Making Sense of Smell:
Classifications and Model Thinking in Olfaction Theory

Submitted by Ann-Sophie Barwich to the University of Exeter
as a thesis for the degree of
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I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

Signature: ………………………………………………………………..

Acknowledgement

A little more than three years ago, when starting my PhD, I had a cunning plan. (In fact, “a plan so cunning, you could stick a tail on it and call it a weasel!”) It involved an ambitious pairing of Gottfried Wilhelm Leibniz’s idea on processual identity and John Dupré‘s promiscuous realism of biological entities, all laced up with a lot of fancy wording! Then came the realist phase. Like gravitational forces act on bodies, a thesis acts on the mind in obscure and rarely understood ways. These forces simply threw over the whole plan when I learned about the invisible and barely conceivable world of smell. And like gravitational forces exerted by the surface of massive objects, the riddles posed by this vivid but ephemeral olfactory world pulled my thesis out of its previous trajectory and into a new orbit, a quite dizzying experience.

For being a great part of this experience, many people have my deepest gratitude. First and foremost, my praise and sincere thanks go to my supervisors John Dupré and Michael Hauskeller, who guided me not only to travel around the surface but, rather, to delve into this new orbit. And I am especially grateful to John, whose profound criticism was the Heisenberg compensator fuelling this thesis journey. I would also like to extend my gratitude to all the friends and colleagues I had the pleasure to meet at Egenis, making this a wonderful and inspiring time of my life. Particular thanks must go to Louise Bezuidenhout, Werner Horn, Ingvar Johansson, Mike Morrison, Cheryl Sutton and David Wyatt for helping me proofreading “the final thing”. My personal debt is to my family that helped me to not join the dark side of the force but asked me to use a better torch.

Abstract

This thesis addresses key issues of scientific realism in the philosophy of biology and chemistry through investigation of an underexplored research domain: olfaction theory, or the science of smell. It also provides the first systematic overview of the development of olfactory practices and research into the molecular basis of odours across the 19th and 20th century. Historical and contemporary explanations and modelling techniques for understanding the material basis of odours are analysed with a specific focus on the entrenchment of technological process, research tradition and the definitions of materiality for understanding scientific advancement. The thesis seeks to make sense of the explanatory and problem solving strategies, different ways of reasoning and the construction of facts by drawing attention to the role and application of scientific representations in olfactory practices. Scientific representations such as models, classifications, maps, diagrams, lists etc. serve a variety of purposes that range from the stipulation of relevant properties and correlations of the research materials and the systematic formation of research questions, to the design of experiments that explore or test particular hypotheses. By examining a variety of modelling strategies in olfactory research, I elaborate on how I understand the relation between representations and the world and why this relation requires a pluralist perspective on scientific models, methods and practices. Through this work I will show how a plurality of representations does not pose a problem for realism about scientific entities and their theoretical contexts but, on the contrary, that this plurality serves as the most reliable grounding for a realistic interpretation of scientific representations of the world and the entities it contains. The thesis concludes that scientific judgement has to be understood through its disciplinary trajectory, and that scientific pluralism is a direct consequence of the historicity of scientific development.

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Curating A Controversy: Making Sense of Smell

1 What's in a Smell? A Different Kind of Case Study

The first responses people offer when a conversation shifts to the sense of smell is to mention its elusive power to evoke memories and trigger emotions, emphasising its strongly subjectively perceived character and, sometimes, bringing up their favourite fragrance. To many, smell is an unlikely or at least not an obvious topic to pursue questions surrounding the production of scientific knowledge and the ways in which scientific practice provides an understanding of the reality of nature. Smell does not appear to be the object of straightforward empirical observation and objective claims, and also not of grand theories that, unlike relativity or quantum theory, might change the way in which science is practiced or theorised in science studies. This popular opinion, however, is misguided. Smell is said to be the most primeval sense.[1] It thus might come as a surprise that there is as yet no proper scientific understanding of how smell perception actually works, especially in humans.

Scientists as well as philosophers have neglected olfaction, the sense of smell. The lack of interest in the nature of smells stems perhaps from its very character. As the most volatile sense of them all, smell does not appear to be sufficiently 'real'; odours are seen as to insubstantial, too brief in their appearance and at best subjectively perceived qualities. Its emotive and deceptive appearance made smell a suggestive descriptive tool in literary and film works, often disclosing a sense of time, space and identity: "[a]t sea one day, you'll smell land where there'll be no land, and on that day Ahab will go to his grave, but he'll rise again within the hour."[2] Nonetheless, in comparison to other senses such as vision or touch, the ability to smell had been considered unimportant. Immanuel Kant in his *Anthropology from a Pragmatic Point of View* even dismissed it as the most 'ungrateful' sense of them all.[3]

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[1] Harel, D., Carmel, L. and Lancet D. (2003): Towards an odor communication system. *Computational Biology and Chemistry* 27(2), 121-133.

[2] Huston, John (Dir.) (1956): Moby Dick. Moulin Productions. USA, Film.

[3] "Which organic sense is the most ungrateful and also seems the most dispensable? The sense of *smell*. It does not pay to cultivate it or to refine it at all in order to enjoy; for there are more disgusting objects than pleasant ones (especially in crowded places), and even when we come across something fragrant, the pleasure coming from the sense of smell is fleeting and

Despite traditional philosophical lack of interest in volatile matters, the sense of smell has acquired an increasingly important role for research in biological and medical studies, especially in the last fifty years. Smells perform a variety of vital functions in organisms. Pheromones, for instance, trigger species-specific responses for communicating mating behaviour, danger situations or food-trails; moreover, they affect the physiology of animals as well as their behaviour.[4] Some animals such as moles rely much more on the senses of smell, taste and touch than vision to interact with their environment.[5] Other interesting subjects of research involving smell-perception comprise, for instance, the phenomenon of canine drug and medical cancer detection.[6]

Scientific interest in human smell perception is fairly recent and closely linked to contemporary advances in genetics.[7] Awareness of olfaction as a crucial research topic was raised by a most intriguing and puzzling genomic discovery: "With roughly 3% of all genes coding for odorant receptors, OR [olfactory receptor] genes are by far the largest gene family in mammalian genomes."[8] The only biological process matching this is the undoubtedly important immune system. This suggests that the sense of smell is evolutionarily important.[9]

The most interesting aspect of olfaction, however, is yet to be explained. How do we actually perceive odours? The truth is, we currently have no answer. The phenomenon involves various mechanisms, and answers must be sought on different levels, starting with the primary molecular interaction in the nose and the subsequent signal transduction and processing at the neurological level.

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transient." Kant, Immanuel (2006[1798]): *Anthropology from a Pragmatic Point of View.* Ed. by R.B. Louden. Cambridge; Cambridge University Press, 50-51.

[4] Wyatt, Tristram D. (2003): *Pheromones and Animal Behaviour. Communication by Smell and Taste.* Oxford: Oxford University Press; Tirindelli, Roberto; Dibattista, Michele; Simone, Pifferi and Menini, Anna (2009): From pheromones to behavior. *Physiological reviews* 89(3), 921-956; Chamero, Pablo; Katsoulidou, Vicky; Hendrix, Philipp; Bufe, Bernd; Roberts, Richard; Matsunami, Hiroaki; Abramowitz, Joel; Birnbaumer, Lutz; Zufall, Frank and Leinders-Zufall, Trese (2010): G protein Gαo is essential for vomeronasal function and aggressive behavior in mice. *Proceedings of the National Academy of Sciences* 108(31), 12898-12903.

[5] Catania, Kenneth (2002): The Nose Takes a Starring Role - The star-nosed mole has what is very likely the world's fastest and most fantastic nose. *Scientific American* (July), 54-59.

[6] Ehmann, Rainer; Boedeker, E.; Friedrich, U.; Sagert, J.; Dippon, J; Friedel, G. and Walles, T. (2012): Canine scent detection in the diagnosis of lung cancer: revisiting a puzzling phenomenon. *European Respiratory Journal* 39(3), 669-676.

[7] Zhang, Xinmin and Firestein, Stuart (2002): The olfactory receptor gene superfamily of the mouse. *Nature Neuroscience* 5(124), 124-133; Keller, Andreas and Voshall, Leslie B. (2008): Better Smelling through Genetics: Mammalian Odor Perception. *Current Opinion in Neurobiology* 18(4), 364-369.

[8] Zhang, Xiaohong; De la Cruz, Omar; Pinto; Nicolae, Dan; Firestein, Stuart and Gilad, Yoav (2007): Characterizing the expression of the human olfactory receptor gene family using a novel DNA microarray. *Genome Biol* 8(5), R86.

[9] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House, 11.

This, in turn, invites studies of hormone releases and of psychophysical interactions. Comprehension of smell and its perception, therefore, requires contributions from various scientific domains. Although much current research is neurological, the uncertainty and lack of understanding of smell perception already begins at the first step, namely the interaction between molecules and the olfactory receptors. This problem, the mechanism of primary odour recognition, is the central topic of this thesis.

2 Contemporary Issues in Olfaction Theory: What's so special about Primary Odour Recognition?

Sometimes scientific controversies are based on more than mere disagreement between scientists about the correct theoretical explanation of a phenomenon. They can touch the foundations on which a science is based, calling into question not only the empirical grounds on which particular scientific claims are established but also whether these claims are rooted in an adequate conception of the investigated phenomenon. Prevailing assumptions about the nature of the phenomenon influence what questions are considered legitimate and what features seem relevant for explaining particular observed effects. Yet what if these assumptions about a phenomenon's nature are the ones in dispute?

One such controversy is currently taking place in olfaction theory. Odour perceptions are caused by a variety of chemicals we encounter, which are processed in the olfactory bulb. When we perceive smells we recognise particular features of the volatile molecules that carry them. But which are the causally relevant features? A large number of structural hypotheses have been put forward, involving steric, electrophilic and nucleophilic characteristics, peripheral functional groups and even infrared frequencies.[10] The odour of a molecule, unlike its shape or electronic properties, is not an intrinsic property but relates to a particular mechanism of primary odour recognition. It is a sensory response that takes place when volatile molecules stimulate the appropriate receptors in the nasal epithelium. The identification of these receptors and their particular character is thus the essential condition for the

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[10] Dravnieks, Andrew (1969): Current status of Odour Theories. *Flavour Chemistry. Advances in Chemistry* 56, 29-52. See also: Heath, Henry B. (1981): *Source Book of Flavors. AVI Sourcebook and Handbook Series.* Dordrecht: Kluwer, 122-127.

construction of any hypothesis about how smells are recognised on a molecular level.

A debate in olfaction surrounds the yet unknown mechanism of primary odour recognition. It is hoped that this mechanism will explain why a particular molecule has a particular smell. For almost the entire 20th century any hypothesis about the molecular basis of odour perception remained speculative, simply because the receptors were unidentified. Nonetheless, being considered as part of a wider group of ligand binding processes such as digestion, metabolism and immune response, primary smell perception was assumed to act according to a shape-sensitive mechanism. Demonstrating the adequacy of this hypothesis appeared to be a local scientific problem and subject to further advancements in technology and measurement. With the discovery of the olfactory receptors (ORs) by Linda Buck and Richard Axel in 1991, the key element for research on the olfactory mechanism was identified at last.[11] Knowing what kind of protein is associated with olfactory responses, it was believed, should enable us to identify what kind of perception mechanism is at work. Fast forward to the present day, however, and insight into the details of the recognition process has not improved greatly. Although the class of proteins to which the ORs belong, namely 7-transmembrane G-coupled proteins, suggests that odorants (odoriferous molecules) dock on a specific primary receptor according to a shape-sensitive mechanism, no conclusive evidence is available. The problem is the experimental inaccessibility of the OR binding site. Studies of transmembrane proteins are notoriously difficult and only very few breakthroughs in elucidating the structure of their binding sites have been made.[12] ORs present a particularly difficult case as standard methods of crystallisation, an essential requirement for protein modelling, have so far been unsuccessful.[13]

Despite this lack of empirical progress there has so far been little reason to suspect that odour perception differs from other molecular responses. Even though unknown in its details, there was no alternative empirically viable mechanism available to explain how olfactory responses were caused other

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[11] Buck, Linda B. and Axel, Richard (1991): A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. *Cell* 65(1), 175-187.

[12] Topiol, Sid and Sabio, Michael (2009): X-ray structure breakthroughs in the GPCR transmembrane region. *Biochemical pharmacology* 78(1), 11-20.

[13] Crasto, Chiquito J. (2009): Computational Biology of Olfactory Receptors. *Curr Bioinform* 4(1), 9.

than by primarily stereochemical, i.e. geometrical, properties. All G-coupled protein receptors (GCPRs) involved in ligand binding processes are assumed to share the same general principle of interaction, molecular shape. Buck and Axel's discovery thus resonated with the widely accepted "shape theory of odours", which was the dominant view in olfaction research over the last century.

Despite its prevalence in the olfactory community up to today, the shape theory and its various modifications leave some fundamental theoretical problems unresolved. These problems concern a variety of irregularities in the accommodation and explanation of molecular data, so-called structure-odour relations (SORs).[14] In light of these problems, and challenging the standard account, an alternative model for primary odour recognition was introduced in 1996.[15] Reviving the formerly abandoned "vibration theory of odours", this model proposes a mechanism for the transduction of molecular infrared vibrations in a biological system. Greeted with disbelief across the wider olfactory community,[16] it has nevertheless received support from two recent isotope perception studies.[17] Although accommodating a vast range of molecular data and furthermore providing predictive results on SORs,[18] it still faces the problem of lacking sufficient experimental evidence from protein studies. At any rate, as long as the nature of the receptor binding site remains elusive, neither model for the mechanism of primary odour recognition can be conclusively demonstrated.

Notwithstanding the polemics in the debate surrounding the olfactory mechanism,[19] the alternative vibration-theory has received sufficient attention

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[14] Turin, Luca and Yoshii, Fumiko (2003): Structure-Odor Relations: A Modern Perspective. In: *Handbook of Olfaction and Gustation 2nd edition*. Ed. by R. Doty and M.Decker. Informa Healthcare, 457-482; Sell, Charles (2006b): On the Unpredictability of Odor. *Angew Chem Int Ed Engl.* 45(38), 6254-6261; Turin, Luca (2006): *The Secret of Scent.* London: Faber and Faber, 46-82; Davies, Emma (2009): The sweet smell of success. *Chemistry World* (February), 41; Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 61-133.

[15] Turin, Luca (1996): A Spectroscopic Mechanism for Primary Olfactory Reception. *Chemical Senses* 21(6), 773-791.

[16] Nature Neuroscience Editorial (2004): Testing a Radical Theory. *Nature Neuroscience* 7(4), 315.

[17] Franco, Maria Isabel; Turin, Luca; Mershin, Andreas and Skoulakis, Efthimios, M.C. (2011): Molecular vibration-sensing component in *Drosophila melanogaster* olfaction. *PNAS* 108(9), 3797-3802; Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780.

[18] Turin (1996): Spectroscopic Mechanism; Turin (2006): *Secret of Scent*.

[19] Nature Neuroscience Editorial (2004): Testing a Radical Theory; Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

through recent studies to provoke scientific debate on whether the standard approach is still acceptable and where its weaknesses lie. The interesting issue emerging between the two competing accounts thus is not merely the degree to which each model explains the available observations, but whether olfaction is more of a chemical or a spectral sense,[20] or possibly a combination of both.[21] For this reason, the olfactory debate has potentially wider implications for the general understanding of molecular recognition, questioning whether, instead of a uniform principle of interaction, there might be various causal processes involved.

3 Complementary Science: A Practice-Oriented Approach for Undertaking Science Studies

The olfactory dispute raises a number of challenges, for scientists as well as for philosophers of science, that must be addressed. One of the most interesting aspects concerns the arguments provided to support the relevance of an experimental result for a theoretical explanation. In the specific case study chosen, a closer look at these arguments will show that there is more to what counts as evidence for an empirical framework than criteria aiming at empirical success and epistemic or pragmatic virtues. Whereas the shape-sensitive mechanism is largely supported by its ontological compatibility with other molecular recognition processes, the vibration account explains and predicts the relevant structure-odour relations with greater reliability. In response to the scientific debate, this thesis analyses the development of the two competing theoretical frameworks, the shape and the vibration theory of odours, and critically assesses the implications of this controversy for a philosophical understanding of science. As an active and unresolved scientific debate, I also draw on this case study to develop an integrated historical and philosophical perspective on science that aims to contribute and benefit the practitioners' discourse.

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[20] Hettinger, Thomas P. (2011): Olfaction is a chemical sense, not a spectral sense. *PNAS* 108(31), E349; Franco, Maria Isabel; Turin, Luca, Mershin, Andreas and Skoulakis, Efthimios M. C. (2011): Reply to Hettinger: Olfaction is a physical and a chemical sense in Drosophila. *Proceedings of the National Academy of Sciences 108*(31): E350-E50.

[21] Solov'yov, Ilia A.; Chang, Po-Yao and Schulten, Klaus (2012): Vibrationally assisted electron transfer mechanism of olfaction: myth or reality? *Physical Chemistry Chemical Physics* 14(40), 13861-13871.

By outlining the trajectory of olfactory research, I will elucidate the different strategies of modelling facts and conducting experiments, exploring the extent to which the evidential status of contemporary practices is bound to previous and existing ontological assumptions. My aim will be to present a philosophically informative picture of a contemporary scientific debate through its historical development. Without relapsing into prescriptive statements about the advancement of science, the philosophical aim is yet more than a descriptive survey; it is rather a critical exposition of the terms of the debate, its conditions as well as its inconsistencies.

Although a central feature of my discussion will be the concept of evidence, my broader focus is on the evolving practices of investigation of the material basis of smell and smell perception. A number of interesting issues were raised by the revival of the vibration theory of odours and its competition with the traditional shape theory. These issues, independently of the adequacy of a vibration-sensitive mechanism for understanding a biological process, shed light of some challenges olfactory research has been facing. One substantial challenge is the fragmentation of research practices addressing smell perception. To date, olfaction – unlike, for instance, cell and molecular biology, systems biology, ecology or proteomics – is not considered a discipline in its own right. Yet, increasing awareness of olfaction as an important research topic fosters the need to organise the hitherto dispersed discussions, particularly regarding the mechanism of primary odour recognition.

Investigations into the molecular basis of odours are mainly located within two domains, fragrance chemistry and molecular biology. Linking smell to molecular features, research in fragrance chemistry focuses on regularities between the structure of molecules and their odour quality, leading to the development of rules for structure-odour relations (SORs).[22] In comparison, studies in molecular biology, seeking for regularities in the activity patterns of the interaction between odorants and ORs, concern the understanding of structure-activity relations (SARs).[23] Although fairly autonomous, each disciplinary domain – molecular biology and fragrance chemistry – acts under the shared working

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[22] Rossiter Karen J. (1996): Structure-odor relationships. *Chemical reviews* 96(8), 3201-3240; Chastrette M. (1997): Trends in structure-odor relationship. *SAR and QSAR in Environmental Research* 6(3-4), 215-254.

[23] Ohloff, Günther (1994): *Scent and fragrances: the fascination of odors and their chemical perspectives.* Trans. by W. Pickenhagen. Berlin, Heidelberg: Springer; Laska, M., Trolp S. andTeubner, P. (1999): Odor structure–activity relationships compared in human and nonhuman primates. *Behavioral neuroscience* 113(5), 998-1007.

hypothesis that the key feature underlying the molecular perception mechanism, determining SARs, must correspond to SORs to a certain degree.[24] This hypothesis, for instance, informs the selection of test odorants for functional analysis in molecular biology on the one hand (investigating which structurally similar molecules bind to what range of receptors)[25] and the selection of parameters for the development of odour rules and olfactophore models in fragrance chemistry on the other.[26]

As a result of the disciplinary fragmentation, it is very difficult to view the olfactory debate surrounding the molecular basis of odours as a coherent enterprise. Although the general consensus of olfactory researchers is to take a shape-sensitive mechanism as responsible for olfactory perception, the different use of concepts, explanations and models in different contexts problematises the interpretation and evaluation of observations. A conceptual organisation and unification of the olfactory debate thus provides more than a philosophical narrative but could help provide a common basis on which a scientific debate can be held.

I will present the present olfactory debate through its historical development, treating it as an emerging discipline. Disciplines are historical entities that arise for different reasons, spurred, for instance, by the impact of new methods on the way in which the research materials are conceptualised, by evolving questions that diverge from previous treatment of these materials and so on. The current interdisciplinary and incoherent character of the olfactory debate and the challenges arising from it can be characterised in terms of Bill Bechtel's account of 'interdisciplinary research clusters'. Interdisciplinary research clusters "develop similar institutional structures as disciplines (professional societies and journals) and are interested in a common domain of phenomena, […] [but] they do not employ distinctive research techniques. Rather, collaborators draw upon the techniques and employ the standards of successful explanation from their home disciplines."[27]

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[24] Laska, M. and Teubner, P. (1998): Odor structure-activity relationships of carboxylic acids correspond between squirrel monkeys and humans. A*merican Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 274(6), R1639-R45.

[25] Malnic, B.; Hirono, J.; Sato, T. et al. (1999): Combinatorial receptor codes for odors. *Cell* 96(5), 713-23.

[26] Ohloff et al. (2011): *Scent and Chemistry*.

[27] Bechtel, William (2006): *Discovering Cell Mechanisms. The Creation of Modern Cell Biology.* Cambridge: Cambridge University Press, 13.

Even though not yet a full-fledged discipline, olfactory research nevertheless exhibits a tendency of gradually merging its participating research clusters. Since contemporary experimental methods fail to discern the unknown olfactory mechanism, researchers try to fill the explanatory gaps by making reference to explanations used by their interdisciplinary collaborators. A variety of explanations and models in fragrance chemistry rely on developments in molecular biology and, conversely, some models in molecular biology refer to data models from fragrance chemistry. However, rather than merging the disciplines equally, it will appear that the tendency is to give priority to explanations derived from molecular biology. This, in turn, leads to a variety of challenges in the explanation of data from fragrance chemistry concerning aberrant structure-odour relations. Dealing with these challenges, a common pattern, as my thesis will show, is the development of explanatory strategies that shape the material culture of the olfactory discourse and, furthermore, impact on the current debate surrounding the two rival theories. As they are evolving from the historical development of research on the molecular basis of odours, a critical exposition of the arguments employed in favour of a theory (or model) thus shows the need for a historically informed perspective to understand the current state of olfactory science.

4 Why Theory and Model Choice? A Note on the Narrative

For a conceptual organisation and unification of the olfactory debate my focus will be on an internalist interpretation of its development. This means that, rather than institutional and social factors, I will concentrate more on the underlying theory and model development. Especially relevant here are the explanatory strategies towards, and changes in the conceptualisations of, the central issue, the primary odour mechanism, and the solutions offered for problems posed either by experimental limitations or conflicting data. My choice of an internalist approach in this thesis does not render an externalist perspective irrelevant and, of course, cannot present a full picture of the debate. It does, however, address an important concern of the practitioners.

Although a hitherto neglected topic, the olfactory discussion surrounding the molecular recognition mechanism has sporadically received some media attention after the revival of the vibration theory by Luca Turin in 1996. Since olfaction researchers form a relatively secluded community, Turin, who worked on membrane proteins in structural biochemistry before turning his attention to the olfactory mechanism, was seen as an outsider. The BBC Horizon documentary "A Code in the Nose" (1995) and the book "The Emperor of Scent" (2002) by Chandler Burr, who subsequently became the NY Times fragrance critic, popularised Turin's model, but further strengthened the alienation between Turin and the established olfactory researchers. Presenting Turin's new model as the struggle of a single revolutionary scientist who fights the established community with its outdated theory, many researchers felt they were portrayed as incompetent or reactionary villains by these popularisations. Some replies to Turin and his mechanism model therefore focussed on its popularity, proposing caution to naively trust non-expert judgements:

> "The media loves controversy, and ever since David and Goliath, the story of a lone hero taking on the establishment has had enduring appeal. Of course, radical ideas from outside the mainstream do occasionally turn out to be right. Of course scientists are sometimes excessively attached to conventional ideas. But in science at least, the mainstream view is usually based on the accumulation of evidence over many years. Journalists are trained to report both sides of any argument, but this can be misleading when both sides are not equally credible."[28]

While the underlying issues of authority, institutional belonging and expertise certainly are important factors in the debate and how it is held, (illustrating the impact of what Miriam Solomon calls "non empirical decision vectors" in scientific controversies,[29]) my analysis of the debate answers the objection that the vibration theory lacks credibility on the scientific level. Adopting a complementary view, I therefore take the scientists' emphasis on judging an alternative theory or model through an accumulative experimental practice as the basis of my analysis of the olfactory debate. Within this perspective, this thesis performs what Hasok Chang advocates as "complementary science".

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[28] Nature Neuroscience Editorial (2004): Testing a Radical Theory.

[29] Analysing the reactions to Turin by the established olfactory community, she presents a first account of the underling social factors under the perspective of social epistemology in Solomon, Miriam (2006): Norms of Epistemic Diversity. *Episteme: A Journal of Social Epistemology 3*(1), 23-36; Solomon, Miriam (2008): Norms of Dissent. London School of Economics. *Centre for the Philosophy of Natural and Social Science Contingency and Dissent in Science Technical Report* 09/08. URL=<http://www2.lse.ac.uk/CPNSS/projects/CoreResearchProjects/ContingencyDissentInScience/DP/SolomonNormsOfDissent0908Online.pdf>

Complementary science describes the pursuit of scientific questions that, for a variety of reasons (e.g. being outdated, too controversial, or simply neglected), are not addressed within the practitioners' discourse. By approaching such issues from a historical and philosophical standpoint, they are given the benefit of the doubt in the sense that it is not their truth or falsity that is primarily in dispute, but their potential utility for some aspects of scientific practice if they were given closer scrutiny.[30]

Given my emphasis on an internalist approach to accommodate the practitioners' concerns about how the olfactory debate is perceived in a wider discourse, I will also follow their use of key notions such as theory, model and mechanism. While there have been a variety of proposals about what a theory, model or mechanism is in the philosophy of science, the use of these notions is less well defined within the olfactory debate. The notion of theory to refer either to the shape or vibration theory of odours nevertheless conveniently contrasts the diverging positions. It does not fit a syntactic understanding of theory as a set of relatively stable propositions,[31] as the historical variability of how to understand the key hypothesis and the flexibility of explanatory strategies accommodating aberrant data will demonstrate. Nor does it help clarifying the olfactory debate by adopting a semantic view in which a theory is defined by a collection of models,[32] because the key models, for instance the mechanisms, are themselves the subject in question and under constant modifications and change. Likewise, the notion of mechanism is used simply to refer to the underlying perception process as a causal process involving particular components, without any reference to philosophical issues concerning what mechanisms in general or mechanisms in biology might be.[33] The notion of models, too, relates to the practices in which different modelling strategies appear without, however, addressing the question what a model is in general. Accordingly, I will use these key notions as the practitioners employ them, examining how theoretical assumptions about the material basis of smell and smell perception are formed and justified. Not being concerned with the abstract

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[30] Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press.

[31] Suppe, Frederick (1972): What's wrong with the received view on the structure of scientific theories? *Philosophy of Science* 39(1), 1-19.

[32] Suppes, Patrick (1960): *A Comparison of the Meaning and Uses of Models in Mathematics and the Empirical Science.* Institute for Mathematical Studies in the Social Sciences.

[33] Glennan, Stuart (1996): Mechanisms and the nature of causation. *Erkenntnis* 44(1), 49-71; Bechtel (2006): *Discovering Cell Mechanisms,* 19-40.

character of “theories”, “mechanisms” and “models”, I will give preference to the details of the strategies by which the olfactory researchers study their materials and argue for the adequacy of their explanations.

The resulting picture of the olfactory debate, as this thesis will demonstrate, is not as unambiguous as the scientific opinion cited above suggests. Quite the contrary, my analysis will elucidate that each theory with its proposed model of the olfactory mechanism is able to accommodate a variety of data and to provide explanatory strategies for aberrant data. In my discussion, I will further show that, given a run for its money, the vibration theory has the potential to provide experiments that enhance the general debate by pointing at overlooked data that require a better explanation on the molecular level than the one that is currently favoured. Likewise, I will also demonstrate the grounds on which the shape theory receives its current dominance. (It should be noted that there is scientific dissent about whether the accepted account should be labelled “shape theory” as there are, in addition to shape – determined by stereochemistry –, further molecular parameters involved. Nonetheless, stereochemistry is considered the key feature and I therefore use shape theory here as an umbrella term to organise the different positions and responses towards the alternative vibration theory in the olfactory debate.[34])

In addition to presenting the merits of each approach, this thesis concerns the benefits of the mutual interaction of different theories and models. Rather than arguing for one of the rival accounts, this thesis questions the scientific emphasis on theory and model choice in an exclusive sense.

5 The Philosophical Context: The Role of Representation in Questions of Scientific Realism

Tracing the trajectory of olfactory practices within this complementary program not only sheds a different light on the scientific debate but also addresses particular issues integral to the philosophy of science. A question that has inspired a broader philosophical debate is to what extent scientific representations such as classifications and models represent reality or are mere conventions. This debate encompasses two positions. Advocates of realism

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[34] Hettinger (2011): Olfaction is a chemical sense, not a spectral sense.

argue for the truth of descriptions provided by scientific theories or at least the existence of the entities involved. Proponents of anti-realism remain sceptical about strong ontological claims such as the truth of scientific theories or the existence of entities posited therein. They prefer to describe scientific theories rather as useful tools for constructing explanations and making predictions about phenomena.[35]

The general problem that underlies this debate concerns both the history and philosophy of science. History abounds with examples of scientific theories about the world that turned out to be false and that have subsequently been overthrown. In parallel with the resulting theory changes, a variety of scientific entities - such as phlogiston, the ether or pneuma - turned out not to exist either. Their falsity (by contemporary lights) casts doubt on the truthfulness of our current scientific explanations. On what basis, if any, can we therefore assume that our present scientific claims about reality are truthful? In addition, and related to the historical changeability of scientific judgement, another problem concerns the growing dependence of scientific practice on mediated forms of observation. Technological advancements increasingly direct scientific focus to phenomena that are impossible to observe directly, and the investigation of which relies on the production and interpretation of experimental traces. The resulting hypothetical character of a number of scientific explanations further opens up inquiry about how to determine whether and when a realist case can be made for explanations of entities of which most of our knowledge relies on model-based inferences.

To examine the grounding for a realistic interpretation of scientific representations of the world and the entities it contains, philosophical analysis must investigate the scientific activity underlying practices of representation such as model building, classification, etc. By emphasising the ‘primacy of the making’, i.e. the methods of measurement and experimentation in research practice, over abstract epistemic justifications of theoretical explanations, recent discussions in the history and philosophy of science have therefore increasingly directed attention toward the mutability of scientific judgement and the

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[35] Hacking (1983): *Representing and Intervening*, 21.

manipulative strategies for turning scientifically relevant phenomena into epistemically accessible objects.[36]

Focus on the variety and mutability of construction strategies and on the experimental conditions under which, and the means with which, phenomena are *transformed* into scientific objects, moreover, has changed philosophical understanding of the reality that science is supposed to address. Philosophical debate on the means by which science does and does not address reality can be roughly divided into three perspectives. First, some philosophers such as Bas van Fraassen and Hans-Jörg Rheinberger have revived scepticism about whether we can justify anything but a pragmatic and instrumental perspective on scientific theories and entities.[37] Here the implicit duality between an instrumentally produced materiality, contained in an experimental system, and an observer independent reality is considered meaningless since science only deals with the former and “nature as such is not a referent for the experiment”.[38] Second, other philosophers such as Brian Ellis restrict scientific realism to a limited number of scientific entities, principally fundamental elements in physics and chemistry that appear to fall under lawlike generalisations - unlike for instance biological entities.[39] Third, another group of philosophers such as Ian Hacking and John Dupré suggest reconsidering the apparently problematic criteria of defining reality.[40] Advocates here argue for an understanding of scientific realism that emphasises that science is a materially bound enquiry. Assessing whether scientific explanations make truthful claims about reality means considering the strategies by which scientists interact with research materials and also being open to suggestions about what constitutes the nature of these materials, i.e. carefully analysing the various theoretical implications of

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[36] Latour, Bruno (1987): *Science in Action. How to follow scientists and engineers through society.* Cambridge M.A.: Harvard University Press; Hacking (1983): *Representing and Intervening*; Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press. Quite often these investigations concern particular case studies such as in debate on model organisms. See: Ankeny, Rachel A. and Leonelli, Sabina (2011): What’s so special about model organisms? *Studies in History and Philosophy of Science Part A* 42(2), 313-323.

[37] van Fraassen, Bas (1980): *The Scientific Image.* Oxford: Oxford University Press; Rheinberger (1997): *Epistemic Things;* van Fraassen, Bas (2008): *Scientific Representations. Paradoxes of Perspective.* Oxford: Oxford University Press.

[38] Rheinberger (1997): *Epistemic Things*, 109.

[39] Ellis, Brian D. (2001): *Scientific essentialism.* Cambridge: Cambridge University Press; Ellis, Brian D. (2002): *The philosophy of nature: a guide to the new essentialism.* Queens: McGill University Press.

[40] Hacking (1983): *Representing and Intervening*; Dupré, John (1993): *The Disorder of Things. Metaphysical Foundations for the Disunity of Science.* Cambridge M.A.: Harvard University Press; Dupré, John (2002a): *Humans and Other Animals.* Oxford: Clarendon Press.

experimental traces. This implies that it is important to consider the nature of the materials under scrutiny as well as the practices that address the materials. Central to all these diverging perspectives is the focus on definitions of materiality. Opinions differ, however, on whether the dependence of science on techniques to manipulate matter for producing specific phenomena poses a problem for a realist interpretation of scientific practice.

Current problems in olfaction theory depend exactly on issues of this kind. As long as the structure of the olfactory receptors remains elusive, proposals about the nature of primary odour recognition are based on theoretical reasoning and hypothetical modelling. Difficulties are exacerbated, as there are two competing and empirically viable theories, for either of which a realist case can currently be made. A striking feature of the olfactory debate, therefore, is that it presents an unresolved and "live-stream" scientific controversy that leaves both scientific reasoning and philosophical analysis to a certain extent speculative. As much as such speculative grounds require a cautiousness of philosophical claims and sensitivity to current scientific practice, this case of contemporary history likewise offers a unique opportunity to reflect on the limits and possibilities of both scientific practice and philosophical understanding of scientific practice.

Addressing contemporary issues in olfaction theory within the philosophical debate on scientific realism, this thesis elaborates arguments supporting a pluralistic realist interpretation of science, sympathising with a position close to John Dupré and Ian Hacking. In *The Disorder of Things* (1993), Dupré advocates a radically pluralistic account of reality and states that there are numerous and equally applicable ways to classify the biological world. In short, there are real distinctions in nature. However, these do not result in a unique set of classes but, rather, in overlapping sets that justify the need for different classifications, signifying different relations serving different purposes. The claim that there are divergent and equally valid descriptions of nature presents a different picture of scientific realism, one that does not "force" nature into a clear-cut and unique structure but, rather, one that suggests investigating the disposition of disorder in the natural world as its very characteristic. Thus, Dupré's argument is fundamentally ontological; the pluralism and mutability of scientific explanations is a direct consequence of the overlapping and changing nature of reality. Hacking's position is more epistemically grounded; it concerns the scientific strategies employed to provide access to scientifically relevant phenomena. In *Representing and Intervening* (1983), Hacking suggests shifting our criteria for realism about scientific entities by not judging primarily whether what we *say* about these entities matches observations by virtue of some abstract criteria of similarity but, rather, to examine what we can experimentally *do* with research materials in light of these assumed explanations.

Resonating with these two approaches, and stressing the intrinsic plurality of nature on the one hand and of manipulative practices on the other, my analysis of olfactory research therefore addresses two issues: the nature of odours and their material basis, and the research strategies involved in investigating the materiality of odours. A slogan once made famous by Hacking states that "if you can spray them, then they are real."[41] Although concerning the reality of electrons, this expression is somehow also true of smells. It does not even need very sophisticated techniques to spray smells; a perfume vial from the drugstore will do. Despite the obvious difference in what is meant by 'spraying' positrons in contrast to spraying smells, Hacking's slogan nevertheless conveys a common denominator in the implicit understanding of what counts as real: materiality and techniques of manipulating this materiality. The basic question here is whether we are perceiving or accessing a phenomenon, and the ability to manipulate is the grounds for saying we are.

Rather than focussing on ontological issues surrounding a realist interpretation of science, however, I will approach the realism question more from an epistemological view. Grounded partly in the ephemeral nature of smell and partly because of the current experimental inaccessibility of the ORs, a variety of the ways in which odoriferous materials are manipulated are closely linked to visualisation strategies. To analyse how these visualisation strategies are used to represent the link between odours and material features and the underlying perception mechanism, I will predominantly address the realism question through the notion of representation. Advancing a multifaceted conception of scientific practices in which no single element can dominate the results of scientific discourse, I will argue that pluralism is a necessary condition for representation.

The case study chosen here provides an especially fruitful and novel perspective on arguments concerning scientific realism. Smells do not, at first

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[41] Hacking, Ian (1983): *Representing and intervening: introductory topics in the philosophy of natural science.* Cambridge University Press, 23.

sight, seem the most obvious choice to engage in questions about realism. Quite the contrary, it seems intuitive to consider odours as a more salient example for antirealism. First, inquiry about smells is inevitably observer dependent; being a sensational response, there are no smells without a perceiving subject. Moreover, descriptions of smells rely strongly on disciplinary conventions and are often fuzzy in character (what does it mean to say, for instance, that something smells “fresh”, “sweet” or “fruity”?). As a result, classifications of smells remain arbitrary to a certain extent.

Second, knowledge about the underlying perception process is limited. The olfactory receptors are currently experimentally inaccessible, emphasising the provisional character of theoretical explanations in the construction of experimental traces. As a result, olfactory research into the molecular basis of odours relies strongly on speculations about what the experimentally produced effects imply.

For these reasons, a realist interpretation of scientific practice grounded in olfaction theory faces several fundamental difficulties including the observer dependence of the investigation, the fuzzy character of smells that result in problems of measurement, the current empirical underdetermination of theory by data and the dependency on instrumental requirements for successful experimental inquiry. Yet, it is exactly because of these undeniable difficulties that olfaction theory offers a strong basis upon which arguments for scientific realism can best be shown to prevail. For my defence of a realist interpretation of scientific practice, I endorse a radical form of scientific pluralism that nonetheless cannot be accused of being just a form of antirealism in disguise.

6 The Chapters and Their Topics: Conceptualisations of Materiality, Representational Pluralism and the Historicity of Scientific Judgment

Addressing issues of scientific realism in light of historical and contemporary developments in research on smells, my project has two interwoven theses. The first thesis concerns the history of science. It is the claim that the changeability of theories and research practices does not pose a problem for scientific realism; only its denial does. The second one is epistemological; it is a thesis about how to assess whether theoretical assumptions, provided by scientific representations such as models, tell us anything about the world. My goal is to show to what extent a plurality of representations does not pose a problem for realism about scientific entities and their theoretical contexts but, rather, that this plurality serves as the most reliable indicator for realism about how science addresses and explores the world and the entities it contains. In addition, I propose a relation between these two theses: arguments for pluralism follow from the inevitability of the historicity of scientific judgement.

For this reason, the approach of this thesis is to argue for the benefits of an integrated historical and philosophical perspective for understanding science through the case study of olfactory research. Although the historical and philosophical issues are intertwined, the structure of this thesis falls into two broad parts. The more historical part of this thesis outlines the development of scientific practices and techniques surrounding research on odoriferous materials. Especially in the first half of this thesis, attention is directed to the variety of disciplinary interests and classificatory practices that concern the material basis of odours and the development of odours as scientifically interesting phenomena. The more philosophical part of this thesis follows up with an in depth analysis of odours concerning a specific modelling context within the recent debate on the molecular mechanism of primary odour recognition. In the second part of the thesis, focus thus shifts from classificatory practices to model building.

Most of the historical issues are dealt with in the first part, where I first explore definitions of materiality in the conceptualisation of odours as scientifically interesting objects (chapter 1) and their classification into kinds (chapter 2), followed by an analysis of the reference of kind terms in scientific practice (chapter 3). Tracing classificatory practices across different disciplinary contexts such as botany, chemistry and perfumery, and spanning about 300 years up to the present, I explore the various criteria considered to define the material basis of odours. Here I demonstrate, with reference to a range of particular classification practices and disciplinary interests, the impact of different definitions of ‘materiality’ on the conceptualisation of odours, presenting an image of taxonomic and conceptual diversity. The overall aim of the first part is to investigate the epistemic implications of different disciplinary practices for the development of odours as scientifically tractable objects. A comparison of historical and present research trajectories sheds light on the non-linear development of scientific enquiry and the conceptualisation of scientifically significant entities. The significance of the pluralistic context in which phenomena are investigated further needs to be mirrored in any account of meaning that is adequate to reflect scientific reality. For this reason, I will propose an alternative perspective on the concept of extension to accommodate the diverse material practices that determine the application of general terms to define scientific objects in science.

In the second part of the thesis, I follow up on the epistemic trajectory of research on odoriferous materials by focussing on the debate surrounding the mechanism of primary odour recognition. Exploring the various modelling and experimental strategies of this particular modelling context, I will show that odours appear here as what Hans-Jörg Rheinberger refers to as “epistemic things”. The concept of epistemic things describes the character of scientific objects as, while under investigation, subject to conceptually flexible lines of enquiry. These research materials are embedded within an “experimental system” that consists of specific modelling strategies, instruments and methods.[42] Investigating research on odours under the concept of epistemic things thus means to focus on the different strategies of model building, experimental design and the construction of empirical evidence for the two competing theories about the molecular basis of smell perception. Within this investigation, I address three major difficulties for scientific realism that result from the reliance of some scientific entities on mediated forms of observation, these address the “underdetermination of theory by data”, the use of non-denoting elements and abstract and idealised concepts in scientific representations such as models, and the problem of “theory-infused” evidence, i.e. the fact that the relevance of many observations rests upon theoretical reasoning.

Central to both parts are the representational techniques surrounding the “scientification” of smell. These not only allow for conceptual thinking about the nature of the phenomenon under investigation, but also serve as graphic

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[42] Rheinberger (1997): *Epistemic Things* See also: Rheinberger, Hans-Jörg (1992): *Experiment, Differenz, Schrift. Die Geschichte Epistemischer Dinge.* Marburg, Lahn: Basilisken-Presse; Rheinberger, Hans-Jörg (2005): A Reply to David Bloor: “Towards a Sociology of Epistemic Things”. *Perspectives on Science* 13(3), 406-410; Rheinberger, Hans-Jörg (2010): *On Historicizing Epistemology: An Essay.* Stanford: Stanford University Press.

reflections on the development of research techniques in olfactory research itself. Applying my pluralist approach, which I defend in this thesis, to representational analysis, I finish by demonstrating the extent to which present olfactory judgement relies strongly on ontological assumptions that are not justified by current modelling practice but that are grounded in the historical trajectory of olfactory research.

PART I

CLASSIFICATION PRACTICE IN OLFACTION STUDIES

“Odours are capable of a very wide diffusion,
so much so, that one can scarcely credit that at all times odour necessarily implies materiality.”
G.W. Septimus Piesse (1862): *The Art of Perfumery*, 24.

Chapter 1

The Disodour of Things I

The Role of Materiality in the Conceptualisation of Odours: An Epistemic History of Odour Materials in the 19th and 20th Century

1 A Historical Trajectory of Odour Materials in Three Stages: From 'Objects in Nature' and 'Materials of Production' to 'Epistemic Things'

This chapter presents an epistemic history of odour materials in the 19th and 20th century, particularly in biology, chemistry and perfumery. The focus here lies on the role played by materiality in the conceptualisation of odours and in the order of odour materials. Materiality is not what first comes to mind when thinking about odours, though. Odours are perceptible qualities and they do not exist without a perceiving subject. It is *subjects that perceive odours*. Yet, caused by small volatile molecules, odours have a complex molecular basis, and it is *materials that* might be said to *carry odours*.

Conceptualisations of materiality played a significant role in understanding the nature of odours. Tracing different classificatory practices surrounding odoriferous materials, I here explore the various criteria considered to define the material basis of odours and analyse the epistemic implications that these practices have on the development of smell as a scientifically significant research topic. Linking odours to a material basis was a reliable means to provide an ephemeral phenomenon with a measurable and stable basis. Yet, the rich diversity of the material origins of odours made them susceptible to become embedded within various observational and experimental practices. Informing the theoretical reasoning of how and why researchers focussed their investigations on particular features of odoriferous materials, my analysis of divergent conceptualisations of materiality will reveal the ongoing interplay between conceptual choices, different modes of investigation, and technological advancements in the formation of odours as scientific objects.

The general material culture that evolved around the study of odour materials has been shaped by shared interest in a variety of materials and methods for their investigation, spawning diverse perspectives on how to classify them. Decisions about the arrangement of odour materials into classes, I want to show, are informed both by the practical imperatives of the practitioners and the natural demarcations of the materials. To highlight the fundamental conceptual connection between pragmatic choices and natural traits in classificatory practice, the following analysis therefore illustrates how different definitions of materiality, relating odours to a material basis, influence the conceptualisation of odours, resulting in a situation of vast taxonomic diversity.

The most general approach to determining the relation between odours and their materials is their conceptualisation according to three criteria, namely natural origins, chemical composition and perceptible qualities. Nonetheless, what these general criteria refer to in particular is open to diverging interpretations, depending on the specific purposes and methods of the various disciplines and sub-disciplines involved, such as botany, chemistry and perfumery but also horticulture, pharmacy and psychophysical studies. By illustrating the impact of classificatory choices, of disciplinary interests and available techniques for determining natural distinctions between largely the same range of materials, the following analysis further highlights the underlying ontological disunity that is reflected by the co-existing ontologies in the classification of odour materials. This disunity is not merely a result of the partially subjective nature of smell perception but, rather, it is grounded in the plurality of materials classified as well as in the multiple interests involved in working with these materials. Taxonomic diversity as a result of co-existing ontologies in classification practices, exemplified by the case of odour materials, is not simply a matter of subjectivity and flawed or scientifically ‘pre-mature’ classifications, but it often directly reflects the complex nature of the materials under investigation.

To analyse the diversity of interests in odours and the classificatory practices addressing their material basis, this chapter does not outline a primarily chronological but a conceptually organised history of odour materials in three main stages, examining odour materials as “Objects in Nature”, “Materials of Production” and “Epistemic Things”. Benefitting from Ursula Klein and Wolfgang

Lefèvre's work on *Materials in Eighteenth-Century Science* (2007),[43] my analysis of these conceptual stages follows three interwoven themes, namely different ontologies of materials, practices of making and identifying materials, and the impact of diverging disciplinary interests.[44]

I begin with a conceptualisation of odours as "objects in nature". Here I first compare different ways in which odours constitute a relevant classificatory tool to explore taxonomic relations of plants in botany, horticulture and other related crafts. I then illustrate the impact of botanic practices on the classification of odours in perfumery and for academic studies on the nature of smells. Although often defining odour types with respect to their largely botanic origins, classifications of odours are further shown to have a tendency to emancipate themselves from botanically informed taxonomic considerations by employing additional and conceptually different criteria such as the comparison with other senses.

Following this, I continue with parallel experimental practices handling odoriferous materials in chemistry. Initially used to investigate the nature of chemical reactions, odour materials were slowly transformed into "materials of production". Developments in chemistry, concerning its various techniques of extraction, are shown to turn the related artisanship of perfumery more and more into a chemical discipline. In the course of this conceptual and disciplinary change, scientific inquiry into odours and their materials increasingly defines them by their use and methods of alteration. With the rise of synthetic chemistry, the investigation of odours as materials of production also paved the way for a significant ontological shift: the possibility of creating synthetic materials directed attention to the molecular basis of odours. Instead of specific materials or methods dealing with the materials, the material basis of odours was now characterised through the chemical composition of these materials.

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[43] Klein, Ursula and Lefèvre, Wolfgang (2007): *Materials in Eighteenth Century Science. A Historical Ontology.* Cambridge M.A.: MIT Press.

[44] In contrast to Klein and Lefèvre's study on chemicals and their properties, odours and their material basis are still poorly explored, and studies in the molecular basis of olfaction are less extended than studies of chemical materials in general. It is therefore intriguing to apply the themes and results of a historical perspective on scientific practices and disciplinary development to a more recent and still ongoing adjacent scientific discourse. Indeed, to date only one major work considering a recent history of odour classification has been undertaken, namely Harper, Roland; Bate Smith, E.C. and Land, D.G. (1968): *Odour Description and Odour Classification. A Multidisciplinary Examination.* London: J. & A. Churchill LTD. It presents a general overview of practices and materials involved in odour classification; however, its historical focus only relies on limited examples of studies in botany and psychophysics, and, furthermore, it does not provide an interpretation of the underlying ontologies and conceptual development of odours as scientific objects.

As a result of this ontological shift, research on odours turned toward the molecular level. Making the imperceptible molecular features accessible to further investigation, this line of enquiry inevitably relied on instruments and technologies of visualisation such as gas chromatography, spectrometry, etc. Increasing insight into the molecular dimensions of odours opened up new scientific inquiries about the physiological conditions responsible for odour recognition, discrimination and identification. Research on the material basis of smells thus further transformed odours into what Hans-Jörg Rheinberger calls "epistemic things". The concept of epistemic things describes the character of scientific objects as, while under investigation, being subject to conceptually flexible lines of enquiries. Addressing scientifically relevant questions, these research materials became embedded within evolving "experimental systems" that consist of specific modelling strategies, instruments and methods.[45] Viewed as epistemic things, contemporary research on the material basis of smell concerns the expanding efforts to understand the underlying mechanisms of odour perception.[46]

The overall aim of this chapter is to trace and analyse how the investigative practices addressing the nature of odoriferous materials transformed odours into scientifically interesting objects. The historical variation of methods for acquiring knowledge about odours and odour materials will demonstrate that scientific objects such as odours can be part of various observational or experimental traditions in which the question of their nature takes different forms for different kinds of enquiry. Drawing attention to these different enquiries and their dependence on contingent technological and disciplinary developments will further show that the epistemic biography of some scientific objects requires a pluralist perspective. Only through a pluralist perspective, it will become clear, can we understand and accommodate the variety of ways in which phenomena are turned into scientifically interesting objects, and how

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[45] Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press. See also: Rheinberger, Hans-Jörg (1992): *Experiment, Differenz, Schrift. Die Geschichte Epistemischer Dinge.* Marburg, Lahn: Basilisken-Presse. (This is the earlier German edition of three lectures that provided the basis for the epistemological chapters in the later book on the History of Epistemic Things.); Rheinberger, Hans-Jörg (2005): A Reply to David Bloor: "Towards a Sociology of Epistemic Things". *Perspectives on Science* 13(3), 406-410. Rheinberger, Hans-Jörg (2010): *On Historicizing Epistemology: An Essay.* Stanford: Stanford University Press.

[46] Since the controversy surrounding the primary odour mechanism, comprising a variety of disciplinary contributions across fragrance chemistry, biochemistry and molecular biology, will be dealt with separately in chapters 4, 5, 7 and 8, my analysis here mainly concerns the instruments and visualisation techniques supporting recent olfactory developments.

knowledge claims about these objects influence each other without, however, leading to coextensive conceptions of a phenomenon.

2 Odours as Objects in Nature

2.1 Odours as Taxonomic Tools in Botany

First attempts to describe odours were undertaken in antiquity, for instance by Theophrastus.[47] In his work on *Enquiry into plants,* odours served as an important taxonomic tool to describe significant traits of certain plants, and even as a means to suggest medical treatments, for instance the use of cabbage against the use of wine "to expel the fumes of drunkenness".[48]

Systematic approaches to characterising odours, however, started with Linnaeus' *Odores Medicamentorum* in 1752. Linnaeus provided seven primary odour classes, which are based on their general appeal (pleasant, unpleasant) and partly on their quality (garlic-like, musk-like).[49] Linnaeus' hedonic approach presented a systematic forerunner to later psychophysical studies. In his later work *Clavis Medicinae* (1766), he further ordered odours into opposite hedonic pairs (sweet-smelling versus evil-smelling) and related these pairs to five principles of antithetic affects (libido/chastity, alertness/sleep, weakness/vitality, lassitude/activity, apathy/consciousness). By virtue of this twofold scheme (fig. 1), he suggested the arrangement of odoriferous material for purposes of therapy, correlating "ways of life" with "properties of nature" to treat certain (imbalanced) affects.[50]

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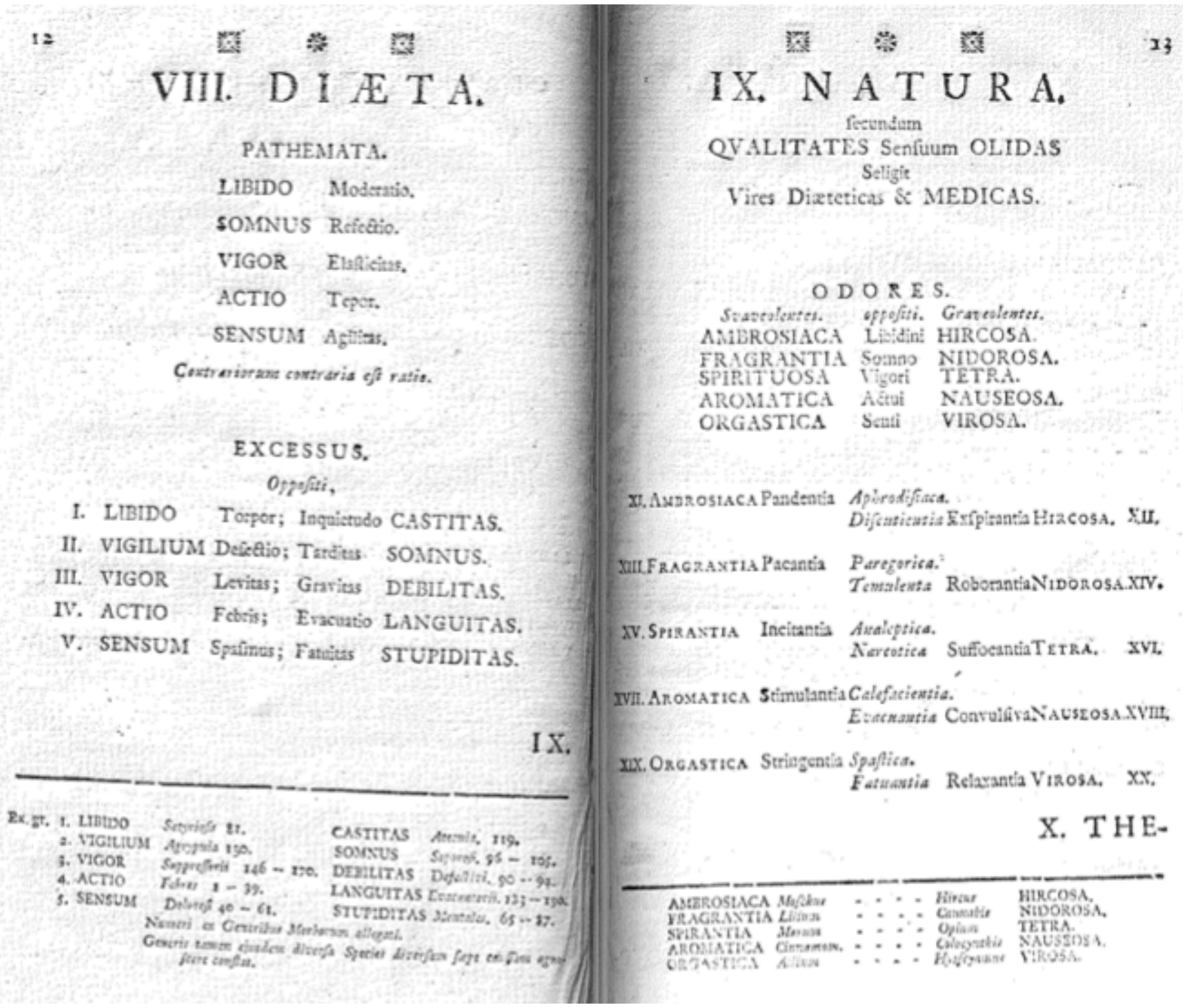
[47] Theophrastus: *Enquiry into plants, and minor works on odours and weather signs, Vol. 2.* Ed. by Sir A. Hort (1916). London: W. Heinemann, 85f., 215, 257, 281, 301, 321, 341, 413, 443.

[48] Ibid., 413.

[49] Linnaeus, Carl and Wahlin, Andreas (2010[1752]): *Dissertatio Medica Odores Medicamentorum Exhibens.* Reprint. Kessinger Publishing.; Harper et al. (1968): *Odour description and classification*, 19.

[50] Linnaeus, Carl (2012[1766]): *Clavis Medicinae Duplex. The two keys of medicine.* Ed. by L. Hansen. Trans. by P. Hogg. London: Whitby, VIII-XXVIII.



12

VIII. DIÆTA.

PATHEMATA.

LIBIDO	Moderatio.
SOMNUS	Refectio.
VIGOR	Elaſticitas.
ACTIO	Tepor.
SENSUM	Agilitas.

Contrariorum contraria eſt ratio.

EXCESSUS.

Oppoſiti,

I.	LIBIDO	Torpor; Inquietudo	CASTITAS.
II.	VIGILIUM	Defectio; Tarditas	SOMNUS.
III.	VIGOR	Levitas; Gravitas	DEBILITAS.
IV.	ACTIO	Febris; Evacuatio	LANGUITAS.
V.	SENSUM	Spaſmus; Fatuitas	STUPIDITAS.

IX.

13

IX. NATURA.

ſecundum
QVALITATES Senſuum OLIDAS
Seligit
Vires Diæteticas & MEDICAS.

ODORES.

Suaveolentes.	*oppoſiti.*	*Graveolentes.*
AMBROSIACA	Libidini	HIRCOSA.
FRAGRANTIA	Somno	NIDOROSA.
SPIRITUOSA	Vigori	TETRA.
AROMATICA	Actui	NAUSEOSA.
ORGASTICA	Sensi	VIROSA.

XI. AMBROSIACA	Pandentia	*Aphrodiſiaca.*		
		Diſcuticutia	Exſpirantia HIRCOSA.	XII.
XIII. FRAGRANTIA	Pacantia	*Paregorica.*		
		Temulenta	Roborantia NIDOROSA.	XIV.
XV. SPIRANTIA	Incitantia	*Analeptica.*		
		Narcotica	Suffocantia TETRA.	XVI.
XVII. AROMATICA	Stimulantia	*Calefacientia.*		
		Evacuantia	Convulſiva NAUSEOSA.	XVIII.
XIX. ORGASTICA	Stringentia	*Spaſtica.*		
		Fatuantia	Relaxantia VIROSA.	XX.

X. THE-

AMBROSIACA	*Moſchus*	. . . .	*Hircus*	HIRCOSA.
FRAGRANTIA	*Lilium*	. . . .	*Cannabis*	NIDOROSA.
SPIRANTIA	*Marum*	. . . .	*Opium*	TETRA.
AROMATICA	*Cinnamom.*	. . . .	*Colocynthis*	NAUSEOSA.
ORGASTICA	*Allium*	. . . .	*Hyoſcyamus*	VIROSA.

Fig. 1 Linneaus' hedonic approach. Odours are arranged by effects, and paired in opposites. Linnaeus (2012[1766]): *Dissertatio Medica Odores*, VIII-IX.

Linnaeus' approach of addressing odours by their hedonic features and degree of (un)pleasantness was later adopted in many late 18th and 19th century olfactory classifications (and serves as a useful distinction even today).[51] Although the specific numbers of odour classes and subclasses varied, Linnaeus' concept remained prominent across the pioneering works of for instance, Albrecht von Haller (1763), Hendrik Zwaardemaker (1895), Hans Henning (1916), and E.G. Boring (1942).[52] Especially in the influential classification of Zwaardemaker (1895), the inventor of the olfactometer,

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[51] Harper et al. (1968): *Odour description and classification*; Rouby, Catherine (2002): *Olfaction, Taste, and Cognition.* Cambridge: Cambridge University Press, 147.

[52] von Haller, Albrecht (1763): *Liber XIV. Olfactus. Elemenata Physiologiae Corporis Humani, Tome 5.* Lausanne: Grasset, 453-458; Zwaardemaker, Hendrik (1895): *Die Physiologie des Geruchs.* Leipzig: Engelmann; Henning, Hans (1916): *Der Geruch.* Leipzig: J.A. Barth; Boring, E.G. (1942): *Sensation and Perception in the History of Experimental Psychology.* New York: Irvington.

Linnaeus' distinctions – and even his specific method of list-making[53] – visibly informed classificatory arrangements (fig. 2).[54]

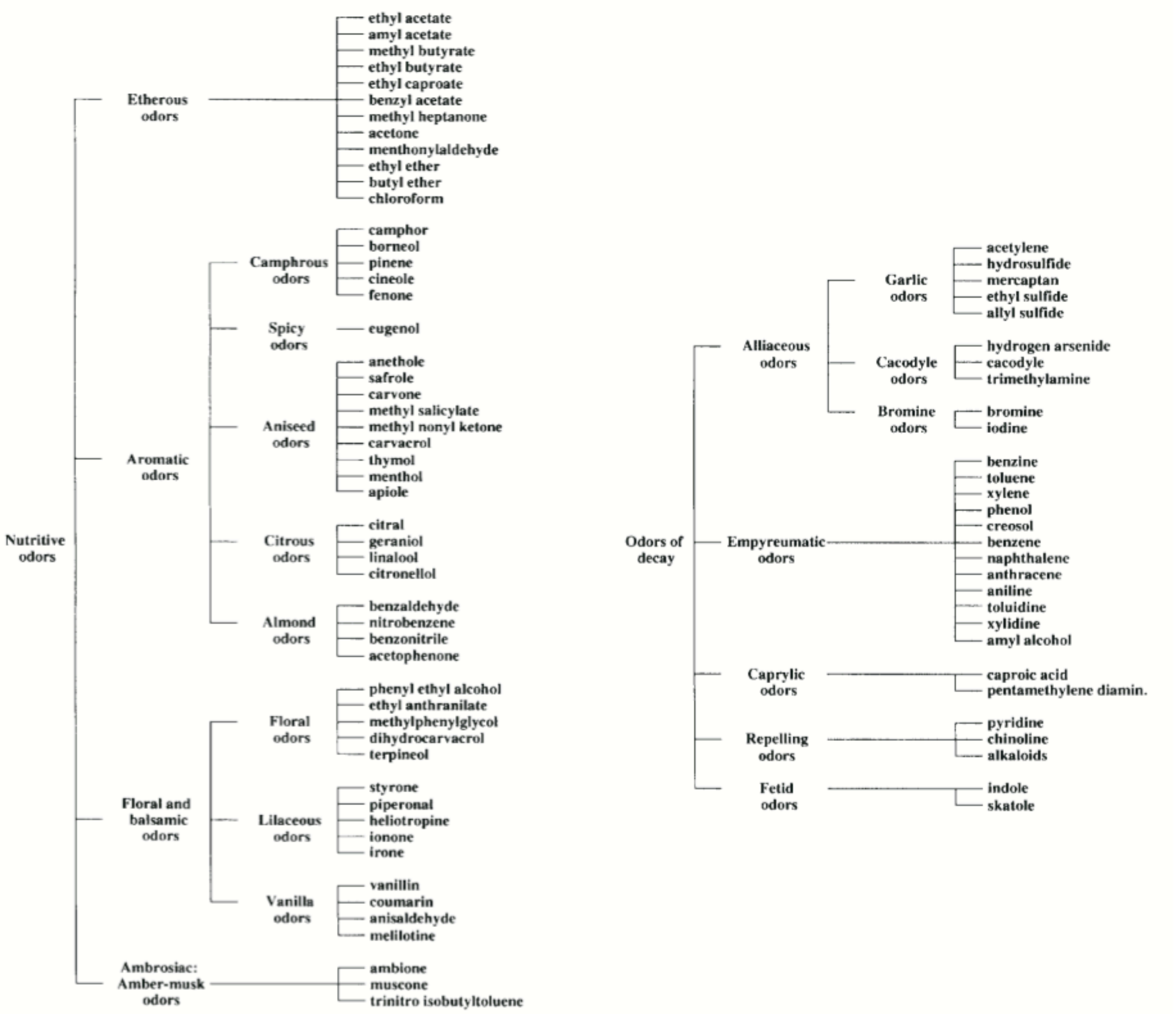

Fig. 2 Zwaardemaker's arrangement analyses odours first by effect (e.g. decay) and second by associated quality (e.g. garlic). Wise et al. (2010): *Quantification of Odour Quality*, 432.

This already indicates the significant influence of natural history on the development of odour classifications. Before analysing odour classifications, an investigation of the relevance of odours in botanic practice will illuminate how the nature of odours was approached before their potential as autonomous scientifically interesting objects was recognised. Understanding odours as taxonomic tools first is useful to explore the later construction of odour classifications based on botanic criteria, as this examination not only explains

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[53] For the conceptual influence of Linnaeus method of list-making for his classification system see: Müller-Wille, Staffan and Charmantier, Isabelle (2012): Lists as Research Technologies. *Isis: international review devoted to the history of science and its cultural influences* 103(4), 743-752.

[54] Zwaardemaker (1895): *Physiologie des Geruchs.*

the selection of odour classes but it also highlights the reasons for developing alternative criteria that exceed botanic considerations.

Odours occur as an important taxonomic auxiliary tool in botany and were repeatedly used to distinguish between different plant species and also to discern different plant parts.[55] In many textbooks and encyclopaedias of 19th century botany, the entrenchment of botanic practices and early attempts at systematic characterisations of odour materials can be seen in the taxonomic emphasis on so-called odoriferous plants and flowers.[56] Classifications of odoriferous plants and flowers mostly concerned the physiology and the morphology of specific plant species.

2.1.1 Plant Physiology: Odour Emission

With respect to their physiology, the first aspect for the classification of odoriferous plants involved their odour emission. On that account, in 1838 and, since it remained unanswered, again in 1839 the Academy of Sciences of Brussels posed the prize-question about "the production of odours in flowers".[57] In answer to this question, Prof. M. Morren and Prof. M. Auguste Trinchinetti de Monga conducted a range of experiments on different emission patterns of odoriferous plants. Based on Trinchinetti's account, odoriferous flowers are arranged into two classes, which are further divided into two subclasses:

1. "Those [plants] in which the intermission of odor is connected with the opening and closing of the flower (…)
    (a) Flowers which are closed and scentless during the day, and are open and odoriferous at night such as *Mirabilis Jalapa, M. dichotoma, M. longiflora, Datura ceratocaula, Nyctanthes arbor tristis, Cereus grandiflorus, C.*

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[55] Berzelius, Jacob (1837): On the Relations of Colour and Smell in the more important Families of the Vegetable Kingdom. *The Edinburgh new philosophical journal: exhibiting a view of the progressive discoveries and improvements in the sciences and the arts* 22, 7ff.; Balfour, John Hutton (1863): *A manual of botany.* Edinburgh: Adam and Charles Black, 483.

[56] Mile, Colin (2008[1805]): *Botanical dictionary: or, Elements of systematic and philosophical botany. H.D. Symonds by Bye and Law.* Reprint. Cambridge M.A.: Harvard University Press; Burnett, Gilbert Thomas (1835): *Outlines of botany: including a general history of the vegetable kingdom, in which plants are arranged according to the system of natural affinities, Vol.1.* J. London: John Churchill; Gray, Asa (1836): *Elements of Botany.* New York: G. & C. Carvill & co; Partington, Charles F. (1937): *The British cyclopaedia of natural history.* Oxford: Oxford University Press; Wood, Alphonso (1851): *A class-book of botany.* Unspecified; Balfour, John Hutton (1870): *Class book of botany: being an introduction to the study of the vegetable kingdom, Vol. 1.* Edinburgh: Adam and Charles Black.

[57] Meyen, F.J. (1841[1839]): Report of the Results of Researches in Physiological Botany made in the year 1839. *Annals And Magazine of Natural History* 8, 31.

nycticalus, C. Serpentinus, Mesembryanthemum noctiflorum, and some species of *Silene*.

   (b) Flowers which are closed and scentless at night, and are open and odoriferous during the day, such as *Convolvulus arvensis, Cucurbita pepo,* and *Nymphaea cœrulea*.

2. Flowers which are always open, but which are odoriferous at one time and scentless at another.

   (a) Flowers always open, and only odoriferous during the day such as, *Cestrum diurnum, Coronilla glauca,* and *Cacalia sepentrionalis.*

   (b) Flowers always open, but only fragrant at night, such as *Pelargonium triste, Cestrum nocturnum, Hesperis tristis*, and *Gladiolus tristis*."[58]

Such a classification, which is based on the performance of odoriferous flowers, is of botanical interest when it comes to specific patterns of reproduction. Supporting considerations about speciation in terms of breeding and hybridisation, physiological studies on odoriferous plants further guided the interpretation of parallel studies of the morphology of flowering plants, exhibiting specific colour-odour relations.[59]

2.1.2 Plant Morphology: Distribution of Odour in Relation to Colour

Another classification scheme of plant materials – provided in the tables of Köhler and Schübler, and promoted by John Hutton Balfour (1863) – is based on the distribution of odoriferous properties in relation to colour, exploring possibly important statistical correlations between these traits. They present white flowers as the most fragrant ones with the greatest use for the perfumer, whilst the least fragrant ones are orange and brown (fig 3). In addition, flowering plants are further examined through their family relations of taxonomic order (fig. 4). Results obtained from such tables were often consulted for the design of

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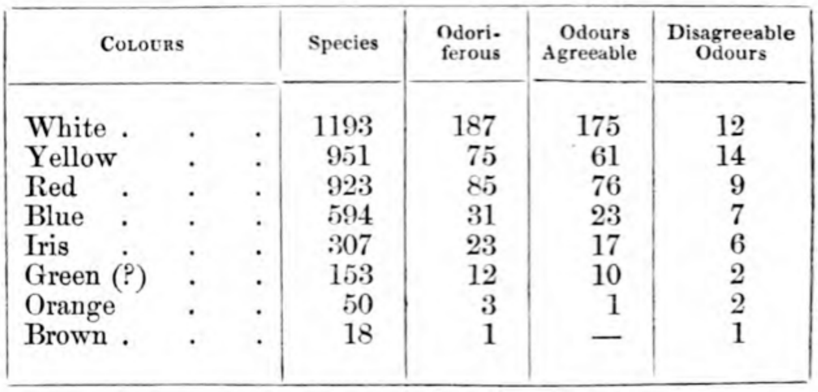
[58] Trinchinetti's account as quoted in: Piesse, George William Septimus (1862): *The Art of Perfumery, and the Methods of obtaining the odours of Plants.* 3rd Edition. London: Longman, Green, Longman and Roberts, 40f.

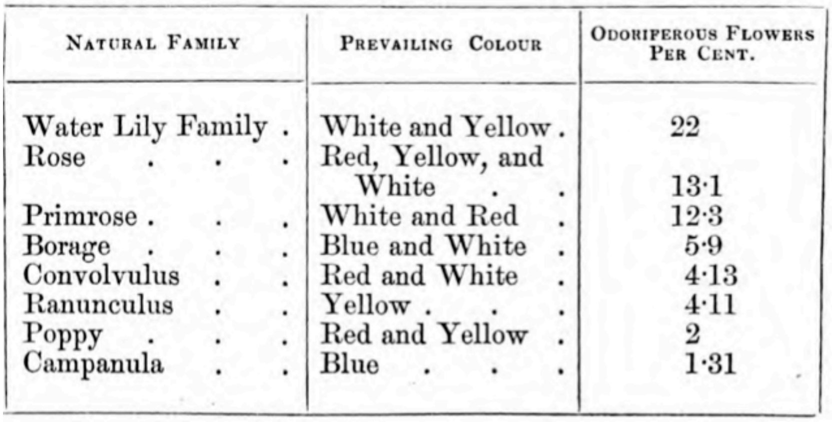
[59] Goodale, George Lincoln (1885): Physiological Botany. *Volume 1 of Physiological Botany: Outlines of the Histology of Phaenogamous Plants. Vegetable Physiology.* Ivison, Blakeman. URL=<http://www.ebooksread.com/authors-eng/george-l-george-lincoln-goodale/physiological-botany-i-outlines-of-the-histology-of-phaenogamous-plants-ii-v-ala/page-44-physiological-botany-i-outlines-of-the-histology-of-phaenogamous-plants-ii-v-ala.shtml>

gardens, arranging flowers according to their most harmonious smell and complementary colours.[60]



COLOURS	Species	Odoriferous	Odours Agreeable	Disagreeable Odours
White . . .	1193	187	175	12
Yellow . .	951	75	61	14
Red . . .	923	85	76	9
Blue . . .	594	31	23	7
Iris . . .	307	23	17	6
Green (?) . .	153	12	10	2
Orange . .	50	3	1	2
Brown . . .	18	1	—	1

Fig. 3 Statistical correspondences between the colour and the odoriferous properties of flowery plants. Tables of Köhler and Schübler. Piesse (1862): *Perfumery Methods*, 42.



NATURAL FAMILY	PREVAILING COLOUR	ODORIFEROUS FLOWERS PER CENT.
Water Lily Family .	White and Yellow .	22
Rose . . .	Red, Yellow, and White . .	13·1
Primrose . . .	White and Red .	12·3
Borage . . .	Blue and White .	5·9
Convolvulus . .	Red and White .	4·13
Ranunculus . .	Yellow . . .	4·11
Poppy . . .	Red and Yellow .	2
Campanula . .	Blue . . .	1·31

Fig. 4 Statistical evaluation of selected plant species and their correspondences in colour and odour. Tables of Köhler and Schübler. Piesse (1862): *Perfumery Methods*, 42.

Statistical correlations between colour and odour also served the purpose of exploring the fertilisation of flowers by insects in order to detect patterns of attraction. In this context, Darwin, acquainted with Köhler's and Schübler's work mentioned before, commented on these tables, remarking that

> "[t]he fact of a larger proportion of white flowers smelling sweetly may depend in part on those which are fertilised by moths requiring the double aid of conspicuousness in the dusk and of odour. So great is the economy of nature, that most flowers which are fertilised by crepuscular or nocturnal insects emit their odour chiefly or exclusively in the evening. Some flowers, however, which are highly odoriferous depend solely on this quality for their fertilisation, such as the night-flowering stock (Hesperis) and some species of Daphne; and these

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[60] Balfour (1863): *Manual of botany*, 342f.

> present the rare case of flowers which are fertilised by insects being obscurely coloured."[61]

Another example where systematic characterisations of odoriferous properties in plants were used to investigate the pollination behaviour of insects is the work of the Italian botanist Federico Delpino. Delpino, in his *Ulteriori Osservazioni sulla Dicogamia nel Regno Vegetale* (1868-1874), systematically divided odours into forty-five kinds based on their botanic occurrences.[62] In light of these studies, odoriferous properties of flowers presented an indispensable tool for 19th century botanic and horticultural practice.

Although initially used as taxonomic aids in the observation and arrangement of plant materials, odours were thus further applied as explanatory tools for deriving meaningful relations from statistical correlations between, for instance, observable properties of plants such as their odoriferous properties and their colour. The uses of such correlations were widespread and included harmonious composition of gardens (arranging flowerbeds according to complementary colours and pleasant odours respectively) as well as studies in plant physiology (observing possible relations between odour-emission patterns and fertilisation).

2.1.3 Species Demarcation? The Curious Cases of Fungi

Odours as a taxonomic tool are not limited to the classification of flowering plants. More recently odours have been suggested as a species demarcation in often less clear-cut cases of different fungi. Although consensus about the utility of odours for taxonomic purposes has not been undivided,[63] a number of case studies supported this approach.[64] For instance, the species of "*Entholoma lividum*, whose mealy odour quickly becomes rather nauseous, can be separated from *E. sinuatum* with its burnt odour, from *E. ameides* which smells

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[61] Darwin, Charles (1876): *Effects of Cross and Self Fertilisation in the Vegetable Kingdom.* London: John Murray, 347.

[62] Goodale (1885): *Physiological Botany*, 44; Delpino, Federico (1868-1874): *Ulteriori Osservazioni sulla Dicogamia nel Regno Vegetale.* Giuseppe Bernardoni.

[63] Josserand, M. (1952): *Description of higher fungi. Encyclopaedia Mycologique.* Paris: P. Chevalier.

[64] Gilbert, M.E.J. (1932): Osmologie Mycologique. *Extrait du Bulletin de la Société Mycologique de France* 48(3), 241-252; Heim, R. (1957): *Champignons. (Odour. It's Taxonomic Importance.).* Paris: N. Boubée et Cie, 141; Harper et al. (1968): *Odour description and classification*, 52f.

of orange blossom, and from *E. prunuloides* which has an odour of fruit and meal".[65]

Overall, the previous subsections presented odours as an integral aid in taxonomic practice that, notwithstanding their shared botanic focus, exhibited related yet conceptually different arrangements. Classification criteria here first comprised the emission behaviour of flowering plants and second statistical correlations between the colour and odoriferous properties across plant species. Although these two criteria were interpreted with respect to the same enquiry, reproduction patterns of flowering plant species, their different conceptual focus nevertheless resulted in varying arrangements of the materials. Moreover, and even more importantly, odoriferous properties as taxonomic criteria were considered to reflect natural distinctions or relations across different flowering plants. Yet, the specific interest that links, for instance, either the performance or the morphology to questions of reproduction, resulted in different applications of odours as a relevant taxonomic criterion.

2.2 The Influence of Botanic Practices on Odour Classifications in Perfumery

Given this influence of odours on taxonomic practice and further considering the fact that plant materials provided the largest quantity of raw materials in perfumery before the rise of synthetic chemistry, overlap of classifications across both fields is not surprising. Even with the increasing application of synthetic materials in 20th century perfumery, classifications of odours still partly rely on botanic categories. Drawing on the botanic origins of odour materials, the most influential works on odour classification in the first half of the 20th century are presented in the studies of Anton Kerner von Maurilaun (1902), Anthony Hampton (1925), Ralph David Bienfang (1941), J.H. Willis (1944) and René Cerbelaud (1951).[66]

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[65] Harper et al. (1968): *Odour description and classification*, 51.

[66] von Maurilaun, Anton Kerner (1902): *The natural history of plants: their forms, growth, reproduction, and distribution,* 2 Vols. Trans. by F.W. Olivier. London: Blackie & son; Hampton, Frank Anthony (1925): *The Scent of Flowers and Leaves. Its purpose and relation to man.* London: Dulau & Co., ltd; Bienfang, Ralph David (1941): Dimensional Characterisation of Odours. *Chronica Botanica* 6, 249-250; Willis, J.H. (1944): Flower Perfumes and their Classification. *The Victorian Naturalist* 61, 131-136; Cerbelaud, René (1951): *Formulaire de Parfumerie.* Editions Opéra, Brussels. (Unfortunately, most of these references are hardly

Since the botanic materials grouped together were extremely diverse, determining odour types on this basis led to several cross-cutting demarcations. From a broad comparative view, these classifications, similar to arrangements of botanic materials in 18th century chemistry,[67] ordered odour materials under five general criteria, namely:

- entire plants and specimens (type flowers such as Jasmine)
- plant parts and organs (roots, leaves, twigs, bark, bulbs, woods, fruits, resins and seeds, etc.)
- raw plant materials (unprocessed materials)
- extracted plant substances (processed materials such as essential and fatty oils or alcohols)
- and odours developed in chemical preparations that resemble odours of certain botanic origins.

Under the focus of these general criteria, the following subsections will illustrate that, although drawing on taxonomic relations, there is a vast variety of odour classifications that not only arise from different practical interests in the materials but also from the diversity of natural demarcations for grouping odour materials into relevant kinds. The link between odours and plant materials, it will further become clear, was systematised by different criteria, each of which related to natural features of the materials under investigation and, thus, equally presenting a natural demarcation to arrange botanic odoriferous substances. Presenting such a variety of demarcations demonstrates that, even within a specific disciplinary context, there are multiple features to define the material basis of odours for their classification.

2.2.1 Specimens, Extracted Plant Substances and Plant Parts

To begin with, a classification based on selected specimens and extracted plant substances is given in Frank Anthony Hampton's *The Scent of Flowers and Leaves* (1925).[68] Hampton proposes ten main odour classes and suggests

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accessible so that my analysis is largely based on Harper et al. (1968): *Odour description and clasification*.)

[67] Klein and Lefèvre (2007): *Materials*, 12f.

[68] Hampton (1925): *Scent of Flowers and Leaves.*

three different reference standards to identify and accommodate a wide range of odours under these classes (fig. 5).

Falling under these reference standards are:

- a significant olfactory quality (verbal descriptors),
- essential and fatty oils or alcohols (extracted plant substances),
- a type flower (specimen).

One common criticism addressing this approach concerns its limited global utility. Not all specimens, for instance, can necessarily be found in every geographic area, impeding successful communication between practitioners such as perfumers, their material suppliers and customers.[69] In addition, the choice of specimens and the number of odour classes likewise reflects a certain degree of arbitrariness.

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[69] Willis (1944): *Flower perfumes and their classification*; Harper et al. (1968): *Odour description and classification*, 45.

INDOLOID GROUP:
Quality: foetid.
Essential oil contains indole.
Type flower: Stapelia.

AMINOID GROUP:
Quality: stale and slightly sweet.
Essential oil contains trimethylamine.
Type flower: Hawthorn.

HEAVY GROUP:
Quality: very sweet and heavy.
Essential oil contains benzyl acetate, methyl anthranilate, indole, etc.
Type flower: Jasmine.

AROMATIC GROUP:*
Quality: sweet, with a spicy quality.
Essential oil contains eugenol, cinnamic alcohol, vanillin, etc.
Type flower: Clove Carnation.

VIOLET GROUP:
Quality: sweet, but less heavy than preceding groups.
Essential oil contains ketones of the ionone type.
Type flower: Violet.

ROSE GROUP:
Quality: sweet, but not heavy.
Essential oil contains geraniol.
Type flower: Rose.

LEMON GROUP:
Quality: light, fresh.
Essential oil contains citral.
Type flower: *Magnolia grandiflora.*

FRUIT-SCENTED GROUP:
Quality: fruity.
Essential oil contains esters of higher fatty alcohols.
Type flower: *Philadelphus microphyllus.*

ANIMAL GROUP:
Quality: animal and unpleasant.
Essential oil contains caproic and valeric acid and their esthers.
Type flower: Lizard Orchid.

MUSK AND HONEY GROUP:
Quality: sweet, often rather dry and dusty.
Essential oil farnesol.
Type flower: Musk Orchid (*Herminium monorchis*)

**The aromatic group is further subdivided into 6 groups (balsamic, clove, aniseed, vanilla, almond and hawthorn type).*

Fig. 5 Hampton's system. Odours are arranged by three standards: quality, essential oil and type flower. Harper et al. (1968): *Odour description and classification*, 39f.

Alternatively, René Cerbelaud in his very influential *Formulaire de Parfumerie* (1951)[70] differentiates between botanic and floral odours by adopting the

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[70] Cerbelaud (1951): *Formulaire de Parfumerie.*

distinction between different fragrant parts and organs of plants (fig. 6), i.e. roots, leaves, fruits and seeds, and the more prominent floral parts. These plant parts are further arranged into forty-five classes, based on the taxonomic distinctions and family relations between botanic odour materials.[71] An advantage of the focus on plant parts instead of the entire plant is that a plant can produce more than one odour in its different organs, and these are also subject to different extraction methods.

Fig. 6 Plant parts of the orange tree. Kurt Stübers online library (2001).

Consider, for instance, the bitter orange tree, which gives rise to three different odours: *petitgrain* gathered from the leaves via steam distillation; *neroli* or *orange flower absolute* elicited from the flowers also by steam distillation, and the essential oil labeled *Portugal* or, more commonly, *orange bitter,* cold pressed from the rind of the fruit.[72]

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[71] Harper, Roland (1966): On Odour Classification. *J. Fd Technol.* 1, 170.

[72] Piesse (1862): *Perfumery Methods*, 38; Soburg, Horst and Panten, Johannes (2006): *Common Fragrance And Flavor Materials: Preparation, Properties And Uses.* Wiley-VCH, 219-225.

Notwithstanding the detailed and elaborate comparison of odour materials and their descriptions, one criticism that Cerbelaud's approach invites is that his lists present an inventory or review of already known materials but do not compose a system under which future materials, natural as well as synthetic, can be assembled.[73] Moreover, many essences produced vary in their odour quality not only because of different extraction methods but also because they differ with respect to seasonal factors of production:

> "Essence of bergamot made in October is of different quality to essences produced in the months of November, December, January and February. Production is carried out for five months of the year and actually results in essences that start off with intense, fresh, green notes and continue with floral and gustatory notes. October essence has the highest content of linalool, a constituent with a floral smell, and February has very little linalool but contains fresh-smelling linalyl acetate. (…)"[74]

2.2.2 The Conceptual Influence of Disciplinary Practices

Comparing the two classifications of Hampton and Cerbelaud, focus on botanic origins allows for variable aspects to distinguish odour materials, such as the plant species and its provenance, the character of extracted plant substances (i.e. fatty and essential oils or alcohols, etc.) or the preparations made only from particular plant parts (roots, leaves, fruits). Relevant substances are thus grouped together in classes by proximate principles drawn from different practical interests surrounding plant science. These principles in fact transcend their initial natural basis by presenting a combination of criteria tied to different classification practices and interests.

Upon closer inspection, Cerbelaud's focus on plant parts and organs, for instance, was influenced by his prominent work on pharmaceutical and cosmetic products.[75] As to the possible uses and combinations of botanic materials, it is specific plant parts that are either used as remedies for illness or as soothing ingredients in oils or crèmes. In comparison, by employing

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[73] Harper et al. (1968): *Odour description and classification*, 73, 114; Harper (1966): *Odour classification*.

[74] Ellena, Jean-Claude (2012): *The Diary of a Nose. A Year in the Life of a Perfumer.* London: Particular Books (Penguin Group), 19.

[75] Georgin, A. (2005): One hundred years after the Geminal law, Rene Cerbelaud publishes secret remedies. *Rev Hist Pharm* 53(346), 257-265.

descriptive properties as well as reference to specimens, Hampton's system relied on extensive knowledge of horticulture. During his lifetime, Hampton, next to his profession as a psychiatrist, established himself as a horticulturalist, publishing gardening books under the pseudonym of Jason Hill.[76]

It is thus worth emphasising that the conceptual relations between the classified materials are entrenched in a range of collective practices of adjacent disciplines dealing with largely the same domain of materials, such as botany and horticulture, organic chemistry, pharmacy, perfumery, etc.[77] At first glance it seems obvious to ascribe the common employment of these classificatory practices, forming conceptual points of intersection, merely to the common botanic materials classified. Yet this disciplinary entrenchment, I argue, presents two further, more important, aspects for a philosophical and historical analysis of scientific objects.

First, it marks a certain stage of inquiry in the historical trajectory of a scientific object, in this case the conceptualisation of odours in relation to their materials. Such stages, as will become clearer in the course of the present analysis and in the following chapter, reflect different dimensions of, and interests in, the materials classified. One reason for this is that the relevance and selection of specific material features is embedded in the available techniques and modelling strategies. Historical work on classifications thereby helps to elucidate the degree to which classifications are grounded in specific enquiries and disciplinary directions. The classification of odour materials exhibits a development of practices and shifts in the conceptualisation of odours and ontologies of materials similar to Klein and Lefèvre's analysis of materials in 18th century chemistry. A historic trajectory of scientific objects thus benefits from a cross-disciplinary comparison of similar conceptual practices.

Second, this disciplinary entrenchment, especially with respect to the focus on chemistry and molecular biology adopted later, also reveals the underlying diversity of material distinctions used to address odoriferous substances. Their multidimensionality presents the materials as a shared basis for quite different conceptual perspectives. Plants, in particular, had already been shown to exhibit various but equally applicable means to divide a wide range of odour materials with respect to informative botanic categories.

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[76] Unspecified (1967): *Gardener's chronicle, horticultural trade journal* 161, 4; Royal Horticultural Society Great Britain (Eds.) (1984): *The Garden* 109, 428.

[77] Klein and Lefèvre (2007): *Materials*, 12f.

2.3 Conceptual Analogies to Other Research Contexts

Developing this pluralistic perspective, the multidimensionality of criteria to divide up odoriferous materials is further illustrated by other influential examples of classification schemes. These examples will highlight the persistent impact of botanic categories on odour classifications but will also explore additional criteria that begin to generate a disciplinary emancipation in the work on odours. Among the various conceptualisations of odours, a variety of classification schemes started to include conceptual analogies to other senses. Historically, cross-reference between perceptible qualities such as colour, sound, smell and taste were not unusual. George Field's *Chromatics* (1845), for instance, presented a scale arranging colours in parallel with a series of sounds.[78] Drawing such analogies between perceptible qualities was supposed to answer a specific inquiry, in Field's case concerning forms of composition and harmony, and also to provide, to a certain degree, means of measurement. This already indicates that different kinds of classifications with diverging purposes may nevertheless coincide by virtue of particular materials or conceptual criteria.

2.3.1 The Analogy between Sound and Odours

In earlier 19th century perfumery, drawing conceptual links to other senses in order to establish systematic characterisations of odours was common practice. Analogies to sounds as a tool to explain relations of harmony for the composition of perfumes were particularly popular (fig. 7 and 8).

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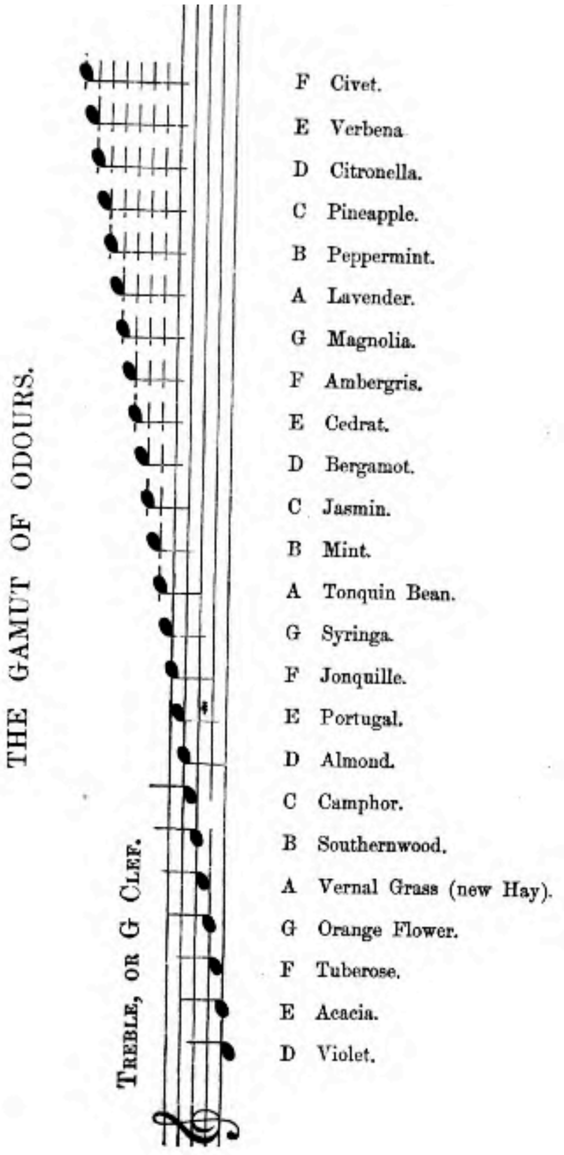
[78] Field, George (1845): *Chromatics; or, The analogy, harmony, and philosophy of colours*. 3rd Edition. London: Moyes and Barclay, 78-176.



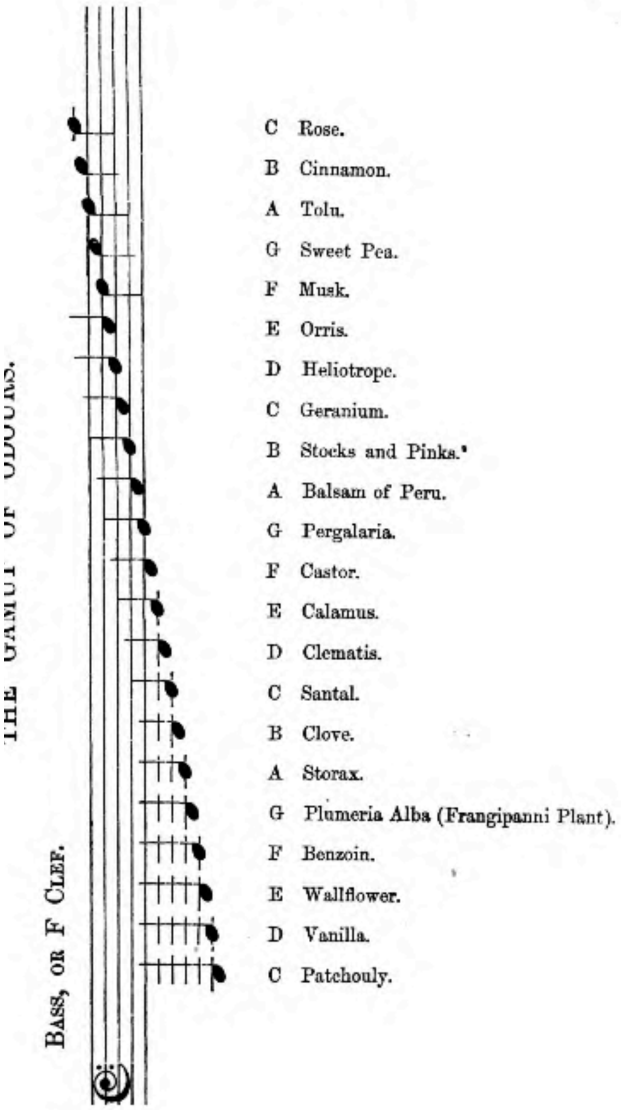


Fig. 7 Odours arranged as notes.
Piesse (1862): *Perfumery Methods*, 28.

Fig. 8 Odours arranged as notes.
Piesse (1862): *Perfumery Methods*, 29.

The perfumer's arrangement of odours comprised more or less basic materials with a stable standard and technique of production such as orange flower, musk, rose, etc. In parallel with tones, odours were arranged into harmonious "chords", involving complementary notes as well as contrasting ones (fig 9).[79] Despite its limited application with respect to the increasingly wider range of odour materials, such a system appeared more useful as an educational tool for perfumers.

It thus seems plausible that the analogy of odours with colours was largely grounded in the comparison of their associated arts and purposes of skilful composition: "as an artist would blend his colours, so must a perfumer blend his

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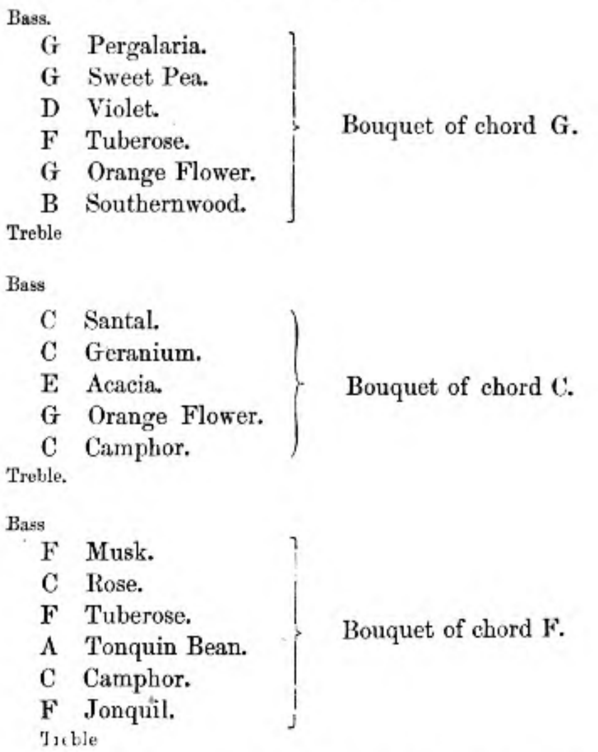
[79] Piesse (1862): *Perfumery Methods*, 30.

scents."[80] Nonetheless, this explanation on its own falls far short of a satisfactory account. In fact, observations on the material production of odours also provided reasons to suggest a similarity between sound, colour and odours. For the case of light and sound, contemporary physicists such as David Bewster were observing the phenomenon that "[t]wo loud sounds may be made to produce silence and two strong lights may be made to produce darkness."[81] Similarly, mutual neutralisations of perceptible qualities had also been noticed in the composition and mixing of odour materials, for instance in the combination of concentrated ammonia (NH_3) and acetic acid (CH_3CO_2H).



Bass.		
G	Pergalaria.	Bouquet of chord G.
G	Sweet Pea.	
D	Violet.	
F	Tuberose.	
G	Orange Flower.	
B	Southernwood.	
Treble		
Bass		
C	Santal.	Bouquet of chord C.
C	Geranium.	
E	Acacia.	
G	Orange Flower.	
C	Camphor.	
Treble.		
Bass		
F	Musk.	Bouquet of chord F.
C	Rose.	
F	Tuberose.	
A	Tonquin Bean.	
C	Camphor.	
F	Jonquil.	
Treble		

Fig. 9 Harmonious odour "chords" or bouquets. Piesse (1862): *Perfumery Methods*, 30.

2.3.2 Bienfang: Conceptual Inferences of an Analogy for Classification Purposes

Further drawing on an analogy of odours and colours, a more contemporary approach is presented in Ralf David Bienfang's work on the *Dimensional*

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[80] Piesse (1862): *Perfumery Methods*, 27.

[81] Brewster, David (1834): *Letters on natural magic, addressed to Sir Walter Scott.* London: John Murray, 195. See also Piesse (1862), 31.

Characterisation of Odours (1941).[82] Like classifications previously presented, his templates for odour classes relate to botanic concepts. And like Cerbelaud, Bienfang referred to different plant parts that have distinct odours; apart from "flowery" most odour classes relate to specific vegetative parts of plants.[83] In addition to this botanic focus, he proposed that odours could be ordered in analogy to colours.

Research on vision has always been far more advanced than studies on smell, and our understanding of colours has therefore always been better developed than our understanding of odours. Perhaps, colours may appear simpler to describe. Using advanced knowledge about colours, Bienfang elaborated on conceptual similarities between the perception of smell and vision. Since it provided specific criteria for how to define perceptible qualities, he suggested determining odours with respect to Munsell's colour system (fig. 10).

Colours in Munsell's system are divided in three dimensions:

- Hue, indicating colour quality (blue, green, yellow, red),
- Value, giving a scale of brightness (1-9),
- and Chroma, displaying a scale of saturation (1-10).[84]

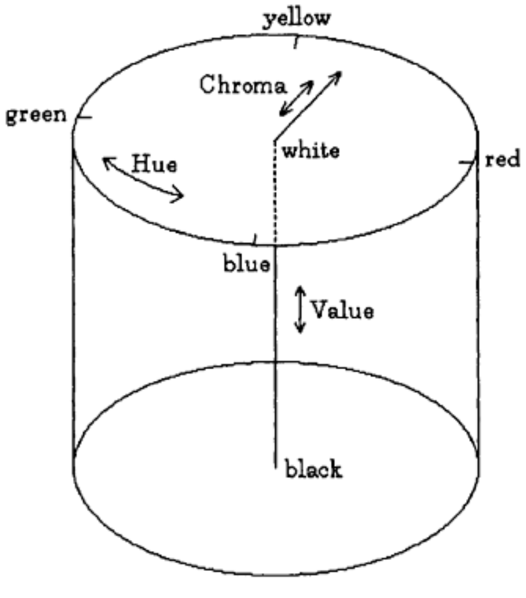

Fig. 2.13. Munsell color space is a cylinder with Value (lightness–darkness) making up the center axis, Chroma radiating outward from the Value axis with circles of constant Hue forming concentric circles around the Value axis (also see color plates 1 and 2).

Fig. 10 Munsell's colour system presented as a cylinder. Nassau (1998): *Color for Science, Art and Technology*, 53.

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[82] Bienfang (1941): *Dimensional characterization of odors.*

[83] Harper et al. (1968): *Odour description and classification*, 43.

[84] Cleland, Thomas M. (1921): *A practical description of the Munsell color system, with suggestions for its use.* Boston: Munsell Color Company.

In parallel with colour dimensions, Bienfang presented three comparative criteria to define odours, namely:

- the circumference of note (like Hue/quality),
- the axis of clarity (like Value/brightness),
- and the radius of strength (like Chroma/saturation).[85]

Stretching the analogy to colours even further, selected odour classes were then arranged into a circle of three prime and six subprime odours (fig. 11). It is worth adding that Bienfang refers to both the *intensity* and the *quality* of odours in his system, a feature not explicitly addressed in previous accounts.

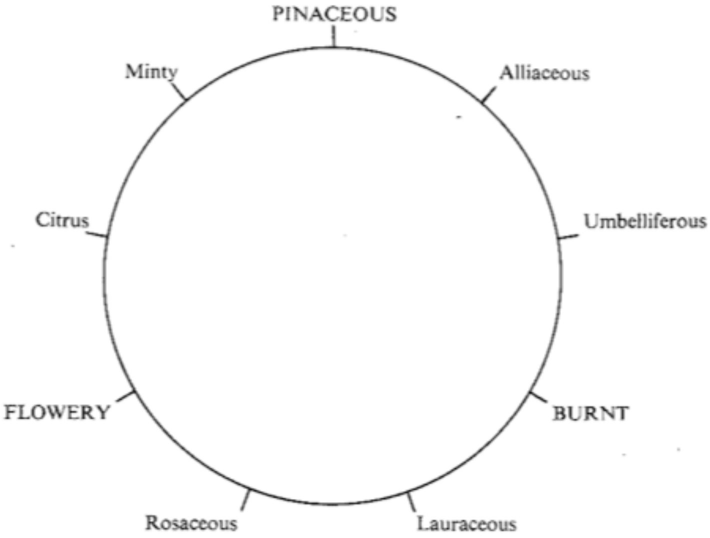

Fig. 3 (1). Bienfang's three PRIMES and six SUB-PRIMES
After Bienfang, 1941.

Fig. 11 Bienfang's odour circle. Harper et al. (1968): *Odour description and classification*, 44.

One particular limitation, inherent in Bienfang's system, is its small range of primary odours. Whereas most odours are complex mixtures, these primes merely apply to 'simple' odours. Amongst the variety of odour materials, however, are dozens of substances that give rise to complex odours, exhibiting quite divergent characteristics and containing 'hidden' or less dominant qualities. The bulk of raw materials and processed substances, and the rise of chemical analysis of odour materials rendered the limits of such a simple system all too visible. Many odour complexes consist of quite different constituents and these complexes change their note significantly when diluted.[86]

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[85] Bienfang (1941): *Dimensional characterization of odors.*

[86] Harper et al. (1968): *Odour description and classification*, 44; Dravnieks, Andrew (1972): Odour Measurement. *Environmental Letters* 3(2), 81-100; Chastrette, M. (1998): Data management in olfaction studies. *SAR & QSAR in Environmental Research* 8, 159.

For instance, ethylamine's ($CH_3CH_2NH_2$) quality in concentrated form is described as "ammoniacal" whereas its diluted form is characterised as "fishy"; similarly, Diphenylmethane ($(C_6H_5)_2CH_2$) concentrated smells like "orange" whereas diluted it resembles "geranium".[87]

A striking feature of Bienfang's classification is the combination of two conceptually different criteria for a systematic arrangement of odour materials. His odour circle sorted odours by reference to two criteria: their botanic origins on the one hand and the perceptible odour qualities in their own right on the other. A lot of names for odour types were taken from plants or plant parts. Therefore, a lot of names assigned to a diversity of odour types refer to most popular or better known botanic origins of odours, providing a recognisable template to relate less well known odours and to further describe the quality of odours of synthetic origin.

This twofold mode in Bienfang's classification exemplifies the possible conceptual overlap between different modes of classification within one system. By reference to their botanic origins, odours are still represented as objects in nature. Yet, the determination of odour quality in parallel with colour dimensions provides this classification with a supplemental standard that, by transcending their specific origins, allow for a more extensive arrangement of odour materials. In addition to object-oriented criteria such as plant parts, the analogy to vision presented sensory descriptions of odours with an additional form of measurement that, within its own limits, made possible the arrangement of non-botanic materials under general categories previously derived from plants. Bienfang's approach thus nicely demonstrates the conceptual plurality with which odours can be defined and the different dimensions of odours on which this plurality is based.

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[87] For more examples see: Moncrieff, Robert Wighton (1944): *The Chemical Senses.* London: L. Hill; Gross-Isseroff, Ruth and Lancet, Doron (1988): Concentration-dependent changes of perceived odour quality. *Chem. Senses* 13(2), 191-204; see also: Dravnieks (1972): *Odour Measurement*.

2.3.3 Henning: Combinatorial Inferences from Analogies between Smell and Colour, Sound and Taste

Another example that utilises analogies to other senses is Hans Henning's odour prism (fig. 12). In *Der Geruch* (1916),[88] Henning considers the similarity between smell, colour, sound and taste as a heuristic source to develop six principle odour categories, mainly in comparison to flavours and colours. In his approach, the first analogy to colours consists of the three-dimensional characteristics in odour quality; a conceptual point that, as I have shown above, had been developed in greater detail by Bienfang. Yet, Henning also points out the limits of this colour analogy, namely the difference in composition: whereas colours are often produced by the merging of primes such as yellow and blue into green, the mixing of smells, he argues by employing a second analogy, must rather be understood like the composition and "tonal fusion" of chords. He further describes the olfactory space between his main primes as 'transitional' in a third comparison to taste. Like taste experiences such as salty and sweet, salty and sour, salty and bitter, a variety of smells exhibit a "transitional character" at different positions in his smell prism.[89]

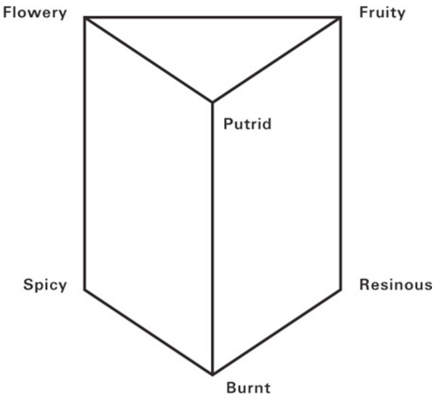

Fig. 12 Henning's odour prism. Jasper and Wagner (2008-2009): *Notes on Scent*.

Although his system is considered outdated today, it significantly influenced the later Crocker-Henderson classification (1927),[90] which reduced these six principal odours to four (fragrant, acid, burnt, caprylic) and which, before John

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[88] Henning (1916): *Der Geruch.*

[89] Gamble, Eleanor Acheson McCulloch (1921): Review of Der Geruch by Hans Henning. *The American Journal of Psychology* 32(2), 293, 295.

[90] Crocker, E.C. and Henderson, L.F. (1927): Analysis and classification of odors. *American Perfumer Essential Oil Review* 22, 325-256.

Amoore's "Stereochemical Theory" (1964, 1970),[91] served as an important educational tool until the Second World War.[92]

Henning's influence, however, is less founded in his odour classification than in his extensive methodological considerations on odour measurement. His psychophysical approach, conducting a series of experiments on subjects trained in psychology, involved 415 test substances, including extracts such as essential oils and raw materials such as dried herbs, which were supposed to represent "the whole qualitative range of *natural odours*".[93] Like previously presented systems he too consulted specific reference materials for odour classes such as violet for floral, lemon for fruity, sulphureted hydrogen for putrid, nutmeg for spicy, frankincense for resinous and tar for burned.[94]

The most significant methodological contribution to olfactory research concerned his argument that the prominent method of "monorhinic" smelling, i.e. test smelling with only one nostril, was unnatural; and he also criticised the associated practice of smelling mixtures "diorhinic", that is first with one nostril open and then, separately, with the other.

In addition, informed by his psychophysical approach, he also introduced a fundamental conceptual distinction between "the true odor (*Gegebenheitsgeruch*), which is obtained by the observer who is smelling with closed eyes and is ignorant of the nature of the scent, and the object-smell (*Gegenstandsgeruch*), which (like color) is projected upon the objects from which it is known to come and apt to be distorted by associative supplementing."[95] This again emphasises the extent to which the conceptualisation of odours inevitably relates to the methods selected and its disciplinary origins. Description of smells and their associated qualities inevitably differs when one is confronted with their visible material origins from when the odour experiences are only accessible by mental associations. Resulting differences in the cognition and the description of perceptive experiences constitute an interesting phenomenon for psychophysical studies.

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[91] Amoore, John E. (1964): Current Status of the Steric Theory of Odor. *Annals of the New York Academy of Sciences Volume 116, Recent Advances in Odor: Theory, Measurement, and Control,* 457-476; Amoore, John E. (1970): *The Molecular Basis of Odor.* Springfield, IL: Thomas.

[92] Wilson, Donald Alan and Stevenson, Richard J. (2006): *Learning to smell: olfactory perception from neurobiology to behavior.* Baltimore: John Hopkins University Press; Harper (1966): *Odour classification*, 170.

[93] Gamble (1921): *Review*, 291. [Italics mine]

[94] Ibid., 292.

[95] Gamble (1921): *Review*, 292.

Showing the impact that methodological choices have on research outcomes, diverging research traditions compete in how to best measure experiential states of perception. “Mentalist” approaches, for example, work with descriptions drawn from mental images, whereas “performance” studies, concentrate more on human powers of discrimination.[96]

Another conceptual feature of Henning’s system is his explicit rejection of linear classifications such as in Zwaardemaker’s lists and its replacement by a three-dimensional system built on more abstract relations by analogy with other senses. Its over-elaborate conceptual character, however, evoked the criticism of his contemporaries such as Eleanor Gamble who, reviewing Henning’s approach in light of the complexity of odour measurement, remarked: “Its very neatness is against it.”[97]

2.4 Conceptual Distinctions and their Disciplinary Entrenchment

To recap the previous section briefly, all the different classifications discussed rest on an empirical basis by defining odours in relation to their botanic origins. By reference to plant materials, these classifications presented an overall object-based approach and conceptualised odours as objects “found in nature”. The selection of relevant criteria to arrange these materials, namely plants, certain plant parts and type specimens, already singled out specific substances among a larger range of odour materials. This selection mirrors, in fact, the particular importance and practical interest that plant materials have for assigning a classificatory link between odours and their material basis.

These various interests resulted in alternative distinctions for the arrangement of odoriferous materials. First, odours as taxonomic tools in botanic classifications of flowers have been shown to rely on different aspects in the study of plants such as physiological and morphological relations. Second, and in addition to the utility of odours as taxonomic tools in botanic classifications, botanic criteria and practices were also employed for odour classifications in perfumery. Hampton and Cerbelaud, for instance, drew on associated disciplinary practices such as horticulture and pharmacy that shaped their

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[96] Wise, Paul M.; Olsson, Mats J. and Cain, William S. (2000): Quantification of Odour Quality. *Chem. Senses* 24, 436.

[97] Gamble, Eleanor Acheson McCulloch (1916): Taste and Smell. *Psychol. Bull.* 13, 137.

specific focus on how to pragmatically select relevant classes. Other approaches such as Henning's and Bienfang's used analogies to other senses to provide more abstract criteria in order to transform inventories of odour materials into systematic schemes.

All these various distinctions drawn from investigating botanic relations resonated with the nature of the explored materials. For instance, plants often produce a variety of different odours, residing in different plant parts, and extracted by diverse methods. Likewise, some odour types are related to selected flower families such as roses, violets, etc. This natural variety in the underlying relations between odours and their materials resulted in cross-cutting classifications that considered plant specimens, plant parts and extracted substances. As a result, although equally drawing attention to botanic traits of odoriferous materials, the selection of criteria led to significant differences in the classifications of odours. It is thus the very entrenchment and overlap of different disciplinary interests and the multidimensional character of the materials themselves which lead to alternative classification practices that, nevertheless, aim to represent natural distinctions.

Yet, one might wonder, why did these odour classifications generally concern botanic materials? Reluctance to arrange odours exclusively in terms of their perceptible qualities suggested the emphasis on source materials. Among the problems of classifying odours is the lack of adequate language to define odour quality. Descriptions of odours often resort in comparisons to objects such as "this smells like apple" to provide a certain degree of intersubjectivity. Reference to material origins thereby provided a principle for collecting, comparing and arranging the vast diversity of odour phenomena that, when only taken as perceptual properties, appeared to have no objective grounds for measurement and classification.

At first glance it does seem intuitive to classify odours according to their botanic sources; they indeed provide the largest resource of raw materials in perfumery. Nonetheless, when thinking of odours as natural objects, i.e. as objects produced and found in nature, important odour materials are found in the animal kingdom as well. Although animal materials such as fats and gland excreta provided indispensible raw materials for perfumery, these appeared nevertheless less suitable for a more systematic classification of odours. Animal materials are either summarised under broad and less specific classes such as "animalic" and "musky" or appear in list form. In addition to the lack of significant taxonomic relations, a second factor responsible for the absence of systematic arrangements of animal materials is their inaptitude for controlled "farming". Many animal materials such as ambergris cannot be systematically reproduced and are sporadic in their occurrence.[98] By contrast, the farming and trade of plant materials constituted an often historically neglected yet important economic factor, especially in Mediterranean countries such as Italy, Sardinia and Southern France.[99] The logistics of breeding, collecting and distributing plant materials requires systematic knowledge about their taxonomic relations, adaptations, different qualities and behaviour. Moving beyond botanic interests, many odoriferous plant materials were of practical concern for other disciplines such as horticulture, pharmacy, and organic chemistry and psychophysics. In addition to academic studies, plant materials and their odours have also often been of commercial relevance for "wine merchants, tea-brokers, drug dealers, tobacco importers".[100] Therefore, an important factor for the dominant focus on botanic materials is their shared significance across various branches of trade.

Nonetheless, classifications relying on botanic criteria do not fully exhaust the wide range of odour materials. Despite their utility for various purposes, they often remained too limited for other conceptual inquiries, for instance seeking an explanation of similar odours of different botanic origins such as camphor, turpentine and rosemary. These limits came into focus with the introduction of synthetic fragrance materials at the end of the 19th century. The increasing industrial growth of perfumery in the 20th century necessitated a different perspective on the material basis of odours and their classification.

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[98] One social consequence of its natural rarity is the evolving competition of semi-professional ambergris seekers and even the peculiar emergence of an "ambergris mafia" patrolling beaches. Kemp, Christopher (2012): *Floating Gold. A Natural (and Unnatural) History of Ambergris.* Chicago: University of Chicago Press.

[99] For an overview of flower-farming statistics in the 19th century see Piesse (1862): *Perfumery Methods*, 36-47; see furthermore: Piesse, George William Septimus (1891): *Art of Perfumery and the Methods of Obtaining the Odours of Plants, the Growth and General Flower Farm System of Raising Fragrant Herbs.* London: Piesse and Lubin.

[100] Piesse (1862): *Perfumery Methods*, 26.

3 Odours as Materials of Production

In parallel with botanic practices, odoriferous materials also played a significant role for developments in early chemistry. Studying chemical reactions, odours served as perceptible criteria for describing material changes occurring during experiments. Surrounded by different techniques to extract, manipulate and blend materials, research here largely investigated odours under the focus of "materials of production".

A lot of the odoriferous materials used across academic disciplines and artisanal arts and crafts were not strictly natural but often already processed substances such as essential oils, balms, butters, etc. Operations on raw materials and their transformation into processed substances involved several practices. Until the end of the 19th century, these practices were mainly mechanical in character. Forming what Hans-Jörg Rheinberger and Staffan Müller-Wille describe as "epistemic space"[101], a variety of related disciplines and commercial sectors such as chemistry, pharmacy, perfumery and other trading arts and crafts such as spirit and food manufacture shared their expertise on techniques of processing materials. Overlapping interests in producing odoriferous products such as perfumes, oils, waxes, remedies, crèmes, spirits, etc. for various purposes led to shared efforts to develop appropriate and efficient extraction techniques. Using and refining the same instruments, the practices surrounding odoriferous materials generated an epistemic space in which to establish standards for the measurement, description and classification of odoriferous substances in order to compare and distribute processed products. Within this productive environment, the evolving practices created new conceptual inquiries into the character of odours and their material basis. Instead of their botanic origins, odour materials became increasingly thought of in relation to their differences in production. Not every technique appeared to be appropriate for every kind of material. Leaves, flowers, roots, fruits and barks, for instance, are of different consistency and, as a result, required different treatment for a successful extraction of their smelling substances.

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[101] Müller-Wille, Staffan and Rheinberger, Hans-Jörg (2012): *A Cultural History of Heredity.* Chicago: University of Chicago Press.

Especially the increasing vicinity to the interests of academic chemistry and perfumery led to a significant change in the understanding of the material basis of odours. Starting out as an alternative to parallel investigations of odours as objects in nature within botany, odour materials were more and more explored in terms of their physical alteration. As a result of this development, insight into the chemical composition of odoriferous substances reinforced an ontological shift in defining the material basis and similarity relations of odour materials.

3.1 The Treatment of Odoriferous Materials in Chemistry

The beginnings of this underlying ontological shift are linked to a more general ontological turn in understanding the nature of materiality. In earlier chemical practice, the fundamental change to understanding material interaction in terms of elementary particles instead of chemical principles signified one of the most revolutionary turns in science.[102] Chemical reactions were long considered to relate to some kind of principles that are inherent in matter. These principles were described as abstract forces acting on materials, causing reactions such as combustion. Suggestions that reactions between chemicals must be understood instead in terms of their composition and the exchange of compositional elements implied a novel conception of the underlying nature of matter in general.

Fundamental changes in the scientific understanding of nature can often be traced by taking a closer look at contemporary experimental reports. Notably, these experimental reports also included work on odoriferous materials, thereby placing them in a different material culture from the preceding taxonomic perspective on odour materials in botany. Since the imperceptible structure of matter was not accessible at that time, perceptible changes of materials such as their odours provided descriptive traits to suggest hypotheses about the character of the underlying reactions and to design experiments on the basis on which these hypotheses were explored.

In *Experiments and Observations About the Mechanical Production of Odours* (1675) Robert Boyle, for instance, presented experiments that addressed

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[102] Chang, Hasok (2010): The Hidden History of Phlogiston. How Philosophical Failure Can Generate Historical refinement. *HYLE – International Journal for Philosophy of Chemistry* 16(2), 47-79.

different techniques for processing odoriferous materials.[103] These reports, written as instructions for experimental reproduction, were part of Boyle's wider criticism of the chymists' dominant doctrine,[104] which was advocated by Paracelsus and the Spagyrists. The chymists' doctrine, namely the *tria prima*, concerned the composition of matter by the three principles of *salt* (principle of fixity and incombustibility), *sulphur* (principle of flammability) and *mercury* (principle of fusibility and volatility).[105] By emphasising the experimental production of perceptible qualities, such as odour and flavour, through the physical alteration of matter, Boyle suggested instead a corpuscular perspective on chemistry.[106] To explore patterns in chemical reactions, the materials were systematically exposed to mechanical force, observing whether particular changes in the quality of materials resonated with particular methods applied. In his experimental reports, smells were explicitly linked to the composition of materials by describing how mechanical force applied to these materials resulted in two co-occurring changes: visible changes in the material make up (e.g. the production of salts) and significant changes in odoriferous qualities:

> "EXPER. I.
>
> *With two bodies, neither of them odourous, to produce immediately a strong Urinous smell.*
>
> Take good Quick-lime and Sal Armoniac [sic], and rub or grind them well together, and holding your nose to the mixture, you will be saluted with an Urinous smell produced by the particles of the volatile Salt, untied by this operation, which will also invade your eyes, and make them to water."[107]

Odours, as part of early experimental chemistry, were thus presented in relation to their materiality. In contrast to botanic interests, however, the materiality of odours in chemistry was determined more by the modes of experimentation, concerning their manipulability in composition, mixture and interaction, than by their taxonomic relations. Boyle, in his *Experiments and Observations*, in fact

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[103] Boyle, Robert (1675): *Experiments and Observations About the Mechanical Production of Odours.* London: E. Flesher.

[104] Boyle, Robert (2003[1661]): *The Sceptical Chymist.* Reprint. New York: Courier Dover Publications.

[105] Principe, Laurence (2000): *The Aspiring Adept: Robert Boyle and His Alchemical Quest.* Princeton, New Jersey: Princeton University Press, 36.

[106] Boyle, Robert (1676): *Experiments, Notes, & c. About the Mechanical Origine or Production of divers particular Qualities: Among which is inserted a Discourse of the Imperfection of The Chymist's Doctrine of Qualities; Together with some Reflections upon the Hypothesis of Alcali and Acidum.* London: E Flesher.

[107] Boyle (1675): *Experiments and Observations*, 4.

presented twelve different operations in the manipulation of odour materials, which can be summarised as following:

1. Combination of odourless materials producing a strong smelling odour
2. Dilution resulting in increased odour
3. Combination of materials producing an odour different from the single components
4. Producing odours via local motion
5. Neutralising strongly odorous materials with nearly odourless ones
6. Combining strong stinking materials with others to produce pleasant ones with enhanced strength
7. Digestion of nearly odourless materials resulting in strong fragrant ones
8. Influence on weak scented materials dissolved in spirits (e.g. wine)
9. Producing odours via heat
10. Combination of nearly odourless materials to produce a distinct odour
11. Steaming odoriferous materials in vessels of different metal (e.g. silver, gold)
12. Enhancing a particular odour quality of materials through composition with other materials

These experiments explore different techniques of material manipulation, which can be summarised in three main categories:

- *Mode of operation* (mechanical force such as pressure; dilution; digestion; heat; local motion),
- *Materials* (metal; spirits; water; salts),
- *Effect* (neutralisation; enhancement; new creation).

Odoriferous materials constituted an integral part of the experimental culture of early chemical practice. Their conceptualisation, along with the general work on chemical materials, suggested the prospect of understanding the nature of things through their alteration. Advancing techniques for material manipulation and intervention, shared across a wider range of disciplines, generated an epistemic space of shared practices that spurred further inquiry into the chemical nature of odour materials. The production-oriented interest in the constitution of materials led the practitioners of different fields to a mutual quest for developing reliable instruments and modes of experimental practice.

3.2 The Mechanics of Odour Extraction in Perfumery

Turning now to parallel practices in perfumery, methods for the extraction and production of odoriferous materials also comprised a variety of operations. Records of techniques for extracting odoriferous substances go well back to the pre-Christian era.[108] At the beginning of the 19th century, several methods of obtaining the desired odours from their materials were available for the perfumer, such as Expression, Maceration, Digestion, Infusion, Absorption or Enfleurage and Distillation.[109] These operations can be categorised into three main operations:

- mechanical force (Expression),
- heat (Distillation),
- solvent extraction/solubility (Maceration and Enfleurage, Digestion, Infusion).

A variety of factors inform their application. One factor relates to the consistency and texture of the materials from which odoriferous substances are extracted. Other factors concern pragmatic considerations such as the price of the raw materials, the desired odour quality of the processed substances and their final application (i.e. essences, waters, oils, pomades, balms, etc.). Quite often these material and pragmatic factors were coinciding (fig. 13):

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[108] Strathern, Paul (2000): *Mendeleyev's Dream - The Quest For the Elements.* New York: Berkley Books, 19.

[109] Panda, H. (2003): *The Complete Technology Book On Herbal Perfumes & Cosmetics.* National Institute of Industrial Research, 311-313.

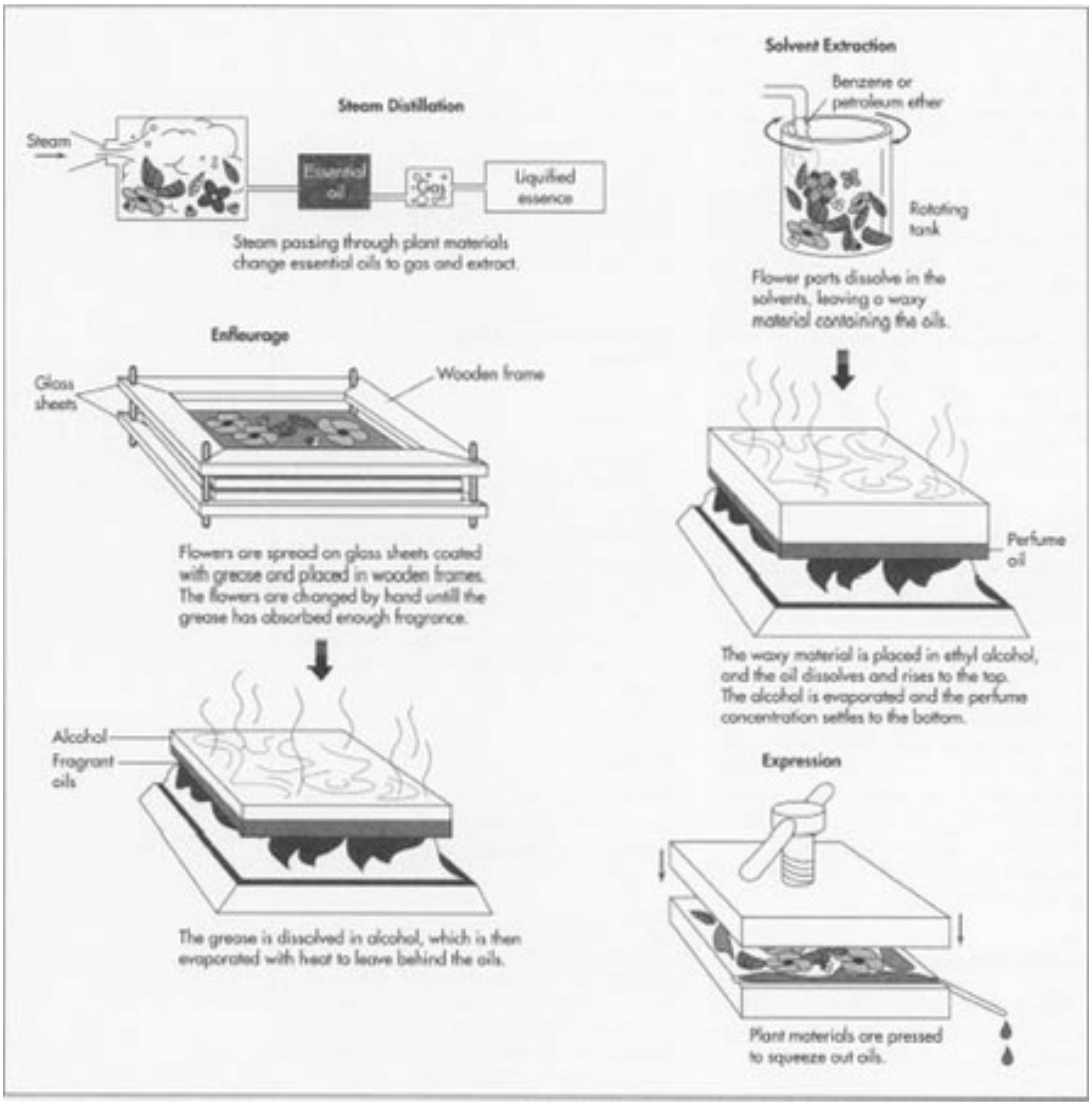

Fig. 13 Odour extraction techniques in perfumery. Dorman (2013): *Perfume.*

(1) Mechanical Force (Expression): Expression describes the method of extracting odours by applying mechanical force in a press. This method is only feasible for plant materials that are very rich in their volatile and essential oils and cheap to farm, such as the peel of oranges. It is mainly used for the production of expressed oils such as citrus oils.[110]

(2) Heat (Distillation): During distillation, the raw materials are exposed to heat in order to collect the extracted fragrant materials by condensation. This procedure may either be done dry, by virtue of steam and water or with a so-called fractionating column, depending on the materials (steaming of fresh

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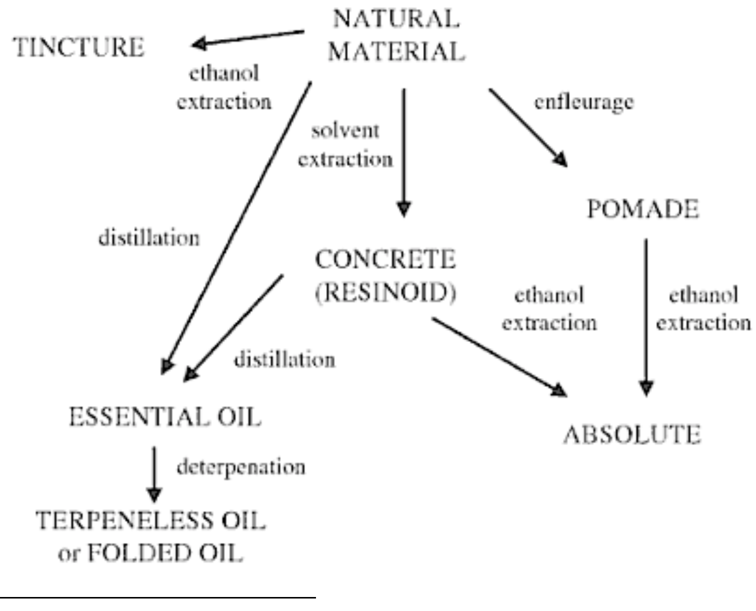
[110] Piesse (1862): *Perfumery Methods*, 48. Sell, Charles (2006a): Perfumery Materials of Natural Origin. In: *The Chemistry of Fragrances: From Perfumer to Consumer.* Ed. by D.H. Pybus and C. Sell. Royal Society of Chemistry, 33; Aftel, Mandy (2004[2001]): *Essence and Alchemy. A Natural History of Perfume.* Reprint. Salt Lake City: Gibbs Smith, 51.

flowers, dry heating of solid ones such as wood) and what the desired odour quality and complexity is.[111]

(3) Solvent Extraction (Maceration and Enfleurage/Absorption): Maceration describes the process of separating particular odoriferous components by treating the raw materials with specific substances such as spirits. The selection of solvents is informed by the constitution of the raw materials. Ethanol extraction, for instance, is largely applied to animal materials such as ambergris whereas fats are largely used to gain ottos[112] and oils of more volatile flowers that would denature in a distillation process, such as Jasmine. The materials gained by maceration are usually semi-solids such as pomades, waxes and similar substances but also so-called absolutes.[113] Enfleurage or Absorption is a procedure adopted only for very delicate and volatile flowers whose odours could not be extracted by any of the previous methods. The flowers are spread over a frame containing a layer of fat, which absorbs their odour within a time frame of seventy-two hours.[114] Needless to say, this method is expensive and time-consuming.

Depending on the materials and desired product type, these different operations are further combined (fig. 14).



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[111] Piesse (1862): *Perfumery Methods*, 49-54; Sell (2006a): *Perfumery Materials of Natural Origin*, 34-36; Turin, Luca and Sanchez, Tanja (2010): *Perfumes: The A-Z Guide.* London: Penguin, 42. Aftel (2001): *Essence and Alchemy,* 52f.

[112] Ottos, also referred to as attars and ittars, is a specific kind of essential oil, long lasting and the purest non-alcoholic perfume oil. It is often used as a fixative for other ingredients in perfumes.

[113] Piesse (1862): *Perfumery Methods*, 54-56; Sell (2006a): *Perfumery Materials of Natural Origin*, 37; Aftel (2001)*: Essence and Alchemy*, 57.

[114] Piesse (1862): *Perfumery Methods*, 57.

Fig. 14 Combination of extraction techniques. Sell (2006a): *Perfumery Materials of Natural Origin*, 36.

The evolving techniques of processing and altering odoriferous materials significantly shaped the material culture of perfumery. The shared use of materials, techniques and instruments, laboratories and knowledge across perfumery and chemistry created an epistemic and pragmatic point of intersection between academics and artisanship. This disciplinary overlap influenced further olfactory work, emphasising the need for standard tools and concepts of measurement.

3.3 A Shift in Ontology: The Rise of Synthetic Chemistry

Disciplinary overlap between chemistry and perfumery, and the resulting conceptualisation of odours as materials of production was pushed even further in light of the discoveries in chemical composition at the end of the 19th century, leading to the development of synthetic materials. With the introduction of new odour materials by chemical synthesis a significant ontological shift occurred in parallel with the newly opened-up conceptual inquiry into the composition of odoriferous materials.

As part of the growing industrialisation of social sectors in 19th century Europe, the promising prospect of producing, manufacturing and, moreover, *creating* new odours with the novel technique of chemical synthesis turned perfumery from an artisanship into an industrial laboratory practice. Higher production rates and demands of fragrant products have made synthetic compounds and a modernisation of perfumery indispensible. In fact, by now many of the raw materials initially used in 19th century perfumery are too rare and too expensive to produce for the large scale commercial distribution of 20th century perfumery. Ambergris, for instance, was one of the most luxurious ingredients in perfumery and is often referred to as “floating gold”, despite its rather insalubrious origins. Natural ambergris is a substance produced in the intestines and found in hardened dung of the sperm whale (*Physeter macrocephalus*). Occurring in only about 1% of the sperm whale population, it has a pleasant smell, combining “exotic woody elements with incense-like, earthy, camphoraceous, tobacco- and musk-like facets surrounded by the smell of the ocean."[115] Today, different synthetic alternatives to ambergris are available, such as *Amberlyn*® (Quest), *Ambroxan*® (Henkel) and *Ambrox*® (Firmenich).[116] Once developed, synthetic alternatives to raw materials are cheaper to produce and thus more widely affordable. Since they do not rely on specific seasons, as for instance in the farming of flowers, another advantage is their availability at all times. For these and other reasons such as ethical, hygienic and legal restrictions for the application of animal products, synthetic alternatives have now widely replaced a variety of raw materials.[117]

The rise of synthetic materials marked a significant change for investigations of odoriferous materials and inspired a new understanding of the material basis of odours at the turn of the 20th century. Stimulating greater interest into the imperceptible dimension of odour materials, the grounds for this ontological shift involves both the diverging practices of handling odour materials and the inherent features of the materials themselves. A new material dimension of odours was brought to light when the chemical composition of one of the most fundamental fragrance materials was found. In 1818, Jacques-Julien Houtou de Labillardiére discovered that turpentine oil is composed of "a relation of five C- to eight H-atoms ($(C5H8)_x$)."[118] This discovery initiated analysis of the composition of similar essential oils. As a result, in 1833 Jean-Baptiste Dumas recognised that essential oils could be classified according to their chemical composition,[119] dividing essential oils into "those containing only hydrocarbons such as turpentine and citron oil, those containing oxygenated compounds such as camphor and anise oil, and those with sulfur (mustard oil) or nitrogen compounds (oil of bitter almonds)."[120] In the following fifty years, studies on chemical analysis undertaken by, for instance, Jean-Baptiste Dumas, Eugène-Melchior Péligot, Friedrich Wöhler, Justus Liebig and Otto Wallach accumulated more knowledge about the constituents and formulas of essential oils most important for perfumery such as menthol, bitter almonds, etc. Most significantly,

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[115] Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 364. See also: Kemp (2012): *Floating Gold.*

[116] Nunes, F.M.N. and Imamura, P.M. (1996): A Convenient Preparation of Ambergris Odorants from Copalic Acid. *J. Braz. Chem. Soc.* 7(3), 181.

[117] Ohloff et al. (2011): *Scent and Chemistry*, 374.

[118] Ibid., 5.

[119] Dumas, J.B. (1833): Über die vegetabilischen Substanzen, welche sich dem Campher nähert und über einige ätherische Öle. *Justus Liebig's Annal. Chem.* 34, 245-258.

[120] Ohloff et al. (2011): *Scent and Chemistry*, 5.

these discoveries went hand in hand with the improvement of techniques for the separation of different odour components from raw materials, techniques involving, for instance, vacuum-distillation and derivatization techniques, producing structurally similar derivates from a particular chemical compound.[121] Such technological developments in 19th century chemistry fundamentally improved insights into the imperceptible nature of materials, i.e. their chemical composition. With the synthesis of coumarin this development was pushed one step further. Coumarin, described as having the smell of freshly mown hay, is naturally found in the Tonka Bean (*Dipteryx odorata*) and melilot (*Melilotus*). A first synthetic version of coumarin was made in 1886 by means of the so-called Perkins condensation. Sir William Henry Perkins, also responsible for aniline dye or, more commonly, mauve,[122] obtained coumarin from the condensation of salicylaldehyde (C_6H_4CHO-2-OH) and acetic anhydride ($(CH_3CO)_2O$).[123] Similar to the experimental reports of Boyle, the recipe for this reaction presented clear instructions how to handle and operate with the materials involved:

> "In a 250 ml round-bottomed flask place 2.1 g of salicylaldehyde, 2 ml of dry triethylamine and 5 ml of acetic anhydride and reflux the mixture gently for 12 hours. Steam distil the mixture from the reaction flask and discard the distillate. Render the residue in the flask basic to litmus with solid sodium bicarbonate, cool, filter the precipitated crude coumarin and wash it with a little cold water."[124]

Notwithstanding the impact of the Perkins condensation, the real revolution within the rise of fragrance chemistry took place only a few years later when Ferdinand Tiemann synthesised vanillin and, together with Wilhelm Haarmann, refined the reaction procedure for the industrial production of synthetic materials.[125]

Within the first half of the 20th century, a striking and growing diversity of synthetic materials was accumulated, opening up enquiry about what specific structural features might be responsible for their odours. A result of these advances was an alternative definition of what is natural and what is artificial. Instead of focussing on the difference between objects found in nature and

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[121] Ohloff et al. (2011): *Scent and Chemistry*, 6.

[122] Garfield, Simon (2002): *Mauve: How One Man Invented a Color that Changed the World.* New York, London: W.W. Norton & Co.

[123] Dudley, Matthew Edward (2009): *Synthesis of Hydroxylarylacrylates and Benzofurans*. ProQuest, 109; Ohloff et al. (2011): *Scent and Chemistry*, 7.

[124] As quoted in: Turin, Luca (2006): *The Secret of Scent.* London: Faber and Faber, 41. For the original see: Vogel, Arthur Israel and Furniss, B.S. (1989): *Vogel's textbook of practical organic chemistry.* Reprint. London: Longman.

[125] Ohloff et al. (2011): *Scent and Chemistry*, 7-9.

objects created in the laboratories, the definition of "natural" became extended and now co-existed with an alternative reference to imperceptible structural features. When "Tiemann and his co-worker Paul Krüger used the similarly smelling but much cheaper orris root oil (*Iris pallida* LAM.) in their investigations on the smelling principle of violets" they were working on the assumption "that the odor of both oils was due to the same *natural product*."[126] Chemical synthesis thus described more than just additional means for physical alterations of matter; it offered a new perspective on the selection of important characteristics on the basis of which to explore whether there is a lawlike relation between odours and their material basis, and which could be used for classificatory purposes.

4 Odours as Material Inscriptions

The rise of synthetic chemistry caused an ontological shift in the understanding of the material basis of odours. Turning from the perceptible to the imperceptible dimension of odoriferous materials, previously dispersed olfactory studies began to manifest themselves as an independent research domain. At the core this development lay the proliferation of novel techniques in the middle of the 20th century. With growing knowledge about the composition of odoriferous compounds, it was suggested that there must be some molecular key features that form regular relations between the structure of a molecule and its odour. The construction of structure-odour relations (SORs) required reliable methods for data production and data processing.

Making the underlying molecular structures accessible, the investigation of these imperceptible features relied heavily on the development and application of visualisation strategies. A variety of novel instruments such as gas chromatographs now allowed delving into the material basis of odours by producing "material inscriptions". Acting as what Bruno Latour and Hans-Jörg Rheinberger label "inscription devices"[127], these instruments are technologies that transform matter into written and graphic traces such as graphs,

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[126] Ohloff et al. (2011): *Scent and Chemistry*, 10. [Italics mine]

[127] Latour, Bruno and Woolgar, Steve (1979): *Laboratory Life: The Construction of Scientific* Latour, Bruno and Woolgar, Steve (1979): *Laboratory Life: The Social Construction of Scientific Facts.* Princeton, New Jersey: Princeton University Press, 51. See also Rheinberger (1997): *Epistemic Things*, 109f.

photographs, x-rays, etc. The construction of graphic traces in olfactory research was like the application of any laboratory technology; it required the establishment of standard experimental conditions and procedures and it involved conceptual choices of how to arrange and interpret the data produced. Influencing and refining these conceptual choices were additional visualisation techniques that supported the process of making hypotheses about SORs. These additional techniques, such as olfactophores and artificial language systems, acted as, in Ursula Klein's terms, "paper tools".[128] Paper tools are modes of representation that facilitate conceptual thinking through replacing the manipulation of materials with the systematic manipulation of visual signs.

Material inscriptions and paper tools, however, are, as it will turn out, not unambiguous. Different visualisation techniques spurred different conceptual enquiries into the material basis of odours. As a consequence, comprehension of the nature of odours and how their materiality must be pursued in further scientific enquiry likewise began to take different forms, starting to transform odours into scientifically interesting research topics within a variety of disciplinary contexts such as fragrance chemistry, molecular biology, neurology, medicine, behavioural studies, etc.

To illustrate the beginning of olfactory research as an independent research domain before it started taking up different disciplinary directions, the next subsections present an overview of the most influential visualisation techniques and their impact on determining the molecular basis of odours in the 20th century. Each technique is elucidated as a specific mode of representation that presents odours under several visual categories with different epistemological implications, namely conceptualising odours as fingerprints, codes, templates and maps.

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[128] Klein, Ursula (1999): Techniques of modelling and paper-tools in classical chemistry. In: *Models as Mediators. Perspectives on Natural and Social Science.* Ed. by M. Morgan and M. Morrison. Cambridge: Cambridge University Press, 146-167; Klein, Ursula (2001a): Berzelian Formulas as Paper Tools in Early Nineteenth-Century Chemistry. *Foundations of Chemistry* 3(1), 7-32; Klein, Ursula (2001b): Paper Tools in Experimental Cultures. *Studies in History and Philosophy of Science Part A* 32(2), 265-302.

4.1 Odours as Fingerprints: Gas-Chromatography

A very important factor in laboratory practices is a clear standard of measurement to draw distinctions. But how is it possible to discriminate individual “smelly molecules” within a complex odour mixture? And how can one identify which of the constituents are responsible for *that* odour? Separating and individuating odoriferous molecules within complex mixtures, one of the most revolutionary instruments for olfactory research is the gas chromatograph. The technique of gas chromatography, more specifically gas-liquid chromatography, was introduced into chemical analysis in the 1950s.[129]

In essence, a gas chromatograph (fig. 15) works as follows. It separates and detects different volatile molecules in a mixture through their varying solubility in the gas phase. To double check peak identities, gas chromatography is usually used in combination with mass spectrometry.[130] A gas chromatograph is essentially a machine, which is:

> “eighty meters of thin silica tube wound up inside an oven, which gradually heats the tube as a steady stream of odorless argon gas is passed through it like a conveyor belt. Put a complex sample of chemicals into one end of the tube, and the sample’s components will break apart (the oven heats them and they will boil off), separate, and travel through the tube on the conveyors belt of helium. The trick is that the components break apart at different times and thus travel at different speeds, which depend on their boiling points: the light, low-boiling ones rush first into the gas belt, the heavier molecules lag behind, and the heaviest follow last, each separate, each coming along in its own time and place.”[131]

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[129] Biemann, Klaus (1985): The Mass Spectrometer as a Detector in Chromatography. Journal of Chromatography Library: *The Science of Chromatography Lectures Presented at the A J F! Martin Honorary Symposium, Urbino, May 2 7-37, 1985.* Ed. by F. Bruner. Elsevier, 43; Gohlke, Roland S. and McLafferty, Fred W. (1993): Early gas chromatography/mass spectrometry. *Journal of the American Society for Mass Spectrometry* 4(5), 367-371.

[130] Hites, Ronald (1997): Gas Chromatography/Mass Spectrometry. In: *Handbook of Instrumental Techniques for Analytical Chemistry.* Ed. by F.A. Setlle. New Jersey: Prentice Hall, 609-626.

[131] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House, 275.

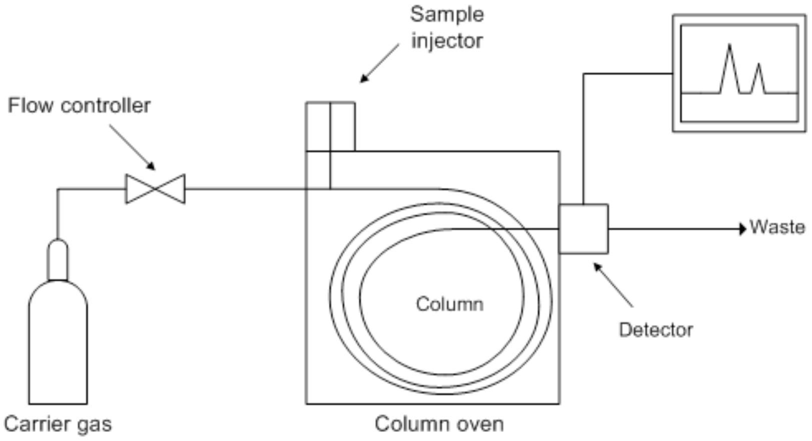

Fig. 15 Wikipedia (2013a): *Gas chromatograph*.

The immediate result of the refinement of technologies for chemical analysis and the invention of gas chromatography was, of course, the increasing acquisition of knowledge about the composition of complex odoriferous mixtures. In separating volatile compounds by virtue of their different grades of solubility, gas chromatography served more than as a mere technological supplement for inquiry into the imperceptible dimension of odour materials. It provided a material practice that *generated* graphic traces of single molecular components.

Converting complex odour mixtures into another form of matter, i.e. the individual molecular constituents of such mixtures, this material transformation allows olfactory researchers to smell and describe the individual components when these are coming out at the end of a gas chromatograph. The process of this conversion is graphically recorded, resulting in so-called chromatograms (fig. 16). Gas chromatography thereby acts as an inscription device, producing graphic articulations of the chemical composition of complex odour mixtures.

These graphic traces radically changed the way in which odours were conceptualised. Accounting for the separate constituents and their specific proportions, complex odour mixtures such as perfumes now became *fingerprinted*: “[a] fingerprint, in this context, is a characteristic chromatogram of a complex mixture of compounds.”[132]

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[132] Dunnivant, Frank M. and Ginsbach, Jake (2011): *Identification of Fragrances.* URL=<http://people.whitman.edu/~dunnivfm/C_MS_Ebook/CH7/7_5_2.html> (accessed 20 February 2013)

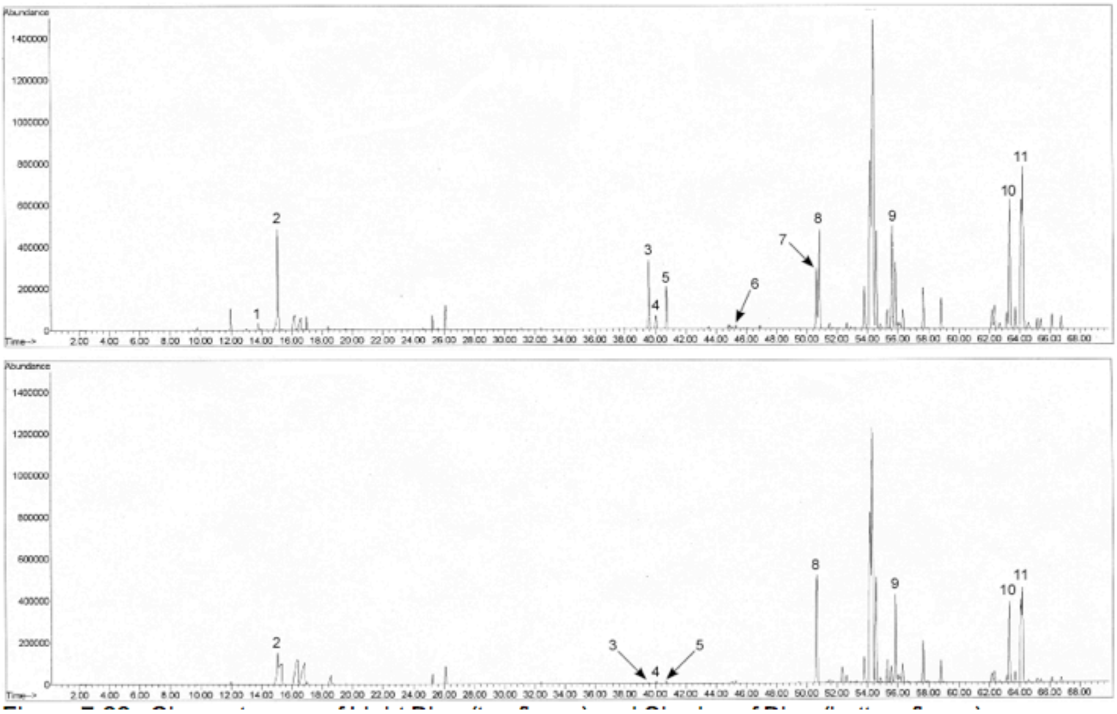

Fig. 16 Chromatogram of two generic perfumes: “Light Blue” (top) and “Shades of Blue” (bottom). Dunnivant and Ginsbach (2011): *Identification of Fragrances.*

The analysis of odour mixtures in terms of fingerprints had major consequences. Providing a visual trace of their individual composition, odoriferous mixtures are bestowed with an objective identity. One consequence of a traceable, i.e. visual, identity is a change in the legal status of complex odour compositions such as perfumes. Although, concerning their individual history of production, single synthetic molecules fell under the terms of intellectual property and patent right claims, for perfumes such a legal status seemed impossible to acquire. Fragrances were considered as too intangible for genuine comparison and, therefore, the scent of a perfume had not been a proper subject of copyright law. In order to be eligible for copyright claims, there must be some basis to compare the composition of perfumes. Scent alone was hard to compare and evaluate. With the introduction of chromatograms, however, the specific composition of constituents, a perfume’s identity formula, became accessible. Gas chromatography allows for a precise analysis of perfumes, ingredients and compositions, thereby making a comparison between the compositions of similarly smelling perfumes possible. In fact, on this account, two precedents concerning copyright infringement of perfumes were recently established with great impact on commercial perfumery. These cases involved, on the one hand, the Dutch Court of Appeal at Den Bosch ruling in favour of *Lancôme* in 2004 (*Lancôme* versus *Kecofa*) and, on the other hand, the Paris Court of Appeal ruling for *L'Oreal* in 2003 (*L'Oreal* versus *Bellure*).[133] The technique of gas chromatography made two significant contributions to the development of olfactory research. First, it offered a way of separating and individuating odoriferous elements from complex mixtures, allowing more precise analyses of the imperceptible dimension of (complex) odoriferous materials; it is now possible to identify and compare single constituents.

Second, producing a visual trace of a fragrant composition this technique strengthened the conceptual link between the perceptible and otherwise intangible odoriferous properties and specific materials. Complex odoriferous mixtures such as perfumes suddenly acquired an objective identity by being assigned a specific, measurable materiality. It is this combination between its operational character, manipulating materials by separating their constituents, and its constitutive function, explicitly correlating the scent and the material composition of odoriferous mixtures, that allowed for further enquiry into possible causal relations between the structure of the molecular materials and their perceptible qualities, so called structure-odour relations (SORs).

4.2 Odours as Codes: SMILES

Further enhancing research into the structural make-up of odoriferous molecules is the construction of artificial languages. A few artificial language systems have been developed to evaluate whether specific structural features somehow correspond with certain qualities of molecules, allowing for model-based inferences about implicit correlations of features. In 1988, David Weininger developed an artificial computational language system to linearly represent complex molecular structures.[134] This system, SMILES or 'Simplified Molecular Input Line Entry System', had since been developed and modified. Its purpose is to facilitate the recording of the vast range of molecular diversity and

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[133] Field, Thomas G. (2004): Copyright Protection for Perfumes. *Idea: The Journal of Law and Technology* 45(1), 19-31; Derclaye, Estelle (2006): One in the nose for Bellure: French appellate court confirms that perfumes are copyright protected. *Journal of Intellectual Property Law & Practice* 1(6), 377-379; See also: Seville, Catherine (2007): Copyrights in Perfumes: Smelling a Rat. *Cambridge Law Journal* 66(1), 49-52. (The latter article cites the wrong year for the Dutch appeal.)

[134] Weininger, David (1988): SMILES, a chemical language and information system. 1. Introduction to methodology and encoding rules. *J. Chem. Inf. Comput. Sci.* 28(1), 31-36.

to enable canonical notations for molecules across large molecular databases.[135] The general idea of SMILES and its many modifications is that every molecule is represented as a word, “each of whose letters represents an atom, and provides built-in instructions on how to connect the ends […] when you have a closed circle, you cut it open and label the ends (C1 connects to C1) etc.”[136] A large amount of information is, in fact, transcribed by these chemical words:

- The length of the word provides, for instance, an indicator of whether the molecule is odorous or odourless in general: The longer the word, the bigger the molecule, and the less likely we can smell it.
- Looking at the word’s ending, it is possible to infer whether the molecules are volatile enough to vaporise: if the end groups have a charge, they are most likely to form bonds and are less likely to fly.
- The arrangement of letters also indicates the existence of highly reactive groups (such as OO and OOO, peroxides and ozonides) that are generally unwanted in perfumery.[137]

In the language of SMILES, the substructure of molecules is represented in a linear notation. This enables an easier computation of various patterns of structural transformations and substitutions of atoms or atom groups. On this account, SMILES acts as what Ursula Klein defines as “paper tools”.[138] Paper tools are representations that facilitate conceptual manipulations of structural patterns without having to deal with the concrete materials. Representations of molecules in terms of their structural arrangements as words on paper allow, for instance, random reorganisations as well as systematic changes in their elementary patterns. And indeed, the molecules computed, starting from paradigmatic molecular structures and applying specific patterns of manipulation, significantly aided in the exploration of structural relations amongst these variations.[139]

Thus, SMILES understood as a form of paper tool offers the opportunity of acquiring knowledge of possible yet unknown SORs by means of the

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[135] Bone, Richard G. A.; Firth, Michael A. and Sykes, Richard A. (1999): SMILES Extensions for Pattern Matching and Molecular Transformations: Applications in Chemoinformatics. *J. Chem. Inf. Comput. Sci.* 39, 846-860.

[136] Turin (2006): *Secret of Scent*, 34.

[137] Ibid., 34f.

[138] Klein (1999): *Paper-tools*; Klein (2001a): *Berzelian Formulas*; Klein (2001b): *Experimental Cultures*.

[139] Bone et al. (1999): *SMILES*, 854.

conceptual manipulation of already known features. What this illustrates is the dependency of insight into the underlying physicochemical structures on the increasing emergence of alternative modes of representation.

4.3 Odours as Templates: Olfactophores

Modelling odours with respect to their molecular basis, the latest odorant models, so-called olfactophore models (fig. 17, right), provide abstract templates to represent statistical correlations between odour families and molecular parameters. They consist of three specific molecular groups – namely, the osmophore, profile and bulky group –, where each group is assumed to have a specific role in the mechanism of primary odour recognition.[140] Providing paradigmatic model structures for odorant groups relevant to fragrance research – such as sandalwood, amber or muguet –, SORs are explored and visualised by the specific spatial and geometrical arrangement of atoms and atoms groups, especially their relative positions and distances from each other. On these accounts, olfactophores present odours with virtual bodies that are used to define and refine the molecular parameters assumed to underlie their recognition.

Like SMILES, they also work as paper tools in the conceptual manipulation and computation of new odorants from scratch or, in this case, on screen. By exploring how specific changes in molecular parameters and configurations influence the overall structure of the odorant, suggestions can be made for the synthesis of future materials. Modelling new materials on screen often serves as a conceptual aid to the creation of new fragrant materials in the laboratory. In an interview Philip Kraft, fragrance researcher at Givaudan, mentioned the conceptual function of these kinds of paper tool models for the creative progress of fragrance research:

> “ ‘You can play with conformational elements that drive a certain molecular shape – for example you can introduce structural elements that cause a molecule to fold itself into a horseshoe shape and thus smell musky,’ explains Kraft. Adding rigidity to molecules often gives more defined odour notes, he adds. ‘Or you can make the molecule more flexible to add new by-notes – you

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[140] For more details see chapter 5.

can cut some parts to make it lighter and more diffusive while conserving its overall shape.' "[141]

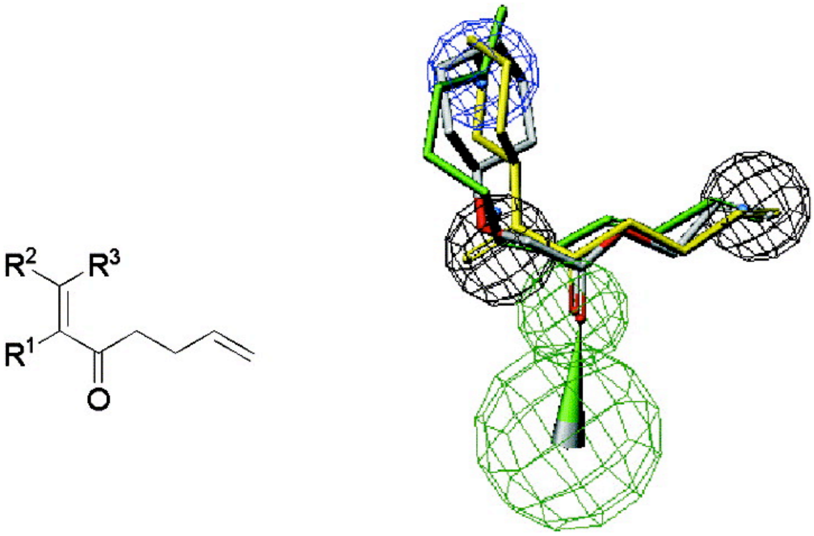

Fig. 17 Olfactophore model (right). Odorants are analysed in terms of the presence of specific atom groups and their stereochemistry, position and distance from each other and their hydrophobic and electronic properties. Bajgrowicz et al. (2003): *Substituted hepta-1,6-dien-3-ones*.

4.4 Odours as Maps: Multidimensional Scaling

Another representational strategy employed in contemporary olfactory research on SORs is the method of multidimensional scaling (MDS). MDS is a statistical technique that correlates two datasets: descriptions of the molecular features of odorants on the one hand and descriptors of the odoriferous properties of these materials on the other, i.e. verbal descriptions of odour quality. Correlations between specific materials and specific odoriferous properties are then spatially arranged, generating maps of so-called "odour perception spaces" (fig. 18).[142]

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[141] Davies, Emma (2009): The sweet smell of success. *Chemistry World* (February), 41.

[142] Zarzo, Manuel and Stanton, David T. (2009): Understanding the underlying dimensions in perfumer's odor perception space as a basis for developing meaningful odour maps. *Attention, Perception, & Psychophysics* 71(2), 225f.; Schiffmann, Susan S. and Pearce, Tim C. (2002): Introduction to Olfaction: Perception, Anatomy, Physiology and Molecular Biology. In: *Handbook of Machine Olfaction: Electronic Nose Technology.* Ed. by T. C. Pearce, S.S. Schiffmann, H.T. Nagle and J.W. Gardner. Wiley-VCH, 11f.

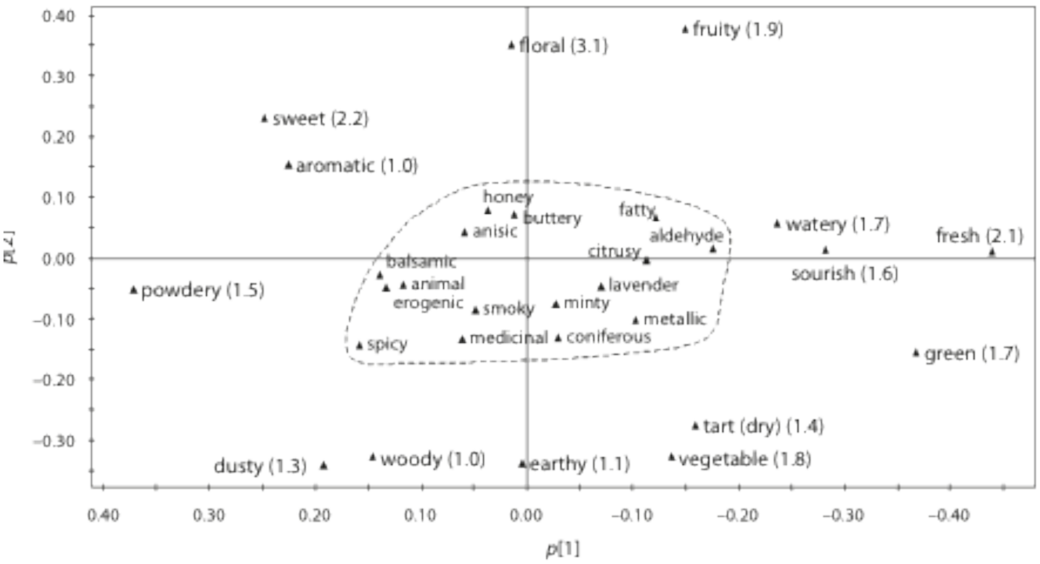

Fig. 18 Odour perception map. Zarzo and Stanton (2009): *Odour maps*, 231. This map presents a statistical calculation of the odorant descriptors given in the Boehlens-Haring database and arranges them on two axes p[1] and p[2]. Relations between odorant aspects are judged as most similar (positive scale on p[1] and p[2]) and most dissimilar (negative scale on p[1] and p[2]).

By virtue of the vicinity in the perceptible quality of certain odour materials, these odour maps rely on the assumption that determining features of odorants must be identifiable by closer analysis of neighbouring materials. Notably, such maps often presented a range of odorants whose close proximity could not be accounted for by a single physicochemical feature – “such as chemical structure, molecular weight, number of double bonds, or dipole moment” – but seemed to express a complex combination of a series of such features which, if only approximately, seemed to relate to the represented odour space of perceptible features.[143]

Spatial maps, revealing correlations of odoriferous properties between structurally different materials, opened up another conceptual dimension of enquiry into the nature of odours that, compared to previous approaches, involved a stronger focus on the perceptible relations between odour materials. It connected odour studies more closely to a wider field of inquiries across biology, neurology and psychophysics. Spatial maps, as an alternative approach to arranging odour materials by evaluating similarities in odour perception, thus drew attention to the evaluation of odour similarities with respect to fundamental aspects of human sense perception. Moving beyond chemical analysis, interest in the material basis of odours is not limited to the

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[143] Schiffmann and Pearce (2002): *Introduction to Olfaction*, 12-13.

molecular features of odorants but also involves the physiological and cognitive conditions of the perceiving subjects.

4.5 Tools for Visualisation: The Structure of What?

Although methods for investigating the molecular basis of odours have vastly progressed in the course of the 20th century, knowledge about structural regularities determining the odour of molecules is still limited and research into SORs is still in its early stages. In the first half of the 20th century, a number of suggestions concerning the nature of SORs have been put forward, involving the size and shape of molecules, their steric properties, electrophilic and nucleophilic characteristics, peripheral functional groups and even far infrared frequencies.[144] Until now, however, no general rule to correlate odour quality with molecular structure has been established that is not riddled with a range of significant exceptions. Despite the large amount of data collected, any theory about the 'molecular smelling principle' is still hypothetical.[145]

Increasing awareness of the limits of investigating the material basis of odours by mere chemical analysis thus turned focus toward the underlying recognition process. Since odours are a sensory response, explanations of their material causes that are based on the molecular level needed to be supplemented with an account of the mechanisms that underlie their perception. Thus, in parallel with studies of SORs, olfactory research started to explore the physiological conditions for the perception of odours. Interpretations of structural irregularities across a vast variety of odorants suggested that odour quality cannot be primarily understood in terms of chemical structure, but must be based on a better understanding of the various underlying recognition processes, including not only the molecular recognition mechanism but also odour discrimination on a neurological level, thus comprising various aspects from molecular, cellular and systems biology.[146]

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[144] Dravnieks, Andrew (1966): Current status of Odour Theories. *Flavour Chemistry. Advances in Chemistry* 56, 29-52; See also: Heath, Henry B. (1981): *Source Book of Flavors. AVI Sourcebook and Handbook Series.* Dordrecht: Kluwer, 122-127.

[145] For details see chapters 4, 5, 7 and 8.

[146] Mamlouka, Amir Madany; Chee-Ruiterb, Christine; Hofmann, Ulrich G. and Bower, James M. (2003): Quantifying olfactory perception: mapping olfactory perception space by using multidimensional scaling and self-organizing maps. *Neurocomputing* 52-54, 591-597; Shepherd, Gordon M. (2004): The Human Sense of Smell: Are We Better Than We Think? *PLoS Biol* 2(5),

Visualisation techniques in laboratory practice significantly informed these diverging disciplinary developments in olfactory research. Although conceptually different, these techniques (presented previously) share a twofold epistemic function. On the one hand, they visualise the practices and interactions with materials in the laboratory. As such they serve as an exploratory device, spurring *conceptual thinking through material practices*. On the other hand they likewise serve as *graphic reflections* on the development of techniques in laboratory intervention itself. Here they allow for reflections on measurement, evaluation and interpretation strategies and also facilitate changes in the conceptualisation of odours and their material basis, linking them to other areas of research. By exposing the sheer variety of odorants and the lack of lawlike structural relations across molecules having the same smell, these modelling strategies drew attention to the limits of purely structurally based explanations of odour materials. In addition, they also facilitated further enquiry emphasising, for instance, interesting relations of perceptual proximity over mere structural similarity such as in perceptual space maps.

5 The Historical Transformation Process: Odours on the Verge of becoming Epistemic Things

The epistemic history I presented in this chapter explored the variety of disciplinary practices, conceptual choices and methods, materials and instruments surrounding the investigation of odoriferous materials. Influenced by the diverse techniques of intervening with the materials, this chapter reconstructed how odours were slowly transformed into scientifically interesting objects that acquired various theoretical and experimental lives across different contexts of research and artisanship. The underlying development outlined presented three main trajectories, which followed the shared practices across disciplines that informed specific inquiries into the material dimension of odours. In the course of the different trajectories, I illustrated the dependency of the selection of conceptual criteria on the available techniques and practices of making and identifying materials.

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e146. doi:10.1371/journal.pbio.0020146; Shepherd, Gordon M. (2005): Outline of a Theory of Olfactory Processing and its Relevance to Humans. *Chem. Senses* 30(1), i3-i5.

Central to each trajectory was a conceptualisation of materiality which differed with respect to the particular material research culture in which it was embedded. In the first trajectory, research on odours and odoriferous materials concerned their occurrence as “objects in nature” based on their largely botanic origins. Odours were first explored as taxonomic tools for the arrangement of plant materials. Following this, I analysed the impact of botanic categories on odour classification in perfumery. Moving beyond botanic categories, the development of odour classifications in perfumery was further explored in their emancipation from botany, starting to form independent classificatory practices by emphasising the perceptible qualities of odours over their botanic origins. This tendency relied on criteria familiar to the measurement of other sensory perceptions. In parallel with classificatory practices surrounding plant materials, odoriferous substances were also embedded in the experimental culture of early chemistry. Tracing the nature of chemical reactions by looking at different strategies for manipulating and altering matter, interest in odour materials here mainly resided in their application as “materials of production”. One result of this focus on the creation of odoriferous substances was the disciplinary merger of chemistry and perfumery into fragrance chemistry. Another result was increased attention to the imperceptible molecular dimension of odoriferous substances. The advancement of new modelling and visualisation techniques such as gas chromatography, spectrometry, computer modelling, etc. further reinforced this shift. These new visualisation techniques facilitated conceptual thinking through material practices, arranging odoriferous materials into structural kinds such as olfactophores or highlighting similarities of perceptible qualities in odour perception maps. While establishing a range of possible standards for the measurement, description and classification of odours across their divergent material origins and composition, the limits of chemical analysis for the understanding of odours became transparent. As a result, scientific research about the nature of odours increasingly concerned the underlying processes of olfactory perception, embedding odoriferous materials into new experimental contexts such as molecular biology, neurology and medicine. Placed in these emerging experimental contexts, odours turned into “epistemic things”, i.e. phenomena that constitute independent scientifically relevant objects within specific research questions about their nature.[147]

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[147] Here I lay emphasis only on the technological conditions of this turn, since this recent

Materiality as the central concept underlying all these trajectories provided the most reliable means to turn the ephemeral and fleeting phenomena of smells into measurable and more stable research objects. The career of odours as scientifically interesting objects was thereby grounded in the various material practices associated with these material practices. Tracing these practices, a comparison of the treatment of odour materials across the three trajectories also showed the co-existence of different ontologies involved. Diverging conceptualisations of materiality underlying research on odoriferous materials resulted in a range of perspectives on what constituted the underlying material nature of odours. From a broader perspective, this nature was either defined by botanic origins or chemical composition, and upon closer inspection these general categories were interpreted by various sub-categories such as specimens, plant parts, method of processing, etc. Especially the most detailed focus on different classificatory practices in the first trajectory emphasised the entrenchment of conceptual choices and the drawing of natural demarcations for the arrangement of odoriferous materials. Considering the resulting taxonomic diversity, the variety of demarcations employed to classify odour materials in fact resonated with the plurality of relevant natural features inherent in these materials. With the rise of synthetic chemistry and the introduction of new odour materials into perfumery, I further demonstrated the impact of advancing technologies, embedded in different research contexts and evolving over time, on an understanding of the material nature of odours. Opening up new perspectives on what material features of smell were considered constitutive of its nature, advanced insight into the general chemical composition of matter indicated a molecularly defined relation between odours and their materials. This shift from observable material properties and interventions (such as the distillation of odoriferous materials) to the imperceptible dimension (of molecular properties) expressed a fundamental ontological change.

The often cross-cutting demarcations in the arrangement of odour materials were shown to mirror an overlap of classificatory interests and shared practices across different disciplines as well as the plurality of relevant material features. Chosen criteria for natural demarcations here thus resonated with different

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transformation of odours into epistemic things within experimental systems will be followed up in greater detail in the following chapters.

techniques of standardisation that emphasised particular features of odoriferous materials to which they are responsive. All of these different ways of conceptual and experimental reasoning, in which knowledge claims about odours and their material basis were established, were related to natural features of odoriferous materials. As a result, the notion of ‘natural’ implicit in the conceptualisation of the material basis of odours was embedded in the material culture in which specific lines of enquiry were pursued. The question of the material nature of odours took different forms in different contexts, constituting odours as different kinds of research objects. My analysis of the origin and the advancement of knowledge about smells presented them as naturally occurring objects, as artificially produced ones in the laboratory, and as objects becoming part of a developing theoretical framework about the underlying perception mechanism. Exploring the ways in which these divergent practices were bound to different conceptual distinctions and disciplinary entrenchments, therefore, showed the extent to which smells require a pluralist account of scientific objects.

Smells as scientifically interesting objects have been shown to evolve over time, and their development was entrenched in the different methods of enquiry within the various research contexts. The epistemic history I outlined may seem to present a linear story of scientific advancement, describing the investigation of odours from objects in nature, to materials of production towards epistemic things. But do not let an impression of linearity mislead you. First, underlying these trajectories in olfactory practices is not a development from some form of “pre-mature” to some form of “mature” science but, rather, the graphic reflections on the development of classificatory practices and laboratory inventions reveal an interesting continuity: traditional graphic techniques employed in natural history such as list making, maps and tables, etc. are in fact still integral to modern olfactory research. Second, the narrative here analysed different inquiries into the nature of odoriferous materials in light of the emergence of new technologies and the resulting ontological changes. In chapter 2 I will show the extent to which the research trajectories above have changed yet continue to persist today.

The diversity in the conceptualisation of smells and their dependency on the notions of materiality employed also revealed them as historical objects of knowledge. By tracing the evolving techniques, the selection of natural demarcations and the parallel ontological changes were shown to be historically contingent. Yet, all of these demarcations responded to real features of the materials classified, showing the multidimensional, complex and heterogeneous character of the material basis of odours. The historical career of odours thereby showed that the historicity of some scientific objects does not lead into a form of scientific relativism that suggests taking these objects as purely constructed and their conceptualisations as merely conventional. But it showed that scientific objects are part of various experimental traditions in which the question of their reality takes different forms for different kinds of enquiry. The historicity of scientific judgement and technological enquiry thus does not mean that the criteria chosen are not natural, as they often reflect inherent features of the materials classified, contributing significantly to scientific enquiry. Rather, what determines our decision to call something natural is a result of disciplinary developments.

Chapter 2

The Disodour of Things II:
After Structure: Where to make the cut? Contemporary Research on Odours and Odoriferous Materials

1 A Whiff of *This* and *That*: Odours as Natural Kinds?

In this chapter, I want to address the multifaceted character of odours and their importance to different contemporary research practices by analysing them as "natural kinds". Natural kinds, according to philosophical tradition, are supposed to define groups of entities whose criteria for membership reflect certain characteristic distinctions. Informing scientific inquiry, these distinctions describe features that guarantee the lawfulness and regularities in the constitution and behaviour of these entities. Therefore, the features, determining "whereby a thing is what it is"[148], are taken to be its 'real essence'. In comparison to the descriptive character of 'nominal essences' (properties that generally help to identify an object without necessarily determining its nature), 'real essences' are largely considered to be causally significant. Traditional philosophical debate thus often defines such essences by reference to intrinsic and microstructural features.[149] On these accounts, groups consisting of such natural kinds are supposed to provide taxonomic distinctions that are objective, in the sense that their correct description is independent of conventional stipulation and whose membership is grounded in intrinsic natural demarcations. Assumed to reflect the underlying structure of reality, these kinds are further expected to fall under unique, distinct and hierarchically ordered categories of things.[150]

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[148] Locke, John (1860[1689]): *An Essay Concerning Human Understanding: And A Treatise on the Conduct of the Understanding.* Ed. by P. Nidditch. Oxford: Clarendon Press, Book III chap. 3-15, 293.

[149] Putnam, Hilary (1975): The meaning of ''meaning''. *Minnesota Studies in the philosophy of science. Lang Mind Knowl* 7, 131-193; Kripke, Saul (1980): *Naming and necessity.* Cambridge M.A.: Harvard University Press.

[150] Hacking, Ian (1991): A Tradition of Natural Kinds. *Philosophical Studies* (61), 110f.; Ellis, Brian D. (2001): *Scientific essentialism.* Cambridge: Cambridge University Press; Ellis, Brian D. (2002): *The philosophy of nature: a guide to the new essentialism.* Queens: McGill University Press.

In light of these criteria, odours appear to be unsuitable to be understood as natural kinds. Not only the diversity of conceptualisations, but also the partially subjective nature of odour perception and odour description, makes it hard to conceive them as natural kinds in a strict sense. Nonetheless, it is this apparent inaptitude, I suggest, that makes an analysis of odours as natural kinds fruitful. The reasons for this are twofold. First, I want to illustrate the extent to which classifications of odours reflect natural distinctions that illuminate the vast plurality of what counts as "natural" in scientific practice. Second, by casting light on the significance odours have for a wider context of scientific research, my analysis also highlights the limited utility that restrictive philosophical definitions of natural kinds have for capturing scientifically relevant entities. Thus, moving beyond a strict tradition of natural kinds, I will demonstrate that odours present and reflect various kinds in nature and, even more importantly, various kinds of nature.

To situate my criticism of an essentialist understanding of natural kinds and to analyse what kinds of "things" odours are, I begin with contemporary classifications in perfumery. Picking up on the themes of the previous chapter, these classifications again illustrate the diversity of methods and interests surrounding odoriferous materials. In addition, I demonstrate that this variety is not a flaw of "premature" scientific practices to be overcome by a better and proper understanding of odours, but, rather, this variety is due to the very nature of odours as multidimensional phenomena. An analysis of this multidimensionality, and the inevitably ephemeral nature of odours, will lead me to criticise the implicit essentialist assumption that the development of scientifically relevant objects will in principle end up in some definition of their structural make-up (as in Putnam's Twin Earth thought experiment leading to the understanding that water is necessarily H_2O).[151] Instead, a closer look at different contemporary practices shows that, despite displaying a general turn to molecular features, research on odours does not progress in a linear fashion

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[151] Putnam (1975): *Meaning of meaning*, 191. Other examples are Kripke's identity statements such as "Light is a stream of photons" and "Heat is the motion of molecules". Kripke (1972): *Naming and Necessity*, 98f., 106, 129-133. For a critical discussion of understanding kinds through aspects of "miscrostructure" (and Putnam's example) see: Needham, Paul (2002): The discovery that water is H2O. *International Studies in the Philosophy of Science* 16 (3), 205-226; LaPorte, Joseph (2004): *Natural Kinds and Conceptual Change.* Cambridge: Cambridge University Press; Chang, Hasok (2012): *Is Water H2O? Evidence, Realism and Pluralism.* Dordrecht, Heidelberg, New York, London: Springer; See also: Klein, Ursula and Lefèvre, Wolfgang (2007): *Materials in Eighteenth Century Science. A Historical Ontology.* Cambridge M.A.: MIT Press, 73.

but, on the contrary, continues to diversify into separate yet related domains within which odoriferous materials are explored through different definitions of materiality. Therefore, a comparative study of historical and present research on odoriferous materials results in a pluricentric image of odours as scientifically relevant entities or demarcations of scientific entities. It is their multidimensional character, informing a variety of different scientific enquiries, which presents odours as most relevant to our understanding of the peculiar relationship between nature and scientific practice. This, in turn, begets questions of how to understand the ways in which scientific practices aim at reality. The questions as to what kind of "things" odours should be seen as, how to measure their perceptible likeness and how to explore their material causes point to bigger issues for the philosophy of science concerning the development of techniques and their impact on conceptual choices for defining scientifically significant phenomena in research practice.

2 Images of Diversity: Classifications of Odour Quality

Contemporary classifications of odours correlate two main aspects to arrange the vast range of odorants. They concern, on the one hand, *verbal descriptions* of sensory perceptions (bitter, sweet, soft) and odour notes (floral, balsamic, waxy, fruity). On the other hand, they refer to the *material basis* according to (i) template materials (vanilla, cedar, bergamot, jasmine) and (ii) structural composition such as chemical classes (alkanes, alkenes, benzenoids, terpenes and heterocycles) and molecular features (molecular weight, number of double bonds, or dipole moment).[152] Fundamental to the classification outcome is the characterisation of odour quality by odour profiling. Odour profiling comprises two methods: odours can be characterised either by semantic descriptions or by direct reference to model substances, so-called benchmark odorants.[153] Despite

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[152] Schiffmann, Susan S. and Pearce, Tim C. (2002): Introduction to Olfaction: Perception, Anatomy, Physiology and Molecular Biology. In: *Handbook of Machine Olfaction: Electronic Nose Technology.* Ed. by T. C. Pearce, S.S. Schiffmann, H.T. Nagle and J.W. Gardner. Wiley-VCH, 11; Zarzo, Manuel and Stanton, David T. (2009): Understanding the underlying dimensions in perfumer's odor perception space as a basis for developing meaningful odour maps. *Attention, Perception, & Psychophysics* 71(2), 225-247; Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 36.

[153] Wise, Paul M.; Olsson, Mats J. and Cain, William S. (2000): Quantification of Odour Quality. *Chem. Senses* 24, 429-443; Ohloff, et al. (2011), 31.

their differences, both methods lead to multidimensional odour profiles: many odorants cannot be reduced to simply one odour note but exhibit a complexity of different qualitative notes. As a result, “the odour of almost all materials resembles a *fragrant mosaic* built up from elements and nuances of other categories.”[154] To accommodate such a mosaic image in a systematic way and to single out relations between the most prominent categories, the olfactory spectrum is represented in different pictorial forms, including dendrograms, circles, tables, diagrams and maps. These different pictorial forms, it is shown in the following subsections, are used to highlight different conceptual criteria for addressing odour quality.

2.1 Dendrograms

Starting with dendrograms such as John Amoore’s (fig. 1), they present a range of odorants (here: 107) that were tested against selected reference odours (here: 7) and judged by their degrees of similarity. The outcome of such dendrograms strongly depends on both the test odorants and the reference odours chosen. Strictly speaking, a dendrogram does not present a proper classification scheme, but, rather, formulates a list that addresses the complexity of odour characteristics in odoriferous materials. A striking feature of this representational form is the overlapping and cross-cutting character of odour profiles that do not offer a single and unambiguous answer to the question of “where to make the cut?”[155]

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[154] Ohloff et al. (2011): *Scent and Chemistry*, 31.

[155] Wise et al. (2000): *Quantification of Odour Quality*, 435.

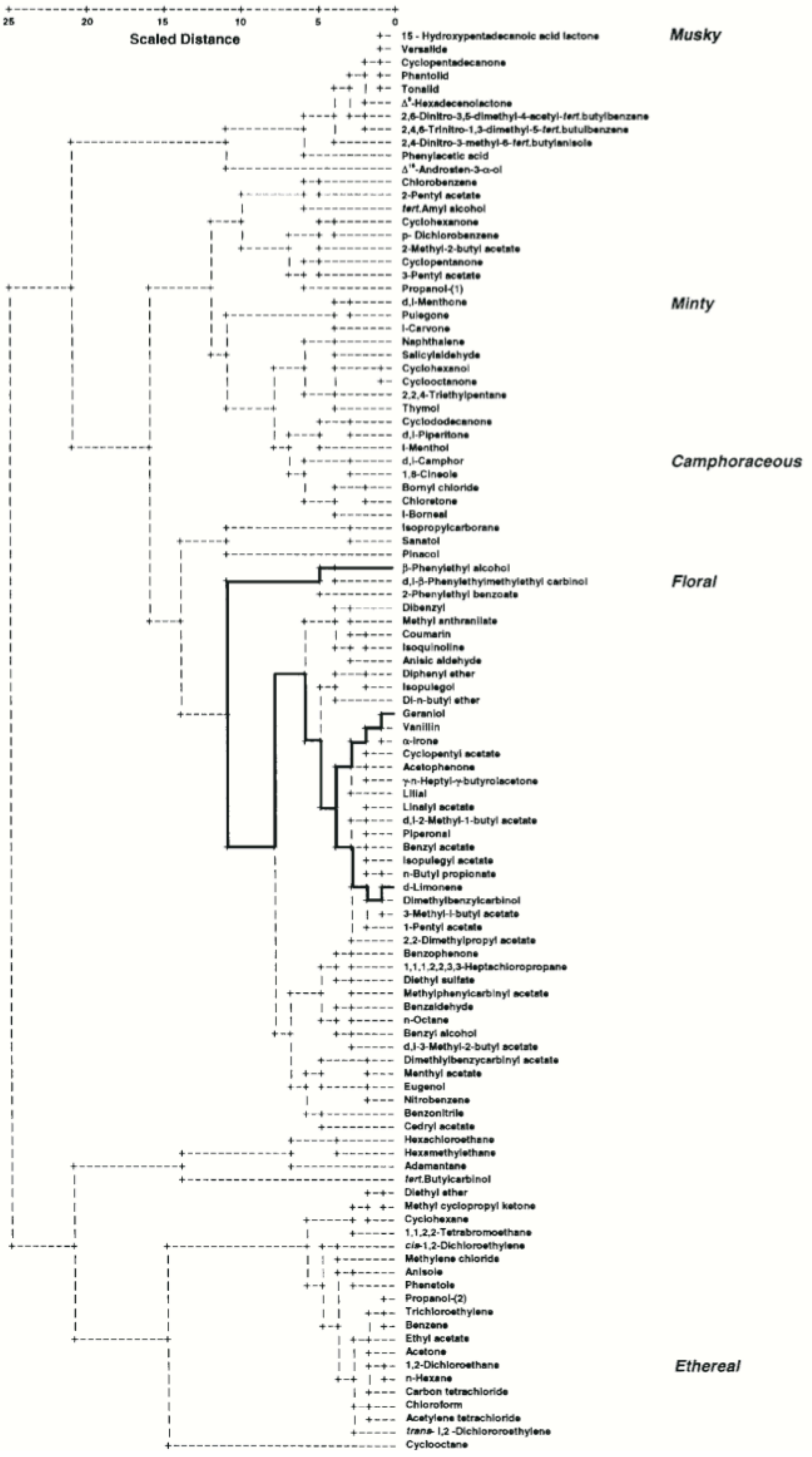

Fig. 1 Amoore’s dendrogram. A range of odorants are compared to reference substances by virtue of their perceived similarity. Wise et al. (2000): *Quantification of Odour Quality*, 434.

2.2 Classification Circles

Another strategy to accommodate the overlapping character of odours is to represent the olfactory spectrum as a fragrance circle. Such a conceptualisation can take various forms. One example is the classification by Ulrich Harder (fig. 2), who defined floral odorants by different dimensions of odour quality. Harder first divided floral odours into three abstract sensory categories, namely "light", "green" and "heavy", which are then further surrounded by seventeen more specific notes. Notably, "the circle is arranged in such a way that related notes are adjacent and blend seamlessly with one another."[156]

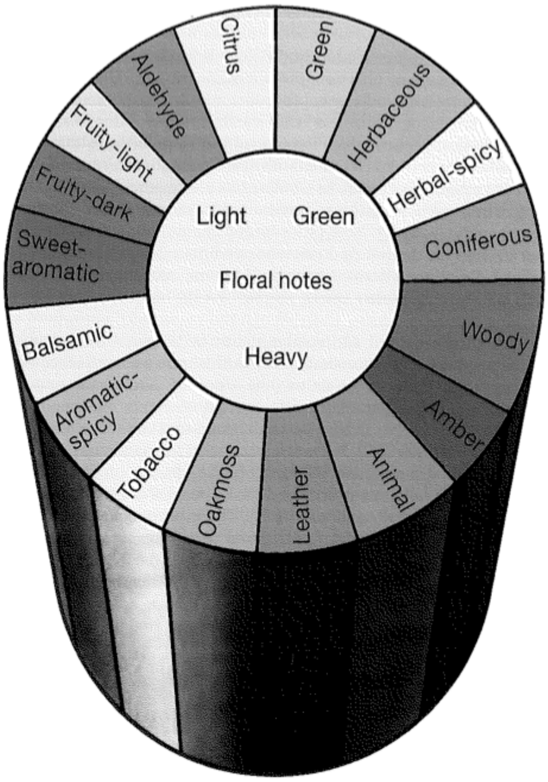

Fig. 2 Harder's fragrance circle. Odours are arranged under very general categories (light, heavy, green, floral) and further divided into more specific qualities associated either with substances (tobacco, woody, leather) or sensory qualities (dark, light, spicy). Ohloff et al. (2011): *Scent and Chemistry,* 32.

Alternatively to such a semantic approach for defining the overlapping dimensions and transition of odour quality, classification circles can also be built on model substances, using benchmark odorants, for instance, in the case of

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[156] Ohloff et al. (2011): *Scent and Chemistry*, 31.

Givaudan's fragrance circle (fig. 3). Here the materials were grouped into eight odour families with the most relevance to perfumers' purposes:

> "These were then arranged around a circle with the help of benchmark odorants, each of them combining odor attributes of two families, and thereby linking odorant families to one another."[157]

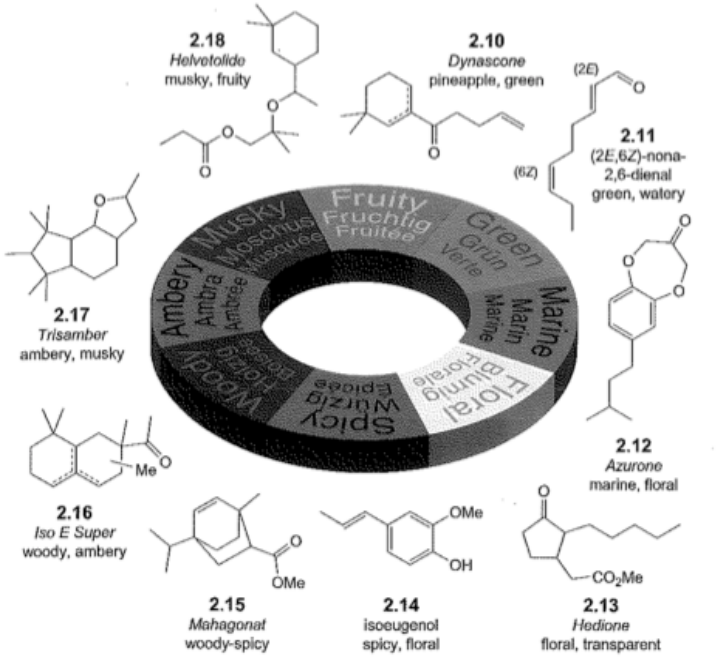

Fig. 3 Givaudan's fragrance circle. Odour types are defined by selected benchmark materials (e.g. dynascone for pineapple, green) and further arranged into a circle, within with the qualities of the various odorants classified can overlap. Ohloff et al. (2011): *Scent and Chemistry*, 33.

Similar to these fragrance circles, another influential classification by Michael Edwards (1983) presents odours within a fragrance wheel (fig. 4).[158] Here too, a range of particular odour families are arranged in a circular form. This range has subsequently been extended by the addition of further subgroups over the years. Using mainly vernacular terms, its purpose is to provide a standard terminology for the communication between perfume consumers and retailers. An interesting feature of this representation is its dynamic character; apart from "fougère", all categories can be rotated to combine the outer dimensions of odour quality and the inner dimensions of sensual impressions in the classification of a specific odorant.[159]

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[157] Ibid., 32.

[158] Edwards, Michael (Ed.) (2013[1983]): *Fragrances of the World. 29th Edition.* Unspecified.

[159] Zarzo and Stanton (2009): *Odour maps*, 244.

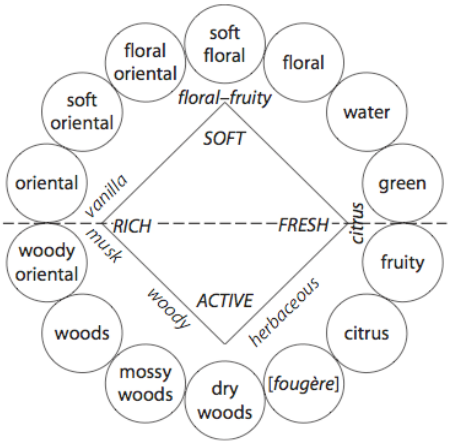

Fig. 4 Edward’s fragrance wheel. To design and combine fragrant compositions outer odour quality classes (circles) can be rotated around sensoty categories (square) and vice versa. Zarzo and Stanton (2009): *Odour maps*, 244.

Semantic family relations are often based on the statistical dominance of particular odour note descriptions, which proves helpful in establishing a standardised use of terminology. In comparison, benchmark odorants are more often used when it comes to the comparison and investigation of selected odour notes and their correlation to chemical structures.[160] It is also worth noting that this spatial representation in the form of a circle, often employed in perfumery and fragrance research, closely resembles the actual workplace of the practitioners: perfume organs (fig. 5), where the creation of new mixtures takes place, present a similarly spatially circular arrangement of essential odorants. Classification schemes thereby can be conceived as occasionally directly reflecting their associated application practices.

Fig. 5 Perfumer’s workplace in Grasse. Wikipedia (2013b): *Perfume organ*.

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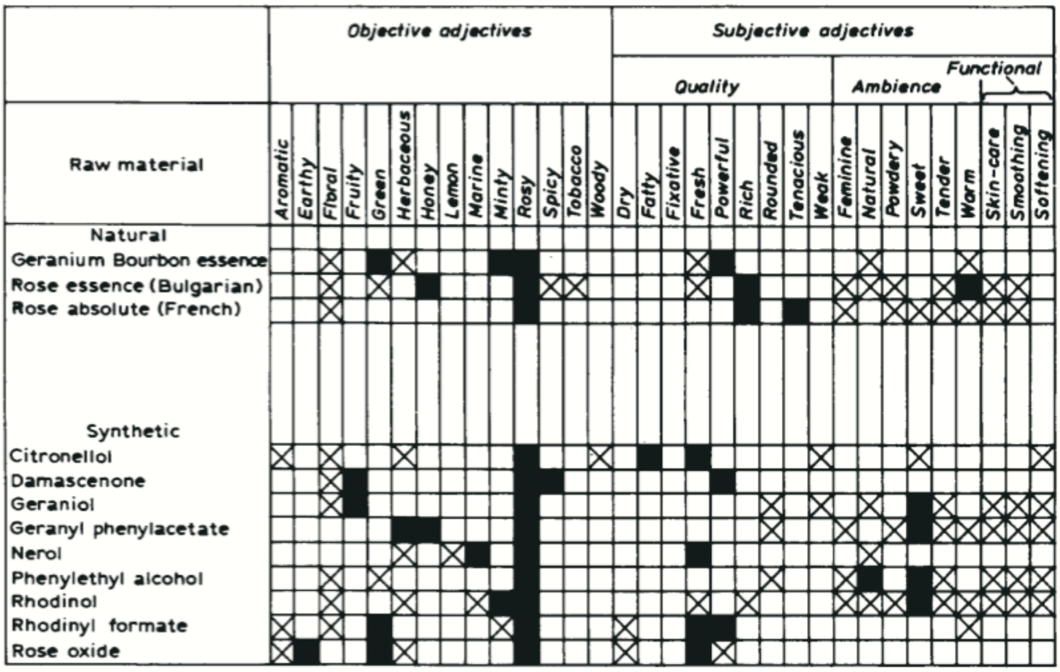
[160] Ohloff et al. (2011): *Scent and Chemistry*, 35-36.

2.3 Classification Tables

Classification in the form of a table offers another way of presenting conceptual distinctions for a systematic arrangement of odours and their materials. Maurice Thiboud (fig. 6), for instance, characterised odours by two conceptually different kinds of descriptors. “Objective” descriptions first present characterisations that relate to the qualities of the raw materials such as “floral” and “herbaceous” for Geranium Bourbon essence. “Subjective” descriptors refer to the sensory qualities associated with their smells such as “fresh”, “natural” and “warm”.[161] Such a classification inevitably requires different skills of the perfumer, partly based on his or her knowledge about the nature of raw materials, natural as well as synthetic, and partly dependent on the sensory interpretations of quality that a fragrance composition is supposed to address. In this form, the character of odours combines descriptions of materially based notes and descriptions of associated sensory impressions.



	Objective adjectives														Subjective adjectives																	
															Quality									Ambience						Functional		
Raw material	Aromatic	Earthy	Floral	Fruity	Green	Herbaceous	Honey	Lemon	Marine	Minty	Rosy	Spicy	Tobacco	Woody	Dry	Fatty	Fixative	Fresh	Powerful	Rich	Rounded	Tenacious	Weak	Feminine	Natural	Powdery	Sweet	Tender	Warm	Skin-care	Smoothing	Softening
Natural																																
Geranium Bourbon essence			☒		■	☒				■	■							☒	■						☒				☒			
Rose essence (Bulgarian)			☒		☒		■				■	☒	☒					☒		■				☒	☒	☒		☒	■	☒	☒	
Rose absolute (French)			☒								■									■		■		☒		☒	☒	☒	☒	☒	☒	
Synthetic																																
Citronellol	☒		☒			☒					■			☒		■		■					☒				☒					☒
Damascenone			☒	■							■	■							■													
Geraniol			☒	■							■										☒		☒		☒		■	☒		☒	☒	☒
Geranyl phenylacetate						■	■				■										☒			☒		☒	■	☒	☒	☒	☒	☒
Nerol						☒		☒	■		■							■							☒							
Phenylethyl alcohol			☒		☒						■										☒			☒	■		■	☒		☒	☒	☒
Rhodinol			☒			☒			☒	■	■							☒		☒				☒	☒	☒	■	☒	☒	☒	☒	☒
Rhodinyl formate	☒		☒		■					☒	■				☒			■	■										☒			
Rose oxide	☒	■			■	☒					■				☒			■	☒													

Fig. 6 Thiboud’s table of odour descriptors (black boxes: main or mode important odour characteristic; ticked boxes: secondary note, or according to dosage). Thiboud (1991): *Empirical classification of odours*, 268.

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[161] Thiboud, Maurice (1991): Empirical classification of odours. In: *Perfumes: Art and Science, and Technology.* Ed. by P.M. Müller and D. Lamparsky. Dordrecht: Kluwer, 255.

2.4 Odour Diagrams and Multidimensional Maps

Another alternative to think about relations between odours are multidimensional sensory odour maps. Consider, for instance, the map developed by Zarzo and Stanton (2009) (fig. 7).[162] Based on psychophysical considerations, these maps spatially arrange odours by statistically evaluating odour stimuli and their most common effects. A first insight into odour families provided through such maps is the formation of descriptive clusters.

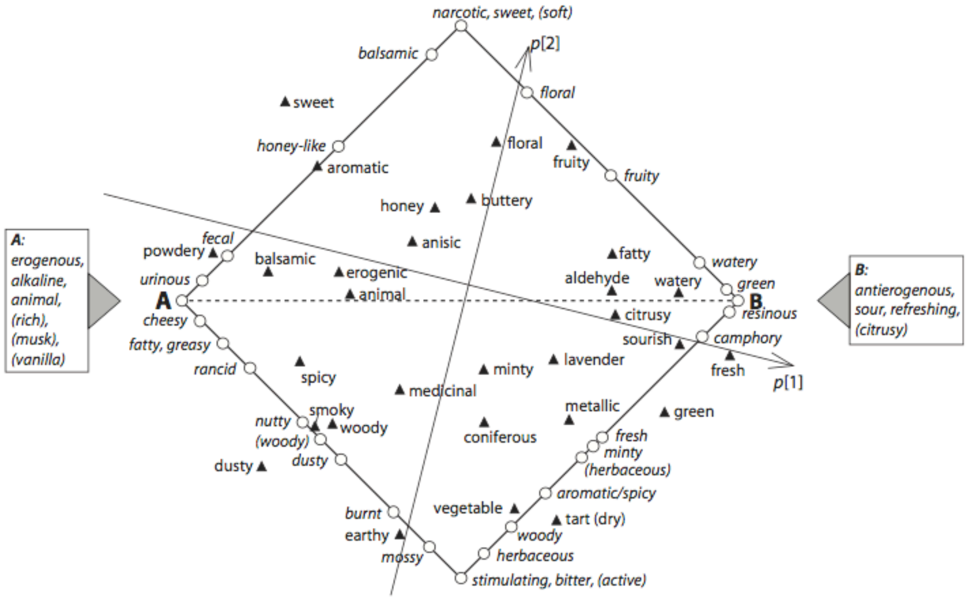

Fig. 7 Multidimensional sensory odour map. Odours are arranged through two axes of opposite pairs (erogeneous vs antierogeneous, and narotic/sweet versus stimulating/bitter). Zarzo and Stanton (2009): *Odour maps*, 236.

These clusters present family relations between prominent smells such as:

- "Smoky – burnt – birch tar – toasted – leather
- Camphoraceous – pine – *lavender* – mint – *conifer* – *rosemary*
- Herbaceous – chamomile – *lavender* – *rosemary* – sage – clary sage
- Resinious – olibanum – gum from trees – *conifer*
- Earthy – dust – moss – forest – soil – mold – must – roots – yeast – mushrooms
- Sweet – balsam – vanilla – heliotropin – honey – syrup"[163]

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[162] Zarzo and Stanton (2009): *Odour maps*, 225-247.

[163] Donna, Laura (2009): Fragrance Perception: Is everything relative? Research presents a leap towards a consensus in fragrance mapping. *Perfumer & Flavorist* 34, 30. [Italics mine]

This list of family clusters highlights an interesting feature of odours. Whereas some odours are considered to form a distinct class of their own, exhibiting a highly unique character such as sulphur, other odours present a more overlapping and diverse image, resulting in cross-cutting classes of odour families. Examples taken from Donna's review of perfumers' practices above are picked out in italics and include rosemary, conifer and lavender which all feature in more than one family.

As well as spatially organised family clusters, Zarzo and Stanton also employed psychological criteria for the interpretation of these relations of odour vicinity and distance. For the identification of reference substances, they first consulted two large odour databases, namely those curated by Boelens-Haring and Thiboud. These databases comprise a variety of odorants that correlate two data sets, molecular parameters of odorants on the one hand and odour descriptors on the other. The reference materials these contain were then scaled and compared with Paul Jellinek's influential odour effects diagram (fig. 8).[164]

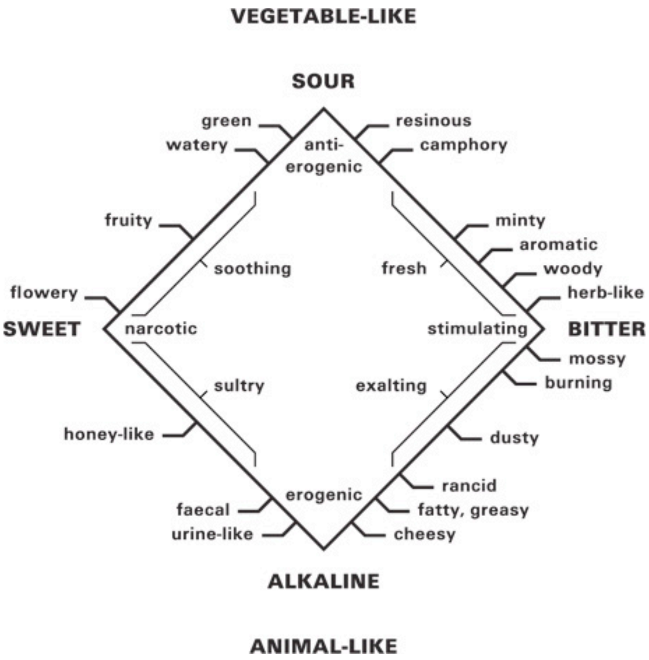

Fig. 8 Jellinek's odour effects diagram. Odour materials are arranged through opposite qualities (sweet vs bitter and sour vs alkaline) that further correspond to two hedonic pairs (narcotiv vs stimulating and anti-erogenic vs erogenic). Jasper and Wagner (2008-2009): *Notes on Scent*.

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[164] Jellinek, Paul (1951): *Die Psychologischen Grundlagen der Parfümerie.* Heidelberg: Alfred Hüthig Verlag; Jellinek, Paul (1997): The psychological basis of perfumery. In: *The Psychological Basis of Perfumery.* 4th Edition. Ed. by J.S. Jellinek. London: Chapman & Hall (1997) 1-162.

On such accounts, the comparison of odours in sensory maps is defined by two axes with opposite poles, describing four key effects: (i) erogenous and anti-erogenous and (ii) narcotic and stimulating. The arrangement of odours under these criteria, however, does not always result in clear cut cases, as the classes formed are often of a hybrid character: "narcotic plus anti-erogenous is calming; anti-erogenous plus stimulating is fresh; stimulating plus erogenous is exalting; erogenous plus narcotic is sultry".[165]

2.5 Paradise lost: The Consistency and Limits of Odour Classifications

From a broad perspective, all these classifications present odours in a systematic way that allows for the arrangement of already known odorants as well as for the allocation of new or unknown odours. New odorants, when profiled – either by semantic descriptions or by direct comparison to a test odorant – are then placed "into the local proximity of these standard odors"[166] and further accommodated within one of the various schemes, depending on what purposes the scheme's application will serve. Considering the material complexity of odour materials, the diversity of odour impression and the overlapping nature of odour quality, these classifications thus offer various schemes to capture and define particular odour dimensions to form family relations, resulting in an image of representational plurality. The previous representational schemes adopt different criteria for the arrangement of odours into relevant classes. The interpretation of their family relations range from:

- *Dendrograms*: expressing how strongly a range of test odorants correlates in odour similarity by comparison to reference materials
- *Circles*: accounting for the gradational and overlapping character of odour families
- *Tables*: drawing distinctions between different descriptor kinds of odour quality (referring to impression of material quality and sensory effect)
- *Diagrams* and *maps*: arranging odour materials spatially and offering additional dimensions to interpret their vicinity.

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[165] Donna (2009): *Fragrance Perception*, 28.
[166] Ohloff et al. (2011): *Scent and Chemistry*, 34.

Practitioners' selection of methods for assigning odour families is driven by their particular interest in odour materials and the specific purposes for which they wish to finding meaningful relations amongst them. Many of the previous classifications maintain criteria from historical accounts. As with Hampton's classification scheme in the previous chapter, current classifications based on fragrance circles still use benchmark materials. Likewise, contemporary psychophysical classifications employ hedonic criteria similar to those proposed by Linnaeus.

In light of this conceptual and representational diversity, the question then arises whether, or to what extent, these classifications correlate. For a comparison of odour classes across various classifications, two criteria have to be considered. It first needs to be seen how *comprehensive* the selected schemes turn out to be with respect to the full range of odour data. A second criterion involves the *homogeneity* and the *sharpness of class boundaries*.[167] In light of these two criteria, three main criticisms can be raised about odour classification in general:

- First, odour classifications are *ambiguous*.

Choices in semantic odour descriptions and their related reference substances vary and, as a result, lead to different arrangements that can either overlap or differ greatly. Consider, for instance, different assignments for the two reference substances "eugenol" and "safrole" (fig. 9):[168]

	Boehlens/ Haring	Jellinek	Zwaardemaker	Zarzo/ Stanton
eugenol	spicy		aromatic/spicy	
safrole		spicy/aromatic	aromatic/aniseed	Herbaceous/anasic

Fig. 9 Comparative table of two reference substances across four classificatory systems

Notably, these classifications differ in some important respects. First, they sometimes use two reference materials that, although they differ in smell, are used to fix the meaning of the same semantic descriptor (Boelens/Haring and Jellinek). Second, these reference materials can also be accommodated under

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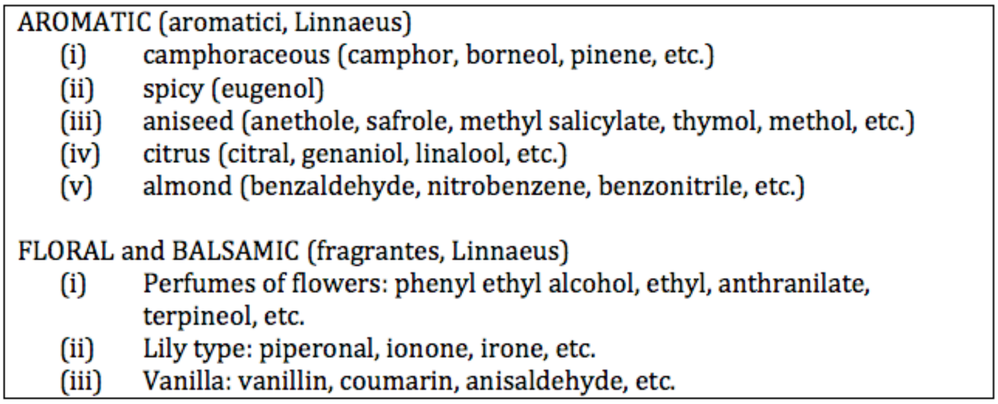
[167] Dupré, John (2002b): In Defense of Classification. In: *Humans and Other Animals*. Clarendon Press, 90.

[168] Donna (2009): *Fragrance Perception*, 33.

two clearly distinct semantic descriptors (Jellinek and Zarzo/Stanton). Third, the substance can fall under two overlapping descriptors (Zwaardemaker). Fourth, classifications can overlap with respect to their descriptor but be inconsistent in the assigned reference substances (Jellinek and Zwaardemaker).

One explanation for these overlapping, inconsistent and cross-cutting kinds across different classification schemes is that semantic descriptor classes are *arbitrary* to some extent. Usually based on the work of individual people,[169] decisions rely heavily on the practitioner's preferences. Quite often, the distinctions drawn between classes, subclasses and reference substances are exchangeable, even within a particular classification. A subclass such as "vanilla" in the scheme of Zwaardemaker, for instance, can easily fall either under "aromatic" or "fragrant" (fig 10).[170]



AROMATIC (aromatici, Linnaeus)
- (i) camphoraceous (camphor, borneol, pinene, etc.)
- (ii) spicy (eugenol)
- (iii) aniseed (anethole, safrole, methyl salicylate, thymol, methol, etc.)
- (iv) citrus (citral, genaniol, linalool, etc.)
- (v) almond (benzaldehyde, nitrobenzene, benzonitrile, etc.)

FLORAL and BALSAMIC (fragrantes, Linnaeus)
- (i) Perfumes of flowers: phenyl ethyl alcohol, ethyl, anthranilate, terpineol, etc.
- (ii) Lily type: piperonal, ionone, irone, etc.
- (iii) Vanilla: vanillin, coumarin, anisaldehyde, etc.

Fig. 10 Excerpt of Zwaardemaker's classificatory scheme. The classes chosen and their specificity are not clear-cut and uniform but ambiguous and selective (e.g. perfumes of flowers versus lily type) Harper et al. (1968): *Odour Description and Classification*, 26.

- Second, odour classifications are *artificial*.

Odour classifications inevitably present a different outcome depending on the selection of semantic descriptors as well as on the selection of odorants which strongly differ with respect to the individual preferences of practitioners. Moreover, and even more importantly, classification outcomes also diverge according to the methods of odour profiling applied. Odour profiling, as mentioned previously, can comprise different methods. In the semantic method, panels of test subjects are presented with odours to which they must attribute descriptions according to either their own associations or a set of prepared

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[169] Such as, for instance, the influential work of Dravnieks, Andrew (1984): *Atlas of odor character profiles.* ASTM.

[170] Harper, Roland; Bate Smith, E.C. and Land, D.G. (1968): *Odour Description and Odour Classification. A Multidisciplinary Examination.* London: J. & A. Churchill LTD, 27.

descriptions rated within a similarity scale. A different method works by direct comparison of a range of test odours to reference substances. The comparison of substances can take place either in a dyadic form, evaluating whether a test odorant is similar or not to a reference odorant (and, based on a scale, to what degree) or by "triadic comparisons", where test subjects are given three substances from which they must pick pairs of the most similar and the most dissimilar.[171]

- Third, odour classifications are *incomplete*.

Considering the utility of odour classifications, they are inevitably bound to their purpose and accordingly limited. Odour cycles such as Harder's and Givaudan's, for instance, arrange odorants most relevant for perfumery and other artisanship's such as wine, tea and coffee tasters, flavourists and food technologists.[172] However, odour classifications are not only limited with respect to relevant family selections and materials but also in comparison to the vast amount of molecular data. The odour map of Zarzo and Stanton, despite its insight into meaningful odour family relations, only covers about 32% of the variety of collected data.[173]

Thus, considering all these pragmatic restrictions, the plurality of metrics for determining odour profiles, the complexity and ambiguity of odour quality and the diversity of odour materials, should odour classification be perhaps seen as futile? Contemporary odour classifications have been shown to result in inevitably ambiguous, overlapping, not hierarchically organised, and partially artificial groups. Odour classifications do not provide unambiguous and distinct classes, nor do they exhibit essences in the strict sense. In addition, such classifications are dependent on the disciplinary context, and do not, therefore, give clear preference to a specific order of odours. All this seems to oppose the idea of understanding odours in the tradition of natural kinds.

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[171] Wise et al. (2000): *Quantification of Odour Quality*, 433-436; Ohloff et al. (2011): *Scent and Chemistry*, 31.

[172] Ohloff et al. (2011): *Scent and Chemistry*.

[173] Zarzo and Stanton (2009): *Odour maps*, 230.

3 Challenging the Distinction between Real and Nominal Essences

Notwithstanding the acknowledged degree of artificiality in the construction of odour classifications, efforts of classifying odours into groups by virtue of their nature mark a general aim in olfactory research. Indeed, Harper et al. (1968) explicitly referred to parallel philosophical discussion of taxonomy and “natural kinds” to emphasise the need for a better theoretical understanding of classification in olfactory research.[174]

Comparison between odour classifications and ‘armchair’ definitions of natural kinds does not lead very far. Odour classification cannot be reduced to some underlying causal “real essences”, nor are they mere descriptive accounts of odour quality. One reason is that the so-called “nominal essences” are not simply an accidental feature of the phenomena to be classified, but, on the contrary, the ‘nominal features’ of smells, namely odour quality, *constitute the phenomenon* in question. Despite their ambiguity, descriptions of quality are thus indispensable and integral to odour classification. Yet, they do not suffice to determine odour families and groups in general but often require a relation to particular reference materials. The material basis of odours was shown to be definable by various criteria that, despite being grounded in the nature of these materials, are also entrenched in the surrounding disciplinary practices and methods. As a result, odour classifications do not fulfil the criterion of natural kinds as being independent from observers’ perspectives.[175]

Determining odours exclusively by reference to some underlying essence and independence from the observers’ purpose is futile. In addition to their dependency on context and methods, odours cannot be reduced to mere structural features. Although having a molecular basis, odours *are* observer-relative features and, as a result, their very nature challenges the strict distinction between nominal and real essences for the classification of kinds. A defender of essences might object here that, notwithstanding the plurality of practices and materials, increasing insight into the imperceptible dimension of odours has led to contemporary research into structure-odour relations (SORs). Although the molecular basis of odours is still underexplored and hypotheses

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[174] Harper et al. (1968): *Odour description and classification*, 102.

[175] Hacking (1991): *Natural Kinds,* 110.

about the key feature are not univocal,[176] this might nevertheless ultimately result in a primarily structural definition of odours.

Even imagining that debate on the key structural feature of primary odour recognition has been settled, this does not imply a turn to an 'essentialist' understanding of odours as kinds. Given the complexity of molecular parameters, it is not clear whether the key feature underlying odour perception is common to all kinds of odours and their recognition. Especially with regards to recent knowledge about the combinatorial nature of odour perception, the molecular basis of odours cannot simply be reduced to the stereochemical parameters of odorants but requires further insight into their relation to receptor activity patterns.[177] It is in fact the combinatorial character of odour detection that explains the overlapping and cross-cutting character of odour notes.[178] Furthermore, the molecular basis only presents one way to determine the causal nature of odour perception. Neurological and psychophysical approaches focus instead on the wider context of brain activity and development. Gordon Shepherd, for instance, suggests an evolutionary reading of the sense of smell in humans:

> "The reduced repertoire of olfactory receptor genes in the human is thus offset by the expanded repertoire of higher brain mechanisms. Rather than being restricted to a tiny part of the brain, olfactory processing of complex smells, such as those produced by human cuisines, draws on the enlarged processing capacity of the human brain."[179]

In addition to the complex causal character of smell perception, the molecular basis of odours presents a causal feature for the *detection* of odours yet not for their *classification*! Consider again odour profiles used in, for instance, Amoore's dendrogram or Givaudan's fragrance circle. These schemes determine odours with respect to benchmark materials, looking for correlations between structurally similar molecules and their odour. They do not, however, offer unique, unambiguous odour families and definitions of odour similarity and, as a result, the decision of 'where to make the cut' in qualitative odour similarity remains to some extent ambiguous. The reason for this is to be found in the diverse qualities of odoriferous materials that, instead of forming neatly distinct

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[176] See chapter 7 for a detailed discussion about studies on structure-odour relations (SORs).

[177] Malnic, Bettina; Hirono, Junzo; Sato, Takaaki and Buck, Linda B. (1999): Combinatorial Receptor Codes for Odors. *Cell* 96, 713-723.

[178] Ohloff et al. (2011): *Scent and Chemistry*, 31.

[179] Shepherd, Gordon M. (2004): The Human Sense of Smell: Are We Better Than We Think? *PLoS Biol* 2(5), e146.

and separate odour classes, exhibit overlapping and cross-cutting odour notes. Exhibiting a transitional image of odour qualities, previous classification schemes approached odour classifications from various angles amongst which none can be given absolute preference.

4 The Pragmatic Purpose of Classification Practices

In contemporary classifications of odour quality in perfumery, there are a variety of odoriferous substances that form overlapping and cross-cutting family relations. Although it is certainly possible to discriminate between the smell of grass, wood or jasmine, the scientific problem that accompanies the classification of odours seems to be how to *measure* and *define* their difference:

> "Did you ever try to measure smell? Can you tell whether one smell is just twice as strong as another? Can you measure the difference between one kind of smell and another? It is very obvious that we have very many different kinds of smell, all the way from the odour of violets and roses up to asafetida. But until you can measure their likeness and differences you can have no science of odour." (Alexander Graham Bell 1914).[180]

Although contemporary studies in olfaction still have no standardised procedure to measure odours, a variety of methods have been developed. One of them, the odour profiling described above, elucidated the limits of measurement regarding the ambiguous, contextually and conventionally determined correlation between descriptors and reference substances. These differences are more than just a mere 'problem of measurement' but are pointers to a bigger issue in our understanding of perception and cognition performances. Studies involving changes of test odorants and descriptors showed that human test subjects not only differ in their *decisions* about odour similarity but moreover, and even more importantly, also show variability in their *criteria of similarity*.[181]

This illustrates the pragmatic purpose classifications serve. By facilitating criteria for a standardisation of materials, classifications are indispensable for comparing research results, since they serve as a common basis for intra- and

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[180] Quoted in: Boland, Wilhelm and Spiteller, Dieter (2001): Electronic Noses. In: *Bioresponse-linked instrumental analysis.* Ed. by B. Hock. Stuttgart, Leipzig, Wiesbaden: Teubner, 57.

[181] Wise et al. (2000): *Quantification of Odour Quality*, 435; Davis, R.G. (1979): Olfactory perceptual space models compared by quantitative methods. *Chem. Senses Flav.* 4, 21-33.

interdisciplinary communication.[182] Guided by these concerns, analysis of classifications thus needs to involve their disciplinary contexts, their strategies for fixing the reference of classes and their underlying methods of measuring and comparing the relevant features.

The multiplicity of classifications in perfumery was shown to employ a variety of methods for odour measurement and comparison. The resulting ambiguous character of odour classes is accommodated by different forms of visualisation – such as dendrograms, tables, circles, maps etc. – that highlight the underlying conceptual plurality of similarity relations for the definition of odours, e.g. structural resemblance in comparison with odour quality, similarity in sensory perception, family relations between descriptions of general odour notes in perfumery, etc. This diversity of classificatory strategies thus resonates with the diversity of research interests in grouping odours into kinds.

All these classifications serve a pragmatic purpose and play an indispensable role in fragrance research practices. These classifications, first, provide a standard terminology for communication amongst different practitioners (researchers, retailers, consumers etc.). Second, they are a conceptual tool for facilitating the skills required to work with the relevant materials, a point that can easily be seen in, for instance, the resemblance between the workplace of a perfumer (the perfume organ) and the spatial representations of odour circles. Third, classificatory practices actively assist in exploring conceptual questions that address research materials, such as underlying and different definitions of measurement and, in further consequence, similarity. In addition, classification practices often act as cross-disciplinary instruments, i.e. the context in which they are applied and are of further utility is not limited to the context in which they are constructed. Going beyond the design of new fragrant compositions in fragrance research, results of odour classifications are for instance of major importance for neurological and psychophysical studies of human cognition. For these reasons, analysis of classificatory practices allows for comparisons that highlight the variety of relevant features of the research materials and the plurality of surrounding research interests. Analysis of classificatory practices, I argue, also aids exploring to what extent these overlapping practices influence

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[182] Harper et al. (1968): *Odour descriprtion and classification*; Chastrette, M. (1998): Data management in olfaction studies. *SAR & QSAR in Environmental Research* 8, 157-181; Sell, Charles (2005): Scent through the looking glass. In: *Perspectives in Flavour and Fragrance Research.* Ed. by P. Kraft and K.A.D. Swift. Wiley-VCH, 67-88; Leonelli, Sabina (2012): Classificatory Theory in Biology. *Theoretical Biology* 7(1), 1-8.

the development of scientifically interesting research objects across different disciplines.

5 Odours as Multidimensional Research Objects

Exceeding mere historical interest, studies of classificatory and experimental practices also inform philosophical analysis on the formation and development of scientific objects. Contrary to traditional assumptions held by some philosophers,[183] the development and the descriptions of scientific objects does not simply move from "premature" stages of science to more "mature" and technically advanced ones that inevitably result in some neat intrinsic structural feature that somehow explains their nature. At least for research on odoriferous materials, such a scientific one-way street does not disclose itself when one takes a closer and comparative look at its historical and contemporary classificatory practices.

In the previous chapter, in which I presented an epistemic history of material practices surrounding odours, the following trajectory emerged (fig. 11). Odoriferous materials were first analysed as objects in nature in relation to their largely botanic origins (trajectory 1). Odours here played a part within different, though related, disciplines such as botany, horticulture, pharmacy and perfumery; they either appeared as a useful taxonomic tool for plant classifications or were presented in perfumers' classifications employing botanic criteria. In parallel with the pluricentric botanic interest in odours, odoriferous materials were also part of the early experimental culture in chemistry (trajectory 2). Although this interest did not initially concern their systematic arrangement, growing knowledge about the manipulability and the underlying structural composition of odoriferous materials led to a fundamental change in the conception of odours. With the rise of synthetic chemistry at the end of the 19th century, enquiry into the material basis of odours started to transform into an independent scientific field, looking for lawlike structure-odour relations

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[183] Popper, Karl (1959): *The Logic of Scientific Discovery.* London: Hutchinson; Kuhn, Thomas (1970[1962]): *The Structure of Scientific Revolutions.* 2nd Edition. Chicago: University of Chicago Press; Imre Lakatos (1970): Falsification and the Methodology of Scientific Research Programmes'. In: *Criticism and the Growth of Knowledge.* Ed. by I. Lakatos and A. Musgrove. Cambridge University Press; Imre Lakatos (1980): *The methodology of scientific research programmes: Volume 1: Philosophical papers*. *Vol. 1*. Cambridge: Cambridge University Press.

(SORs). This shift was further enforced by the development of new techniques of visualisation, exploring and modelling the molecular basis of odours. Increasing insight about the structural diversity of odorants did not generate lawlike SORs rules but spurred further scientific inquiry into the underlying perception process of odours, relating olfactory research to other scientific disciplines such as molecular biology and neurology (trajectory 3).

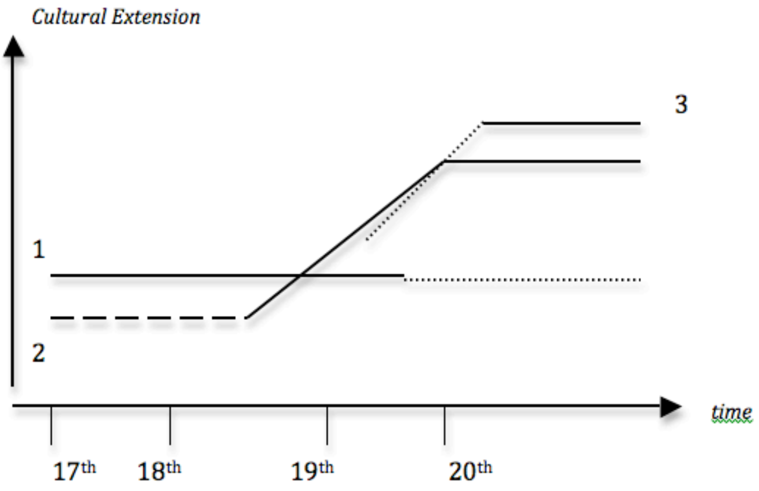

Fig 11[184] Trajectories of the different conceptualisations of the material basis of odours

Trajectory 1: Pluricentric culture of botanic practices surrounding odoriferous materials
Trajectory 2: Experimental culture of chemistry and perfumery
Trajectory 3: Emerging experimental system of molecular odour recognition

Although parts of these three trajectories overlap in terms of the materials investigated, the methods employed for processing these materials etc., they nevertheless form conceptually different enquiries, defining odours as objects in nature, as materials of production and as parts of experimental systems respectively. These trajectories do not simply display a linear progression of the research on odours over time. From a distant perspective, it might appear that the history of odours as scientifically interesting entities might be described as a transition of scientific interest in odours from botany to chemistry to molecular biology and neurology. This appearance, however, changes when taking a closer look at the individual developments of these trajectories.

The individual strands of these three trajectories continued to develop independently. Interest in odours as objects in nature (trajectory 1) and the

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[184] This display of trajectories is similar to Klein, Ursula (2003): *Experiments, Models, Paper Tools. Cultures of Organic Chemistry in the Nineteenth Century.* Stanford: Stanford University Press, 220.

variety of the “natural origins” of their materials did not cease. It just changed. Biological interest in odoriferous substances expanded to include, for instance, studies on pheromones and biodiversity in biology. In addition, expeditions for the discovery of new fragrances, so-called Scent Treks in commercial perfumery and fragrance chemistry,[185] explore remote territory in order to find new fragrant materials and new plant species and to capture their fragrance. In parallel with these plant based projects, interest in odours as chemical structures (SORs) also persists in fragrance chemistry (trajectory 2)[186] along with autonomous, though, related research on the perception process in molecular biology, psychophysics and neurology (trajectory 3).

What this amounts to is that the complexity of understanding odours and their material basis can neither be fully reduced to perceptible features, nor to molecular structures, nor to one particular stage in the perception mechanism. Instead, the existence of multiple conceptualisations of odours, odoriferous materials and aspects of odour perception requires their investigation through various disciplines. This multi-disciplinarity highlights the necessity to define scientifically relevant phenomena under a less reductive perspective. Entrenched in different experimental systems, odours act as scientifically significant objects and also provide demarcations of other scientifically interesting objects across different disciplines that are loosely linked by overlap in interest, methods and materials.

Scientific interest in odours is not even exhausted by the focus on SORs and the perception process. Contemporary research on odours and their materiality includes studies on biodiversity and on the behaviour of humans and other animals as well as studies in clinical medicine and neurology. To demonstrate the non-linearity not only of the historical but also of the contemporary developments and to provide an outlook on the inevitably multi-centred progression of research on odours, the two following subsections will briefly introduce two different perspectives on the divergent scientific interests in and approaches to odours.

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[185] Kaiser, Roman (2010-2012): *Scent Trek.* Givaudan. URL=<http://www.givaudan.com/Fragrances/Innovation/ScentTrek>

[186] Jenner, Karen (1999): The Search for New Fragrance Ingredients. In: *The Chemistry of Fragrances.* Ed. by C. Sell. Royal Society of Chemistry, 254-293.

5.1 Odours as Semiochemicals: Pigs, People and Goldfish

Odours in contemporary biology are mainly explored as signalling chemicals, or so-called *semiochemicals.*[187] Here odours inform research concerning a wide range of different aspects of behaviour such as, for instance, mate recognition within a species, predator-prey relations, or learning processes and memory responses to experiential states. In this research, the materiality of odours is interpreted as comprising natural signs of a particular physical condition or of species identity.[188]

As signs of species identity or initiators of behavioural responses, odours are relevant to inquiry in biodiversity and interspecies relations. One important discovery, for instance, was that, when they are ready to mate, female Asian elephants release a specific pheromone in their urine, namely (Z)-7-dodecenyl acetate. This finding revealed an unexpected inter-species connection: “Who would have predicted that the largest living land animal would have the same pheromone as the turnip looper, the cabbage looper and at least a 100 other species of butterflies and moths (Lepidoptera)?”[189] Other cases for inter-species similarities in the structure of particular chemical signals were found, for instance, between beetles, trees, moths and mice[190] or even between pigs, people and goldfish.[191] Similarity of chemical signals across different and unrelated species can serve a variety of functions, which are not yet fully explored. One more apparent function includes strategies of sexual deception, describing cases of pheromone mimicry. Consider, for instance “[t]he "sexually deceptive" orchid *Chiloglottis trapeziformis*” that “attracts males of its pollinator species, the thynnine wasp *Neozeleboria cryptoides*, by emitting a unique

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[187] Abate, Agnese; Brenna, Elisabetta; Fuganti, Claudio; Gatti, Francesco G. and Serra, Stefano (2005): Odour and (Bio)diversity: Single Enantiomers of Chiral Fragrant Substances. In: *Perspectives in Flavour and Fragrance Research.* Ed. by P. Kraft and K.A.D. Swift. Wiley-VCH, 55.

[188] Jellinek, J.S. (1991): Odours and Perfumes as a System of Signs. In: *Perfumes: art, science, and technology.* Ed. by M. Müller and D. Lamparsky. Glasgow: Chapman & Hall, 51-60.

[189] Kelly, David R. (1996): When is a butterfly like an elephant? *Chemistry & Biology* 3(8), 595.

[190] More specifically between or western pine beetles (*Dendroctonus brevicomis)*, Norway spruce trees, mice and two African antelopes (the grey duiker *Sylvicapra grimmia* and the red duiker *Cephalophus natalensis*). Kelly (1996): *When is a butterfly like an elephant?*, 595.

[191] Ibid., 596f.

volatile compound, 2-ethyl-5-propylcyclohexan-1,3-dione, which is also produced by female wasps as a male-attracting sex pheromone."[192]

Overall, interest in odours as pheromones is focussed on three different issues, namely (i) their chemical similarity, (ii) their behavioural function – such as to sexually arouse and attract, repel, warn, etc., and (iii) their production and transmission, i.e. the various forms of pheromone transport and release. The latter refers both to the material origins of pheromones such as specific glands, excreta, body surfaces etc. and to different ways of distributing pheromones into the environment such as wing fanning, fish gills washed by water, etc.[193]

5.2 Odours as Diagnostic Markers

Another quite different disciplinary interest in the material basis of odours is their use as "diagnostic markers" in clinical medicine and neurology. Obviously, inquiry into the material basis of odours and their identification here serves a different purpose from the study of odours in biology, chemistry and perfumery. Odours in medicine often present very useful diagnostic tools for a variety of diseases, among which the most are grounded in metabolic and dermatological dysfunctions. Although medical interest in odour is grounded in a causal relation to their material origins, it differs significantly from the concern with SORs in fragrance research. In medicine, odour identification involves two aspects. Medical diagnosis can concern, on the one hand, significant changes in the patient's odour perception and, on the other hand, significant changes of odour in the secreta and excreta of the patient's body (i.e. "sweat, sebum from the skin; secreta from the nose, mouth, throat, bronchi, and lungs; urine, stool and vaginal discharges; wound suppuration; and from necrotic tissue").[194]

Tracing significant abnormalities in body odour, practitioners identify and classify certain symptoms typical of disease. A variety of metabolic and dermatological diseases are associated with significant abnormalities of body odour, often linked to particular enzyme deficiencies or infections. Odours

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[192] Schiestl, Florian P.; Peakall, Rod; Mant, Jim G.; Ibarra, Fernando; Schulz, Claudia; Franke, Stephan and Francke, Wittko (2003): The Chemistry of Sexual Deception in an Orchid-Wasp Pollination System. *Science* 17 Vol. 302(5644), 437-438.

[193] Kelly (1996).

[194] Cone Jr., Thomas E. (1968): Diagnosis and Treatment: Some Diseases, Syndromes, and Conditions associated with an unusual odour. *Pediatrics* 41(5), 993-995.

signalling particular medical conditions include: PKU (*Phenylketonuria*); diabetic ketosis; organ failures involving Uraemia (kidney) or the liver; infections such as typhoid or diphteria; dermatological diseases such as *hidradenitis suppurativa*, etc. Some changes in body odour are even associated with cases of mental disorders such as paranoias and phobias, indicating physiological causes.[195]

One standard example of a disease with a very characteristic change of body odour is the so-called "fish odour syndrome" (*trimethylaminuria*). This syndrome is described as follows:

> "Fish odour syndrome (trimethylaminuria) is a metabolic syndrome caused by abnormal excretion of trimethylamine in the breath, urine, sweat, saliva and vaginal secretions. Trimethylamine is derived from the intestinal bacterial degradation of foods rich in choline and carnitine and is normally oxidised by the liver to odourless trimethylamine N-oxide which is then excreted in the urine. Impaired oxidation of trimethylamine is thought to be the cause of the fish odour syndrome and is responsible for the smell of rotting fish. Certain foods rich in choline exacerbate the condition and the patients have a variety of psychological problems. (…)".[196]

Another example, named after the peculiar smell of infants' urine, is the "maple syrup urine disease" (MSUD). If not treated properly within a short period of time, the results are irreversible neurological damages, seizures, coma and, finally, death.[197] Similarly, recent studies on the detection of skin cancer also focussed on changes of body odour. In order to identify basal cell carcinoma, these studies have generated specific odour profiles for human skin to further develop different methods of diagnosis.[198]

The utility of odours as diagnostic markers is in fact twofold. First, despite the development of more precise methods, advanced diagnostic tests are not always available, either because the equipment is too expensive or it requires specially trained personnel. Diagnosis is thus often based on identification of immediately observable symptoms one of which is abnormal odour. Second, focus on abnormalities in odours and their material causes often spurs inquiry into the nature of the associated disease. Consider the case of schizophrenia. A

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[195] Ibid.; Liddell, K. (1976): Smell as a diagnostic marker. *Postgrad Med J* 52, 136-138.

[196] Rehman, H.U. (1999): Fish Odour Syndrome. *Postgrad Med J* 75, 451-452.

[197] Saudubray, Jean-Marie (2011): Clinical approaches to Inborn Errors of Metabolism in Pediatrics. In*: Inborn Metabolic Diseases: Diagnosis and Treatment.* 5th Edition. Ed. by J.M. Saudubray, G. Van Den Berghe and J.H. Walter. Berlin, Heidelberg, New York: Springer, 9.

[198] Nelson, Roxanne (2008): Smelling Skin Cancer: A Potential Tool for Detection and Diagnosis. *American Chemical Society Annual Meeting*, presented August 20th, 2008. URL=<http://www.medscape.com/viewarticle/579408>

study by Smith and Sines (1960), elicited a remarkable difference in odour between the sweat of schizophrenic and non-schizophrenic persons.[199] This difference was linked to trans-3-methyl-2 hexenoic acid, which was only present in the sweat of schizophrenic patients. This discovery did not only prove useful for diagnostic purposes, but also fostered debate about whether to identify schizophrenia as "an inborn error of metabolism"[200]. Although not entertained in contemporary diagnostic classifications anymore,[201] this hypothesis was nevertheless considered until the mid 1980s.[202]

In addition to body smell, medical interest in odour also concerns smell perception. Changes in and loss of smell perception, in fact, are a first symptom and an integral tool for pre-clinical detection of major diseases such as frontal lobe tumors, Alzheimer's, Parkinson's or epilepsy.[203] [204] Differences in the course of hyponosmias (loss of smell perception) furthermore serve as an indicator for the distinction of similar diseases such as the Lewy Body Disease and Alzheimer's.[205]

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[199] Smith, Kathleen and Sines, Jacob O. (1960): Demonstration of a peculiar odor in the sweat of schizophrenic patients. *Archives of General Psychiatry* 2(2), 184.

[200] Liddell (1976): *Smell as a diagnostic marker*, 137.

[201] Apart from mentioning olfactory hallucinations in the perception of patients in the International Classification of Diseases (version10), neither the ICD nor the Diagnostic and Statistical Manual (version 4) provide any reference to the body odour of patients. See: ICD (International Statistical Classification of Diseases and Related Health Problems) 10th Revision (2013): *Schizophrenia.* URL=< http://apps.who.int/classifications/icd10/browse/2010/en#/F20> and American Psychiatric Association (2000): *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR : Text Revision.* American Psychiatric Pub, 297-344.

[202] Horrobin, D.F. (1977): Schizophrenia as a prostaglandin deficiency disease." *The Lancet* 309(8018), 936-937; De Wied, D. (1979): Schizophrenia as an inborn error in the degradation of β-endorphin—a hypothesis. *Trends in Neurosciences* 2, 79-82; Haug, J.O. (1984): Pneumoencephalographic evidence of brain atrophy in acute and chronic schizophrenic patients. *Acta Psychiatrica Scandinavica* 66(5), 374-383.

[203] Liddell (1976): *Smell as a diagnostic marker*, 136; Ward, Christopher D.; Hess, William A. and Calne, Donald B. (1983): Olfactory impairment in Parkinson's disease. *Neurology* 33(7), 943-946; Doty, Richard L.; Reyes, Patricio F. and Gregor, Tom (1987): Presence of both odour identification and detection deficits in alzheimer's disease. *Brain Research Bulletin* 18(5), 597-600; Doty, Richard L.; Perl, D.P.; Steele, J.C.; Chen, K.M.; Pierce Jr., J.D.; Reyes, P. and Kurland, L.T. (1991): Clinical Aspects of Parkinson's Disease. Odour identification deficit of the parkinsonism□dementia complex of Guam. Equivalence to that of Alzheimer's and idiopathic Parkinson's disease. *Neurology* 41 (5, Suppl. 2), 77-80; Morgan, Charlie D.; Nordin, Steven and Murphy, Claire (1995): Odour identification as an early marker for Alzheimer's disease: Impact of lexical functioning and detection sensitivity. *Journal of Clinical and Experimental Neuropsychology* 17(5), 793-803.

[204] Doty, Richard L. (1995): Practical approaches to clinical olfactory testing. In: *Taste and Smell Disorders.* Ed. by A.M. Seiden. New York: Thieme, 38-51; Katzenschlager, Regina and Lees, Andrew J. (2004): Olfaction and Parkinson's syndromes: its role in differential diagnosis. *Current Opinion in Neurology* 17(4), 417-423.

[205] Westervelt, Holly James; Stern, Robert A. and Tremont, Geoffrey (2003): Odour Identification Deficits in Diffuse Lewy Body Disease. *Cognitive & Behavioral Neurology* 16(2), 93-99.

A basic requirement for comparing abilities and differences of perception between healthy and ill test subjects is a standardised identification set of test odours. The most commonly used one in the US is the “University of Pennsylvania smell identification kit” (UPSID). It consists of four booklets, each containing 10 test substances.[206] Another test kit developed is the so-called “sniffing sticks”, widely used in Germany, Austria and Switzerland.[207] This consists of three test subsets, addressing three different aspects of odour perception: odour identification (test to identify a range of common odours), odour discrimination (test to distinguish between odour pairs) and olfactory threshold (test to determine at what concentration an odour is detected).[208] To be useful, the odour profiles of such tool kits need to be commonly known and easily identifiable by lay people.[209]

Nonetheless, the lack of standardisation in odour profiling poses experimental difficulties for such studies. A recent and extensive study of olfactory loss, for example, found that the choice of kit produced different research outcomes.[210] Such a divergence of results reflects the way in which measurement methods must always be considered in the evaluation of published results. For a comparison of results across laboratories and research literature, these different standards therefore need to be made as explicit as possible.

6 The Promiscuous Character of Nature

The present chapter presented an overview of contemporary interests and research on odours and odoriferous materials. Conceptualisations of odours, I demonstrated, reflect a multidimensionality of natural demarcations and definitions of materiality. This multidimensionality, in fact, forms and informs enquiry into different and equally valuable perspectives on what is broadly the

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[206] Doty, Richard L.; Shaman, P. and Dann, M. (1984): Development of the University of Pennsylvania smell identification test: a standardized microencapsulated test of olfactory function. *Physiol. Behav.* 32, 489-502; Chang, Louis W. and Slikker, William (1995): *Neurotoxicology: approaches and methods.* London: Academic Press, 733.

[207] Kobal, G.; Hummel, T. Sekinger, B.; Barz, S.; Roscher, S. and Wolf, S. (1996): “Sniffin' sticks”: screening of olfactory performance. *Rhinology* 34, 222-226.

[208] Hummel, T.; Sekinger, B.; Wolf, S.R.; Pauli, E. and Kobal G. (1997): ‘Sniffin’ sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chem. Senses* 22, 39-52.

[209] Ibid., 40-41.

[210] Lötsch, Jörn; Reichmann, Heinz and Hummel, Thomas (2008): Different Odor Tests Contribute Differently to the Evaluation of Olfactory Loss. *Chem. Senses* 33 (1), 17-21.

same domain of phenomena. In fragrance research, odours form a mosaic of odour families that are related to molecular properties. Demarcations between odour families and their suggested correlation to chemical classes further aids in modelling the mechanism of primary odour recognition. Difficulties in the measurement of the related structure-odour relations again shed light on the wider context of cognition and differences in intersubjective criteria of similarity. In other contexts too, odours are interpreted as natural demarcations. In clinical medicine they informed inquiry about the nature of a disease by referring to physiological grounds such as changes and deficiencies in metabolism. Likewise, odours as pheromones inform studies on biodiversity and intra-species relations such as sexual deception. All of these perspectives – historical and contemporary – focus on a material basis of odours and it has been shown that all exhibit different conceptualisations of the underlying materiality.

Drawing attention to these different conceptualisations of materiality, two things came to the fore. First, an epistemic trajectory of the history and present of research interests in odours and the surrounding classification practices revealed that scientific advancement is not linear but pluricentric. Despite a general turn to understand odours and their material basis by focus on their molecular features, odours as scientifically significant entities or as the grounds for demarcation of scientifically significant entities are not exhausted by a reference to “structure” but involve a variety of additional criteria. Definitions of what counts as “structure” are thus not unambiguous but depend on the specific research interest in odours – e.g. does the definition of structure relate to research on SORs, odours as semiochemicals, or molecular recognition? In addition, odours cannot be stripped of their sensory qualities and limited to the “real” molecular structure of the materials that carry them, because odours *are* these hard-to-grasp sensory qualities.

In none of the diverging research contexts were odours fully reduced to chemical structure. Neither were they exclusively explored as perceptible qualities, but always determined in relation to some form of materiality. In fact, the plurality of ways in which odours were defined and grouped (or used as a tool to define and group other kinds of things) illustrated that neither the material basis nor the phenomenological nature of smell provided a privileged basis for an understanding of odours. Instead, the study of odours required a combined perspective involving both material features and sensory qualities of odoriferous materials. This combined perspective, in turn, was modelled on different criteria constituting a link between selected material and sensory aspects, thereby disclosing odours as a multidimensional phenomenon. As a result, the question of how to investigate the nature of odours and their material basis was shown to have different yet equally valid answers. In fact, it is their very promiscuous character – being a sensory quality yet inextricably linked to a variety of structurally diverse materials, embedded in a perception mechanism and of relevance to a variety of physical and behavioural responses of organisms and their environment – that make odours interesting for a variety of parallel, partly overlapping and partly independent scientific endeavours.

Second, this multidimensionality, resulting in multidisciplinary perspectives, points to a plurality of what counts as 'natural' in scientific practice. Odours might not be natural kinds in a strict philosophical sense but they constitute indispensable categories and classes for a wide variety of purposes. Odours in medicine and neurology, on the one hand, *are relevant natural demarcations;* by virtue of their specific material causes they serve as useful diagnostic markers to distinguish categories of diseases and physiological processes. On the other hand, odours *exhibit natural distinctions* in their perceptible qualities that *form natural kinds* as overlapping and cross-cutting families. Moreover, this overlap in odour group characteristics has been shown not to be a flaw of the classifications but, rather, to reflect the very nature of odours.

On that note, recalling the question with which this chapter started, what kind of things are odours? Having presented a variety of ways in which odours were transformed into objects of scientific enquiry or were integrated as tools in the formation of objects of scientific enquiry, the answer to this question must be: many kinds of things. But how or why consider them as natural kinds? Concerning the classification of odour types, odours do not always come in groups that are 'reasonably homogeneous' or exhibit 'reasonably sharp boundaries between groups'.[211] Whereas some odours are easier to discriminate from others (such as sulphurous, coffee or faecal), the distinctions between other odour notes are sometimes more subtle (such as the difference between earthy and mossy or woody, nutty and spicy). Furthermore, not only do many odour qualities appear transitional, i.e. merging into each other, but odoriferous materials often also exhibit more than just one odour note,

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[211] Dupre (2001): *In Defense of Classification*, 210.

presenting a mosaic of odour qualities. All these complexities of odour quality exacerbate attempts to arrange odoriferous substances into something such as a ‘periodic table of odours’. In addition, odour materials do not fall into structurally similar or homogeneous classes either, as can be seen, for instance, in the case of structurally diverse musk odorants. This all seems to speak against taking odours as natural kinds from a traditional philosophical perspective.

Nonetheless, all of these complexities and lack of neatness were shown to be grounded in the nature of odours and their materials. Odours presented a variety of natural demarcations that are not fully reducible to a unique conceptualisation of the materiality of odours. Grounded in their own ambiguous perceptible qualities, the variety of their material causes and the complexity in their recognition process, odours were shown to inform a variety of enquiries and to constitute multiple categories for diverging scientific purposes. Even within the more specific domain of odour classifications in fragrance research, there is no unique way to sort odoriferous substances into classes. Instead, they result in overlapping classes of transitional family relations that justify the need for a plurality of classifications.

In response to this complexity, perfumers and scientists developed various classificatory practices containing different conceptual criteria relating odour qualities to materials. Each practice suited the task for which it was designed, whether it enabled communication between different practitioners, addressed forms of measurement or aided in the creation of new fragrances. In turn, this complexity and need for different practices led to increased knowledge about odours, their material basis and their involvement in significant biological processes as well as the refinement of measurement techniques. In this way the achievements in understanding odours, as presented here, come from exploring the material multidimensionality and mosaic qualities of odours, not by eliminating it.

For these reasons, odours mirror what John Dupré in his *Disorder of Things* (1993) advocated as a promiscuous understanding of nature and ‘natural kinds’ as groups of entities in nature. Dupré advocates a radically pluralistic account of reality and states that there are numerous and equally applicable ways in which scientists classify the (biological) world. The need for different classifications, signifying different relations serving different purposes, he demonstrates, is a result of the overlapping, complex and evolving nature of the entities classified. His view that there are divergent and equally valid descriptions of nature opposes a philosophical understanding of science in which nature is given the appearance of falling into unique, hierarchical classes. Deconstructing the multiple classificatory choices for biological taxa, he stresses that the disposition of disorder in the natural world is its very characteristic. Because of the inherent pluralistic character of nature, there are equally good reasons for drawing divergent distinctions between biological entities.

In support of this pluralist position, the previous analysis of odour classifications illustrated the underlying disunity that is reflected by the existence of co-existing classifications of odours and odoriferous materials. This disunity, it became clear, was built on two aspects, namely, on the one hand, the various material and sensory dimensions of odours classified and, on the other hand, different ways of knowing and working with these materials. The different criteria of odour classification, although each relying on natural features of the grouped materials, diverged to an extent which made a uniquely comprehensive classification of odours not only impossible but, given the variety of materials, practices and scientific interests involved in their investigation, undesirable.

On this account, odours form natural kinds in two significant ways. First, odour as an umbrella term for the many phenomena of smells and smell perception present us with a general category of a natural kind. Opening up diverging directions of research into the material conditions underlying biological processes and sensory qualities, odours present us with many ways in which nature and what counts as natural can be explored and defined. Second, types of odour quality as a more specific category of a natural kind showed that taxonomic diversity in classification practices is not simply a matter of subjectivity and flawed scientifically ‘pre-mature’ classifications, but it often reflects the complex nature of the materials. The link between odours and their materials is too complex and interconnected to be divided in a unique comprehensive way. And, considering the multidimensionality of odours and their relevance to many branches of research, why should scientists and philosophers of science work with a restrictive notion of natural and natural kinds when a pluralist perspective accommodates both the nature of a phenomenon and its associated classificatory practices better?

Analysis of the various classificatory practices surrounding such a promiscuous phenomenon, I showed, aids in understanding the development of scientific objects and guards against a limited and reductive perspective on scientific reality. It also shows that the history of these practices is not simply history, left on a shelf. For these reasons, and in order to understand nature and the scientific reality surrounding the investigation of nature, it is the plurality of practices and the multidimensionality of the phenomena, rather than restrictive 'armchair' criteria of natural kinds, that should serve as a basis for investigating underlying and relevant demarcations and groups in nature. The character of odour materials, in a (mis)quotation of Shakespeare, can thus perhaps be summarised as being "[a] little more than kin, and less than kind".[212]

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[212] Shakespeare, William: Hamlet. Act 1, scene 2, 64-67. In: *Complete Works. By William Shakespeare. The RSC Shakespeare.* Ed. by B. Jonathan and E. Rasmussen (2007). New York: Modern Library.

Chapter 3

A Pluralist Approach to Extension: The Role of Materiality in Scientific Practice for the Reference of Natural Kind Terms[213]

1 Theories of Meaning and the Reference of Natural Kind Terms

This chapter argues for a different outlook on the concept of extension, especially for the reference of general terms in scientific practice. Scientific realist interpretations of the two predominant theories of meaning, namely Descriptivism and the Causal Theory, contend that a stable cluster of descriptions or an initial baptism fixes the extension of a general term such as a natural kind term. These views, in which the meaning of general terms is presented as monosemantic and the reference as stable, homogeneous, and unchangeable, do not reflect the various practices involved in the investigation of research materials and the related application of general terms in scientific practice. By drawing on the taxonomic diversity of structure-based classifications in chemical databases, this chapter illustrates the limited utility of such a concept of extension. Research materials often exhibit a plurality of material dimensions that, within different research contexts, allow for various and often equally significant taxonomic demarcations. In light of this, the extension of a general term cannot be uniquely determined by a supposedly independent nature of the referent but is relative to the context of the model under which the materials are investigated. The significance and plurality of the model context, I claim, needs to be mirrored in an account of meaning that is adequate to reflect scientific reality. The aim of this chapter, therefore, is to present an alternative perspective on the concept of extension able to accommodate the diverse material practices that determine the application of general terms in science.

In the following I present a brief overview of the two main theories of meaning and explain why each falls short of explaining the application of scientific terms.

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[213] An earlier and shorter version of this chapter is published as: Barwich, Ann-Sophie (2013): A Pluralist Approach to Extension: The Role of Materiality in Scientific Practice for the Reference of Natural Kind Terms. *Biological Theory* 7(2), 100-108. URL=< http://link.springer.com/article/10.1007/s13752-012-0083-x>

The two predominant theories, Descriptivism and the Causal Theory, introduce general accounts of reference by explaining how terms get attached to things in the world. Reference is thus considered to be a two-part relation between terms and objects in the world.[214] Descriptivism holds that terms have an associated descriptive content and the referents of a term are those objects that fit this description.[215] By contrast, the Causal Theory maintains that reference is fixed by an initial baptism and transferred by a causal chain of communication.[216]

Of particular concern for advocates of both theories are so-called "natural kind terms". Natural kind terms are terms assigned to groups of objects sharing specific underlying features that allow for generalisations and inferences about the nature of these objects and their interconnections. Although the subject of natural kinds has been discussed extensively, no general consensus about their nature has been reached.[217] Debate about the ontology underlying kind membership presents an image of conceptual diversity, ranging from traditionally essentialist[218] towards pluralistic positions.[219] For the purposes of this chapter I cannot review the ontological aspects of natural kinds but, rather, will focus on the possible applications of natural kind terms in and for scientific practice.

The existence of natural kinds is of importance to the philosophy of science when it comes to arguments about whether our classifications reflect real distinctions in nature or merely offer useful taxonomic tools that may represent conventional demarcations at most. As part of the wider debate surrounding issues of scientific realism, comprising a variety of positions that concern the existence of entities and processes described by scientific theories, natural kinds are supposed to illuminate the extent to which scientific concepts might explore a language-independent reality.

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[214] Bloor, David (2005): Toward a sociology of epistemic things. *Perspect Sci* 13, 286.

[215] Searle, John R. (1958): Proper names. *Mind* 67,166-173; Searle, John R. (1983): *Intentionality: an essay in the philosophy of mind.* Cambridge: Cambridge University Press.

[216] Putnam, Hilary (1975): The meaning of ''meaning''. *Minnesota Studies in the philosophy of science. Lang Mind Knowl* 7, 131-193; Kripke, Saul (1980): *Naming and necessity.* Cambridge M.A.: Harvard University Press.

[217] Riggs, P.J. (Ed.) (1996): *Natural kinds, laws of nature and scientific methodology.* Dordrecht: Kluwer.

[218] Ellis, Brian D. (2001): *Scientific essentialism.* Cambridge: Cambridge University Press; Ellis, Brian D. (2002): *The philosophy of nature: a guide to the new essentialism.* Queens: McGill University Press; Devitt, Michael (2008): Resurrecting biological essentialism. *Philos Sci* 75, 344-382.

[219] Kitcher, Philip (1984): Species. *Philos Sci* 51, 308-333; Dupré, John (1993): *The Disorder of Things. Metaphysical Foundations for the Disunity of Science.* Cambridge M.A.: Harvard University Press.

For natural kind terms, the question of realism is how it is possible to address such a language independent reality, meaning what particular features of an entity should be recognised as inherently natural and determinant of its nature, e.g. its structural constitution, its causal role or its temporal persistence and unchangeability. The assignment of a referent to a term based on these features is supposed to reflect how linguistic practices relate to the structure of the world and the entities it includes.[220] A wide range of arguments in this debate can thus be subsumed under the question: what determines whether a term properly denotes?

Proponents of Descriptivism argue that definite descriptions or a cluster of descriptions constitute the definition of a term, which determines its reference. This definition governs the correct use of a term within a language community. Such a definition might either directly address observable features of an object or, in the case of terms that depend on the theoretical framework in which they are embedded, reflect a term's definition within its specific theoretical context.[221] A description of a bus, for instance, can be "a vehicle for public transport", or the definition of an electron, "a negatively charged subatomic particle".

Problems with this theory fall into two categories. One problem involves the possibility of theory change that, for theoretical terms, implies a change of meaning.[222] If a theoretical term, however, is supposed to pick out natural kinds, these must be theory independent to a certain degree. Another problem concerns the contingency of descriptive features. This contingency is twofold. Not every description, on the one hand, picks out the referent; some entities may lack certain descriptive features or may not share the same cluster of properties while still being assigned kinship as, for example, in the case of biological species.[223] Positions can vary depending on whether conjunctive or disjunctive property clusters determine kind membership. On the other hand, descriptions can be too unspecific. It is possible to discover entities that

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[220] Psillos, Stathis (2012): Causal descriptivism and the reference of theoretical terms. In: *Perception, realism, and the problem of reference.* Ed. by A. Raftopoulos and P. Machamer. Cambridge: Cambridge University Press, 212-238.

[221] Barnes, Barry (1982): On the extensions of concepts and the growth of knowledge. *Sociol Rev* 30, 23-44.

[222] Feyerabend, Paul K. (1962): Explanation, reduction, and empiricism. In: *Scientific explanation, space, and time.* Ed. by H. Feigl and G. Maxwell. Minneapolis: University of Minnesota Press, 28-97; Kuhn, Thomas (1970[1962]): *The Structure of Scientific Revolutions.* 2nd Edition. Chicago: University of Chicago Press; Psillos (2012): *Causal Descriptivism*.

[223] Ereshefsky, Marc (2001): *The poverty of the Linnaean hierarchy: a philosophical study of biological taxonomy.* Cambridge: Cambridge University Press.

correspond to the same cluster of descriptions without necessarily being members of the same kind, as in the controversial case of jade. There are two substances that fall under the term “jade”, nephrite (having the formula $Ca_2(Mg,Fe)_5Si_8O_{22}(OH)_2$) and jadeite (having the formula $NaAl(SiO_3)_2$). What is curious about this case is that although these substances differ in their chemical composition, they resemble each other very closely in their observable features, a specific greenish colour and the particular hardness of the stones. In fact, the decision whether the reference of the term ‘‘jade’’ was sufficiently determined by these superficial features, including both substances, or needed to further include the underlying chemical composition, possibly restricting the term jade to nephrite, ended up being a matter of considerable debate.[224] This example illustrates a possible infinite regress of specification: in order to restrict the extension of a term to natural kinds only, additional descriptions of features may be required as soon as similar nominal kinds are discovered. Otherwise a more heterogeneous extension has to be accepted.[225] For these reasons, Descriptivism, if used within the essentialist tradition of natural kinds, has been heavily attacked as unable to provide a term with stable reference and homogeneous extension.

In response to the problems of Descriptivism, proponents of the Causal Theory contend that the referent of a term is assigned by an act of naming, and that reference is further transmitted by other speakers within a causal chain of communication that reaches back to the original baptism.[226] An advantage of this position is that it allows for reference to the same entities across different theoretical frameworks.[227] Nonetheless, the proposed direct relation between a term and a referent, unmediated by a concept, has been called into question. Although an act of baptism explains the reference of proper names to individuals, it still requires further criteria for the reference of natural kind terms. In order to explain how natural kind terms pick out entities that form natural kinds, it needs to be determined whereby certain entities are referred to as being members of the same natural kind. Reference to natural kinds thus requires a form of “same essence relation”, and every instance that exhibits

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[224] LaPorte, Joseph (2004): *Natural kinds and conceptual change.* Cambridge: Cambridge University Press, 94-99.

[225] Barnes (1982): *Extensions of concepts*, 25f.; LaPorte (2004)*: Natural Kinds*, 66f.

[226] Kripke (1972): *Naming and Necessity*, 54, 59 footnote 22, 77, 93, 96 footnote 42, 109 footnote 51.

[227] Psillos (2012): *Causal Descriptivism*, 212f.

such a same essence relation is a member of a kind referred to by a particular natural kind term.

In reply to this, Putnam proposed four different features to describe the meaning of natural kind terms, viz., the syntactic marker, the semantic marker, the stereotype, and the extension of a term. His distinction between the stereotype and the extension of a term provides a useful suggestion to explain the relevance of the sameness relation in picking out natural kinds and its relation to the meaning of natural kind terms. The stereotype consists of descriptions that reflect the speaker's competence in the use of a term, and these descriptions are transitional in the causal chain of communication. The extension is the set of referents of a term. These referents were introduced by a baptismal act, and to guarantee that the referents are members of the same natural kind, the extension of a term is determined by a description of the referents' nature or essence, i.e. a selection of intrinsic and exclusive features of these referents.[228]

Recent philosophical discussion, derived from this account, identifies the same essence relation that holds between members of the same natural kind with the microstructure or some other theoretically significant aspect.[229] A consequence of this position is that the reference of a natural kind term is determined by an identity relation necessary a posteriori, such as "water is H_2O" or "light is a stream of photons".[230]

Critics of this position contend two serious flaws. First, many examples have been provided to highlight the limits of the associated essentialist position, particularly with respect to biological entities and other categories in the life sciences. Attempts to determine unambiguous essences for biological species not only fail to distinguish between species as taxonomic and evolutionary units,[231] but also fail to acknowledge the variety of classification practices and the ontological diversity of biological entities.[232] Second, the selection of same essence relations often relies on the theoretical framework in which scientific

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[228] Putnam (1975): *The meaning of meaning*, 191.

[229] Kripke (1980): *Naming and Necessity*; Ellis (2001): *Scientific Essentialism*; Ellis (2002): *New Essentialism*; Psillos (2012): *Causal Descriptivism*.

[230] Putnam (1975): *The meaning of meaning*, 140-142; Kripke (1972): *Naming and Necessity*, 98f., 106, 129-133.

[231] Dupré, John (2002b): In Defense of Classification. In: *Humans and Other Animals*. Clarendon Press, 81-100. Also published in *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 32(2) June 2001, 203-219.

[232] Dupré (1993): *Disorder of Things*; Ereshefsky (2001): *Linnaean hierarchy*.

entities are investigated. Many entities, in fact, exhibit several equally significant features that allow for different groupings. Whether, for instance, chlorine and its isotopes are grouped into one or different kinds, according to either their electronic or nuclear structure, depends on the specific context.[233] On this account, undifferentiated talk of ‘‘microstructure’’ has been criticised. With increasing knowledge about chemical structures, many more different structural aspects relevant for chemical classifications became apparent.[234]

Without any description of the referent’s nature, however, the utility of the Causal Theory for a realist position is limited. If the reference of terms was to be described only by virtue of a baptismal act and a causal chain of communication, then even terms that fail to refer such as phlogiston can be argued to refer by pointing out that “phlogisticating” and “dephlogisticating” agents in Priestley’s ontology can be thought to correspond with what we call “reducing” and “oxidising agents” today.[235]

In both theories of meaning the referential relation between a term and the objects that fall under it mainly concerns the question of how to find the right criteria to identify the referents. For a realist position, these criteria, if based on the underlying nature of the referent, provide a term with a stable, continuous, and homogeneous extension.[236] In the following, however, I will examine three aspects of mutability, integral to scientific practice, that render this position problematic.

2 The Application of General Terms and Mutability in Research Practice

Realism about scientific entities draws on their materiality. Its material character determines why an entity has certain properties and behaves as it does. In the

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[233] Mellor, D.H. (1977): Natural Kinds. *The British Journal for the Philosophy of Science* 28(4), 303f.; Barnes (1982): *Extensions of concepts*, 28f.

[234] Needham, Paul (2002): The discovery that water is H2O. *International Studies in the Philosophy of Science* 16 (3), 205-226.

[235] Kitcher, Philip (1993): *The Advancement of Science: Science without Legend, Objectivity without Illusions: Science without Legend, Objectivity without Illusions.* Oxford: Oxford University Press, 100f.; Ladyman, James (2009): Structural realism versus standard scientific realism: the case of phlogiston and dephlogisticated air. *Synthese* 180, 87-101.

[236] Concerning a combination of Causal Theory and Descriptivism, so-called Causal Descriptivism, it will, I think, will face the same problem for the concept of extension that I criticise in the other two accounts if it is rigidly conceived as unchangeable, homogeneous, and stable.

course of scientific progress various techniques, models, and instruments have been developed to explore, manipulate, and trace the materiality of scientific entities. Failure to describe science in terms of stable conditions of knowledge production or logical relations between a concept and its former application has lately turned the attention of philosophers and historians of science towards the importance of these research practices.[237] As a consequence, discussions of scientific realism increasingly addressed the different aspects of mutability underlying research practice, namely the mutability of nature, the mutability of scientific development, and the mutability of scientific judgment.

First, concerning the mutability of nature, nature does not consist of timeless and stable building blocks. Particularly in the biological world things are rather messy. A number of processes such as mutation, recombination, and random drift prevent species from exhibiting any traits that are both universal and unique.[238] Biological entities continuously develop, evolve, adapt, mix, separate, etc., and features that once were abnormal may become the norm. For this reason, biological entities, rather than corresponding to a fixed standard, form ‘‘moving targets’’ of investigation. This led to the suggestion that the character of biological entities is processual and changeable.[239] Even if, as some philosophers such as David Hull argue, it is disputable whether species form genuine natural kinds (and not, for instance, individuals),[240] the species category nevertheless has always been a fundamental concept in biology; the lack of neat essences did not render ‘‘species’’ irrelevant for classification purposes. To the contrary, their overlapping and contingent character helped to frame relevant questions about the diversity of natural processes and demarcations. The problem for any realist trying to establish a stable referential relation for a species term thus appears to be the changeable and overlapping

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[237] Hacking, Ian (1983): *Representing and intervening: introductory topics in the philosophy of natural science.* Cambridge: Cambridge University Press; Rheinberger, Hans-Jörg (1997): *Toward a history of epistemic things: synthesizing proteins in the test tube.* Stanford: Stanford University Press; Morgan, Mary and Morrison, Margaret (Eds.) (1999): *Models As mediators: perspectives on natural and social science.* Cambridge: Cambridge University Press; Radder, Hans (Ed.) (2003): *The philosophy of scientific experimentation.* Pittsburgh: Pittsburgh University Press; Klein, Ursula and Lefèvre, Wolfgang (2007): *Materials in eighteenth-century science: a historical ontology.* Cambridge M.A.: MIT Press.

[238] Hull, David (1965): The effect of essentialism on taxonomy—two thousand years of stasis (I). *Brit J Philos Sci* 15, 314-326; Ereshefsky (2001): Linnean poverty; Ereshefsky, Marc (2007a): Species, taxonomy, and systematics. In: *Philosophy of biology.* Ed. by D.M. Gabbav, P. Thaggard and J. Woods. Amsterdam: Elsevier, 403-428.

[239] Ereshefsky, Marc (2007b): Foundational issues concerning taxa and taxon names. *Syst Biol* 56, 295-301.

[240] Hull, David (1976): Are Species Really Individuals? *Systematic Zoology* 25(2), 174-191.

nature of the referents. Reference to species, lacking not only intrinsic essences but even stable descriptive features, is not to be fixed by specific irreversible criteria.

Second, considering the mutability of scientific development, research objects are rarely well defined and stable, and the discovery and selection of relevant features is often what is at stake. In light of the ongoing production of scientific knowledge, any assignment of a concept-object relation, even a theoretical relation of a concept to other concepts, is subject to constant revision. Unmediated reference, as the Causal Theory proposed in answer to this problem, does not accurately reflect research practice. Quite to the contrary, especially in laboratory practice the investigation of materials requires mediation through models. These models provide concepts regulating under what conditions the objects of inquiry are manipulated and, further, how their materiality is defined; for instance, ‘‘[h]andling the virus as a gene, that is, on the model of a gene, can take the experimental form of trying to mutate the building blocks of its nucleic acids. It depends of course on what a gene is understood to be at a particular point in time’’.[241] Scientific concepts in their empirical application are therefore not merely representational but constitutive; they provide tools to outline specific expectations and questions in order to address the materials and to form them into particular objects of scientific inquiry. The integration of such objects into experimental systems, sometimes across different but related fields, further requires scientific concepts to be to some extent vague in their descriptive content.

Pace the Causal Theory, it is clear that the reference of scientific terms in research practice is usually mediated by concepts. For this reason, reference to ‘‘essences’’ is not context-insensitive, as the selection of relevant features is determined by the concept under which a specific object is modelled. Quite often the same domain of materials can be investigated from various perspectives across related conceptual systems, leading to different groupings. Particularly in the life sciences, subdisciplines often overlap with respect to a common domain of materials studied (bacteriology; virology; botany; mycology; zoology), employing shared methods (genetics; immunology; ecology; molecular biology; physiology) and frequently having similar applications

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[241] Rheinberger, Hans-Jörg (2005): A Reply to David Bloor: “Towards a Sociology of Epistemic Things”. *Perspectives on Science* 13(3), 408.

(medicine; agriculture).[242] Furthermore, research concepts are clear-cut only on paper, but prove to be more dynamic in their empirical application. This dynamism is twofold; it not only concerns diachronic changes in the content of concepts but also synchronic differences. Reconciling disciplinary specialisation with the importance of interdisciplinary links, the definition of a scientific concept is inevitably fuzzy and context-sensitive. A rigid cluster of descriptions is, in fact, not always desirable. This conceptual overlap is a consequence of the multidimensional character of materials, which I will discuss in more detail in the following section.

The final point concerns the mutability of scientific judgment that correlates a concept with its referents. Descriptivism, to begin with, cannot avoid this problem. If the referent is fixed by fitting specific definite descriptions, then a change in these descriptions or the discovery that those descriptions were erroneously assigned suffices to terminate the correlation between a concept and its instances. Within the Causal Theory this problem seemed resolved. Reference was fixed by a baptismal act, assigning a term to a paradigmatic instance, and a causal chain of communication further transmits this referential relation. This strategy promised to avoid the contingencies of meaning change by eliminating mediating concepts and descriptions from reference and substituting it with a baptismal act.

By drawing on reference to paradigmatic instances, the Causal Theory provided an answer to the problem of conceptual change. Yet, this act of reference to particular specimens too is not generally incorrigible, even in the case of relatively stable concepts. An example of this is the concept of ‘‘mutation’’ introduced by Hugo de Vries, who investigated mutable periods in plants resulting in species variation. The paradigmatic plant he used for breeding experiments was the evening primrose (*Oenothera Lamarckiana*). De Vries’ discovery was the occurrence of occasional phenotypic differences in offspring that were passed on to further generations, creating a new species. The idea of hereditary changes was correct; the observed phenomena of the specimen, however, were not. Many variations in the evening primrose, as known today, are caused by polyploidy, i.e. aberrant chromosomal segregations, instead of

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[242] Temmerman, Rita (2000): *Towards new ways of terminology description: the sociocognitive approach.* Amsterdam: Benjamins, 47.

changes in genes as units of heredity.[243] Despite the abandonment of the initial referent and a lack of stability in extension, the concept of “mutation”, however, did not become meaningless or vacuous.

In general comparison of the two theories of meaning, Descriptivism and Causal Theory, the essential thesis for a realist account is that reference is determined by the independent nature of the referent that allows for either specific stable descriptions or reference to an intrinsic feature of the referent. Upon closer inspection the application of empirical terms in scientific practice exhibits a dynamic character that is not compatible with the standard realist accounts of either theory of meaning. The reason for this, I argue in the following, is grounded in the very materiality of research objects. Research materials exhibit a plurality of material dimensions that, within different research contexts, allow for various taxonomic demarcations and conceptual distinctions. This plurality, it will be shown, is in conflict with the previous two theories of meaning that provided a monosemic account of general terms and justifies the need for an alternative polysemic perspective on meaning and extension.

3 The Plurality of Material Dimensions for Classification Purposes

Extension has been characterised in terms of ‘‘the same sort of objects’’ in previous accounts. For reference to natural kinds, this sameness relation is usually defined based on shared structural features across the members of a kind. These features, independent of human cognition and not relative to the context of experimentation, were supposed to provide terms with a stable reference for a realist interpretation. Non-realist philosophers, however, criticise this position by arguing that the reference of scientific terms is neither atemporal nor context-insensitive. The latter thus contend that direct and unmediated reference is not possible and that scientific terms are inevitably entrenched within a specific theoretical framework that is not necessarily true but at best empirically adequate.[244]

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[243] de Vries, Hugo (1909): *The mutation theory: experiments and observations on the origin of species in the vegetable kingdom.* Chicago: Open Court; Barnes (1982): *Extensions of concepts*; Hull, David (1990): *Science as a process: an evolutionary account of the social and conceptual development of science.* Chicago: University of Chicago Press.

[244] van Fraassen, Bas (1980): *The Scientific Image.* Oxford: Oxford University Press.

Exploring the empirical practices of science, the mutability of nature, scientific development, and scientific judgment seems often to favour a non-realist view. Nonetheless, the problematic cases illustrated above might also lead to a different conclusion. The problem for a realist position is not the presence of mutability and contextuality in scientific practice, but its denial. A number of philosophers have already addressed this issue, advocating a more modest and pluralist view of science.[245] A pluralistic ontology such as John Dupré's ‘‘promiscuous realism'' in his *The Disorder of Things* (1993), for instance, states that there are numerous and equally legitimate ways to classify the world. Rather than methodological constraints, pluralism is a result of nature, which is too complex and interconnected to be divided in a unique comprehensive way. On this account, there are real distinctions in nature yet there is no unique set of such distinctions, but rather overlapping classes that justify the need for different classifications, which in turn signify different relations serving different purposes.[246] Although such a position might be considered as minimally realist and close to a non-realist perspective, it nonetheless accommodates two important aspects integral to science: the previously illustrated mutability and the complexity of partially related classifications. From such a minimal realist point of view, these two aspects, mutability and complexity, are a result of the multifaceted nature of materials and the variety of technologies applied to them.

One way to demonstrate the multidimensionality of research materials and the related technologies involved in their investigation is to take a look at scientific databases comprising largely the same domain of materials. The function of such databases is to organise a large quantity of research materials into meaningful groups so that multiple sources of data can be accumulated and compared. Key databases are mainly web-based and continuously updated. General databases for chemical materials include, for instance, SciFinder,[247]

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[245] Hacking (1983): *Representing and Intervening*; Kitcher (1993): *Advancement of Science*; Cartwright, Nancy (1999): *The dappled world: a study of the boundaries of science*. Cambridge: Cambridge University Press; Giere, Ronald (2006): *Scientific Perspectivism. Science and Its Conceptual Foundations Series.* Chicago: University of Chicago Press.

[246] Dupré (1993): *Disorder of Things*; Dupré, John (2002a): *Humans and Other Animals.* Oxford: Clarendon Press.

[247] SciFinder (2013) *American Chemical Society.*
URL=<https://scifinder.cas.org/scifinder/login.jsf?TYPE=33554433&REA LMOID=06-b7b15cf0-642b-1005-963a-830c809fff21&GUID=&SM AUTHREASON=0&METHOD=GET&SMAGENTNAME=-SM-VS R14pTQX5XGubkDwkogX2Mmb%2bsNTuTuF7B1Flcl1uUn9xeAD a8ECKxgk%2bA2MJVP&TARGET=-SM-http%3a%2f%2fscifinder %2ecas%2eorg%3a443%2fscifinder%2f

Reaxys (formerly Beilstein),[248] Science of Synthesis,[249] BIOSIS,[250] and the Chemical Entities of Biological Interest (ChEBI).[251] Currently these databases include over 8 million molecular structures and provide an indispensable resource for research in chemistry and related disciplines such as biology and life sciences, medical studies and materials science, thus further deepening interdisciplinary links and demands for data sharing. A recent analysis of the ontology in one of the largest chemical databases, ChEBI (Chemical Entities of Biological Interest), exemplifies the variety of features used for the classification of chemical materials. Hastings et al. (2012)[252] distinguish between structure-based and non-structure based classifications. The latter involve different categories such as the origin of materials – whether they are of a natural or synthetic origin – and their function or activity in a biochemical context. A lot of materials in this context have a similar role, yet do not necessarily share common structural features, for instance in the case of ‘‘analgesic’’ compounds.[253]

Structure-based classifications likewise refer to different structural aspects. The materials are arranged according to five categories, namely according to specific parts (an atom group or the scaffolding of a molecule), basic chemical properties (such as charge, molecular weight), topological features (presence of rings or chains), mechanical connectivity and shape, and the structural formulae. These different categories can but need not appear in combination. In fact, many complex molecules can fall under several classes, and the selection of the feature most relevant for defining a group is embedded within the experimental system in which the material is investigated. In addition to these different structural features under which chemical materials can be arranged, the definition of such chemical groups can be subject to stricter or vaguer

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[248] Reaxys (formerly Beilstein) (2013) *Elsevier.* URL=< http://www.elsevier.com/online-tools/reaxys>

[249] Science of Synthesis 4.0 (2013) *Thieme Chemistry.* URL=< http://thieme-chemistry.com/en/formate/referenzwerke/science-of-synthesis.html>

[250] BIOSIS (Biosis Life Sciences database) (2011) *Thomson Reuters.* URL=< http://wokinfo.com/media/pdf/BIOSIS_FS.pdf
a-z/biosis/.

[251] ChEBI (Chemical Entities of Biological Interest) (2013) *European Molecular Biology Laboratory-EBI.* URL=< http://www.ebi.ac.uk/chebi/>

[252] Hastings, Janna; Magka, Despoina; Batchelor, Colin; Duan, Lian; Stevens, Robert; Ennis, Marcus and Steinbeck, Christoph (2012): Structure-based classification and ontology in chemistry. *Journal of cheminformatics* 4(8). doi:10.1186/1758-2946-4-8

[253] Objections to ‘‘analgesic’’ as a natural kind term might be answered with reference to Putnam for whom ‘‘acid’’ constituted a natural kind term. Putnam, Hilary (1977): Is semantics possible? In: *Naming, necessity and natural kinds.* Ed. by P. Schwartz. Ithaca, New York: Cornell University Press, 105.

boundaries. Whether groups such as hydrocarbons do or do not include derivatives such as chlorohydrocarbons depends on the context in which these categories are applied.[254]

This variety of structural features reflects the multidimensionality of materials under different research perspectives. Even within the same field, the significance of structural features strongly depends on the model chosen. From the perspective of a fragrance chemist, for example, structure-odour relations of odorants are addressed either by homology, olfactophore, or receptor models. Homology models are essentially based on the assumption that the odour of a volatile compound is determined by its stereoelectronic structure (Fig. 1).[255] This approach is defined by systematic experimental modifications of a paradigmatic compound with selected molecular parameters. Olfactophore models work with characteristic conformational elements assumed to underlie odour recognition, namely hydrophobic groups, H-bond donors and acceptors. Like olfactophore models, receptor models are based on the spatial configuration of particular molecular groups. For this reason, compounds are modelled and tested with respect to the complementary binding sites of the olfactory receptors. Nonetheless, olfactophore and receptor models of odours are not strictly identical. Olfactory receptors are broadly tuned and combinatorial, meaning they can receive a wider range of odours and some odorants can be identified by different receptors. As a result, olfactophore models may partially overlap with receptor models yet present a wider and more combinatorial range of significant key features for the design of new odorants.[256]

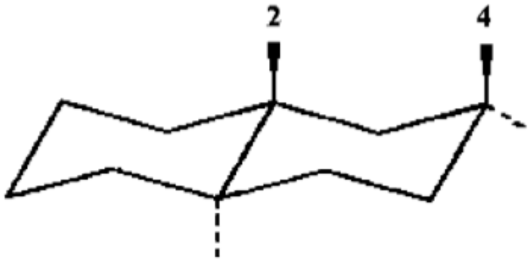

Fig. 1 Triaxial rule for ambergris. Ohloff's rule defines ambergris odorants by the presence of a decalin structure, i.e. a bicyclic compound, and the requirement that the atom groups in the positions 2, 4, and 1 (marked by a dotted line opposite 2) be axial. Ohloff (1971): *Decalin Ring Compounds*.

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[254] Hastings et al. (2012): *Structure-based classification*.

[255] Ohloff, Günther (1971): Relationship between Odor Sensation and Stereochemistry of Decalin Ring Compounds. In: *Gustation and Olfaction.* Ed. by G. Ohloff and A.F. Thomas. New York: Academic Press, 118-183.

[256] Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and chemistry: the molecular world of odors.* Wiley-VCH, 117-127.

A striking feature of this situation is that the chosen model contexts generate material practices that lead to different material demarcations. As has been illustrated in the case of olfactory models, the selection of molecular features is deeply entrenched in different experimental practices: chemical substitution patterns, statistical homology between a range of known odorants, and receptor expression patterns. Such model contexts are determined by the practical entrenchment of materials on one hand, and the technologies and conceptual implications that shape these materials on the other. The same domain of materials can thus be carved up in different ways, depending on the model and related experimental application chosen. To meet this plurality of model contexts, and for a better understanding of the application of empirical terms in science a multidimensional perspective on the meaning of kind terms is needed.

4 Open Extension and Encyclopaedic Meaning

The previous two sections illustrated the role played by materiality in the conceptualisation of scientific objects under general terms, presenting an image of taxonomic diversity. This diversity is grounded in the multiple dimensions of the materials and also in the varying research interests involved in working with these materials. These two aspects are, in fact, intertwined and constitute three different dimensions that underlie taxonomic diversity. First, there is taxonomic diversity over time, which concerns the general growth of knowledge and, more specifically, the development of new technologies and experimental strategies that lead to different taxonomic distinctions. Second, there are differences in taxonomic practices across different disciplines and social groups that often rely on different practical interests in the materials explored. And, finally, one and the same scientific community might work with different assumptions about what features are relevant and significant in the classification of substantially the same domain of objects.[257]

For the dominant accounts of meaning, Descriptivism and Causal Theory, this image of taxonomic diversity poses a problem. By drawing on a stable and independent nature of the referent, i.e. a nature not relative to the context of experimentation, a standard realist interpretation of these two theories does not

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[257] Klein and Lefèvre (2007): *Materials*, 74f.

exhaustively accommodate the scientific practices dealing with the materials in question. On both accounts, the extension of a term presents itself as ‘‘closed’’ in the sense that the criteria for determining the sameness relation between members of a kind, either in terms of a stable cluster of descriptions or some intrinsic feature, are incorrigible and irreversible (fig 2 and 3).[258] Such a view, however, is limited in its ability to accommodate the multidimensionality of materials within different research practices and interests. Considering the previous example of a chemical database, a general term can comprise miscellaneous conceptualisations that may either form co-extensive, overlapping, and even disjoint classes of materials. For an account of the reference of general terms in research practice, possibly identifying natural kinds, the concept of extension thus needs to be adjusted in order to meet the dynamic and polysemic character of scientific terms.

Figure 1 Description theory

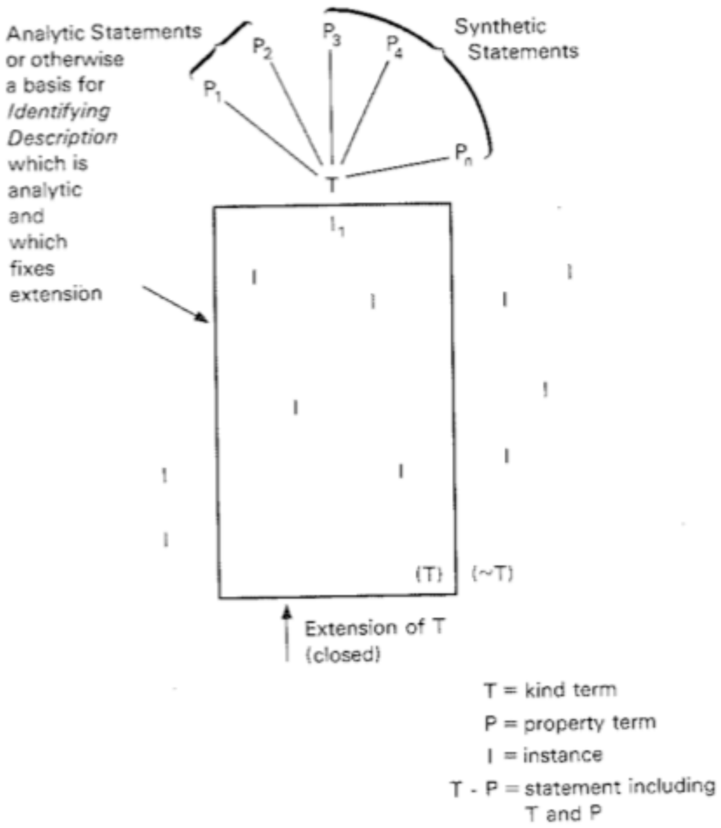

Fig. 2 Description Theory. The extension of a term is determined by a closed (incorrigible) set of descriptions. Barnes (1982): *Extensions of concepts*, 39.

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[258] Barnes (1982): *Extensions of concepts*.

Figure 2 Realist theory

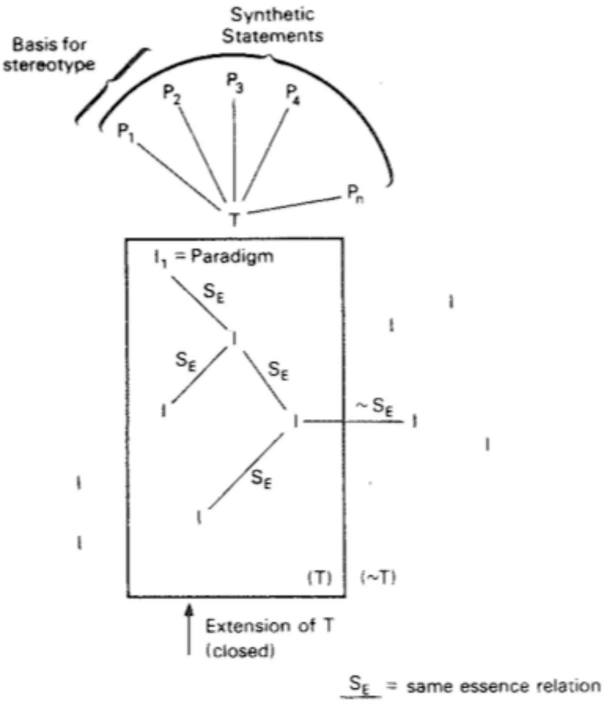

Fig. 3 Causal Theory. The extension of a term is determined by a closed (incorrigible) definition of an essential feature (e.g. microstructure). Barnes (1982): *Extensions of concepts*, 40.

Instead of focussing on the problematic idea of a conceptually independent nature of the referent, I suggest adopting Barry Barnes' revisionary account of extension. Barnes proposed to define the extension of a term in relation to the judgment of what constitutes the sameness relation.[259] He makes the fundamental point that scientific judgment is revisable. As result, the criteria employed for fixing the reference of a term in previous usage need not be the same for determining the reference of a term in later application (fig 4). Barnes' account leaves furthermore open whether these criteria address particular structural features, a cluster of descriptions, or operational hypotheses of measurement. The judgment about what constitutes the sameness relation of scientifically significant kinds needs to reflect the particular scientific practices that surround the investigation of research materials and must thereby be assessed on a case-by-case basis.

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[259] Barnes (1982): *Extensions of concepts*, 33-38.

Figure 3 Finitist semantics

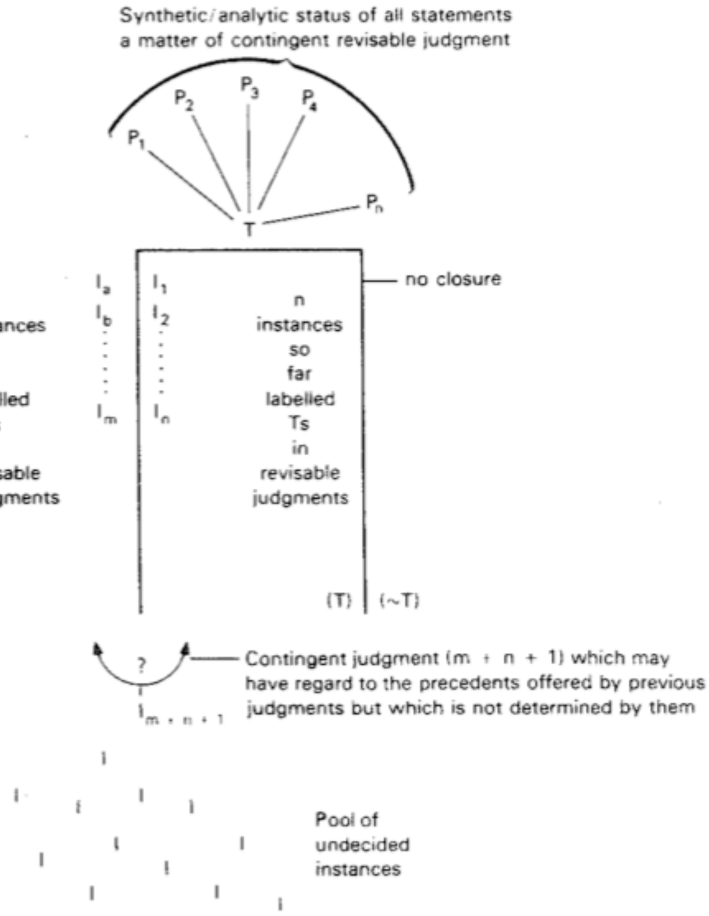

Fig. 4 Finitist semantics. The extension of a term is determined by an open (corrigible) definition (e.g. descriptions, microstructure, operational form of measurement, etc). Barnes (1982): *Extensions of concepts*, 41.

The selection of the relevant sameness relation is not merely conventional but is also embedded in the material culture in which the investigated materials are defined as specific objects of research. Hans-Jörg Rheinberger nicely described different material cultures in research practice as experimental systems, which are "basic unit[s] of experimental activity combining local, technical, instrumental, institutional, social, and epistemic aspects."[260] The meaning of a term, I suggest along the lines of Barnes' account, is determined by the contextual application of a term such as its involvement in an experimental system. It is mediated by concepts embedded in model contexts and empirical settings in which the term is applied. These research contexts then inform the judgment of what constitutes a sameness relation. Being contingent and

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[260] Rheinberger (1997): *Epistemic Things*, 238. For a more historical analysis of the interaction of different material cultures in the disciplinary development of 18th-century chemistry see Klein and Lefèvre (2007): *Materials*.

contextual, this judgment is inevitably revisable. As a result, the extension of a term can change in parallel with the development of scientific hypotheses and the discovery of new features and material applications. In other words, the features consulted to fix the extension of a term are subject to a revisable judgment and depend on the research culture that works with and, through material intervention, often realises specific material features. Fixing reference by the application of a term thus renders the extension of a general term ''open'' and multidimensional.

An implication of this is the possibility of multiple meanings of a general term, subsuming co-extensive, overlapping, or even disjoint classes of referents according to the different criteria and models chosen. In his *Theory of Semiotics* (1979), Umberto Eco compared the application of the more contextual meanings that can fall under a general term with the application of codes, forming rules for different (combinatorial) semantic units.[261] Along these lines, I want to refer to the specific applications of general terms within specific research contexts as the rule meaning of a general term. A so-defined rule meaning describes the specific procedure that allows for generating specific classes, and governs their application in different empirical practices.

For an example of such different rule meanings forming meaningful related groups under the banner of a general term, consider the array of structurally diverse musk odorants.[262] As one of the most important fragrance ingredients, musks are well explored and thus serve as important classes for the investigation of structure-odour relations. Musk odorants fall within different families such as nitro, polycyclic, macrocyclic, linear, and dienone musks, and each family involves different structural features for their definition. Macrocylic musks, for instance, are mainly defined by topological features (ring structure with 14-18 members) and the number of a specific atom group (exactly one carbonyl or imino group), while nitro musks are mainly determined by a specific atom group (tert-alkyl group and either two nitrogen dioxides or one nitrogen dioxide and an alkoloxy group) and specific chemical properties (molecular

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[261] Eco, Umberto (1976): *A Theory of Semiotics.* Bloomington: Indiana University Press, 49f. Eco speaks of rules for generating of signs in communicative acts; this semiotic procedure resonates with the postulation of classes in a taxonomic system.

[262] Philosophical scepticism about treating odorants as natural kinds is nicely met by fragrance chemists' desire to classify odours into natural kinds, explicitly using this term with reference to the discussion about classification in the philosophy of science. See: Harper, Roland; Bate Smith, E.C. and Land, D.G. (1968): *Odour Description and Odour Classification. A Multidisciplinary Examination.* London: J. & A. Churchill LTD, 102.

weight below 300g/mol). These classifications are largely derived from homology models. In comparison, an olfactophore model of musk odorants in identifies two molecular fragments, one referring to a topological feature and one to specific molecular parts, namely an ‟H-bond acceptor symmetrically flanked by 2 Me or methylene groups” and, independently, 2 Me or methylene groups.[263] It is worth noting that all these classes have many exceptions, yet they provide basic rules and classes for the synthesis of musk odorants in fragrance chemistry.

What these different classes have in common is that they all are musk odorants, i.e. they all are materials having a musk odour. As a general term, ‟musk” thus refers to different classes of odorants, encompassing musk groups of different structurally meaningful relations. Similar to Wittgenstein's notion of family resemblance, ‟musks” are not defined by a unique, exhaustive definition but exhibit cross-cutting demarcations. Following this, the representation of the meaning of a general kind term such as musk resembles a spatial map more than a linear dictionary. A general term such as a natural kind term, I argue, again in accord with Eco's semiotics, exhibits a form of encyclopaedic meaning, by which is meant that a general term subsumes various conceptualisations of specific materials relative to the selected material dimensions and the domain of application.[264]

In comparison, and to further illustrate such an encyclopaedic map of meaning, similar cases occur within the analysis of the meaning of general vernacular terms in comparative linguistics. Although some words in different languages basically concern the ‘same matter', they nonetheless reveal different conceptual demarcations in comparison. Hjelmslev illustrated this with his example of the different translations of ‟wood” (Fig. 5).[265] For an (admittedly sketchy) comparison, one may compare the words for ‟wood” across different languages with concepts from different conceptual domains. The picture that emerges presents different distinctions, resulting in co-extensive {/skov/;/Wald/}, overlapping {/Holz/;/Wald/; /bois/} and disjoint concepts {/trae/;/skov/}.

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[263] Fráter, Georg; Bajgrowicz, Jerzy A. and Kraft, Philip (1998): Fragrance chemistry. *Tetrahedron* 54(27), 7641.

[264] Eco, Umberto (1984): *Semiotics and the philosophy of language.* Bloomington: Indiana University Press, 77.

[265] Hjelmslev, Louis (1961): *Prolegomena to a theory of language.* Madison, Wisconsin: University of Wisconsin Press, 54.

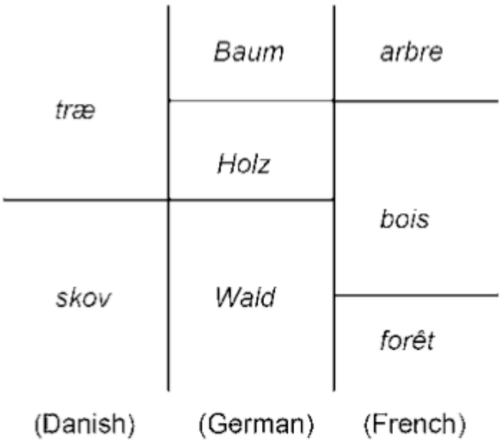

Fig 5 Different translations of the English term “wood” into Danish, German and French. Hjelmslev (1961): *Prolegomena*, 54.

The conception of general terms as encyclopaedic maps provides an alternative account to the previous standard theories of meaning. General terms describe a conglomerate of specific applications for a domain of materials that form its encyclopaedic meaning. The specific applications are determined by the criteria formed in the research context in which the materials are modelled. Such criteria can involve descriptions, operational hypotheses, structural features, and so on. Like Nancy Nersessian’s ‘‘meaning scheme’’ that specifically addresses the problem of meaning change and incommensurability within historical conceptual development,[266] the focus lies on the explanatory function of concepts in the process of knowledge production. Thus, this chapter’s outlook for understanding the reference of general terms including natural kind terms is not linked to a metaphysical understanding of scientific kinds or objects but is based on their methodological role, which in turn is determined by the model context and experimental systems in scientific practice.

In closing, I want to address what my proposed account of meaning and reference in this chapter adds to the general discussion on ‘meaning as use’. One of the issues associated with meaning as use is that what it is that applies as a rule to the different uses of a word need to be fully determinate. For the later Wittgenstein a rule, generating the meaning of a word through its conventional acceptance, is not a fixed all-encompassing notion describing an abstract entity under which suitable instances are accommodated. Rather, it is

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[266] Nersessian, Nancy (1984): *Faraday to Einstein: constructing meaning in scientific theories.* Dordrecht: Martinus Nijhoff Publishers, 134-161.

part of an activity, a language game that is of open-ended character.[267] Viewing scientific activities as a particular example of language games spurs enquiry into the character of rules that might be said to distinguish scientific language games from, let's say, politics, religion or poker. Philosophers of science advocating meaning as use, such as Nersessian, often addressed the nature of scientific terms and the problems of meaning change through the notions of explanation and conceptual change associated with theory development.

With respect to the increasing attention to modelling practices and material intervention, however, more emphasis needs to be directed at the relation between the modelling practices guiding the formation of scientific concepts and the associated material practices. The application of general terms in science, as I have shown, is governed by mediating concepts. The formation of these concepts, in turn, was further shown to be embedded in particular experimental contexts. To understand the meaning of a term through it use, therefore, requires sensitivity to the experimental context and the associated strategies for operating on the materials. These strategies can vary across different experimental contexts dealing with largely the same domain of materials. Furthermore, since these strategies take place in historical time, the rules governing the use of a term must be historicised, in the sense that these rules will not only develop over time but also give rise to other meanings when different experimental contexts fertilise each other. Fruitful philosophical analyses tracing the meaning of a general term in scientific practice thus require a notion of rules that goes beyond Wittgenstein's to accommodate the contextual and historical sensitivity to accommodate the flexibility of general terms. In addition to focus on theoretical frameworks, this contextuality needs to encompass more strongly the material practices involving instruments, experiments, techniques of measurement etc.

The expansive notion of meaning that I propose here facilitates the specifity with which some general terms are applied in diverse ways, such as in the case of musks. It also accommodates the historicity involved in generating different and/or related rule meanings of a general term. By allowing a heterogeneous and open extension, rather than a dyadic and determinate relation between a

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[267] Wittgenstein, Ludwig (2009[1953]): *Philosophical Investigations.* Trans. by G.E.M. Anscombe, P.M.S. Hacker and J. Schulte. Revised 4 Ed. Wiley & Sons.

term and its referents, it encompasses the multidimensionality of meaningful relations in which a term can be used.

It is also worth noting that the present account, by allowing a cluster of descriptions or a specific feature as a rule meaning of a term, does not necessarily conflict with the benefits of either Descriptivism or the Causal Theory. However, it goes beyond these theories by expanding the concept of extension for scientific terms. Accepting an open and revisable concept of extension, it can accommodate two central aspects of scientific practice, viz., meaning variance and cross-cutting classifications. As has been seen earlier in the case of a chemical database, meaning variance and cross-cutting classifications are based on the multidimensional character of materials, which allow for a comparable variety of material applications.

With this encyclopaedic account of meaning in hand, I want to close by briefly commenting on its position within the divide between scientific realism and anti-realism. Of course, such an account of meaning does not require a realist stance on scientific practice; it works equally well for an anti-realist. But it does provide an account under which a realist interpretation of scientific practice can be best accommodated by focussing more on the material practices in which the application of general terms and their mediating concepts are embedded. The present chapter emphasised the entrenchment of material practices and the relevance of mediating concepts in the classification of entities exhibiting scientifically meaningful relations. Of course, not every philosopher of science may want to accept this as a realist position. Nonetheless, I believe that any realism about science needs to take account of the actual activity and practices of research. Likewise, any theory of the meaning and reference of general terms in science must mirror the application of general terms in the investigation of research materials.

Accepting different aspects of mutability integral to scientific practice, namely the mutability of nature, scientific development, and scientific judgment, the question concerning scientific realism turns toward the relation between different model contexts and experimental practices for the classification of a specific domain of materials. In their actual scientific development, these relations reveal continuities as well as discontinuities that need to be examined on a case-by-case basis. In defending a realist stance, it is therefore important to review the role of materiality in these cases, and the ways in which different experimental practices visualise and realise different aspects of materials and form them into particular objects of study. The proposed multidimensional understanding of the application and meaning of general terms thus reflects the dynamic nature of research and does not present science as a finished business but, rather, as it is: a constantly developing field of knowledge.

PART II

MODEL THINKING
IN OLFACTION THEORY

“Start with the deepest mystery of smell.
No one knows how we do it.”
Chandler Burr (2002): *The Emperor of Scent*, 3.

Chapter 4

The Dissent of Scent: Contrasting Approaches to Define the Molecular Basis of Odour Perception

1 *The Scene of Inquiry:* Prevailing Issues in Olfaction Theory

Before the rise of synthetic chemistry at the end of the 19th century, smell appeared to be an enigmatic sense and was long thought to involve "some form of remote communication between the smelling object and our sense" or "action at a distance".[268] With growing insight into the imperceptible dimension of odoriferous materials after the advancements of chemical synthesis, evidence began to accumulate that indicated a molecular basis of smell perception.[269] Although vague at the start, first hypotheses about molecular features responsible for odour quality emerged at the beginning of the 20th century. The crucial question arising was what, if anything, is the relation between the structure of an odorant, i.e. an odoriferous molecule, and its odour? Essentially, this expresses the idea that, underlying smell perception, there must be a key feature that determines why a specific molecule carries its particular odour. Why, for instance, do sulphur molecules always smell of sulphur and not, perhaps, of musk? Pursuing this question, the two prominent approaches that continued to persist and spurred further insight into the molecular basis of odours throughout the following decades of the 20th century were the so-called "shape theory" and the "vibration theory of odours". Whilst the shape theory refers to geometric and spatial features as the causal features of odorants, the vibration theory states that the odour of a molecule is linked to its vibrational frequency.

At present neither theory is conclusively confirmed while empirical insight into the molecular dimension of olfactory responses is still meagre. Nonetheless, contemporary olfactory debate surrounding these two accounts is highly

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[268] Turin, Luca (2006): *The Secret of Scent.* London: Faber and Faber, 116.

[269] Dumas, J.B. (1833): Über die vegetabilischen Substanzen, welche sich dem Campher nähert und über einige ätherische Öle. *Justus Liebig's Annal. Chem.* 34, 245-258; Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 5-10.

skewed towards the shape theory. Although facing a range of empirical inconsistencies, the majority of researchers adopted the conservative shape theory of odours. These inconsistencies are, however, addressed and accommodated by the revived vibration theory. Given that the latter received further empirical support and attention through a few recent studies on isotope perception in humans and other animals,[270] it is worth questioning what informs the current bias of scientific judgement on theory choice in this debate and what epistemic and scientific consequences might be said to follow.

Theories, for many philosophers are said to be "inevitably involved in the solution of problems; the very aim of theorizing is to provide coherent and adequate solutions to the empirical problems which stimulate enquiry."[271] Traditional philosophical analysis of competing theories, therefore, often addressed the degree to which one of these rivals provided a better resource for solving problems. On this account, the utility of a theory and the criteria for theory choice have been analysed in terms of a variety of epistemic and pragmatic desiderata such as parsimony, operationality, generativity, explanatory power, predictive power, unifying capacity, completeness, internal consistency, scope, elegance, measurement etc.[272] However, philosophical analysis of theory choice as applying these criteria already presupposes two important issues, namely that the debate shares common grounds on (1) how the problem is defined and (2) what is recognised as confirmation for problem solving explanations.

It will be the central claim of this chapter that the latter issue, concerning the evidence supporting explanations, needs to be historicised in order to account properly for the scientific reasoning that underlies theory choice. Historicising evidence means that the basis of confirmation has to be analysed not only within the specific temporal context within which an observation is made, but

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[270] Franco, Maria Isabel; Turin, Luca; Mershin, Andreas and Skoulakis, Efthimios, M.C. (2011): Molecular vibration-sensing component in *Drosophila melanogaster* olfaction. *PNAS* 108(9), 3797-3802. doi:10.1073/pnas.1012293108; Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780. doi:10.1371/journal.pone.0055780;

[271] Laudan, Larry (1977): *Progress and its problems. Towards a Theory of Scientific Growth.* London: Routledge, 70.

[272] Hempel, Carl G. (1966): Philosophy of Natural Science. Prentice-Hall; Kuhn, Thomas (1979[1977]): Objectivity, Value Judgment, and Theory Choice. In: The Essential Tension: *Selected Studies in Scientific Tradition and Change.* University of Chicago Press; van Fraassen, Bas (1980): *The Scientific Image.* Oxford University Press; Lycan, William G. (1988): *Judgment and Justification.* CUP Archive.

also through the impact on later scientific judgements of the historical trajectory through which a scientific practice is reached. By outlining the conceptual development of the two rival olfactory theories over the 20th century, this chapter will elucidate the different strategies of modelling facts and conducting and interpreting experiments implicit in the competing accounts. Approaching the olfactory controversy through its disciplinary trajectory, I will demonstrate that what is considered as evidence for (or against) a theory is informed by the way in which the history of the debate structures the explanations it provides which, in turn, is formed by its historical development. Rather than using the knowledge of history for an objective de-historicised account of theory choice, I will emphasise the need for a historical perspective on scientific judgement. This, I hope, will enable philosophers of science to participate in scientific debates in a complementary fashion.[273]

Adopting a historical approach, the trajectory of these theories reflects much of the development of the discipline of olfaction itself, particularly its hybrid nature. Research on the molecular basis of odours comprises two salient experimental contexts, fragrance chemistry on the one hand and molecular biology on the other. Research in fragrance chemistry investigates regularities between the structure of molecules and their odour quality, leading to the development of rules for structure-odour relations (SORs). Studies in molecular biology seek for regularities in the activity patterns of the interaction between odorants and the olfactory receptors, informing the understanding of structure-activity relations (SARs).

The prevailing acceptance of the shape theory of odours in the wider research community over the last century, I argue, can be seen as an outcome of the investigative stream of parallel disciplines studying other molecular responses such as metabolism, digestion and immune reactions. Certainly the idea of a shape-sensitive mechanism, being the generally established model for explaining specificity in molecular recognition processes, provided the most credible basis to understand odour perception as a molecular biological response. Nonetheless, the shape theory of odours leaves some fundamental theoretical problems unanswered and faces several severe experimental problems. Most of the experimental problems surround the still poorly

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[273] Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press.

understood nature of the olfactory receptors (ORs). Due to the failure of standard methods such as X-ray crystallography, the structure of the OR binding site remains experimentally inaccessible.[274] Another problem is that the structural hypothesis of shape for determining SORs hardly translates into successful laboratory practice in fragrance chemistry.[275]

In addition to the persistent internal problems of the shape theory of odours, the resurrection of the alternative vibration theory in 1996 has opened up a philosophically interesting scientific controversy. The revived vibration theory has been widely disregarded, though it has not been possible to reject it on experimental grounds.[276] Providing a different model for the recognition mechanism, it not only explains a wide range of problematic molecular data but it also leads to impressive predictive results of SORs. Attempts to solve the problem of smell perception have thereby led to two theories each of which suggests a different view of the underlying molecular perception process, the mechanism of primary odour recognition.

Central to this scientific controversy is the concept of evidence. Debate about the role of evidence in theory assessment and interpretations of what constitutes a viable theory has also been important to the philosophy of science. Concerns about the characteristics of a good theory can be subsumed under the following questions: To what degree are scientific theories supported by observations? Why are some explanations evaluated as epistemically superior to others? And how can we decide between two empirically valid alternatives? Given the experimental problems accessing the ORs and the theoretical problems accommodating SORs, the grounds for theory choice in the olfactory debate are far from entirely empirical. Problems of determining acceptable standards for evaluating what kind of observation counts as evidence for (or against) a theory in the olfactory debate are exacerbated by the current empirical underdetermination of both theories. The problem of the

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[274] Crasto, Chiquito J. (2009): Computational Biology of Olfactory Receptors. *Curr Bioinform* 4(1), 9.

[275] Sell, Charles (2006b): On the Unpredictability of Odor. *Angew Chem Int Ed Engl.* 45(38), 6254-6261; Turin (2006): *Secret of Scent*, 46-82.

[276] To date, only one study experimentally challenged the vibration theory of odours. See: Keller, Andreas and Vosshall, Leslie B. (2004): A psychophysical test of the vibration theory olfaction. *Nature Neuroscience* 7, 337-338. Its results have been recently challenged by Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780.

underdetermination of theory by data, or the so-called Duhem-Quine thesis, is characterised as follows:

> "[A]t any given stage of a scientific inquiry the available data will in principle be compatible with many different, mutually incompatible theories. This is because theories always outstrip the data on which they are based, if only by universal generalization – the inference from data to theory is always deductively invalid."[277]

The situation here outlines the problem of rational choice between empirically equivalent theories. Empirical equivalence is defined as two or more theories having "exactly the same deductive observational consequences"[278] and also being "compatible with all *actual* and *possible* observations".[279] This scenario does not exactly fit the olfactory debate. Rather, this case resembles Kyle Stanford's riddle of "new induction".[280] Similar to the general problem of underdetermination, the riddle of new induction describes the situation of an empirical gap between the theoretical descriptions and the underlying phenomena. Posing a philosophical problem for determining reliable grounds on which to assess what constitutes a viable theory, the theories involved in this scenario are not conceptually identical and the cause of underdetermination is transient, i.e. subject to further technological advancement.[281]

Although the currently available observations support both theories as long as the 3D structure of the OR binding site remains elusive, it is assumed that future data about the receptors will settle this question in the end. The cause of underdetermination, the experimental inaccessibility of the receptors, is considered a temporal difficulty. Intense efforts in molecular biology surround the advancement of standard techniques such as 3D crystallography for transmembrane proteins;[282] to date, however, only a few breakthroughs such as in the case of rhodopsin have been achieved.[283] Meanwhile, neither theory is

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[277] Okasha, Samir (2002): Underdetermination, Holism and the Theory/Data Distinction. *The Philosophical Quarterly* 52(208), 303-304.

[278] Boyd, Richard N. (1973): Realism, Underdetermination, and a Causal Theory of Evidence. *Nous* 7(1), 2.

[279] Newton-Smith as quoted in Bergstrom, Lars (1984): Underdetermination and Realism. *Erkenntnis* 21 (3), 350. [Italics, mine]

[280] Stanford, P. Kyle (2001): Refusing the Devil's Bargain: What Kind of Underdetermination Should We Take Seriously? *Philosophy of Science* 68, 1-12.

[281] Magnus, P.D. (2006): What's new about the new induction? *Synthese* 148, 295-297.

[282] Pusey, M.L.; Liu, Z.J.; Tempel, W.; Praissman, J. Lin, D.; Wang, B.C.; Gavira, J.A. and Ng, J.D. (2005): Life in the fast lane for protein crystallization and X-ray crystallography. *Prog Biophys Mol Biol.* 88(3), 359-86.

[283] Topiol, Sid and Sabio, Michael (2009): X-ray structure breakthroughs in the GPCR transmembrane region. *Biochemical pharmacology* 78(1), 11-20.

conclusively confirmed and there is no unambiguous way to substantiate the truthfulness of their claims. Therefore, the central epistemological problem remains: on what grounds is one theory appraised to be strongly supported by the evidence *now*?[284]

An answer to this question for the olfactory debate must reflect the implications of the conceptual differences between the rival theories. Although proposing distinct hypotheses determining the key molecular feature underlying the recognition mechanism, both theories aim at a common target system by means of the same concepts and the same line of inquiry: Whereby do ligands interact with the olfactory receptors, and what is the structural relation between molecules and their odour? The theories vary in their answer but not in the outline of the scientific problem they are modelled to solve. Thus, it would be a misconception to describe the two theories as incommensurable. Nonetheless, the conceptual differences provide, within their current formulations, incompatible explanations for the same range of phenomena[285] and, even more importantly, lead to divergences in the deductive observational consequences. Consider isotopic variants, i.e. molecules with the same shape but different vibrational frequencies, the question arising is whether they smell similar or not and the observation is supposed to support either shape or vibration. A few studies on isotope perception in humans have been conducted without leading to an unambiguous answer.[286] Measurement of sensory responses is notoriously difficult and, especially in the case of smells, results are hard to compare. The contemporary controversy in olfaction theory does not surround two theories that are empirically equivalent with respect to the target system but two theories that are epistemically competitive in the interpretation of the available observations. In fact, the available observations and their epistemic status, as either supporting or conflicting with a particular model framework, are as much in dispute as the theoretical explanations. Interpretations of observations might be said to result in an asymmetry of data accommodation in the future,[287] yet the issue is what justifies these interpretations in the first place.

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[284] Earman, John (1993): Underdetermination, Realism and Reason. In: *Midwest Studies In Philosophy* 18(1), 19-38; Okasha (2002): *Underdetermination*, 310-312.

[285] Worrall, John (2009): Underdetermination, Realism and Empirical equivalence. *Synthese* 180(2), 157-172; Bergstrom (1984): *Underdetermination and Realism*, 351.

[286] See footnote 5. See also chapter 7.

[287] Earman (1993): *Underdetermination, Realism and Reason*; Okasha (2002): *Underdetermination*, 312.

Therefore, it is important to explore whereby particular concepts acquire a greater authority for supporting a theoretical framework.

An explanation, I argue, must be sought in the historical development of a discipline. Outlining the conceptual development of the two olfactory theories within the narrative of an ”historical epistemology”, this chapter elucidates the different strategies of modelling the phenomenon implicit in the competing accounts. Recent work promoting a historical perspective on epistemology and the production of scientific knowledge has already emphasised the need to understand scientific reasoning through attention to the particular context within which hypotheses are developed.[288] This context concerns aspects of the evolving research practices such as advancements in technology, methods of experimental standardisation, and disciplinary interests surrounding a specific line of scientific enquiry. Using a historical perspective for a philosophical analysis of a contemporary controversy, the strategy of this chapter is to identify the historical benchmarks in the evolution of the rival theoretical frameworks in olfaction, namely:

(1) The development of rival hypotheses for structure-odour relations after the rise of synthetic chemistry at the end of the 19th century (1920s-1950s)
(2) The influence of interdisciplinary model thinking and the growth of knowledge within the context of the “lock and key” model of enzyme reactions (1940s-1970s)
(3) The impact of technological intervention and molecular visualisation techniques on the search for predictive odour rules (1970s-2000)
(4) The discovery of the olfactory receptors (1991-2013)
(5) The revival of the vibration theory of odours (1996-2013)

A focus on critical points in these advances will help to introduce the multiple research methods, instruments and experimental conditions employed to explore the molecular basis of odours. As a thorough answer to the broader issues surrounding the concept of evidence and the implications of empirical underdetermination for theory assessment would exceed the scope of this chapter, it addresses the issue of scientific evidence by “retreating” to claims

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[288] Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press; Arabatzis, Theodore (2005): *Representing Electrons: A Biographical Approach to Theoretical Entities.* Chicago: University of Chicago Press; Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press.

with a narrower scope. After presenting an epistemic history of the olfactory contoversy, analysing the evolving set of issues both theories were dealing with, I will explore the grounds on which contemporary scientific judgement is based. These, I will demonstrate, are considerably historical. Given the current underdetermination, each attempt to interpret data as evidence for (or against) either theory is open to objection that the assumed explanations rest on an incomplete picture of the phenomenon and, as a result, present indeterminacy of interpretation instead of a faulty theory. A consequence of the limited empirical basis is, as I will show, a strong reliance on established explanatory strategies which have evolved throughout the last decades as a result of attempts to address previous problems. An answer to the question what counts as evidence in the olfactory debate *now*, therefore, must adress the general explanatory structure of the debate and, in turn, the historical processes that supported the entrenchment of this structure. The approach I want to pursue through the following analysis is thus to explore what a historical perspective on a contemporary controversy can contribute to a philosophical understanding of the concept of evidence in scientific reasoning.

2 *The Epistemic History of an Experimental System:* Modelling the Molecular Basis of Odours

2.1 The Birth of a Scientific Controversy: Rival Hypotheses for Structure-Odour Relations (1920s-1950s)

Although advancements in synthetic chemistry at the end of the 19th century indicated a link between the structure of molecules and their odour, the investigation of this link remained highly speculative up to the mid-50s of the last century. One of the first structural hypotheses, referring to molecular vibrations, was proposed by Malcolm Dyson between the late 1920s and 1930s.[289] Dyson's idea originated from his early studies involving element substitution of chlorine compounds with heavier bromine and iodine elements (fig. 1).

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[289] Dyson, Malcolm (1928): Odour and Conetitution among the Pt II. *Perfumery and Essential Oil Record* 19, 88-91; Dyson, Malcolm (1938): The scientific basis of odour. *Journal of the Society of Chemical Industry* 57, 647-651.

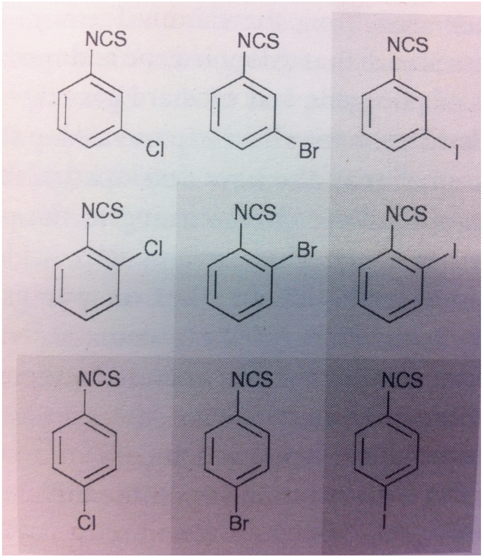

Fig. 1 Dyson's substitution of Chlorine with Bromine and Iodine elements (the darker the shade in the picture, the heavier the molecule). Turin (2006): *Secret of Scent*, 116.

Two observations caught his attention. First, molecules of the same shape can smell dissimilar whilst molecules with different shapes can smell alike. Second, the smell of a molecule gradually and constantly changes the heavier the substituted atom is. Could this mean that there is a causal connection between the odour of molecules and their molecular mass? Yet Dyson's emerging hypothesis about molecular vibrations remained vague and, as there was no form of measurement available at the time, was partly grounded in an analogy to vision and hearing.[290] Only with the discovery of the Raman effect of light diffraction and photon emission did his hypothesis receive empirical support.[291] Following this, Dyson identified molecular vibrations in the Raman spectrum to correlate with odour quality. However, it remained unclear how molecular vibrations were supposed to be detected by a biological system.

Shortly after Dyson presented a systematic account for a vibration theory of odours in 1938, Linus Pauling pursued an alternative strategy published in 1946.[292] Rather than looking for structural correspondences between molecules and subsequently finding a mechanism to explain them, his approach adopted the reverse strategy. Starting with a possible mechanism, his theoretical inspiration for thinking about odour recognition arose out of the earlier development of models for enzyme reactions. Pauling proposed a shape-

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[290] "If it be assumed that osmic perception is due to the intramolecular vibrations of the molecules concerned, then there is a very sound parallel between the three senses of sight, hearing and smell." Dyson as quoted in Turin (2006): *Secret of Scent*, 117.

[291] Ibid., 116f.

[292] Pauling, Linus (1946): Molecular architecture and Biological Reactions. *Chem. Eng. News* 24, 1375-1377.

selective mechanism for olfactory recognition according to the widely popular "lock and key" model originally proposed by Emil Fischer in 1894. In Fischer's model a molecular interaction takes place if a molecule has a correct fit with a complementary shaped receptor, addressing the presumed specificity relation between a substrate and its binding receptor (fig. 2).[293] For this reason, he suggested a correlation between the shape and size of a molecule and its odoriferous properties.

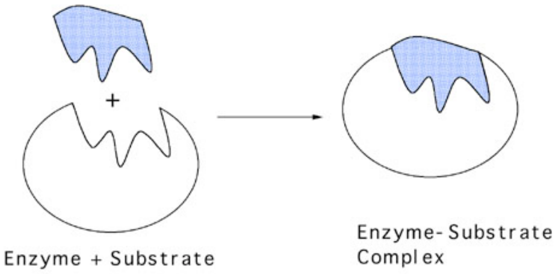

Fig. 2 Lock and Key Model. Casiday and Frey (1998): *Carboxypeptidase*.

Other approaches focussing on the importance of molecular features for smell perception were surprisingly concrete and modern, referring to the possible binding capacities of molecules; in 1920 Leopold Ruzicka, for instance, was the first to address the role of the osmophoric group, which he thought to be responsible for the orientation of the molecule within the receptor site.[294] Thus, unlike the vibration theory exploring the chemical similarities of odoriferous molecules, the shape theory of odours started with implications drawn from the developing models of protein interactions. These models served as a preliminary basis for understanding primary odour recognition and in due course led to a description of molecular properties considered to be responsible for odour detection. The contribution of a biological model to a phenomenon previously addressed chemically highlights the impact of interdisciplinary approaches on theory development. By exploiting the growing knowledge of early molecular biology, olfactory theory started investigating the nature of smell not as a chemical but as a biochemical problem.

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[293] Lichtenthaler, Frieder W. (1995): 100 Years "Schlüssel-Schloss-Prinzip": What Made Emil Fischer Use this Analogy? *Angewandte Chemie* [International Edition in English] 33(23-24), 2364-2374.

[294] Ruzicka, Leopold (1920) *Chemiker-Zeitung* 44, 93-94; Ruzicka, Leopold (1920) *Chemiker-Zeitung* 44,129-131.

2.2 *The Impact of Interdisciplinary Model Thinking: The Rise of the Lock and Key Mechanism (1940s-1970s)*

Systematic investigations of the molecular basis of odours started in the middle of the 20th century. Reinforcing the explanatory centrality of molecular shape were contemporary technological innovations such as X-ray crystallography, liquid gas chromatography and mass spectrometry that now allowed for more detailed knowledge of the structural arrangement of molecular compounds.[295] Under the premise of a shape-sensitive mechanism, Robert Wighton Moncrieff (1949) worked out a more detailed hypothesis, referring to ”steric”, i.e. geometrical, properties of molecules underlying odour perception.[296] Labelled the “Steric Theory of Odours”, John Amoore (1964; 1970) expanded this approach by proposing a range of odour types in relation to their space filling properties.[297] As a rule of thumb, molecules with a similar geometrical and spatial configuration were supposed to smell alike.

As a pioneer of olfaction theory, the key strategy of Amoore comprised two steps. Since the receptors were unknown, experimental evidence about the molecular recognition of odours, other than the construction of SORs, was meagre. Olfactory research thereby relied heavily on methods of chemical analysis such as the synthesis of analogues, i.e. systematic alterations of the parent molecule through element substitution and slight adjustments of molecular parameters (e.g. the distance between atom groups).[298] After testing the extent to which structurally similar odorants matched in odour quality, odour materials were classified into distinct primary odour types, mainly with relevance to categories from perfumery such as musky or minty. Under the premise of a lock and key model, the classification into structural odour types was further used to postulate models for the binding site of the unknown receptors. Given their particular configuration, odorants were thought to interact with a complementary shaped receptor, and, based on their space-filling properties,

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[295] Wright, D.W. (1997): Application of multidimensional gas chromatography techniques to aroma analysis. In: *Food Science and Technology.* Ed. by R. Marsili. New York: Marcel Dekker, 113-142; Turin (2006): *Secret of Scent*, 126.

[296] Moncrieff, Robert Wighton (1949): What is odor? A new Theory. *American Perfumer* 54, 453.

[297] Amoore, John E. (1964): Current Status of the Steric Theory of Odor. *Annals of the New York Academy of Sciences Volume 116, Recent Advances in Odor: Theory, Measurement, and Control,* 457-476; Amoore, John E. (1970): *The Molecular Basis of Odor.* Springfield, IL: Thomas.

[298] Ohloff, Günther (1994): *Scent and fragrances: the fascination of odors and their chemical perspectives.* Trans. by W. Pickenhagen. Berlin, Heidelberg: Springer, 27.

odour types served as the negative blueprint for hypothetical models of the complementary receptor types (fig. 3).

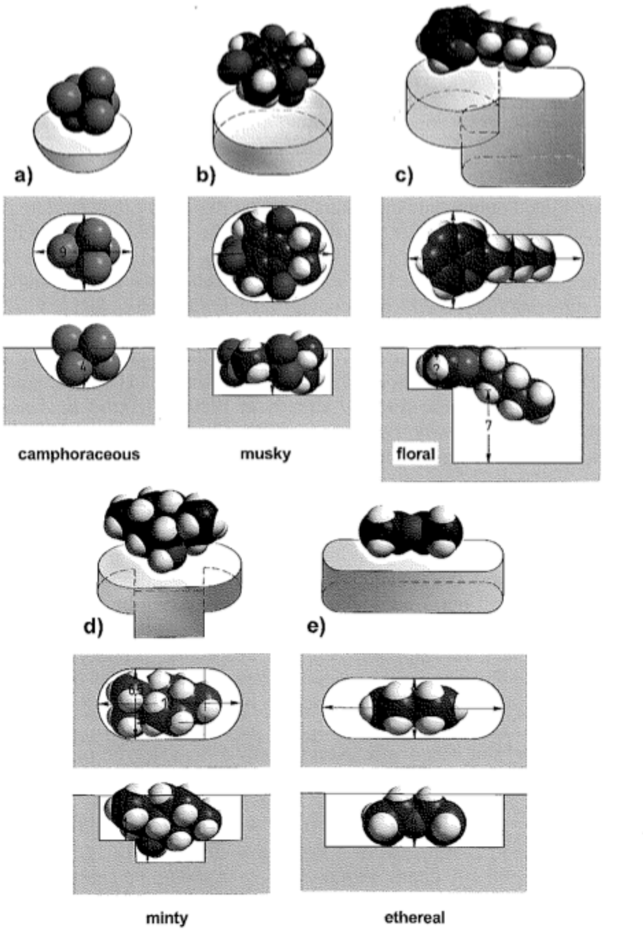

Fig. 3.9. Presumed odorant-binding cavities of the five shape-dependent primary odors

Fig. 3 Amoore's hypothetical receptor models. Ohloff et al. (2011): *Scent and Chemistry*, 74.

The empirical basis on which the stereochemical approach was built relied on chemical classifications of odorants and techniques of chemical analysis. But the lock and key model from which the hypothesis of shape was derived as yet lacked an empirical foundation. For this reason, the lack of knowledge about the receptors resulted in a primarily theoretical approach to the understanding of the molecular perception of odours. To compensate for the unbridgeable empirical gap, the development of olfaction theory continued to draw heavily on the growing knowledge of other disciplines studying molecular recognition processes. And perhaps it is not surprising that a widely applicable model for biological processes was the most successful, even though insufficiently supported empirically, proposal for the olfactory mechanism.

Due to the success of the shape theory, Dyson's hypothesis about molecular vibrations was considered outdated. Nonetheless, stereochemical classifications of odour types were riddled with exceptions and Amoore's stipulation of primary odours appeared to be too simplistic to explain the huge structural diversity of odorants. When these weaknesses of Amoore's account began to become conspicuous, modifications were called for while the adequacy of the general theoretical framework remained unquestioned. Meanwhile, however, Robert Wright (1964, 1970) felt that the vibration theory had been abandoned prematurely and, taking up Dyson's idea, he considerably expanded and modified the original account.[299] Envisaging a possible mechanism for the transduction of molecular vibrations, the idea of a "spectroscope made out of flesh" was the theoretical vision that drove Wright's efforts for the revival of vibration. Optical spectroscopy seemed out of the question for several empirical reasons. One is the problem of an infrared light source that does not toast its organic surroundings. Another one is the amount of water in human bodies: "water is absolutely black to infra-red and would soak up all the energy, leaving none for the smelly molecules to absorb."[300] The only alternative, he reasoned, was to postulate a mechanical interaction, a strategic move with major theoretical implications. It implied that the only energy source exciting the receptors must be thermal motion, meaning that the energy involved is small and, as a result, the detectable range of molecular vibrations is restricted to a maximum of 1000 wavelengths.[301] Unlike Dyson, Wright thereby identified far-infrared frequencies to underlie odour perception but excluded near-infrared ones. Notwithstanding his exemplary studies on bitter-almonds, exhibiting a regular correspondence of vibration patterns and odour quality (fig. 4), the restriction to frequencies below 1000 wavelengths posed insoluble empirical problems. Wright's mechanical model failed to explain the strong smell of small molecules whose frequencies lie outside the theoretically detectable range such as, for instance, ammonia (NH_3) and hydrogen cyanide (HCN).[302] Another pragmatic obstacle to the success of Wright's idea was the instrumental requirement for the measurement of far-infrared frequencies. A far-infrared spectroscope was not a readily accessible instrument for contemporary researchers and, as a consequence, most of Wright's experimental results

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[299] Wright, Robert H. (1964): Odor and molecular vibration: the far infrared spectra of some perfume chemicals. *Annals of the New York Academy of Sciences* 116, 552-558; Wright, Robert H. (1977): Odor and Molecular Vibration: Neural Coding of Olfactory Information. *Journal of Theoretical Biology* 64(3), 473-474.

[300] Turin (2006): *Secret of Scent*, 133.

[301] See also chapter 7.

[302] Klopping, H.L. (1971): Olfactory theories and the odors of small molecules. *J Agric Food Chem* 19, 999-1004.

could not easily be reproduced.[303] However, the final straw that would make his contemporaries completely give up the vibration theory was the case of enantiomers. Enantiomers are mirror-imaged molecules. Identical in their shape *and* their vibration spectrum, the only difference is their spatial orientation. Increasing studies of enantiomers in the 1970s, showing that some enantiomers with identical vibrations have a different smell, were thus seen as the most irrefutable objection to the vibration theory.[304]

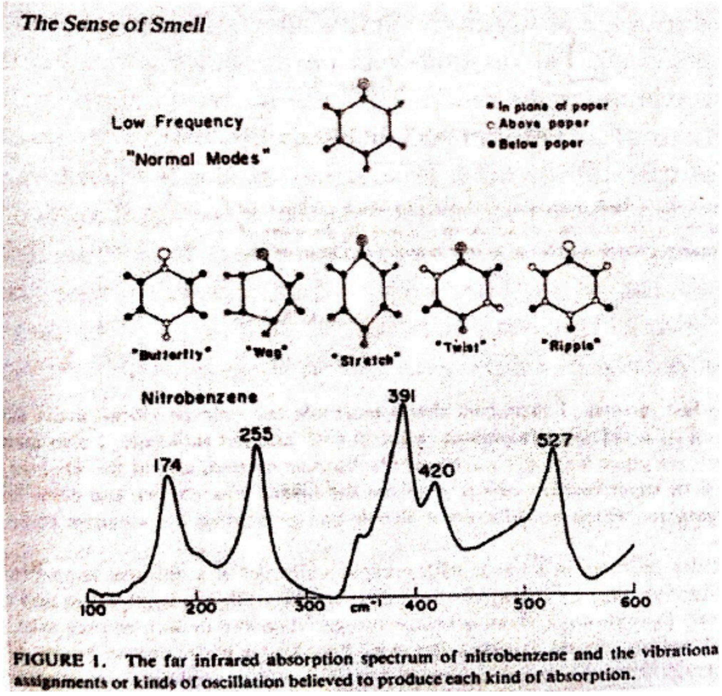

FIGURE 1. The far infrared absorption spectrum of nitrobenzene and the vibrationa assignments or kinds of oscillation believed to produce each kind of absorption.

Fig. 4 Wright's bitter-almond studies. Turin (2006): *Secret of Scent*, 136.

2.3 The Unpredictability of Odour from Odour Rules (1970s-2000)

By the 1980s, sporadic interest in the vibration theory of odours had passed,[305] and olfactory research proceeded to pursue the systematic study of stereochemical similarities between odorants. The rapidly growing accumulation of synthetic materials and the improvement of statistical techniques for the comparison of molecular parameters led to developments of the first successful

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[303] Turin (2006): *Secret of Scent*, 135.

[304] Russell, G.F. and Hills, J.I. (1971): Odor differences between enantiomeric isomers. *Science* 172(3987), 1043-1044; Kafka, W.A.; Ohloff, G.; Schneider, D. and Vareschi, E. (1973): Olfactory discrimination of two enantiomers of 4-methyl-hexanoic acid by the migratory locust and the honeybee. *Journal of comparative physiology* 87(3), 277-284; Wright, Robert H. (1978): Odor and molecular vibration: optical isomers. *Chemical Senses* 3(1), 35-37; Turin, Luca (1996): A Spectroscopic Mechanism for Primary Olfactory Reception. *Chemical Senses* 21(6), 783; Turin (2006): *Secret of Scent*, 141-143.

[305] With the exception of the research group around Clifton Meloan at Kansas State University who worked on insect repellents. Turin (2006): *Secret of Scent,* 153-157.

odour rules. Designed to facilitate predictions of odour quality from molecular structure, odour rules give approximate measurements of the spatial orientation and geometric configuration of atoms and atom groups within odorants, also including their position and distance from each other.

One of the earliest and most influential odour rules is Günther Ohloff's (1971) "triaxial rule for ambergris".[306] It states that ambergris odorants are distinguished by the presence of a decalin, i.e. a bicyclical compound (fig. 5), and that atom groups in positions R1, R2 and R3 must be axial (fig. 6). Over the following decades this rule underwent several modifications, for instance into the "ambergris triangle" by Pavel F. Vlad and co-workers (1985).[307] Despite its overall success, however, this rule began to face a lot of exceptions, most significantly in the form of Karanal® (fig. 7), a compound scrupulously rebutting any definition of structural regularity by differing in both electronic and topological properties.[308]

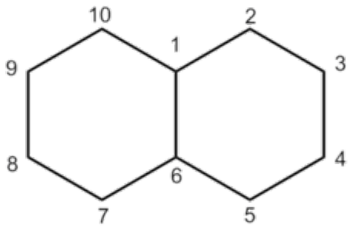
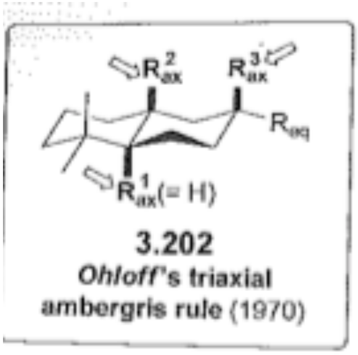


Fig. 5 Wikipedia (2013c): *Decalin*



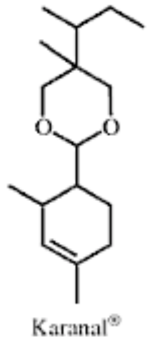


Fig. 6 Triaxial Ambergris Rule.
Ohloff et al. (2011): *Scent and Chemistry*, 98

Fig. 7 Karanal. Sell (2006b): *Unpredictability*, 127.

Other odour rules proposed within the last decades – such as the sandalwood rules of Naipawer (1981), Chastrette (1990), Buchbauer (1994) and Dimogolo

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[306] Ohloff, Günther (1971): Relationship between Odor Sensation and Stereochemistry of Decalin Ring Compounds. In: *Gustation and Olfaction.* Ed. by G. Ohloff and A.F. Thomas. New York: Academic Press, 118-183.

[307] Vlad, P.F.; Bersuker, I.B.; Dimoglo, A.S.; Gorbachov, M.Yu. and Koltsa, M.N. (1985): Structural and electronic origin of ambergris odor of cyclic compounds. *New. J.Chem.* 9, 211.

[308] Turin (2006): *Secret of Scent*, 82.

(1995), and the musk rules by Bersuker (1991) and Jain (1994)[309] – share this fate. Instead of reliable principles for the design of new odorants from scratch, these rules function as helpful guidelines with limited claims to success. A recent assessment of the Bersuker rule for musk, for instance, showed it to successfully predict the odour only 59% of the time, whilst the remaining percentage of synthesised molecules exhibited an odour substantially differing from musk.[310] Far from being lawlike, all these rules exhibit many significant exceptions.

Rather than pinning down structural regularities, odour rules directed attention to the unpredictability of odours.[311] To this day, the structural hypothesis of shape has failed to provide a reliable guideline for rational odorant design in fragrance research. An illustration of the problem is best given through practitioners' records (fig. 8). The page shown here comes from a notebook of Jacques Vaillant, a fragrance chemist in the 1970s. Starting with campholate as a parent structure, it depicts forty-five molecules he designed while working on a new sandalwood odorant. Even though all of these molecules look fairly similar, the results were mostly failures and only one of them possessed the desired smell.[312]

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[309] Naipawer, E.R.; Purzycki, K.L.; Schaffer, G.W. and Erickson, R.E. (1981): A Structure-Odor Relationship for Sandalwood Aroma Chemicals. In: *Essential Oils*. Ed. by B.D. Mookherjee and C.J. Mussinan. Wheaton: Allured Publishing, 105; Naipawer, E.R. (1988): Synthetic Sandalwood Chemistry – A decade in Review. In: *Flavours and Fragrances: A World Perspective.* Ed. by B.M. Lawrence, B.D. Mookherjee and B.J. Willis. Amsterdam: Elsevier Science, 805-818; Chastrette, M.; Zakarya, D. and Pierre, C. (1990): Relations structure-odeur de bois de santal: recherche d'un modèle d'interaction fondé sur le concept d'hypermotif santalophore. *Eur. J. Med. Chem.* 25, 433-440; Chastrette, M. and Zakarya, D. (1991): Molecular Structure and Smell. In: *Human Sense of Smell*. Ed. by D.G. Laing, R.L. Doty and W. Breipohl. Berlin: Springer, 77-92; Buchbauer, G.; Hillisch, A.; Mraz, K. and Wolschann, P. (1994): Conformational Parameters of the Sandalwood-Odor Activity: Conformational calculations on sandalwood odor. *Helvetica Chimica ActaVolume* 77(8), 2286-2296; Dimoglo, A.S.; Beda, A.A.; Shvets, N.M.; Kheifits, L.A. and Aulchenko, I.S. (1993) *Dokl. Akad Nauk SSSR, Ser. Khim.,* 328, 570-572; Dimoglo, A.S.; Beda, A.A.; Shvets, N.M.; Gorbachov, Y.; Kheifits, L.A. and Aulchenko, I.S. (1995) *New J Chem* 25, 433; Bersuker, B.I.; Dimoglo, A.S.; Gorbachov, M.Y.; Vlad, P.E. and Pesaro, M. (1991) *New J Chem.* 15, 307; Jain, A.N.; Dietterich, T.G.; Lathrep, R.H.; Chapman, D.; Critchlow Jr, R.E.; Bauer, B.E.; Webster, T.A. and T. Lozano-Perez (1994). *J Comput Aided Des* 8, 635.

[310] Kansy, M.; Ulmschneider, M. and van de Waterbeemd, Han. (1995): 3D Structural Databases in the Olfactophore Generation of Musk Odor. In: *QSAR and Molecular Modelling: Concepts, Computational Tools and Biological Applications: Proceedings of the 10th European Symposium on Structure-Activity Relationships, QSAR and Molecular Modelling; 1994 September 4 - 9; Barcelona, Spain.* Ed. by F. Sanz, J. Giraldo and F. Manaut. Barcelona: J. R. Prous Science Publishers, 633-638; Ohloff et al. (2011): *Scent and Chemistry*, 102.

[311] Emma Davies (2009): The sweet smell of success. *Chemistry World* (February), 41; Ohloff et al. (2011), 61-133; Sell (2006b); Turin (2006), 46-82.

[312] Turin (2006): *Secret of Scent*, 78f.

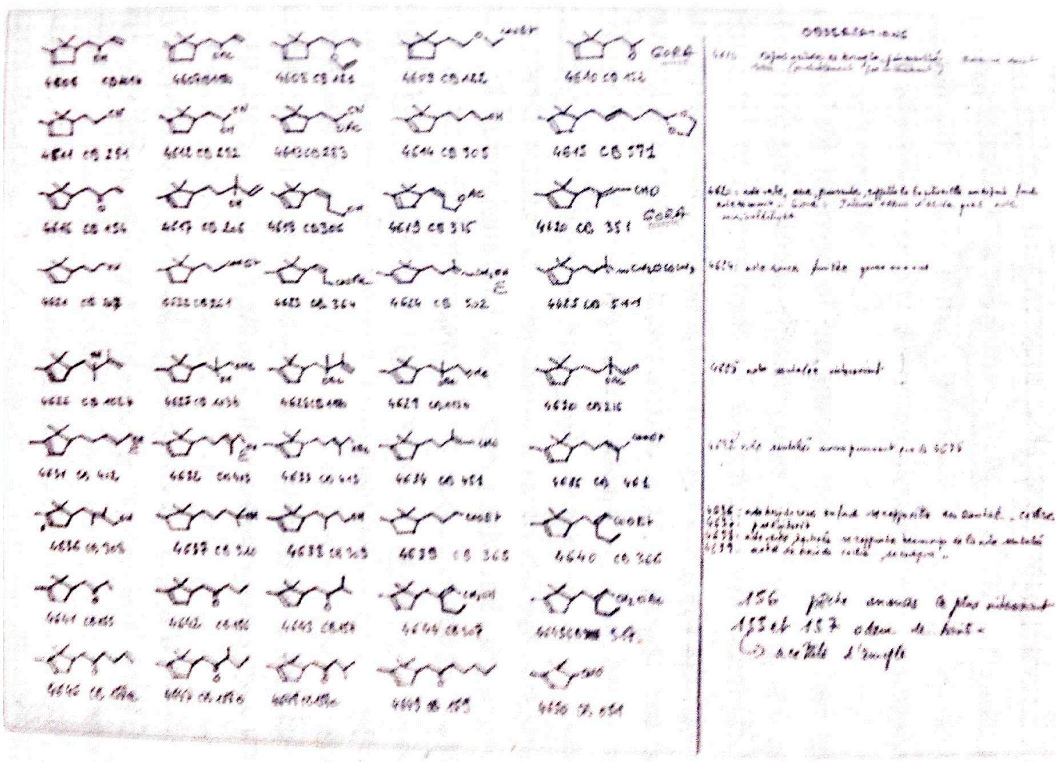

Fig. 8 Notebook page of Jacques Vaillant with forty-five molecules he derived from the parent compound campholate. Only one smells of sandalwood. (It is the molecule numbered 4629 – fourth column, fifth row.) Turin (2006): *Secret of Scent*, 79.

Established lines of work on SORs were overshadowed by this limited level of success in fragrance design. Once again, the persisting problems called for modifications without challenging the overall theory. The theoretical force for reasoning about the molecular basis of odours continued to be the conceptual bond to disciplinary developments modelling other molecular recognition processes. Adopting J.B.S. Haldane's earlier work on enzyme reactions,[313] olfactory researchers started to entertain the idea that the binding site of the unknown ORs might consist of a small and very specific binding area and a less specific one. Rather than the entire shape of the odorant, only those atom configurations binding to the specific receptor site thought to be responsible for its particular odour. Known as "weak shape" or "odotope theory", odorants were measured according to the potential binding capacity of atom groups.[314] Determining "odotopes", i.e. the parts responsible for molecular odour specificity, required taking a variety of molecular parameters into account. In addition to stereochemical features, emphasis was also given, for instance, to

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[313] Haldane, J.B.S. (1930): *Enzymes.* London: Longmans, Green and Co.

[314] Shepherd, Gordon M. (2005): Outline of a Theory of Olfactory Processing and its Relevance to Humans. *Chem. Senses* 30(1), i3; Turin, Luca (2005): Rational Odorant Design. In: *Chemistry and Technology of Flavour and Fragrance.* Ed. by D.J. Rowe. Oxford: Blackwell, 261-273.

electronic and hydrophobic features. An important part in this conceptual change was the advancement of data processing techniques. Especially with the introduction of computer based three-dimensional modelling in the early 1990s, it became possible to conduct a more comprehensive survey of odorants and to compare and statistically evaluate a larger number of more detailed structural aspects.[315] Without insight into the nature of the ORs, however, all these considerations lacked an empirical foundation and rested entirely on theoretical reasoning about the transferability of models developed for other molecular processes.

2.4 *Locks Found but Keys Lost? The Discovery of the Olfactory Receptors (1991-2013)*

For almost the entire 20th century, any hypothesis about the molecular basis of smell and the underlying primary perception mechanism remained speculative. Although a variety of structural hypotheses were put forward,[316] the theories of shape and vibration dominated conceptual thinking about SORs. Until recently biologists were unable to conclusively determine the molecular features underlying the recognition process because the mammalian ORs were simply unknown. It was assumed that once these receptors were discovered, knowledge about the recognition process would inevitably follow. When in 1991 Linda Buck and Richard Axel discovered a multigene family encoding the olfactory receptors in the mammalian genome, the debate seemed to be settled at last.[317] The discovery had important implications for further olfactory research, because it identified smell receptors as a class of 7 transmembrane G-coupled proteins, which strongly suggested that molecules (causing a particular odour) dock on a specific primary receptor according to some kind of shape-sensitive mechanism.

It was the background of advancements in genetics and growing experimental evidence for an involvement of a G-coupled protein that paved the way for this

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[315] Ohloff et al. (2011): *Scent and Chemistry*, 96-133.

[316] Dravnieks, Andrew (1969): Current status of Odour Theories. *Flavour Chemistry. Advances in Chemistry* 56, 29-52. See also: Heath, Henry B. (1981): *Source Book of Flavors. AVI Sourcebook and Handbook Series.* Dordrecht: Kluwer, 122-127.

[317] Buck, Linda B. and Axel, Richard (1991): A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. *Cell* 65(1), 175-187.

groundbreaking discovery.[318] Previous studies on olfactory responses already indicated the presence of cAMP (cyclic AMP), a messenger molecule that activates ion channels when a cell is activated. Because of its function of stimulating the formation of cAMP, the involvement of a G-coupled protein was considered to be likely before its ultimate discovery. Although G-coupled proteins take part in a variety of physiological processes, ranging from vision to the regulation of behavioural and immune responses to digestion, those proteins active in chemical ligand binding were all considered to act according to a shape-sensitive mechanism. Therefore, the theoretical implications of Buck and Axel's discovery were not a complete surprise but, rather, reflected orthodox opinion about primary smell perception, which had always taken aspects of molecular shape to be the key feature responsible for odour detection. If this discovery had led to increasing insight into the nature of the olfactory perception mechanism, the trajectory of the shape theory of odours might have been a story of scientific success. However, it did not quite turn out this way. Things went surprisingly quiet on the OR research front. The experimental inaccessibility of the highly unstable ORs – becoming dysfunctional or disintegrating when isolated, crystallised and tested in vitro – was an important factor in the limited progress since the 1990s. Relying on the theoretical implications drawn from the discovery of the protein class, the mechanism of primary odour recognition was left to be explained until further advancements allowed for closer scrutiny.

What the discovery of the receptors did not resolve were significant cases of conflicting data in SORs. Consider, for instance, isosteric molecules which, despite having almost the same stereochemical configurations, exhibit distinctively different smells. Explanations for such aberrant data were again sought by reference to model-based inferences adopted from related disciplines. Challenges to rigid structural explanations for enzyme-ligand binding in other processes, exhibiting a lack of lawlike binding principles in molecular recognition as well, had spurred further inquiry into the nature of the underlying mechanisms. Abandoning the rigidity of the lock and key model, a proposal to accommodate the structural diversity of ligands by David Koshland

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[318] Buck and Axel (1991): *Novel multigene family*; Buck, Linda B. (2005): Unraveling the Sense of Smell (Nobel Lecture). *Angew. Chem. Int. Ed* 44, 6128-6140; Keller, Andreas and Voshall, Leslie B. (2008): Better Smelling through Genetics: Mammalian Odor Perception. *Current Opinion in Neurobiology* 18(4), 364-369.

in the late 1950s suggested a more flexible interaction. Koshland thought that particular changes in protein conformation were involved in molecular recognition processes.[319] With growing insight into the intrinsically disordered nature of a variety of proteins since the 1990s, this dynamic and flexible model for enzyme reactions received greater attention. In some contexts further modified into the "shifting specificity model"[320] for enzyme catalysis,[321] this modified account led to significant changes in understanding molecular recognition. Attempts to develop general structural principles for ligand binding have been considered futile and had to give way to locally targeted explanations, exploring why a particular substrate binds to a particular protein.[322] Accommodating the failure to discern lawlike odour rules, the hypothesis of conformational change in ligand binding was thus widely welcomed by olfactory researchers, particularly those who were still pursuing a stereochemical explanation for primary odour recognition and who now assumed that irregularities in SORs were due to the deformation of molecules within the receptor site.[323]

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[319] Koshland, Daniel E. (1995): The Key–Lock Theory and the Induced Fit Theory. *Angewandte Chemie International Edition in English* 33(23-24), 2375-2378.

[320] Britt, Billy Mark (1993): A shifting specificity model for enzyme catalysis. *Journal of theoretical biology* 164(2), 181-190; Britt, Billy Mark (2004): Understanding enzyme structure and function in terms of the shifting specificity model. *Journal of Biochemistry and Molecular Biology* 37(4), 394-401.

[321] "Many enzymes have two folded conformations. For bovine adenosine deaminase, the low-temperature (< 30ºC) conformation appears to be better optimized for interaction with the reaction transition state than does the physiological conformation. The SSM requires two global conformations of the enzyme unlike the HPKM which requires only one." Britt, Billy Mark (2009): Testing the Shifting Specificity Model for Enzyme Catalysis. FASEB J. (Meeting Abstract Supplement) 502.1.

[322] Drews, Jürgen (2000): Drug Discovery: A Historical Perspective. *Science* 287(5460), 1960-1964.

[323] Turin, Luca and Yoshii, Fumiko (2003): Structure-Odor Relations: A Modern Perspective. In: *Handbook of Olfaction and Gustation 2nd edition*. Ed. by R. Doty and M.Decker. Informa Healthcare, 457-482. Cited is the online version URL=< http://www.annindriya.com/_mcms/_data/files/Luca%20Turin%20structure%20odor%20theory.pdf>; See also Leslie B. Vosshall quoted in Ball, Philip (2013): Controversial theory of smell given a boost. *RSC Chemistry World* (28 January 2013) URL=< http://www.rsc.org/chemistryworld/2013/01/controversial-molecular-vibration-theory-smell-olfaction> or Charles sell interviewed in BBC Horizon (1995): *A Code In The Nose.* Producer: Isabelle Rosin. Documentary, UK. (27 November 1995)

2.5 *An Echo from the Past: The Possibility of a Biological Spectroscope? (1996-2013)*

Despite the internal problems for the different interpretations of the shape theory of odours, the paradigm of shape has been paramount as there was no reasonable and empirically plausible alternative. It was not until 1996, when Luca Turin published his original research paper,[324] that there was sufficient reason to doubt the predominant model of a shape-sensitive mechanism. Turin questioned the premise of causal similarity between olfactory responses and other molecular recognition processes. Insisting on a general lawlike criterion linking odour quality to molecular features, he criticised the shape theory of odours as posing a flawed structural assumption to begin with. Dissatisfied with the explanation of aberrant data by reference to conformational changes, Turin reasoned how SORs might fit another explanatory pattern. Taking up the abandoned vibration theory, the task was to identify where Dyson and Wright erred and to correct these past mistakes.[325]

Challenging prevalent scepticism about the idea that smell might be a spectral sense was his impressive predictive result of SORs through calculations of the vibration spectrum. For his prediction to make an impact, the experimental set-up required finding two molecules that correspond in both odour quality and vibration frequency but that exhibit a different stereochemical configuration. To remove any doubts about their odoriferous similarity, the odorants were further required to have a distinctive smell. The choice fell on sulphur due to its perhaps unique odour and the frequency of the SH-bond, which lies outside the vibrational range of most known odorants. Calculating simple vibration patterns of diatomic molecules, a frequency close to the SH-bond (2500 wavelengths) occurred in the BH-bonds of boranes (2550 wavelengths). Independently of Turin's study, the vibration spectrum of various boranes had been analysed in 1941 without, however, being explicitly linked to smell perception.[326] What strikes the eye is that "Borane and Sulphur are not in the same column of the periodic table. They have no shape and no chemistry in common."[327] As a

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[324] Turin (1996): *Spectroscopic Mechanism.*

[325] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House; Turin (2006): *Secret of Scent*.

[326] Stitt, Fred (1941): Infra-Red and Raman Spectra of Polyatomic Molecules XV. Diborane. *Journal of Chemical Physics* 9(11), 780-785.

[327] Turin as quoted in Burr (2002): *Emperor of Scent*, 416.

consequence, the geometrical configurations and electronic properties of molecules composed of borane bonds differ significantly from those of sulphur.[328] The question was whether sulphur and boranes smell similar. Defying an answer by simply sniffing them, boranes are rocket fuels and explode spontaneously in contact with air. A test with a less reactive (though toxic) decarborane ($B_{10}H_{14}$) nonetheless presented the anticipated result: boranes smell sulphurous. In support of Turin's assessment, Alfred Stock, the inventor of boranes, had likewise reported their smell as being "reminiscent of sulphur" as early as 1912.[329]

Reviving the vibration theory, however, required more than an explanatory pattern for SORs but an empirically viable model for the transduction of molecular vibrations in a biological system. Abandoning Wright's mechanical account and accepting the impossibility of optical spectroscopy, Turin introduced another possibility, the detection of molecular vibrations through inelastic electron tunnelling spectroscopy (IETS). Drawing on the earlier invention of a device involving electron spectroscopy by Robert Jacklevic and Joseph Lambe in 1966,[330] he proposed a mechanism that, even if highly hypothetical, is grounded in the empirical features of the olfactory receptors.[331] Demonstrating the empirical possibility of biological spectroscopy, the viability of this mechanism was further supported by a study of Brookes et al. (2007).[332] Under the premise of IETS and the deflection of electrons in the recognition process, even formerly recalcitrant data such as that from enantiomers found an explanation, which was furthermore put to the test successfully.[333]

The proposal of an IETS mechanism for olfactory responses was met with disbelief across the wider olfactory research community. This criticism must be seen in the context of its time. To date, introducing quantum physics into

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[328] Ibid., 97.

[329] Legrum, Wolfgang (2011): *Riechstoffe, Zwischen Gestank Und Duft: Vorkommen, Eigenschaften Und Anwendung Von Riechstoffen Und Deren Gemischen.* Wiesbaden: Springer, 68-69.

[330] Jaklevic, R.C. and Lambe, J. (1966): Molecular vibration spectra by electron tunnelling. *Physical Review Letters* 17, 1139-1140.

[331] See Chapter 5.

[332] Brookes, Jennifer C.; Hartoutsiou, Filio; Horsfield, A. P. and Stoneham, A. M. (2007): Could humans recognize odor by phonon assisted tunneling? *Phys Rev Lett.* 98(3), Article 038101.

[333] Turin and Yoshii (2003): *Structure-Odor Relations*, 18; Turin (2006): *Secret of Scent*, 142, 173, 367-385.

molecular biology appears to be a perhaps fascinating but fanciful idea.[334] In the conservative disciplinary context of olfaction theory, even though poorly supported by the failure of the methods available, quantum biology appeared to be some form of magic trick.[335] Despite, or perhaps because,[336] of the wider interest it received from the media,[337] Turin's idea was greeted with polemics that were excessive. Scientists working with the standard model, feeling themselves portrayed as "incompetent villains", defended their work against audiences that "love controversy (…) ever since David and Goliath" but "who were ill qualified to judge its scientific content."[338] Nonetheless, since unambiguous experimental evidence against the revised vibration theory proved impossible to obtain, it was simply edited out of history: the vibration theory of odours seldom appears in historical summaries in recently published olfactory handbooks.[339] Other studies further supporting a molecular vibration sensing mechanism in olfactory perception do not seem to change this.[340] Quite the contrary, a recent paper by Gane et al. (2013)[341] confronting the only study[342] that experimentally challenged Turin's proposal brought to the foreground the epistemic bias that underlies current olfactory debate. Whereas the paper supporting the vibration theory was quickly dismissed as insufficient because "it doesn't seem a useful endeavour to use behavioural responses as an

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[334] Turin, Luca (2002): A method for the calculation of odor character from molecular structure. *Journal of Theoretical Biology, 216* (July), 367-385; Turin (2006), 173.Turin (2006), 142; See Chapter 7.

[335] "The magician James Randi, debunker of paranormal claims, once said that if you claim to have a goat in your backyard, people will probably believe you, but if you say you have a unicorn, you must expect closer scrutiny. The editors at *Nature* used to classify manuscripts on a 'zoological scale' that ranged from goats to unicorns, and Turin's paper was toward the far end of that scale. Despite the forcefulness of his assertions, most scientists in the field were unconvinced by his proposal." Nature Neuroscience Editorial (2004): Testing a Radical Theory. *Nature Neuroscience* 7(4), 315.

[336] Nature Neuroscience Editorial (2004): *Testing a Radical Theory*; Bentley, Ronald (2006): The nose as a stereochemist. Enantiomers and odor. *Chemical reviews* 106(9), 4099; Solomon, Miriam (2006): Norms of Epistemic Diversity. *Episteme: A Journal of Social Epistemology 3*(1), 23-36; Solomon, Miriam (2008): Norms of Dissent. London School of Economics. *Centre for the Philosophy of Natural and Social Science Contingency and Dissent in Science Technical Report* 09/08.
URL=<http://www2.lse.ac.uk/CPNSS/projects/CoreResearchProjects/ContingencyDissentInScience/DP/SolomonNormsOfDissent0908Online.pdf>

[337] BBC Horizon (1995): *A Code In The Nose*; Burr (2002): *Emperor of Scent*.

[338] Nature Neuroscience Editorial (2004).

[339] Ohloff et al. (2011): *Scent and Cemistry.*

[340] For scientists' responses to Turin's study see: Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013)
URL=<http://www.bbc.co.uk/news/science-environment-21150046>

[341] Gane et al. (2013): *Molecular Vibration-Sensing Component*.

[342] Keller and Vosshall (2004): *Psychophysical test*.

argument”,[343] the preceding critical study by Keller and Vosshall was a little too eagerly cited as evidence against the vibration theory although it too is based on behavioural responses.[344]

3 *Errors and Discovery:* Disciplinary Challenges to Contemporary Issues in Olfaction Theory

Following this micro-epistemic history of research on the molecular basis of smell across the 20th century, I now want to analyse the underlying scientific reasoning that seems to inform theory choice here. The trajectory of olfaction theory exhibited a highly unbalanced debate between the majority of scientists working with the standard shape theory of odours and a small group of researchers promoting the vibration theory of odours. Although the vibration theory, particularly in its latest version, addressed and accommodated explanatory shortcomings of the standard theory, such as the irregularity of SORs, it nevertheless has not yet reached the status of a serious theoretical contender for explaining the molecular basis of smell. Given the inadequate support for either theory in view of the continuing inability to experimentally access the binding site of the ORs, the current bias cannot be fully explained by the available empirical results. An understanding of the prevalence of the shape theory on the one hand and the endurance of the vibration theory on the other, therefore, rests on the identification of the source of scientific disagreement. For this reason, I want to address how judgement about what kinds of observations count as evidence in the current olfactory debate is related to the historical development of the discipline. This, I argue, not only provides a useful resource for recognising the scientific dissent on background assumptions, but also offers a partial philosophical explanation of why this debate is so difficult to resolve. Rather than suggesting the futility of appeals to evidence, my analysis of the olfactory debate elucidates how what counts as evidence is closely linked to the trajectory of the discipline, meaning that the explanatory structure within which observations are considered to be relevant for theory assessment must be related to its historical development. Such a historicised perspective will

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[343] Richard Axel as quoted in Palmer (2013): *Quantum smell*.

[344] Nature Neuroscience Editorial (2004); Hettinger, Thomas P. (2011): Olfaction is a chemical sense, not a spectral sense. *PNAS* 108(31), E349.

elucidate why, in this particular debate, predictive results on SORs via the vibration theory are not seen as a sufficient challenge to the standard account, notwithstanding the fact that the latter has been struggling to provide systematic links between structural parameters and the odour of a molecule.

Bridging the persistent internal inconsistencies and the continuing failure of determining SORs, the prevalence of the shape theory of odours can be best understood through its central role in the disciplinary development of olfaction theory. By drawing on parallel discourse in molecular biology at the beginning of the 20th century, it presented the only empirically viable model on the basis of which structural assumptions about the nature of smell were justified and developed, and, furthermore, the methods employed to assess SORs such as the synthesis of analogues were also primarily directed at stereochemical features. The pervasiveness of the shape theory thus is grounded in the "epistemic iteration" of central concepts in modelling practice. Epistemic iteration, as introduced by Hasok Chang (2004), reflects the developmental character of knowledge production in scientific research. Here the production of knowledge is characterised as a process "in which successive stages of knowledge, each building on the preceding one, are created in order to enhance the achievement of certain epistemic goals… [T]he whole chain exhibits innovative progress within a continuous tradition."[345] Although successive stages do not follow logically from their preceding ones, their manifestation is nevertheless informed by and grounded in previously established techniques and concepts.

Consisting of more than mere repetition of central concepts, the process of epistemic iteration is a progressive one. It is progressive insofar as it reflects the efforts by which researchers revisit their knowledge claims and which, within successive stages of scientific development, lead to their improvement. This improvement is not exclusively empirical but also comprises various other epistemic advances, such as accuracy, unifying and explanatory power, consistency, scope, etc.[346] A successful theory, on this account, does not have to be a theory that merely produces robust empirical data but, alternatively, can be a theory that serves as the most reliable means for question-driven investigation, data collection, and technology-oriented research. It is through

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[345] Chang (2004): *Inventing Temperature*, 226.

[346] Elliott, Kevin C. (2012): Epistemic and methodological iteration in scientific research. *Studies in History and Philosophy of Science Part A* 43(2), 376-382.

this process of epistemic iteration that the shape theory of odours established its success within olfactory studies. Even though accompanied by an evolving set of empirical problems such as the persistent irregularity of SORs, the evidential deficiencies grounded in the experimental inaccessibility of the receptors, etc., the shape theory provided the most profound theoretical basis through which the relevant concepts and measurements of molecular data could be introduced and refined.

Assuming the presence of a ligand binding process for olfactory responses in the first half of the 20th century, the adopted lock and key model had a firm experimental basis in the broader biochemical understanding of molecular recognition processes. Drawing on the ontological premise of causal conformity across all molecular mechanisms, I have shown, significantly aided the articulation of olfaction theory as an independent research domain. Lacking empirical knowledge about the receptors, the application of the lock and key model served as a conceptual tool to first identify the scope of key molecular features and to compare methods of measurement, further informing the interpretation of data irregularities. Adjustments of the hypothesis of shape, starting from the overall shape to the selection of specific odotope or profile groups, were a result of model-based inferences in the changing understanding of enzyme binding. Almost entirely unchallenged by alternative explanations throughout the 20th century, unresolved irregularities in SORs under the shape framework were left to be explained by molecular interaction processes such as conformational changes. After the discovery of the ORs, identifying them as belonging to the same class as other proteins acting according to a shape-sensitive mechanism, the assumption of the shape theory achieved further empirical support. This discovery served as an empirically grounded justification that model-based inferences and auxiliary assumptions explaining irregular SORS were not unwarranted ad hoc modifications.[347] Instead of being considered as a rift in the explanatory scope of the shape theory and instead of fostering the need for novelties of theory, irregularities in SORs data were judged as another element whose explanation must be integrated within a larger, yet to be told story about primary odour recognition. As a result, most olfactory researchers were not under the impression that their discipline was in some sort of crisis. Stepping into this increasingly conservative research

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[347] This will be addressed in more detail in chapter 5.

tradition, the revival of the vibration theory thus was widely regarded as uncalled for and often received less than charitable reviews.[348]

The current scientific response to the explanatory limits of the shape theory by reference to the yet to be explored perception mechanism is a strategy that, indeed, carried further consequences for the more general explanatory structure of olfaction theory. Throughout the 20th century, before the discovery of the ORs and the growing impact of molecular biology on olfaction theory, most olfactory researchers investigated the molecular basis of odours through the chemical analysis of SORs. It was assumed that regularities in SORs must correspond to regularities in the interaction between molecules and the appropriate receptors. Before becoming an element of post hoc justified modifications of model-based inferences, strongly conflicting data such as those from isosteric molecules, therefore, presented an apparent flaw in the previous theoretical account of shape. Given that many irregularities of SORs remain unresolved within the shape theory, and given the surprising predictive success of the revived vibration theory, one might still wonder what further reasons guided the olfactory scientists not to consider the vibration account as a possible, even though speculative, alternative.

In parallel with the persistent problem of the unpredictability of odour from structure within the shape theory, different versions of the vibration theory, demonstrating correspondences between odour and vibration frequency, were proposed across the 20th century. Without a mechanism for the detection of molecular vibrations in a biological system, however, the approaches by Dyson and Wright failed to demonstrate empirical possibility. Yet, the latest revival by Turin granted vibration theory the long sought requirement to turn it into a serious contender: with the model of the IETS mechanism, a biological form of spectroscopy became in principle empirically feasible. In addition to an empirical foundation, the revived version also allowed for a better accommodation and even prediction of SORs. So, given the widespread scepticism and exclusion from the wider research community, what kind of evidence is missing to consider this theory as a serious candidate for truth?

From a broader perspective, traditional philosophical considerations on theory choice seem to be at odds with the contemporary judgement in the olfactory

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[348] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House; Nature Neuroscience Editorial (2004): Testing a Radical Theory. *Nature Neuroscience* 7(4), 315.

debate. In addition to having two empirically viable yet underdetermined theories, each of those theories also exhibit a redeeming epistemic virtue: whereas the shape-sensitive mechanism is largely supported by its ontological compatibility with other molecular recognition processes, the vibration account explains and predicts the relevant structure-odour relations with greater reliability. As a result, there seems to be no criterion on which an unambiguous rational choice is based here. A striking aspect of the olfactory debate is thus its strong bias towards the shape theory of odours. Perhaps more easily comprehensible within the experimental context of molecular biology, this bias even holds in the context of fragrance chemistry with its focus on the successful determination of SORs.

As many philosophers of science have argued and analysed, theoretical frameworks provoking a contentious debate face the challenge of surpassing an established research program. To prove their superiority, they are required to identify oddities arising from standard explanations and to accommodate the problematic data. Furthermore, they need to deepen scientific knowledge by collecting new data and to show how the phenomenon is better accounted for in this new context.[349] The recurrent appeal of the vibration theory was its capacity to identify the conflicting data arising from the shape theory of odours and to accommodate them within an alternative explanatory pattern. Extending scientific knowledge, the IETS mechanism provided a feasible model for a process that had been thought empirically impossible. Clearly, the vibration theory fulfils the epistemic criteria of a serious contender, again raising the question of what kind of evidence seems to favour the shape theory of odours in contemporary scientific reasoning. What is left out of consideration is that these criteria concentrate on the surpassing of an established and older paradigm or research program by a new and progressive one. Yet the vibration theory is not a new theory but almost as old as it rival and, most importantly, it was twice considered outdated. Previously abandoned and later revived theoretical frameworks, even with a new livery, thus face an additional and greater challenge: finding the error and recovering from it.

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[349] Lakatos, Imre (1970): Falsification and the Methodology of Scientific Research Programmes. In: *Criticism and the Growth of Knowledge.* Ed. by I. Lakatos and A. Musgrove. Cambridge: Cambridge University Press; Lakatos, Imre (1980): *The methodology of scientific research programmes: Vol. 1: Philosophical papers. Vol. 1.* Cambridge: Cambridge University Press; Laudan, Larry (1981): A Confutation of Convergent Realism. *Philosophy of Science* 48(1), 19-49; Worrall, John (2012): Theory-Confirmation and History. In: *Rationality and Reality.* Ed. by C. Cheyne and J. Worrall. Springer, 49-60.

Though the mistakes of its predecessors were found and eliminated – i.e. lacking a mechanism (Dyson) or proposing one that is at odds with the range of perceptible materials (Wright) – the greater challenge for the revised theory was to recover from its errors and to convince the wider scientific community that this version had got it right at last. The process of recovery, however, is not history-neutral but deeply dependent on the underlying disciplinary developments. Turin's sulphur-borane prediction, even though fundamental to the revival of the vibration theory due to its demonstrated superiority in explaining SORs, is not judged as strong evidence today. Although studies on SORs presented the main strategy in olfactory research across the 20th century, after the discovery of the olfactory receptors in 1991 the disciplinary focus in olfaction theory changed emphasis. As a collective strategy for dealing with irregular SORs, focus shifted from primarily investigating a link between odour quality and molecular features through chemical analysis in fragrance chemistry to finding explanations of the underlying recognition mechanism, drawing on parallel research in molecular biology. This strategy had two consequences for the general explanatory structure of olfaction theory. First, the concept of chemical similarity to systematically link odour quality to molecular features became extended to include, in addition to steric interactions, other factors such as molecular weight, polarity, acidity, or basicity.[350] Second, the compositional character of different structural features responsible for odour perception allowed interpreting the lack of regular SORs as a natural consequence of chemical complexity rather than a failure of theory. On that account, contemporary opinion holds experiments on SORs or, for that matter the recent study on sensory responses, as "the kinds of experiments [… that] would not resolve the debate - only a microscopic look at the receptors in the nose would finally show what is at work." Rather than chemical, the scientific problem in current olfactory debate is judged to require a molecular biological explanation. Although Turin solved the issue of the empirical possibility of biological spectroscopy, his model still needs to be experimentally linked to studies on G-coupled protein receptors. As long as the IETS mechanism is not embedded in the research culture of molecular biology, it seems to remain a merely conceptual tool without experimental tractability. Future experiments, such as

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[350] Hettinger, Thomas P. (2011):Olfaction is a chemical sense, not a spectral sense. *Proc Natl Acad Sci U S A* 108(31): E349.

the measurement of electron flow in olfactory responses,[351] might however lead to a gradual change in scientific judgment, potentially giving the vibration theory of odours greater credibility in the wider community.

As for the current debate, the kind of molecular evidence demanded for accepting the new vibration theory as a serious contender to shape points at an interesting disparity between what is considered as viable evidence in the olfactory community and what is not. Although judged as insufficient, the SORs data produced in fragrance chemistry provide a complex but experimentally accessible resource for the assessment of theoretical claims about the molecular basis of smell. By contrast, the empirical resources available from molecular biology are mainly derived from research on other recognition processes and, as long as the ORs remain experimentally inaccessible, serve more as a theoretical justification for a shape-sensitive mechanism than as providing it with empirical tractability. Nonetheless, given the historical trajectory of olfaction theory presented in this chapter, it is not difficult to see that the persistent irregularities of SORs, rather than being seen as a resource for theory evaluation, became a source of frustration for researchers that were largely trained in the tradition of the standard shape theory.[352]

The grounds for scientific disagreement in the current olfactory debate, as I identified here, are closely linked to its historical trajectory. To recap briefly, the widely accepted shape theory of odours, uncontested for almost the entire 20th century, was the basis on which research on the molecular basis of odours started to emancipate itself. Moreover, it provided the most reliable resource for developing explanatory strategies for the accommodation of the huge structural variety of odorants. Given that it provided a relatively stable body of knowledge, and given the lack of an empirically conceivable alternative available, the remaining irregularities were not recognised as a significant breakdown of the problem solving ability of the shape theory. Especially after the discovery of the ORs, these irregularities were explained through the complexity of factors determining chemical similarity in molecular binding processes. This disciplinary trajectory gave reason for the prevailing success of the shape theory, despite the evolving set of issues it continues to struggle explaining.

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[351] Turin in personal conversation.

[352] An approach still conducted in fragrance chemistry edutcation today as it can be seen in Frey, Regina F. and Donlin, Maureen J. (2006):Chemistry 257Experiment 6:NMR Analysis, IR Analysis and Smell Testing. URL=<http://www.chemistry.wustl.edu/~edudev/Smell/smell.html>

In response to these issues, the disciplinary development also had an impact on what kinds of observations were considered as significant evidence for theory assessment. The change in disciplinary emphasis from fragrance chemistry to molecular biology arose when the latter started promising to explain shortcomings and irregularities in the data of the former. A result of this change in emphasis was that previous limits of research strategies were now interpreted as temporal indeterminacies within the overall explanatory structure surrounding the mechanism of smell perception. Though individual scientists may have differed in their opinion about the degree to which data irregularities continued to pose a serious problem for the standard theory of shape,[353] it was a shared conviction that these problems were subject to further modifications once the molecular mechanism was better understood. It was against this disciplinary background that the revived vibration theory came into the picture.

The bias underlying the issue of theory choice in the current olfactory debate, therefore, rests on the absence of a common understanding about whether the persistent irregularities in SORs pose an objection to the integrity of the standard theory. Advocates of the rival theories thus not only disagree about what structural features are considered relevant to accommodate phenomena under an encompassing theory. They also differ in their reactions to the persistent irregularities surrounding current explanations of the molecular basis of odours. Are the persistent issues a fatal problem for the standard theory, or can they be resolved through further additional assumptions? In the course of the historical trajectory and within the disciplinary phases I identified, olfactory debate started from scientific disagreement about the identification of the key structural feature before its attention turned to the heuristic role of an empirically feasible mechanism for further theory development. The vibration theory did not merely dispute details of the mechanism, but it revived questions about the structural key feature, an explanatory element that was assumed being firmly established by now.

Nonetheless, despite the disciplinary predominance of shape, the vibration theory has gained more attention throughout the last decade, beginning to change the scientists' assessment of whether or not their field has reached a

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[353] Strong proponents for shape-based explanations are, for instance, Ohloff et al. (2011) whereas others remain cautions about whereas there are any general stereochemical configurations (or general relations at all) that explain SORs such as Sell, Charles (2005): Scent through the looking glass. In: *Perspectives in Flavour and Fragrance Research.* Ed. by P. Kraft and K.A.D. Swift. Wiley-VCH, 67-88.

methodological impasse and whether it would benefit from considering seemingly speculative possibilities.[354] Not least because of the explanatory potential of the vibration theory, accommodating those SORs most persistent and problematic for shape, a couple of researchers have started to mention the vibration theory as a possible complementary alternative. The likelihood of further change in scientific judgement on theory choice, however, depends on the underlying disciplinary development to which future experimental approaches relate.

As for the current situation, considering the arguments presented by both sides, the revival of the vibration theory and the resulting growing controversy benefits the olfactory debate in general by pointing at some deeper underlying issues. It first draws attention to the need to articulate the methodological and experimental requirements for resolving the still outstanding issues. These issues concern not only the theoretical explanation of irregular and conflicting SORs, but also the experimental question whether further research into the OR binding site will mediate successfully between attempts to elucidate the underlying mechanism at work and theory-informed interpretations of molecular data. Second, the dynamics of the controversy also shed light on the increasingly inconsistent use of terms within which the olfactory debate is expressed. Because the wider olfactory debate, apart from its currently collective scepticism towards a vibration sensitive mechanism, is far from a homogeneous field. Divided into two salient experimental contexts, molecular biology and fragrance chemistry, different versions of a shape-sensitive mechanism co-exist simultaneously across these different contexts. Since the flexible induced-fit model is ill-suited for a systematic development of SORs and for the design of new molecules in fragrance research, modernised models of odotopes (so-called olfactophores) remain prominent as a heuristic tool.[355] Simultaneously, persistent anomalies in SORs are explained by reference to conformational changes. At the same time, stereochemical parameters inform the selection of test odorants for the investigation of receptor activity patterns, and also guide the development of hypothetical receptor models and computer

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[354] Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

[355] Ohloff et al. (2011): *Scent and Chemistry*, 79.

simulations of olfactory ligand binding.[356] A result of this disciplinary entrenchment is the overlap of different model-based inferences for the explanation, comparison and evaluation of data. The lack of conceptual coherence, persisting empirical irregularities and, if nothing else, polemics in this debate present an unmistakable indicator of the growing rift between the reliance on standard explanations and, because of their failure, the search for alternatives.

In light of developments such as those in the present case of olfaction theory, I argued that the philosophical concept of evidence for understanding scientific reasoning must be historicised. When we think about what is the basis for scientific judgements on theory choice, it is not enough to consider just the stability of knowledge a theory generates and the range of data it does or does not explain. A problem of theory choice, particularly in cases of underdetermination such as in the olfactory debate, is that each attempt to invoke data in support of a theoretical explanation is open to objection that the purported similarities or irregularities rest on an incomplete picture of the phenomenon and, as a result, present indeterminacies rather than a flaw of theory. Since the interpretation of data as potential evidence for or against a theory is in question, when comparing two rival theories and addressing a controversy, one must thereby also ask what makes a particular interpretation of data more significant than another. Informed by the olfactory scientists' approach to theory choice, I decided to reflect on the grounds on which a range of data is seen either as conflicting or not with a particular theory by consulting the disciplinary trajectory. This, in turn, helped to bring out some characteristic features of the general explanatory strategy in olfaction theory that offered a partial philosophical explanation of (1) the prevalence of the shape theory as the standard account, (2) the endurance of the rival vibration theory, and (2) why this controversy is so difficult to resolve.

The historical trajectory of olfaction theory, as I illustrated in this chapter, had a profound impact on present approaches to theory choice. What observations were considered as evidential or problematic for (or against) a theory depended on the dominant explanatory strategy in olfactory research. This strategy, in turn, was influenced by the conceptual progression and successive disciplinary

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[356] Malnic, Bettina; Hirono, Junzo; Sato, Takaaki and Buck, Linda B. (1999): Combinatorial Receptor Codes for Odors. *Cell* 96, 714; Crasto (2009): Computational Biology. See Chapter 8.

stages. What counts as evidence, therefore, became a question of what observations are considered as anomalies, indeterminate or affirmative data, and the evaluative interpretation of these observations as evidence was shown to be changeable throughout the historical trajectory. By historicising evidence, as undertaken in this chapter, I did not merely refer to the specific temporal context in which an observation is made or an experiment is conducted, but also addressed the historical disciplinary trajectory with its impact on later scientific judgements. Such a historicised perspective on evidence, rather than using the knowledge of history for de-historicising evidence, was shown to provide the basis on which the substantial differences underlying the olfactory controversy were rendered visible. These differences concerned more than just disagreement on basic assumptions about the structural features responsible for molecular odour recognition, but also pointed towards other substantial issues of disagreement in this controversy. Elucidating the different aspects under which a theory is considered successful, the process of epistemic iteration described further illustrated that whether empirical irregularities are evaluated as anomalies or as yet unexplained data remained a matter of interpretation. The interpretation of available observations and their epistemic status as either supporting or conflicting with a particular model framework, however, was shown to be as much in dispute as the theoretical explanations and, moreover, sensitive to historical change. On this account, there was no ahistorical basis to isolate and identify unambiguously what counts as evidence for theory choice in the olfactory debate. Paying attention to the underlying historical developments that characterise the concept of evidence within a scientific debate is central to identifying and understanding the epistemic and scientific consequences that followed from the criteria of theory choice thereby adopted. A critical exposition of theory choice, therefore, must both address the developmental potential of scientific concepts within their experimental context and identify their source of stability within a particular discourse. Philosophers of science as well as scientists thus have to direct closer attention to the historical tendencies that underlie scientific judgement about what constitutes the source of evidence for (or against) a theory.

Chapter 5

The Descent of Scent: Modelling the Mechanism of Primary Odour Recognition

1 What Informs successful Model-based Inference?

In the past decades between the first hypotheses suggesting a molecular basis of smell (1920s) and the discovery of the olfactory receptors (1991), olfaction theory has come a long way, even though it remained more of a niche subject. During this time, informed by theoretical reasoning that relied on the success of parallel developments in molecular biology, olfactory researchers have developed a variety of modelling strategies to compensate for the lack of empirical insight into the molecular perception mechanism. It is, however, not without significance that, even after the groundbreaking identification of the receptors, the empirical gap between model-based inferences and the physical target system has not been bridged and theories about olfactory perception have not been substantiated. Quite the contrary, contemporary issues in olfaction surround two rival explanations for the mechanism of primary odour recognition as I illustrated in the previous chapter. Orthodox opinion about primary smell recognition continues to take shape to be the key feature underlying molecular recognition. The alternative account, questioning shape and referring to molecular vibration in the infrared range, has been widely disregarded – yet not sufficiently challenged on its experimental basis.

Whereas the previous chapter addressed the issue of theory-choice in the olfactory debate through its general historical disciplinary trajectory, this chapter follows with an analysis of the more specific arguments of model-choice surrounding the mechanism of primary odour recognition. The rivalry between these two mechanism models, as part of the contemporary and unresolved olfactory controversy, results in a question central to a philosophical understanding of scientific reasoning: what informs successful model-based inference? And, in this specific case: how and on what grounds are causal explanations inferred from a theoretical model justified? Causal reasoning informs our beliefs about the fundamental reality underlying the phenomena we aim to explain. By identifying the conditions under which particular phenomena are thought to happen, causal explanations determine the characteristics of the entities involved and their predispositions to produce the effects observed.[357] But, given the situation of two rival explanations of molecular odour perception, on what grounds do scientists infer the causal structure? Limited by the experimental inaccessibility of the key entity, the receptor binding site, any reconstruction of the mechanism rests on too meagre an empirical basis to know what is truly at work here. So far the available observations lend insufficient grounds to assess the facticity of the competing model claims and it is currently impossible to unambiguously decide between the two mechanisms on purely empirical considerations.[358] Future studies and advancements in protein modelling might alter the course of olfaction theory, but the question remains how to understand contemporary scientific judgement that takes one causal explanation to be more likely than another.

Addressing this conflict, the present chapter analyses the implicit modelling strategies in the reconstruction of the two olfactory mechanisms to assess the epistemic considerations that apparently credit some observations with greater or lesser authority in support of a specific theoretical framework. For this, I will first examine how each mechanism is built on limited but empirically sound observations, and to what extent epistemic virtues such as explanatory unity assist in the construction of facts. Most observations in laboratory practice are not mere givens of a directly accessible phenomenon but rely on the *production* and *interpretation* of effects through experimental reconstruction. By demonstrating the extent to which the interpretation of empirical data is inseparable from epistemic considerations, I will show that current olfactory judgement does not rest on an unequivocal basis for model assessment and choice. Instead, I suggest directing attention to the model building process and the historical trajectory in which model assessment takes place. This, I argue, is the essential perspective for elucidating the grounds on which scientific judgment in research practice is based. The following analysis therefore proceeds as follows. Section 2 explores what constitutes the empirical support for the two rival mechanisms of primary odour recognition. Section 3 analyses

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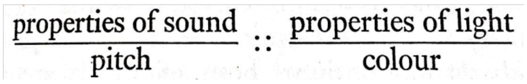
[357] Cartwright, Nancy (1983): *How the Laws of Physics Lie.* Oxford: Clarendon Press, 6.
[358] For more details see chapter 8.

the different epistemic considerations that favour each model. Central to both model building and evaluation, I will show, is a form of analogical reasoning, especially with respect to the widely favoured shape-sensitive model of olfactory responses. Section 4 addresses the issue of when the argument for either mechanism is decisive and argues for a historicised perspective on scientific judgement in order to understand and analyse arguments on model choice.

2 The Use of Analogical Reasoning for Model Building

To analyse what observations support each mechanism, I want to take a first look at how their models are constructed. What strikes the eye is that the causal explanations of both models rely on a form of analogical reasoning. Before I can introduce the underlying correspondence relations on which these models are built, it is useful to begin with what is meant by analogical reasoning. For this I refer to Mary Hesse's work on *Models and Analogies in Science*.[359] Hesse defines the general character of an analogical relation as a four-term relation where two terms form one analogue that is assumed to correspond to another analogue such as, for instance, the similarity relation between the properties of sound and the properties of light (fig. 1):



$$\frac{\text{properties of sound}}{\text{pitch}} :: \frac{\text{properties of light}}{\text{colour}}$$

Fig. 1 Analogy between the properties of sound and light. Hesse (1963): *Models and Analogies*, 75.

This formal scheme provides an abstract similarity relation that defines a one-to-one correspondence between certain characteristics of two otherwise separate phenomena. Serving as a heuristic tool, analogical relations aid in the articulation of theoretical terms to investigate a less well known phenomenon by reference to a better known one. To accomplish this heuristic task, Hesse elucidates, requires two further sorts of dyadic relations that characterise every analogy, horizontal and vertical. The horizontal level comprises similarity relations that hold between specific features of the phenomena. The vertical

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[359] Hesse, Mary B. (1963): *Models and Analogies in Science.* London, New York: Sheed and Ward.

level describes causal relations that, because they are supposed to be of ‘the same kind’, are assumed to correspond (fig. 2).[360]

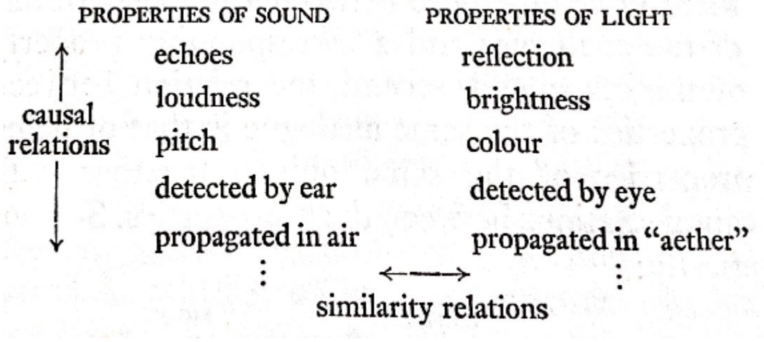

Fig. 2 Horizontal (similarity) and vertical (causal) relations of an analogy. Hesse (1963): *Models and Analogies*, 66.

Similar reasoning takes place in the olfactory debate. Since the nature of the olfactory receptors is unknown, current observations are interpreted within more established models of other mechanisms. Whereas the shape theory of odours started out from the standard “lock and key” model of enzyme binding to define the relevant terms of the olfactory mechanism, the mechanism of the vibration theory is linked to the method of spectroscopy. By noting horizontal similarities between the features of the analogy – lock and key on the one hand and spectroscopy on the other – and the available data of olfactory recognition, it is inferred that the same kind of vertical causal relations may hold as well.

2.1 The Ontological Compatibility of Locks and Keys

The shape-sensitive mechanism proposed by the proponents of the shape theory of odours, as I illustrated in the previous chapter, has its historical roots in the emergence of olfaction theory as an autonomous field. After it became clear at the dawn of the 20th century that odours must have a molecular basis, Linus Pauling reasoned that odour perception might work similarly to other molecular recognition processes such as metabolism, immune responses and digestion. Drawing on the widely popular lock and key model for enzyme binding, the odour of a molecule was presumed to be detected through its size and shape by a complementary shaped receptor.[361] Over the past decades, this

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[360] Hesse (1963): *Models and Analogies*, 96.

[361] Pauling, Linus (1946): Molecular architecture and Biological Reactions. *Chem. Eng. News* 24, 1375-1377; Lichtenthaler, Frieder W. (1995): 100 Years “Schlüssel-Schloss-Prinzip”: What

model has been constantly modified but has retained its central premise that the stereochemistry of a molecule is the key feature underlying the recognition process.[362] Contemporary opinion adopts a shape-sensitive mechanism according to the “induced fit” model of molecular responses which, like the lock and key idea, explains the specificity of ligand binding through the recognition of particular atoms groups by the receptor. Abandoning the structural rigidity of the lock and key analogy, however, the induced fit account states that underlying the recognition process are conformational changes between the molecules and the receptor binding sites.[363] Nonetheless, without experimental access to the olfactory receptor (OR) binding site the application of this model for an explanation of olfactory responses remains empirically underdetermined.

Based on the hypothesis of shape, statistical models assessing similarities of stereochemical parameters across molecules have been an integral part of research practice determining the binding capacity of odorants. The resulting models, so-called olfactophores (fig. 3), then further facilitate inferences to the binding capacities of the unknown receptor site and thereby assist in the construction of computational OR models.[364] Because ORs are broadly tuned and combinatorial[365] – meaning they can detect a wider range of odorants and some odorants can be identified by different receptors – olfactophore models are not identical but partially overlap with receptor models.[366]

Made Emil Fischer Use this Analogy? *Angewandte Chemie* [International Edition in English] 33(23-24), 2364-2374.

[362] Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 61-140.

[363] Koshland, Daniel E. (1995): The Key–Lock Theory and the Induced Fit Theory. *Angewandte Chemie International Edition in English* 33(23-24), 2375-2378.

[364] See Chapter 8.

[365] Malnic, Bettina; Hirono, Junzo; Sato, Takaaki and Buck, Linda B. (1999): Combinatorial Receptor Codes for Odors. *Cell* 96, 713-723.

[366] Ohloff et al. (2011): *Scent and Chemistry*, 117-127.

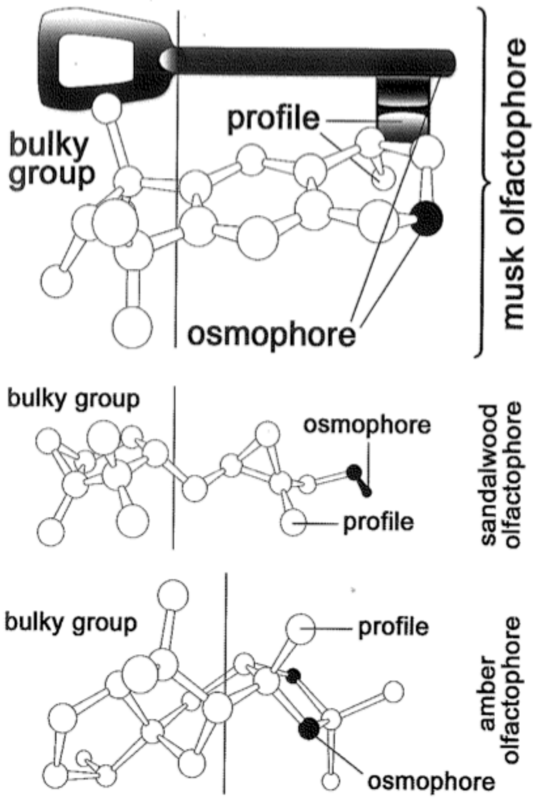

Fig. 3 Olfactophore models presented with the Lock and Key Analogy. Ohloff et al. (2011): *Scent and Chemistry*, 79.

Olfactophore models comprise three specific groups and describe their particular position within the odorant. First, with respect to the binding capacity of the molecule, the *osmophore* or OH-group functions as an H-bond donor. By forming a hydrogen bond with the receptor site, it basically 'inserts' the molecule and 'docks on' to the receptor. Second, encoding most of the olfactory information, the *profile group* binds to a more specific part of the binding site. Profile groups often involve functional groups such as thiols (-SH), nitriles (-CN), aldehydes (-C(=O)H) or esters (R-CO-O-R'). Finally, when interacting with the receptor, the *bulky group* of the molecules fills out the less specific part of the binding site and gives the molecule a firm grip within the receptor.[367]

Informing the construction of a shape-sensitive mechanism is a mediated analogical relation. Other molecular recognition processes, such as digestion, metabolism or immune responses, were modelled analogous to a lock and key interaction. Like the specificity of a key inserted into a lock, if a ligand has a correct fit it interacts with a complementary shaped receptor. Only on the assumption that the same causal process is also responsible for odour

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[367] Ibid., 78-80.

detection can we make inferences about similar characteristics between the entities involved (fig. 4).

Lock and Key Analogy	**Shape-Sensitive Mechanism** (Other Molecular Responses)	**Olfactory Mechanism**
Key	Ligand	Odorant
Lock	Enzyme	GCPR
Complementary Design	Specificity/ (Aspects of) Molecular Shape	Specificity/ (Aspects of) Molecular Shape

Fig. 4 Similarity relations between the Lock and Key model and molecular recognition mechanisms

The model of a shape-sensitive olfactory mechanism thus draws its plausibility from the compatibility with the broader theoretical understanding of other molecular responses. Empirical support for this analogical relation was obtained through the discovery of the ORs, identifying them as G-coupled protein receptors (GCPRs) and, as a result, as part of the class of proteins generally involved in shape-sensitive recognition processes. Yet, the argument that the discovery of the ORs suggests a shape-sensitive mechanism rests on an implicit ontological assumption about the unity of nature. Unity here expresses the idea that similar processes composed of similar entities generate similar causal relations. Even though GCPRs exhibit a great structural diversity, they nevertheless are instances of a class of proteins mostly thought to be involved in shape-sensitive binding processes. The preference for the structural hypothesis of shape in olfaction theory is thus "the preference for a hypothesis which implies as few deviations as possible from what we already know to exist."[368] Notwithstanding its intuitive appeal, the question remains to what extent such an inter-theoretic paradigm for the unification of causal explanations is justified, at least in this particular case study.

The inter-theoretic model of a shape-sensitive mechanism was the most successful approach for explaining molecular processes over the last century and down to today. It is applicable to a variety of phenomena and exhibits a broad explanatory scope. For research on the molecular basis of smell, the lock and key analogy served as a profound theoretical basis on which the selection of the key molecular feature was justified, spurring further enquiry into empirical structure-odour relations (SORs). Moreover, being its starting point, it defined the disciplinary identity and course of olfaction theory and has subsequently

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[368] Hesse (1963): *Models and Analogies*, 142.

developed into an established research paradigm. Since there has been no experimental evidence from other disciplines that contradicted the generally adopted theoretical framework of a shape-sensitive ligand binding mechanism, this inter-theoretic reference appeared to support the specific case aligned to it. Given its pragmatic success and the long-standing absence of a serious contender, there was thus no reason to doubt the adequacy of this model and its application to the olfactory mechanism.

2.2 The Shroud of Turin: A Spectroscope made of Flesh?

Although the shape theory of odours was not wholly unchallenged through the last century, its rival, the vibration theory of odours, lacked an empirically feasible model for the recognition of its proposed key feature responsible for odour perception. Robert Wright's assumption of a mechanical recognition of vibration frequencies in a biological system was thought impossible.[369] But what other option was there? Detecting and measuring vibration frequencies usually requires a spectroscope, an instrument that shoots photons at a molecule. When these photons hit the atoms within a molecule, pulling them out of their minimum energy position, the electron bonds holding these atoms together are stretched. Once the atoms rebound, their bonds are excited and vibrate at a specific frequency that is unique for each type of electron bond. In analogy to plucking the string of a guitar, when you "pull one of them atoms away and release it, it would go *boing*".[370] This molecular *boing* is measured in wavelength. Notwithstanding the technological possibility, photons are not a common functional item in mammalian physiology.

This situation, however, changed with the discovery of *electron* spectroscopy by Robert Jacklevic and Joseph Lambe.[371] Transport chains involving electrons are an integral component of molecular cell biology. Yet, the process of electron spectroscopy does not relate to common biological activities of electron transport. It is instead based on quantum physical electron tunnelling. The

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[369] Wright, Robert H. (1964): Odor and molecular vibration: the far infrared spectra of some perfume chemicals. *Annals of the New York Academy of Sciences* 116, 552-558; Wright, Robert H. (1977): Odor and Molecular Vibration: Neural Coding of Olfactory Information. *Journal of Theoretical Biology* 64(3), 473-474.

[370] Turin (2006): *Secret of Scent*, 119.

[371] Jaklevic, R.C. and Lambe, J. (1966): Molecular vibration spectra by electron tunnelling. *Physical Review Letters* 17, 1139-1140.

fundamental idea here is that, being highly dynamic particles, electrons jump gaps. Constantly buzzing around a donor site, electrons can cross small distances to a nearby acceptor. These jumps, referred to as “elastic electron tunnelling”, only take place when both electron donor and acceptor have the same energy level (fig. 5 left side). If these two sites differ in their energy level, the electrons simply buzz back and forth around the donor without travelling to the acceptor. Tunnelling between two sites with different energy levels is only possible if something absorbs enough of the electron’s energy to match the difference between donor and acceptor (fig. 5 right side). This something, allowing for so-called “inelastic electron tunnelling”, can easily be a molecule.[372]

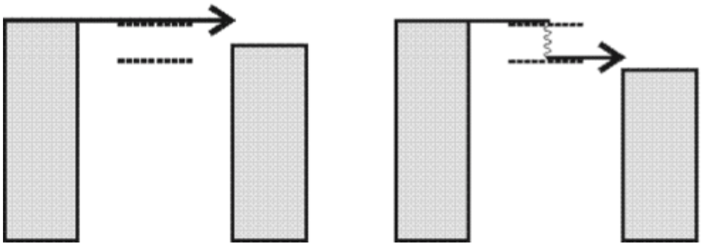

Fig. 5 Elastic (left) and inelastic electron tunnelling (right). Wikipedia (2013d): *Inelastic electron tunnelling spectroscopy.*

With the occurrence of electron spectroscopy the previously purely conceptual analogy of a spectroscope made out of flesh turned into a material possibility. When Luca Turin revived the hitherto abandoned vibration theory in 1996, he proposed the possibility of inelastic electron tunnelling spectroscopy (IETS) for olfactory responses.[373] Unlike the shape-sensitive mechanism, his model first required the demonstration of its empirical possibility. For this he needed to establish three empirical requirements: the conductivity of proteins, the presence of an electron source and the existence of a metal binding site in the ORs. The first requirement was possibly the easiest to supply; studies on the semi-conductive character of proteins were already available and Turin’s previous research had led him to the design of a US-patented device within which proteins act as a Schottky diode. This device consists of two mercury-zinc drops coated with protein (egg will do) that, when wired together, result in a

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[372] Wolf, E.L. (2011): *Principles of Electron Tunneling Spectroscopy.* 2nd Edition. Oxford: Oxford University Press, 366f.; Wang, Wenyong; Lee, Takhee and Reed, Mark A. (2004): Elastic and Inelastic Electron Tunneling in Alkane Self-Assembled Monolayers. *The Journal of Physical Chemistry B* 108(48), 18398-18407.

[373] Turin, Luca (1996): A Spectroscopic Mechanism for Primary Olfactory Reception. *Chemical Senses* 21(6), 773-791.

current flow.[374] The other two requirements, however, did not concern a general feature of proteins but the specific character of the ORs.

Electron sources in biology are commonly found in phosphate groups such as NADPH (nicotinamide adenine dinucleotide phosphates). As a biological battery, NADPH indeed provides the minimum energy requirement for the detection of molecular vibrations up to 4000 wavelengths. Current methods showing the presence of NADPH rely on its ability to bind to a specific amino acid sequence, namely GXGXXA or GXGXXG where “G is Glycerine, A is Alanine, and X can be any neutral (uncharged) amino acid at all”.[375] Turin’s proof of the presence of this sequence in the amino acid motifs of the ORs therefore strongly suggests the presence of NADPH.[376]

Finally, concerning the ‘wiring’ of a biological spectroscope, a similar test demonstrates the presence of a metal co-factor; metal co-factors too bind exclusively to specific amino acid sequences. A metal known for its supreme binding capacity is zinc, a metal co-factor that is furthermore involved in various physiological conditions of olfactory responses – for instance, loss of smell perception is often associated with zinc deficiency.[377] Turin thus searched for zinc binding sequences in the olfactory receptors. Here success was not immediate, though. Starting with zinc-related sequences listed in enzyme databases, no matches of zinc protein sequences for the olfactory receptors were found. However, reversing the strategy, starting from OR sequences and searching for matches in other proteins, led to a surprising result. One sequence, namely CGSHL, was detected; a sequence otherwise almost exclusively found in insulin (fig. 6). And in fact insulin binds extremely well to zinc. The reason why there had been no initial match with amino acid sequences of the olfactory receptors was that in the first approach the sequences were taken from enzymes; insulin, however, is a hormone.[378]

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[374] US Patent 5.258.627 see Turin (2006): *The Secret of Scent*, 166.

[375] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House, 198.

[376] Turin (1996): *Spectroscopic Mechanism*, 776; Burr (2002): *Emperor of Scent*, 198-201.

[377] Beauchamp, Gary K. and Bartoshuk, Linda (1997): *Tasting and Smelling. Handbook of Perception and Cognition.* 2nd Edition. London: Academic Press Inc., 186; Burr (2002): *Emperor of Scent*, 203; Bijlani, R.L.; Bijlani, R.L. and Manjunatha, S. (2011): *Understanding Medical Physiology: A Textbook for Medical Students.* 4th Edition. JP Medical Ltd., 408.

[378] Turin (1996): *Spectroscopic Mechanism*, 776-777; Burr (2002): *Emperor of Scent*, 201-210.

INS_RABIT	FVNQHL	CGSHL	VEALYLVCG
OLFO_RAT	GICKVFST	CGSHL	SVVSLFY GTIIGLYLCP
OLF1_CHICK	KDGKYKAFST	CTSHL	MAVSL FHGTVIFMYL
OLF1_RAT	VRGIHKIFST	CGSHL	SVVSL FYGTIIGLYL
OLF2_CHICK	KDGKYKAFST	CTSHL	MAVSL FHGTVIFMYL
OLF2_RAT	TVQGKYKAFST	CASHL	SIVS LFYSTGLGVY
OLF3_CHICK	KDGKYKAFST	CTSHL	MAVSL FHGTVIFMYL
OLF3_MOUSE	VEGRRKAFNT	CVSHL	VVVFL FYGSAIYGYL
OLF3_RAT	VHGKYKAFST	CASHL	SVVSL FYCTGLGVYL
OLF4_CHICK	KDGKYKAFST	CTSHL	MAVSL FHGTVIFMYL
OLF4_MOUSE	REGKFKAFST	CSTHI	SAVAI FYGSGAFTYL
OLF4_RAT	IQDIYKVFST	CGSHL	SVVTL FYGTIFGIYL
OLF5_CHICK	KDGKYKAFST	CTSHL	MAVSL FHGTVIFMYL
OLF5_MOUSE	ATGQRKAFST	CASHL	TVVVI FYTAVIFMYV
OLF5_RAT	PRGGWKSFST	CGSHL	AVVCL FYGTVIAVYF
OLF6_CHICK	KERKYKAFST	CTSHL	MAVSL FHGTIVFMYF
OLF6_RAT	IPSARGRHRAFST	CSSHL	TV VLIWYGSTIF
OLF7_MOUSE	EEGQRKAFST	CSSHL	CVVGL FYGTAIVMYV
OLF7_RAT	AAGRHKAFST	CASHL	TVVIIFYAAS
OLF8_MOUSE	KGWSKALGT	CGSHI	TVSLFY**GSGLLA**YVK
OLF8_RAT	SIHKVFST	CGSHL	SVVSLFY GTIIGLYLCP
OLF9_RAT	SIHKVFST	CGSHL	SVVSLFY GTIIGLYLCP
OLFD_CANFA	IGICKVFST	CGSHL	SVVSLF YGTVIGLYLC
OLFE_HUMAN	VSKKYKAFST	CASHL	GAVSL FYGTLCMVYL
OLFI_HUMAN	SKGICKAFST	CGSHL	SVVSL FYGTVIGLYL
OLFJ_HUMAN	VEGRKKAFAT	CASHL	TVVIV HYSCASIAYL
GU58_RAT	SQGKYKAFST	CASHL	SVVSLFYSTLLGVYL
GU33_RAT	SSTVSKYKAFST	CGSHL	CVVCLFYGSVIGV
GU38_RAT	SLLGGMYKAFST	CGSHL	SVVSLFYGTGFGV
GU45_RAT	SSAEGKYKAFST	CVSHL	SVVSLFYCTLLGV

Figure 2 Sequence homologies between insulin (top line) and olfactory and gustatory receptors. The motif indicated in red (box) is the zinc-binding motif of insulin, which is also present in all the olfactory and gustatory receptors with small variations. The blue motif of olf8_mouse is a highly conserved NADPH binding sequence.

Fig. 6 Amino acid sequence homologies (between ORs and insulin) obtained from BLITZ email server.[379] Turin (1996): *Spectroscopic Mechanism*, 777.

Linked to these empirical features of the receptors, Turin modelled a possible spectroscopic mechanism for olfactory responses, the so-called swipe card model. In his model of the receptor (fig. 7), we have an electron donor (NADPH) and an acceptor (zinc). Donor and acceptor are not on the same energy level so that a ligand is required to initiate a response. As long as the binding site is unoccupied, no reaction takes place. Once an odorant enters the olfactory receptor, electrons cross the gap in the binding site – but only if the vibration spectrum of the odorant matches the energy difference between donor and acceptor. In this case, a form of electron spectroscopy occurs: when the electrons shoot through the molecule, hitting its atoms, they excite the electron bonds and thereby activate the molecule's vibrational mode. In the course of this, and depending on the particular vibration spectrum of the odorant, the electrons lose a specific amount of energy that is absorbed by the molecule. It

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[379] BLITZ email server (1993): *EMBL-Heidelberg.* URL=<http://www.gen-info.osaka-u.ac.jp/eserver/blitz.html>

is also assumed that binding sites exhibit different energy levels and thus react to odorants with a corresponding vibration spectrum. When the electrons lose enough energy in this process, they travel across the receptor and dock on to the metal binding site. A further consequence is that the disulfide bridge, connecting the G-protein with the receptor via the zinc ion, is reduced. After splitting up the disulfide bridge and thus releasing the G-coupled protein from its bond to the 7-transmembrane receptor, the subsequent signal transduction takes place.[380]

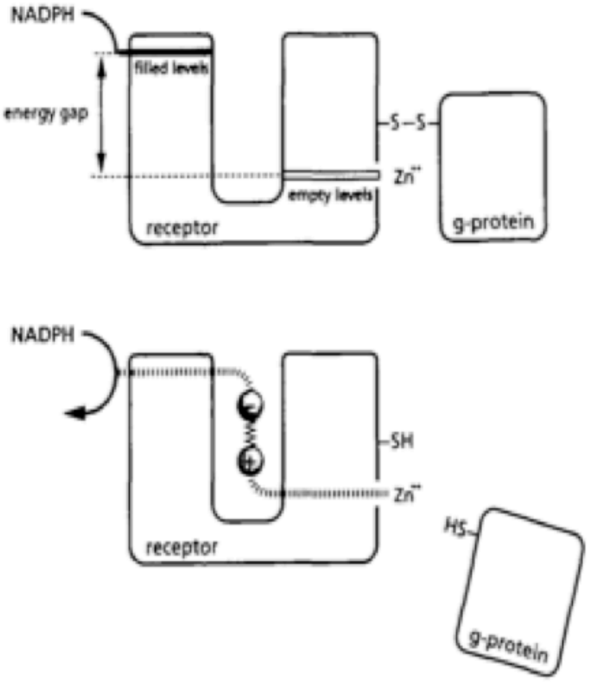

Fig. 7 Swipe card model. Turin (1996): *Spectroscopic Mechanism*, 774.

Turin's construction of a plausible model that describes the biological transduction of molecular vibrations relied on a modification of an existing physical system whose basic empirical requirements had to be brought in correspondence with features of the ORs such as the semi-conductivity of proteins, a soluble electron donor and a metal-cofactor. Only by locating these discrete characteristics in the ORs was Turin able to establish an empirical link between two otherwise completely disparate causal processes, namely spectroscopy and molecular recognition (fig. 8). In further support of the IETS mechanism, another study attested Turin's model to be empirically feasible, even though highly hypothetical, according to current knowledge:

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[380] Turin (1996): *Spectroscopic Mechanism*, 772-775; Turin (2006): *Secret of Scent*, 159-189.

> “Using values of key parameters in line with those for other biomolecular systems, we find the proposed mechanism is consistent both with the underlying physics and with observed features of smell, provided the receptor has certain general properties.”[381]

Electron Spectroscopy	Swipe Card Model
Conductivity	Semi-Conductivity
Electron Donor	NADPH
Electron Acceptor	Metal Co-Factor/Zinc
Gap	Receptor Site
Energy Absorbing Entity	Odorant

Fig. 8 Similarity Relations between Electron Spectroscopy and Olfactory Recognition

Criticism addressing the IETS mechanism concerns its causal nature. Unlike the shape-sensitive mechanism, Turin’s model presents a mechanism that is not only highly hypothetical but currently unique in its ontological character. The proposal of a biological spectroscope is seen as unduly speculative in comparison to the well established alternative of shape. Although the characteristics for an olfactory IETS mechanism analogous to an electron spectroscope are not arbitrary (as they are grounded in the demonstration of its empirical requirements within the structure of the ORs), they nevertheless do not prove whether the physical process acts like the model. Moreover, compared to the broader explanatory scope of the shape-sensitive mechanism, the explanatory function of the swipe card model might not exceed the scope of its particular explanandum.

3 The Limits of Analogical Reasoning for Model Assessment

The situation outlined above describes the rivalry of two mechanisms each of which states a different causal explanation for primary odour recognition. Although both models are currently empirically underdetermined, a strong tendency in the olfactory debate is to dismiss the IETS mechanism in favour of the more traditional shape-sensitive one. My focus of discussion in the remainder of this chapter thus concerns the scientific reasoning that informs this bias. Having introduced the competing theoretical models previously, it became

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[381] Brookes, Jennifer C.; Hartoutsiou, Filio; Horsfield, A. P. and Stoneham, A. M. (2007): Could humans recognize odor by phonon assisted tunneling? *Phys Rev Lett.* 98(3), Article 038101.

clear that analogical reasoning played an important part in their generation. By helping to find similarities between two model systems, analogies provided the source on which the selection of descriptions for the qualitative character of the olfactory mechanisms were based, leading to the individuation of significant elements and the specification of the conditions on which the presumed causal interaction is supposed to take place.

Moving beyond their heuristic role for model construction, I now want to address another role of the analogies employed in this particular debate surrounding the olfactory mechanisms. Given the strong presupposition of model-choice in favour of the shape-sensitive mechanism, how does analogical reasoning play into the justification strategies underlying this preference? And why, with respect to the particular case study chosen, is the argument for the lock and key analogy (rather than the idea of a biological spectroscope) seen as more persuasive?

Although either model of the olfactory mechanism is in principle empirically possible, the wider scientific community accepts a shape-sensitive mechanism as the more 'likely' cause of olfactory recognition. What I want to know is what difference there is between the evidence for this allegedly more likely causal explanation and the evidence we have for a feasible alternative. It seems to me that the two mechanisms are probably on an equal footing epistemically. In support of shape is its explanatory unifying character through reference to an inter-theoretic framework that treats a variety of molecular processes in a similar way. Yet this approach comes up against a broader range of conflicting SORs data. In favour of vibration are its predictive success and the SORs data about which shape remains silent. Nonetheless, the causal process by which odour perception is assumed to act here appears to be potentially unique to the sense of smell.

There is, I think, an important constraint that guides current scientific judgement in this debate – the premise of an ontological unity of similar causal processes. Given that all known ligand-binding processes are assumed to act according to a shape-sensitive mechanism, why should this be different for olfactory recognition? Despite its persuasive power, such an argument from ontological unity is conditional, though. We can infer to the more likely cause legitimately if there are no alternatives that account for the phenomenon in an equally explanatory satisfying way. Having an alternative explanation for the same phenomenon, ontological unity can be considered a reasonable criterion for model or theory choice. But given the limits of the shape theory for explaining SORs in comparison to the predictive success of the rival vibration account, there are also good reasons to question the premise of ontological unity. Thus, even though explanatory power does not imply truth, as Nancy Cartwright rightly pointed out in *How the Laws of Physics Lie* (1983),[382] in the case of two rival models it serves as reasonable grounds to question our beliefs about the legitimacy of our established inferences. These grounds divide the olfactory community. Considering the experimental inaccessibility of the ORs, it is not obvious what observable features and data of the olfactory perception process are in fact ‘essential’ for determining its underlying causal nature.

The scientific reasoning for the selection of stereochemical features as the causally ‘essential’ ones was shown to be primarily analogical and theory-driven. Only on the grounds of the established lock and key model and its firm experimental basis within the wider research culture on molecular recognition did the hypothesis of stereochemistry as the causally relevant feature seem less speculative than, for instance, the hypothesis of vibration frequencies. Empirical support for the theoretical reasoning suggesting a shape-sensitive mechanism was eventually obtained though the discovery of the ORs. Enforcing the analogical relations underlying the adopted lock and key model was the co-occurrence of essentially the same causal entities in what seems to be the same causal pattern: signal transmission through ligand docking on G-coupled protein receptors (GCPRs). Given the dominance of the shape theory, which at that time lacked a genuine rival, the discovery of the ORs indeed followed a research strategy that acted upon the premise of ontological unity. One of the core assumptions involved in the discovery process was a possible involvement of some type of GCPRs, as these were part of all other known ligand-binding processes acting according to a shape-sensitive mechanism. These empirical findings therefore strengthened this account and it is not surprising that this result was seen as post hoc evidence for the legitimacy of the lock and key analogy. Even though not part of any explicit hypothesis testing, the discovery of the ORs thereby presented a form of ‘generative justification’, i.e. a

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[382] Cartwright (1983): *Laws of Physics*, 4, 76.

confirmation of a hypothesis through its productive involvement in further discoveries.[383]

In favour of the shape-sensitive mechanism were thus its intuitive appeal and its exemplary success through the discovery of the ORs. Despite these valid considerations, however, the tendency to unify explanations of somewhat similar phenomena under an umbrella theory can also lead to a misleading and even severely distorted picture. Unification generally involves an abstraction from particular cases, which might not only vary structurally from instance to instance, but the subsumed cases can also differ in their causal characteristics. In whatever way the individual entities, the GCPRs, may structurally resemble or differ from each other, the predominant focus on the nature of the causal *constituents* diverts attention from the characteristics of the causal *process*. What is not considered, therefore, is whether molecular recognition processes may differ in other significant aspects.[384] Consider the factor of time, central to understanding processes. A temporal comparison of molecular reactions such as digestion, immune responses and olfactory recognition in fact suggests that there are differences in their causal structure.

Digestive processes are limited to specific nutriment elements such as lipids, proteins and carbohydrates. Being an only slowly evolving inventory of the evolutionary available menu, most of the elements digested by our ancestors will be the same elements digested by our descendants. These elements are also processed a few hours after ingestion to provide the organism with the energy constantly required to sustain itself. In comparison, the (trained) immune system demands a high degree of flexibility because it needs to constantly adapt to new and yet unknown elements that the organism encounters. It cannot rely on a fixed catalogue of elements that our ancestors might have come across but it has to adjust to an ever-changing and evolving environment. The identification of an indefinite range of elements and the production of antibodies do not happen swiftly but, as one is vividly reminded with every new flu season, take a considerable amount of time. Digestion and immune responses thus differ in two important aspects: the scope of ligands detectable and the time involved for their recognition.[385]

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[383] Kirschenmann, Peter P. (1991): Local and Normative Rationality of Science: The ‘Content of Discovery’ Rehabilitated. Journal for General Philosophy of Science 22, 67.

[384] Dupré, John (2002c): The Lure of the Simplistic. *Philosophy of Science* 69, 284-293.

[385] Burr (2002): *Emperor of Scent*, 7-9.

Exactly these two aspects mark an important difference in the sense of smell. A significant characteristic of olfactory responses is the broad scope of structurally diverse and complex elements recognised; there is – apart from general size restraints – no innate limitation of the mechanism to what we can smell. Our noses are indifferent as to whether they encounter an odorant known by our ancestors or an odorant just synthesised in the laboratory. Moreover, and most importantly, the smell of these odorants is perceived immediately.[386] Perfumery would not be a profitable business if we were only able to smell a new fragrance after we left the store. Unlike digestion and immune responses, which may be said to *begin* very quickly, smelling an unfamiliar smell is thus something that one *does now*. Although the broad range of structurally diverse odorants is explained through the combinatorial nature of odour recognition,[387] the rigid lock and key model and also its more flexible induced fit sibling (in their current formulation) do not account for the *immediateness* of the response.

In addition to empirical observations casting doubt on an alleged ontological conformity of molecular processes, there are also epistemic concerns regarding the strategy of explanatory unification. The normative tendency to unify phenomena under a familiar explanation and an inter-theoretic framework sometimes "unduly restricts the *novelty* of theories which have model-interpretations."[388] Putting aside the question of whether Turin's mechanism turns out in the future to be factual for olfactory responses, the present significance of his proposal is the demonstration of an empirical possibility for biological spectroscopy – the possibility of a causal process that had been universally denied previously. Even though the model of a biological spectroscope remains highly hypothetical, there is neither an *a priori* nor an empirical reason to reject its proposed causal explanation. Since the material requirements of the initially merely conceptual model have been experimentally demonstrated, the idea of a "spectroscope made out of flesh" received an empirical foundation. Criticism directed at the causal interpretation of the vibration-sensitive mechanism thus rests on a theory-infused perspective on the causality of biological processes in general.

This, I think, indicates a crucial conflation occurring in the olfactory debate. Rather than being established by causal reasoning, the shape-sensitive

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[386] Ibid., 9.

[387] Malnic et al. (1999): *Combinatorial Receptor Codes*.

[388] Hesse (1963): *Models and Analogies*, 143.

mechanism has its origins in analogical reasoning. Consider how causal reasoning is commonly defined: “we reason backwards from the detailed structure of the effects to exactly what characteristics the causes must have in order to bring them about.”[389] Arguments for a shape-sensitive mechanism, however, were shown to follow a different reasoning pattern. Rather than linking a suggested causal feature with observed effects through structure-odour relations, the scientific reasoning underlying the construction of the shape-sensitive mechanism started with a theoretical model drawn from explanations of other molecular processes. In fact, the irregularity of SORs and the failure of systematically relating observations of molecular structure to olfactory properties, required constant modifications of the theoretical shape-mechanism.[390] Since many irregularities remain unresolved, these ad hoc modifications required further justification. This justification was found in the discovery of the ORs eventually. Exploring the process of model construction and justification strategies for a shape-sensitive mechanism, one thing stands out in particular. Assumptions about an ontological uniformity in the causal structure of molecular processes did not only guide the introduction of the lock and key analogy into the olfactory debate, they also carried some probative weight for judging it legitimate. Furthermore, its generic involvement in the discovery process of the ORs seemed to present the theoretical reasoning spurring the lock and key analogy with greater credibility. Underlying this entanglement of the lock and key analogy in both the construction and justification process of the shape model is the same epistemic virtue, the unity of explanations through the unity of nature.

By contrast, the vibration theory started from a comparison with SORs data and hypothesis testing leading to a (successful) prediction. This, in turn, led to the search for a theoretical model that explained which characteristics were responsible for the observable (SORs) effects. Spurred by causal and not analogical reasoning, the justification strategies for a vibration-sensitive mechanism were shown to be independent from the generation process. Whereas the generation of the IETS-mechanism was based upon the analogy with a biological spectroscope, its justification relied on the accommodation and prediction of SORs. Nonetheless, emphasis on the predictive success of

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[389] Cartwright (1983): *Laws of Physics*, 6.

[390] See chapter 7.

vibration theory seems not to carry enough weight for many olfactory researchers today.

The manifest asymmetry in evidential weight between ontological unity and predictive success in the olfactory debate on model choice highlights a nice point about scientific judgement. Questions of empirical support, as can be seen in this case, are entrenched within epistemic considerations. These, in turn, seem to play a role not only in the invention but also the evaluation of heuristic strategies such as the use of analogical reasoning. In fact, in the case of the widely accepted model of a shape-sensitive mechanism, the analogical reasoning that aided in its construction was part of the same thought process that guided its justification. In comparison, the epistemic virtue supporting the rival vibration-sensitive mechanism, i.e. the predictive power of its hypothesis, was only involved in questions of empirical support and hypothesis testing. As a result, the conceptual boundaries between heuristic and confirmative approaches appeared increasingly blurred in the olfactory debate.

Although it is difficult to see, from an abstract philosophical perspective, how evidence that comprises predictions is considered less valuable than that obtained from data used in the construction process of a model, the scientific judgement underlying the olfactory debate is not irrational by any means but, rather, displays a reasoning pattern which, as I will argue in the following, is deeply grounded in its disciplinary historicity. In the next section, I will therefore clarify the impact that historicity has on the reasoning pattern that informs scientific judgement by illustrating the extent to which justification strategies in scientific practice closely relate to the trajectory within which a model was developed. In spite of its locality – the olfactory debate currently forms only a niche discourse – the reasoning patterns and explanatory strategies employed are of exemplary character and present a case study against which analyses of other scientific discourses can be compared to benefit further philosophical understanding of scientific judgement and analyses of model choice.

4 Historicising Scientific Judgement for Understanding Model-Choice

Emphasis on the historical character of science, exploring the contextual embedding of theories instead of their abstract epistemic virtues,[391] has increasingly entered debate in the philosophy of science within the last few decades. Most of the arguments concerning a historically informed philosophical perspective on science can be subsumed under the question: to what extent does the plausibility of scientific theories and models depend on their historical context, development and application? A variety of philosophical work already points to the significance of the historical changeability of important factors underlying scientific advancement such as, for instance, changes concerning forms of measurement and standardisation, technological innovations and conceptual change in general.[392] A general consensus emerging out of this, as Alan Musgrave already advocated, is the need to include background knowledge in theories of confirmation.[393] He argued that significant changes to the background by which a certain model is characterised, also affects its source of confirmation.[394]

This perspective ascribes an inevitably historical character to the theoretical interpretation and epistemic evaluation of observations as evidence. Using such a historical perspective on theory choice in the olfactory debate, I already demonstrated the impact of disciplinary developments and changes in background knowledge on what kinds of observation are taken as evidentially

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[391] Philosophers of science have considered variety of epistemic and pragmatic criteriasuch as parsimony, operationality, generativity, explanatory power, predictive power, unifying capacity, completeness, internal consistency, scope, elegance, measurement etc. See: Carl G. Hempel (1966): Philosophy of Natural Science. Prentice-Hall; Thomas Kuhn (1979[1977]): Objectivity, Value Judgment, and Theory Choice. In: The Essential Tension: *Selected Studies in Scientific Tradition and Change.* University of Chicago Press; Bas van Fraassen (1980): *The Scientific Image.* Oxford University Press; William G. Lycan (1988): *Judgment and Justification.* CUP Archive; Lycan, William G. (1998): Theoretical (Epistemic) Virtues. In: *Routledge Encyclopedia of Philosophy 9.* Ed. by E. Craig. London: Routledge, 340-343.

[392] See for instance the works of Koyré, Alexandre (1957): *From the Closed World to the Infinite Universe.* Baltimore: John Hopkins University Press; Collingwood, Robin George (1960): *The Idea of Nature.* Oxford: Oxford University Press; Rheinberger, Hans-Jörg (2010): *On Historicizing Epistemology: An Essay.* Stanford: Stanford University Press; Chang, Hasok (2012): *Is Water H2O? Evidence, Realism and Pluralism.* Dordrecht, Heidelberg, New York, London: Springer.

[393] Musgrave, Alan (1974): Logical versus Historical Theories of Confirmation. *The British Journal for the Philosophy of Science* 25(1), 1-23.

[394] Musgrave (1974): *Logical versus Historical*; Worrall, John (2012): Theory-Confirmation and History. In: *Rationality and Reality.* Ed. by C. Cheyne and J. Worrall. Springer, 49-60. Cited is the prepublished paper: URL=< www.error06.econ.vt.edu/Worrallb.doc>, 32.

adequate for contemporary discourse in the previous chapter. In comparison, this chapter focussed on the related but more model-specific arguments surrounding the mechanism of primary odour recognition. Here I first explored the use of analogical reasoning as a heuristic strategy employed in the model building process of the competing mechanisms. Following this, I analysed the extent to which these analogies were also part of the arguments in the models' justification. Although integral to the construction process of either model, the role analogies played for justification strategies were shown to differ. It turned out that the analogical reasoning that spurred enquiry into a shape-sensitive mechanism was part of the same process that underlay its justification. By contrast, analogical reasoning only played a part in the construction process of the rival vibration-sensitive mechanism but not in its justification, which was largely grounded in hypothesis testing concerning SORs.

This opens up an interesting perspective for understanding the scientific reasoning underlying model choice in the olfactory debate. Why is it that the evidence for a shape-sensitive mechanism, relying on arguments involved in both its construction and its justification, are not considered question-begging? And why is it that predictions, despite being fairly independent of data used in the construction process, possess *less* evidential weight? The grounds for this, I argue, lie in the particular historical trajectory of the olfactory debate. For this reason, tracing the developmental character of knowledge production, attention needs to be directed at the historical entrenchment of theoretical assumptions and interpretations of empirical data. This entrenchment, I argue, serves as the basis on which we can understand the emphasis given to particular explanations and to particular epistemic considerations in scientific discourse today. In the remainder of this chapter, I will therefore show how a perspective on the historical trajectory of a discipline elucidates the process by which theoretical assumptions and epistemic considerations can become "blackboxed" into an ontological premise.

The philosophical concept of "blackboxing" has been mainly used to analyse technological advances and their influence on scientific development. When Bruno Latour and Hans-Jörg Rheinberger introduced this concept, they used it to describe the process of turning results of previous scientific enquiry into technological objects. That means that instead of further exploring the previously unknown nature of a phenomenon, we have developed techniques that allow for its stable and coherent reproduction such as, for instance, the technology of DNA sequencing that, while being under active development over more than ten years ago, is now a standard laboratory routine no longer challenged. By becoming the standard means through which further enquiry takes place, objects or procedures become “blackboxed”. In other words, the epistemic context of a phenomenon and its surrounding scientific practices changed.[395]

This epistemic process of blackboxing not only concerns the instrumental context surrounding research materials but also describes the historical transformation of a theoretical assumption into an ontological premise. To address this issue, and to extend my historical argument in the previous chapter, I will now suggest that, in order to understand the evidential weight attributed to epistemic considerations in a scientific debate, one must also take the particular *order of events* defining the trajectory of rival theories into account. A closer look at the continuities and discontinuities underlying scientific developments will elucidate that the particular order of events significantly shapes the background ontology defining a phenomenon’s nature. This background ontology in turn provides the basis on which later scientific judgement decides on the adequacy of explanations and the desirability of particular epistemic virtues for a model providing these explanations. For a demonstration of the epistemic impact that historical developments have on contemporary judgement let me therefore present two brief stories, one of which is the real trajectory of the olfactory debate and the other one is a counterfactual version.

Suppose we are given two rival theories, T_1 (shape) and T_2 (vibration) that address the same phenomenon of smell perception by appeal to either of the two distinct molecular features B_1 (stereochemistry) and B_2 (wavelength frequency) of which one is assumed to be the cause C for a sensory quality A. Although T_2’s structural hypothesis H_2 (All A are linked to B_2) corresponds with a variety of molecular data, only T_1 proposes an empirically feasible mechanism M_1 that presents its hypothesis H_1 (All A are linked to B_1) with causal credibility.

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[395] Latour, Bruno (1987): *Science in Action. How to follow scientists and engineers through society.* Cambridge M.A.: Harvard University Press, 21; Rheinberger, Hans-Jörg (1992): *Experiment, Differenz, Schrift. Die Geschichte Epistemischer Dinge.* Marburg, Lahn: Basilisken-Presse, 70-73, see esp. pp. 70 footnote 15; Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press, 30f.

Throughout the course of a century, T_1 dominated the research tradition, becoming embedded in a variety of data processing techniques and experimental strategies. The late introduction of a feasible mechanism M_2 now challenges the causal explanation of T_1, because B_2 is not included in the formulation of H_1/M_1. It is furthermore supported by a successful experiment where A is predicted by a calculation of B_2 and its result is also in conflict with H_1. Given this constellation, the introduction of the model M_2 into T_2 seems to *weaken* the claim of T_1 without, however, refuting it.

Imagine now a different story: what if M_2 was introduced into the debate *before* M_1? In this scenario, T_2 facilitates successful predictions through H_2 and has a mechanism M_2 that grants it with empirical feasibility. As long as there is no comparative predictive success of the inductively better supported model M_1, the choice for T_2 over T_1 appears not only legitimate but also more reasonable. The reason for this is that the claim of T_2 in this counterfactual trajectory remains not only *unrefuted* but also *unaffected* by T_1.

Looking at the olfactory debate in this way, it seems justification strategies for scientific theories are informed not only by the content-related change of background knowledge, but also by the temporal *sequence* or the *course* of a scientific trajectory. Why a particular model remains prominent, despite having an available alternative the testing of which does not rely on the data employed for its construction, as in this case, depends on the significance of the epistemic virtue that supports its application. The epistemic virtue of the shape model, its explanatory unity, rested on the explanatory success this model had gained in other, related modelling contexts. “Existing and emerging discoveries of DNA structure, progress toward cracking the genetic code, and the known commonalities in metabolic pathways all seemed to justify the assumption of the universality of molecular processes.”[396] The empirical weaknesses of the shape model were considered to reflect the chemical complexity underlying the perception process which, rather than demanding a different model, required further adjustments. Being involved in a variety of associated experimental and modelling practices (such as the synthesis of analogues, the development of olfactophore models and hypothetical receptor modelling) it gathered continuity and robustness of its underlying structural hypothesis over the last decades. By

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[396] O’Malley, Maureen A.; Elliott, Kevin C.; Buran, Richard M. (2010): From genetic to genomic regulation: iterativity in microRNA research. *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 41(4), 408.

contrast, the model of a vibration-sensitive mechanism lacked any historical or experimental practice in the sense that it was not affiliated with the relevant research context. Although relying on an established quantum physical process, it appeared disconnected from generic concepts embedded in molecular biology. Its only connection to olfactory research practices concerned its mainly conceptual relation to the old vibration theory. As a result, it lacked an affiliation with experimental practices relevant to olfactory practices with which it could be better positioned in comparison to the established shape model. The latter's weaknesses on the theoretical level were compensated by its experimental entrenchment in a wider experimental context, which it obtained through the gradually evolving background ontology it was embedded in and which was shaping the character of olfactory research throughout the last decade.

However, recalling my counterfactual trajectory, if the vibration model were introduced into olfaction theory before the shape model, its predictive success would have had more weight in considerations about model choice. The lack of continuity, through which the shape model gained its hegemony in the actual trajectory, would have at least weakened the epistemological strength of assumptions of the universality of molecular processes. Moreover, as I argued already in the previous chapter, the strength of the vibration model, predicting odour from structure, would have occurred at a time when SORs were considered to be more relevant for understanding primary smell perception than they are today.

Therefore, a striking feature of the brief comparison above is that the particular order of events appears to play a crucial role in determining the evidential *priority* or *weight* of the underlying competing epistemic virtues, namely ontological unity versus predictive power. This suggests that the support for a theory is not simply evaluated on a strictly cumulative empirical basis or by a comparison of epistemic virtues put on the same level. Rather, the priority given to particular considerations underlying evaluation of a scientific debate partly derives from the history of a discipline. Such a history might even explain to what extent post hoc modifications sometimes overrule a simpler or empirically more successful alternative. For almost the entire 20th century, a shape-sensitive mechanism served as the only empirically feasible model for research on the molecular basis of smell perception. Unchallenged by any empirically possible alternative, the theoretical premise on which the shape model's application rests, i.e. the ontological unity of molecular processes, gradually transformed into the paradigm which now stands in dispute.

Whether or not further experiments on the viability of a vibration-sensitive mechanism gather enough momentum must be left open to the future. Its contemporary persistence despite the hegemony of the shape theory, however, represents the first cracks in the image of an ontological unity of molecular processes. “The fact is that nobody has been able to unequivocally contradict [Dr Turin]. […] There are many problems with the shape theory of smell – many things it does not explain that the vibration theory does.”[397] Since the contemporary olfactory debate cannot be “unequivocally settled by logic and experiment alone”,[398] attention to past events and the development of future ones might help to achieve a better understanding of the dynamics underlying scientific development and change.

In closing, I have made the case in this and the previous chapter that the olfactory debate can neither be understood nor resolved through an abstract and ahistorical assessment of the epistemic virtues of the competing theories. A comparison between the rival mechanisms in this chapter showed that whereas each is built on analogical reasoning, only the shape model’s analogy also plays a role in its justification. Support for the legitimacy of such a blurred line between heuristic and confirmative strategies in model choice was found in the historical development and the continuity of practices in which the lock and key analogy gathered its epistemic strength. Understanding of why one model is given preference over another, therefore, must be sought in the historical development that supports its epistemic entanglement in a particular research context. In the course of the olfactory trajectory the initially theoretical considerations gradually turned into ontological background assumptions. Considering the impact of these ontological assumptions on theory assessment and model choice in current olfaction theory, I argue for taking a historicised perspective to explain what informs contemporary scientific judgement. By elucidating the impact of disciplinary history on present scientific judgement, we can explore the extent to which experimental practice is bound to particular

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[397] Tim Jacob as quoted in Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

[398] Kuhn, Thomas (1970[1962]): *The Structure of Scientific Revolutions.* 2nd Edition. Chicago: University of Chicago Press, 94.

epistemic virtues which currently grant some model-based inferences with greater credibility than others.

Contemporary olfactory judgement was demonstrated not to rest on an unequivocal basis for theory and model choice but to be strongly linked to contingent factors in scientific developments. Tracing these developments, a closer look at the historical (dis)continuities and shifts, I claim, will further aid in explaining future developments taking place, whether these be in favour of shape, vibration, a combination of both or other possibilities. Therefore, by historicising scientific judgment, i.e. understanding its present position through its disciplinary trajectory, it is possible for philosophers and historians of science to participate in scientific debates without mainly resorting either to normative prescriptions or merely descriptive reviews. Rather, by providing a critical exposition of a debate concerning its conditions as well as inconsistencies, philosophical work can elucidate what informs successful model-based inference in a particular context. And, in further consequence, philosophers can participate in the question of whether these inferences are sound or to what extent we can (or cannot) justify a causal explanation inferred from a theoretical model, as I will continue to show in the following chapters.

Chapter 6

Science and Fiction: Analysing the Concept of Fiction in Science and its Limits

This chapter departs from the overall narrative of the thesis and presents a philosophical interlude concerning more general analyses of modelling in the philosophy of science. I will use the concept of fiction in recent debates about models and representation as the background to my analysis of olfactory modelling strategies in the subsequent chapters. A fast growing debate in the philosophy of science has taken an interest in fictionalisation strategies for scientific reasoning. Unlike other areas of philosophy such as metaphysics, ontology, aesthetics, philosophy of language and mathematics, the concept of fiction in this debate does not concern issues surrounding the problem of truth in fiction,[399,400] the existence of fictional entities such as Pegasus,[401] or the existence of mathematical entities and the interpretation of existential quantifiers.[402] Fiction here refers to the role played by particular methods of model building such as abstractions, idealisations and the employment of highly hypothetical entities. Since a variety of concepts and models in scientific practice – e.g. frictionless planes, ideal gases or *Homo economicus* – do not

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[399] This concerns propositions such as “Sherlock Holmes is a detective” versus “Sherlock Holmes is the fifth member of the Sign of Four.”

[400] This concerns propositions such as “Sherlock Holmes is a Detective” versus “Sherlock Holmes is the fifth member of the Sign of Four.” See for instance: Lewis, David (1978): Truth in Fiction. *American Philosophical Quarterly* 15(1), 37-46; Salmon, Nathan (1998): Nonexistence. *Noûs* 32(3), 277-319.

[401] See for instance: Meinong, Alexious (1904): Über Gegenstandtheorie: In: *Untersuchungen zur Gegenstandtheorie und Psychologie*, Leipzig: Barth. Reprinted in *Gesammelte Abhandlungen* (Gesamtausgabe bd. II), Graz: Akademische Druck- und Verlagsanstalt, 1971, 481-535. Also In: *Realism and the Background of Phenomenolog.* Ed. by R. Chisholm Trans. by I. Levi, D.B. Terrell and R.M. Chisholm. Glencoe: Free Press, 1960, 76-117; Kaplan, David (1973): Bob and Carol and Ted and Alice. In: *Approaches to Natural Language*. Ed. by K.J.I. Hintikka, J.M.E. Moravcsik and P. Suppes. Dordrecht: Reidel, 490-518; Kripke, Saul (2011): Vacuous Names and Fictional Entities. In: *Philosophical Troubles: Collected Papers, Vol. 1.* Oxford: Oxford University Press, 52-74.

[402] See for instance: Balaguer, Mark (1998): *Platonism and Anti-Platonism in Mathematics*. New York: Oxford University Press; Priest, Graham (2003): Meinongianism and the Philosophy of Mathematics. *Philosophia Mathematica* 11, 3-15; Priest, Graham (2005): *Towards Non-Being.* Oxford: Oxford University Press.

denote any particular physical target system, the question emerging is how science aims at describing reality.[403]

Addressing the underlying question of scientific realism, the claim I want to defend is that denoting, i.e. referring to a particular physical entity, is not a necessary condition for scientific representations to make claims about reality. By using the concept of fiction as a tool for analysing non-denoting elements in science, this paper aims to address the ways in which scientific representations, even though employing non-denoting elements, are said to provide information about the world. Rather than structural criteria such as the degree of similarity a representation exhibits towards its represented entity, I will argue that the reference of representations is determined by their epistemic function. This function does not merely concern the capacity of a representation to allow for inferences about an intended physical target, but is also defined by its relations towards other representations making similar or conflicting claims about the same target system. The reason for this, I will argue, is that elements, even if identical in semantic content, only denote by virtue of their contextual embedding. To analyse epistemic relations, my argument points out, requires a form of enquiry different to the interpretation of fiction.

To introduce my argument, this paper proceeds as following. First I will present the context in which the concept of fiction became part of the philosophical debate on scientific realism. Following this, I will focus on the hybrid character of representations that, employing both denoting and non-denoting elements, makes it hard to mark a distinction between representations that refer and those that do not. After emphasising the limits of structural criteria such as similarity, I want to make use of the concept of fiction in science by drawing a distinction between the interpretation of a representation as either fictional or non-fictional. The aim of this approach is to present reasonable ground to distinguish between fictional entities and non-denoting elements in science. The basis for this distinction is the context in which denoting and non-denoting elements are used. This, I hope, will also provide further insight into the characteristics of scientific enquiry.

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[403] Cartwright, Nancy (1983): *How the Laws of Physics Lie.* Oxford: Clarendon Press; Suárez, Mauricio (Ed.) (2009): *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* London: Routledge; Suárez, Mauricio (2010): Fictions, inference and realism. In*: Fictions and models: new essays.* Ed. by J. Woods. Munich: Philosophia Verlag, 225-245.

1 Fiction in Science?

Most of the philosophical difficulties that spurred interest in the concept of fiction in the philosophy of science are a consequence of fundamental changes in the scientific understanding of nature. The legacy of, on the one hand, the substitution of phlogiston for oxygen in 19th century chemistry and, on the other hand, radical theory changes in earlier 20th century physics led to growing scepticism about the reference of scientific concepts and cast doubt on the reality of scientific objects.[404] These changes suggested that even supposedly fundamental scientific concepts are dependent on the theoretical framework in which they are embedded. If this framework is replaced, the concepts may either change their meaning or become redundant.

The history of science provides a rich inventory of concepts of entities abandoned in the course of theory changes such as phlogiston, the ether or pneuma. What all these examples have in common is that the entities described were once assumed to exist but later turned out to have no instantiations in the world, neither in a literal nor in an idealised sense. When Galen assumed the existence of *pneuma*, it was considered to be the principle of life and served as an explanation for three different life processes: visual perception, blood flow and metabolism.[405] Albeit the *explanandum*, in the case of the blood flow the process and its physical parts such as the heart and arteries were real, the *explanans* was not. Nevertheless, the concept of pneuma served a theoretical purpose by providing a model under which certain life processes were fruitfully investigated.

Philosophical scepticism raised by historical changes resonates with further doubt about the reality of scientific entities and phenomena that are not directly observable. Contemporary scientific theories often subsume entities under concepts that assume specific experimental settings and conditions under which certain effects are produced. The interpretation of these effects facilitates claims about the nature and existence of particular entities that are assumed to underlie these phenomena. Examples for such entities are genes and electrons

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[404] Kuhn, Thomas (1970[1962]): *The Structure of Scientific Revolutions.* 2nd Edition. Chicago: University of Chicago Press; Feyerabend, Paul K. (1962): Explanation, reduction, and empiricism. In: *Scientific explanation, space, and time.* Ed. by H. Feigl and G. Maxwell. Minneapolis: University of Minnesota Press, 28-97; van Fraassen, Bas (1980): *The Scientific Image.* Oxford: Oxford University Press.

[405] Johansson, Ingvar and Lynøe, Niels (2008): *Medicine & philosophy: a twenty-first century introduction.* Heusenstamm: Ontos Verlag, 82.

that are investigated as causes for phenomena of inheritance and electricity. However, these entities are only indirectly traceable and our knowledge of them remains hypothetical to a certain extent. For these reasons, the border between the concept of an entity and the entity conceptualised are called into question and seem to blend. Perfectly sharp distinctions between 'hypothetical' and 'real' objects in science can no longer be expected. By drawing on the influence of models and experiments in guiding research practice, awareness of the not only descriptive but also constitutive function of scientific concepts and representations has been raised in the last few decades.[406] Models often determine the conditions under which materials are transformed into epistemically accessible research objects.[407]

Indeed, it is the striking theoretical usefulness of many scientific concepts and models that nevertheless lack proper reference to physical target systems and objects, which became the centre of recent philosophical attention. Familiar examples involve models such as frictionless planes, ideal gases or *Homo economicus*. Models such as these are often idealisations and imply assumptions seldom realised in the physical world,[408] Consider, for instance, the model of the pendulum that assumes an environment lacking air resistance. To apply this model to an environment that is not a vacuum additional calculations about the variables have to be made, which serve as approximations of the real situation. Yet, taken in its literal and unmodified sense, the pendulum does not refer to any physical system and therefore does not seem to have a denoting character.[409]

What brings these two related concerns together, the abandonment of scientific concepts in the course of theory change and the distortions brought about by contemporary model building, is the problem of the reference of scientific representations. The question emerging here is how to decide *whether* and

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[406] Cartwright (1983): *Laws of Physics*; Hacking, Ian (1983): *Representing and intervening: introductory topics in the philosophy of natural science.* Cambridge: Cambridge University Press; Rheinberger, Hans-Jörg (1997): *Toward a history of epistemic things: synthesizing proteins in the test tube.* Stanford: Stanford University Press; Morgan, Mary and Morrison, Margaret (Eds.) (1999): *Models As mediators: perspectives on natural and social science.* Cambridge: Cambridge University Press; Radder, Hans (Ed.) (2003): *The philosophy of scientific experimentation.* Pittsburgh: Pittsburgh University Press; Suárez (2009): *Fiction in Science*.

[407] Rheinberger, Hans-Jörg (2005): A reply to David Bloor: Toward a sociology of epistemic things. *Perspect Sci* 13, 408.

[408] Cartwright (1983): *Laws of Physics*; Suárez (2009): *Fiction in Science*.

[409] Morrison, Margaret (1999): Models as autonomous agents. In: *Models as Mediators. Perspectives on natural and social science.* Ed. by M. Morgan and M. Morrison Cambridge: Cambridge University Press, 49, 63.

when a particular scientific representation makes truthful claims about the world. A number of philosophical arguments have addressed this question by exploring criteria for denoting such as “similarity”, “resemblance”, or definitions of “structure” that determine the relation between a representation and its intended target system.[410] The insufficiency of these criteria for an understanding of scientific representations, however, has directed philosophical debate towards an analysis of the construction of models as a fictionalisation technique.[411] Guiding scientific reasoning, the application of models often lacks accuracy and truthfulness in favour of making highly idealised or abstract claims about their intended target system. Likewise, many models employ hypothetical entities that serve a heuristic role, e.g. aiding in calculations or hypothesis-making, rather than presenting real entities.[412] The concept of fiction in the philosophy of science, therefore, is used to explore the strategies that underlie model thinking in scientific reasoning.

Two responses should be offered to the employment of the concept of fiction in science. First, and most obvious, the alleged similarity of scientific model building with fictionalisation techniques involves two meanings of fiction.[413] One meaning concerns distortion techniques such as idealisations and abstractions. These, when compared with fiction, are described as cases of mimesis. Even though they closely resemble some entities in the world, they do not denote anything in particular but, rather, provide a more abstract understanding of the world and its affairs. By contrast, abandoned scientific concepts such as phlogiston or pneuma, like fiction, do not denote real entities.[414] On this account, the second meaning of fiction concerns whether some concept denotes an entity or not. Unlike fictional characters that were never thought to

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[410] Goodman, Nelson (1969): *Languages of Art. An Approach to a Theory of Symbols.* Oxford: Oxford University Press; Frigg, Roman (2002): Models and Representation. Why Structures are not enough. *Measurement in Physics and Economics Project Discussion Paper Series*, DP MEAS 25/02, London School of Economics. URL=<http://www.romanfrigg.org/writings/Models_and_Representation.pdf> (accessed 21 February 2013); van Fraassen, Bas (2008): *Scientific Representations. Paradoxes of Perspective.* Oxford: Oxford University Press; Frigg, Roman (2010): Fiction in Science. In: *Fiction and Models. New Essays.* Ed. by J. Woods. Munich: Philosophia Verlag, 247-287.

[411] Sugden, Robert (2000): Credible worlds: the status of theoretical models in economics. *Journal of Economic Methodology* 7, 1-31; Suárez (2009): *Fiction in Science*; Suárez (2010a): *Fictions, inference and realism*; Toon, Adam (2012): *Models as Make-Believe: Imagination, Fiction and Scientific Representation.* Palgrave Macmillan.

[412] Suárez (2010a): *Fictions, inference and realism*.

[413] Frigg (2010): Fiction in Science, 247.

[414] Existence here means the physical existence of entities, that is their concrete being in space and time, and does not involve any possible metaphysical existence of fictional entities. Ibid., 248.

denote, however, scientific entities are commonly assumed to exist. If they turn out to be fictitious, such as in the case of phlogiston or pneuma, their lack of reference is not intended. Even in the case of highly hypothetical entities such as the Higgs boson particle (where, until debate reignited recently, there was no general consensus about its alleged ontological status within the scientific community), these entities are still handled as candidates for truth.

Corresponding with these two meanings of fiction, i.e. mimesis and non-existence, are two positions in the philosophical debate. For some philosophers such as Cartwright, Suárez, Frigg and Fine, who argue for *wide fictionalism*, the comparison of scientific representations with fiction involves both meanings of fiction. Other philosophers such as Morrison, Teller, Giere and Winsberg, who advocate *narrow fictionalism*, restrict the concept of fiction in science to concepts of non-existent entities only.[415]

My second response to the concept of fiction in science is that the two positions just distinguished nevertheless have one major aspect in common. With philosophical debate focussing on the general problem of reference, the concept of fiction in science appears to be associated with different forms of *non-denoting elements* in scientific representations. The central idea of identifying non-denoting elements with fiction is to understand the ways in which our modelling strategies may or may not reflect reality. Notwithstanding their conceptual affinities, I tend to be sceptical about conceiving particular representational elements in science as fiction only on the grounds that neither of them denotes. The question that interests me here is thus: is something similar to fiction because it does not denote, or do such non-denoting elements in science have other characteristics that distinguish them from proper fiction? Furthermore, if there is a characteristic difference between fiction and non-denoting elements, what does this difference tell us about the character of scientific enquiry? Therefore, the issue that guides the following sections is whether ‘non-denoting elements’ in science really are fictions, and where the limits of such a comparison are.

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[415] Suárez (2009): *Fiction in Science.*

2 The Hybrid Character of Fictional and Non-Fictional Discourse

The common denominator I identified in the widespread debate on fiction in science is the involvement of different kinds of non-denoting elements in scientific practice. In comparison to the problem of non-denoting elements addressed by the concept of fiction in science, a similar difficulty occurs in other discourses such as history and literary theory. Consider, for instance, the interpretation of historical documents and the assessment of the authenticity of their embedded claims. Historical documents are used to account for past events; they are thought to prove, certify or witness something that really happened and are used to inform later generations about, for instance, political decisions and social norms of earlier times. Yet the border between fiction and historical documents often seems to blur. Like the first meaning of fiction as forms of distortion mentioned above, a range of fictional works such as Victorian novels do not denote particular people but can be employed as a historical source to provide information about the society and manners of that time. Furthermore, many fictional works employ historical documents as props for their plot setting and, conversely, elements and characters of fiction also appear in historical documents, for instance as satire or for illustrative and political purposes.[416] With respect to the second meaning of fiction, regarding non-existent entities, historical documents can likewise turn out to be forged and completely fictitious, for instance, in the spectacular fraud of “Hitler’s diaries”.[417]
Common to all these representations, whether these be works of fiction, historical documents or models in science, is their “hybrid character”. By hybrid character I mean that representations as public devices of description are permeated by denoting as well as non-denoting elements. Non-fictional representations such as models in science or historical documents can include elements that do not denote anything particular in the world whereas fictional works can employ elements known from reality, containing real places, events or people such as Napoleon in *War and Peace,* London in *Sherlock Holmes*, or the Cuban Crisis in *X-Men.*

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[416] Werle, Dirk (2006): Fiktion und Dokument. Überlegungen zu einer gar nicht so prekären Relation mit vier Beispielen aus der Gegenwartsliteratur. Non Fiktion 1, 113.

[417] Henry III, William A.; Lee, Gary and Ludtke, Melissa (1983): Press: Hitler's Diaries: Real or Fake? *Times Magazine* 9 May 1983.
URL=<http://www.time.com/time/magazine/article/0,9171,923630,00.html>

Approaching the hybrid character of fiction, this hybridity resonates with Terence Parson's analysis of fictional elements and his distinction between "objects *native* to the story versus objects that are *immigrants* to the story".[418] "Objects native to the story" are those that are a genuine creation of a representation such as Sherlock Holmes. Immigrant objects are elements that are not inventions originating from a particular representation but are 'imported' from other contexts such as the element of London. However, this distinction does not necessarily provide a basis to decide whether such immigrant objects (when employed in fictional contexts) are properly referring to the real counterparts on which they are modelled. "Immigrant objects", e.g. the character of Napoleon in *War and Peace,* are nevertheless part of a particular fictional discourse and their interpretation is informed by their occurrence in this particular representation.

Such mixtures of real and unreal elements in the composition of fictional representations are not surprising. Fist, the interpretation of fiction relies on the same principles and conventions about language that also give meaning to words and signs in non-fictional discourse. When Barbarella and Jane Fonda are, for instance, both portrayed as blondes, we say the same about both of them. Even though one is a fictional character and the other one is a real person, by describing the two of them as blonde we attribute a particular hair colour to them. Convention about the meaning of words is external to fictional discourse. Unless a different meaning is made explicit in fictional discourse, a word has the same meaning as it has in non-fictional discourse.[419] Second, fiction is often based on knowledge about particular places, events and people. Previously mentioned examples such as Napoleon in *War and Peace,* London in Sherlock Holmes, or the Cuban Crisis in *X-Men* illustrate that the interpretation of fictional discourses often requires knowledge about elements of non-fictional discourses. By virtue of this, fiction has been described as dependent or even 'parasitic' on non-fictional discourse.[420] This twofold dependency of fiction on non-fictional discourse thus constitutes the grounds for its often 'hybrid character'.

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[418] Parson, Terence (1980): *Nonexistent Objects.* New Haven: Yale University Press, 51.

[419] Heintz, John (1979): Reference and Inference in Fiction. *Poetics* 8, 89.

[420] Searle, John R. (1975): The Logical Status of Fictional Discourse. *New Literary History 6(2): On Narrative and Narratives*, 326; Eco, Umberto (1994b): *Six Walks in the Fictional Woods.* Cambridge M.A.: Harvard University Press, 95.

Comparing the hybrid character of fictional with non-fictional representations, the question arises how to evaluate whether a representation has a denoting or a fictional character, i.e. whether and when its claims truthfully refer to the world or are merely fictitious? For many representations, the case seems intuitive. When chemists investigate the transformation of chemical substances, they assume that the underlying elements indeed correspond to their concepts of atoms and molecules. If, however, Star Trek's Captain Picard gives the order to engage to Warp 3, it would not convince people that this refers to an actual velocity. Nonetheless, it would not be considered as either false or non-sense. Although there is nothing in our world to which Warp 3 refers, it makes sense when understood as a construct within a particular fictional context. In the case of fiction reference to the world is therefore suspended.[421] For other examples, however, the case appears less obvious. What anecdotes of Casanova's memoirs are factual or fiction,[422] and what elements of hypothetical computer models of olfactory receptor proteins are real?[423] Scientific discourse is permeated by idealised or often figurative descriptions and the issue is how literally to take them. To emphasise the importance of DNA in life processes, for instance, DNA is often referred to as "the book of life" in analogy to its coding function; yet this vivid metaphor has developed a problematic life of its own.[424] Moreover, the concept of 'metaphors' has been used to describe the function of theoretical models in biology and economics.[425] Metaphors are figurative descriptions that are not understood literally but, although they conflict in their literal sense, they convey an element of meaning.[426]

The issue at stake is the epistemic function served by non-fictional elements. The epistemic function of denoting representations is to tell us something about the world.[427] To the contrary, fiction deals with entities and descriptions that are not bound to be truthful descriptions of our world. Even though fiction contains entities that have familiar counterparts in the world, these elements are not

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[421] Werle (2006): Fiktion und Dokument; Eco (1994b): *Six Walks*.

[422] Casanova, Giacomo (2007[1725-1798]): *The Complete Memoirs of Jacques Casanova.* Ed. by A. Symons. Trans. by Arthur Machen. Clue.

[423] Crasto, Chiquito J. (2009): Computational Biology of Olfactory Receptors. *Curr Bioinform* 4(1), 8-15.

[424] Kay, Lily E. (2000): *Who Wrote the Book of Life? A History of the Genetic Code*. Stanford: Stanford University Press.

[425] Morgan, Mary (2002): Models, Stories and the Economic World. In: *Fact and Fiction in Economics.* Ed. by U. Mäki. Cambridge: Cambridge University Press, 178-201; Sudgen (2010): *Credible worlds.*

[426] Eco (1994b): *Six Walks*, 68, 139.

[427] Sudgen (2000): *Credible worlds*, 1.

automatically seen to serve as a truthful description of their counterparts.[428] Consider, for instance, Tolstoy's *War and Peace*, which, contrary to historical fact, describes a victorious Napoleon in Russia. Tolstoy neither *lied* to his reader nor *assumed* something historically inaccurate. He merely used the knowledge about a historical character and created a fictional course of history, which is not bound to be accurate or true of the actual historical events. Hence, fictional discourse is not required to *prove* or *argue for* the truth of its presented claims. For these reasons, fiction lacks an epistemic function; it is not used to truthfully reflect states of affairs in the world.[429]

Concerning this divergence over epistemic function, how does one determine the grounds for the adequate epistemic use of a representation? Addressing so-called fictions in science, Hans Vahinger suggested considering them as useful heuristic tools that, unlike hypotheses referring to real phenomena, are not verifiable by observation.[430] A problem with this suggestion is that the distinction between what counts as observable and unobservable in science had been called into question.[431] How are assumptions assessed as fictional or non-fictional if the model context from which they are derived relies strongly on mediated forms of observation? Although Vahinger admits that distinctions between fictional and non-fictional elements in science are not fixed but can

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[428] A question arising here is whether fiction might be said to be accidentally true. Consider, for instance, the possibility that we find a real person that matches every description of a fictional character's biography without the author's knowledge. Is the fictional character now a true description of the real person? A discussion of such an example can be found in Ryle, Gilbert (1933): Imaginary Objects. *Proceedings of the Aristotelian Society* Suppl. 2, 39: "Now suppose by sheer chance, without any knowledge of Dickens, one person had existed, such that the Pickwick Papers were in fact faithful biography. […] it seems obvious that we could not say of the real Mr. Pickwick >Oh, he is not identical with the hero of the story<." An alternative answer is given in Danneberg, Lutz (2006): Weder Tränen noch Logik. Über die Zugänglichkeit fiktionaler Welten. In: *Heuristiken der Literaturwissenschaft. Einladung zu disziplinexternen Perspektiven auf Literatur.* Ed. by U. Klein, K. Mellmann and S. Metzger. Paderborn: Mentis Verlag, 35-83. Quoted is the extended online version: URL=<http://fheh.org/images/fheh/material/danneberg-fiktion.pdf>, 14. I agree with Danneberg that the reason why we intuitively suggest the fictional character is a faithful depiction of a real person only rests on intuition based on a structural similarity by coincidence. There is, however, no causal connection that would allow for the justification of this inference. Therefore, fiction might seem accidentally true, but still lacks an argumentative basis for the truthfulness of its claims.

[429] Albrecht, Andrea and Danneberg, Lutz (2011): First Steps Toward an Explication of Counterfactual Imagination. In: Counterfactual Thinking/Counterfactual Writing. Ed. by D. Birke, M. Butter and T. Köppe. Berlin, New York, 12-29. Cited it the extended online version: URL=<http://fheh.org/images/fheh/material/counterfact.pdf>, 8.

[430] Vaihinger, Hans (2008[1928]): *The Philosophy of As If.* London: Taylor & Francis; Fine, Arthur (1993): *Fictionalism. Midwest Studies in Philosophy* 18(1), 7.

[431] Maxwell, Grover (1962): The Ontological Status of Theoretical Entities. In *Scientific Explanation, Space and Time, Minnesota Studies in the Philosophy of Science, Vol. 3*. Ed. by H. Feigl et al. Minneapolis: University of Minnesota Press, 3-27.

change over time (and, furthermore suggests approaching these elements as fictions first), he does not provide "firm grounds for sorting and grading into fictional versus nonfictional" elements.[432] It is these grounds that I want to address in the following sections. Vahinger excluded proper fiction in literature and art from his analysis of fictional elements in science. However, I suggest reconsidering this move and using proper fiction for a comparison with apparently fictional elements in science. This, I claim, will provide a basis on which the grounds for distinguishing between apparently fictional and non-fictional elements in science can be clarified.

Previous philosophical comparisons of scientific models with works of art, for instance in the work of Goodman, Suárez, Frigg and van Fraassen, have demonstrated that there is no intrinsic structural trait that can unambiguously distinguish them.[433] This alleged ambiguity has been taken as a good reason to support an antirealist interpretation of scientific practice. Since many scientific models lack accuracy or truthfulness to their physical target system and, the argument continues, if taken literally, are false, there are no grounds on which the claim that science aims at truth can be defended.[434] In response to this view, I argue that concern about the truth of claims given in scientific representations and, in further consequence, the relation of representations to the real world should not address structural criteria such as similarity but the interpretation of representations.

3 Transposing Fiction and Reality

Arguments for understanding representations in terms of their interpretation instead of their internal structure have already been given in the works of Kendal Walton and Adam Toon.[435] According to their theory of *make-believe*, fiction is considered to simulate particular affairs under the assumption that these are not to be taken literally. Here representations are "props" in a

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[432] Fine (1993): *Fictionalism*, 12.

[433] Goodman (1969): *Languages of Art*; Frigg (2002): *Models and Representation*; van Frassen (2008): *Scientific Representations*.

[434] van Fraassen (1980): *Scientific Image*; van Fraassen (2008): *Scientific Representations*.

[435] Walton, Kendall (1990): *Mimesis as Make-Believe: On the Foundations of the Representational Arts.* Cambridge M.A.: Harvard University Press; Toon, Adam (2010): *Models as Make-believe.* URL=<http://philsci-archive.pitt.edu/3227/1/Adam_Toon_-_Models_as_make-believe.pdf>; Toon (2012): *Make-Believe: Imagination, Fiction and Scientific Representation.*

conventionalised form of game play. The interpretation of scientific representations is understood as intentionally accepting a set of definitions and rules. Interpreting them in an *as if* relation to the world, these rules are used to derive “fictional truths”, i.e. to provide theoretical inferences about real phenomena within a particular model framework.[436]

The concept of fiction employed here is an umbrella term for a variety of interpretative acts, ranging from children’s games to scientific modelling in the laboratory. This use of fiction may thus explain strategies of imagination, yet it lacks an answer to the question of how to distinguish the particular epistemic differences that seem to underlie the use of genuine fiction in contrast to the use of scientific models. Let me emphasise this issue by considering examples of the misinterpretation of fictional works.

First, consider the tragic case of a Japanese woman who died in the snow of North Dakota woods.[437] She was looking for the fictional treasure of $1m that was buried in the fictional placement of North Dakota woods in the Coen brother's film *Fargo* (1996).[438] Police stated that, before she was found dead, she had been reported wandering around with a crude map of these woods taken from the movie. What happened was that the she failed to distinguish between fiction and reality. Since North Dakota Woods is an element known from reality she assumed a proper referential relation between the representation and the actual place. But she did not understand that “North Dakota Woods” was only a fictional placement of a denoting element and therefore it did not suffice to make proper inferences to the ‘real thing’. The descriptions of North Dakota Woods in Fargo are part of the fictional story in which they take place. Their only function is to provide the space of action for the fictional characters of Jerry Lundegaard and others.

A second example is *Foucault's Pendulum* by Umberto Eco. In Chapter 115 the character of Causabon walked along the Rue Saint-Martin in Paris on the night of 23-24 June 1984. Eco described this scenery as realistically as possible, even consulting weather reports of that night. Yet when a passionate reader went to the archives he found out that on this very night there was, in fact, a fire on Rue Saint-Martin. This fire was not mentioned in the novel! But if Causabon

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[436] Fine (1993): *Fictionalism*; van Fraassen (2008): *Scientific Representations*.

[437] Berczeller, Paul (2003): Death in the Snow. *The Guardian* Friday 6 June 2003. URL=<http://www.guardian.co.uk/culture/2003/jun/06/artsfeatures1>

[438] Coen, Joel and Coen, Ethan (Dirs.) (1996): *Fargo.* PolyGram Filmed and Metro-Goldwyn Mayer. Film, USA.

had *really* walked along that street that very night he must have seen the fire. So why was it not mentioned, the reader questioned? Despite Eco's rather mocking answer (that Causabon might have had his reasons not to mention the fire that may be beyond the author's knowledge), the reader's enquiry is clearly an over-interpretation. The detailed knowledge about the real place was adopted to generate a strikingly realistic fictional counterpart. The descriptions of this counterpart, however, cannot be held epistemically accountable for their truthfulness. Whilst it is not used to make any proper claims about the real place, it was in fact this striking similarity that caused the reader to "believe that my story took place in "real" Paris".[439]

Both examples of misinterpretation have the assumption in common that some elements known from reality embedded in fiction provide a truthful source of information about their counterparts in reality. This, however, is an act of transposing fiction and reality. By 'transposing' fiction and reality I mean that a fictional element is used as if it genuinely refers to a real thing only because it resembles a non-fictional counterpart. That being said, it is neither impossible nor forbidden to transpose fiction and reality, and quite often this presents a fascinating cultural phenomenon. The many tourists visiting the real Baker Street in the real London looking for Sherlock Holmes' fictional whereabouts are an entertaining (and for the city of London quite lucrative) example of over-interpretation, i.e. the act of assigning to an element of fiction reference to real things. Nonetheless, such fiction-tourism is an *intended* over-interpretation.[440] It is in the light of the straightforward fictionality of the Holmes stories that, although people are visiting the real Baker Street in the real London, no one expects to really go to the real place Sherlock Holmes lived since he never actually lived. The function of the fictional placement of London as "the place where Sherlock Holmes lived" is not to provide genuine statements about London nor is it bound to do so. Instead, the element of London here is part of a fictional discourse and thereby it is not bound to provide accurate claims about the real London.

Fiction-tourism such as in the case of Sherlock Holmes' London is a form of game-play as it is described by Walton and Toon. Yet, what distinguishes this case of fiction tourism from the previous two examples that seem to present

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[439] Eco (1994b): *Six Walks*, 76f. Note Eco's own quotation marks!
[440] Eco (1994b): *Six Walks*, 84.

less adequate interpretations of fiction? On the account of make-believe, the intuitive answer would be convention, or alternatively in Searle's terminology, institutional or collective agreement.[441] Even though this solution appears attractive, it is obviously insufficient in this simple form. Convention is a fickle friend, and collective agreements are arbitrary to a certain extent. As a radical example, consider Duchamp's *readymades*. Readymades, basically being random and trivial objects of utility such as a urinal or bottle racks, were claimed as art in order to challenge rigid definitions of art and representation. Now, however, readymades are an established part of art discourse. They partake in this discourse not because of Duchamp's intention alone but due to the collective acceptance of the wider audience involved in this judgement. Likewise, Galileo's telescope was not accepted immediately as a proper technique of observation but invoked a now infamous controversy among his contemporaries.[442]

Therefore, reference to convention does not explain *on what grounds* something is used to provide a truthful description of reality or only taken to be a fiction. The theory of make-believe explains how we use representations as vehicles for imagination and interpretation but, moving beyond convention, it does not provide a satisfactory answer to the question on what basis we distinguish between scientific models and fictional works. I therefore propose an alternative answer, suggesting that the divergent use is visible when we take a look at *how* these fictional and non-fictional representations and their embedded claims are interpreted differently.

4 Denoting Elements versus Images of Denoting Elements

My claim is that strategies of interpretation and not structural criteria such as similarity or semantic content elucidate the suggested epistemic difference between fictional and non-fictional representations. To analyse the difference in the interpretation of fictional and non-fictional works, I argue that we should reconsider the hybrid character of representations more carefully. Starting with the interpretation of fictional representations, I focus on the particular relation of

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[441] Searle, John R. (2010): *Making the Social World. The Structure of Human Civilization.* Oxford: Oxford University Press, 7.

[442] Harries, Karsten (2002): *Infinity and Perspective.* Cambridge M.A.: MIT Press, 282.

denoting and non-denoting elements to the representational context in which they occur. For comparison, I then consider the interpretation of non-denoting and apparently fictional elements in non-fictional representations. This will aid me in showing why the interpretation of these hybrid elements is dependent on the overall representational context in which they are embedded. This context concerns the particular representation in which specific elements are embedded as well as the wider discourse in which the representation is interpreted.

The interpretation of a representation can focus on two things; it can concern, on the one hand, the entire representation or, on the other hand, the individual elements contained. To distinguish between fictional and denoting representations I want to follow Lutz Danneberg's proposal. He suggests that only reference to the entire representation provides feasible grounds to discern between fictional and non-fictional uses of representations.[443] The basis for this claim has nothing to do with the particular character of the elements involved; it does not concern the issue of whether these elements might be considered to denote or not. Rather, this claim is based on the function these elements are assigned. As the following examples will show, this function depends on the entire representation and its wider use.

My first example in support of this claim is the *X-Men: First Class* movie (2011).[444] Based on the Marvel comic series, it tells the story of a young group of mutants preventing a cold war scenario from turning into a third World War. Halfway through the storyline the group watches the president of the United States give a speech on TV. This is a curious case, because the president's speech is in fact not a re-enactment but an original recording of a Kennedy speech. Not only does the movie utilise a person known from reality but, moreover, it uses the copy of a proper historical document, the recording. Nonetheless, this denoting element does not lead to doubt about the fictionality of the entire story told. Although the recording is an historical artefact, the fictional story is not; the representation, of which this recording is an element, is not used to provide any explanation of the real events taking place during the Cuban Crisis. Furthermore, the recording itself in its fictional context is not used to provide an explanation of past events. The function of this element, in fact, only reflects its own placement within the *X-Men* story: it sets up a historically

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[443] Danneberg (2006): *Weder Tränen noch Logik*, 10.

[444] Vaughn, Matthew (Dir.) (2011): *X-Men: First Class.* Marvel Studios and 20th Century Fox. Film, USA.

grounded and convincing background for the fictional characters to act in. By employing a copy of a proper historical document the fictional story does not suddenly become factual; it cannot be used, for instance, to argue for an alternative interpretation of real historic events. Thus, individual elements cannot be judged on their own for referentiality. Examples of this kind are legion.[445]

The general point of this example is that denoting elements are self-referential when used in fictional discourse, meaning that their placement only serves a particular function within the specific context in which they appear. The implicit consequence is that denoting elements and their counterparts in fiction are somewhat different. This difference concerns their function for and within a representation and, as it will become clearer in the remainder of this paper, its relation to knowledge claims made by other representations. To examine this difference, I suggest distinguishing between *denoting elements* and *images of denoting elements*.[446] The original recording of the Kennedy speech in this sense is a denoting element whereas the copy of the Kennedy recording in *X-Men* is only an *image of a denoting element.* The basis for this distinction, however, is not that the image of a denoting element is just a copy of the denoting element since there are various copies of the original speech also in historical documentaries. The point I want to emphasise instead is that, although all these elements – the original Kennedy speech, copies used in historical documentaries or copies used in fiction like *X-Men* – are *structurally identical,* i.e. identical in semantic content, they are not *epistemologically equivalent*.

On this account, although fiction employs copies of denoting elements, these are merely images of denoting elements as long as they are only used as features to back up the fictional story. To the contrary, if an element is used to refer, its function is to present a claim about some element in the world. Any claim about elements in the world, however, is subject to argumentation and justification, and can be judged as either true or false. A seemingly denoting element when used in fiction thereby constitutes an *image of a denoting element*, because it refers to *the conventional knowledge of* a particular

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[445] Eco (1994b): *Six Walks*; Werle (2006): Fiktion und Dokument; Danneberg (2006): *Weder Tränen noch Logik*.

[446] Werle (2006): Fiktion und Dokument.

denoting element but not strictly to *the element denoted*.[447] To illustrate this difference, consider the following case. A novel employs a denoting element of an entity assumed to be real. In the course of time, however, it turns out that this entity has never really existed. Yet the novel is not suddenly giving a false account of reality but only mirrored the state of knowledge for when it was created. Fiction draws on knowledge without assuming this knowledge is necessarily a truthful account of reality; it just sets up a scenario to convince the reader of a particular act of make-believe. In contrast, any denoting representation employing this non-existent element and assuming it properly represents, becomes a false or inaccurate representation of reality. A model, once its postulated entity turns out not to exist, must either be modified or rejected. No such change is needed for the novel. In light of this, even if some elements in fiction closely resemble and are even modelled on denoting elements, they are not denoting themselves.[448]

Having argued that denoting elements when used in fiction are only images of denoting elements, the converse case also holds for apparently ‘fictional’, i.e. non-denoting, elements in non-fictional discourse. If an element in a scientific representation is non-denoting, the representation does not necessarily become less factual or suddenly lacks reference. The second example in support of this claim is “Twin Earth” in Putnam’s *The Meaning of Meaning*.[449] Twin Earth is a fictitious place almost identical to our earth; it only differs in the molecular structure of water. This non-denoting element clearly does not refer to any real place; nonetheless, it is part of a philosophical argument about actual language practice. Of course, the accuracy of Putnam’s theory of meaning might be disputed, but within this argument Twin Earth is assigned an epistemic function. It is used to support Putnam’s position. In parallel with my previous example of

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[447] The hermeneutic rules that regulate the reference to general knowledge are the so-called *reality principle* and the more restrictive *mutual belief principle*. The principle of reality states that the interpretation of a representation is guided by the assumption of its closest resemblance to the external world. This means that unless there are descriptions suggesting otherwise, for instance, by leading to a contradiction or formulating explicit differences, a representation depends on the same language conventions and truths as the real world. A contextually and historically restrictive version of the reality principle is the mutual belief principle; closest resemblance here is characterised by the norms and conventions that had been held true at the time of the creation of the representation. Walton (1990): *Mimesis as Make-Believe*, 144-161; Margolin, Uri (1992): The Nature and Function of Fiction. Some Recent Views. *Canadian Review of Comparative Literature – Revue Canadienne de Littérature Comparée* 19, 109f..

[448] Eco (1994b): *Six Walks*, 125; Werle (2006): Fiktion und Dokument, 120.

[449] Putnam, Hilary (1975): The meaning of ‘‘meaning’’. *Minnesota Studies in the philosophy of science. Lang Mind Knowl* 7, 131-193.

the *X-Men*, by employing a non-denoting element Putnam's argument does not suddenly become fictional or lose its overall reference to language phenomena. Whether such non-denoting elements are a useful contribution to non-fictional discourse, in fact, depends on the strength on the argument these non-denoting elements are employed to support.[450]

In light of this, the position I want to advocate is to define the reference of representational elements with respect to their epistemic function rather than their degree of similarity to a particular entity. This epistemic function is derived from the interpretation of the representation in which these elements occur and its wider use within specific fictional or non-fictional discourses. According to my proposal, the status of non-denoting elements in science is thus not equivalent to fiction. Even if some elements such as idealisations and non-denoting concepts in science are somewhat similar to fictional elements they nevertheless differ fundamentally in their epistemic character. In contrast to scientific representations, fiction is not used to serve as an explanation nor is intended to be a truthful description of the world. While scientific representations are epistemic items, proper fictions are not. In light of this, the difference between denoting and non-denoting elements is not subject to structural resemblance to a physical target system, but concerns their assigned epistemic role.

Like an inferential account of scientific representations, advocated, for instance, by Mauricio Suárez and Jesus Zamora-Bonilla and Xavier de Donato-Rodríguez,[451] my account of representation, therefore, concerns the capacity to facilitate 'surrogate reasoning' about the world. Rather than defining a structural relation between the representation and its target system, scientific representations are understood as vehicles of reasoning, which often require specific skills of the practitioner for its correct application. Depending on the

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[450] By virtue of their similarity to fiction yet their different epistemic function, examples such as thought experiments, counterfactuals and ceteris paribus clauses have been characterised as 'Neighbouring Notions' elsewhere. See: Albrecht and Danneberg (2006): *Counterfactual Imagination*. An analysis of idealisations and theoretical models in comparison with thought experiments, counterfactuals or ceteris paribus clauses might thereby be insightful (Sudgen (2000): *Credible Worlds*, for instance, nicely explores theoretical models in economy in this context), yet these do not necessarily describe cases of 'fiction' and would, unfortunately, go beyond the scope of this chapter.

[451] Suárez, Mauricio (2004): An Inferential Conception of Scientific Representation. *Philosophy of Science, 71*, 767-779; Zamora-Bonilla, J. and de Donato-Rodríguez, X. (2009): Explanation and Idealization in a Comprehensive Inferential Approach. EPSA09: 2nd Conference of the European Philosophy of Science Association (Amsterdam, 21-24 October, 2009) > EPSA 2009 Contributed Papers. URL=<http://philsci-archive.pitt.edu/5263/>

purposes of enquiry, scientific representations “provide us with specific information regarding their targets […] in the sense that it could not be equally conveyed by any other arbitrarily chosen sign.”[452] In light of this, an apparently denoting element (such as the Kennedy speech) denotes if the representation in which it occurs is interpreted to make claims about the world. If such an element is only interpreted with respect to the internal narrative of the representation in which it is embedded, then it is not used to refer. Likewise, if an apparently non-denoting element (such as Twin Earth) is used to support claims about the real world, this element may not strictly denote anything in particular, yet in its argumentative context it is used to make claims about phenomena in the world. On this account, I suggest that the epistemic character of apparently denoting and non-denoting elements depends on the interpretation of the representational context in which these elements occur.

My claim, therefore, is that elements in fiction resembling elements known from reality do not strictly denote because they are not used to provide a genuine description of these real entities. What such *images of denoting elements* and properly *denoting elements* have in common is that they refer to a certain body of knowledge about the world. Only if they are used to make claims about the world, do these elements have a *denoting* character. The use of an element as denoting, instead of being merely an image of a denoting element, depends on a different relation to the wider body of knowledge. This relation, I will show, is determined by two conceptually distinct forms of enquiry. Unlike the inferential account, my distinction between *images of denoting elements* and *denoting elements* therefore implies that the representational force of a scientific representation is defined not only by its capacity to derive claims about the world. Rather, these claims must be furthermore analysed and compared with claims derived from other representations aiming at the same target system. Only by being embedded in a polyphonic network of representational sources can a representation exercise its epistemic function. That is to say, if a representation is said to allow for inferences about elements in the world, it is necessary to define a basis on which these inferences are evaluated as ‘providing information’ about a particular target. Its relation to other representations, I will argue in the remainder of this paper, is what grounds a representation’s capacity to allow informative inferences about particular

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[452] Suárez (2004): An Inferential Conception, 772.

elements in the world. Whether a representation is assigned an epistemic function and, moreover, whether it fulfils this function, therefore, must be explored in its wider context of use and on a case-to-case basis. With respect to the initial comparison of scientific representations with fiction, I shall clarify this contextuality in the following section.

5 Fictional and Non-Fictional Enquiry

As I have argued throughout this paper, no element is denoting on its own account but only by virtue of the use within its wider contextual embedding. This context concerns, on the one hand, the representation in which a certain element is contained and, on the other hand, how this representation is used in the wider discourse with other representations.

To analyse the epistemic function an element is assigned in the interpretation of the overall representation in which it is contained, I suggest drawing a distinction between two kinds of enquiry: fictional and non-fictional. This, I hope, will provide further insight into the characteristics of scientific enquiry. When we question the function of an element for the interpretation of a particular representation I consider it to be a *fictional enquiry*.[453] Such an inquiry only concerns the placement of an element and its character within the framework of a particular representation, but it is not used to make claims about the world. This means that if the relevance of an analysis is limited to the construction of a representation, the use of a representation is defined as fictional. By contrast, interpretations of an element that address questions exceeding its placement in and function for the composition of a particular representation I consider to form a *non-fictional enquiry*. These interpretations concern claims that are not bound to a particular representational context but address issues about the world that could also be investigated through alternative and partly independent representations dealing with the same phenomenon. On this account, non-fictional enquiry is inevitably related to a plurality of representations and shows a degree of independence of the investigated element to its particular representational context. The claims made by non-fictional interpretations of individual representations are therefore in constant cooperative and competitive

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[453] Danneberg (2006): *Weder Tränen noch Logik*, 31.

comparison and revision with claims derived from other representations. The pluralistic access to descriptions external to the representation, I propose, is the ground for the epistemic function of scientific representations to prove, witness, certify or support claims about the world.

It is crucial emphasising here that the distinction between fictional and non-fictional enquiry is not to be confused with a definition of fictional and non-fictional representations such as novels and scientific models. Given the earlier described hybrid character of representations, (non-)fictional enquiries define the *use* and *interpretation* of a representation as purporting a fictional or non-fictional claim.

Putting the use of this distinction to the test, I want to address the interpretation of two different examples, a scientific model employing a non-denoting element on the one hand and a historical text in which fictional and non-fictional elements blend on the other. For the first case, consider Eric Winsberg's analysis of "silogens" in computer modelling.[454] Silogens are hypothetical atoms that aid in the calculation of silicon fractures in nanomechanic models. By having some properties of silicon and some properties of hydrogen, their hybrid character is used to combine the algorithms and the descriptions of two different theories involved in this modelling procedure, namely quantum mechanics and classical molecular dynamics. Silogens do not denote real atoms. Although the overall model in which they are contained makes "good enough" claims about the world, Winsberg argues that these silogens are fiction since, taken individually, they have no identifiable physical target system. I agree with Winsberg insofar as that the overall model is non-fictional and that the individual silogen atoms are non-denoting elements within this model.[455] Where I disagree is to describe silogens as fiction just on the basis that they are non-denoting elements. Instead, I propose to take a look at two different ways in which the element of silogens can be interpreted here. On the one hand, as part of the overall model and its application, silogens are used to make claims about the world. These claims can be furthermore investigated and compared with claims derived from alternative models, resulting in further corrections, confirmations etc. On the other hand, considered separately with respect to their individual

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[454] Winsberg, Eric (2009): A Function for Fictions. Expanding the Scope of Science. In: *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* Ed. by Mauricio Suárez. London: Routledge, 179-190.

[455] Ibid.

placement and function for the model, silogens are not used to make claims about the world but about the particular structure of the representation in which they are embedded. According to my definition, whereas the first interpretation is a non-fictional enquiry, the latter is fictional. Therefore, it is not the element per se that is fictional or non-fictional, and it is not the denoting or non-denoting character of an element that makes it fictional or not, but its use within an interpretation of a representation. As a result, the distinction between fiction and non-fiction is not to be based on the structure of the representation and its individual elements but to be determined by the interpretation strategies addressing the representation.

Let me consider another, literary example to stress this point a little further. In 1634 Johannes Kepler's *Somnium seu Opus de Astronomia Lunari – The Dream, or Posthumous Work on Lunar Astronomy* was published. The enigmatic charm of this book is its twofold character, which places it in an apparently intermediate position between science and fiction. In order to analyse this ambiguous character and determine its denoting or fictional characteristics I will start with a brief summary of its content. Kepler's book narrates a dream that is divided into three levels. The book begins with a first person narrator who describes a dream in which he is reading a book of a fictional author called Duracotus. The second level of narration concerns Duracotus's own story about his life, which involves his academic study of astronomy and also his relation to his mother, who practices forms of magic. She gains her knowledge from spirits and it is because of her that Duracotus encounters the voice of the 'Daemon ex Levania', who constitutes the third narration level. The Daemon holds a monologue on the moon that is, indeed, a brief account of Kepler's own argument in support of Copernicus' heliocentric worldview.[456]

The poetic structure of the text is a technique of *reduplication,* that is to say the frames of narration are embedded within each other. On the first level somebody is telling a dream about a book, on the second level there is the tale of the book itself and, by the third level, the story has turned into a self-contained monologue of the Daemon within this book. The effect created is an inverse relation between content and structure: the more fictional elements the

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[456] Kepler, Johannes (1965[1634]): *Kepler's Dream.* Ed. and trans. by L. John. Berkeley: University of California Press.

text evokes – beginning with a dream leading to a fictional character and ending with a daemon – the more scientifically relevant its content appears. Although introduced by a complex fantasy framework, the astronomic descriptions match the Copernican theory.[457] What is fairly clear in this case is that the *Somnium* distinctively exhibits denoting and non-denoting elements. Slightly more problematic is the decision whether to interpret this representation as fiction or a denoting representation. With its astronomic descriptions in mind, is Kepler's *Somnium* a scientific explanation disguised by its poetic structure? Or are these astronomic descriptions merely background descriptions for a story about a fictional journey?

If one consults the historical background it becomes apparent that Kepler's own view on the Copernican system was of outspoken advocacy; and he already openly stated this position before and whilst working on the *Somnium.*[458] On this account, the fictionalisation might have had a different function if it was not to be a disguise to strategically hide academically controversial thoughts. The point I want to make again is that interpretations focussing on the peculiar poetic structure of this representation and its relevance constitute what I consider to be a *fictional enquiry*; they only reflect the placement of the elements and their relations within a particular representation but do not extend to make claims about the world. This means that if the relevance of an enquiry is limited to a particular and, moreover, *only this* particular context, the use of a representation is defined as fictional.[459] (It is worth adding at this point that whether the embedded description of the lunar sphere in the case of Kepler’s *Somnium* is adequate or not has no relevance for such a fictional enquiry. Whether the *Somnium* reflects true or false claims about the lunar sphere does not affect the fictional framework.)

By contrast, if one wants to use Kepler’s *Somnium* as a historical document, investigating the astronomic views held at his time, the enquiry exceeds the scope of this particular representation but makes (historical) claims about the world. These historical claims can be addressed by a variety of sources and need not be limited to the *Somnium.* In fact, in order to see, for instance,

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[457] Schneider, Christian (2006): Science as Science Fiction. Johannes Kepler’s *Somnium* and the Poetics of Invention. In: *Imagination und Innovation, Paragrana, Internationale Zeitschrift für Historische Anthropologie* (Beiheft 2). Ed. by T. Bernhart and P. Mehne. Berlin: Akademie Verlag, 262.

[458] Danneberg (2006), 31.

[459] Danneberg (2006), 31.

whether Kepler presented an adequate account of Copernicus' theory, interpretations have to be related to other representations dealing with the same topic. On this account, *non-fictional enquiry* is inevitably related to a variety of representations and shows a certain independence of the investigated element to its particular representational context. This independence grants representations an epistemic function to participate in the scientific endeavour of making claims about the world.

6 Fictionalism and the Issue of Scientific Realism

This paper argued for a distinction between fiction and non-denoting elements in science by emphasising the different strategies involved in their interpretation. Grounded in two forms of enquiry directed at the interpretation of a representation, rather than a feature of the representation itself, this distinction accommodated the diversity of ways in which scientific representations aim to address the world, for instance, as mathematical or material models, graphs, computer simulations and so on. The way in which representations were assigned an epistemic function, i.e. were argued to facilitate claims about the world, was grounded in their relation towards other representations making similar or conflicting claims about the same target system. In contrast to fictional enquiry, questions that exceeded the function of an element within a particular representational context but relating it to a plurality of representations were defined as non-fictional. On this account, my approach also provided a heuristic strategy for evaluating to what extent an inference drawn from a representation can be said to present a claim about the world, rather than merely being a result of the representational structure.

I would like to end the discussion of the preceding distinction between fictional and non-fictional enquiry with a brief comment on its implications for the wider philosophical debate on fiction in science. Although a comparison of fiction with non-denoting elements in science may be justified with respect to the shared lack of unambiguous reference to the world, it nevertheless reveals an important epistemic difference for the interpretation of scientific representations. This epistemic difference concerns the evaluation of the claims given in a representation in relation to the claims of other representations.

Instead of employing the concept of fiction in science for non-denoting elements in general (whether this concerns only non-existent entities such as silogens in the case of narrow fictionalism or includes abstractions such as frictionless planes in the case of wide fictionalism), the concept of fiction is best used to understand the question we address with such non-denoting elements. Does this question concern claims about the world? Then it is important to see to what extent the descriptions given by a particular representation relate to other representations with a similar topic, i.e. do their claims conflict, support or complement each other? In these cases, we can speak of a non-fictional use of these non-denoting elements. By contrast, if we address the construction of a particular representation, for instance to analyse the workings of a model and its limits, the interpretation does not primarily concern the world but the structure of the representation. In these cases, we can speak of a fictional use of a representation.

The distinction between fiction and non-denoting elements in science, I conclude, is important for examining the use of scientific representations and to further understand the nature of scientific inquiry. In fact, the distinction advocated here between fictional and non-fictional enquiry provides a useful tool to explore to what extent the descriptions given by a model can be justified as making claims about the world or, rather, are a consequence of the model's particular construction. Applying the model to specific cases and not forgetting the complexity of the world, it can be evaluated where the potential as well as the limits of a particular model lies. The adequacy of the link modelled between the claims made in the representation and the phenomenon explained cannot be evaluated through the model and its structure alone but inevitably requires further investigation and comparison to other models, statistics and case studies. Even highly idealised models or models employing elements that have no direct relation to any physical system can be interpreted as making claims about reality, if their represented explanations can be explored beyond the limits of this model. The use of representations is thereby not determined by literal reference but by the extent to which their claims relate to the world by comparison to other representations, models, experiments, etc.

On this account, the plurality of representations likewise provides a useful tool to draw a line between fictitious and real enquiries about the world. Is something addressed only by a particular model or can it be further explored by alternative representations? The usefulness of a particular scientific enquiry about the world can be assessed by means of this representational plurality. In light of this, I suggest that representational pluralism is not a problem, but rather a very useful indicator to adopt a realist stance on scientific models and concepts.

Chapter 7

Bending Molecules or Bending the Rules? The Application of Theoretical Models in Fragrance Research

1 Models in Experimental Systems

The main aim of this chapter is to explore the question of what models do, and to justify my claim that the referential capacity of models must be analysed through their epistemic relations with other models. The general philosophical problem that attends the empirical application of scientific representations such as models is twofold. Models, on the one hand, are said to often make “false” claims about the world, i.e. claims not literally realised in the physical systems they are supposed to represent. On the other hand, models have often been shown to lack forms of resemblance to the physical system they are used to address. These issues can be summarised in the following question: Under what particular conditions do we take models as a representation of the empirical phenomena they aim to explain?[460]

To answer this question, I propose to focus on representation as a practice-oriented notion. Drawing on my argument in the previous chapter, this chapter exemplifies how scientific models are used in relation to other models aiming at the same target system. Forming what I described as epistemic relations, models interact in different ways by competing with, cooperating and complementing each other. Like Hans-Jörg Rheinberger and Hasok Chang, my usage of epistemic concerns knowledge-making practices rather than abstract notions of ‘truth-bearing’ or facticity.[461] The reason for this, as I will illustrate, is that any notion of truth-bearing and facticity only holds retrospectively. But to define the capacity of models to represent the world, no notion of truth or facticity is applicable to those representations in scientific practice that are not yet fully established. My account of representation, which I will further develop

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[460] Bailer-Jones, Daniela (2009): *Scientific Models in the Philosophy of Science.* Pittsburgh: University of Pittsburgh Press,177.

[461] Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press; Chang, Hasok (2011): The Persistence of Epistemic Objects Through Scientific Change. *Erkenntnis* 75, 413f.

here, is thereby in contrast to a more conventional one that takes representation as a dyadic relation between models and target systems and that is defined by notions such as similarity or resemblance. Instead, I want to argue that representation is an epistemic activity that requires a pluralist as well as historicised perspective on scientific practice. I will exemplify my account of representation here through a detailed reconstruction of the practices involved in applying two rival theoretical models concerning the mechanism of primary odour recognition for accommodating structure-odour relations (SORs) in fragrance chemistry.

Concerning the notion of facticity in representational analysis, Nancy Cartwright (1983) raised profound criticisms of the practice of defining the reference of models simply by virtue of their explanatory function, i.e. their capacity to bring certain observations into a scientifically relevant (e.g. causal) relation. Cartwright's "simulacrum account" draws a distinction between the potential explanatory value a model might have and the factual truth of its descriptions. Although a model might explain certain phenomena by accommodating the data and fitting them into a general theoretical framework, this does not guarantee their truth or the truth of the theory from which they are derived. Instead of representing what really happens, some models provide only abstract relations under which observations are organised to investigate a specific phenomenon.[462] Cartwright's criticism gives us good reason to evaluate the extent to which the claims made by models do indeed reflect reality and to consider models as investigative tools rather than factual representations.

Cartwright distinguishes two ways in which a model is said to be realistic or unrealistic. The first concerns the relation between "the model and the situation depicted by the model".[463] The second addresses the function of models that explain the mathematical structures of a theory by describing the conditions under which a phenomenon occurs.[464] In both cases a model's function is to give a theoretical description of the behaviour of a phenomenon, and its degree of realism is measured by how well the descriptions given in the model match the substructures of the represented phenomenon. The extent to which a model replicates these substructures thereby determines its factuality. Nonetheless, models that fail to replicate may not be factual but may still be explanatory.

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[462] Cartwright, Nancy (1983): *How the Laws of Physics Lie.* Oxford: Clarendon Press, 143-162.

[463] Ibid., 147.

[464] Ibid., 150.

Although I agree with Cartwright that models do not need to replicate the relations that hold between elements in the world, my problem with her assessment of realism concerns her use of the notion of the "factual". This usage presupposes that, although theoretical frameworks and models may be able to explain phenomena, they may nevertheless not be "true to" the character of the underlying relations between elements in the world. The problem with this account of truthfulness, however, is that it only holds in hindsight. Judging a model's degree of realism in terms of its facticity (even though Cartwright only defines this for phenomenological regularities and not fundamental causal laws) implies that we already know what part of the model descriptions are factual replications or explanatory distortions. Cartwright's simulacrum account "says that we lay out a model, and within the model we 'derive' various laws which match more or less well with bits of phenomenological behaviour".[465] What is left out here, however, is how we judge whether model-based inferences and descriptions match the phenomenon. This problem becomes more prominent for cases where different models are available that compete in their explanation of a phenomenon and its behaviour. My problem with Cartwright's argument thus does not concern the suggested distinction between explanation and factuality but, rather, whether this distinction contributes to our understanding of how models (are used to) represent reality.

In order to determine the representational capacity of models, the notion of facticity and its utility for describing how models make realistic or mere explanatory claims has to be considered more carefully. To address this question we might first consider the relation between models and observations: what determines the facticity of a model? For my analysis I turn to contemporary issues in olfaction theory regarding the molecular basis of odours. Attempts to explain the primary perception of smells led to two theories, the shape theory and the vibration theory of odours, each of which suggest a different theoretical model of the underlying recognition mechanism. Drawing attention to the conceptually distinct structural hypotheses implied in the two rival theories, I will analyse the application of the theoretical mechanisms and how these are used to accommodate the vast range of structurally diverse odorants (i.e. odoriferous molecules). This leads to a consideration of the

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[465] Ibid., 161.

complex role that models play in research practice. Focussing on how the same range of data is analysed and interpreted within two rival theoretical models will first illustrate that the relation between the theoretical and the empirical is inevitably of a mediated character. Philosophical attention to the mediating character of models has been growing, and there are, of course, various forms of mediation for linking our theoretical assumptions to observations, involving models, instruments, methods of measurement etc.[466] It is important to emphasise the extent to which models and the model context further provide the grounds on which competing explanations are judged and assessed. Asking how empirical observations are turned into evidence for (or against) a theoretical framework, the application of models is shown to be integral to the evaluative process of theory assessment.

What is considered to be a factual representation, I argue, must therefore be analysed more closely with respect to the particular context in which models, instruments and experiments are placed. For these reasons, I suggest that we direct attention to the different ways in which models *produce* a relationship with the world by interacting with other models and with the information that is available about the phenomenon. The capacity of models to represent must then be explored and evaluated with respect to the epistemic functions they exhibit in the experimental environment within which they are applied and the specific purpose(s) for which they are constructed.

The experimental environment within which models interact is best defined by Hans-Jörg Rheinberger's (1997) notion of "experimental systems" that refers to "the evolving practices and objects involved in experimentation."[467] This means that a number of different elements – models, materials, instruments, measurement techniques, but also social factors such as the spatial and social qualities of the laboratory – must be consulted to understand how scientific objects (*Wissenschaftsobjekte*) are formed and how they continue to develop with their own dynamics. An analysis of this development in terms of the

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[466] Morgan, Mary and Morrison, Margaret (Eds.) (1999): *Models As mediators: perspectives on natural and social science.* Cambridge: Cambridge University Press; Suárez, Mauricio (Ed.) (2009): *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* London: Routledge.

[467] Leonelli, Sabina (2011): Review of An Epistemology of the Concrete by Hans-Jörg Rheinberger. *International Studies in the Philosophy of Science* 25(4), 420; Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press; Rheinberger, Hans-Jörg (2010): *On Historicizing Epistemology: An Essay.* Stanford: Stanford University Press.

entrenchment of practices has to proceed by evaluating how a specific question is used to gather and interpret data, design instruments and develop further techniques to handle aberrant results. Scientific enquiry is often accompanied by a range of structural assumptions that also reflect back on the assessment of conflicting data (and possible alternative explanations). Tracing the individual development elements in models and their impact on the overall theoretical framework, a number of modifications and additional assumptions enter the experimental system so that the different models, instruments and experiments can be adjusted to accommodate each other.[468] This adjustment and the role played by models within this process is the topic of my subsequent analysis of the establishment and theoretical development of structure-odour relations in fragrance research.

In the following, I illustrate that, as part of such dynamic experimental systems, models can have various functions. Drawing on Daniela Bailer-Jones (2009), these functions can be divided into three general categories: theoretical models, models of experiments, and data models. Theoretical models such as the rival olfactory mechanisms aim to describe physical systems in their qualitative character: by individuating the elements involved and by further determining the nature of the interaction between those elements, they specify the conditions under which a specific phenomenon occurs. Models of experiments present instructions about how to test assumptions such as the specific structural hypotheses concerning the key feature of odour recognition implicit in a theoretical model. Data models address the materials, such as the vast range of odoriferous molecules, and arrange them into a form that allows comparison and analysis of observations with respect to the structural claims implicit in the theoretical model.[469]

I address the function of models and their relations toward each other first by introducing data models in fragrance chemistry, so-called olfactophore models. These consist of statistical comparisons of a wide range of molecules of the same odour type and, as I will show, are deeply embedded in a theoretical framework that takes stereochemistry to be the key feature determining the molecular basis of odours. Yet, as it will turn out, the accommodation of molecular data under stereochemical criteria faces many exceptions. These are

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[468] Hacking, Ian (1992): The Self-Vindication of the Laboratory Sciences, 29-65. In: *Science as Practice and Culture.* Ed. by A. Pickering. Chicago: University of Chicago Press, 29-64.

[469] Bailer-Jones (2009): *Scientific Models*, 170ff.

explained through reference to the model of the mechanism of primary odour recognition. Since the mechanism is yet unknown, however, this model still has a purely theoretical character. In fact, current olfactory debate surrounds the rivalry of two possible models for the recognition mechanism. I will next explain how, proposing two different key features, each model makes sense of a range of problematic data and how each theoretical model aids in the construction of experiments aimed at testing its implicit structural hypotheses. This will provide the basis on which I shall explore the interaction between these models and further refine my account of representation as an epistemic and historical activity.

2 Data Models for Evaluating Structure-Odour Relations

Integral to research on the molecular basis of odour perception is the question of what constitutes the specific relation between the structure of an odorant and its odour. Determining what part of the molecule carries its olfactory information, telling the receptor what its particular smell is, means positing a mechanism explaining the interaction between odorants and receptor proteins. Assumptions about the nature of this mechanism, however, remain highly speculative. Since the nature of the binding site of the olfactory receptors (ORs) is unknown and currently experimentally inaccessible,[470] hypotheses about structure-activity relations (SARs) between odorants and receptors rely strongly on statistical comparisons of a wide range of molecules. These statistical comparisons allow particular molecular parameters of odorants to be assigned to specific odour types, establishing structure-odour relations (SORs).

A range of databases – owned by large industrial fragrance companies such as Quest International, Givaudan, Henkel, Firmenich etc. and for patent right reasons often restricted in their accessibility to the wider public and academic researchers – contain a huge number of structurally diverse odorants.[471] Addressing this vast amount of data, the most advanced models for a systemic comparison of odorants are so-called olfactophore models (fig. 1). With the introduction of computer-based three-dimensional modelling techniques to

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[470] Crasto, Chiquito J. (2009): Computational Biology of Olfactory Receptors. *Curr Bioinform* 4(1), 9.

[471] Burr, Chandler (2002): *The Emperor of Scent.* London: Random House, 306-309.

fragrance research in the 1990s, it is now possible to conduct a comprehensive survey of odorants and to compare and statistically evaluate a larger number of more detailed structural aspects.[472] Olfactophore models have two main tasks. They first allow for the accumulation of data by employing different statistical and computational techniques, comparing a vast range of molecular parameters. Second, such olfactophore models reduce and interpret the otherwise unmanageable data and serve as a means of data processing. By selecting particular molecular parameters for data analysis, these models are based on specific structural hypotheses and therefore are not strictly theory-neutral.[473]

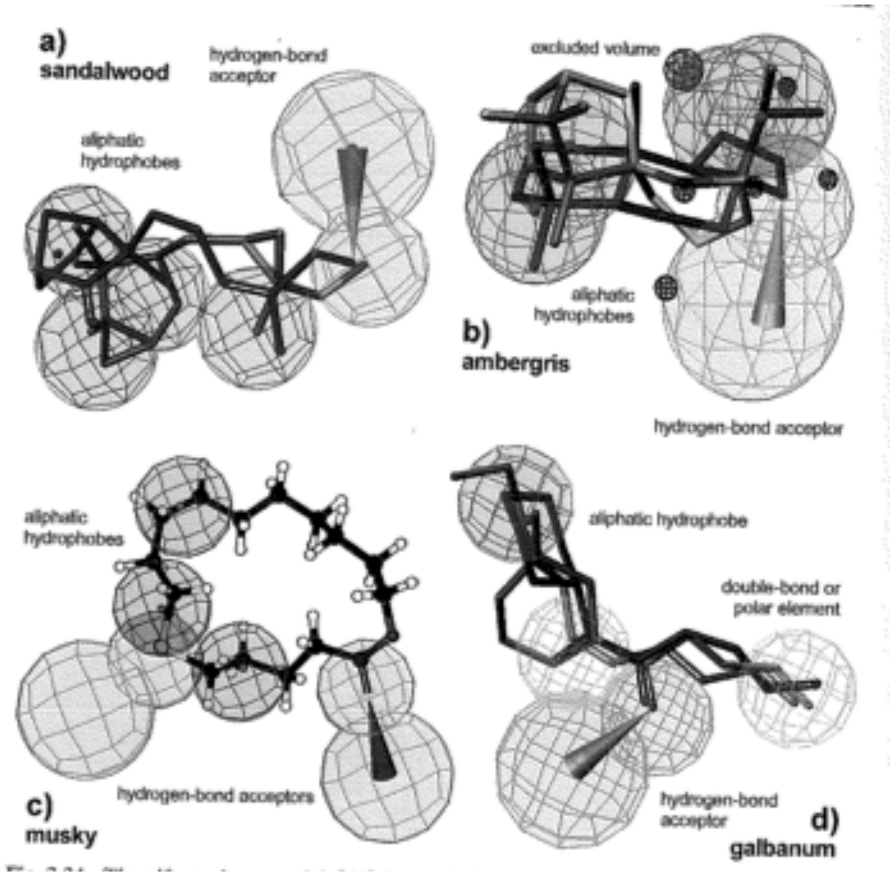

Fig. 1 Olfactophore models. Odorant types are analysed in terms of their stereochemistry, atom positions and distances of atom groups from each other, as well as other molecular parameters such as hydrophobicity. Ohloff et al. (2011): *Scent and Chemistry*, 126.

Relying on assumptions of a shape-sensitive mechanism, olfactophores consist of three specific molecular groups, namely the osmophore, profile and bulky

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[472] Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH, 96-133.

[473] Thereby also combining three elements of data processing – data reduction, data analysis and data interpretation – as proposed by Hacking (1992): *Self-Vindication of Laboratory Sciences*, 48.

groups. Defined by particular molecular features such as hydrophobicity, each group is assumed to have a specific role in the mechanism of primary odour recognition. Visualising the specific spatial and geometrical arrangement of atoms and atoms groups, involving their position and distance from each other, these olfactophores serve as template model structures for specific odorants (mostly odorants with relevance to fragrance research such as sandalwood, amber or muguet).[474] Other forms of data models, collecting materials and grouping them into kinds, rest on common structural classifications in chemistry that comprise categories such as chemical groups, isosteric molecules, isotopes and enantiomers.[475]

The scientific problem arising from these data models with respect to currently proposed structural hypotheses about SORs is the apparent lack of lawlike regularities. The majority of fragrance scientists assume stereochemical features to be responsible for primary odour recognition. Until now, however, no stereochemical odour rule has been established which has not been riddled by a range of significant exceptions.[476] This difficulty is more than a technicality. Rather, it raises questions about the integrity of the predominant theoretical framework from which most of these structural hypotheses are derived and under which most of the data are analysed. Challenging this theoretical basis, a rival theory suggests an alternative feature determining SORs, referring to molecular vibration in the infrared range as the key feature of primary odour recognition. Instead of assuming a shape-sensitive recognition mechanism, the vibration theory proposes that odour recognition works by virtue of a biological transduction of molecular vibrations.[477] Although highly speculative in its nature, a proposal for such a mechanism to detect molecular vibrations in a biological system has nevertheless been demonstrated to rest on viable empirical assumptions.[478] My concern here is not the nature of the recognition mechanism but, rather, how the implicit structural hypotheses of the two rival mechanism models accommodate the range of structurally diverse odorants. By virtue of

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[474] Ohloff et al. (2011): *Scent and Chemistry*, 126.

[475] Sell, Charles (2006b): On the Unpredictability of Odor. *Angew Chem* Int Ed Engl. (38), 6255; Turin, Luca (2005): Rational Odorant Design. In: *Chemistry and Technology of Flavour and Fragrance.* Ed. by D.J. Rowe. Oxford: Blackwell, 261-273.

[476] Sell (2006b): *Unpredictability*; Turin, Luca (2006): *The Secret of Scent.* London: Faber and Faber, 46-82; Ohloff et al. (2011): *Scent and Chemistry*, 96-133.

[477] Turin, Luca (1996): A Spectroscopic Mechanism for Primary Olfactory Reception. *Chemical Senses* 21(6), 773-791.

[478] Brookes, Jennifer C.; Hartoutsiou, Filio; Horsfield, A. P. and Stoneham, A. M. (2007): Could humans recognize odor by phonon assisted tunneling? *Phys Rev Lett.* 98(3), Article 038101.

selected examples of conflicting data, I explore how the theoretical models of the rival mechanisms are applied and modified and, furthermore, how experiments to test affiliated auxiliary assumptions are designed.

3 Theoretical and Experimental Models: Data Accommodation and Hypothesis Testing

What is striking about a general comparison of the rival olfactory theories is that, although working on two conceptually clearly distinct assumptions, both of their proposed mechanisms are more or less able to explain a range of problematic data. The role of the mechanisms assumed in each theory in the process of data accommodation appears twofold. The mechanisms, as theoretical models, first provide an inferential basis from which auxiliary assumptions to explain aberrant data are derived. A lot of exceptions in SORs are explained through reference to additional molecular features or by particular effects evoked throughout the perception mechanism. Second, following this development, the theoretical models of the mechanisms are modified appropriately. Integrating additional parameters or particular effects into the theoretical mechanism often requires a modification of the initial model. The relation between the theoretical models and the data models and experiments thus appears to have a peculiar kind of circularity. As a preliminary formulation we can say that in order to accommodate the conflicting data and to serve as a ground to derive possible explanations, the theoretical models themselves must be flexible enough to accommodate a range of additional theoretical assumptions. To illustrate this flexibility, the following subsections explore four examples that pose problems for the underlying structural hypothesis of the rival theories and their suggested mechanisms, namely the strong smell of small molecules and functional groups, isosteric molecules, isotopic variations and enantiomers.

3.1 The Strong Smell of Chemical Groups and Small Molecules

One perplexing aspect of odour perception is our ability to smell very small molecules and to identify specific chemical groups such as thiols (-SH), nitriles (-CN), isonitriles (-NC) oximes (-NOH), nitro groups (NO_2), aldehydes (C=O(H)).[479] Small molecules like these initially posed problems for each of the rival olfactory theories, shape and vibration. These problems are extensively reviewed by Klopping (1971).[480]

Certain small molecules such as hydrogen sulphide (H_2S), ammonia (NH_3) and hydrogen cyanide (HCN), Klopping remarks, are not accounted for by the initial formulation of the vibration theory, proposed by his contemporary Robert Wright.[481] Although they exhibit frequencies outside Wright's suggested perceptible vibration spectrum, these small molecules nevertheless possess extremely powerful odours. Wright's response was to suggest some form of chemical reaction that might take place during the causal interaction between the molecule and the receptor.[482] However, this suggestion corresponded neither to his own nor to the accepted contemporary view that odour recognition is physical rather than chemical in its nature.[483] "In other words, the odorant molecule does not need to undergo chemical conversion in order to be perceived."[484]

In comparison, attempts to explain the strong smell of small molecules also face difficulties within the shape theory of odours, because of the sheer absence of

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[479] Turin, Luca and Yoshii, Fumiko (2003): Structure-Odor Relations: A Modern Perspective. In: *Handbook of Olfaction and Gustation 2nd edition*. Ed. by R. Doty and M.Decker. Informa Healthcare, 457-482. doi: 0.1201/9780203911457.ch13 Cited is the online version URL=< http://www.annindriya.com/_mcms/_data/files/Luca%20Turin%20structure%20odor%20theory.pdf>, 11.

[480] Klopping, H.L. (1971): Olfactory theories and the odors of small molecules. *J Agric Food Chem* 19, 999-1004.

[481] Although it was not Wright but Malcolm Dyson who first proposed an olfactory theory of vibration, it is Wright who developed a systematic account of how such a theory was to look like. Wright, Robert H. (1964): Odor and molecular vibration: the far infrared spectra of some perfume chemicals. *Annals of the New York Academy of Sciences* 116, 552-558; Wright, Robert H. (1977): Odor and Molecular Vibration: Neural Coding of Olfactory Information. *Journal of Theoretical Biology* 64(3), 473-474; Wright, Robert H. (1982): *The sense of smell.* Boca Raton, Florida: CRC Press.

[482] "He assumed that H2S undergoes a chemical reaction in the nose which turns it into a larger molecule, i.e. one possessing vibrations below 1,000 [wavelengths]:
$4H_2S + O_2 = 2H_2S_2$ [+ $2H_2O$]
$2H_2S_2 = H_2S + H_2S_3$." Turin (2006): *Secret of Scent*, 135.

[483] Roderick, William R. (1966): Current Ideas on the Chemical basis of olfaction. *Journal for Chemical Education* 43(10), 510; Klopping (1971): *Olfactory theories*; Turin (2006): *Secret of Scent*.

[484] Klopping (1971): *Olfactory theories*, 999.

any distinct stereochemical, i.e. shape-size related, features that could explain the extremely intense and distinct odours of these molecules. Needless to say, efforts were made to resolve these anomalies for both theories. The solutions within each account resided in a modified model of the recognition mechanism. With respect to the impossibility of optical spectroscopy in a biological system, Wright assumed that the transduction of molecular vibrations is of a mechanical character. As a result, only vibrations under 1000 wavelengths were considered, because of the limited amount of energy available for thermal motion at body temperature.[485] This energy is far too low for detecting frequencies of, for instance, 2500 wavelengths but rather resides around frequencies of 250 or 800 wavelengths.[486] When Luca Turin revived the vibration theory in 1996, he corrected Wright's calculations and developed the first concrete and empirically viable model for a biological spectroscope that was based on electron spectroscopy and inelastic-tunnelling frequencies.[487] It is therefore not mechanical but quantum in character and, as a result, the energy available is enough to extent the detection of molecular vibrations to the upper limit of 4000 wavelengths.[488] Thus, the vibration frequencies of small molecules such as ammonia (NH_3) are no longer outside the range of what is understood as perceptible. In addition to explaining the strong odour of small molecules, the likewise puzzling ability to discern the smell of small chemical groups such as thiols embedded in bigger molecules is less puzzling within the vibration theory. Independently of their sheer structural diversity (fig. 2), functional groups exhibit quite distinct vibrational frequencies corresponding to different odour types.[489]

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[485] "The problem with thermal motion is that the energy involved, whether at room or body temperature, is small, of the order of 250 wave numbers, which is around 10 per cent of the SH stretch energy. One might think that the effect of a 250 bump on a 2,500 vibration would be to play it *pianissimo*. That would be if things weren't quantum. In the quantum world things work like flutes, not like pianos. When you blow into a flute (or a beer bottle) very softly you get no sound. It is only when you get beyond a threshold intensity of blowing that the flute emits a sound. Blow harder, and the sound jumps an octave higher. Same with Brownian motion: a 250 wave number bump is tantamount to the gentlest puff of air, and stands almost no chance of exciting a 2,500 wave number vibration. What this boils down to is simply that if the nose is going to feel vibrations mechanically, then only vibrations below 1,000 wave numbers need concern us." Turin (2006): *Secret of Scent*, 134.

[486] Turin (1996): *Spectroscopic Mechanism*, 774; Turin (2006): *Secret of Scent*, 134.

[487] Turin (1996): *Spectroscopic Mechanism*.

[488] Turin, Luca (2002): A method for the calculation of odor character from molecular structure. *Journal of Theoretical Biology, 216*, 367-385; Turin (2006): *Secret of Scent*, 135.

[489] Turin (1996): *Spectroscopic Mechanism*, 774.

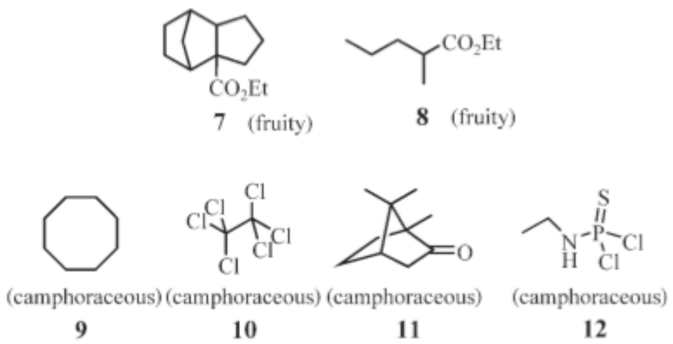

Fig. 2 Stereochemical diversity of functional groups that exhibit the same smell. Sell (2006b): *Unpredictability*, 6255.

Although the strong smell of small molecules still poses a puzzle for shape-based theories, a suggestion accommodating this phenomenon and the diversity of functional groups was discussed under the “profile-functional group” (PFG) concept.[490] Here small molecules and functional groups are interpreted as so-called profile groups, which are assumed to bind to a more specific part of the receptor-binding site. A few problems arise with this suggestion though.

One characteristic of profile groups is that their position in the molecule within which they are embedded sometimes seems to play a more important role than their stereochemistry. Studies with systematic element substitutions showed that “whether the substituents are acetyl, methoxy, or ethoxy, the para position is inevitably connected with ethereal odours and the ortho and meta positions with pungency.”[491] A proposal to simply combine the features of shape *and* position into an overall explanation, however, leads into conflict with other observed substitution phenomena, for instance, “if an aldehyde group is introduced in the para position of phenyl isothiocyanate a strong odour of an entirely different type, namely of heliotropine, is obtained.”[492] To accommodate this additional conflicting data, the latter results were explained by a competition between different functional groups, indicating the perception of either a more dominant chemical group or a combination of both groups given that these occur in a neighbouring position.[493] By rescuing the phenomena, these auxiliary assumptions respectively enter and modify the theoretical model of the perception mechanism: only if it is assumed that specific functional groups (e.g.

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[490] Beets, M.G.J. (1957): Molecular Structure and Organoleptic Quality. In: *S.C.I. Monograph No 1.* London: Society of Chem. Ind., 54-90; Klopping (1971): *Olfactory theories*, 1001.

[491] Klopping (1971): *Olfactory theories*, 1001.

[492] Ibid., 1001.

[493] Ibid., 1001.

"energetically favoured ones" that participate in the hydrogen-bonding of the osmophore group) determine the overall orientation of the molecule within the receptor-site, it is possible to explain its dominance in odour quality.

A significant change occurring in both olfactory theories concerns the rival structural hypothesis under which SORs are modelled. Even though the general theoretical framework retains a shape-sensitive or vibration-sensitive mechanism, the structural details of the hypotheses change and, as a result, so do also the conditions under which the odorants are supposed to interact with the receptors. The vibration theory became extended with respect to the range of detectible frequencies, whilst the shape theory directed attention to particular molecular groups rather than the stereochemical character of the entire molecule. Only in light of a different causal process explaining the transduction of molecular vibrations was the vibration theory able to accommodate the perception of small molecules. Its rival, a shape-sensitive mechanism, was modified to the extent that the perception of odours was no longer determined by the entire molecule but by a complex interaction of functionally different groups, introducing further molecular parameters such as their electronic profiles into the model.

Data accommodation, however, is only one function these theoretical models serve. In addition to articulating explanations for aberrant data, the mechanisms also provide a basis on which these explanations can be tested and assessed in direct comparison with their rivals. What form must an experiment take to compare the structural conditions that each modified mechanism entails? A suggestion put forward by Alan Musgrave is that in order to explore whether a theoretical framework is superior to its rival one should directly compare their specific underlying assumptions in such a way that both cannot entail the same result of a possible test ('not entailed' in this case means that either the observations conflict with one of the rivals or present a result on which the rival remains silent).[494] Therefore, developing a model of an experiment for the detection of functional groups must make one of the required structural features inaccessible to the receptors.

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[494] Musgrave, Alan (1974): Logical versus Historical Theories of Confirmation. *The British Journal for the Philosophy of Science* 25(1), 16; Worrall, John (2012): Theory-Confirmation and History. In: *Rationality and Reality.* Ed. by C. Cheyne and J. Worrall. Springer, 49-60. Cited is the prepublished paper. URL=< www.error06.econ.vt.edu/Worrallb.doc>, 33.

A promising candidate for such an experiment, proposed by Turin and Yoshii (2003), concerns the inaccessibility of stereochemical features. They suggested designing a molecule that contains a distinct functional group hidden (or "buried") in its structural configuration. "Hidden" here means that the functional group is sterically inaccessible to the olfactory receptors and, as a result, the only (currently conceivable) way to detect its odour is in terms of its molecular vibrations. Unfortunately, this experiment seems impossible, because such a molecule is too bulky and possibly exceeds the biological size restraints for perceiving odoriferous molecules. Alternatively, Turin and Yoshii suggested to use a molecule with sterically "hindered", i.e. hardly accessible, functional groups instead:

> "Sterically hindered phenols provide a first approximation to this goal. The presence of an OH group on a substituted benzene ring gives the molecule a distinctive "phenolic" odor, which the corresponding benzene does not have. Once again, if one assumes that the OH group is an odotope [a profile group], then making it less accessible to molecular recognition should silence its smell. This idea is easily tested by comparing the smell of di-tert-butyl derivatives of phenol, which are readily available commercially. *The results go against the odotope theory. 2,6 di-tert-butyl phenol, in which the OH group is strongly hindered smells as phenolic as, say, the 2,4 derivative in which it is more accessible."*[495]

Although not providing conclusive evidence, the model of the experiment allows for a test of the structural hypotheses implied by the theoretical models of the mechanism. Similar experiments, constructing further evidence, might follow. Comparing the modifications of both mechanisms, two interesting relations occur in this example. First, the theoretical change in the descriptions of the models altered the structural hypotheses implied and, as a result, had an impact on further data collection and assessment. Instead of the stereochemical configuration of the entire odorant, shape-based explanations came instead to focus on particular atom groups and included additional molecular features. The vibration theory of odours meanwhile extended the range of frequencies considered detectable by including near-infrared as well as far-infrared frequencies. As a near-infrared source is significantly weaker in comparison to a far-infrared one, this extension also required different instrumentation for

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[495] Turin and Yoshii (2003): *Structure-Odor Relations*, 14. [Italics mine]

measurement and data collection.[496] Second, both modifications of the theoretical models not only served as explanations for aberrant data but also suggested possible experimental tests of the structural assumptions involved. Whilst for the shape hypothesis these tests applied classic element substitution as a means to test for competition among functional groups, the claims made by the vibration mechanism led to the design of an experimental model for comparing the detection of sterically hindered functional groups.

3.2 Isosteric Molecules: Same Shape, Different Odour

Other data posing problems for the structural hypothesis underlying a shape-sensitive mechanism are isosteric molecules. Isosteric molecules are molecules of the same or a very similar shape that, nevertheless, have quite different odours. Conversely, there is also the opposite case involving molecules with the same or similar odours but entirely unrelated shape/size profiles (fig. 3).[497]

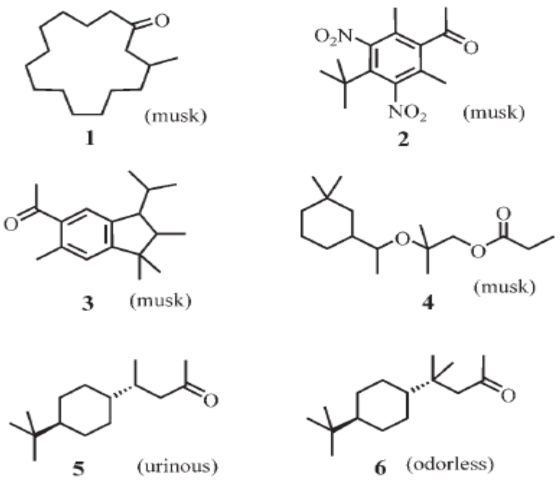

Figure 1. Different molecules, similar odors; and vice versa.

Fig. 3 Isosteric molecules are molecules with either a similar stereochemistry but a different odour (bottom). A converse case also appears for molecules with a different stereochemistry and a similar odour (top). Sell (2006b): *Unpredictability*, 6254.

Methods investigating the odoriferous character of isosteric molecules largely consist of systematic element and element pattern substitution. Possibly the

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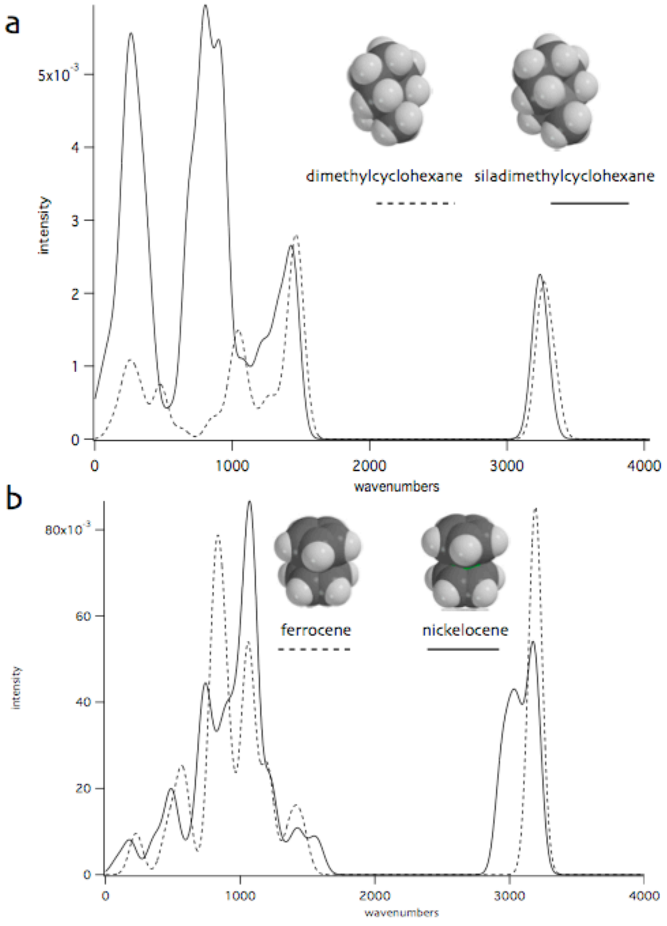
[496] Griffiths, Peter R. and Homes, Christopher (2006): Instrumentation for Far-infrared Spectroscopy. In: *Handbook of Vibrational Spectroscopy*. Wiley and Sons, S0207.
[497] Sell (2006b): *Unpredictability*.

most significant example is the replacement of carbon atoms with (periodically neighbouring) sila compounds:[498]

> “This preserves bond angles, increases bond lengths slightly and modifies partial charges, because the Si-C bond is more polar than is C-C congener. […] The sila replacement amounts to a relatively small structural change, accompanied by a striking change in odor character, from camphoraceous to harsh, bleach-like.”[499]

This phenomenon does not pose any particular problem for the vibration theory. Since the sila substitution changes the mass and charge of the molecule, the spatial configuration remains constant yet the vibration spectrum of these molecules differs sufficiently. Similar results arise in the case of metallocenes, where ferrocene and nickelocene, despite their similar structure, exhibit quite different smells (fig. 4).



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[498] Wannagat, U.; Damrath, V.; Huch, V.; Veith, M. and Harder, U. (1993): Sila-Riechstoffe und Riechstofffisostere XII. Geruchsvergleiche homologer organoelementverbindungen der vierten hauptgruppe (C, Si, Ge, Sn). *J. Organometallic Chem.* (443), 153-165; Turin and Yoshii (2003): *Structure-Odor Relations*; Turin (2002): *Method for the calculation of odor character*, 6f.

[499] Turin (2002): *Method for the calculation of odor character*, 6.

Fig. 4 Shape and vibration spectra of (a) a carbon compound with its sila-substituted counterpart and (b) two metallocenes in comparison. Turin (2002): *Method for the calculation of odor character*, 372.

The significance of isosteric molecules resides in their being nearly identical in their stereochemical features, i.e. atom positions as well as spatial and geometrical configurations, yet differing significantly in their odours. This structural similarity in contrast with their diverging odour quality obviously challenges a stereochemical hypothesis about SORs. Although still unaccounted for, attempts for a possible explanation have been made that refer to the compositional flexibility of molecules. It is assumed here that when odorants interact with the receptors, some molecules 'bend' within the binding site to such an extent that they adopt the shape of another odorant and therefore resemble each other in odour (fig. 5). Testing the validity of this explanation under so-called "conformational analysis", odorants are manipulated to abandon their minimum energy configuration and are deformed to adopt the configuration of other odorants in order to see whether their odours are also similar.[500] Certainly additional explanations are required to account for when, and under what conditions, a molecule is perceived in its minimum energy or in a deformed state. Nonetheless, this explanation resonates with contemporary assumptions about the general nature of molecular recognition where the interactions between ligands and receptors are considered to be more flexible and dynamic. To avoid the problems inflicted by the rigidity of the "lock and key" model of receptor-ligand interaction, modifications of the mechanism of primary odour recognition refer to the so-called "induced fit" model, where the ligand partly determines the complementary conformation of the flexible enzyme binding-site.[501] The dominant shape-related model-context for investigating enzyme reactions spurs further inquiry into shape sensitive olfactory mechanisms and acts as a resource for modifications of the existing shape-sensitive model.

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[500] Turin and Yoshii (2003): *Structure-Odor Relations*, 2; Yoshii, F.; Hirono, S. and Moriguchi, I. (1994): Relations between the odor of (R) Ethyl citronellyl oxalate and its stable conformations. *Quantitative Structure-activity Relationships* 13(2), 144-147. A similar explanation was also given by Charles Sell in BBC Horizon (1995): *A Code In The Nose.* Producer: Isabelle Rosin. Documentary, UK. (27 November 1995)

[501] Koshland, Daniel E. (1995): The Key–Lock Theory and the Induced Fit Theory. *Angewandte Chemie International Edition in English* 33(23-24), 2375-2378.

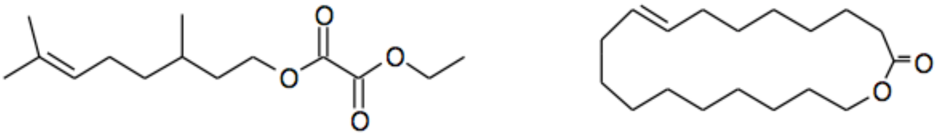

Fig. 5 “left: Ethyl citronellyl oxalate, a molecule possessing a macrocyclic musk odor but linear in shape. Right: a macrocyclic musk, cyclopentadecanolide. Shape-based theories assume that the linear musk assumes a conformation close to that of the macrocyclic when binding to the receptor, hence the similarity in odor.” Turin and Yoshii (2003): *Structure-Odor Relations*, 2.

3.3 Isotopes: Different Vibrations and Different Smell?

Definite experimental evidence for either theory, as has become clear, is not readily obtained. The development and modifications of both theoretical mechanisms in support of two conceptually distinct hypotheses highlight the importance of models and model development in the process of theory assessment. Contemporary rivalry between the shape theory and the vibration theory of odours only arises if their hypotheses are taken to exclusively determine the key molecular feature.[502] Considering the claims of both theories as mutually exclusive, odorants identical in composition that differ in molecular vibrations such as isotopic variants of a solution present a good basis to assess the structural hypotheses implicit in these rivals. Isotopes are variants of a chemical element with a different number of neutrons. Even though they exhibit subtle physical and chemical differences,[503] isotope compounds are nearly identical to their parent structure, except for molecular mass and, as a result, their vibration spectrum. Since isotopic variants are lighter or heavier than their parent structure, their electron bonds vibrate at different frequencies. The question that arises here is whether isotopic variants of an odorant smell similar, potentially posing a problem for the vibration hypothesis.

Most research on odour differences between isotopic variants concerns animal studies. Tests on insect repellents, for instance, suggest that insects such as flies and cockroaches not only detect isotopic differences but also that they

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[502] With respect to the persisting rivalry and ambiguous data accommodation, a suggestion to combine both structural assumptions, shape and vibration, has been made by Solov'yov, Ilia A.; Chang, Po-Yao and Schulten, Klaus (2012): Vibrationally assisted electron transfer mechanism of olfaction: myth or reality? *Physical Chemistry Chemical Physics* 14(40), 13861-13871.

[503] Wade, D. (1999): Deuterium isotope effects on noncovalent interactions between molecules. *Chem Biol Interact* 117(3), 191-217; Turin and Yoshii (2003): *Structure-Odor Relations*, 16.

[503] Keller, Andreas and Vosshall, Leslie B. (2004): A psychophysical test of the vibration theory olfaction. *Nature Neuroscience* 7, 337-338.

respond to specific versions which appear to share only a common pattern in their vibration spectrum.[504] Similar studies with fish have reached comparable results.[505] Another more recent study (2011), systematically linking these phenomena with the hypothesis of molecular vibrations, set out to test whether fruit flies are able to discriminate between normal and deuterated versions of odorants,[506] finding indeed that "*flies sniff out heavy hydrogen*".[507] Despite their suggestive power these animal studies on the perceptible differences of isotopes are not considered conclusive proof for the viability of the vibration hypothesis, especially not for explaining human smell perception.[508]

Concerning human smell perception, three major studies involving a panel with human test subjects presented diverging results. The widely cited study by Keller and Vosshall (2004) recorded that the participants were unable to tell a difference in the odour of deuterated acetophenone and its parent compound.[509] By contrast, an earlier study by Haffenden et al. (2001), using analogues of benzaldehyde, and a recent study by Turin's team in Gane et al. (2013), using deuterated cyclopentadecanone, came to the opposite result.[510] So do isotopes smell similar or not? As these conflicting results suggest, a conclusive answer

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[504] For studies concerning cockroaches see: Meloan, Clifton E., Wang, V.-S.; Scriven, R. and Kuo, C.K. (1988): Testing Wright's theory of olfaction with deuterated compounds. In: *Frontiers of Flavor, Proceedings of the 8th International Flavor Conference*. Amsterdam: Elsevier, 29-48; Kuo, C.K. (1982): *The effects of deuterating an attractant of the American cockroach, Periplaneta americana L, as a test for the frequency theory of olfaction.* M.S. Thesis. Manhattan: Kansas State University; Scriven, Rory and Meloan, Clifton E. (1984): Determining the active component in I,3,3-trimethyl-2-oxabicyblo [2,2,2] octane (cineole) that repels the American cockroacj, periplaneta americana. *Ohio J Sci* 84(3), 85-88; Havens, Barry R. (1993): *The applications of deuterated sex pheromone mimics of the American cockroach, Periplaneta americana L to the study of Wright's vibrational theory of olfaction.* Ph.D. Thesis. Manhattan: Kansas State University; Decou, D.F. (1993): *The study of Wright's theory of olfaction with trans-Z-hexen-l-al and related deuterated compounds.* Ph.D. Thesis. Manhattan: Kansas State University; Havens, Barry R. and Meloan, Clifton E. (1995): The Application of Deuterated Sex Pheromone Mimics of the American Cockroach (Periplneta americana, L.), to the Study of Wright's Vibrational Theory of Olfaction. In: *Food Flavors: Generation, Analysis and Process Influence*. Ed. by G. Charalambous. Elsevier Science, 497-524. For a review of the Meloan story see also: Turin (2006): *Secret of Scent*, 153-157.

[505] Hara, J. (1977): Olfactory discrimination between glycine and deuterated glycine by fish. *Experientia* (Switzerland: Birkhäuser) 33(5), 618-619.

[506] Franco, Maria Isabel; Turin, Luca; Mershin, Andreas and Skoulakis, Efthimios, M.C. (2011): Molecular vibration-sensing component in *Drosophila melanogaster* olfaction. *PNAS* 108(9), 3797-3802.

[507] Ball, Philip (2011): Flies Sniff Out Heavy Hydrogen. *Nature News* URL=< http://www.nature.com/news/2011/110214/full/news.2011.39.html>. See also a previous article by Ball, Philip (2006): A Rogue Theory Gets A Boost. *Nature News* URL=< http://www.nature.com/news/2006/061204/full/news061204-10.html>.

[508] Ball (2011): *Flies Sniff Out Heavy Hydrogen*.

[509] Keller and Vosshall (2004): *Psychophysical test*.

[510] Haffenden, L.J.; Yaylayan V.A. and Fortin, J. (2001): Investigation of vibrational theory of olfaction with variously labelled benzaldehydes. *Food Chem.* 73(1), 67-72.

cannot be given yet.[511] The incompatibility of these studies, however, points toward bigger issues underlying current olfactory research.

Even though the widely assumed subjective character of smell perception poses problems for methods of measurement, more profound difficulties for comparing experimental records reside in the lack of overall standardisation.[512] Measurements of sensory responses, like most measures of human performance, constitute a continuous variable. This is what makes them so difficult to evaluate and makes methodological reflections on forms of measurement so indispensible. The lack of 'scientific rigor' regarding experimental standardisation and explicit discussion of terminology presents a limit to the comparability of olfactory studies. Unless there is an accepted basis for the comparability of experimental results, addressing performance execution of experiments in different laboratories as well as the discussion of results across the wider research community, a general comparison of experimental results, especially of behavioural response studies, is futile.[513]

3.4 Enantiomers: Mirror Imaged Molecules

The last group of molecules integral to research on SORs are enantiomers. Enantiomers are mirror imaged molecules, which means they are identical in both their shape *and* vibration spectrum, and their only difference lies in their chirality (fig 6). (Chirality means that the mirror imaged molecules are not

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[511] Leading, in fact, to scepticism about whether experiments relying on behavioural responses should even be admitted as experimental evidence for the mechanism of primary odour recognition. Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

[512] In comparison, and although Keller and Vosshall did not discuss their methods extensively, a few suggestive methodological differences across these conflicting studies catch the eye. For instance, unlike the study by Keller and Vosshall, both studies of Haffenden et al. and Gane et al., who obtained a positive result, employed *trained* human subjects. Furthermore, the test panel size of Haffenden consisted of 30 people, whereas Vosshall and Keller here provided no information. In addition, it is also not clear whether the purification method for the test materials is sufficiently comparable in these studies, as Vosshall and Keller do not elaborate enough on this factor either. The measurement and procedure of material (im)purity, however, is one of the most crucial factors for preparing and comparing odoriferous materials, and impurities can lead to distorted experimental results.

[513] Sell, Charles (2005): Scent through the looking glass. In: *Perspectives in Flavour and Fragrance Research.* Ed. by P. Kraft and K.A.D. Swift. Wiley-VCH, 86.

superimposable.)[514] It is thus a most puzzling occurrence that some enantiomers smell different whilst others smell identical.

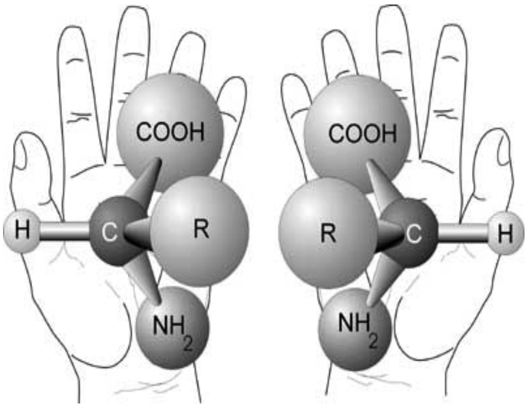

Fig. 6 Enantiomers, i.e. mirror imaged molecules, have the same stereochemistry but a different spatial orientation (similar to hands or feet). Wikipedia (2013e): *Chirality*.

The fact that two molecules have identical vibrations but different smells has long been the most convincing objection against the vibration theory. A well-known example of enantiomers with distinctively different odours are carvones: whilst (S) carvone smells dominantly minty, (R) carvone has the smell of caraway. Only after Turin developed a model of the olfactory mechanism acting on electron spectroscopy was an explanation for this perplexing phenomenon devisable. Enantiomers exhibit identical vibrations when measured under *unpolarised light* (within a customary infra-red spectroscope).[515] However, when the probes are treated with polarised light, the spectrum “depends on the relative orientation of the molecular dipoles [in the probe] to the plane of light polarization”.[516] Turin assumed that a biological spectroscope, detecting molecular vibrations by inelastic electron tunnelling spectroscopy (IETS), works in the same manner.[517] Here the chirality, i.e. the orientation of the odorant, is argued to result in a *polarisation effect* of the tunnelling electrons. This means that, as an effect of the odorant’s orientation within the receptor binding-site, electrons are deflected in specific directions and particular vibrations are ‘hidden’ and, thus, remain undetected.[518]

To test this auxiliary assumption, Turin proposed another model of an experiment. Considering a polarisation effect, it is assumed that the vibrations

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[514] Oxford English Dictionary (3rd Ed.) (2005): *Chirality.* Oxford: Oxford University Press.
[515] Turin (2006): *Secret of Scent*, 142.
[516] Turin and Yoshii (2003): *Structure-Odor Relations*, 18.
[517] Turin (2002): *Method for the calculation of odor character*, 367-385.
[518] Turin (2006): *Secret of Scent*, 173.

of those electron bonds causing the minty smell of (S) carvones are not detected by the deflection of electrons. If one were to constantly add a solution consisting almost entirely of the supposedly undetected C=O bonds to a solution of (R) carvones, the odour of the mixture must shift from caraway to minty at some specific concentration.[519] A test conducted and recorded for the BBC Horizon documentary *A Code in the Nose* (1995),[520] involving three professional perfumers, led to the following positive outcome: when (R) carvone is mixed 3:2 with acetone ($(CH_3)_2CO$), its caraway smell is replaced by a minty quality. A similar experiment, using the similar but less rapidly evaporating butanone ($CH_3C(O)CH_2CH_3$) instead of acetone, reveals a similar change in odour quality.[521] As fascinating as this results is, in order to assume a regularity of smell differences caused by deflected electrons, additional tests with other strong dipoled enantiomers (i.e. those enantiomers assumed to differ in smell) are required.

Nonetheless, Turin's explanation of odour differences between enantiomers results in an interesting epistemic turn of events. After accommodating cases of differently smelling enantiomers within the vibration theory, the opposite question arises as to how those enantiomers that smell similar are dealt in the rival theory of shape. Since they are assumed to bind to different receptors, odour differences between enantiomers here are explained through their chirality. But what about enantiomers that have the same smell? Two explanations are offered.

One option suggests that enantiomers might bind *equally well* to chiral receptor sites. This seems implausible though: if the perception mechanism acts in a similar fashion to a stereochemical complementary receptor model, a mirror-imaged key hardly fits equally well into its counterpart's lock (fig. 7 and 8). (Similarly, your left foot will not be comfortable in your right shoe.) Why and under what conditions should this general principle then be different for some

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[519] The reason for this is that, rather than smelling the components of odoriferous mixtures separately, we perceive the smell of an entire composition. Consider perfumes, taken separately, the materials involved smell nothing like the overall composition. See: Ellena, Jean-Claude (2012): *The Diary of a Nose. A Year in the Life of a Perfumer.* London: Particular Books (Penguin Group), Appendix. This is due to the combinatorial nature of smell perception, meaning that each odorant relates to a specific perception pattern of responding receptors in the nose. These patterns are further combined and processed in the brain. See: Malnic, Bettina; Hirono, Junzo; Sato, Takaaki and Buck, Linda B. (1999): Combinatorial Receptor Codes for Odors. *Cell* 96, 713-723.

[520] BBC (1995): *Code In The Nose.*

[521] Turin and Yoshii (2003): *Structure-Odor Relations*, 18; Turin (2002): *Method for the calculation of odor character*, 174.

enantiomers? Another option suggests that different receptor sites interacting with those enantiomers are joined in such a way that they activate the very "same pattern of nerve excitation". This too has been considered as unlikely.[522] Hence, current theoretical issues surrounding the problematic nature of enantiomers remain unresolved. Nonetheless, enantiomers present a good example for the significance of theoretical models for the assessment of data and, moreover, its transformation into facts supporting or conflicting with a particular theory.

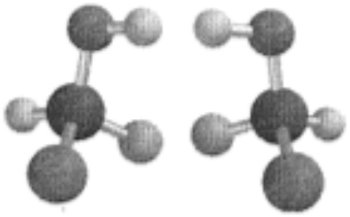

Fig. 7 Chiral molecules
Turin (2006): *Secret of Scent*, 102.

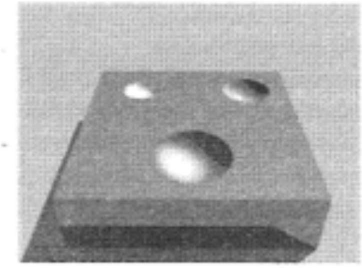

Fig. 8 Receptor fitting one of the chiral molecules.
Turin (2006): *Secret of Scent*, 103.

4 Conceptual Manipulations: Observation and Evidence

In discussing the different modelling strategies within the rival theoretical frameworks of shape and vibration, I was deliberately vague about how these models might be said to represent but, rather, concentrated on how they are used to accommodate data and test hypotheses. I have avoided this issue thus far because I wanted to focus first on the ways in which these models acted as tools of scientific knowledge production and to highlight the ambiguity in the interpretation of molecular data within each account. It is precisely because of this ambiguity that I will now emphasise the need to view models in context and in relation to each other, before attempting to address them in terms of their capacity to represent.

In presenting the efforts to accommodate the vast range of diverse molecules, the models employed were shown to have a number of functions. Data models such as olfactophores are used to manage the sheer quantity of odoriferous materials and embody assumptions about what constitutes relevant structural relations between odorants. In the comparison of data models and the

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[522] Turin and Yoshii (2003): *Structure-Odor Relations*, 18-19.

competing hypotheses of shape and vibration, a number of anomalies emerged. In light of these, theoretical models – the two rival mechanisms – provided the source from which auxiliary assumptions about the causal interaction between receptors and odorants were derived. In return, these assumptions led to a modification of the theoretical descriptions made by the model. In addition to their explanatory function, theoretical models aided in the design of models of experiments, for instance testing the accessibility of sterically hindered odorants. The interaction between data models, theoretical models and models of experiments thereby resulted in enhanced knowledge about apparent anomalies, explanations for these anomalies as involving additional aspects of the recognition mechanism and tests regarding the regularity of presumed SORs correspondences.

Promoting further theory development, these different types of models interact by suggesting strategies under which certain observations can be turned into evidence for (and against) a specific theory. Models can play different roles in the process of evidence construction. In the case study chosen, they inform the selection of features and aid in the accumulation of data, identifying SORs regularities as well as irregularities. They are also involved in the transformation of these features into parameters used to explain specific observations that seem to form exceptions or that require further tests of what is assumed to be at work on the molecular level. This reinterpretation of molecular parameters often reflects back on data accumulation and selection. Different models thereby have different functions, depending on the specific aims for which they are built. Facilitating and integrating these different modelling practices, the olfactory theories adopted a coordinating function. By channelling between the underlying research commitments and required model modifications, the theories themselves become subject to changes, feeding back into the models.

One insight gained through the detailed reconstruction of SORs explanations through model-based reasoning therefore concerned the theoretical commitments that are tied to the application and interaction of the different models. Providing different tools to explain SORs and facilitate epistemic access to the unknown process of primary odour olfactory recognition, modelling decisions were determined both by the observed features of odorants and by the theoretical commitments entrenched in the model construction. Reconsidering the ambiguity of molecular data for explaining olfactory responses, the application of models involved continuous mediation between observed regularities, theoretical commitments, apparent anomalies and possible additional factors for the latter's accommodation. This mediation also points to a distinction between what are taken as observations and what is considered to be evidence, leading to the following kind of circularity:

> "[a] piece of evidence for (and against) a theory is a construction in the context of that theory from (raw) data. In this construction, a set of auxiliary assumptions is employed. The auxiliaries may be themselves theoretical in character. From the same (raw) data it is possible to construct different evidence for (or against) different theories since the auxiliaries employed in connection with different theories can be different."[523]

A striking feature of such a process of theory-infused evidence construction for SORs in fragrance chemistry is the flexibility of epistemic relations that hold between observations, models and theory. Consider the case of enantiomers again. These presented the most profound objection to vibration theory for a long time. Yet, in light of the revived vibration-sensitive mechanism, acting on inelastic electron tunnelling instead of mechanical spectroscopy, an explanation for the puzzling case of differently smelling enantiomers appeared, which it was also possible to test experimentally. The significance of this epistemic shift, turning an initially conflicting into a supporting datum, is that this observation was further used to form an objection against the competing theory. As a result, the evidential relation between observations about enantiomers and the competing theories changed.

How observations are turned into evidence, therefore, is a matter of how the models are applied to serve the theoretical framework in which they are embedded. "Observation, in order to be (evidentially) relevant for a theory", meaning "transformed into evidence for a hypothesis, phenomena, or a theory", is theory-informed.[524] The validity of these transformations is dependent on the specific stage of theoretical development. Distinguishing among different types of models enables this theoretical development to be traced. It first helps in pinpointing the underlying research commitments tied to the application of models. Second, it allows the analysis of the modifications and (dis)continuities associated with the interaction of different models. Not only are there many

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[523] Basu, Prajit K. (2003): Theory-ladenness of evidence: a case study from history of chemistry. Stud. *Hist. Phil. Sci.* 34, 357.
[524] Ibid., 356.

strategies for processing data and accommodating observations but also, in the course of being modelled, the interpretation and significance of these observations changes. Thus, there is no ahistorical criterion of evidence construction and theory evaluation that reflects research practice. Evidence, unlike the observations from which it is constructed, appears to be a historical category.

Models and model-based inferences, as the previous sections have shown, play a central and active role in turning observations into evidence for (or against) a theory. Within the process of evidence construction they are modified, leading to a re-evaluation of observations as evidence. Justifications of why certain observations are taken to be evidential for (or against) a theory in general or a theoretical model in particular must therefore be judged against the contextual background in which they are introduced. This implicit iterativity and circularity of evidence construction forms an epistemic system of "self-vindication" as analysed by Ian Hacking (1992). Within laboratory sciences, i.e. those sciences whose study of phenomena require techniques to isolate and interfere with materials that rarely appear observable in a "pure state", any theoretical explanation is judged against an organised system of types of analysis, techniques, instruments and specifically chosen research materials. This contextual environment, what Hacking calls "apparatus" and Rheinberger refers to as an "experimental system", constitutes a relatively stable yet dynamic background against which theoretical explanations are judged. Since this apparatus has its own historicity, evolving in conjunction with a theoretical framework, any test of a theory embedded within it remains irrefutable as long as it fits the data to a sufficient degree.[525]

For these reasons, scepticism toward the alternative vibration theory and the predominance of the shape theory is less surprising, but resonates with the disciplinary history of fragrance chemistry, which has largely been built on assumptions underlying a shape based approach to SORs. Although each theoretical framework manages to make sense of problematic molecular data, the hegemony of the shape-sensitive model is not established through a comparative evaluation of how well the rival mechanisms fit the data. How well the models are seen to fit the data was demonstrated to be ambiguous and subject to continuous negotiations between model-based inferences and data

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[525] Hacking (1992): *Self-Vindication of Laboratory Sciences*, 30.

management. Given the ambiguity of data, the strength of the shape theory lies in its well-adjusted model system, which has shaped researchers' understanding of the character of olfactory perception over the last century (as chapters 4 and 5 have stressed). A careful reconstruction of how models are aimed at a specific target system such as the molecular basis of smells, therefore, cannot be reduced to a dyadic comparison between the features of the phenomenon and the setting of the model, but must also include the justification strategies associated with the model's wider role within a theoretical framework and experimental system.

5 Representing as Epistemic Relation and Historical Activity

Independently of the unresolved question of which olfactory theory is true, I now want to approach the question of how these different models, especially the rival and hypothetical mechanism models, are said to represent. In arguing for analysing models through their epistemic relations, that is as aiding in knowledge production through their cooperative and competitive character towards each other, I am manifestly engaging in a pluralist approach to representation. Yet, given the emphasis on a model's interaction with other models rather than its relation to the target system, what is it that is being represented and in what sense do we have a representation?

What my analysis of the olfactory debate surrounding SORs showed so far is that for modelling strategies of data accommodation and subsequent evidence construction in fragrance chemistry, each theoretical model of the suggested olfactory mechanism requires for its empirical application a network of auxiliary assumptions, conceptual modifications and instruments together with additional models of experiments and data models. The theoretical models are thus not "directly compared" to the phenomenon they are supposed to explain but, rather, are linked to observations of this phenomenon by means of different techniques that mediate between the theoretical assumptions made in the model and the features of the phenomenon. In light of the current possibility of organising the same domain of data and providing meaningful causal explanations about the underlying mechanism within two rival accounts, the question remains how to conceptualise the way in which the two theoretical mechanisms may be said to represent the olfactory perception mechanism. How are the claims of the rival models assessed as “matching the phenomenon”?

Coming back to the beginning of my chapter, Cartwright’s suggested distinction between providing an explanation for a phenomenon and being a factual representation of it appears difficult to apply to the present case of the theoretical models of the olfactory mechanism. Surely, one of the two rivals might turn out to be wrong and, although providing reasonable explanations, nevertheless fail to be a factual representation at some point in the future. But what use does this distinction have for describing the *current* application of both models to represent – as in to explore – the nature of their target system? The notion of facticity when applied to an active debate such as olfaction theory is in fact linked to the justification of theoretical models, and the justification of theory is not ahistorical. Whatever counts as evidence for (or against) a theory or model is, as I demonstrated in the previous section, a result of a contingent historical process of evidence construction. Evidence, thus, is a historical category and so is factuality. It appears that being a “factual representation” in contrast to merely “providing an explanation” does not contribute much to the understanding of how models are used to represent reality. Instead of introducing some retrospectively defined notion of “factuality” to judge their degree of realism, the capacity of models to “represent”, i.e. match the structure of their target system, is better defined by their *contemporary use.*

Considering thus what the two theoretical mechanisms are employed *to do*, they act as the basis for *conceptual manipulations* that allow *convergence between* theoretical assumptions and the data “to the point where the resemblance between what can be observed and what is sought is […] ‘very satisfactory’.”[526] Therefore, the activity of models is determined by their role in contextualising and thereby transforming observations into relevant evidence for (or against) a theory. Theoretical models such as the rival olfactory mechanisms, I suggest, represent by their capacity to form and allow for specific enquiries about their supposed target system that can further be explored through other models, instruments and techniques.

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[526] Gooding, David (1992): Putting Agency back into Experiment. In: *Science as Practice and Culture.* Ed. by A. Pickering. Chicago: University of Chicago Press, 65-112. Quoted after Hacking (1992): *Self-Vindication of Laboratory Sciences*, 32.

Instead of defining "representing" as a dyadic relation of some form of correspondence between a representation and a physical target system, the notion of representation that I here proposed emphasises the different functions of, and interactions between, models. Depending on the purpose of the model, its capacity to represent may take different forms. In arguing for the epistemic function of models, I am however not claiming that there might be no correspondence relations between models and target systems at all. Data models such as olfactophores, for instance, can be said to relate more directly to a target system as a statistical arrangement of molecular parameters. But I do argue that this is not the only way to understand representation, as it does not reflect the full range of modelling. It also does not account for the importance of theoretical assumptions entrenched in the model to make it work within a wider context of other models addressing the same target system. Olfactophore models were shown to be theory-informed in their selection of atom groups responsible for odour detection. In comparison, models such as the rival mechanisms were shown to work effectively as a heuristic to inform the selection of parameters in data models; to derive explanations for irregular SORs data, thereby aiding in further theory development; and to aid in the design of models experiments, testing model-based inferences. On this account, some models may rather be said to represent by providing a theoretical platform for further inquiry into the nature of the target system.[527]

For that reason, the theoretical mechanisms represent the process of primary odour perception not as something being "beyond" the experimental system but as something that is embedded in it. As Rheinberger stated, "nature as such is not a referent for the experiment"[528] or, in this case, model. Models have been shown to mediate between features of the phenomenon and theoretical commitments. Therefore, there is no isolated model procedure reaching out to isolated target systems in the world, but a productive interaction between different modelling techniques and features of the materials being modelled under these. Representing, therefore, is a process that is defined as a productive interaction between research commitments and materials. For this

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[527] Related criticism addressing a dyadic understanding of representing is found in: Knuuttila, Tarja and Voutilainen, Atro (2003): A parser as an epistemic artifact: A material view on models. *Philosophy of Science* 70(5), 1484-1495; Knuuttila, Tarja (2010): Some Consequences of the Pragmatist Approach to Representation. In: *Epsa Epistemology and Methodology of Science*. Ed. by M. Suárez, M. Dorato and M. Rédei. Dordrecht, Heidelberg, London, New York: Springer, 139-148.

[528] Rheinberger (1997): *Epistemic Things*, 109.

reason, even models with different theoretical assumptions such as the rival olfactory mechanisms can be said to represent the same target system, if they possess a heuristic power to productively interact with other models addressing the same materials. The sense in which I use the notion of representation here is thus as a partial reflection of the target system, transforming some of its features into parameters used to further explore and explain its nature. It is not a strict representation of the target system, but a representation of the target system within a particular theoretical framework. The interactivity between the different model strategies, leading to implementations of new or conflicting data and modifications of the theoretical framework, further ensures that the modelling process exceeds its initial theoretical commitments. The nature of the target system not only allows, but, as my analysis of SORs explanations has shown, in fact requires a constant development of models in order to continue to represent its target.

To find out whether the assumptions on which an inquiry is based are adequate with respect to the available observations, it thus needs to be seen to what extent these claims conflict, contradict or converge with the claims of other – either complementary or rival – representations. It is their relative epistemic function of turning observations into evidence and further fitting together a variety of models, experiments, forms of data analysis, etc. into a more or less coherent experimental system that defines the application of theoretical models. Any notion of “matching the phenomenon” relevant here is thus not determined by a single model’s resemblance to its target system but as an organisational and modifiable aspect for integrating results from the various elements within the experimental system it acts in.

A consequence of this practice-oriented conception of “representing”, defined as an activity of forming epistemic relations across various modelling practices, is that “representing” is inevitably historical and contingent. As soon as a model is no longer used to direct inquiry about its supposed target system, its function to represent expires. That does not mean that an outdated model might not be used and revived to represent again in a later scientific context. It only means that its function to represent depends on its application within an active research context. A model thus represents if it is used to represent, and this use requires its integration into an active and dynamic research context such as an “experimental system”.

Chapter 8

Chasing Fiction? Exploring the Reality of “Hidden Mechanisms” and The Issue of Olfactory Receptor Modelling

1 Model-based Inference and the Question of Scientific Realism

Discussions of scientific realism comprise a variety of positions that concern the existence of entities and processes described by scientific theories or models. While the reality of desks and cats seems to be a minor issue, the reality of electrons and genes appears less easy to determine. The primary function of theories about what electrons are and what genes can and can’t do is to interpret the phenomenon they are supposed to explain such as electricity and inheritance.[529] Contemporary scientific theories often assume the existence of entities that are not directly observable but are only traced indirectly by the effects produced under specific experimental conditions. These effects are used to support claims about the nature and existence of such theoretical entities. The resulting hypothetical character of some scientific explanations directed philosophical attention towards the strong reliance of research practices on mediated forms of observation and model-based inference.[530] The mediated relation between scientific models and their physical target system divides philosophical opinion about how to decide *whether* or *when* a realist case can be made for hypothetical claims about the existence of a phenomenon. Philosophical debate surrounding theoretical entities occupies two positions. Realists argue for either the truth of the descriptions provided by scientific theories or the existence of the entities described by scientific theories (or both). Anti-realists consider scientific theories as useful tools for constructing explanations. Rather than making strong ontological claims such as for the truth

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[529] Moss, Lenny (2004): *What genes can't do*. Cambridge M.A.: MIT Press; Arabatzis, Theodore (2005): *Representing Electrons: A Biographical Approach to Theoretical Entities.* Chicago: University of Chicago Press; Barnes, Barry and Dupré, John (2008): *Genomes and what to make of them*. Chicago: University of Chicago Press.

[530] Hacking, Ian (1983): *Representing and intervening: introductory topics in the philosophy of natural science.* Cambridge: Cambridge University Press; Rheinberger, Hans-Jörg (1997): *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube.* Stanford: Stanford University Press; Morgan, Mary and Morrison, Margaret (Eds.) (1999): *Models As mediators: perspectives on natural and social science.* Cambridge: Cambridge University Press.

of scientific theories or the existence of theoretical entities, they judge a theory by its empirical adequacy.[531]

A growing trend in the philosophy of science engages in this debate by employing the concept of fiction. Positions vary, however, about the role of fiction in science, as I have already addressed in chapter 6. Philosophers such as Cartwright, Suárez and Fine use the concept of fiction to describe both a variety of non-denoting elements in science, and a range of strategies, especially idealisation and abstraction, that introduce such elements into models. In contrast to advocates of this position, referred to as *wide fictionalism*, other philosophers such as Morrison, Giere, Teller and Winsberg subscribe to a position of *narrow fictionalism*. Here the concept of fiction is restricted to non-existent entities only.[532] What all positions have in common, though, is that the concept of fiction is used to understand the application of scientific models that facilitate conceptual reasoning about phenomena that does not depend on reference to the world and may even employ concepts of entities that may not exist.

In this chapter, I want to employ the concept of fiction in science to address current limits of receptor modelling in olfaction theory. My focus here is only on narrow fictionalism and the question of how to evaluate the hypothetical character of many scientific entities and their descriptions. I will not, for instance like Winsberg, be concerned with entities such as ‘silogens’ which are known to be constructions and which do not purport to provide a genuine referent.[533] Rather, I will address arguments about scientific entities whose reality is not certain and which, therefore, are discussed as theoretical entities. Problems surrounding theoretical entities comprise the extent to which model-based inferences about such entities are warranted or merely reflect assumptions that feed into the model construction. Contemporary problems in olfaction theory depend on issues of this kind.

Aspects of theoretical entities are widely seen as constructed and thus, as some philosophers argue, closely resemble fiction.[534] Unlike fiction, however, theoretical entities are assumed to be candidates for truth. Fictional entities

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[531] Hacking (1983): *Representing and Intervening*, 21.

[532] Suárez, Mauricio (Ed.) (2009): *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* London: Routledge.

[533] Winsberg, Eric (2009): A Function for Fictions. Expanding the Scope of Science. In: *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* Ed. by Mauricio Suárez. London: Routledge, 179-190.

[534] Suárez (2009: *Fiction in Science.*

such as Captain Jean-Luc Picard, Hercule Poirot or Madame Bovary all have one thing in common. They do not exist.[535] They are furthermore not thought to do so. Although such fictional characters may occasionally resemble people known to us, they have no proper instantiations in the world and, therefore, their names lack reference.[536] Nonetheless, we sometimes like to be inspired by fiction as if it was real, for instance when we are trying to learn how to make brilliant deductions in a similar fashion to a famous ~~French~~ Belgian detective and his little grey cells.[537] Is this why fiction and some postulated scientific entities could be argued to resemble each other? Even though scientific entities such as phlogiston, pneuma or the ether were once intended to refer to something real, these entities turned out to not exist and their names consequently lack reference.[538] Nevertheless, these entities had previously been an integral part of an experimental culture that aimed to provide explanations about the world. For this reason, it is hard to tell the difference between these failed concepts of entities and theoretical entities currently employed in science. How can we be certain that our presently favoured entities are better candidates for truth than their historical predecessors? Should not some of these entities be handled as fiction because of their highly hypothetical and constructed character? It appears to me that one of the reasons that compel some philosophers to compare theoretical scientific entities with fiction is an implicitly normative one: it is a recommendation of caution about taking contemporary concepts of entities as more truthful than their historical siblings. Carefulness about the grounds on which contemporary claims are based seems good advice. Nonetheless, I remain sceptical whether a comparison with the concept of fiction is always appropriate.

I have argued for the limited grounds for a comparison of the concept of fiction with model elements in science in a previous chapter, and instead suggested that representations should be interpreted either as fictional or as non-fictional. I

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[535] Whether these entities might be argued to metaphysically “exist” in some philosophical obscure realm is of no matter for the present argument.

[536] Eco, Umberto (1994a): *The Limits of Interpretation.* Bloomington: Indiana University Press, 125.

[537] Books written to teach readers about the art of deduction of fictional characters such as Hercule Poirot or Sherlock Holmes are, for instance: Bullimore, Tom (2000): *Sherlock Holmes' Puzzles of Deduction.* New York: Sterling Juvenile; Konnikova, Maris (2013): *Mastermind: How to think like Sherlock Holmes.* Viking Adult; O’Brien, James (2013): *The Scientific Sherlock Holmes: Cracking the Case with Science and Forensics.* Oxford: Oxford University Press.

[538] Johansson, Ingvar and Lynøe, Niels (2008): *Medicine & philosophy: a twenty-first century introduction.* Heusenstamm: Ontos Verlag, 82.

would now like to extend this argument by focussing on the distinction between our understanding of real and fictional entities that is reflected in a different relation between these entities and their representations. Fiction and most scientific entities, even if highly hypothetical, differ in one fundamental respect: the latter are handled at the very least as potential candidates for truth.[539] This difference, I claim, is important when it comes to inferences about properties not explicitly given in the descriptions of a representation, but the interpretation of which rests on knowledge external to the representation.

Drawing on the concept of fiction and exploring its use for debate in the philosophy of science, the argument of this chapter is twofold. In the first part I will develop an argument about the evaluation of model-based inferences to theoretical entities based on the concept of fiction; in the second part I will exemplify my conclusions with reference to receptor modelling practices in the olfactory debate.

In the fiction part of this chapter, I will begin by exploring the conceptual difference between fictitious and real entities by analysing their different relations toward their representational sources. A representational source, for the purpose of my argument, is rather loosely defined. It can be any device of public description in which knowledge is embodied, including images, documents, novels, material or mathematical models, instruments, and so on. The conceptual difference between fictional and real entities will lead me to a significant distinction regarding model-based inferences to unknown properties of a represented entity. This distinction concerns legitimate and illegitimate inferences to properties of an entity and implies a difference in the interpretation of real and fictional entities. In order to demonstrate how this distinction has implications for the evaluation of theoretical entities in science, it will then be applied to the example of phlogiston. The general philosophical focus of this section is the question of how to make successful model-based inferences about the existence and properties of (experimentally) hardly or only indirectly accessible entities.

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[539] For that reason, it has been suggested to speak of “hidden” rather than “theoretical entities” as the latter “conveys the misleading impression that hidden entities do not transcend the theoretical framework in which they are embedded. Arabatzis, Theodore (2007): “Hidden Entities and Experimental practice: Towards a Two-way Traffic between History and Philosophy of Science.” In *HPS1: Integrated History and Philosophy of Science,* vol. 1. http://philsci-archive.pitt.edu/id/eprint/3639, 3.

As regards to subject matter, the thematic focus of the second part of this chapter is to explore issues of inference to the nature of hidden entities using the example of contemporary research culture and model thinking in olfaction theory. Although the class to which the olfactory receptors (ORs) belong was determined in 1991, identifying ORs as 7-transmembrane G-coupled proteins,[540] no insight into the structure of the receptor binding site has yet been obtained. Standard experimental methods such as X-ray crystallography have failed due to the highly unstable nature of these transmembrane proteins. As a result, any hypothesis about the recognition mechanism by which the ORs interact with their ligands, i.e. odoriferous molecules, resides in theoretical reasoning and remains to a degree speculative. The predominant shape-sensitive model of primary odour recognition, which is not without recognisable problems, has recently been challenged by the proposal of an alternative mechanism. This has led to a contemporary controversy surrounding two rival theories, for either of which, it seems, a realist case can be made. The presence of these two rival mechanisms, in addition to the lack of empirical knowledge, presents an even greater challenge to the assessment of model-based inferences and the truth of theoretical claims. By addressing the experimental gap between the theoretical mechanisms and the available observations, I would like to explore the ways in which alternative models are designed to facilitate access to the unknown molecular dimension of the receptor proteins and, as a result, how they spur further inquiry into the nature of the perception mechanism. An analysis of these model strategies, and exploring their potential, conditions and limits, will provide a good basis to assess the grounds on which scientists make model-based inferences to unknown features of a phenomenon. It will also show the extent to which definitions of structure are deeply entrenched in the model building process and, therefore, are ill-equipped for the substantiation of a particular theoretical framework from which these definitions are derived.

This chapter therefore proceeds in two steps. I will begin by exploring the conceptual difference between fiction and theoretical entities in science, leading me to a significant distinction for model-based inferences to unknown properties of a represented entity. This distinction will then be applied to the limits of

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[540] Buck, Linda B. and Axel, Richard (1991): A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. *Cell* 65(1), 175-187.

olfactory receptor modelling and the contemporary controversy surrounding two models of the unknown and "hidden" mechanism of primary odour recognition. The overall aim of this chapter is to demonstrate the extent to which the presumed success of model-based inferences, rather than having a purely empirical basis, is often in part theoretically and historically justified.

2 Fiction in Science and the Limits of Interpretation

2.1 Fictional and Non-Fictional Entities

Considering the fact that fictional entities have no instantiations in the external world, fictional entities and their representations form, I argue, a relation of *strict identity*.[541] Captain Jean-Luc Picard, for instance, only corresponds to the descriptions of a character in a series of stories about the adventures of the spaceship USS Enterprise (NCC-1701-D). Likewise, other characters such as Hercule Poirot or Hamlet only correspond to entities embedded in a very specific and limited representational context. As a result, fiction presents a case of strict co-extension and synonymy between the fictional character and its representational source. The representation, acting as the existential grounds for a fictional entity, is the only basis for inferences about that entity. Therefore, the representation provides an exhaustive description of its fictional entity and, conversely, any fictional entity is fully determined by its representational source.

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[541] Identity here is defined according to Leibniz' Law. This law states that two things are strictly identical if they are identical in *all* their properties, so that: everything that can be said to be true of x also must be true of y, and vice versa. For a discussion of Leibniz' Law see: Ishiguro, Hidé (1990[1972]): *Leibniz's Philosophy of Logic and Language.* Cambridge: Cambridge University Press, 17; Mates, Benson (1986): *The Philosophy of Leibniz. Metaphysics & Language.* Oxford: Oxford University Press, 123. There is disagreement, however, whether the law of identity commonly known as Leibniz' Law is actually the same as Leibniz' Principle of Indiscernibles. See Mates (1986): *Philosophy of Leibniz*, 123. Mates distinguishes between both laws, however, he does not provide criteria but identifies Leibniz' Law with the truth principle of substitution, i.e. *salva veritate.* Ibid., 97. Ishiguro remains sceptical about this distinction. Ishiguro (1990[19972]): *Leibniz's Philosophy*, 17. Concerning the identity of a fictional entity with its representation I am using the interpretation of Leibniz' Law as the Principle of Indiscernibles. Although attributed to Leibniz, who explicitly stated this as a principle of identity, it was in fact Aristotle who first mentioned the idea of identity as mutual likeness. Aristotle stated that likeness means that if we have two things alike then what can be said about and attributed to one thing has to be equally said of and attributed to the other, and vice versa. See: Aristotle: *Topics Books I and VIII, With excerpts from related texts. Translated with a commentary.* Ed. and trans. by R. Smith (1997). Oxford: Clarendon Press, Topic I 17[5]. The first symbolic formulation of this Law of Identity, however, was done by Charles S. Peirce. See: Wessel, Horst (1998): *Logik.* Berlin: Logos Verlag, 221.

Every description of Hamlet in Shakespeare's play is a property of Hamlet and, vice versa, all there is to be known about the character of Hamlet is given in the descriptions in this play.[542]

By contrast, real entities exist independently and "outside" a particular representational source that portrays them. The actual entity is not part of the representation, only its image is. This is likewise expressed by Alfred Korzybski's slogan "the map is not the territory."[543] Although this point appears trivial at first, its importance becomes clear in light of the distinction between the *representation of an entity* (i.e. the image of an entity) and the *entity represented* (i.e. the referent of a representation). For many entities this distinction is intuitively applied. Of course, there were fiery objects in the heavens before the natural philosophers developed the first models of celestial movements. Likewise, there must have been something different in the nature of trees when taxonomists divided them into classes such as oak and elm. For other entities the case appears less intuitive. It is not easy to see how to describe, for instance, the reality of quantum phenomena without any notion of an observer and previous to any intervention with instruments acting as (what Latour and Rheinberger call) "inscription devices",[544] i.e. instruments producing material traces of otherwise unobservable phenomena. Yet, if the phenomena underlying representations of such theoretical or "hidden" entities are real, I claim, they must not be exhaustible and, in further consequence, not fully reducible to their representational sources. But what constitutes a sufficient degree of ontological independence for a hypothetical entity from its representational source, especially if its investigation is to some extent dependent on the surrounding theoretical apparatus?

My answer to this question is the claim that, unlike fiction, there is no privileged representational origin or access to real entities. Whereas our knowledge of Sherlock Holmes is restricted to the stories of Sir Arthur Conan Doyle, our knowledge about London is grounded in various sources such as tube maps,

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[542] Danneberg, Lutz (2006): Weder Tränen noch Logik. Über die Zugänglichkeit fiktionaler Welten. In: *Heuristiken der Literaturwissenschaft. Einladung zu disziplinexternen Perspektiven auf Literatur.* Ed. by U. Klein, K. Mellmann and S. Metzger. Paderborn: Mentis Verlag, 35-83. Cited is the extended online version: URL=<http://fheh.org/images/fheh/material/danneberg-fiktion.pdf>

[543] Korzybski, Alfred (1994[1933]): *Science and sanity: an introduction to non-Aristotelian systems and general semantics.* 4th Edition. Reprint. Institute of General Semantics, xvii.

[544] Latour, Bruno and Woolgar, Steve (1979): *Laboratory Life: The Social Construction of Scientific Facts.* Princeton, New Jersey: Princeton University Press, 51. See also Rheinberger (1997): *Epistemic Things*, 109f.

historical documents, holiday travels, etc. Thus, access to hypothetical entities, if they are assumed to be candidates for truth, must in principle be facilitated by multiple representational means. The issue is how to determine the extent to which our knowledge about the nature of an entity is grounded in one or in many representational sources. For this reason, I suggest drawing attention to the interpretation of representations, and taking a look at the inference to properties not explicitly given in a representation.

2.2 Legitimate and Illegitimate Inferences

Imagine two people in a restaurant; you might read about this scenario in a novel or hear it in a conversation. Perhaps, you are told whether these people sit in a TexMex or a Sushi bar, whether they meet for private or business purposes, and so on. What is not mentioned is whether they have a heart (in a non-metaphorical and strictly anatomical sense that is). Despite the missing information about this biologically crucial feature, no one would assume that these people lack a heart if it is not explicitly stated otherwise, simply for the reason that people usually do have a heart.[545] Descriptive gaps like these usually do not pose difficulties when we interpret a representation as long as they concern implicit properties of entities that can be complemented and affirmed through common knowledge and convention.[546] Successful inferences to implicit features rest on other, explicit properties of the entity portrayed in the representation. Consider King Lear, "although no production ever portrays Lear's consort, he must have had one – Cordelia, his daughter, provides the evidence."[547]

Nonetheless, there are also limits of interpretation concerning the inference to features for which no explicit descriptions are provided in the representation. Ask yourself, for instance, as L.C. Knight famously did, *How many Children has Lady Macbeth?*[548] Looking at Shakespeare's play, it turns out there is no definite answer. Despite the impression that Lady Macbeth's character is not

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[545] Danneberg (2006): *Weder Tränen noch Logik,* 23.

[546] See Chapter 5 on the "parasitic" character of fiction. Searle, John R. (1975): The Logical Status of Fictional Discourse. *New Literary History 6(2): On Narrative and Narratives,* 326; Eco, Umberto (1976): *A Theory of Semiotics.* Bloomington: Indiana University Press, 95.

[547] Heintz, John (1979): Reference and Inference in Fiction. *Poetics* 8, 86.

[548] Knight, L.C. (1973[1933]): *How many children had Lady Macbeth? An essay in the theory and practice of Shakespeare criticism.* New York: Haskell House.

exactly of the maternal type, she nevertheless might have had one, or many or no children at all. Not only is there no information to answer this question, it also does not concern or affect the story of the play. To engage in speculation about unknown properties of entities – those that are not accessible through the representation, for instance, by reference to explicit properties – is to construct "a world outside the given material of the play."[549] Any attempt at such a construction implies some obscure realm 'beyond' the world described in the play that is neither part of the representation nor the external world. Thus, "[w]hat they [the representations] fail to tell us, either explicitly or by implication, simply does not exist."[550]

These limits of interpretation do not apply exclusively to fiction. All representations, whether fictional or not, share one crucial feature: the selected descriptions of their embedded entities are limited in comparison to the external world and, as a result, there are various possible features that are not mentioned. Consider, for instance, the early atomic models by Dalton and Berzelius in 19th century chemistry. Berzelian formulas were based on his "theory of chemical proportions", which was similar – yet not identical – to Dalton's conception of atoms. The two accounts supported the hypothesis of "discontinuous bits or proportions of chemical elements and compounds, defined by their invariable and characteristic combining weight."[551] Unlike Dalton, Berzelius remained agnostic about mechanical properties of atoms. This divergence in the conceptualisation of atoms is reflected in the representational methods chosen. Dalton's pictorial account (fig. 1) implies classical mechanical properties such as an element's size, shape and its place in space, whilst Berzelius' formal account (fig. 2) neglects these properties. Other properties such as proportional composition, however, are expressed in both approaches.[552]

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[549] Original in: Pettet, E.C. (1949): *Shakespeare and the Romance Tradition.* London: Staples Press, 192. Quoted after: Britton, John (1961): A.C. Bradley and those Children of Lady Macbeth. *Shakespeare Quarterly* 12(3), 349.

[550] Heintz (1979): *Reference and Inference in Fiction*, 92.

[551] Klein, Ursula (2001b): Paper Tools in Experimental Cultures. *Studies in History and Philosophy of Science Part A* 32(2), 276 footnote 11.

[552] Klein (2001b): *Paper Tools*, 276.

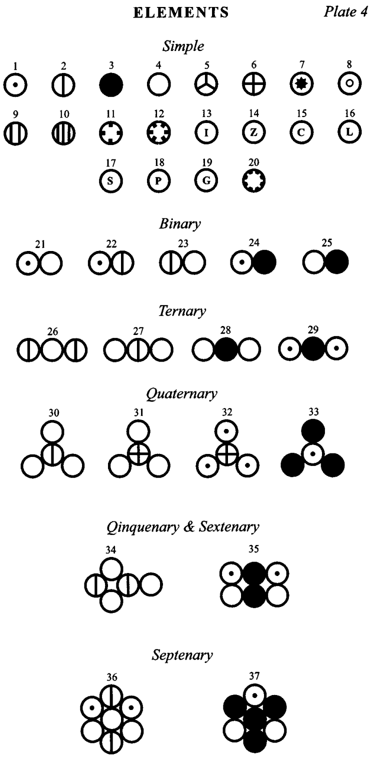
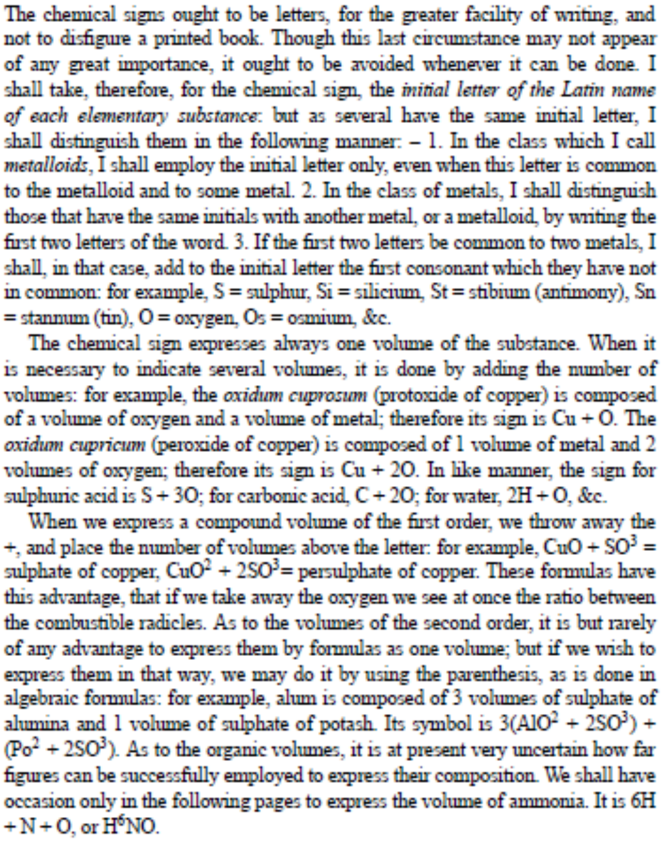


Fig. 1 Dalton's atomism.
Atoms are presented as spherical bodies, implying features such as shape/size.
Klein 2001a, 8.



The chemical signs ought to be letters, for the greater facility of writing, and not to disfigure a printed book. Though this last circumstance may not appear of any great importance, it ought to be avoided whenever it can be done. I shall take, therefore, for the chemical sign, the *initial letter of the Latin name of each elementary substance*: but as several have the same initial letter, I shall distinguish them in the following manner: – 1. In the class which I call *metalloids*, I shall employ the initial letter only, even when this letter is common to the metalloid and to some metal. 2. In the class of metals, I shall distinguish those that have the same initials with another metal, or a metalloid, by writing the first two letters of the word. 3. If the first two letters be common to two metals, I shall, in that case, add to the initial letter the first consonant which they have not in common: for example, S = sulphur, Si = silicium, St = stibium (antimony), Sn = stannum (tin), O = oxygen, Os = osmium, &c.

The chemical sign expresses always one volume of the substance. When it is necessary to indicate several volumes, it is done by adding the number of volumes: for example, the *oxidum cuprosum* (protoxide of copper) is composed of a volume of oxygen and a volume of metal; therefore its sign is Cu + O. The *oxidum cupricum* (peroxide of copper) is composed of 1 volume of metal and 2 volumes of oxygen; therefore its sign is Cu + 2O. In like manner, the sign for sulphuric acid is S + 3O; for carbonic acid, C + 2O; for water, 2H + O, &c.

When we express a compound volume of the first order, we throw away the +, and place the number of volumes above the letter: for example, $CuO + SO^3$ = sulphate of copper, $CuO^2 + 2SO^3$= persulphate of copper. These formulas have this advantage, that if we take away the oxygen we see at once the ratio between the combustible radicles. As to the volumes of the second order, it is but rarely of any advantage to express them by formulas as one volume; but if we wish to express them in that way, we may do it by using the parenthesis, as is done in algebraic formulas: for example, alum is composed of 3 volumes of sulphate of alumina and 1 volume of sulphate of potash. Its symbol is $3(AlO^2 + 2SO^3) + (Po^2 + 2SO^3)$. As to the organic volumes, it is at present very uncertain how far figures can be successfully employed to express their composition. We shall have occasion only in the following pages to express the volume of ammonia. It is 6H + N + O, or H^6NO.

Fig. 2 Berzelius' formalism.
Atoms are represented through letters, their proportions by numbers.
Klein 2001a, 8.

The limits of interpretation outlined above emerge when we compare the range of properties that are attributed to an entity in a particular representation with the range of properties that it could have based on our knowledge of the external world. Given these limits, I argue that there are two forms of inference involved in the interpretation of a representation, concerning implicit features on the one hand and unknown features on the other. Inferences to properties not explicitly given in a representation appeared legitimate when these were implicit, meaning that their interpretation could be backed up by reference to other explicit descriptions and convention. Other inferences were illegitimate, as they had no sufficient grounds either in the descriptions offered by the representation or by reference to convention, and the features thus remained unknown. Although one might, for instance, wonder whether Sherlock Holmes had a mole on his left shoulder, there is no legitimate basis on which a definite answer can be justified.[553]

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[553] Zipfel, Frank (2001): *Fiktion, Fiktivität, Fiktionalität: Analysen zur Fiktion in der Literatur und zum Fiktionsbegriff in der Literaturwissenschaft.* Wuppertal: Erich Schmidt Verlag, 94.

Nonetheless, the boundary between legitimate and illegitimate inferences is not a sharp and clear-cut one but a boundary that needs to be evaluated on a case-to-case basis. Whereas the scope of illegitimate inferences might be considered indefinite,[554] the scope of legitimate inferences is determined by the complexity of the representation in which a represented entity is embedded. By that I mean that the limits of interpretation are posed by the details and descriptions given in a representation and these limits, therefore, need to be assessed on a case-by-case basis. These inferential limits are often taken to enforce a methodological demand for the plurality of representational resources in science:

> "The multiplicity of models is imposed by the contradictory demands of a complex, heterogeneous nature and a mind that can only cope with a few variables at a time; by the contradictory desiderata of generality, realism and precision; by the need to understand and also to control; even by the opposing esthetic standards which emphasize the stark simplicity and power of a general theorem as against the richness and the diversity of living nature."[555]

This demand for representational pluralism in science has more than methodological reasons.[556] Other approaches such as, for instance, Bill Wimsatt's concept of "robustness" also rests on the limits of human beings that require a piecemeal approach to understand the vast complexity of nature. Yet he, like me, understands pluralism as an indicator of the reality of an entity and the truth of our claims about it. The more independent perspectives we have on a phenomenon, he argues, the more are we assured of its reality and our knowledge of it.[557] The subtle difference of my argument from Wimsatt's is that I do not primarily focus on plurality as evidence for reality but the relevance of pluralism for the process of interpretation itself. Pluralism, I argue, is the basis on which the possible reality of a theoretical or hidden entity can be explored. By investigating which model-based inferences are legitimate and illegitimate,

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[554] Danneberg (2006): *Weder Tränen noch Logik,* 27.

[555] Levins, Richard (1966): The Strategy of Model Building in Population Biology. *The American Scientist* 54(4), 431.

[556] Another argument concerns the complexity of the phenomenon that leads to inconsistent but complementary models such as currently incoherent nuclear models. See: Morrison, Margaret and Morgan, Mary (1999b): Models as Mediating Instruments. In: *Models as Mediators. Perspectives on Natural and Social Science.* Ed. by M. Morgan and M. Morrison. Cambridge: Cambridge University Press, 23, 28; Morrison, Margaret (1999): Models as autonomous agents. In: *Models as Mediators. Perspectives on natural and social science.* Ed. by M. Morgan and M. Morrison Cambridge: Cambridge University Press, 62; Morgan, Mary (2011): One phenomenon, many models: Inconsistency and Complementarity. *Studies In History and Philosophy of Science Part A* 42(2), 342-351.

[557] Wimsatt, William C. (2007): *Re-Engineering Philosophy for Limited Beings: Piecewise Approximations to Reality.* Cambridge M.A.: Harvard University Press.

we can determine the extent to which our insight into the features of a represented entity is (in)dependent of a representational source. How do the results of legitimate inferences relate to other models of the same entity? And how can other alternative models address unknown properties? Unlike the interpretation of fiction, enquiries about unknown properties of allegedly real entities are not put on hold. When the properties in question are considered to be relevant for a better understanding of this entity, other sources are sought in answer to this line of enquiry.

2.3 Implications for Realism about Theoretical or Hidden Entities

Inferential limits have different implications for the interpretation of representations depicting fictional or real entities. A result of the exhaustive relation between fictional entities and their representational source is that for fictional entities *every* description given in a representation is a true description of this entity and, vice versa, every knowable property of a fictional entity is entailed in its representational source. The same does not hold for real entities; not every knowable property is displayed in the representation and not every description in the representation needs to be a property of the referent. For this reason, the properties of a real entity and the descriptions given in its representation do not need to match.[558] What this mismatch implies is that our access to knowledge about a real entity cannot be restricted to a particular representational source. My suggestion, therefore, is to investigate the reality of theoretical entities with respect to the following two considerations. First, it needs to be evaluated whether unknown properties are accessible through alternative representational sources. Second, to what extent do the inferences about an entity's nature correspond with the inferences drawn from other sources?

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[558] Consider a similar perspective on the discrepancy between the properties of an entity and the descriptions given in a representation in Hesse, Mary B. (1963): *Models and Analogies in Science.* London, New York: Sheed and Ward. Hesse distinguishes between positive, negative and neutral analogies in modelling. Positive analogies refer to properties of a model analogy that can be found in the target system whereas negative analogies describe properties that cannot be projected onto the target system; neutral analogies are those properties of an analogue that have yet to be evaluated to be present in the target system or not. Hesse argues that the productive power of analogies for modelling rests in this neutral analogy. The implicit mismatch between representations such as analogical models and reality constitutes a heuristic source to investigate unknown properties of a phenomenon.

Now let me briefly give some historical flesh to this suggestion. Many philosophers of science have chosen the case of phlogiston as the prime example for discussing the (un)reality of theoretical entities.[559] In contrast to concepts of other scientific entities such as oxygen or atoms, and even though their theoretical descriptions underwent substantial changes, the concept of phlogiston, rather than being considered partially false, has been abandoned completely. Before the success of Lavoisier's system, however, phlogiston was of fundamental importance for the explanation of chemical reactions. The referential failure of representations involving phlogiston thus advises caution towards claims surrounding modern examples of theoretical entities. As phlogiston was an integral part of experimental practice, linked to observable phenomena and concrete operations, the question is how phlogiston differs from entities in contemporary research practice which, even though assumed to exist, are also strongly founded in model-based inferences. Although many reasons can be put forward explaining phlogiston's demise,[560] one central problem relates to the persistent issue that the different representational and experimental contexts within which it was investigated couldn't be made to cohere properly. Presenting significantly contradictory interpretations about phlogiston's weight, an important property for contemporary researchers, this was more than merely a problem of inconsistent measurement and the integration of data derived from different sources. To illustrate the independence of theoretical entities from their representations through alternative representational resources, consider the foundations on which the investigation of phlogiston relied. The experimental practices surrounding the investigation of phlogiston have been argued to exhibit two limitations, concerning the instrumental resources on the one hand[561] and its ontological foundation on the other.[562]

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[559] Kitcher, Philip (1993): *The Advancement of Science : Science without Legend, Objectivity without Illusions: Science without Legend, Objectivity without Illusions.* Oxford: Oxford University Press; Ladyman, James (2009): Structural realism versus standard scientific realism: the case of phlogiston and dephlogisticated air. *Synthese* 180, 87-101.

[560] Chang, Hasok (2011): The Persistence of Epistemic Objects Through Scientific Change. *Erkenntnis* 75, 413-429; Chang, Hasok (2012): *Is Water H2O? Evidence, Realism and Pluralism.* Dordrecht, Heidelberg, New York, London: Springer.

[561] Kim, Mi Gyung (2008): The Instrumental Reality of Phlogiston. *HYLE – International Journal for Philosophy of Chemistry* 14(1), 27-51.

[562] Chang, Hasok (2010): The Hidden History of Phlogiston. How Philosophical Failure Can Generate Historical refinement. *HYLE – International Journal for Philosophy of Chemistry* 16(2), 47-79.

Beginning with the first limitation, phlogiston's "instrumental reality" was mainly grounded in investigative analysis using Tschirnhaus' burning glass according to Homberg's system. By melting substances such as iron, it was tested whether there is a difference in weight before and after the reaction, indicating a loss of material for which the underlying "inflammable principle" of phlogiston was taken to be responsible. With the introduction of further methods such as thermometric measurement and instruments such as the hydrometer, gasometer and calorimeter, inferences to the nature of phlogiston were soon challenged. Attempts to reconcile inferences from different experimental resources led to conflicting interpretations of the characteristics of phlogiston. Experiments with the burning glass seemed to suggest that the element of phlogiston possessed weight whereas it appeared to be weightless within thermometric measurements. Although the divergent weight seemed to be experimentally measurable, each result remained bound to a specific instrumental setting and could not be reconciled and coordinated beyond its particular instrumental source.[563] The limits of the investigation of this important feature presented a severe impediment that slowly spurred further inquiry into the alleged grounds of phlogiston's reality.

Another limit to investigations of phlogiston concerned its strong reliance on a specific ontology. Inferences to phlogiston's theoretical identity as the material cause of combustion were based on an ontology within which chemical principles rather than elementary building blocks underwent chemical reactions. Instead of being empirically disproven, phlogiston became slowly redundant with the rise of an alternative ontology of chemical elements.[564] Unlike phlogiston, not all concepts of scientific entities are abandoned in the light of changing ontologies but they often become modified and accommodated. The concept of oxygen, for instance, originated in the so-called "building block" ontology[565] but was further adopted within the succeeding atomistic ontology by Dalton and his contemporaries, whereas oxygen's "sister compound" in Lavoisier's system, caloric, was dismissed.[566] Nonetheless, considering Chang's convincing historical argument that there were no better empirical or

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[563] Kim (2008): *Instrumental Reality of Phlogiston*, 44-46; Macquer, Pierre-Joseph (1749): *Elémens du chymie – théorique.* Paris: J.T. Hérissant.

[564] Chang (2010): *Hidden History of Phlogiston*, 70.

[565] Klein, Ursula (1999): Techniques of modelling and paper-tools in classical chemistry. In: *Models as Mediators. Perspectives on Natural and Social Science.* Ed. by M. Morgan and M. Morrison. Cambridge: Cambridge University Press, 151.

[566] Chang (2010): *Hidden History of Phlogiston*, Ibid.

epistemic grounds to keep oxygen but not phlogiston,[567] I might add that the emerging ontology within which phlogiston became redundant placed an even stronger emphasis on the property of weight. Irresolvable differences in the measurement of phlogiston's weight thus remained a central focus in debates about its nature and reality. Even though properties of phlogiston remained stable within specific representational contexts (such as the burning glass experiments), the results derived from these individual contexts could not be made to cohere with each other. Facing these instrumental limits and ontological constraints, the concept of phlogiston was hard to translate into alternative emerging experimental practices. Here the plurality of investigative methods and the emerging limits of inference to unknown properties caused a serious rift in the image of the theoretical entity phlogiston. It was not simply a matter of experimental inconsistencies that led to scepticism about its existence but, rather, an insoluble problem of determining a fundamental property that, within the ontological context of its contemporaries, phlogiston either must have had or not. Whether the criteria on which an enquiry into an unknown property of a theoretical entity is based are adequate, of course, is another significant question. Yet, when a property is considered fundamental to its nature, the account of representational pluralism presented here serves as a good indicator for assessing a theoretical entity's reality.

2.4 *Preliminary conclusions on model-based inferences*

In the first part of this chapter, I have presented an account of how to deal with theoretical entities in science and how to evaluate their disputed reality. By relating to the wider debate on fictionalism in the philosophy of science, I contrasted real with fictional entities through the different relations of these entities and their representations. Fictional entities were determined by a relation of synonymy and strict-identity with the descriptions in their representational sources. By contrast, non-fictional entities were argued to exhibit a degree of ontological independence from their representations and to have no privileged representational origin. This conceptual divergence, I have

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[567] Chang (2011): Persistence of Epistemic Objects; Chang (2012): *Is Water H_2O?*, see especially chapter 1.

shown, resulted in a difference in the interpretation of represented entities, especially with respect to the interpretation of properties not explicitly given in a representation. Here I distinguished between two kinds of inference, legitimate inferences to implicit properties on the one hand and illegitimate inferences to unknown properties on the other. Unlike fiction, for real entities the latter did not pose a limit of interpretation when it was possible to consult additional representational resources of the same entity addressing the property in question. I therefore suggested that the reality of a theoretical entity, and its degree of ontological independence from particular representational resources, could be explored by virtue of the plurality of alternative representations. Although this approach must be assessed further on a case-by-case basis, I exemplified its application by discussing the historical example of phlogiston. Endorsing representational pluralism and the partial and mosaic character of many scientific representations and investigative approaches, rather than denying it, I think, provides a valuable heuristic strategy to assess when a realist case about a theoretical entity can be made.

3 *Chasing Unicorns?* Inferential Boundaries in Olfactory Receptor Modelling

In the remainder of this chapter, I will exemplify my argument on model-based inferences by addressing contemporary limits of receptor modelling in olfaction theory. Since the character of the olfactory receptor (OR) binding site currently remains elusive, the question here is how to make successful model-based inferences about the nature of experimentally inaccessible or difficult to assess materials. What models and methods exist for studying these materials? There are as yet very few successful material studies of ORs and most alternative methods consist of computer modelling and simulation techniques. The lack of empirical insight into the structure of ORs renders any hypothesis about the underlying molecular recognition process to some extent speculative. This problem is exacerbated by the rivalry of two empirically feasible models for this mechanism. Orthodox opinion about primary smell recognition takes stereochemical configurations to be the key feature underlying molecular recognition.[568] An alternative account proposed by Luca Turin questions a shape-sensitive mechanism and, referring to molecular vibrations in the infrared range as the key feature instead, suggests a recognition process by inelastic electron tunnelling spectroscopy (IETS).[569] Although both mechanisms are in principle empirically possible,[570] the IETS mechanism was widely disregarded when initially proposed and it has not been recognised as a serious candidate for truth in the wider research community.[571] With the publication of additional studies supporting Turin's model,[572] however, the olfactory debate has been reignited. A striking feature of the growing controversy surrounding the rival olfactory mechanisms is that in some of the olfactory scientists' responses, the vibration theory was compared to fiction and its proponents accused of chasing a fiction:

> "The editors at Nature used to classify manuscripts on a 'zoological scale' that ranged from goats to unicorns, and Turin's paper was toward the far end of the scale."[573]
>
> "I like to think of the vibration theory of olfaction and its proponents as unicorns. The rest of us studying olfaction are horses. (…) The problem is that proving that a unicorn exists or does not exist is impossible. This debate on the vibration theory or the existence of unicorns will never end, but the very important underlying question of why things smell the way they do will continue to be answered by the horses among us."[574]

The polemic use of fiction in the olfactory debate may at first seem to have little to do with the concept of fiction as discussed in the philosophy of science. It does not address the employment of non-existent entities that are nevertheless an integral part of successful modelling practice, such as 'silogens' in

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[568] Amoore, John E. (1970): *The Molecular Basis of Odor.* Springfield, IL: Thomas; Ohloff, Günther; Pickenhagen, Wilhelm and Kraft, Philip (2011): *Scent and Chemistry. The Molecular World of Odors.* Wiley-VCH.

[569] Turin, Luca (1996): A Spectroscopic Mechanism for Primary Olfactory Reception. *Chemical Senses* 21(6), 773-791.

[570] Brookes, Jennifer C.; Hartoutsiou, Filio; Horsfield, A. P. and Stoneham, A. M. (2007): Could humans recognize odor by phonon assisted tunneling? *Phys Rev Lett.* 98(3), Article 038101.

[571] Franco, Maria Isabel; Turin, Luca; Mershin, Andreas and Skoulakis, Efthimios, M.C. (2011): Molecular vibration-sensing component in *Drosophila melanogaster* olfaction. *PNAS* 108(9), 3797-3802; Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780.

[572] Gane et al. (2004): *Vibration-Sensing Component.*

[573] Nature Neuroscience Editorial (2004): Testing a Radical Theory. *Nature Neuroscience* 7(4), 315.

[574] Leslie Vosshall as quoted in: Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

nanomechanic models.[575] It does, however, address the problem of model-based inferences to unobservable phenomena and the resulting question of whether currently accepted scientific concepts explaining these phenomena are truthful or, as in the case of phlogiston, possibly fictitious. Not without a trace of irony, the philosophical agenda, advocating caution about the conviction with which we take contemporary established scientific concepts to have a better foundation than historical failures, seems to be skewed in the olfactory debate. Fiction here is used as an objection to an alternative hypothetical model that challenges an established research paradigm. The question that interests me is whether the scientific opinion that the IELTS mechanism for olfactory responses is as real as unicorns is justified empirically.

To address this question, this section proceeds in two steps. It will first explore the material culture of receptor modelling in general and the failure of the standard methods for studying ORs in particular. Deeper insight into the model building process will elucidate the limits of considering “structure” as a criterion for determining how models refer to the nature of their target system. Instead, the capacity of models to represent a physical phenomenon is introduced as being based on a mediating chain of model ingredients. The purpose of this first step is to emphasise the dependency of successful model-based inferences on specific instrumental and material conditions and the involvement of different definitions of structure. Focus on these conditions will also enable me to demonstrate how, despite its mediated character, a model relates to and thereby represents its target system through the interconnection of the different modelling stages.

Second, this section investigates the development of alternative model strategies to facilitate access to the unknown OR binding site. Demonstrating how multiple models interact by complementing and refining each other, the purpose of this part is to analyse the contemporary practices and conditions under which claims about the nature of the ORs are made. Drawing attention to the interaction between different models will show to what extent the theoretical assumptions integrated in the model building procedure play a central part not only in the generation of model-based inferences but also in their justification. This is necessary to demonstrate the extent to which the competing olfactory

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[575] Winsberg, Eric (2009): A Function for Fictions. Expanding the Scope of Science. In: *Fiction in Science. Philosophical Essays on Modelling and Idealisation.* Ed. by Mauricio Suárez. London: Routledge, 179-190.

mechanisms can be related to current results, and to provide the background for my claim in section 4 that, far from being a fiction, inferences to an IELTS mechanism are empirically as well grounded as inferences to a shape-sensitive mechanism.

3.1 Modelling as a Mediating Chain: X-Ray Crystallography

One of the two standard methods of protein modelling is X-ray crystallography, the other being nuclear magnetic resonance (NMR). For the purpose of this section, unfolding the internal structure of models and the process of model building, I only address the first method here. The method of X-ray crystallography is pictorially represented (fig. 3) and basically works as follows. The protein materials are prepared in a specific detergent so that they form a crystalline structure. They are then placed within a goniometer, an instrument that allows for the constant rotation of its inserted object. Inside the goniometer the crystals are then treated with beams of x-rays. Expressing a specific diffraction pattern, the scattered x-rays are subsequently collected either on an image plane or an x-ray film. The data thereby collected reflect the electron density within the crystal structure and serves as the basis to infer atom positions and, consequently, the molecular structure of the crystal.[576]

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[576] Drenth, Jan (1999): *Principles of Protein X-Ray Crystallography. Advanced Texts in Chemistry.* 2nd Edition. New York: Springer, 37; Pattabhi, V. and Gautham, N. (2002): *Biophysics.* Springer, 105-106; Serdyuk, Igor N.; Zaccai, Nathan R. and Zaccai, Joseph (2007): *Methods in Molecular Biophysics: Structure, Dynamics, Function.* Cambridge*:* Cambridge University Press, 860.

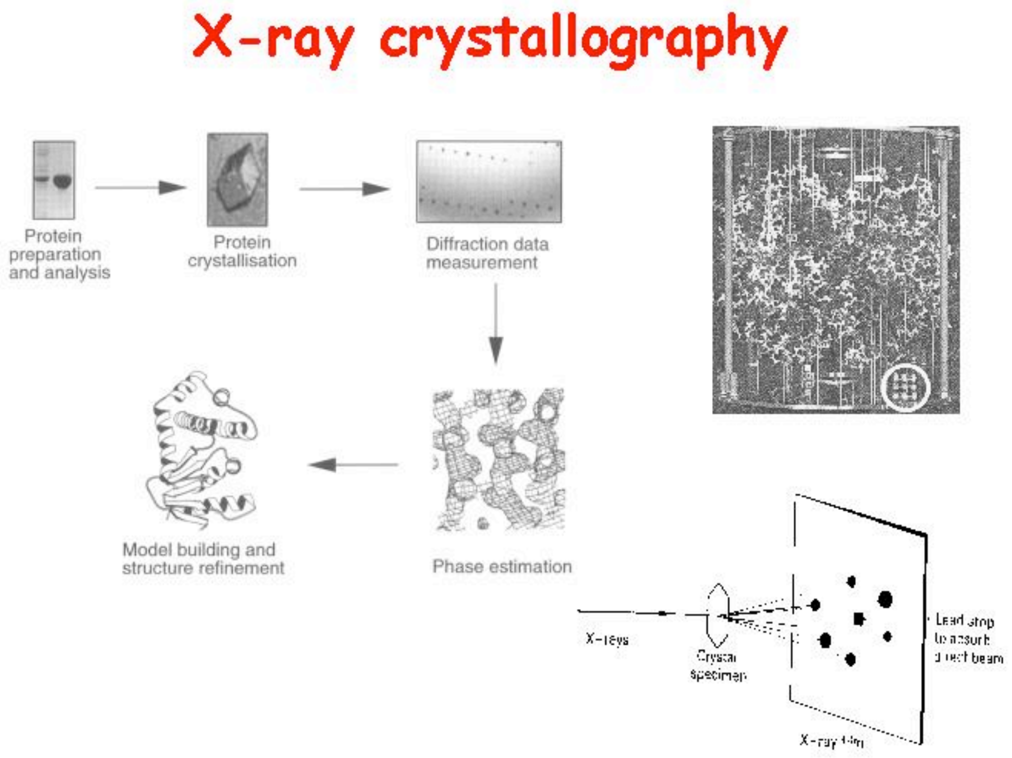

Fig. 3 The different modelling steps involved in the method of X-ray crystallography. Kobe (2004): *Protein three-dimensional structural data*.

The application of this procedure is not without difficulties. Proteins, when treated with x-rays, disintegrate quickly and, as a result, the collected diffraction data are not always complete. An enhanced problem for studies of ORs, in comparison to other proteins, concerns their extremely delicate nature. It is the high instability of transmembrane proteins that prevent ORs from building regular crystalline structures, but current applications of X-ray crystallography only work

> "[…] if you can make 3-D crystals of proteins. You slowly remove the water and as the protein gets dry they spontaneously form nice big crystals (a millimetre or so is sufficient, as long as the crystal is nice and regular). But the proteins we're interested in, the receptors, are membrane proteins and they do not easily form 3-D crystals because they live in a flat, nearly 2-D environment. So crystallographers are stuck with flat crystals […]."[577]

Crystallography with flat crystals is unsuccessful, because they do not exhibit symmetric structures. Symmetry is indispensible to combine the series of diffraction images acquired while the crystal is rotated, and to apply the mathematical interpretations of diffraction patterns for the development of

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[577] Turin, Luca (2006): *The Secret of Scent.* London: Faber and Faber, 93-94.

electron density maps. The diffraction data obtained from 2D crystals, however, is incomplete and distorted and cannot be accommodated within the available mathematical models.[578] Therefore, the problem of distorted and indeterminate data results in important limits for legitimate inferences to the structure of the research materials. Diffraction patterns of protein crystals present a complex picture within which it is not easy to distinguish what part of the image is the actual diffraction data (fig. 6) and what is mere ‘background noise’.[579] Nonetheless, this distinction is crucial for further calculations and to transform the diffraction data into readable electron density maps (fig. 7).

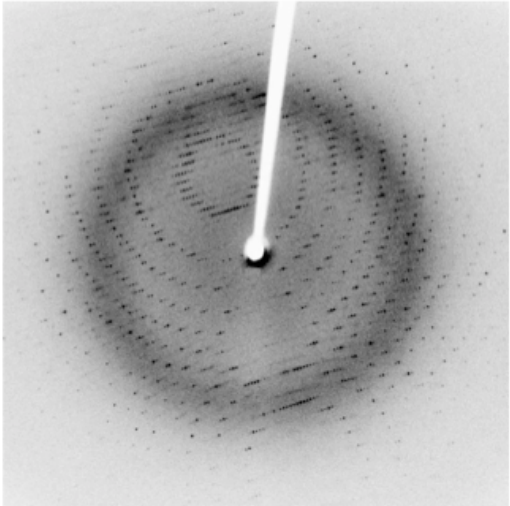

Fig. 6 Diffraction data
(concentrated spots indicate electron clouds)
Hardinger (2012b): *Instrumentation.*

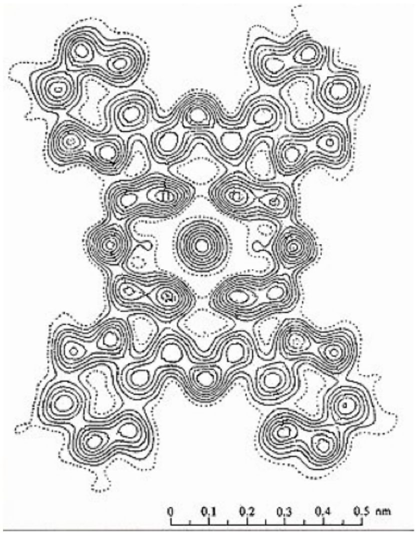

Fig. 7 Electron density map
(concentrated rings indicate atom positions)
Hardinger (2012b): *Instrumentation.*

Although the main impediment to OR modelling appears to be the material condition of crystallisation, the underlying issue of unknown and distorted data elucidates a point that is more than a mere transient technicality. It marks the methodological dependency of experimental research on the available instrumental tools and the aspects of structure to which they are responsive. Serving as the foundation for successful inferences to the molecular dimension of proteins is not the underlying structure of the materials per se, irregular and flexible when untreated, but an artificially produced symmetry. Experimental access to the OR binding site, therefore, is facilitated by manipulating materials

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[578] Smyth, M.S. and Martin, J.H.J. (2000): x Ray crystallography. *Mol Pathol.* 53(1), 8-14.

[579] For a good and short tutorial in the art of “reading electron maps” see: Hardinger, Steve (2012a): *XRAY CRYSTALLOGRAPHY 101: The Who’s What’s and Why’s.* URL=< http://www.chem.ucla.edu/harding/ec_tutorials/tutorial60.pdf>

to fit the model procedure rather than simply mapping models onto the materials.

Rather than reconstruction, the basis for inferences about the constitution of proteins is the very *production* of structures, artificially generated and very different from untreated materials. The success of claims about the nature of proteins is dependent on the techniques for bringing the materials in correspondence with the requirements of the model procedure. As products of this material intervention, structure and structural correspondence are not a mere givens of the materials simply waiting to be disclosed. Elucidating the process of model building shows that what is conceived as an essential structure often reflects only a methodological utility for the model rather than an inherent ontological feature of the material. Presumptions about structural similarities are an integral part of modelling and, therefore, do not provide independent criteria for the evaluation of model-based inferences.

The production of symmetric crystals is not the only methodological requirement for successful receptor modelling. In addition to the experimental manageability of the research materials, further factors play an important role, for instance the production of a sufficient range of data, the availability of appropriate methods to translate the diffraction data into an electron density map and the introduction of data processing techniques such as molecular graphic programs.[580] These factors are involved in a sequence of material and conceptual operations before resulting in a final receptor model:

- first, the material transformation of flexible proteins into stable and rigid crystal structures (fulfilling the requirement of symmetric patterns);
- second, the material transformation of the crystallised protein structure into diffraction data (relying on Bragg's model of diffraction or Bragg's law)[581]
- third, the conceptual transformation of diffraction data into an electron density map (through Fourier transformation)
- and fourth, the subsequent conceptual transformation of the electron map into a protein model (employing computer programs to calculate the positions and relations of atoms from the electron clouds).

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[580] Serdyuk et al. (2007): *Methods Molecular Biophysics*, 35-37, 243, 873, 858, 870; Pattabhi (2002): *Biophysics*; Drenth (1999): *Protein X-Ray Crystallography*, 223.

[581] Ghosal and Srivastava (2009): *Fundamentals Of Bioanalytical Techniques And Instrumentation*. PHI Learning Pvt. Ltd., 237.

Unfolding the process of model building and dissecting it into its ingredients brought to the foreground that the final model does not present a direct but a mediated image of the structural composition of proteins. Protein models are not inferred from a single, intrinsic or essential trait of the materials but are a result of various material and conceptual manipulations. Rather than a direct relation between the models and the materials, there is a mediating chain of multiple inferential stages. Understanding of how a model carries out its representational function by allowing for the generation of reliable descriptions or hypotheses about an intended target, therefore, cannot be reduced to dyadic notions such as the structural similarity or resemblance between the model and its target system. The modelling procedure was shown neither to involve a unique and unambiguous notion of isomorphic structure nor to involve any directly connective similarity relation between the model and the materials. Instead, the relation between the materials and their models rests on the interdependence of the multiple inferential steps involved in the model building procedure. Although the successive modelling steps do not follow logically from each other, the manifestation of these steps is informed by, and grounded in, the inferences established through their preceding ones. Focus on these steps thereby enables the analysis of how model-based inferences are derived. Only by taking a closer look at the multiple modelling steps can we explain how these models are linked to the materials and, in further consequence, allow the generation of inferences about them. Presenting a mosaic of ingredients and inferential steps, models, as analysed here, are not freely floating objects. Therefore, any evaluation of a model and the inferences drawn from it must be set against the background knowledge on which the modelling procedure is based. Every model has a history that determines its construction and use and, consequently, its potential and limits for inferences to the properties of the modelled materials. To elaborate on this point further, the next section will continue with an analysis of the interplay between multiple models that are currently adopted in hypothetical OR modelling. By illustrating the interactive and iterative relation between these different modelling procedures, I will demonstrate that the representational function of models is best understood as a pluricentric activity. Instead of analysing a model’s capacity to represent solely by its relation to the target system, I propose to further include its relation to other models designed to address the same target. My analysis of models by their mediated and interactive character will then aid me to evaluate the entrenchment of procedural assumptions integral to model building that may also impact on justification strategies for inferences.

3.2 Simulations and Speculations: Hypothetical Receptor Modelling

Despite the experimental inaccessibility of the ORs, research on the structural composition of the binding site is not put on hold. One suggested alternative to experimental receptor modelling is the development of hypothetical computational models. These are based on so-called “homology modelling”, and their utility rests on two additional complementary procedures, namely functional analysis and ligand docking simulations.

Developing computational OR models, in a first step the modeller generates the hydrophobicity profiles for the olfactory receptors, identifying the domain with the seven transmembrane helixes:

> “Olfactory receptors (OR) are part of a family of proteins that have 7 transmembrane regions. That is they pass through the cell membrane 7 times. The interior of the cell membrane is hydrophobic while both the exterior and interior of the cell are hydrophilic. Therefore, the regions of the protein that pass through the membrane should contain mostly hydrophobic amino acids while the portion outside of the membrane should be mostly hydrophilic.”[582]

Resulting from these profiles is a rough sketch of the spatial arrangement of the receptor site. Yet, what is still needed is some “flesh” to this receptor model “skeleton”, for which the modeller employs models of other proteins. These template proteins, which are part of the same receptor class as the ORs, are experimentally accessible and, therefore, we have better insight into their structure, such as the proteins Bovine rhodopsin (PDB ID: 1u19), Beta-adrenergic receptor (PDB ID: 2r4r, 2r4s &2rh1), Adenosine A2A receptor (PDB ID: 3qak, 2ydo & 2ydv). Drawing inferences from structural homologies, the protein templates (usually rhodopsin) are used to ‘fill out the gaps’ in the OR helix “skeleton” through a comparison of their amino acid sequences with the sequences of the ORs. Matches in parts of these sequences are assumed to

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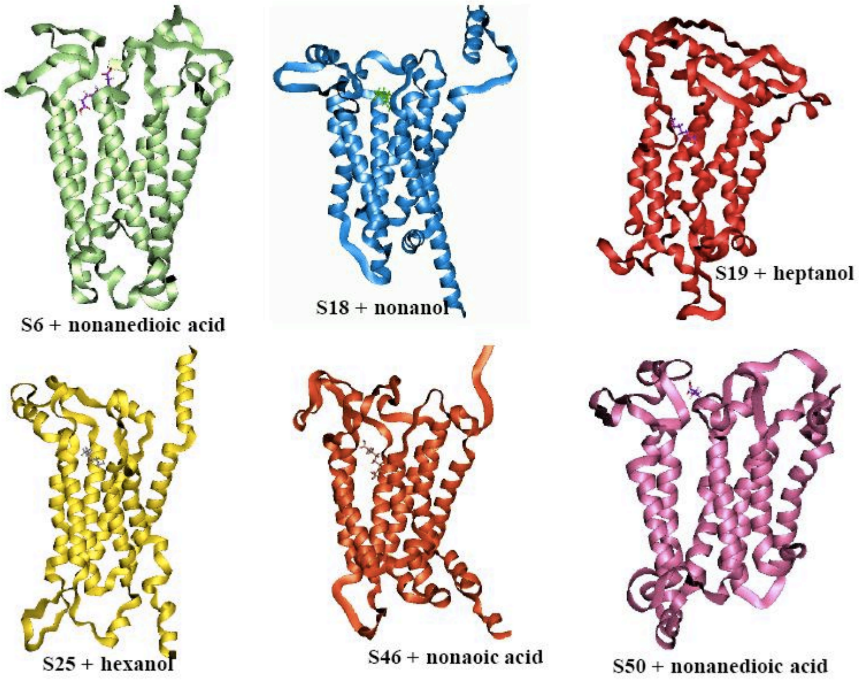
[582] Computational Genomics (2006): *OLFACTORYRECEPTORS Example of use of HMM in sequence analysis.* URL=<http://www.computational-genomics.net/case_studies/olfactoryreceptors_demo.html>

allow for inferences to structural similarities. The molecular structure corresponding to the template sequences is then mapped onto the OR helix sketch, “creating the transmembrane scaffold”.[583] Since ORs vary greatly in their amino acid sequences, they are also assumed to form various OR types with different binding capacities for a variety of structurally diverse odorants (fig. 8).[584]

An issue with this procedure is its strong reliance on structural homology, as the matches of amino acid sequences across the ORs and rhodopsin amount to 40% at best. Thus, even though similarities in these sequences might suggest structural similarities, the presumed correspondence remains to a certain extent speculative. Some structural differences between the target and the template proteins were already noticed, for instance, differences in the length of the loops connecting the transmembrane helixes. For this reason, it is not undisputed which structural features of rhodopsin can and cannot be translated to the computational model of the ORs.[585]



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[583] Crasto, Chiquito J. (2009): Computational Biology of Olfactory Receptors. *Curr Bioinform* 4(1), 8-15; Crasto, Chiquito J. (2011): *Preferential binding odorant- olfactory receptors as a predictor of OR excitation or inhibition.* URL=< https://docs.uabgrid.uab.edu/w/images/c/c6/Crasto_SIM_01_21_11.pdf>

[584] Buck and Axel had already put forward this assumption in 1991. The sequence variability was taken to possibly explain the capacity of receptors to interact with the vast range of structurally diverse odorants. Buck and Axel (1991): *Novel multigene family*; Buck, Linda B. (2005): Unraveling the Sense of Smell (Nobel Lecture). *Angew. Chem. Int. Ed* 44, 6128-6140.

[585] Crasto (2009): *Computational Biology*; Crasto (2011): *Preferential binding*.

Fig. 8 Computational OR models. OR types are derived from the different amino acid sequences of different Olfactory Sensory Neurons (each of which hosts only one gene). OpenWetWare (2006): *BIO254:ORs.*

To further facilitate insight into the underlying recognition mechanism, current olfactory research employs two additional methods: functional analysis and simulations of ligand docking. Functional analysis is an experimental method exploring the range of odorants that bind to particular receptors. Simulations of ligand docking compare and analyse the molecular parameters that might correlate between these odorants and the hypothetical receptor models.

One of the first and most crucial studies of functional analysis was the work by Bettina Malnic, Junzo Hirono, Takaaki Sato and Linda Buck (1999).[586] They tested a range of ORs and their responses to a selected group of odorants. The chosen odorants, namely aliphatic aldehydes, have different smells and exhibit an overall structural affinity with distinct sub-structural differences regarding their embedded functional groups and the length of their carbon chain (involving 4-9 carbon atoms). Because ORs are highly unstable entities, becoming dysfunctional when isolated and tested in vitro, odorant response tests were conducted on the olfactory sensory neurons (OSNs), those cells in the nasal epithelium whose surface cilia are covered with ORs. Using the method of Calcium Imaging, positive responses to odorant exposure (resulting in calcium release) are monitored on OSNs (of mice) that were previously treated with fura-2, a fluorescent dye responsive to calcium (fig. 9).

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[586] Malnic, Bettina; Hirono, Junzo; Sato, Takaaki and Buck, Linda B. (1999): Combinatorial Receptor Codes for Odors. *Cell* 96, 713-723.

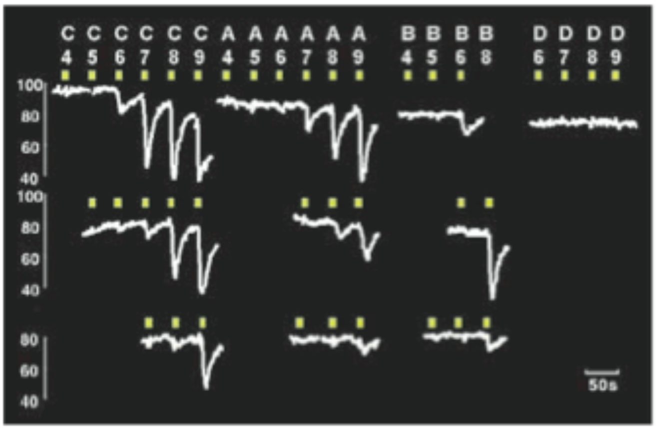

Figure 7. Responses of a single olfactory sensory neuron to different odorants. Fluorescence emission was monitored during sequential exposure of a neuron containing an indicator dye (Fura-2) to a series of odorants (C4–D9). Responses to lower odorant concentrations are shown below. Adapted from Ref. [20].

Fig. 9 ONS response tests with Calcium Imaging. Buck (2005): *Nobel Lecture*, 6135.

OSNs responsive to at least one odorant (98 out of 647) were isolated, and the gene expressed in these OSNs was extrapolated by reverse transcriptase polymerase chain reaction (RT-PCR), meaning that RNA strands of the OSNs are transcribed into their complementary DNA. Following this, the cDNA sequences were compared and searched for matches within the known amino acid sequence motifs of the mammalian OR genes. By determining the genes expressed in the OSNs, it was discovered that each OSN only expresses one particular gene, indicating that each OSN hosts a particular type of ORs. This discovery allowed for further inferences about the response patterns of OSNs to particular odorants (fig. 10):

> “These data make three important points. First, each OR can recognize multiple odorants (…). Second, each odorant can be detected by multiple different ORs. Finally, and most importantly, different odorants are recognized by different combinations of ORs.”[587]

In other words: the perception of odours is a combinatorial process, and each odorant relates to a specific perception pattern of responding receptors in the nose.

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[587] Buck (2005): *Nobel Lecture*, 6135.

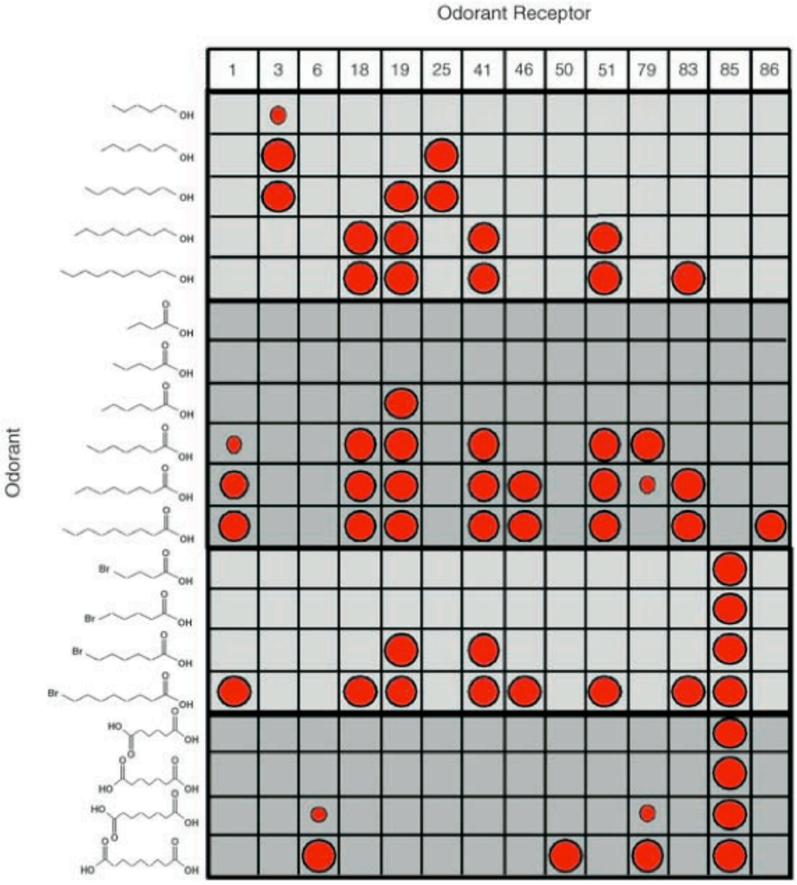

Figure 8. Odorant receptors are used combinatorially to detect odorants and encode their identities. The recognition profiles of individual odorant receptors to a series of odorants were determined by calcium imaging and single-cell RT-PCR. The sizes of circles reflect response intensity. Adapted from Ref. [20].

Fig. 10 OR activation pattern (presenting a series of odorants interacting with different ORs). Buck (2005): *Nobel Lecture*, 6136.

The results of the two methods mentioned, computational receptor modelling and functional analysis, are further combined to make assumptions about the perception mechanism and to explore possible structural correspondences between odorants and hypothetical OR models. Using ligand-docking simulations, the perceptive range of an OR can be analysed with respect to the molecular features of the odorants to which it responds. For this, the first step involves a calculation of the binding capacity of odorants, concerning their hydrophobicity and energy profiles, and, in a second step, these molecular parameters are compared with the energy structures of the computational OR models. A statistical comparison of these parameters is thought to reveal to which part of the receptor site the odorant binds: starting with the electron structure of the amino acid sequences, it is simulated where a responsive odorant must locate itself to ‘dock on’ (fig. 11).[588] Since Malnic and Buck’s discovery of the combinatorial nature of odour recognition, it is also assumed that ORs have multiple binding sites for the interaction with different odorants. The purpose of such ligand binding simulations is the refinement of the original computational OR models and to correct structural ambiguities, resulting from the differences between rhodopsin and OR proteins. For this reason, computational models and docking simulations mutually inform each other and stand in a relation of constant revision and adjustments. Even though this OR model procedure *in vacuo* remains highly speculative, it is the most advanced modelling alternative to standard protein studies such as X-ray crystallography.[589]

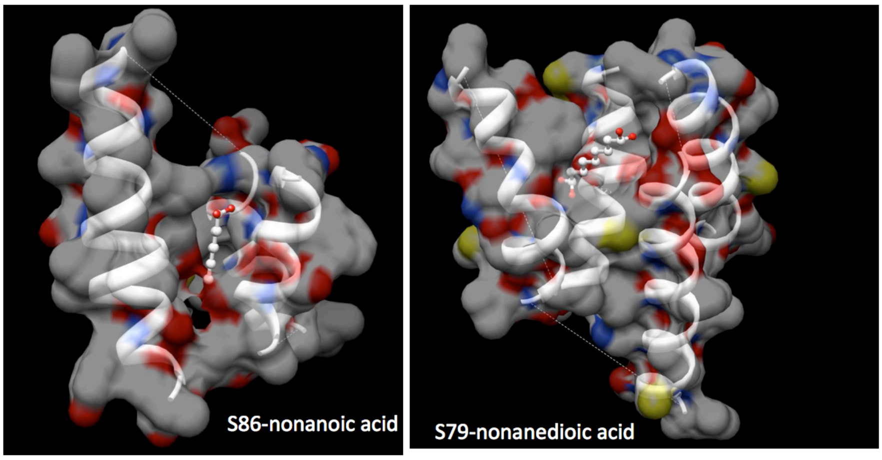

Fig. 11 Ligand-docking simulation screenshot. It is simulated where an odorant should bind to the computational receptor site (according to specific parameters such as hydrophobicity, electronic structure, etc.). Crasto (2011): *Preferential binding*.

The models and methods introduced above are all used to facilitate access to the yet unknown structure of the OR binding site. Facilitating access means to provide strategies for exploring a phenomenon, for instance by relating it to other models of more familiar phenomena, to serve as aids in the visualisation of structural hypotheses, or to present a guide for further experimentation.[590] Attempts to facilitate access to the ORs were shown to rest on the combination of multiple modelling strategies, namely computational models, functional analysis and ligand docking simulations. Instead of acting as separate building

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[588] For an example of a ligand docking simulation (representing the first 5nanoseconds of the interaction) see: Crasto UAB (2011): *OR17-209-5ns.mpeg*. URL=< http://www.youtube.com/watch?v=z8UPl_wP8K8>

[589] Crasto (2009): *Computational Biology*; Crasto (2011): *Preferential binding*.

[590] Bailer-Jones, Daniela (2009): *Scientific Models in the Philosophy of Science.* Pittsburgh: University of Pittsburgh Press, 102.

blocks, the application of these models requires a dynamic interaction. This interaction can be best characterised as a form of iterativity. Building on Hasok Chang's account of "epistemic iterativity" that describes the gradual process of scientific advancement,[591] Maureen O'Malley et al. (2009, 2010) introduced a similar notion of "methodological iteration".[592] Methodological iteration especially describes the interactivity of various modes of research strategies ranging from the conceptualisation of phenomena, model building, the development of new instruments, and experimental techniques to the generation of research questions and hypothesis. Rather than being linear, this process is ongoing back and forth, resulting in mutual model corrections and revisions such as in the feedback relation between hypothetical computational OR models and ligand binding simulations. It is this "corrective evolution"[593] in the interplay of modelling that compensates for and accommodates particular empirical uncertainties and limits. The strong reliance on structural homology in computational OR modelling, for example, was shown to rest on 40% of similarities across the amino acid sequences of ORs and rhodopsin at best. The ensuing structural ambiguities in the model were then corrected and adjusted through the results of ligand docking simulations. On that basis, even empirically impoverished and hypothetical models are seen to yield relatively reliable results compensating for the current experimental inaccessibility of the OR materials. By complementing the limits of other models, the aggregate therefore exceeds the limits of the individual models and widens their grasp on the target system. For this reason, analysing the representational capacity of a model in scientific research means analysing its productive interaction with other models, instruments and experimental practices. Only by tracing the intermediate stages and combinations of models and by making the conditions of model-based inferences explicit, can we explain how these models relate to the materials. Modelling, therefore, is a pluricentric practice, consisting of multiple steps, assumptions and elements. This pluricentricity holds true for the

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[591] For more detail see chapter 4; Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press, 226.

[592] O'Malley, Maureen, Elliott, Kevin C.; Haufe, Chris and Burian, Richard M. (2009): Philosophies of Funding. Cell 138, 611-615; O'Malley, Maureen; Elliott, Kevin C. and Burian, Richard M. (2010): From genetic to genomic regulation: iterativity in microRNA research. Studies in History and Philosophy of Biological and Biomedical Sciences 41, 407-417; Elliott, Kevin C. (2012): Epistemic and methodological iteration in scientific research. *Studies in History and Philosophy of Science Part A* 43(2), 376-382.

[593] Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press.

combinatorial use of and iterativity between different models and methods. It also applies to the successful application of individual models, which rest on multiple mediating modelling and inferential steps as I illustrated earlier by unfolding the mediating model chain of X-ray crystallography.

4 The Discovery and Combinatorial Nature of *What*?

Having delved into the details of current OR modelling practices, the question I want to resume is whether the opinion that the IELTS mechanism for olfactory responses is as real as unicorns is justified. This question I want to pursue now by comparing the empirical grounds for inferences to an IELTS mechanism with the grounds for inferences to a shape-sensitive mechanism. Such questions are addressed by assessing the extent to which the competing olfactory mechanisms accommodate the currently available observations. The crucial question guiding me is the one that resulted from my discussion of fiction in comparison with theoretical entities: to what degree are the model-based inferences (in)dependent of a particular model or model-context? Can these interpretative descriptions about a phenomenon be traced, explored and assessed across a variety of (partially independent) models? This line of enquiry, I argue, will help to evaluate whether and on what grounds a structural hypothesis or a model-based inference is justified.

With respect to the lack of empirical insight into the interactions between ORs and odorants, what the rival theoretical mechanisms do is to identify specific features and to propose hypothetical mechanical links between these features. These regularities must be somehow traceable in the results of the OR model building procedure. This also resonates with the wider scientific opinion voiced after Turin’s latest study on isotope perception, further supporting vibration theory, was published in 2013:[594]

> “Columbia University's Richard Axel, whose work on mapping the genes and receptors of our sense of smell garnered the 2004 Nobel prize for physiology, said the kinds of experiments revealed this week would not resolve the debate - *only a microscopic look at the receptors in the nose would finally show what is at work.* "Until somebody really sits down and seriously addresses the

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[594] Gane et al. (2013): *Vibration-Sensing Component.*

> mechanism and not inferences from the mechanism... it does not seem a useful endeavour to use behavioural responses as an argument," he told BBC News."[595]

Axel's comment is significant. Although true in its de-contextualised content, his statement turns out inconsistent as long as it is only directed at the IELTS mechanism and not the shape-sensitive model too. So let's take Axel at his word and take a closer look at the conditions and empirical implications of OR modelling to see what we can currently assume to be at work.

What catches the eye is that there is only one part of the entire OR modelling process that deals with the actual OR proteins, namely functional analysis. In contrast, ligand binding relies heavily on computational OR models, and the latter are built on the template protein rhodopsin. The employment of template proteins in the model building process rests on the premise that matches in amino acid sequences suggest structural similarities between rhodopsin and ORs. This thus conveys the implicit assumption that similarity in structure allows for inferences to similarity in function. Even though this assumption has proved useful in other proteinomic studies, it is not wholly undisputed. Strengthening the premise of structure-function correspondence was the discovery of the olfactory receptors and their identification as a specific class of G-coupled proteins. Although structurally diverse, G-coupled proteins involved in ligand binding all are assumed to act according to a shape-sensitive mechanism. As a result, current receptor modelling *starts* from the assumption of a shape-sensitive interaction. Ligand docking simulations too are not theory-neutral models because only molecular parameters assumed to be relevant for a shape-sensitive mechanism are compared but not those relevant within the IETS model. Nonetheless, the fact that a premise is central to the contemporary model building procedure does not guarantee its truth. So how valid is the premise of shape? If there were no rival explanations, there would be no sufficient grounds to doubt a shape-sensitive olfactory mechanism, especially as it is compatible with models of other molecular recognition processes such as digestion, metabolism and immune responses. But with the introduction of the IELTS mechanism by Turin in 1996, the situation changed and the indefeasibility of these theory-informed model-based inferences was

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[595] Palmer (2013): *Quantum smell*. [Italics mine]

challenged. The question, therefore, is: to what extent are the model-based inferences (in)dependent from the construction premise?

Consider again the only method in OR model building that empirically deals with the actual ORs: functional analysis. With the groundbreaking study by Malnic et al. (1999), the combinatorial nature of odorant recognition was discovered. This study, resulting in an odorant-OR recognition pattern (fig. 10), was likewise built and interpreted within the theoretical framework of a shape-sensitive mechanism. The selection of test odorants was visibly informed by stereochemical considerations (fig. 12), and the interpretation of combinatorial patterns further emphasises the focus on stereochemical configurations of particular atom groups as the key feature explaining OR-odorant interactions (fig. 13).[596]

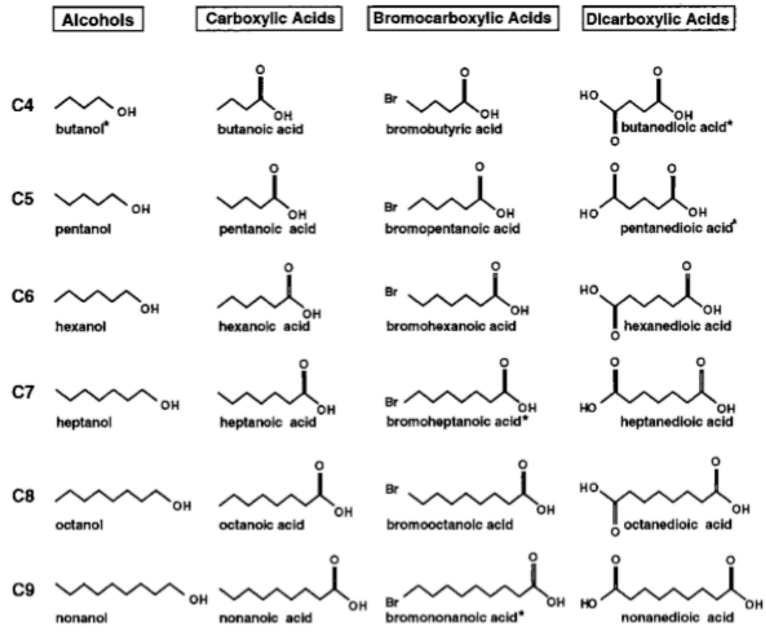

Fig. 12 “The test odorants used were aliphatic alcohols with straight carbon chains ranging from 4 to 9 carbons in length (C4–C9), and the corresponding aliphatic carboxylic acids, bromocarboxylic acids, and dicarboxylic acids. *, not tested.” Malnic et al. (1999): *Combinatorial Receptor Codes*, 714.

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[596] Malnic et al. (1999): *Combinatorial Receptor Codes*; Buck (2005): *Nobel Lecture*.

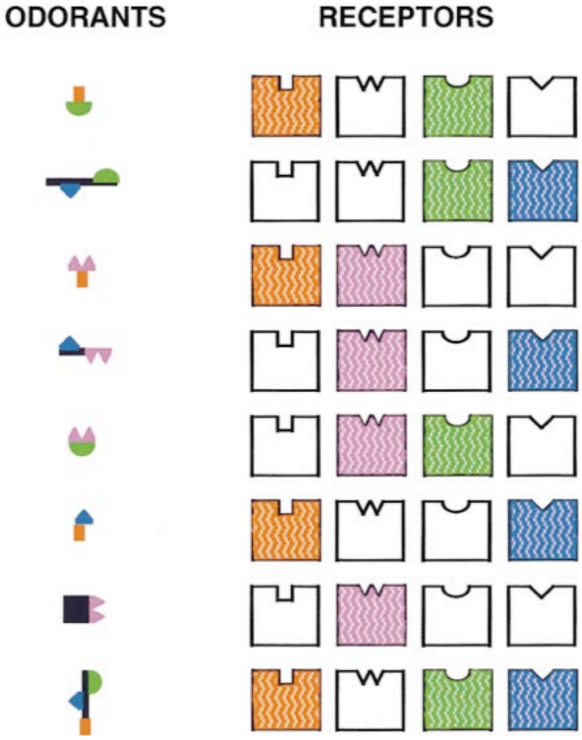

Fig. 13 "(…) The identities of different odorants are encoded by different combinations of receptors. However, each OR can serve as one component of the combinatorial receptor codes for many odorants. Given the immense number of possible combinations of ORs, this scheme could allow for the discrimination of an almost unlimited number and variety of different odorants." Malnic et al. (1999): *Combinatorial Receptor Codes*, 720.

However, if the theoretical framework within which it is interpreted is stripped away, one must question what is really known about the perception mechanism through current OR modelling. Given the combinatorial OR activation pattern, consider an alternative interpretation. Analysing Malnic et al.'s odorant-OR study, Turin and Yoshii proposed another structural feature accommodating this correspondence pattern. They suggested that the number of ORs responding to an odorant increases with the length of the carbon chain (resulting in different vibration patterns). In support of their hypothesis, they calculated the hydrophobicity profiles of ORs and odorants (as the determining factor in molecular selectivity) and matched these profiles with the scattering intensity of the odorants' vibration patterns (fig. 14).[597]

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[597] Turin, Luca and Yoshii, Fumiko (2003): Structure-Odor Relations: A Modern Perspective. In: *Handbook of Olfaction and Gustation 2nd edition*. Ed. by R. Doty and M.Decker. Informa Healthcare, 457-482. Cited is the online version URL=< http://www.annindriya.com/_mcms/_data/files/Luca%20Turin%20structure%20odor%20theory.pdf>

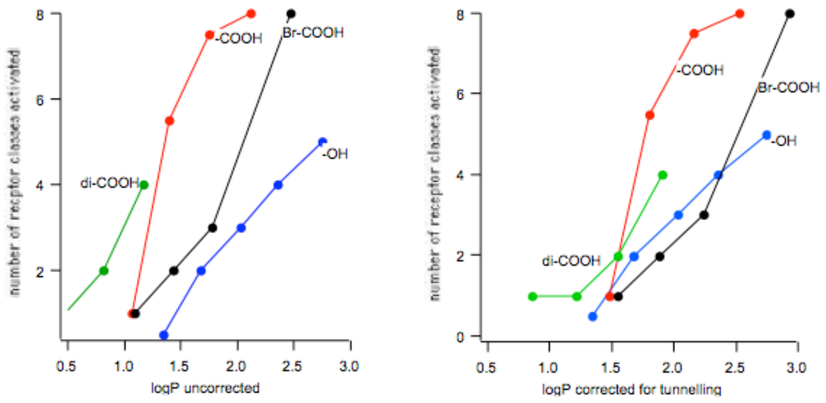

Figure 20 A reanalysis of the published data of Malnic et al on the response of expressed olfactory receptors to a variety of odorants. When the number of different receptor classes activated (ordinate) is plotted against the water-octanol partition coefficient (logP, abscissa), it becomes clear that a determining factor in molecular selectivity is hydrophobicity. When the data is corrected for scattering intensity in a vibrational mechanism (right) , the correlation improves. Weak responses obtained at 100μM (small circles in original figure) were treated as 0.5.

Fig. 14 Turin and Yoshii (2003): *Structure-Odor Relations*, 21.

Therefore, the question remains: what do we actually know about the recognition mechanism from current OR modelling? The only empirical observation derived is the discovery of the combinatorial nature of odour recognition through functional analysis. Nonetheless, not only are OR activation patterns accommodated within the two rival mechanisms but, they are also relatively theory-independent as they are not derived from previous versions of the rival frameworks, neither from the shape nor vibration theory of odours. In comparison, all other model procedures were built on the premise of a shape-sensitive mechanism without resulting in either empirical observations or independently assessable results. Quite the contrary, model-based inferences from computational OR modelling and docking simulations do not result in but rest on an empirical finding: the discovery that ORs are part of the same class as other proteins the majority of which acts according to a shape-sensitive mechanism.[598] This discovery is taken as the empirical foundation for current computational models, providing the shape-sensitive mechanism with greater credibility than its IETS rival in the wider scientific community.

But what did the discovery of the ORs actually *prove* about the mechanism of primary odour recognition? By presenting an empirical link allowing for possible inferences about structural similarities between related proteins, it undoubtedly

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[598] DeMaria, Shannon and Ngai, John (2010): The cell biology of smell. *The Journal of cell biology* 191(3), 443-452.

facilitated further model building. However, moving beyond this suggestive role, it must be recognised that no independent foundation for the assessment of the implied structure-function premise is currently available. Concerning the validity of inferences to a shape-sensitive mechanism on this premise, contemporary insights into protein folding cast doubt on the predominant structure-function paradigm. Growing knowledge about intrinsically disordered proteins – i.e. proteins that exhibit a high degree of structural flexibility and the function of which is determined by the folding process rather than merely amino acid sequences – led to scepticism as to whether shared amino acid sequences allow for inferences about structure-function correspondences.[599] Although the widely accepted causal explanation for ligand binding still rest on assumptions about shape and size alterations between molecules and receptors,[600] awareness of irregular protein folding leaves model-based structure-function inferences on weaker empirical grounds.

Contemporary support for a shape-sensitive olfactory mechanism rests strongly on its ontological compatibility with other models of molecular recognition, despite lacking an independent empirical basis for its justification. Enforced by its impact on the disciplinary development of olfaction theory,[601] the evidential strength of a shape-sensitive mechanism relates to its explanatory centrality and its integral role in model construction. Rather than having an empirically independent source, the premise of shape presents a theoretical assumption that, in the course of its historical entrenchment in research practice, has been transformed into a fundamental ontological premise underlying scientific judgement in the olfactory debate. Nonetheless, being an integral component of the continuity of practices throughout the last century does not guarantee its truthfulness. The history of science abounds with examples of scientific theories that, despite their persistent explanatory and ontological appeal, have subsequently been overthrown. Reliance on the previous pragmatic success of a theory, therefore, is not a sufficient argument for its facticity.

In conclusion, there currently is no fundamental empirical reason and independent model source on which claims about a shape-sensitive mechanism

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[599] Lutz, Diana (2012):Intrinsically disordered proteins: A conversation with Rohit Pappu. *PhysOrg* (20 September 2012) URL=< http://phys.org/news/2012-09-intrinsically-disordered-proteins-conversation-rohit.html>

[600] Kokkinidis, M.; Glykos, N.M. and Fadouloglou, V.E. (2012): Protein Flexibility and Enzymatic Catalysis." In: *Advances in Protein Chemistry and Structural Biology* 87, 210.

[601] See chapter 4.

are better justified than claims about the IELTS mechanism. Given the empirical possibility of biological spectroscopy,[602] successful predictions of structure-odour relations,[603] and explanations for a variety of data that remains unresolved within the shape theory of odours,[604] there is good reason to consider the vibration theory of odours and its IETS mechanism as a serious, even though highly hypothetical, theoretical contender and candidate for truth.

5 Why Model-*Choice*?

This brings me, in closing, briefly to reflect on an underlying commitment I made in this and previous chapters. Given the IETS-mechanism a run for its money, and also to make more explicit the suggestions that follow from an attempted neutral comparison relating both mechanisms to current OR modelling results. The question I want to pose is, quite simply, why all this pressure to take a decision? The strong focus on *choice* in this debate seems to be more grounded in the scientists' preferences than the available observations. A careful examination reveals that the status of current explanations of molecular data is a great deal more ambiguous than the widespread commitment to the dominant stereochemical theory suggests.

The conceptual differences between the two theories and their proposed mechanisms led to divergent interpretations of SORs and SARs data. Although the interpretations rested mainly on inferences from the mechanism models, the modes of evaluation for these interpretations were considerably different. Whereas the justification for a shape-sensitive mechanism was shown to be its central role in current OR model building, the IETS-mechanism has not yet been integrated sufficiently into research practices within molecular biology. The IETS-mechanism, however, has been shown to provide impressive explanations of SORs, even resulting in predictions of odour from structure. I therefore suggest reconsidering the assumption that an either/or choice between theories is required. Rather than eliminating other (different) theories, there are good reasons to entertain alternatives *in parallel with each other* given

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[602] Turin (1996): *Spectroscopic Mechanism*; Brookes et al. (1999): *Phonon assisted tunneling.*

[603] See Chapter 4 and 5; Turin (1996): *Spectroscopic Mechanism*; Turin (2006): *Secret of Scent*.

[604] See Chapter 7; Turin and Yoshii (2003): *Structure-Odor Relations*; Turin (2006): *Secret of Scent*.

that these possess heuristic power. Heuristic power means that these theories, for instance, aid in the design of experiments that potentially produce new data or open up enquiry into overlooked or irregular data.

The prevalence of the shape account, as I argued throughout this thesis, is grounded in the disciplinary centrality it obtained throughout the historical development of olfaction theory. As an exemplary study of scientific reasoning and development, the trajectory of olfaction theory presented a research culture building on successive stages of different modes of practice, ranging from data gathering, interdisciplinary model-building, exploratory conceptual manipulations, the design of experiments and the introduction and development of new techniques and technology. Based on the lack of knowledge about the ORs and the resulting underdetermination of theory by data, the developing research culture was shaped significantly by the background ontology it shares with the wider context of molecular biology.

Even though the trajectory of olfactory research was strongly hypothesis driven, resting on the assumption of a primarily stereochemical interaction, it progressed more through inductive, theory-informed reasoning than hypothesis testing. Partially grounded in the remaining experimental inaccessibility of the ORs, another reason for the background ontology was that, being short of a genuine rival for a long time, the shape-sensitive mechanism did not need to be strictly tested. By contrast, the revived vibration-theory was under a stronger obligation to justify its underlying hypothesis. A number of experiments, testing inferences drawn from the model, were conducted. These mainly concerned SORs such as predicting the sulphurous smell of boranes; testing the effects of a polarisation effect with carvones; comparing the smell of stereochemically hindered with the smell of easily accessible functional groups; and testing the ability to discriminate the odour of isotopic variants.

Nevertheless, despite their suggestive power, these tests were not considered sufficient evidence within the wider olfactory community. An explanation for this was given in previous chapters by focussing on the historical development of olfaction and explanations for irregular SORs within the shape theory. The historical trajectory revealed a conceptual shift that moved from ‘simple’ stereochemical lock-key interactions to a mechanism that, even though primarily stereochemically determined, involves a complex combination of a range of molecular features. On this account, contemporary opinion in olfaction theory considers SORs to be explainable through better insight into the perception mechanism and, in turn, judges the latter to be the basis in which claims about the molecular basis of smell need to be grounded.

Thus, moving beyond SORs in fragrance chemistry, one might justifiably question wherein the heuristic power of the IETS mechanism lies for current OR model practice in molecular biology. Whereas the shape-sensitive mechanism provides a basis on which further model strategies are developed, where is the productivity of the IELTS model in all of this? Breaking through the circularity of current olfactory modelling illustrated above, or what Hacking calls the "self-vindication of the laboratory sciences",[605] attempts to design models that further support a vibration-sensitive mechanism are in fact in progress. Turin's proposal is to measure possible electron flow occurring in OR-odorant interactions:[606]

> "**From:** luca turin <lucaturin@me.com>
> **Subject: Re: Quantum smell**
> **Date:** 13 March 2013 11:51:23 GMT
> **To:** "Barwich, Ann-Sophie" <ab478@exeter.ac.uk>
>
> Hi Ann
>
> It's really quite simple in principle, though fraught with unknowns in practice: a straightforward prediction of an electronic receptor mechanism is that there should be movement of electrons somewhere in the receptor when the ligand [odorant, or whatever] binds. The electrons are likely to be unpaired and therefore to have spin.
>
> The idea is therefore to measure spin of a biological prep containing receptors using an ESR spectrometer before and after adding a ligand. The difficulties are 1- ESR spectrometers are not that sensitive, they need at least 10*10 [10^{10}] spins to see a signal. 2- ESR machines do not like water which absorbs microwaves like mad, and the maximum volume of water tolerated by the machine is approx 100 microlitres. So you have to get 10*10 [10^{10}] spins in 100 microlitres.
>
> Assuming that binding of the ligand to the receptor frees up one electron [probably pessimistic] we need 10*10 [10^{10}] receptors in 100 microliters. We also want as little extraneous spin as possible, i.e. no melanin, no iron, etc. We decided to go for yeast. Yeasts come in two flavors, "a" and "alpha" and each type responds to the mating pheromone made by the other type. You can grow yeast to abt 10*7 [10^{7}] cells per 100 microliters, and each yeast cell has about 1000 receptors, which gets us in the right ballpark.
>
> But the most important thing is this: the receptor for the mating pheromone is a GPCR with all the downstream machinery fully functional. In fact you can replace the yeast's own receptor with any number of other GPCRs including

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[605] Hacking, Ian (1992): The Self-Vindication of the Laboratory Sciences, 29-65. In: *Science as Practice and Culture.* Ed. by A. Pickering. Chicago: University of Chicago Press, 29-64.

[606] Luca Turin in personal conversation.

> olfactory receptors and neurotransmitter receptors, and they mostly work fine. So if [huge if] we see a spin signal on receptor activation, we've shown that an early event in receptor activation involves electrons. No such thing should occur with lock and key.
>
> We'll know in the next month or so.
>
> All the best
> Luca”

Other possible experiments might involve studies of functional analysis explicitly based on the selection of vibration frequencies.[607] Since these experiments are all in preparation while this chapter is written, the results (and the reactions to such a study) have yet to be seen. Regardless of the future outcomes of this debate, favouring a shape-sensitive or a vibration-sensitive mechanism (or possibly a combination of both),[608] my analysis of current receptor modelling brought to the foreground that no sufficient basis exists at present to reject either model on purely empirical grounds.

The fact that the olfactory mechanism is currently only addressed by mediated modelling strategies within either theory does not necessitate abandoning hypotheses prematurely. Contemporary OR modelling has been shown to rely on the assumption of a background ontology shared with other molecular processes without its results, however, being assessable independently. Awareness thus needs to be directed to the implicit processes of “ontological blackboxing” – ontological assumptions obtaining normative force for the assessment of model-based inferences – through theory development and its impact on contemporary scientific judgement. The dependence of ontology on its historical role in theory development, if not backed up by further and independently accessible empirical resources, serves as a reasonable basis to doubt, but not a sufficient basis to reject an empirically viable alternative. In fact, the only unicorn grazing in this debate is the conviction that scientific judgement, strategies of evidence construction and model-based inferences are theory-neutral and, even more importantly, history-independent.

In conclusion, given the current experimental limits for OR modelling, the range of irregular SORs and the remaining ambiguity of theoretical interpretations, the strong focus on theory and model choice in the olfactory debate appears

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[607] Turin in personal conversation.

[608] Solov'yov, Ilia A.; Chang, Po-Yao and Schulten, Klaus (2012): Vibrationally assisted electron transfer mechanism of olfaction: myth or reality? *Physical Chemistry Chemical Physics* 14(40), 13861-13871.

counterproductive. Considering the historical development of both theories throughout the last century, it became clear that both theories exhibit the potential to further change and develop in response to new observations and objections. No theory has ever been born fully-fledged but has been subject to amendments of various degrees. A result of the continuous and iterative theoretical developments and changes, as one could see in the olfactory case, were “partial answers that modif[ied] the original aim of inquiry, tighten[ed] its focus, [… gave] rise to additional lines of research” and “yield[ed] an expansion of the domain”.[609] On that account, the modification of the underlying experimental and descriptive strategies went hand in hand with a reconfiguration of the theoretical frameworks. A healthy competition between the two rival frameworks, each having its own heuristic power, thereby carries the potential to capture further aspects of the molecular basis of smell that either were overlooked or require a better explanation than so far provided. An example of this is the recently published study on human sensory performance in distinguishing isotope variants by Gane et al. (2013),[610] which will be dealt with in more detail in the concluding chapter. Moreover, one does not even have to define the fertility of theory and model pluralism in terms of their competition, as there also can be fruitful interactions between the different explanations. A study by Solov'yov et al. (2012), for instance, suggested a combinatorial account of the two hypotheses, shape and vibration.[611] There is thus one conclusion to research be drawn, especially in light of the current empirical uncertainty about the mechanism of primary odour recognition: there is no sufficient reason why olfactory ought to work exclusively with one theory but, rather, there are many possible ways to go.

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[609] O’Malley et al. (2010).

[610] Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780.

[611] Solov'yov, Ilia A.; Chang, Po-Yao and Schulten, Klaus (2012): Vibrationally assisted electron transfer mechanism of olfaction: myth or reality? *Physical Chemistry Chemical Physics* 14(40), 13861-13871.

Concluding Chapter: *Comments on Concrete Things*

The Scientification of Scent: Philosophical Implications of Disodour

Understanding the nature of smell is an unresolved but largely neglected mystery of our time. Like gravitation, odours are ubiquitous. And like gravitation, we have no idea about what is truly at work here. Smell is a sensory phenomenon with a material basis. Carried by a huge diversity of volatile molecules and perceived under complex physiological conditions, its material basis is yet hard to determine. In fact, wider scientific interest in olfaction is fairly recent, and before groundbreaking genomic discoveries in the 1990s it constituted more of a niche subject throughout the 19th and 20th century. Yet, its relatively young disciplinary history presented it as a most fruitful case study for an integrated philosophical and historical approach to understand science. If the issues that have been addressed in the previous chapters have shown anything, it is that neither historical nor present research on the material basis of smell neatly fits the characteristics that some philosophers of science generally ascribe to the advancement of science. The general image of olfaction did not exhibit a linear progression or strong tendencies of unification (Part 1).[612] Even in more specific contexts such as research on molecular smell perception, the trajectory did not nicely respond to a rational reconstruction of scientific development, where the success of a research program is defined by criteria such as greater explanatory or predictive power and empirical adequacy (Part 2).[613]

Exploring the gradual "scientification" of smell, this thesis started out with a broadly defined approach to the historical roots of olfactory research. Analysing the diversity of material cultures that evolved around the study of odoriferous materials across the 19th and 20th century, my focus lay on the definitions of materiality that informed different classificatory practices. Instead of following a

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[612] Kitcher, Philip (1993): *The Advancement of Science : Science without Legend, Objectivity without Illusions: Science without Legend, Objectivity without Illusions.* Oxford: Oxford University Press.

[613] Lakatos, Imre (1970): Falsification and the Methodology of Scientific Research Programmes. In: *Criticism and the Growth of Knowledge.* Ed. by I. Lakatos and A. Musgrove. Cambridge: Cambridge University Press; Lakatos, Imre (1980): *The methodology of scientific research programmes: Vol. 1: Philosophical papers. Vol. 1.* Cambridge: Cambridge University Press.

linear trajectory, earlier research on smell started out from divergent conceptualisations of materiality, investigating odours as ‘objects found in nature’ and as ‘materials of production’ up to their transformation into ‘epistemic things’ (Chapter 1). Even the general turn to molecular structure did not result in a convergence or unification of these domains but olfactory research continued to disperse in several related yet independent directions (Chapter 2). The resulting diversity in the classification of odours into kinds like “musk” further corresponds with the application of general terms in other scientific practices, fostering the need for a more general but still contextual understanding of the meaning and reference of scientific terms (Chapter 3). Olfactory research was shown to consist of a mosaic of practices, comprising various academic disciplines such as plant science, fragrance chemistry, neurology, clinical medicine, psychophysics, and molecular biology as well as artisan and craft activities such as perfumery, spirits and food manufacture, horticulture and pharmacy. Each of those disciplines is independent yet overlaps through shared interests in the development of adequate technologies for measurement and standardisation, and efforts in providing informative descriptions and classifications of the materials and their sensory qualities. Olfaction, defined as a set of practices surrounding the systematic investigation of smells and the sense of smell, is thus a mixed bag.

Taking a pick out of this bag and exploring one experimental system that evolved around a specific line of olfactory enquiry in the second part of the thesis, scientific debate about the mechanism of primary odour recognition likewise resisted telling a classic story of scientific success. Issues concerning model thinking, inference and the concept of evidence surrounding an unresolved controversy between two rival olfactory theories posed interesting riddles for a philosophical understanding of the dynamics that underlie scientific development. Rather than empirical or epistemic support, the roots of the currently predominant support of the shape theory of odours over its rival, the vibration theory, were argued to be historical. Historicising scientific judgement, i.e. understanding its present focus through its disciplinary trajectory, brought two things to the foreground. First, it demonstrated the influence of disciplinary changes in background knowledge on what kinds of observation are taken as evidentially significant within contemporary discourse (Chapter 4). Second, in order to understand the evidential weight attributed to epistemic grounds in a scientific debate, it also emphasised the particular order of events in the trajectories of the rival theories (Chapter 5). Moving beyond an analysis of the historical reasoning that informs current judgement, attention was directed at the modelling strategies and techniques that inform scientific reasoning. After exploring the way in which the plurality of representational sources acts as an indicator for the truthfulness of our theoretical descriptions (Chapter 6), I exemplified the importance of model thinking in the two overlapping and salient experimental contexts in olfaction, fragrance chemistry and molecular biology. An exploration of the theoretical development of the two mechanisms through the construction of facts in evidence for (or against) the rival theories in fragrance chemistry emphasised the dynamic character of models. Illustrating the historical contingency of “facticity”, it stressed a flexible understanding of evidence in relation to the complexity and plurality of model relations (Chapter 7). An analysis of the methods employed in current receptor modelling further highlighted the extent to which interpretations of experimental practices are bound to existing ontological assumptions in order to be accepted as evidential (Chapter 8).

Although having the appearance of an ‘immature science’ – not only with respect to its disciplinary youth but also regarding the continuing issues of measurement, standardisation and conflicting theoretical explanations – olfaction, rather than starting from “scratch”, relied strongly on modelling strategies of parallel, more matured disciplines. Drawing analogies to other senses, for instance, was a common approach in olfactory classifications, and analogies to other molecular processes was integral to modelling the mechanism of primary odour recognition. These interdisciplinary influences persist down to today and, unlike Wittgenstein’s metaphor, olfaction theory has not discarded the ladder on which it moved up. Quite the contrary, current debate was shown to exhibit a conservative strategy to preserve what is considered normal olfactory practice and, moreover, normal scientific practice in general, in contrast to excessive speculation about “good vibrations”.[614] Nonetheless, underlying the olfactory controversy about the perception mechanism and the question of evidence is a broader problem that that resonates throughout the entire history of olfaction.

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[614] Leslie Vosshall compared the vibration theory to “unicorns” and went (strategically) even further by comparing Turin’s persistence with the creationists. Vosshall as cited in Schrader, Christopher (2013): Schwingungen in der Nase. *Süddeutsche Zeitung* 25 February, 16.

To Grasp A Sense So Rare: The Reality of *What?*

A striking motif throughout the history of olfaction is an ambiguous relationship with, and a fragile understanding of, the nature of smells. Smell is materially bound and research on smells pursued different lines of enquiry into its material basis. Nonetheless, although smells imply materiality, they are not reducible to the materials that carry them, and their sensory qualities refuse to correspond unequivocally with the molecular features of these materials. Unlike Kripkean identity statements of heat and light perhaps, it seems implausible to limit smell to molecular structures such as “the smell of fresh cut green grass is cis-3-hexenol” or, alternatively, “the smell of fresh cut green grass is receptor pattern XYZ”. Apart from the issue whether a quality-structure equation of an odour will tell you anything about experiencing that smell, such a statement fails to explain *what smell is*. The phenomenal features do not describe an accidental feature; these sensory qualities *are the phenomenon of smell.* Therefore, in addition to structural irregularities and experimental difficulties with unruly materials in the laboratories, there is another factor that makes it difficult to comprehend the nature of smells, namely the ambiguous “scientification” of their sensory nature.

Contemporary practices still struggle to present standardised methods and unambiguous criteria for determining odour quality, for instance in the case of odour profiling (Chapter 2). Difficulties posed by the lack of standardisation and, furthermore, the unreliability of sensory responses for a systematic comparison of odour quality led to the conclusion that behavioural performance studies on odour identification and discrimination cannot be used as evidence for hypotheses about the molecular perception mechanism, only ‘molecular data’ on the OR proteins can (Chapter 8). The emerging scientification of scent thereby led to a paradoxical situation in some domains of olfaction: since the phenomenological nature of smells does not comply with the scientific methods available, its sensory characteristics are excluded from providing evidence for research on smell recognition. In other words, research on smell perception without the perception of smells. This attitude, like some philosophical arguments for essentialism and reductionism, aims at a fundamental level of reality defined by the ontological priority of some undisclosed microstructure over mere phenomenological appearances. This tendency is problematic, because it precludes the very nature of the phenomenon it tries to explain. But how, then, is the nature of smell to be conceived?

Concerning the phenomenal nature of smell, some odours form distinct and separate classes whilst others do not. The smell of coffee is clearly distinguishable from the smell of sulphur, violets or grass. Looking at other smell types such as lemon, orange and grapefruit, their qualities only gradually differ while falling under a general label such as “citrus”. And what about the odour of structurally different odorants of the same class (such as nitro-musks, polycyclic musks, macrocyclic musks and alicyclic musks), whose subtle differences require a highly trained nose?[615] Any scientific practice surrounding odours and their materials must thus address the often ambiguous, gradual, overlapping and complex characteristics of odour quality. The taxonomic diversity in odour classifications, I argued, is not simply a matter of subjectivity and flawed or scientifically pre-mature classifications but, rather, it reflects the complex nature of smells (Chapter 1 and 2). Therefore, instead of denying the multifaceted nature of a phenomenon and the resulting demand for a plurality of scientific approaches, this diversity should inform our understanding of nature and its various kinds and, consequently the interpretation and application of scientific concepts to describe these kinds (Chapter 3).

Investigating odours, whose nature comprises both molecular as well as phenomenal features, as natural kinds (Chapter 2) might raise philosophical objections similar to the reluctance of some scientists to accept sensory responses as empirical evidence. Odours seem not exactly the most reliable or objectively measurable sensation. But why? Despite their ephemeral character that (ironically) seems to be easier to capture in vials than in words, they nevertheless imply a form of physical concreteness and materiality. Odours present something like “comments on concrete things: people, things, places,

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[615] For an untrained nose they may all just be musks, for a perfumer (and an entire billion dollar industry) their subtle quality differences matter. Consider the possible ban of one main ingredient of Chanel No.5 in the EU, which led to an outrage in perfumery – even using a similar ingredient as a substitute, it is protested, would change the entire composition and. As a result, the signature scent of No.5 would no longer exist. See: Wendlandt, Astrid (2012): Exclusive: Perfume-makers fear EU legal blow to industry. *Reuters* (31 October 2012). URL=<http://www.reuters.com/article/2012/10/31/us-luxury-perfumes-eu-idUSBRE89U1CC2012103>; Hsu, Tiffany (2012): Chanel No. 5 ban in Europe, edible perfume, sushi cologne. *Los Angeles Times* (12 November 2012). URL=<http://articles.latimes.com/2012/nov/07/business/la-fi-mo-chanel-perfume-edible-sushi-cologne-20121107>; Laurance, Jeremy (2013): Fashion houses' defence of toxic perfume has whiff of inaccuracy, says top scientist. *Independent* (15 February 2013). URL=<http://www.independent.co.uk/life-style/fashion/news/fashion-houses-defence-of-toxic-perfume-has-whiff-of-inaccuracy-says-top-scientist-8305054.html> (accessed 28 February 2013)

situations. (…) Olfactory perception always triggers a sense of physical presence (…).”[616] Perfumers are masters in the art of manipulating these olfactory perceptions of physical presence by creating and bottling concrete sensory illusions of something that isn’t actually there: artfully conjuring the appearance of freshly washed white linen, chocolate, freshly mown hay or lemon trees. Achieving such powerful sensory images, practitioners such as Jean-Claude Ellena employ a variety of materials that, taken individually, seem to bear no relation to the created overall effect:[617]

> “*In this summary I have reduced smells to the level of signs. This is how smells, such as amber, cherry or jasmine, are achieved using a minimum of juxtaposed materials. Taken separately, the materials smell nothing like the subject headings I give*. (…)
>
> “APPLES
> *A colourful basket of apples.*
>
> GREEN APPLES
> fructone
> benzyl acetate
> cis-3 hexenol
>
> YELLOW APPLES
> fructone
> hexyl acetate
> benzyl acetate
>
> RED APPLES
> fructone
> allyl caproate
> hexyl acetate”
>
> “GRAPEFRUIT
> *If there is one disappointment for perfumers, it must be grapefruit because, although it has its own essence, this essence smells of oranges. Fortunately, our arsenal includes sufficient artifice to satisfy the enthusiast.*
> sweet orange (essence)
> rhubofix”
>
> “LILY
> *Lilies ‘announce’! In the fifteenth century many paintings by Italian masters depicted the angel Gabriel handing lilies to Mary as he announces that she is to be a mother. The choice of lilies is never made innocently. Their shape and colour are symbolic, but their smell also contributes to their symbolism.*
> benzyl salicylate
> phenyl ethyl alcohol
> methyl anthranilate
> *Depending on botanic varieties, you can add linaool, indole or geraniol.*”

Ellena’s compendium creates the olfactory impression of something physical

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[616] Jellinek, J.S. (1991): Odours and Perfumes as a System of Signs. In: *Perfumes: art, science, and technology.* Ed. by M. Müller and D. Lamparsky. Glasgow: Chapman & Hall, 59.

[617] Ellena, Jean-Claude (2012): *The Diary of a Nose. A Year in the Life of a Perfumer.* London: Particular Books (Penguin Group), Appendix.

without the occurrence of the materials associated. These impressions exhibit a striking precision. Consider the lilies, whose olfactory recreations are subtle to the extent that they even refer to species specific odiferous differences of botanic varieties. So what is the element of unreality here? Noses may not be deceived in what is perceived but we seem confounded about what material we think creates this perception. There is, I think, a pervasive impression that odours act as "indicators of the essence of things",[618] meaning that when we smell something, this smell *should* tell us what is *really* there. The absence thereof and the resulting sense of unreality, however, springs from the nature of the perception process and, not without a trace of irony, its materiality. Because when we are

> "smelling something, we are touching it, there is the direct contact between the molecules of what we smell and our receptors. In such an intimate encounter, there is no room for deception."[619]

The judgement that smells are deceptive and convey an element of unreality only makes sense if we assume that the underlying correspondence relation between the materials causing smells and the smells perceived is understood semantically: is it a deception when I smell 'green apple' without green apples being present? If it was not for a semantic interpretation, playful impressions such as Ellena's odour puzzles might be considered 'inventions' rather than 'deceptions'. Enforcing the implicit "semantic fallacy" of smell perception, we also seem to lack an adequate language to describe odours, often relapsing into object-related associations or comparisons to other sensory qualities, even in the vocabulary of perfumers (e.g. a green note scent). Nonetheless, our inability to adequately describe and unambiguously identify smells as well as other sensory impressions such as vision again resides in the nature of the perception process. Explanations why it is harder for the untrained nose to analyse and break down single smell components and why, further clouding objective descriptions, emotional reactions sometimes piggyback on smell experiences, are found in the particular material conditions of olfactory processing:

> "[t]he fact that odour perception is based on material, molecular contact […] lends to olfaction, along with taste and touch, a very concrete quality. In somewhat simplified terms, this quality is further emphasised in the processing

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[618] Jellinek (1991): *Odours as a System of Signs*, 58.
[619] Ibid., 58.

> of the various sensory inputs in the brain: while the neurones of the visual and the auditory system lead to the cortex, the seat of abstract reasoning and analysis, the neurones of the olfactory system first lead to the hypothalamus, to the primitive part of the brain which responds to inputs in their totality rather than analysing them; it is also the part which directly controls the hormonal system that affects our moods and feelings."[620]

A lot of the difficulties that seem to impede research on olfaction are thus not mere technical issues but elucidate the very characteristics of smell that seem not to respond well to our available methods, such as the problem of ambiguity in smell perception, the lack of analytic language and the huge qualitative and structural heterogeneity of the perceived materials. Scientific understanding of smell, therefore, must take a multiplicity of factors into account, ranging from the different processual stages and physical conditions of smell perception to the chemical complexity of materials.

The Lure of The Discontinuous

Given the complexity of smell and the difficulties involved in measuring its qualitative aspects, the preclusion of sensory performance studies from research on the primary perception mechanism is understandable but nevertheless unjustified. For purposes of theory assessment, the fundamental issue at work here is between what is considered to be adequate empirical support for a model of the primary mechanism and what is not. Responses to the latest study supporting a vibration sensing mechanism in olfaction[621] were widely uniform: these tests only addressed inferences drawn from a hypothetical model (do isotopes smell the same?) but not the mechanism (do we smell molecular vibrations?). For this reason, Richard Axel concluded:

> "[u]ntil somebody really sits down and seriously addresses the mechanism and not inferences from the mechanism… it does not seem a useful endeavour to use behavioural responses as an argument. […] Do not get me wrong, I'm not writing off this theory, but I need data and it has not been presented."[622]

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[620] Ibid., 59.

[621] Gane, S.; Georganakis, D.; Maniati, K.; Vamvakias, M.; Ragoussis, N. et al. (2013): Molecular Vibration-Sensing Component in Human Olfaction. *PLoS ONE* 8(1), e55780.

[622] Richard Axel as quoted in Palmer, Jason (2013): 'Quantum smell' idea gains ground. *BBC News Science & Environment* (28 January 2013) URL=<http://www.bbc.co.uk/news/science-environment-21150046>

Given the lack of empirical insight into the molecular structure of the protein binding site, however, sensory performance studies currently present one of the few experiments that allow for empirical hypothesis testing. Thus, although I agree with Axel that the theoretical model of the vibration-sensing mechanism needs to be linked to experiments on ORs, I do not agree with him that behavioural studies do not present any considerable data at all, especially since neither mechanism can currently be substantiated through molecular protein studies (Chapter 8). Sensory response studies may not present conclusive proof of what precisely is at work on the molecular level, but they do lead to findings that may require further thought about what is assumed to be at work on the molecular level. Let me explain this by taking a closer look at the study that caused Axel's comment.

This study by Turin and the team of Gane et al. was a response to an earlier study by Keller and Vosshall, the only experimental study that presented a challenge to the revived vibration theory of odours. Keller and Vosshall showed that a panel of (untrained) subjects was unable to distinguish between isotopes that have little difference in their vibrational spectrum (deuterated acetophenone).[623] A repetition of their study by Gane et al. led to the same result. In reply to this negative finding, Turin considered the option that the difference in frequency between the isotopes might be too weak to result in an odoriferous difference strong enough to be perceived. To test this explanation, the team specifically designed a musk molecule with enhanced features (deuterated cyclopentadecanone). These isotopes contained more hydrogen and deuterium bonds that, if Turin's assumption about the nature of isotope perception is right, must surely result in a perceivable odour difference. The assumption turned out to be supported by the experimental results: people in this study were able to tell the isotopes apart. (In fact, neither the experimenter nor the (trained) test subjects were informed about the nature of the samples.)

In addition to Axel's judgement that this study is no proof for assumptions about a vibration-sensing mechanism, another reply pointed to an apparent inconsistency, which is the really interesting issue, I believe:

> "[t]hat's all well and good, says Eric Block, professor of chemistry at the University at Albany in New York State. But, he says, it hardly proves the vibration theory, which faces some contrary evidence. For one, he points out

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[623] Keller, Andreas and Vosshall, Leslie B. (2004): A psychophysical test of the vibration theory olfaction. *Nature Neuroscience* 7, 337-338.

> that Turin once claimed humans, like drosophilia, could sniff out a deuterated version of the molecule acetophenone from the regular stuff, yet in 2004 *Nature Neuroscience* published a contrary claim, that human noses can't smell the presence of deuterium in acetophenone (*…*). And, Turin himself says in his new paper that he has confirmed the negative 2004 finding, although he thinks he has an explanation for the failure: deuterated acetophenone has relatively few deuteriums in it and thus may generate a weak vibrational signal that is too weak for humans to detect. *Block says Turin can't have it both ways: either noses can smell deuterium or they can't.*"[624]

Block claims Turin cannot have it both ways. But why can't he? Examinations of sensory responses, like most measures of human performance, present a continuous variable. This is what makes them so difficult to evaluate and methodological reflections of measurement so indispensible. Yet, unlike Axel, Block's issue with this study is not methodological but bottom-line ontological. The question emerging from Turin's experiment is not if we detect differences between isotopes per se, but under what conditions are these differences detected. Block's objection that Turin cannot have it both ways reveals the conviction that either we must detect an odour difference in *all* deuterated versions of molecules or we detect *none at all*.[625] This, however, only makes sense if sensory responses were to act like a mechanistic version of a binary code – with a 0 for no response and a 1 for activation. There is no empirical reason or observation, however, suggesting that receptors cannot act selectively to specific factors such as, in this case, strengths of vibration frequency. Quite the contrary, an explanation of irregularities by reference to feature selectivity also takes place within the shape theory. The perception of only one odour quality despite the presence of two competing and distinct functional groups, for instance, is explained by the selection of one stereochemical feature that is favoured, for instance, by its position in the molecule (Chapter 7).[626]

Nonetheless, Turin's assumption differs fundamentally from the shape theory. Considering the latter's explanation of feature selectivity, the unperceived

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[624] Anderson, Mark (2013): Study Bolsters Quantum Vibration Scent Theory. *Scientific American* (28 January 2013). URL=<http://www.scientificamerican.com/article.cfm?id=study-bolsters-quantum-vibration-scent-theory&page=1> [Italics mine]

[625] Turin's initial assumption that, like fruit flies, humans should detect an odour difference between acetophenones may just be seen as a premature assumption that turned out to be wrong.

[626] Klopping, H.L. (1971): Olfactory theories and the odors of small molecules. *J Agric Food Chem* 19, 1001.

functional group would have been definitely detected if it were not for the presence of a stronger competing functional group. In Turin's account, there is no competing factor involved but the undetected feature is simply not strong enough. Turin's explanation, therefore, implies that olfactory molecular recognition might be a gradual phenomenon. On this account, the recognition process does not only depend on particular features being present but, moreover, it requires a minimum strength of the key feature to be recognised. This implication stands in direct conflict with the shape theory of odours. If olfactory molecular recognition were gradual, the explanation of isosteric molecules within the shape theory would not make any sense. Isosteric molecules are structurally similar with only minor conformational differences but quite distinct smells (Chapter 7). There is thus no possibility of a gradual odour detection from structurally similar odorants in SORs explanations of the shape theory. As a result, the rivalry of the olfactory mechanisms does not only present a fundamental ontological disagreement regarding the causal *structure* underlying molecular recognition in biology but, moreover, it presents an emerging ontological conflict concerning the nature of the causal *process* of molecular smell perception in particular: its potentially gradual character.

Whether or not Turin's new study presents significant proof for the presence of a vibration-sensitive mechanism is therefore one issue. (As long as there's no experimental link to the GCPRs, it does not.) The other issue is that this study presents sensory results that require a molecular explanation.[627] Although this phenomenon of selective isotope perception does not depend on Turin's proposed causal explanation (there may be another reason), it nevertheless allows for a supportive interpretation. The scientifically relevant question is thus how these results are explained under the premise of a shape-sensitive mechanism. There are two possible responses. The first is a molecular explanation for shape yet to be given. The other is to reject behavioural studies as interesting but unreliable. It seems that the latter is the one currently adopted. Considering the emerging ontological implications of this study, I find this response unsatisfactory. Under the premise of shape, it is assumed that our noses categorically do or do not perceive a structural feature (unless it is overpowered by a competing factor). Yet, if our experience of smelling

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[627] Whether these results need further confirmation through repeated studies is again a methodological issue.

something does not match this premise, it seems that it is not the theoretical assumption that is questioned but the reliability of this perception and our methods of measurement. Given the sensory nature of smell and the lack of insight into the molecular dimension of smell perception, this is a questionable choice to make. Evidential primacy of molecular data for judging hypotheses about the mechanism of primary odour recognition should not lead to overlooking other non-molecular data that require a better molecular explanation than the one that is currently adopted.

Complementary Science and Historicising Scientific Reality: An Argument for Pluralism

Acknowledging the unpredictability of future developments, it is crucial to thoroughly analyse the directives that guide the present olfactory debate, as its future is something that is constantly produced by the practitioners. And it is here, at the intersection of fundamental experimental, technological and conceptually driven choices that an integrated historical and philosophical approach benefits scientific debate. Pursuing what Hasok Chang advocates as "complementary science", the aim is to accompany scientific practice in an attentive yet critical fashion by addressing

> "[…] scientific questions that are excluded from current specialist science. It begins by re-examining the obvious, by asking why we accept the basic truths of science that have become educated common sense. Because many things are protected from questioning and criticism in specialist science, its demonstrated effectiveness is also unavoidably accompanied by a degree of dogmatism and a narrowness of focus that can actually result in a loss of knowledge. History and philosophy of science in its "complementary" mode can ameliorate this situation […]."[628]

As part of such a program, this thesis carried out a complementary analysis of scientific development by exploring contemporary issues in olfaction theory through their historical roots. Investigating the background and systematically analysing the arguments made for both olfactory theory developments casts an alternative light on the present olfactory discourse. Rather than empirical or

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[628] Chang, Hasok (2004): *Inventing Temperature. Measurement and Scientific Progress.* Oxford: Oxford University Press, 3.

epistemological, the basis on which current debate is held rests strongly on historically determined disciplinary grounds. A variety of the arguments made for the rejection of the revived vibration theory were further shown to be no longer valid.

Whatever future turns may shape the course of olfaction theory, the present debate might present the first cracks in a uniform theoretical image of molecular processes. Questioning the broader understanding of molecular recognition, the model of a vibration-sensing olfactory mechanism may very well turn out to be fictitious but its current persistence is an indicator of emerging problems in the traditional approach of explaining ligand binding through a shape-selective mechanism. With increasing insight into the functional plasticity of binding surfaces and the evolvability of recognition sites in receptor proteins, the complexity underlying molecular interactions resists falling under the orthodox structure-function paradigm. For these reasons, the growing demand for alternative explanations in parallel with the conservation of established explanatory models, results in a rapidly developing but internally inconsistent scientific discourse surrounding the nature of molecular recognition.

The importance of olfaction theory and its advancement thus reaches farther than to the end of our nose. As a young but advancing model system, the olfactory mechanism with its peculiarities and specificities is expected to facilitate further knowledge about the characteristics and behaviour of other molecular processes.[629] Although knowledge of other molecular processes is more advanced than knowledge of the olfactory mechanism, there also remain a variety of unresolved issues concerning irregular structure-function relations. Whether an interdisciplinary influence of olfactory research will strengthen or cause a rift in the broader inter-theoretic image of molecular processes, of course, needs to be seen. Theoretical changes in the olfactory community, however, are slowly emerging. For instance, Klaus Schulten, a previous vibration sceptic, and his team recently suggested the possibility of a combinatorial olfactory mechanism that includes features of both shape *and* vibration.[630] Other studies further support the possible involvement of quantum-

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[629] Stuart Firestein in an interview with big think (2010): *The Importance of Olfaction Beyond Smell.* URL=< http://bigthink.com/videos/the-importance-of-olfaction-beyond-smell>

[630] Solov'yov, Ilia A.; Chang, Po-Yao and Schulten, Klaus (2012): Vibrationally assisted electron transfer mechanism of olfaction: myth or reality? *Physical Chemistry Chemical Physics* 14(40), 13861-13871.

based processes in olfactory responses.[631] A third tendency is to refer to an alternative, electrochemical approach that might either surpass or complement shape or vibration.[632]

For this reason, complementary work on the developmental character of knowledge production and the impact of disciplinary history in olfaction might transform or at least inform the course of the present debate. Attention to the entrenchment of theoretical assumptions in data interpretation displayed the extent to which ontological premises about the nature of a phenomenon become an integral and often unquestioned part of theory and model assessment. The dynamics underlying the entrenchment and fixture of ontological assumptions throughout disciplinary trajectories, therefore, deserve further thought and are of more than "just" historical interest. This is not only because they explain why a particular theoretical account is favoured at a specific time, but also because these dynamics have an impact on subsequent decisions of theory or model choices. A vivid example was Block's response to Turin's explanation of isotope perception. Block first relied on an assumption about how the recognition mechanism acts (noses recognise a key structural trait as a distinct smell or not) and then used this assumption to reject an alternative explanation (we perceive an odour caused by a structural trait only if the trait is strong enough) without, however, having sufficient insight into the perception mechanism to justify his primary assumption as a valid criterion for theory assessment. A judgement like this puts the cart before the horse.

Scientific discourse, therefore, requires sensitivity to such an implicit "blackboxing" of ontological assumptions in research practice. Yet such sensitivity may exceed the available time, resources and responsibility of many practitioners. Scientific practice, on the one hand, rests on the acceptance of many theoretical assumptions, technological procedures and data interpretations which, while once in dispute, are now accepted and established as standard. As a stable and reproducible apparatus, these models and methods are "used as foundations or tools for studying other things".[633] Having seen the pragmatic success of the lock and key model for olfactory research through most of the 20th century and the heuristic role of shape-based

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[631] Bittner, Eric R.; Madalan, Adrian; Czader, Arkadiuz and Roman, Gregg (2012): Quantum origins of molecular recognition and olfaction in drosophila. *arXiv preprint arXiv:1207.2796*

[632] Kovacic, Peter (2012): Mechanism of smell: electrochemistry, receptors and cell signaling. *Journal of Electrostatics* 70(1), 1-6.

[633] Chang (2004): *Inventing Temperature*, 237.

explanations in hypothetical receptor modelling today, a variety of effective scientific practices are organised around a relatively stable theoretical framework that allows for the development of further models and explanations. On the other hand, scientific discourse is not free of social hierarchies, peer pressure and the reputational prospect that comes along with pursuing more or less "respectable" ideas. These, what Miriam Solomon calls, "non-empirical decision vectors" in theory choice likewise inform scientific consensus and, as a result, the distribution of judgement.[634] "And although many more scientists are taking the vibrational theory seriously than back in 1996, it remains an extraordinarily polarised debate. "He's had some peripheral support, but... people do not want to line up behind Luca," Prof Jacob said. "It's scientific suicide."'"[635]

A complementary approach to scientific discourse is not affected by the same restrictions as the scientific research community. Alternative lines of enquiry and theoretical directions that seem outdated or too fanciful for the practicing specialist can nevertheless render great service to science. Unimpressed by the orthodox consensus, a critical picture of a scientific issue through complementary analysis can carve out the inconsistencies in and evidential grounds of a debate such as the olfactory one. This, of course, requires careful consideration of and attention to the specific modelling strategies and technologies employed across historical as well as present research practice. Analysis of the competing theoretical explanations must thus focus more on the applications rather than the retrospectively fixed facticity of their classifications, models and methods. For this reason, in this thesis a lot of consideration was given to detailed and technical aspects of classifying and modelling the material basis of odours. In order to analyse and evaluate the ways in which practitioners aim to explore and interpret the nature of smell, I therefore focussed on the various representational practices that shaped olfactory research 'through the ages'. This focus on representations not only allowed the tracing of the conceptual assumptions and manipulations informing different scientific understandings of smell and smell perception. Representations also

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[634] Solomon, Miriam (2008): Norms of Dissent. London School of Economics. *Centre for the Philosophy of Natural and Social Science Contingency and Dissent in Science Technical Report* 09/08. URL=<http://www2.lse.ac.uk/CPNSS/projects/CoreResearchProjects/ContingencyDissentInScience/DP/SolomonNormsOfDissent0908Online.pdf>, 6.

[635] Palmer (2013): *Quantum smell*.

served as graphic reflections on the underlying scientific development, presenting its continuities and discontinuities.

For my preferred account of “representation” I analysed the representational capacity of scientific representations by means of two intertwined questions: *how* and *why* is a representation used to represent its intended target system? First, in order to understand *how* a representation is used, I argued for abandoning a dyadic approach of linking representations to the world by criteria such as structural resemblance. Instead, attention was directed at the representation’s *epistemic* role within a network of different investigative methods, models, experiments and technologies surrounding an experimental context. Second, in order to understand *why* a representation is used, I proposed to analyse the *historical* conditions that underlie model building and development. By historicising model thinking, the interpretation of data and the legitimacy of model-based inferences were shown to be grounded in the ongoing development of research trajectories.

In light of this, the account of representation, which I developed throughout this thesis, articulated a conception of scientific practice that is defined through a historically mediated relation between conceptual interpretations and material interventions. As an integral part of scientific practice, representation was characterised as an epistemic activity that embodied various forms of action, ranging form the stipulation of potentially significant properties and correlations between materials and the systematic formation of research questions, to the design of experiments that explore particular hypotheses. A variety of models, maps, diagrams, lists, classificatory circles and tables, etc. were each shown to suit different purposes and to spur different kinds of enquiry into the nature of the research materials. Thus, if there is any theme that unites these heterogeneous ways in which something can be understood to represent, then activity is a good candidate.

Arguments for defining representations in terms of their use and as an epistemic activity have been increasing in recent philosophical debate. Abandoning the idea of a dyadic relation between a representation and the world, most of these approaches focussed on notions of agency attributed to the modeller and that underlie the construction process.[636] For instance, abstraction, rather than a property of a representation, was considered to be an intentional activity of the modeller that becomes manifested in a model and its application.[637] The application of a model was defined by its capacity to generate inferences about an intended target system.[638] I find this approach insightful as it has elucidated a variety of problems arising from a dyadic understanding of representations that excludes the intentions and activities underlying representational practices, especially scientific ones. Yet something was missing from these studies. Despite stressing the need to understand representations as an epistemic activity, they neglected two important conditions under which representing as an epistemic activity takes place. These conditions are the plurality and the historicity of representational practices.

First, why is pluralism a condition of representation? The reason for this is that only through pluralism can we explain how novelties are introduced into a representational context such as an experimental system. There is only so much one can do with a single model, and some of the inferences drawn are consequences of the theoretical assumptions that entered the model building process. If it were merely a relation between one representation and its target system, scientific practices such as modelling and classifying would become highly repetitivein their outcomes. But representations and the people who use them to gain insight into the nature of a phenomenon do not act in a vacuum. First, the construction of a representation, whether it be a model a map or a picture, is not something that can be done in isolation. As I have shown with the example of olfaction theory, any form of classification and model building is embedded in a disciplinary context with its already established methods and practices from which it draws criteria to arrange materials or form concepts under which these materials are investigated. Second, by relating a representation to others, the different representations form an interactive network to which each representation contributes. Since each model has its own limits and potential, it can relate to each other in ways that are specific and distinct, forming competitive, cooperative or complementary links. On this

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[636] Knuuttila, Tarja (2005): *Models as epistemic artefacts: Toward a non-representationalist account of scientific representation.* University of Helsinki, Faculty of Arts, Department of Philosophy. Doctoral Dissertation. URL=< https://helda.helsinki.fi/handle/10138/19380>

[637] Leonelli, Sabina (2008): Performing abstraction: Two ways of modelling arabidopsis thaliana. *Biology and Philosophy* 23(4), 509-528.

[638] Suárez, M. (2004). An Inferential Conception of Scientific Representation. *Philosophy of Science, 71*, 767-779.

account, representations create an epistemic space together with other scientific practices such as experimentation, measurement etc., in which the scientist as actor can fruitfully engage with the research materials.

The introduction of novelty through representational plurality into a scientific discourse is facilitated by the variety of ways in which multiple representations can relate and enter a discourse. Whereas some representations form 'harmonious' relations, such as in the case of the different practices in current hypothetical receptor modelling, others create tension, for instance in the case of the rival mechanisms and the different interpretations of isotope studies. By acting in concert, presenting harmonies and discords, representations create epistemically fruitful interactions that allow thinking "representatively" about a phenomenon under investigation. On this account, thinking representatively means to create a number of different perspectives through a variety of related representational practices. The epistemic space established thereby then calls for actions to compare, adapt, modify or alter the individual representations employed in it and, in turn, to develop and change the scientific discourse that takes place.

As a manifestation of plurality, representation becomes unpredictable to a certain extent. Unpredictability is necessary to make the introduction of novelties and the discovery of anomalies possible. As each representation and its application makes possible different processes of interpretation, it enters into an inextricable entanglement of actions and events in an experimental system to which other representational practices contribute. The result of this entanglement is that the research results can never be predicted from the interpretation of a particular model, and no particular model can control the final trajectory of an experimental system.

This leads me to the second necessary condition of representation, namely historicity. As a consequence of their entanglement, it is not always certain what the application of representations will reveal about a phenomenon or how these revelations are correctly to be understood. Only retrospectively, that is, only through the disciplinary trajectory that will arise from the continuous scientific activities and their products will the capacity of a representation to investigate a phenomenon become manifest. A retrospective, however, is not given in advance. It arises gradually from the performances and interpretations of the researchers within a scientific discourse defined by a plurality of methods, interests and materials. Why particular representations such as models gain greater credibility than others then depends on their productive role within such a discourse. In the case of the olfactory mechanism, the shape-sensitive model, for instance, received a lot of support from its constitutive role and continuous participation with other models and techniques in olfaction theory as an emerging experimental system (but also in the more general context of molecular biology). The weaving of a narrative under which the interpretation of representations takes place, therefore, is partly constitutive of their meaning within a scientific discourse, because it enables the retrospective articulation of their significance.

Yet, a scientific debate such as the olfactory one might also run a course in which the preferred narrative of the scientists results in judgments that are determinant of representational practices without, however, being sufficiently justified by the actual outcomes of these practices. The criterion for deciding whether a representation is adequate to its target system often reflects the *sensus communis* of a particular research culture. A critical exposition of the *sensus communis* through complementary science contributes to scientific discourse by providing a parallel narrative that highlights the extent to which the preferred narrative of the scientists might or might not have correlated with the trajectory of historical and contemporary practices.

To provide such a complementary narrative, attention has to be directed at the multiple practices underlying a particular discourse and the course of events that formed its trajectory. A complementary approach presents a standpoint from the present that looks back to what has happened. By reconstructing and analysing the ways in which representational practices interact and inform each other, it is possible to analyse the gradually evolving epistemic space in which contemporary scientific judgement takes place. The role of the philosopher and historian as a complementary scientist is thus crucial not only for the preservation of knowledge, but also for a better disclosure of the conditions, limits and potential of a scientific debate.

What my complementary narrative of olfaction theory contributed was to elucidate the historical conditions under which current scientific judgement is based and, furthermore, to demonstrate the limitations for further progress in this debate posed by an emphasis on theory and model choice in an exclusive sense. Not only did this thesis illustrate the merits of each rival theory with its proposed mechanism, but it also pointed out that it is better to entertain alternative models and theories rather than just to maintain the currently predominant one. Especially with respect to the reactions to the recent isotope perception studies discussed above it became clear that the revival and persistence of the vibration theory started to affect the standard model. First, its endurance in parallel with the standard account highlighted the latter's persistent problems in accommodating a wide range of molecular data. Instead of being explained as data whose correct interpretation is yet lacking a fuller picture of the perception mechanism, the revived vibration theory questioned the grounds on which these explanations as post hoc adjustments were justified. Second, only through the competitive interaction between vibration and shape did the latest results derived from the isotope study point at hitherto overlooked data that require a better molecular explanation than the one that is currently adopted. With respect to the general philosophical and scientific debate, the arguments provided through a complementary narrative thereby not only showed *that* a pluralist perspective on scientific practice is required but it also demonstrated *why* a pluralist perspective is beneficial.

The historical variability of knowledge that becomes manifest through such a complementary perspective might first appear as an erosion of a realist interpretation of scientific practice. But this would be a short-sighted view. Concerning the complementary perspective on olfaction theory that I developed in this thesis, judgements about what constitutes the nature of odours were grounded in different contextual practices and developing methods that gave rise to multiple and often equally valid ways to understand the material basis of smell and smell perception. The historical mutability of these judgements through a changeable, evolving and advancing experimental environment was shown to be not a flaw but the very character of science, and the historicity of scientific practice does not pose a problem for scientific realism, only its denial does. The realism question can take different forms within different research contexts, even for contexts that concern largely the same range of materials. Accepting different aspects of mutability integral to scientific practice, namely the mutability of nature, scientific development, and scientific judgment, requires a flexible and pluricentric perspective on representational activities such as model-based inferences and the assessment whether and when the theoretical descriptions provided by representations tell us anything about the world.

Representing in scientific practice, therefore, is inevitably a pluralistic and historical activity. Moreover, the pluralist character of representing, in addition to the empirical and epistemological advantages it provides, was shown to be a direct philosophical consequence of the historicity of scientific practice.

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