

The Role of Normal Development in Experimental Embryology

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## **Abstract**

This thesis presents an examination of the notion of ‘normal development’ and its role in biological research. It centres on a detailed historical analysis of the experimental embryological work of the American biologist Edmund Beecher Wilson in the early-1890s. Normal development is a fundamental concept in biology, which underpins and facilitates experimental work investigating the processes of organismal development. Concepts of the normal and normality in biology (and medicine) have been fruitfully examined by philosophers. Yet, despite being constantly used and invoked by developmental biologists, the concept of normal development has not been subject to substantial philosophical attention. In this thesis I analyse how the concept of normal development is produced and used in experimental systems, and use this analysis to probe its theoretical and methodological significance. I focus on normal development as a technical condition in experimental practice. In doing so I highlight the work that is required to create and sustain both it and the work that it enables.

Variation between embryos can cause problems for scientists trying to produce valid and comparable results. In my study of Wilson’s work, I examine how the practices associated with normal development deal with the variation between embryos. In the 1890s, Wilson became increasingly interested in which causes were responsible for the processes of differentiation (the production of different cells and organs) and determination in the process of embryonic development. He performed a series of experiments on the marine invertebrate *Amphioxus*, which exhibits considerable variability in early development (Wilson, 1893a). Wilson carefully observed his samples and outlined a normal development based on them, which included a considerable range of variation. How Wilson treated variation was reflected in the different way in which he conceived of the process of development compared to other prominent embryologists, such as Hans Driesch and Wilhelm Roux.

Having introduced and assessed normal development, I use two analytical approaches to make further sense of it. Furthermore, these approaches identify why appreciating the role of normal development enables us to understand important aspects of scientific practice, such as experimental methodology and making causal attributions based on the results of experimental manipulations. The two main analytical approaches I use are James Woodward's manipulationist theory of causation (Woodward, 2003 and 2010), and Hans-Jörg Rheinberger's experimental systems approach (Rheinberger, 1997). The former assesses the factors involved in assessing proposed causal factors, rather than simply demarcating between causes and non-causes. The latter focuses on the way experimental set-ups are configured by scientists in ongoing series of experiments to frame phenomena of interest: "epistemic objects".

My analysis establishes the centrality of the concept of normal development to the way experimental systems are produced and reproduced, and to how attributions of causality which arise from experimental work are made.

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## **Introduction**

The concept of normal development is central to experimental work in developmental biology. It provides researchers with standardised controls, against which the results of experimental manipulations can be compared. It is at the heart of developmental biology. But it is a concept that remains hidden in plain sight, for biologists and philosophers alike. I aim to find out how normal development is produced, distributed, and used, and what the implications are of how it is produced and used.

In this introduction, I provide some background on how philosophers and biologists have analysed and interpreted the normal – and normal development – in biology. Following this, I detail why focusing on normal development provides a valuable way of understanding key features of scientific practice in experimental biology, and I touch on two of the accounts I will use to help me do this. I then detail the methodological aspects of my thesis, clarifying the nature of my integrated history and philosophy of science (HPS) approach, which centres on practice, on how normal development is generated and put to work by scientists. Central to my thesis is my case study on the early experimental embryology work of Edmund Beecher Wilson (1856-1939), and I outline what role that has in the thesis in the methodology section. Finally, I provide a plan of the thesis.

The concept of normal development (including related terms) is frequently invoked by biologists, in one form or another. Despite this, definitions of it are rare. Jonathan Slack is one of the few developmental biologists to actually define it. He defined normal development as “the course of development which a typical embryo follows when it is free from experimental disturbance.” Normal development, thus defined, “must not be confused with pathways of development which give a normal outcome” (Slack 1983, 11).

Slack’s definition is interesting because of its rarity, but also because it misrepresents the ways in which terms such as normal and normal development are actually used by biologists, for example in the following quotes

which demonstrate that normal development is sometimes used to denote “pathways of development which give a normal outcome”:

Parasitism by this species elevates dopamine levels in the nerve cord and hemolymph, slows normal development, and delays pupation of the host

Goodman and Granger, 2009: 328

[B]oth blastomeres of the two-cell mouse embryo can give rise to normal embryos if separated...normal development can still occur even after cells are removed or added to a preimplantation embryo...in normal development, individual blastomeres in early embryos have different developmental properties and fates

Wolpert *et al*, 2011: 138

[B]oth the maternal and the paternal genome are necessary for normal mammalian development...both are required for the normal development of the embryo and the placenta.

Wolpert *et al*, 2011: 340

In more complex organisms, such as vertebrates, in which the regenerative power is primarily limited to the appendages (limbs and tail), regeneration may recapitulate normal development.

Minelli, 2003: 131

[D]uring normal development, differences in cytosine methylation are critical in telling a nucleus which genes can be expressed, and which genes are expressed determines what type of cell it will become

Gilbert and Epel, 2009: 43

Slack may have been attempting to discipline the use of the term, but he was far too late. By the time he wrote about normal development, it had become entrenched, conceptually and in practice, with a different meaning, one which does in fact include “pathways of development which give a normal outcome”.

An additional problem with Slack's definition is that it presents a conception of normal development as passive, something which is given or revealed to the scientist. For Slack, all the scientist needs to do is observe (this of course is not merely a passive process) development and not interfere. However, as we shall see, producing normal development is in fact an active process, which involves much scientific and technical work to produce, circulate, use and maintain. It is this work that I wish to examine. As I will show in this thesis, to establish normal development is not as simple as allowing development to unfold unmolested. Normal development is not merely just a control or non-manipulated arm of an experiment. The conditions to allow normal development to 'happen' must be constructed. Observations and results must be abstracted – an active rather than a passive or automatic process – to produce a standard. Furthermore, a neat conceptual distinction between a course of development followed free from external intervention, and pathways resulting in a normal outcome, is not easily (or actually) made in practice. Partly, this is because assumptions concerning what normal outcomes of developmental processes actually are help to establish what is normal in the first place, a process I will describe in more detail in my account of Wilson's experimental work.

Although biologists have generally not explicitly assessed their use of the normal, some philosophers have, particularly in the philosophy of medicine. In his work on the concepts of the normal and the pathological, Georges Canguilhem observed two linked meanings of normal, remarking that "[s]ometimes it designates a fact that can be described through statistical sampling; ... And yet it also sometimes designates an ideal, a positive principle of evaluation, in the sense of a prototype or a perfect form" (Canguilhem, [1965] 2008: 122). Thus, there is a more descriptive sense of normal, describing what is most common, or typical. This can be conflated with the more evaluative or normative sense of the normal.

This conflation, or elision between the two senses, has been of concern to philosophers dealing with disability and mental health. In this respect, the relationship between the descriptive and normative senses of the term normal



has been examined by John Dupré in his work analysing the concept of 'normal people' (1998) and Ronald Amundson assessing what constitutes normal functioning (2000).

The term 'normal' originally derives from geometry, with the Oxford English Dictionary citing examples from the seventeenth-century in which 'normal' meant right-angled. In the eighteenth-century, it came to mean 'standing at right angles to', or 'perpendicular to'. In Latin it means 'conforming to a rule' (as well as 'right-angled'), and before the nineteenth-century, in French it meant 'which serves as a model'. It is in the nineteenth-century that the use of the term becomes more common, and the meanings of it multiply. Ian Hacking has identified medicine in the 1820s as the root of this explosion in the use of the term 'normal', though he has also identified "nonmedical routes to the normal" related to the increasing importance of standardisation in an industrialising world (Hacking, 1990: 164-165). Hacking observes that once the notion of normal had been established in medicine, "it moved into the sphere of – almost everything" (Hacking, 1990: 160).

One sphere it was able to move into with ease was the science of physiology, which studies the proper functioning of organisms. Towards the end of the nineteenth-century, experimental embryology adopted many of the methodological precepts of physiology, including causal analysis, strict control of conditions, and the existence of experimental control arms (Churchill, 1973). The concept of the normal therefore did not have far to travel to arrive in experimental embryology, and the more normative sense imported from medicine via physiology would rest alongside a more descriptive sense of the term used in the embryology of Karl Ernst von Baer (1792-1896) (Hopwood, 2005). As Nick Hopwood (2005, 2007) detailed, in comparative embryology normal development was formalised at the end of the nineteenth-century in tables of normal stages. Normal stages or series became used in experimental embryology as well. In experimental embryology, normal development became a stable and standardised comparator against which the effects of experimental manipulations could be observed, measured and evaluated.

Variation within and between species makes it difficult to make comparisons, in both non-experimental and experimental embryology. This, and the fact that organismal development is a continuous process, makes necessary the development of certain procedures of abstraction. Ways to abstract from variation and process were (and are) absolutely necessary to ensure that investigative work can be done at all in the biological sciences, not least those concerned with ontogeny. Precisely how this abstraction is done, for what purpose, and to what effect, is the main question of this thesis. One way it is done is by establishing a normal development.

This thesis demonstrates the role of normal development in biological practice and thought, particularly in how biologists set up experiments and interpreted their results. Based on this, I analyse how the role of normal development in practice as a ‘technical condition’ and a ‘background condition’ provides us with a way of understanding attributions of causality and how these relate to experimental practices. These terms derive from the experimental systems approach of Hans-Jörg Rheinberger (1997, 2010, 2012) and some developments of the manipulationist theory of causation promoted by James Woodward (2003, 2010). Elements of these approaches have been used to form the analytical framework I use in this thesis.

The experimental systems approach focuses on the ways in which scientists investigate what they do not yet know – “epistemic objects” or “epistemic things” – by directing, assembling and coordinating various resources termed ‘technical conditions’ to bound or frame the epistemic object to enable its contours to be traced. A technical condition functions to “set the boundary conditions of experimental systems and in the process create the space in which an epistemic object can unfold” (Rheinberger, 2010a: 218). In this way, “technical conditions determine the realm of possible representations of an epistemic thing” (Rheinberger, 1997: 29). The technical conditions may be conceived of as particular technologies, techniques and materials configured in particular ways. I interpret normal development as a technical condition which is, in part, a methodological norm as well as involving or being related to particular materials and techniques. Rheinberger’s approach is attractive as it focuses on the

dynamics of the establishment and development of experimental systems. My concern is how embryologists such as Wilson were able to establish experimental systems to satisfactorily approach the problems they wished to investigate. Some of Rheinberger's insights provide me with conceptual tools to assess Wilson's actions.

Woodward's theory of causation posits that "causal and explanatory relationships are relationships that are potentially exploitable for purposes of manipulation and control" (Woodward, 2003: v). The details of a manipulationist or interventionist theory of causation are not important to my account. I am more interested in what more recent work based on it allows philosophers of biology to do. The identification of three kinds of criteria – of specificity, stability and proportionality – which define how strong or weak candidate causes can be considered to be, provides a valuable basis for analysing how scientists make causal attributions. It sidesteps the question of whether a particular factor is a cause or not and instead focuses attention on how causally relevant the factor is. This approach allows me to assess how attributions of causality may be made in developmental biology, in which attributions of normality and relegating certain factors to background conditions are commonplace, and relevant for assessing causal factors.

When biologists want to identify what relevance particular factors have for development, one way in which they can proceed is to divide the factors into internal and external factors. Internal factors are commonly those internal to the organism, or more precisely, internal to the cells contained in the organism. External factors are often those outside of that, for example, what we might call 'environmental conditions', such as the temperature (or range and gradient of temperatures) or pH (or range and gradient of pH) in the medium surrounding the organism. The distinction between internal and external factors is less clear when we consider the role of the organism in shaping the environmental conditions in which it lives, for example by releasing chemicals (including waste products, but also signals). There is also (as identified by Claude Bernard), the internal environment, the environment within an organism and outside the cells within it, which mediates between cells in the same body, and also between the

external environment and the cells. In terms of biological practice, factors in the external environment are generally easier to control than internal factors or the internal environment, with the exception of being able to control the genome of organisms through practices of pure breeding and cloning.

If an investigator wanted to investigate the role a particular internal factor has, they will attempt to keep all other factors (internal and external) constant – they will relegate them to background conditions. Through the use of a heuristic idealisation known as the instructive-permissive distinction, internal and external factors play different roles in attributions of normality, and consequently external factors are more likely to be relegated to background conditions to be kept constant. This is evident in the distinctions and methodological choices made by Wilson. The instructive-permissive distinction distinguishes between two kinds of factor that have different explanatory roles in a given explanation or causal account. Internal factors are often attributed as instructive causes, causes that make a difference, that exhibit greater specificity, stability and proportionality. External factors, on the other hand, are often deemed to be permissive conditions, factors that can allow normal processes to occur, or to not occur, but not specify in any level of fine-grained detail how normal processes might produce different results. These permissive conditions or causes are thought to exhibit less specificity and stability.

In addressing the role of normal development in experimental systems, I concentrate on how normal development is produced, how it functions as a technical condition, and how aspects of that role affect how causal inferences and attributions are made. This, together with my analysis of how normal development can become entrenched as a possibly inappropriate technical condition for certain epistemic objects, provides a basis for assessing in concrete situations what normal development is doing, which might assist efforts to make it a more appropriate technical condition for the task at hand.

### ***Methodology***

I take an HPS – integrated history and philosophy of science – approach in this thesis. This means that I take a detailed historical case study and an

examination of scientific practices as a necessary foundation for my philosophical analysis. I embed my analysis of normal development in late nineteenth-century experimental embryology, developing a historical case study based on the career and work of the biologist Edmund Beecher Wilson. Wilson was a well-connected and highly respected biologist, active in research for over four decades, whose work ranged over numerous modern disciplines of biology. Wilson became interested in the nascent field of experimental embryology in the early 1890s, and conducted experiments with the marine invertebrate *Amphioxus* (Wilson, 1893a) that I reconstruct, describe and interpret in detail. I draw upon close reading of Wilson's published work as well as historical scholarship on Wilson and contemporary scientific developments, particularly in embryology. I use my interpretation and analysis of Wilson's published works and the existing historical scholarship to pose questions and draw conclusions about normal development, its role in practice, and in mediating practical and more theoretical concerns. The case study and subsequent analysis of it will provide the basis for the later analysis of normal development in chapters 6 and 7 using the framework developed from the work of Rheinberger and Woodward. Given the centrality of the case study, however, in chapters 2 to 5 I do not draw heavily upon my framework, as I will need to spend a considerable amount of the thesis detailing the case study and its consequences.

The historical material is aimed at providing the material for a conceptual clarification of normal development. It will allow me to assess the role of normal development as a technical condition in experimental systems and the consequences of this for attributions of causality in biology. In taking a wider view of the historiography of embryology, I intend to avoid the criticised selectivity and particularity (with consequent evidential limitations) of case studies used in philosophy of science (Kinzel, 2015). I acknowledge this, and the related criticisms of the 'confrontation model' of HPS in which "[t]he role of history was to provide the data for the evaluation of philosophical theories about science" (Schickore, 2011: 464). Instead, the historiography I assess, and the history I examine, is there to provide the basis for an interpretive conceptual analysis that highlights and interprets the origin and role of particular aspects of scientific practice revealed by the histories. It uses the concrete historical

examples to “extract abstract insights”, but not to generalise inductively from particulars (Chang, 2012: 110).<sup>1</sup> My thesis is intended to be historically rigorous in the same way that it is intended to be thoroughly naturalistic – I aim to be faithful to and draw inspiration from the histories as I do from natural science and the practices of scientists.

As I take an integrated HPS approach, historical detail is vital in establishing the basis from which my conceptual analysis will proceed. My historical approach reconstructs changes in practices and research interests using the work of Wilson and his contemporaries, contextualised and situated using some of the existing historical and philosophical literature. I identify the decisions, problems and questions that Wilson encountered in a particular phase in his research career, which helped guide the direction of his research. So much of the progress of science involves a form of rational reconstruction; making the contingent, the uncertain and the nonlinear into something naturalised, necessary, linear, and rational.<sup>2</sup> A classic example is the transformation from convoluted trains of thought and trial-and-error bench work with hunches and promising approaches attempted, modified and discarded, to a resultant well-organized, logically presented scientific paper in a journal. In such papers, the questions motivating the partial representation of some of the work done and a selection of results may not have appeared until late in a series of experimental procedures (Schickore, 2008). My interest in the methods and practices of science means that I do not merely present the science I examine as just a linear temporal series of connected questions, hypotheses, results and conclusions concerning organismal development, though temporal sequence is still important to my account. The relation of the methods and materials to those

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<sup>1</sup> In my thesis I aim to demonstrate the two key criteria of cogency and range of application for demonstrating the worth of such abstract ideas (Chang, 2012: 111).

<sup>2</sup> My approach, and use of the term ‘rational reconstruction’ should not be taken to be an endorsement of a rigid distinction between ‘internal’ and ‘external’ factors in the history of science, nor should it be interpreted as an adherence to Lakatosian rational reconstruction in the strict sense, or logical positivist conceptions of rational reconstruction. Acknowledging the difficulties of truly integrated HPS (which would imply doing history as much as philosophy), I restrict my aim to conducting historically (and historiographically) informed philosophy of biology, which does more than “fabricating examples”, an accusation directed by Kuhn at Lakatosian philosophy of science (Kuhn, quoted in Chang, 2011). Lakatos developed the insight that “[p]hilosophy of science without history of science is empty,” (Lakatos, 1970: 91), but he also acknowledged, albeit in the form of a humorous coda to his paper, that “rational reconstructions are frequently caricatures of actual history” (Lakatos, 1970: 122).

questions, hypotheses, results and conclusions will in fact be my main focus. My intention is not to unpick the linear threads sown into the scientific literature by logically presented papers, but to see how they have been sown, and how the individual strands move through the fabric, change direction, and relate to other threads. I do not adjudicate the rationality or otherwise of Wilson's research path, but rather examine how the internal logic of Wilson's research proceeded from the late-1880s and into the 1890s. There are differences between my approach and the historiographical approach of considering competing research programmes. For instance, I focus on one scientist, and track his development.<sup>3</sup> Wilson might be interpreted as someone who moved from one research programme (which one might say was degenerating) to another which was progressive. Interestingly, taking the approach I do blurs the lines between research programmes – there was not a saltation-like leap from one programme to another, but a gradual shift in research priorities, and a change in methods to accompany them.

I compare Wilson's experimental work, and the role of normal development in it, to the other key early experimental embryology work carried out by Wilhelm Roux (1850-1924) and Hans Driesch (1867-1941). Analysing the methodological and epistemic features of early work in a field allows us to see the plurality of different approaches taken before that field becomes sufficiently stabilised and standardised. This is even more the case here, in the era 'before there were standards' of all sorts: educational, material, informational, communicative, organismal (Logan, 2002). This allows us to compare current practices to the plurality of practices which were pioneered by the likes of Wilson, exposing certain features, assumptions and implicit structures lying behind them and in association with them. The historical analysis therefore allows us to conceive of alternative ways in which normal development can be produced and used in experimental systems in embryology and developmental biology.

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<sup>3</sup> Though I do compare him to contemporaries such as Roux and Driesch, I do not consider their trajectories in any depth, and use my depictions of them in contrast to Wilson, to enable me to demonstrate what differences between their work and Wilson's were significant.

On the latter point, it is practice that I am concerned with, particularly the relationship of practice – how scientists generate and use experimental systems – to attributions of causality. It is therefore a practice-oriented or pragmatic lens through which I examine the development of experimental systems and elements of them (see Ankeny *et al*, 2011 for a programmatic introduction to the philosophy of science in practice). This lens focuses attention on the role of the conceptual apparatus of science and methods as tools for producing knowledge, as opposed to a concern solely with theory (Gimmler, 2012). These tools must be produced, and scientists must learn (how) to master them, adapt them, and make them productive, as well as integrating them with the other tools in their toolbox. Normal development is one such tool (or set of tools). While a focus on practice is a lens, and informs my analysis of the materials at my disposal, it was not an undergirding methodology in the sense of conducting ethnographic or archival work to reconstruct ways of working and ways of making and reproducing elements such as normal development in experimental systems.<sup>4</sup> I am primarily concerned with experimental practices and methods relating to the technical condition of normal development, not the theories which arise from them or uncovering *exactly* how the experiments actually happened (as with historians of science in the mould of Holmes, e.g. 2001).

What does the pragmatic lens offer? Firstly, it asks questions of the everyday, the seemingly mundane, the accepted, the invisible, and the naturalised. It therefore offers an approach suited to the analysis of the role of normal development, something which is present yet invisible, hidden in plain sight. It is a central part of the furniture of developmental biology, and the daily work of developmental biologists, yet it recedes into the background like the hum of a refrigerator. Of course, this is inevitable. The process of coming to belong (by education, training, and acculturation) to a particular discipline, research tradition and research group is one of naturalising the contingent and the produced, including the material and conceptual elements of experimental work, infrastructure, and analysis (Bowker and Star, 1999; Knorr-Cetina, 1999). Even when that system is as unnatural as a laboratory, this point stands. It is

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<sup>4</sup> As a consequence, though I draw on the approach of Rheinberger, it would not be accurate to consider my thesis as a work of historical epistemology (see Rheinberger, [2007] 2010b).



therefore the job of outsiders to identify what is contingent and produced and how it could be produced differently. That is the final task of this thesis on normal development.

### ***Plan of the thesis***

In the first chapter, I outline my framework of analysis for the thesis. I detail the parts of the experimental systems approach developed by Hans-Jörg Rheinberger (1997, 2010) that are relevant for my purposes. I define the elements of the experimental system – epistemic objects and technical conditions – and indicate the interplay and dynamics between them. Additionally, using this framework I assess the ways in which experimental systems can change. The second part of my framework is one aspect of the interventionist account of causation developed by James Woodward (2003, 2010). Rather than identify criteria for distinguishing between causes and non-causes, Woodward has developed criteria for assessing how strong or relevant a cause might be in an experimental system of interest. The three main criteria are stability, specificity, and proportionality and I indicate linkages between all three in my opening chapter. I identify the role of background conditions in Woodward's analysis of attributions of causation, and link this to the role of normal development as a way of managing the relationship of the phenomena of interest to certain background conditions. This is examined later in the thesis, alongside the implications of considering normal development as a technical condition in experimental systems. This chapter picks out the elements of the two main approaches which provide me with the tools I need for my analysis.

In chapter 2, I begin the historical account by describing the changes that occurred in the biological sciences in the latter half of the nineteenth-century, to provide a context for the work and research trajectory of Wilson. After briefly outlining the history of embryology and morphology in the first half of the nineteenth-century, I establish what the key questions, approaches and concepts were in those disciplines. This illustrates the historical roots of the problems of investigating and understanding organismal development, particularly the identification of homologies, and the debates over the significance of germ-layers in embryos (and their homology). I establish the

context of evolutionary morphology in the latter half of the nineteenth-century, the area of biology in which Wilson was trained and worked early in his career. The use of embryology for identifying (evolutionary) relationships between organisms was challenged in the late nineteenth-century by advocates of experimental methods such as Wilhelm Roux. I detail what this meant, and how it related to a change in the sorts of problems tackled by embryologists. It was also related to a shift in interest from historical causation of organismal form, of the phylogenetic explaining the ontogenetic; to a proximate or mechanistic understanding of the generation of form. Leading on from this, I review the differing historical and philosophical perspectives on this period in biology.

Methodological changes, such as the increasing experimentalisation of embryology (Allen, 1978; Churchill, 1973; Coleman, 1977; Maienschein, 1986, 1991), were linked to changes in the types of questions asked and problems tackled by biologists. To understand this more clearly, I follow with a more conceptual section, assessing the epistemic and methodological challenges that conducting comparative (and also experimental) work in embryology entails. One of the key challenges is making comparisons. This challenge provided impetus towards the creation of standards, and also the drive to divide the process of embryonic development into stages. I discuss the role of abstraction and idealisation in the production of normal stages and series of stages, and how one such standardised system of stages, the Hamburger-Hamilton normal stages of the chick, worked (Hamburger and Hamilton, 1951). One of the ways in which stages are produced is through abstraction of variation, a procedure I revisit throughout the thesis. This section establishes many of the key problems faced by embryologists. Debates between biologists concerning those problems raged in this period, and still do today.

As a way of narrowing the focus, in the third chapter I introduce the biologist Edmund Beecher Wilson (1856-1939), the first half of whose career forms the spine of much of the rest of the thesis. Wilson's long career spanned the zenith of evolutionary morphology, and the classical genetics of the Morgan laboratory. He had a wide range of interests and activities, from field naturalism, to detailed morphological work, cytology, sex-determination, heredity, embryology and

evolution. H. J. Muller's 1943 obituary of his former teacher Wilson acknowledged the latter's role in straddling scientific epochs:

Wilson's contact with science began when the establishment of the theory of evolution and even of the cell theory in its primitive form was still fresh in men's minds...experiment had hardly entered the fields of morphogenesis, cell study or evolution. As for the teaching of biology, it and other sciences were practically unknown...Thus Wilson's life spans practically the entire period of growth, not only of genetics, but of biology as we know it. More-over, his own scientific activities largely illustrates this growth, for as improved methods of approach – either those of hand or brain – arose, Wilson time and again was to be found among the vanguard of those adopting them.

Muller, 1943: 5-8

Considering Wilson's career trajectory, I look at the development of the methodologies he employed, and the problems he attacked in his first full decade as a professional scientist. In particular, I examine his work on cell-lineages (Wilson, 1892a) which emerged from the problems and questions generated by his previous work in evolutionary morphology. This cell-lineage work, in turn, led him into areas where cell-lineage work would no longer be sufficient for answering newly posed questions.

This chapter provides the springboard for an examination of the changes occurring in Wilson's interests, methods and practices in the wider context of such changes (and continuities) in the sciences of morphology and embryology. Wilson's morphological interests led him to embryological study, and those very same interests, and the challenges of embryological research and interpretation, led to new research questions being generated. These included questions on the determination of development, on how the developmental potential of cells changed in embryogenesis. Most significantly, many of these new research questions were prompted by the variation he found to be exhibited in early embryogenesis. I therefore highlight variation as an object of research. The morphological and embryological research of the late nineteenth-century, Wilson's work in particular, has not previously been examined in this

way. But I argue that an interest in variation and its morphological significance is crucial in understanding how questions concerning determination became established as a key part of Wilson's overall research interests.

The fourth chapter deals with Wilson's adoption of experimental methods, which he used to try to answer the questions his previous work had produced. These questions concerned the variability of cleavage forms in early development, their significance, the determination of development and the causes of differentiation and emerging form during the process of development. One such experimental approach involved manipulating embryos by shaking apart cells at early stages of development. This was carried out in addition to some of the previous ways he studied development, including careful descriptive, observational, and comparative studies. When experimental methods accompanied comparative methods, Wilson needed to characterise a normal development. This arose from descriptive and observational work, but was given a normative edge by the need to establish a standard against which experimentally manipulated embryonic development could be compared. In as much detail as possible, I re-construct his experiments with *Amphioxus*, and focus in particular on how he produced a normal development. This concept of normal development conditioned how Wilson conceived of the interaction of internal factors within the organism with external factors during development. The concept of normal development arose as a way of dealing with the variation exhibited in early development, for the purpose of making comparable the manipulated and non-manipulated embryos in his experimental set-up. It led to variations away from a specified 'normal range' being treated as deviants to be explained. Wilson's normal development incorporated considerable variation in the early stages of development. As well as focusing on the way Wilson observed and represented embryos, I analyse the nature and significance of Wilson's production and use of normal development, and compare it to the way normal development was used by Driesch and Roux.

In chapter 5 I build on this comparison with Driesch and Roux by moving from the strictly methodological to the realm of theory. In this chapter, I begin to examine the relationship between biological variation and normal development. In examining the way Wilson presented and interpreted his results from the

*Amphioxus* experiment, I identify how the management and explanation of variation is related to normal development. To further explore this, I compare Wilson's conceptualisations with those of Roux and Driesch. I detail how their ideas relate to six parameters which characterise conceptualisations of development: mode of differentiation, type of cause, source of causation, mode of transmission, type of cell division and metaphor of cell relations. I especially focus on the explanation of differentiation and determination of development, and use this to characterise certain elements of theories concerning the developmental process. I argue that some of the differences between Wilson's theory and the dichotomous difference between Driesch and Roux's theories can be explained by the differences in the production and methodological role that normal development had for the three men.

In the sixth chapter I account for the role of normal development in experimental embryology and developmental biology, and how the practices of biologists in treating and conceptualising variation relate to this. I build on the insight that there exist various types of 'normal' in embryological and developmental biological work, what I term a 'taxonomy of norms', and that these correspond to different ways of managing variation (DiTeresi, 2010). Normal development as generated and used by Wilson does not fit into the existing categories of the normal that have been outlined, so I propose an additional one. To develop this analysis, I consider these varieties of normal as, at least in part, methodological norms. I then make the case for considering normal development as a technical condition of an experimental system, and that the methodological norms previously described form part of the technical condition of normal development. I conclude by speculating that if the questions to which experimental systems are directed change to include interest in variation (e.g. its significance, origin and maintenance), then the technical conditions required to frame the epistemic object in that experimental system must change, by incorporating methodological norms which include new ways of abstracting variation. Combining the 'taxonomy of norms' with the experimental systems approach highlights the distinctive roles that different types of normal development can play in experimental systems.

In the seventh chapter I extend the ideas originally introduced in the first chapter concerning change in experimental systems, using the example of normal development as a technical condition. I detail in what circumstances a particular technical condition may affect the nature and dynamics of change in experimental systems. In characterising normal development as a technical condition in experimental systems, I have been able to identify conditions in which normal development may become entrenched in experimental systems. , I propose some consequences of this, which includes the limiting of the types of questions that can be generated by an experimental system. Such an entrenchment may therefore prevent other types of questions from being investigated, such as those concerning the production and significance of biological variation. Additionally, normal development as a technical condition and methodological norm enables certain ways of attributing normality to other elements in an experimental system (including epistemic objects), and in identifying and controlling background conditions. As both attributing normality and identifying and controlling background conditions are key parts of the criteria of specificity, stability, and proportionality for assessing causal claims, the role of normal development in helping biologists to generate and evaluate causal claims is important. These findings emphasise the importance of carefully assessing how normal development impacts on the practical and theoretical aspects of investigations into the nature of organismal development, and whether for some purposes it is produced and used in ways appropriate to those purposes.

I conclude with a chapter detailing the key philosophical lessons derived from the thesis, and possible consequences for the analysis of scientific practice concerning developmental biology, including the role of normal development. I then outline some possible opportunities for, and problems faced by, a more variation-sensitive developmental biology. I close with a series of questions opened by this present work concerning the philosophical examination of variation in biology.

## **Chapter 1 – Framework of analysis**

### **1.1. Introduction**

The task of this chapter will be to establish the analytical framework, which I will then use for the rest of the thesis. The two key elements which constitute this framework are experimental systems and the assessment of the significance of purported causal factors in organismal development. The analytical framework will be used in an investigation of the nature and role of normal development within early experimental embryology, and in embryology and developmental biology more generally. Using the two elements of the framework, my case study will demonstrate the links between the need to produce, maintain, and evolve experimental systems, and the assessment of putative causal factors in development. In terms of normal development, the task will be to establish a link between the nature of normal development as a key component of experimental systems and more ontological conceptions of normal development and variation in development.

I begin by outlining the Rheinbergerian experimental systems approach, and elaborating upon what I take to be its key aspects. The notion of the experimental system introduced by Hans-Jörg Rheinberger (1997) is a way of conceptualising the progress of research as an investigation into epistemic objects or epistemic things (as yet unclear objects of investigation) by directing various resources (technical conditions) to bound the circumstances in which the epistemic object's contours can be traced. I will use what are for my purposes the key aspects of experimental systems, with the intention of using them to highlight the role of normal development within a nascent experimental system.

The ability to successfully identify the causes of phenomena is central to the scientific and social worth of the biological sciences. However, the phenomena biologists deal with – not least, the complexity of the development of organismal form – often means that factors in biological systems are not merely partitioned into the categories of cause and non-cause. Instead, different candidate causes are considered to have more or less weight. One influential way of assessing

the extent to which a proposed cause is relatively strong or weak has been proposed by James Woodward (2010). Woodward's manipulationist theory of causation (2003) has been used by participants in the debate concerning the precise causal role of different factors in organismal development. One example is the question of whether DNA has causal primacy (Waters, 2007), or if instead there is a "causal democracy" involving significant causal contributions from non-DNA factors (Griffiths and Stotz, 2013). This demonstrates that, although Woodward's approach is not uncontested (cf. Bogen, 2004; Cartwright, 2002; Imbert 2013), it can be taken as common ground by participants on either side of a fundamental debate in the philosophy of biology and theoretical biology.

I will describe the criteria of specificity, stability and proportionality outlined by Woodward, draw out relations between them, and identify how they provide the means for understanding the links between methodological practices and causal explanations in developmental biology.

## **1.2. The experimental systems approach**

My account foregrounds the role of practice in driving scientific agendas. In this respect, I am following a path well-worn by philosophers and historians who have, in the past thirty years, attempted to correct for previous (and still extant) theory-dominated/centric accounts of scientific episodes and change. The historian of science Hans-Jörg Rheinberger is a prominent exponent of the focus on experimental practice. For my own purposes, I employ elements of his framework of experimental systems with which he makes sense of his own detailed research.

The first full exploration using an experimental systems approach was Rheinberger's account of the activities of a group of protein synthesis researchers in the 1950s and 1960s. This work, arising out of cancer research and biochemistry, led indeterminately through a meandering path to the characterisation of messenger RNA and transfer RNA (Rheinberger, 1997). The experimental system is a notion which seeks to make sense of the uncertain trajectories of research. Rheinberger analyses an experimental system in the making, and in the process elucidates many aspects of the nature of



experimental systems: their constituents, properties and uses for historians and philosophers.

An experimental system has two main features – an “epistemic thing” (or, using a term Rheinberger came to adopt, an ‘epistemic object’), and technical conditions or objects. The epistemic object is the object of inquiry – an entity or a process which “present themselves in a characteristic, irreducible vagueness” due to them embodying “what one does not yet know” (Rheinberger, 1997: 28). Epistemic objects are “things contained within the arrangements of technical conditions in the experimental system” (Lenoir, 2010: xiv). Epistemic objects, being less known, and therefore less amenable to control, are the relatively unstable elements of experimental systems. Conversely, technical conditions are produced and deployed in combination with each other as a stable context for experimentation, being arrangements that allow “operational redefinition” of the epistemic object by adding items to the “list of its constitutive actions” (Rheinberger, 1997: 29; Latour as quoted by Rheinberger, 1997: 29). Technical conditions have also been described as “tools to produce answers about epistemic objects” (Green, 2013: 171). It is through technical conditions “that the objects of investigation become entrenched and articulate themselves in a wider field of epistemic practices and material cultures...and the floating theorems or boundary concepts attached to them”. In this way, “technical conditions determine the realm of possible representations of an epistemic thing”. This means “that within a particular experimental system both types of elements [epistemic things/objects and technical conditions] are engaged in a nontrivial interplay, intercalation, and interconversion” (Rheinberger, 1997: 29).

It is important to bear in mind the role of the technical conditions in framing the epistemic object, and in providing the conditions in which the epistemic object gradually gains contours and becomes less of a vague entity or process. Additionally, one must be mindful of the fact that technical conditions must work together and mutually adapt to each other to frame an epistemic object. Therefore, if a new technical condition is added, or an old one modified, through addition of some aspect of what was once an epistemic object, we would expect the assemblage of technical conditions (or, the *technical assemblage*) to also

change. It adapts to accommodate the new or modified technical condition. A change in epistemic object might also be expected to cause such a change.

In the “experimental situation...there are scientific objects and the technical conditions of their coming into existence, there is differential reproduction of experimental systems, there are conjunctions of such systems, and graphematic representations. All these are notions related to the process of producing...epistemic things. ...Within these complex, tinkered, and hybrid settings of emergence, change, and obsolescence, scientific objects continually make their appearance and eventually recede into technical, preparative subroutines of an ongoing experimental manipulation. As a result, there is again a continuous generation of new phenomena, which need not have anything to do either with the preceding assumptions or with the supposed goals of the experimenter. They usually begin their lives as recalcitrant “noise,” as boundary phenomena, before they move on stage as “significant units” (Rheinberger, 1997: 21). It is therefore a characteristic of an experimental system that “sufficiently stabilized epistemic things turn into the technical repertoire of the experimental arrangement” (Rheinberger, 1997: 29). While this means that “Epistemic things turned into technical objects become integrated as stable subroutines into other, still growing experimental systems and may help to produce unprecedented events in different contexts”, these very technical conditions, while generating “a historical burden” constraining the future development of experimental systems, are usually “completely replaced by subroutines that embody the actual stabilized knowledge in a subtler way” (Rheinberger, 1997: 80-81). The outputs of prior experimental systems therefore condition the way that future experimental systems are configured, which in turn shapes future outputs.

The experimental systems approach focuses on the dynamics of experimental enquiry; how one experimental set-up, with particular epistemic object and attendant technical conditions leads to the next. This is not a logical step, nor a predictable one. The experimental system functions as a “generator of surprises” producing results (and re-definitions of epistemic objects) that could not be anticipated at the outset of the particular experiment or series of experiments. Furthermore, it presents a surplus of possibilities open to the

researchers following the surprise(s) (Rheinberger, 1997: 161). The particular resources, skills, theoretical commitments, histories, collaborations and conjunctures experienced by the scientists working with a particular experimental system conditions which one (or a few) of the multitude of open paths are taken.

Rheinberger identifies three processes by which the relation of different experimental systems can be understood: conjuncture, hybridization, and bifurcation. A conjuncture is “the emergence of unpredictable constellations in the development of experimental systems resulting from a connection of phenomena that do not derive from an expected relation of cause and effect but that, once set in place, can enter into a kind of structural coupling” (Rheinberger, 1997: 135). Hybridizations are “linkages between mutually independent systems” (ibid.). A hybridization carries with it the production of a hybrid system potentially (and unpredictably) qualitatively different from the pre-hybrid systems (Rheinberger, 1997: 136). Bifurcation is the formation of separate “offspring systems” from a ‘parent’ experimental system. This tends to occur when an experimental system “has reached a certain complexity that allows researchers to pursue slightly diverging epistemic tracks but which are sufficiently different to enable them to arrive at significantly different results” (ibid.). Such offspring experimental systems may share materials, techniques, skills, personnel, theoretical commitments, data, methods, equipment, and so forth, but also may diverge from each other to make such sharing less possible or necessary.

An experimental system is ‘successful’ if it continues to (differentially) reproduce, but also if its practices, materials, objects and empirical data are transmitted to become part of other experimental systems, either by conjuncture, hybridization, or bifurcation.<sup>5</sup> When this happens, they may not simply slot into a pre-existing system, but in substituting for another element, or simply being added to a system, it can itself “reconfigure that very system –

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<sup>5</sup> Rheinberger uses the term reproduction “to indicate that experimentation has to be seen as an ongoing and uninterrupted chain of events through which the material conditions for continuing this very experimental process are maintained” (Rheinberger, 1997: 75).

sometimes beyond recognition”, a process known as “supplementation” (Rheinberger, 1997: 4).<sup>6</sup>

What relevance does all this hold for Wilson, normal development, and experimental embryology? First of all, it provides us with a handle for getting to grips with the messy uncertainties of a nascent programme of experimentalisation. Rheinberger’s point is that while certain experimental systems (and, indeed, model systems) have their “own time” and ageing process, even well-established fields are messy. The experimental systems may be “future-generating machines” (Rheinberger, 1997), but no-one is quite sure of that future at the time. If they were, it would not be research. Peripheral results, annoyances, or ‘noise’ could transfer to the centre of investigation. The surplus of possibilities presented at any one stage could lead down many different paths, with time and resources dictating that only a few might be pursued with vigour. Contingency and uncertainty abound.

Second, the insights about the fates of experimental systems, the transmission of concepts, materials, objects, conditions and processes between them, gives us a way of assessing the fate and significance of Wilson’s own experimental system, both for experimental embryology as the 19<sup>th</sup> turned into the 20<sup>th</sup> century, but also for Wilson’s own research trajectory and focus. In the course of this thesis I will therefore outline the role of normal development within experimental systems, using Rheinberger’s experimental systems approach.

An experimental system does not provide a stable platform for the progressive delineation of an epistemic object by chance, or by design from scratch.

Rheinberger refers to the production of epistemic objects in “complex, tinkered, and hybrid settings of emergence, change, and obsolescence” (Rheinberger, 1997: 21). The totality of the technical conditions (the technical assemblage) are constantly modified, added to, and subtracted from, and the relations between technical conditions and their spatial and temporal deployment may alter. Often, the nature and role of a technical condition depends on its context within the assemblage, and its relation with other elements. In many cases, technical conditions are elements of an experimental system which include objects and/or

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<sup>6</sup> A term Rheinberger borrowed from Jacques Derrida.

processes outside of the immediate experimental situation or the technical assemblage framing a given epistemic object. Normal development as a technical condition is a good example of this, as it comprises of elements such as normal stages, specially-bred strains of organisms, the tacit and embodied knowledge of experimenters, and the theoretical and normative background to not only that experimental system, but a whole discipline. The need for a mutual adaptation of the parts of the technical assemblage is required for two reasons: to provide a sufficiently well-constituted platform for the investigation of the epistemic object, and also because of the interrelatedness, interaction, and sometimes cross-over and merging between the parts.

### **1.3. Assessment of causal factors in development**

James Woodward has characterised an manipulationist or interventionist framework of causation (Woodward, 2003) and then used this as a basis to identify the attributes of a causal explanation in the biological sciences (Woodward, 2010). These allow us to make judgements about the nature of any particular causal explanation.

Woodward identified stability, proportionality, and specificity as three interrelated attributes of causal relationships. Stability is the criterion that depends on a “relationship of counterfactual dependence” holding against a range of changes in background conditions. A causal relationship can therefore be more or less stable depending on the amount of changes to background conditions that can occur and the relationship still hold (Woodward, 2010: 292). Woodward alternatively labels stability the “non-contingency of association” to recognise this. He identifies that more stable relationships are generally more proximate relationships, as there are less intermediate links in the causal chain, which themselves have their own range of background circumstances in which they are associated with the effect of interest. In many instances, this will mean that the range of background conditions in which the more upstream factor is causally associated with a particular outcome is narrowed, and therefore it can be deemed to be less stable (Woodward, 2010: 294).

Proportionality captures situations where the level of explanation or causal account is appropriate to a given *explanandum*. That is, it is not too broad and general, or too narrow and particular. Any posited causes must fit with their effects. In Woodward's interventionist account, this means that the cause is characterised in such a way that alternative states of it are associated with changes to the effect, and the conditions which result in changes in the way in which the alternative effects are produced are characterised (Woodward, 2010: 298).

Woodward identifies two notions of causal specificity in the biological sciences. The first is that a cause is specific if it has a fine-grained influence on the effect, the second "that a causal relationship is specific to the extent that a single (type of) cause produces only a single (type of) effect, and to the extent that each single type of effect is produced only by a (type of) single cause" (Woodward, 2010: 308). On the first notion, if many different states of a putative cause are associated with many different states of an effect of interest, that cause can be judged to be specific than a second putative cause which has many different states associated with just two different states of an effect. Woodward makes an analogy with a radio – the less specific cause of the programme we hear is the on/off switch, which can only turn on or off the particular programme we hear, and the more specific cause is the dial, which allows us to change the programme by turning it (provided the radio is switched on) (Woodward, 2010: 307).

This principle has formed the basis for arguments concerning the causal role of DNA in organisms. This debate centres on the question of whether DNA has a causal specificity not exhibited elsewhere inside or outside the organism. For example, C. Kenneth Waters has used Woodward's analysis of specificity to argue that while DNA is causally specific in generating RNA sequences, other non-DNA factors such as RNA polymerase are not (Waters, 2007). Changes in the sequence of nucleotides in a stretch of DNA are associated with changes in the sequence of nucleotides in RNA. Changes in the amount of RNA polymerase (the enzyme which transcribes the DNA) are not. In the absence of RNA polymerase, there are simply no RNA molecules transcribed. If there is a sufficient quantity of the enzyme, the RNA molecule thus produced will reflect

the DNA transcribed. The RNA polymerase therefore functions as more of a switch than a dial. Countering this, Griffiths and Stotz, who also accept Woodward's framework, have argued that Waters' account only applies to the Precursor-mRNA, the RNA transcript of DNA. They observe that processes of post-transcriptional modification such as splicing may produce mature mRNA quite different to the Precursor-mRNA. It is this mature mRNA which exits the nucleus for the ribosome, to be transcribed in the process of polypeptide (and after that, protein) formation. When the effect is taken to be the protein produced, Griffiths and Stotz argue that not only DNA, but other extra-DNA factors, are causally specific, or as they term it, "*specific actual difference maker[s]*" [italics in original] (Griffiths and Stotz, 2013).

Woodward frames the second sense of specificity by asking whether it is "the case that within the specified range of kinds of effects, a particular kind of cause produces only one kind of effect from that range and is it the case that for a given effect, it is (capable of being) caused only by a single kind of cause within some pre-specified set of alternatives?" (Woodward, 2010: 311). He answers this by stating that "C will be a more (rather than less) specific cause (in the one to one sense) to the extent that it causes only a few different kinds of effects within a pre-specified range" [italics in original] (ibid.). The reference to a "pre-specified range" is Woodward's way of getting around the objection that as in the biological sciences many-many causation (rather than one-one causation) seems to prevail as a rule, this notion of specificity is not particularly useful for considering causation in biology. Woodward suggests that this objection can be overcome if for a "given candidate cause, we consider only possible kinds of effects within some limited set or range of alternatives, rather than all possible effects to which the cause may contribute...[and similarly,] for the causes of particular kinds of effects: we consider only whether there are alternative possible causes that fall within some pre-specified class all of which can produce the effect of interest" (ibid.).

The three attributes are interlinked in various ways. For example, the need to be proportional can in many circumstances demand that the association one draws is also stable, by ensuring that it is more proximate than distal. For example, in the effects of changes to a particular gene, some may be directly related to

changes in the gene, and therefore proportional and stable, others may be more downstream or secondary effects, and therefore less proportional and stable. However, Woodward acknowledges that, in some cases, satisfying the criterion of proportionality is independent of satisfying the criterion of stability (Woodward, 2010: 299).

A cause that is specific in the first sense identified by Woodward, that it has fine-grained control over the effect, is linked by him to proportionality: “To the extent that...there are states of *E* that cannot be reached by realizing states of *C*, there will be a failure of proportionality.” [italics in original] (Woodward, 2010: 306). If the proposed cause acts more like an on-off switch than a dial, the proposed cause will also be viewed as too poor a fit, too coarse-grained, to match the level of explanation required.

Connections are therefore present between the three criteria. But as well as their more logical interrelation, one must also acknowledge that they are not considered separately when a potential cause or causes are considered. Together they form part of the more or less intuitive apparatus with which biologists (and non-biologists considering biological work or systems) approach a particular proposed causal mechanism, or the design of experiments, or a wider programme of work to examine the causal mechanisms at play in a particular biological system of interest., with a view to assessing the ways in which such criteria are (implicitly, or explicitly in different ways from that in which Woodward detailed them) conceived and employed in the generation of questions, experimental situations, observations, interpretations, and communication of new biological knowledge.

The criteria of specificity, proportionality, and stability link explanatory concerns with methodological and epistemic practices. Furthermore, they are not interest-neutral. As I shall demonstrate in chapter 7, assessing how stable, proportional or specific a given causal relationship is depends on a prior determination of background conditions and subject-related judgements of what is ‘normal’.<sup>7</sup> One might add that pragmatic issues concerning what background conditions can be measured and/or controlled may also lead to the specification of which

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<sup>7</sup> To this we might also add community standards and the backgrounds of the experimenters.



background conditions should be employed in assessing the stability of the causal relationship. This is easiest to envisage in experimental psychology where experimenters cannot control or even know precisely what their experimental subjects are doing when outside the laboratory context. But it is also manifested even where the subjects aren't human, and are confined to the laboratory.

One example might be that the organisms used in experimental laboratory studies must be brought into the laboratory from 'the wild', and are not capable of being bred and standardised by specialist breeders or the laboratory itself. Sacoglossans, also known as 'sap-sucking sea slugs', are one such creature. They are the only known animal to exhibit a behaviour known as 'kleptoplasty', in which they 'steal' and subsequently use the chloroplasts from the algae they eat. To study them, researchers must steal them from the sea, as they are incapable of raising them in the laboratory. The collected sacoglossans are placed in controlled, artificial conditions as soon as possible, but researchers have little knowledge of the backgrounds of their samples, and it is usually even not possible to discover their ages. The only background conditions that can be specified here are the ones which the researchers know about, from having controlled them in the laboratory (Rumpho *et al*, 2007: 461). This is also a problem for the organism which Wilson works with, the marine invertebrate *Amphioxus*, in the experiment described in chapter 4.

Even where organisms or parts of them are not plucked directly from nature, but are the result of standardisation and control, factors that may remain unknown and unspecified might cause variation between ostensibly identical organisms kept in ostensibly the same conditions. The acknowledgement of this fact leads experimenters to either ignore the variation, attribute it to error, and to try and discern the source of it to extend the level of control. To a complete extent this is not possible (Carlson Jones and German, 2005: 83). Two organisms cannot have identical life histories, or even the same position in space.

## 1.4. Conclusion

I have outlined the key elements of the analytical framework with which I will approach the role of normal development in experimental systems, the topic which will constitute the bulk of the rest of this thesis.

Rheinberger's account offers us a dynamic practice-oriented way of framing the progress (with no normative weight attached to that term) of experimental research. This allows me to conceive of the role of normal development as a technical condition in experimental systems, both historically (in my late nineteenth-century case study) and in drawing out possible implications for modern experimental systems in developmental biology. Implicit in any experimental system is the generation of background conditions. My aim will be to link the experimental systems approach with some of the insights I have drawn from Woodward, to elucidate the intertwined ongoing relationships between changes in practice, and changes in ontological conceptions of development, once again using normal development as a touchstone.

The strength of Woodward's account is that it provides us with a way of conceiving how an historical and philosophical analysis of scientific practice can illuminate questions of a seemingly pure philosophical nature – that of causation. How Woodward's attributes of causes are assessed is dependent on context, the questions asked by scientists, and the pragmatics of their work. He would perhaps demur from the characterisation, but Woodward's assessment of the attributes which can be used to weigh different proposals of causal factors might even allow us to construct an historical epistemology of causal attribution.

Woodward's framework has not gone unchallenged, but it is an influential account which has been used as the basis for debates between, for example, those who promote a view of development in which the genome has "causal primacy" (e.g. Waters, 2007) and those who argue for a perspective based on "causal parity" (e.g. Oyama 2000a, Griffiths and Stotz 2013).<sup>8</sup> Some philosophers have argued that it is more fruitful to concentrate on knowledge of mechanisms rather than causes (Darden, 2013). However, focusing on

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<sup>8</sup> Regarding challenges to Woodward, see the previously cited sources for a more critical view of Woodward, and Saatsi and Pexton 2013 for a reappraisal.

causation serves my purposes better than focusing on mechanisms. Firstly, as the discussion of Woodward's work will shortly illustrate, the attribution of causation by biologists is not a simple affair, and as the rest of my thesis will demonstrate, it is rich with complexity, judgement, and historical context. It is bound up with practice. Secondly, as will become clear, scientists in the period I focus on were not necessarily seeking mechanisms (in the modern sense). They were attempting to discern what kinds of causes were valid, experimentally accessible and explanatorily relevant; to find out exactly which causes were responsible for the effects they observed and created. The words mechanism and mechanical were used, but it is through discussing the use of these words in terms of causality that we will best discern what exactly they meant, and what exactly mattered about that. Thirdly, and related to the second point, the term mechanism has a complex history with different and intertwined meanings diachronically and synchronically, sometimes even in a single person's work. Using the term 'mechanism' and the philosophical framework associated with it would for these three reasons be more confusing than clear.<sup>9</sup> Woodward's approach is more than adequate to the task of allowing me to highlight how scientists have used different criteria to assess the relative strength of proposed causes, and how this relates to the experimental systems they are involved in.

A fruitful leavening of Rheinberger and Woodward's approaches with the insights of other philosophers (of science) will enable me to draw this out of the historical examples, and suggest implications for modern biological practice and theory. I begin this in the next chapter, when I discuss the history of embryology (with several nods towards morphology) throughout the nineteenth-century, the latter half of which was consumed with precisely a debate over the type of causation that was worth invoking and exploring.

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<sup>9</sup> However, where necessary, I have described certain causes that are invoked by biologists as mechanistic causes, as this best reflects the type of cause being appealed to. Here, causation rather than mechanism is still the primary focus.

## **Chapter 2 – The role of embryology in nineteenth-century biology**

### **2.1. Introduction**

The purpose of this chapter is to establish the historical context in which the following chapters are embedded, and also to provide an indication of the historical roots of the problems which still persist today of actually investigating the processes of development.<sup>10</sup> This also establishes a context for chapters 3 and 4, but also the more conceptual issues concerning embryological practice that are covered in subsequent chapters.

In this chapter I provide an account of the history of morphology and embryology in the nineteenth-century, and their interaction in particular. I outline key concepts and debates, such as the definition of homology and the significance of the embryonic germ-layers. Both of these would become entwined in the ‘embryological criterion of homology’, which motivated the work conducted by Edmund Wilson which I outline in chapter 3. The science of embryology was therefore recruited in the search for a way to produce a Natural System, a way of classifying and ordering species and collections of species that was based on real (genealogical and phylogenetic) affinities and relationships, not artificial ones based on the arbitrary or pragmatic choice of one parameter or criterion. The advent of Darwinism raised the prospect – soon capitalised on – that embryology could provide a means to help classify the natural world along the new Darwinian lines. In turn, it was hoped by some that the new outlook on life could inform a new way of looking at organismal development, and the causes of the production of organic form. Almost from the outset, such projects invited criticism, and alternative ways of investigating and interpreting organismal development and its relationship to evolutionary processes.

The debates within evolutionary morphology and embryology concerning the relationship between ontogeny, the observed process of development, and phylogeny, the inferred genealogy and relations of species, involved

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<sup>10</sup> See Caron (1988) for an examination of some of the wider debates concerning the changes occurring in biology in the late nineteenth century.

methodological and epistemic grounds of disagreement and dissent as well as empirical ones. In chapter 3 I deal with the historical debates concerning the overshadowing of evolutionary morphology and embryology by experimental approaches. In this chapter, I outline the nature of the experimentalist programme proposed towards the end of the nineteenth-century by Wilhelm Roux, a prominent German embryologist, and discuss how this related to the evolutionary morphology that was being left behind. The factors which drove Roux to develop new experimental systems also drove him to partition putative causes. My historiographical position, which will be fleshed out in the third chapter, emphasises continuities that can be drawn from evolutionary morphology to experimental embryology.<sup>11</sup>

The discussion of new ways in which embryological research was conducted necessitates a focus on the challenges that scientists face when working with embryos and developmental processes. I discuss various strategies that scientists have used, such as the comparative method, staging, and the use of model organisms. I relate these methods to the crucial practices (and processes) of abstraction as a way of managing the variation exhibited by developing organisms.

## **2.2. Morphology and embryology in the nineteenth-century**

The study of embryos dates back thousands of years.<sup>12</sup> Joseph Needham's classic account of the history of embryology traces concerns with eggs, generation and the production of adult form back to ancient Egypt (Needham, 1959). Aristotle was therefore not the first to investigate embryos, but he outlined his observations and insights in a particularly systematic way, and so is of considerable interest to the story of embryology. Aristotle will be examined shortly, and also re-visited later in the thesis. There is a rich subsequent history of natural philosophical and natural historical investigation and thinking on embryos between Aristotle's time and the nineteenth-century (Gasking, 1967;

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<sup>11</sup> These continuities do not, however, imply that change was gradual. It is possible to accept many of the points from different sides of the debate concerning the 'revolt from morphology' if one considers the differences between the dichotomies of continuity/discontinuity and evolution/revolution.

<sup>12</sup> While the term 'embryo' refers to a specific stage of early development, embryology has encompassed the study of that and other developmental stages, such as foetal and larval stages.

Needham, 1959; Oppenheimer, 1967; Roe, 1981; Roger, [1963] 1997).

However, what concerns us here is the state of embryology at the beginning of the nineteenth-century.

While important work had been done by observers and empirical workers such as Marcello Malpighi (1628-1694), William Harvey (1578-1657), Albrecht von Haller (1708-1777) and Caspar Friedrich Wolff (1735-1794), the early stages of development were still shrouded in mystery. The mammalian egg had not been located, and the nature and function of the sperm was in question.<sup>13</sup> The conflict between theories of preformation or pre-existence and epigenesis was sparked in the seventeenth-century, and prominent biologists such as Edmund Wilson (1896) and Oskar Hertwig (1849-1922) (1896) still discussed it at the end of the nineteenth-century. The basic divide between the two doctrines was that theories of preformation and pre-existence posited that the form of the organism is substantially present from the 'start', whereas theories of epigenesis proposed that the parts of the organism progressively form over time, and are not present at the 'start'.<sup>14</sup> However, despite its place in late-nineteenth century discussions, the conflict did not assume the centrality or importance it enjoyed before the nineteenth-century.<sup>15</sup> As the eighteenth-century drew to a close, there were mounting empirical and theoretical problems with theories of preformation and pre-existence (Roger, [1963] 1997: 308-366). At the same time, the dominant Newtonian metaphysics was conducive to opposing epigenetic theories, by allowing natural philosophers to posit 'forces' which would help explain the progressive formation of the parts and whole of the embryo from homogeneous undifferentiated material.

The discoveries of the first half of the nineteenth-century are often presented as a "triumph of epigenesis" (Coleman, 1977: 43), the destruction of theories of preformation and pre-existence, and, furthermore, a transformation of the

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<sup>13</sup> If indeed it had any function at all. The full name of 'spermazooan' betrays the theory held by some that the sperm were parasites present in the semen, and not relevant for procreation (Pinto-Correia, 1997: 195-196).

<sup>14</sup> For rich historical discussions of preformation/pre-existence and epigenesis before the nineteenth-century, see in particular Bowler (1971), Detlefsen (2006), Gasking (1967), Roe (1981), Roger ([1963] 1997) and van Speybroek *et al* (2002).

<sup>15</sup> Oscar Hertwig may have boldly pronounced the debate to be the "biological problem of to-day" (Hertwig, 1896), but it served more as an interpretive frame to discuss the real biological problems he and his contemporaries were facing.

problems faced by biologists from explaining generation to explaining reproduction and individual development. Karl Ernst von Baer (1792-1876) observed “that younger embryos are coarser in outline than older ones and simply do not exist in miniature below the resolving power of the common microscope of the day”, and some historians have claimed this to be “fatal to the doctrine of preformation” (Churchill, 1991: 10). It was increasingly clear that form was produced during development, through unknown but surely existent processes. Therefore, the task was to observe, describe and explain these processes.<sup>16</sup> Scientists set about this with copious observation and description, the aim being to identify “general descriptive or phenomenological laws” (Gasking, 1967: 151). This was the birth of comparative and descriptive embryology, which reached its apogee in the work of von Baer.<sup>17</sup> Crucially, von Baer’s investigations started with the fertilised egg and its subsequent development, evidence of very different concerns to the theorists of generation. Modern embryology, if we may speak in such terms, began when the process of interest to investigators became how the individual organism got to point B from point A, when point A did not precede its own coming into being by the fertilisation (or, in the case of parthenogenesis, activation) of an egg.<sup>18</sup>

Morphology is a far younger pursuit. While admirable anatomical work was conducted on various species in the early modern period, this was generally of a natural historical or systematic nature (Russell, 1916: 22). It was only in the closing decades of the eighteenth-century that detailed observation, comparison and interpretation of features of different organisms was to be conducted for different – morphological – purposes (Bowler, 1996: 46; Russell, 1916: 45-51). It was 1817 before the term ‘morphology’ was used in print, and the late 1840s and 1850s before it gained wider currency among scholars (Nyhart, 1995: 36).

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<sup>16</sup> Some historians have emphasised the role of *Naturphilosophie* in freeing scientists from the burden of the eighteenth-century’s failed attempts to solve the problem of generation, by taking (epigenetic) development as a given, fundamental property of the Universe and proceeding on that basis (Lenoir, 1989; Look, 2006).

<sup>17</sup> Though it must be stressed that von Baer was a *Naturphilosoph* in the same way William Harvey was an Aristotelian – taking much methodological and theoretical inspiration, without rigidly adhering to theoretical *content*.

<sup>18</sup> This characterisation of the process of interest owes something to Griesemer’s identification of development and heredity as the same process, investigated from different directions (Griesemer, 2007).

Morphology is the science of organic form.<sup>19</sup> In the study of living organisms, morphology can be approached in two different ways. In one sense, it entails studying living organisms in terms of their form. This opposes morphology to physiology, which investigates living organisms (and parts of them) in terms of function. But in another sense, organic form is the *object* of investigation in itself. This sense does not preclude functional approaches, which may be fruitful in understanding the development or presence of certain forms (see Winther, 2006 for an account of different approaches in morphology, focusing on the twentieth-century).

The early years of morphology established two key themes that dominated debates throughout the nineteenth-century. In modified forms they continue to pervade morphology today. These are the concept of a 'type' and associated terms, and the tension between functional and non-functional (structural) explanations of form.<sup>20</sup>

The 'type' is a fundamental kind of form, an abstract basic plan, archetype or 'idea'. All organisms belonging to the class which is characterised by this basic 'type' possess this basic plan. The zoologist Georges Cuvier (1769-1832) identified four, as did the later pioneer of 'modern' embryology von Baer.<sup>21</sup> Cuvier, like von Baer, based his 'types' on years of careful observation, recording, drawing, interpretation and comparison of specimens. These acts served to engrave the particular details of the specimens into Cuvier's mind, and as Eigen (1997) observes, "Once words or images are graven in the mind, no matter what their origin, they inevitably shape all subsequent observations. 'Type' was the name Cuvier gave to such molds of perception and interpretation" (Eigen, 1997: 181). However, Cuvier was immersed in the works

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<sup>19</sup> At its inception, it was conceived by Goethe as a "science of the necessary and primordial forms of living bodies and their transformations", which included the study of form, formation, and transformation of organic beings (and, initially, minerals) (Steigerwald, 2002: 295-296).

<sup>20</sup> The term structural can be used to apply to formal approaches and explanations in general. However, it can also mean non-functional explanations of form. Due to this confusion, I will continue to use the terms 'form' and 'formal', despite their connotations.

<sup>21</sup> Cuvier's were: "Vertebrates, Molluscs, Articulates, and Radiates" (Russell, 1916: 41), while von Baer's were peripheral/radiate, longitudinal, massive/molluscan and vertebrate (Russell, 1916: 123). It is worth noting that von Baer preferred the term 'scheme' to archetype or type, given the Platonic connotations of the latter terms (Brauckmann, 2011: 387). A key difference between Cuvier and von Baer was that while Cuvier thought each type was a distinctive mode of *functional* organisation, von Baer believed each type to be a distinctive mode of *structural* organisation (Amundson, 2005: 42).

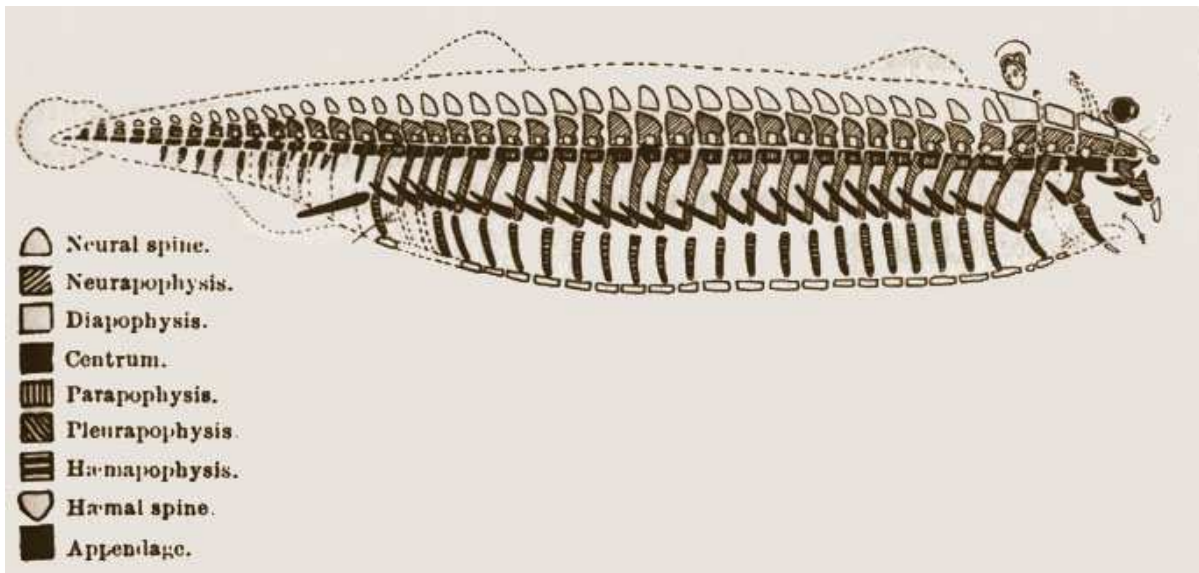


of Linnaeus and Buffon, so his ‘molds of perception and interpretation’ had some structure prior to, and alongside, his own observation and interpretation.<sup>22</sup> Furthermore, his method in discerning types was not completely unconstrained. Indeed, he came to develop a firm, explicit, methodological basis for his work (Eigen, 1997: 199). But Cuvier’s scientific practice neatly demonstrates the significance of the construction of expectations, not least expectations of *type*, by accumulated observation and interpretation of organisms.

A later morphologist, Richard Owen (1804-1892), famously produced a diagram depicting what he deemed to be the ‘archetype’ of the vertebrate skeleton, which is reproduced in **Figure 1** below. The diagram does not depict an actual skeleton in an actual vertebrate species. It represents instead the structure – the skeletal elements and their arrangement – that Owen believed to be common to, and underlying the structure of, vertebrates. Owen defined ‘archetype’ as “that ideal original or fundamental pattern on which a natural group of animals or system of organs has been constructed, and to modifications of which the various forms of such animals or organs may be referred” (Owen, 1848; quoted in Rupke, 1993: 235). Vertebrates were produced by addition to the archetype, and the ‘higher’ the species, the greater the departure from the basic scheme (Rupke, 1993: 243).

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<sup>22</sup> Though, as Eigen points out, for Cuvier, “Observation was inseparable from interpretation and criticism” (Eigen, 1997: 187) so his own findings therefore necessitated engagement with the works of the greats preceding him, as well as other workers of his own and previous eras. As his work matured, and the depth and breadth of his knowledge, appreciation and interpretation of living forms expanded, the “earlier process of emulating and correcting his masters gave way to producing his own standards of judgment in the form of the types” (Eigen, 1997: 199).



**Figure 1 – Richard Owen's archetype of the vertebrate skeleton, originally published in 1848's 'On the Archetype and Homologies of the Vertebrate Skeleton'. Source: <http://www.ucmp.berkeley.edu/history/owen.html> Last accessed 13.05.2015**

An archetype is a fundamental (ideal) plan, of geometrical relations of parts, which is manifested in all organisms within a given type. Differences between taxa within the scope of the plan were said to be the result of different modifications of the same underlying plan (Russell, 1916: 52).<sup>23</sup> Morphological types were and are representations of unities above the level of the species, never at the level of the species (Amundson, 2005: 81).

The tension between functional and structural morphologists centred on disagreements about the relative role of structural and functional causes of the resemblance of form.<sup>24</sup> The debate centred on the relative importance of structural constraint (due to manifesting a 'type') and adaptive modification. This adaptive modification was not merely a functional adaptation to external (environmental) conditions, but an internal co-adaptation of parts and organs (what Cuvier termed the "conditions of existence"). The debate was relevant for classification, as it went to the heart of how morphologists could compare organisms, and parts of them, with a view to establishing greater or lesser

<sup>23</sup> There is a stronger claim, of a unity across or between types, of the sort made by É. Geoffroy St. Hilaire, in contrast to the weaker doctrine of unity within a type or archetype that I deal with here (Greene, 2001: 190).

<sup>24</sup> The classic example is the debate between Cuvier and É. Geoffroy St. Hilaire (see Appel, 1987)

resemblances or similarities (the levels of affinity, we might say) between them. The task of discerning relevant relationships and affinities between organisms and their parts was central to the larger task of how one could (begin to) construct a 'natural system' to classify nature, as opposed to the artificial systems which already existed.<sup>25</sup> The search for a natural system provided the impetus for much biological work, especially in morphology and embryology, in the early nineteenth-century (Di Gregorio, 1982).<sup>26</sup>

### **2.2.1. Defining homology**

All of the key concepts just outlined relate to, rely on, and inform, the crucial notion of *homology*, which was central to the search for a natural system. The concept of homology was a reformulation of the prior concept of affinity, meaning a 'real' rather than merely superficial or phenomological relationship. The Oxford English Dictionary cites the first usage of the word 'homology' to 1656, when it was used to mean "an agreement" (OED, [1989] 2015a).<sup>27</sup> Its appearance in the biological sciences came only in the 1830s (ibid.). However, the practice of seeking and proposing homologies is ancient. Drawing on his inference of a unity of plan for different types or classes of animal, Aristotle detected the sameness of particular parts in animals of the same type. He went deeper in attempting to also distinguish "the essential resemblance underlying the differences in certain parts" (Russell, 1916: 8; see also Rieppel, 1988 for a historical account of the concept of homology).

Richard Owen provided a classical distinction between homologies and analogies, and also analysed the concept of homology into three types.<sup>28</sup> In

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<sup>25</sup> The distinction between artificial and natural systems, at least in the sense in which it came to be understood in the nineteenth-century, originated in the work of Linnaeus. He rejected artificial systems – characterised by *distinction* – based on procedures of logical division in which successive divisions were not deduced from prior divisions. Instead he sought to construct systems in which genera were described and *grouped* following an inductive procedure to ascertain relations based on commonalities of morphology (Müller-Wille, 2013).

<sup>26</sup> There were diverse reasons why the search for a natural system was deemed to be of importance, including the presumed stability of such a system (for the purposes of communication and exchange; Müller-Wille, 2013: 315-316), the potentially practical consequences of knowing what species are closely related to a species of economic value (Müller-Wille and Charmantier, 2012), and the natural theological desire to uncover and revel in the order of God's creation (Di Gregorio, 1982).

<sup>27</sup> Ironic, given the lack of agreement by biologists on exactly what homology *is* (Hall, 1999: 1-2).

<sup>28</sup> However, Owen believed that homologies and analogies "were not mutually exclusive" (Panchen, 1999: 16).

1840 Owen defined homologies as “fundamental similarities which underlie superficial adaptive modifications” (Owen, quoted in Bowler, 1996: 46). An analogy was defined as a similarity based on those superficial adaptive modifications. Owen was a structuralist, and for him homology was based on structure, analogy on the functional modifications of a structural plan (Amundson, 2005: 83). He proposed that two forces operated during embryonic development to produce the individual organism, the structural and the adaptive. The interplay of these forces was supposed to account for the general adherence to an overall (structural) archetype, while modifying elements of it to produce variation and diversity within and between organisms (Amundson, 2005: 87-88). Understanding the processes of embryonic development was therefore central to understand the origin of the diversity of species (ibid.). We might note here the proposed role of two forces which have different sources – the structural being a historical cause of certain aspects of an organism’s development, the adaptive a more proximate, ontogenetic and physiological cause of certain aspects of development.

Today we would include as superficial adaptive modifications examples of *convergent evolution*, where different elements of the body plan are used to produce structures performing the same or similar functions. A fundamental similarity could, on the other hand, underlie diversity of appearance and function. An example of this, the pentadactyl forelimbs of vertebrates, can be seen below (Bowler, 1996: 46-48). The task of the morphologist was to sort out the homologies from the analogies to aid the task of classification.<sup>29</sup> Morphology acted as a handmaiden for classification in the pre-Darwinian era, but also was to do so post-Darwin.

The three main types of homology Owen identified were special, general, and serial (Rupke, 2009: 113; Russell, 1916: 108-109).<sup>30</sup> The division of homology into three kinds enabled (but did not entail) the separation of an idealistic conception of homology (the general, which is the relation to a fundamental type) and the empirical conceptions (serial and special). This separation was

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<sup>29</sup> And consequently, “The main purpose of training in morphology was to develop the intuitive sense of which relationships are genuine homologies” (Bowler, 1996: 46).

<sup>30</sup> To which we could add a fourth, lateral homology, which is defined as “the relation of corresponding parts on the two sides of the body” (OED, [1989] 2015a)

not present in the French morphologist Étienne Geoffroy St. Hilaire's previously influential conception of homology (Jardine, 1967: 126).

A relation of general homology “is that in which a part or series of parts stands to the fundamental or general type, and its enunciation involves and implies a knowledge of the type on which a natural group of animals, the vertebrate for example, is constructed” (Owen, 1848: 7).

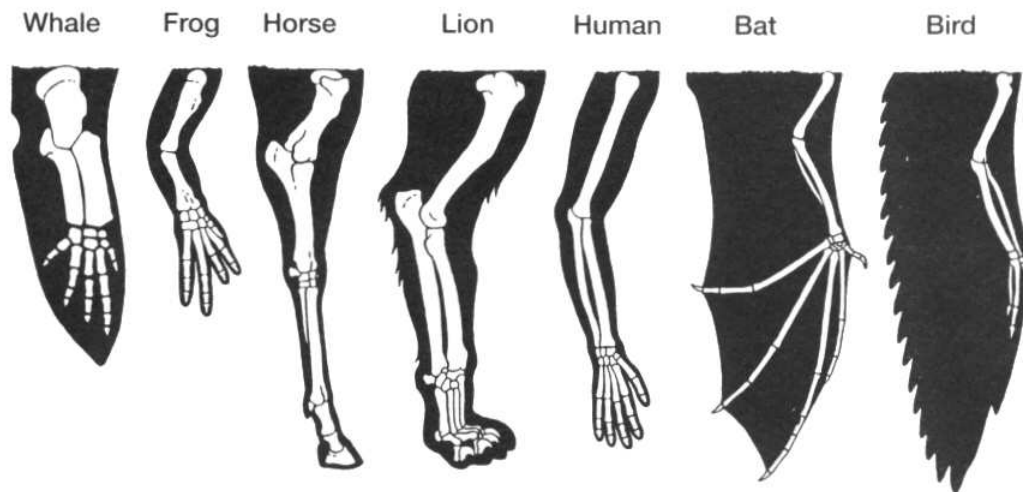
A serial homology is a repeating part within an organism, such as the vertebrae of the spine. The repeating part need not assume the exact same form or function, but could be modified. An example of this kind of serial homology is found in crustaceans. Crustaceans have segmented bodies. On each segment is a pair of ‘biramous’ (two-branched) appendages. Within the same organism, these appendages take very different forms, and perform different functions (see **Figure 2** for an example of this).



**Figure 2 – Serial homology of biramous appendages in a stomatopod (a mantis shrimp). L-R appendages: antennule (sensory), antenna (sensory), mandible (for crushing/grinding food), first and second maxillae (for chewing and shredding food), first through fifth maxillipeds (used to manipulate food), 3 walking legs, 5 pleopods with pinkish gills (swimming legs), and a uropod (tail). Source: <http://www.ucmp.berkeley.edu/arthropoda/crustacea/appendages.html> Last accessed 13.05.15**

A special homology is the same organ or part found in different organisms. Owen, in 1843, defined a special homology as “the correspondency of a part or organ, determined by its relative position and connections, with a part or organism in a different animal” (Owen, 1843, quoted in Russell, 1916: 108). This differs from the general homology in being a relation between parts of two

(or more) organisms, rather than being a relation between a part or parts of an organism and a 'type'. An example of special homology is the vertebrate forelimb, with its five digits (see **Figure 3**).



**Figure 3 – Special homology: the pentadactyl forelimbs of vertebrates. Note that this special homology is one where the organ or part, despite being homologous, has evolved very different functions. Source: <http://facstaff.cbu.edu/~seisen/Darwin.htm> Last accessed 15.05.2015**

The identification of such homologies was problematic for morphologists. How could a true homology be distinguished from a mere superficial resemblance or analogy? The work of morphology, insofar as it was about the discovery of archetypes, needed a robust practical basis for the identification and justification of homologies. What was to be this basis?

In the late eighteenth-century, morphologists compared the anatomical structure, and relations between parts, of adult organisms. The search for homologies between different organisms was not simply a case of looking to see which structures looked like one another. Functional adaptations could make structures look very similar, what we now call *convergence*. Instead, the relations of structures to each other would provide the criterion for establishing homologies. Étienne Geoffroy St. Hilaire (1772-1844) formulated and used the “principle of connections” which supposed that functional changes could do

many things to an organ, but they could not alter its structural relations to other parts (Rieppel, 1988: 39-40; Russell, 1916: 53 and 63).<sup>31</sup>

Étienne Geoffroy St. Hilaire is significant also for proposing an idea which was to develop in the hands of his protégée Étienne Serres and Johann Friedrich Meckel into the 'law of parallelism', that 'higher' animals repeat in their own embryonic development the adult stages of 'lower' animals (Rieppel, 1988: 70-72; Russell, 1916: 70). This idea faded towards the middle of the nineteenth-century. Russell claims that it was grievously wounded by the attacks made upon it by von Baer (Russell, 1916: 120-123), a view echoed by others (Amundson, 2005), but other accounts have downplayed the effects of von Baer's rejection of the 'law' (Ruse, 1999). Regardless of the reasons for the decline, ideas related to parallelism emerged again and gained adherents after the publication of Darwin's work in 1859. The most notable was Ernst Haeckel's biogenetic law.

The final contribution we may note from Geoffroy St. Hilaire is another consequence of his distrust in the method of comparing the form of (rather than the connections between) particular organs in order to ascertain homologies. Instead, he believed that the question of whether a particular organ is homologous between two different species could be determined by looking at whether the "materials of organisation" (the morphological units or building blocks) from which the organ is formed are homologous between species. This led Geoffroy St. Hilaire to study not the adult form, but the *embryonic development* of organisms, where the origin of such building blocks could be discerned, before their transformation during development (Appel, 1987: 85; Russell, 1916: 71-72).<sup>32</sup>

Geoffroy St. Hilaire's work established a key theme that dominated morphological theory and practice throughout the nineteenth-century: the

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<sup>31</sup> However, Geoffroy St. Hilaire recognised that this was not always the case, and introduced the principle of 'metastasis' to account for when this did not occur and the principle of connections was found wanting (Russell, 1916: 55-56). A metastasis was a movement of a part from its 'type' place for functional reasons. This concept was used to 'save' Geoffroy St. Hilaire's idea by accounting for seemingly completely different bones found in fish compared to other vertebrates (Russell, 1916: 55-56).

<sup>32</sup> Goethe had also, independently, looked to embryos to find homologies that the process of development might otherwise obscure (Russell, 1916: 72).

debate on the criterion of homology – should it be comparative adult anatomy, or comparative embryology?

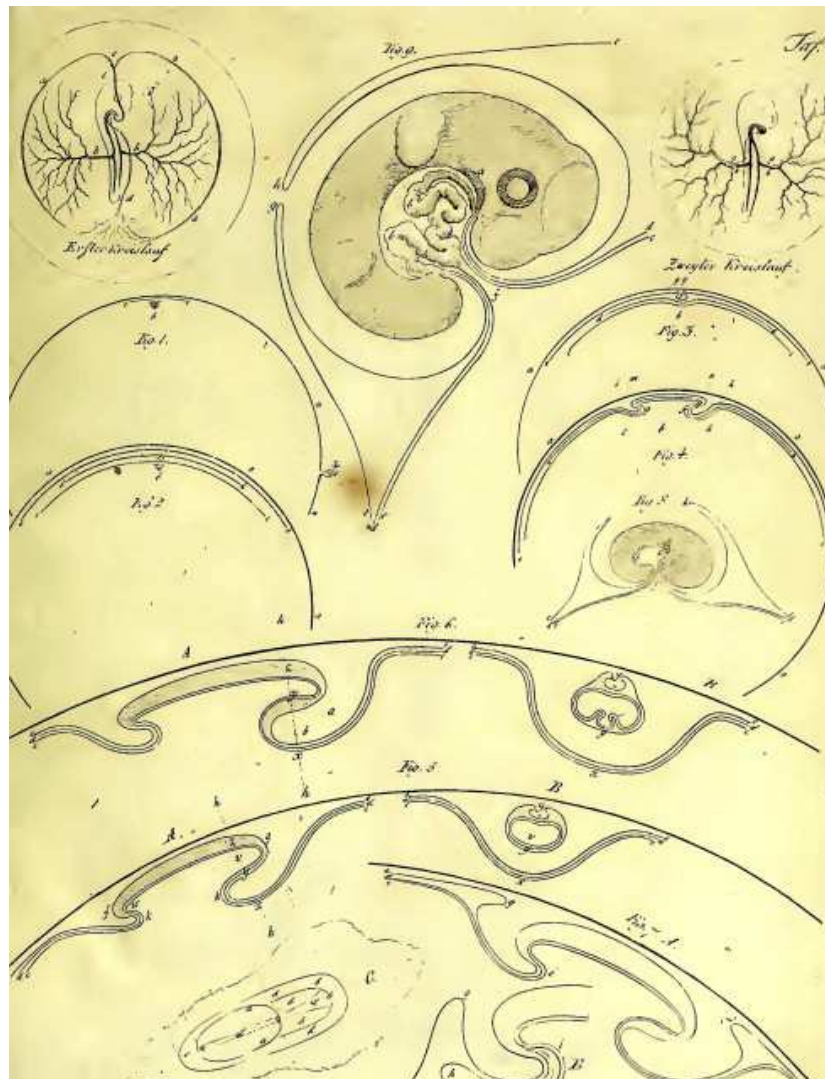
Comparing adult anatomy was certainly easier than comparing embryological structure. And yet, towards the middle of the nineteenth-century, the *embryological criterion* of homology became increasingly popular and important (Hall, 2000; Lenoir, 1989; Russell, 1916: 136-141). One reason for this development was the discovery of the germ-layers in embryos, and the proposed significance of this discovery for the demonstration and justification of homologies. If a proposed homology based on the evidence of adult anatomies was called into question, the discovery of a common embryological origin from the same germ-layer or part derived from a germ-layer (or not) would add greater weight (or undermine) the proposal.

The organisation of the early embryo into specific layers was recognised in the early-nineteenth-century. The 1817 description by Christian Pander (1794-1865) of the three layers he discovered in the chicken embryo (see **Figure 4**) was soon generalised to all vertebrates by his friend, Karl Ernst von Baer (Oppenheimer, 1967: 259). The establishment of primary germ layers in the embryo was a key empirical foundation for the science of embryology (Oppenheimer, 1967: 141; Russell, 1916: 115-118). Von Baer conceived of the formation of the germ layers as the first differentiation that occurred in the embryo.<sup>33</sup> After the formation of the germ layers, within each layer there would subsequently be formation of tissues, and then formation of organs.

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<sup>33</sup> Though for von Baer, the term 'embryo' did not encompass the very earliest stages of development (Sander and Schmidt-Ott, 2004: 71). Indeed, von Baer wonders "whether by going further and further back [in development], we may not eventually attain a stage in which the embryos of the Vertebrata agree with those of the Invertebrata" (von Baer, Huxley trans., [1828] 1853: 212). At the beginning of development, then, the organism is merely an *animal*. It is with the establishment of four main types of development – radiate, spiral, symmetrical and doubly symmetrical – that the embryo is formed and the Type established (von Baer, Huxley trans., [1828] 1853: 215-216). These correspond to the different ways in which the fertilised egg is divided without overall growth (the process of cleavage) in the very earliest stages of development. Von Baer sees great significance in this, declaring "that every organic form, as regards its type becomes by the mode of its formation [the particular form of cleavage that takes place—JL] that which it eventually is. The scheme of development is nothing but the becoming type, and the type is the result of the scheme of formation. For that reason the type can only be wholly understood by learning the mode of its development. This introduces differences into the germs, which at first are alike in all essential points. Different conditions or formative powers must act upon the germ in order to produce this multiplicity" (von Baer, Huxley trans., [1828] 1853: 232).

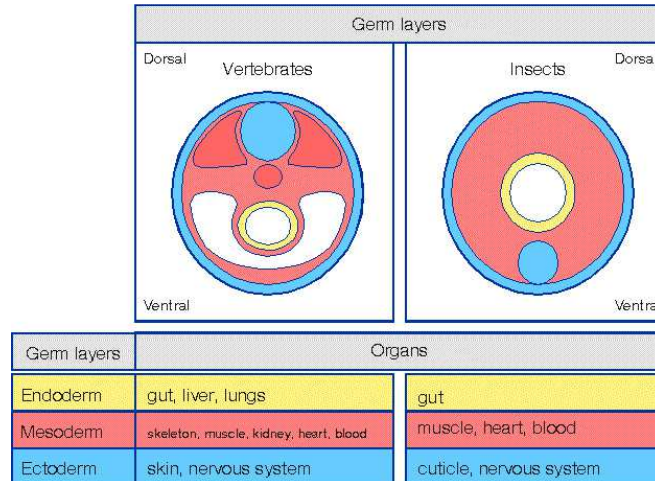




**Figure 4 – Pander's 1818 idealised diagram of the early development of the chick. In the middle of the diagram, four figures can be made out. Pander's figure 1 shows just one layer, figures 2, 3 and 4 (depicting later stages than figure 1) show the three layers he observed. Source: Brauckmann, 2011.**

The existence of these 'germ-layers' has not been in doubt since that time, and continues to form a key foundation of modern embryology. Modern developmental biology recognises the existence of germ-layers in all metazoans (multi-cellular animals), with the exception of sponges. Jellyfish (*Cnidaria*) and comb jellies (*Ctenophora*) exhibit two germ-layers, and are thus termed diploblastic (Gilbert, 2006: 43). The rest of the metazoans, including vertebrates and creatures such as the marine chordate invertebrate *Amphioxus*, sea-urchins, starfish, insects, worms, sea squirts and other wildly differing organisms, exhibit three germ-layers, and are thus termed triploblastic (ibid.).

Diploblastic organisms possess an ectoderm and an endoderm, while triploblastic organisms possess a mesoderm in addition to these. The ectoderm contains the cells that go on to form the epidermis and the nervous system; the endoderm, the lining of the digestive tract, respiratory tract (including the lungs) and endocrine glands; the mesoderm, the heart, blood, kidneys, gonads, muscles, bones and connective tissue (Gilbert, 2006: 8) (see **Figure 5** below).<sup>34</sup>



**Figure 5 – Diagram depicting germ layers and the organs produced in them. Source: Wolpert and Tickle, 2011: 16.**

The significance of these germ-layers, their nature and the role they play in the development of individual organisms, was a matter of considerable debate in the nineteenth-century.<sup>35</sup> Some of the key points of contention were whether the mesoderm was a germ-layer, whether the germ-layers were universal (and homologous), their significance for understanding phylogeny and evolution, and what the role and fate was of the germ-layers in organismal development (Oppenheimer, 1967: 256-277). The latter problem came to be associated with debates concerning the cause of differentiation in the developing organism, the fates of cells (in germ-layers, for example) and their descendants, the role of context in development, and related questions.

<sup>34</sup> At least, that is the textbook story. The reality, as always in biology, is a little more complex and laden with exceptions.

<sup>35</sup> For more detailed accounts of the history of germ-layer theory, see Oppenheimer (1967: 256-277) and Russell (1916: 115-120, 208-212, 288-299).

The reason why many of these questions were deemed to be important lay in the significance that germ-layers were thought to hold for the embryological investigation of homologies. Before the development of more reliable microscopes in the second half of the nineteenth-century, germ-layer formation was the earliest stage of embryogenesis that could be clearly observed.<sup>36</sup> Furthermore, it was significant because adult structures could be traced back to the germ-layer and its products (such as particular parts of the germ-layer and tissues). If a particular adult structure in two different species could be traced back to the same embryological origin and derivation it could be deemed homologous. If it could not, it would be deemed to be a mere superficial (functional) adaptation and labelled as analogous. It was believed that common embryological origin would indicate a more fundamental or deeper level of similarity.

The landmark Croonian Lecture delivered by T. H. Huxley (1825-1895) in 1858 gives us an indication of the role embryology played in morphological theory and practice, but also the state of morphology on the eve of the publication of *On the Origin of Species*. Entitled 'On the Theory of the Vertebrate Skull', it dealt with the theory that the skull was a modified vertebra. Huxley identified that "the phrase "Theory of the Skull" is ordinarily employed to denote the answers to two very different questions; the first, Are all vertebrate skulls constructed upon one and the same plan?—the second, Is such plan, supposing it to exist, identical with that of the vertebral column?" (Huxley, 1858: 384). He noted that "As there are two problems, so there are two methods of obtaining their solution. Employing the one, the observer compares together a long series of the skulls and vertebral columns of adult Vertebrata, determining, in this way, the corresponding parts of those which are most widely dissimilar, by the interpolation of transitional gradations of structure. Using the other method, the investigator traces back skull and vertebral column to their earliest embryonic states, and determines the identity of parts by their developmental relations" (ibid.). While acknowledging that each method has its role for the

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<sup>36</sup> The Pander diagram reproduced in **Figure 4** shows this, but also von Baer's observations using low-powered lenses which found that the embryo "develops first by the primary separation into layers" (Brauckmann, 2011: 387). Von Baer preferred a low magnification because he believed "that a higher one would have obscured the minute differences of texture and would have attenuated the contrast too" (ibid.).

particular problem it is used to explore, he argued “that to one, and to one only, can the ultimate appeal be made, in the discussion of morphological questions. For seeing that living organisms not only are, but become, and that all their parts pass through a series of states before they reach their adult condition, it necessarily follows that it is impossible to say, that two parts are homologous or have the same morphological relations to the rest of the organism, unless we know, not only that there is no essential difference in these relations in the adult condition, but that there is no essential difference in the course by which they arrive at that condition. The study of the gradations of structure presented by a series of living beings may have the utmost value in suggesting homologies, but the study of development alone can finally demonstrate them” (Huxley, 1858: 384-385).

Huxley therefore concluded that, while the inspection of comparative adult anatomy may be extremely useful in suggesting possible homologies, only comparative embryology could definitively establish them. One could say that Huxley’s position was that anatomy proposes, while embryology disposes. Furthermore, embryology allowed Huxley to establish a unity of plan of all vertebrate skulls, a task which comparative anatomy was unable to fulfil (Russell, 1916: 160). The early development of a variety of forms revealed an “embryological archetype” (Russell, 1916: 161).

Despite the debates over the relative merits of homologies established through comparative embryology or comparative adult anatomy, embryology had by the late-1850s been established as an important part of morphological research. Both morphology and embryology were about to be transformed by the advent of Darwinism, and the new popularity of evolutionary theories.<sup>37</sup>

### **2.2.2. The impact of Darwinism**

Darwin’s theory of descent with modification was supported by morphological and embryological evidence (Amundson, 2005: 96-98; Ruse, 1999: 196-197).

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<sup>37</sup> I stress that this was a *new* popularity, and that the significant function of Darwinism at this point in time was to popularise, and make scientifically respectable, the notion that species had a history and that they had genealogical relationships as well as (or perhaps instead of) relations of or to a type. See Bowler (1996) for an account of precisely how Darwinism transformed morphology.

Darwin, while not a morphologist, did reflect on the ways that his theory might change morphological thinking and practice.

For example, rather than reflecting modifications of an *ideal* archetype (idealistic morphology), relationships between different species could be recast as the result of differential modification of *real* ancestors (evolutionary morphology).<sup>38</sup> Darwin asked us to “suppose that the ancient progenitor, the archetype as it may be called, of all mammals, had its limbs constructed on the existing general pattern, for whatever purpose they served, we can at once perceive the plain signification of the homologous construction of the limbs throughout the whole class” (Darwin, [1859] 1985: 416). The archetype and unity of plan could therefore be reinterpreted as the consequence of descent from a common ancestral form, rather than membership of a common type exhibiting a particular archetype (Russell, 1916: 235). However, in so doing, Darwin changed the explanatory function of the unity of type. Rather than being invoked to explain the origin of form, it was now invoked to explain the change in form (Amundson, 2005: 104-106). In the former case, the ontogeny of form was central, and this was where embryology could be of service to morphology. In the latter case phylogeny was crucial and the investigation of embryonic development would only be valuable insofar as it contributed to an understanding of phylogeny.

In moving away from a typological conception of species and typological and idealistic conceptions of organisms and their relations with other organisms in general, Darwinism transformed how *variation* was dealt with by biologists. The typological conception of species (and higher-level taxa) conceived of variations (away from the ideal type) as ‘accidental’ deviations constituting “an obstacle to clear understanding, rather than an object of study” (Gliboff, 2007:274). Darwin turned this on its head. Rather than variation being the exception to the rule, variation (and its constant production and maintenance both within and between species) was the rule. Quite why this was so became an active research

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<sup>38</sup> This shift was not so dramatic for morphologists like Carl Gegenbaur (1826-1903), who had already conceived within the framework of idealistic morphology relations between the different (seven, later nine, in Gegenbaur’s case) types before being convinced of the theory of descent with modification (Coleman, 1976). These relations, and the accompanying diagrams illustrating them, could therefore be reinterpreted, but only slightly modified, in the light of Darwinism (ibid.).

question post-Darwin.<sup>39</sup> Variation as the object of research could draw in many different approaches and many different disciplines, owing to its manifoldness as a concept and its central importance to many distinct problems and avenues of research. In recent years, typological approaches have been revisited by historians and philosophers, and in chapter 6 I deal with these revisions of the picture I have briefly painted here. Additionally, it is not necessarily the case that Darwinism undercut the possibility of or the search for typologies, as the evolutionary typology practised by the likes of Gegenbaur and Haeckel demonstrated (Di Gregorio, 1995).

As well as changes in the understanding of variation, after Darwin the concepts of homology and analogy could be reformulated to take account of genealogical relationships. Homology was recast in terms of genealogy, and explained in terms of derivation from a common ancestor, rather than derivation from an archetype or ideal form (Ruse, 1999: 196; Russell, 1916: 247).<sup>40</sup> Analogous traits were therefore now recast as similarities that were not derived from a common ancestor. However, the task of the evolutionary morphologist, like the idealist morphologist, was still “to study modern forms and try to determine which were the ancestral characters” and which were ‘superficial’ adaptations (Bowler, 1996: 55).

Darwin noticed that embryos of different species resemble each other more than the adult forms do. Darwin attributed this to the fact that adaptive modifications occur later in life, and are inherited by offspring at that same later stage (Gould, 1977: 71; Russell, 1916: 237). However, Darwin did not only recount the similarity of embryos of different animals. He also observed the divergence from this “when an animal during any part of its embryonic career is active, and has to provide for itself.” As a consequence of the resulting “special adaptations, the similarity of the larvae or active embryos of allied animals is

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<sup>39</sup> Generally speaking. There were some scientists, such as H. G. Bronn (1800-1862), who were concerned with explaining variation before Darwin (see Gliboff, 2007). Darwin himself proposed a number of ways in which heritable variation could be generated – indirect external (the environment acting on the reproductive organs of the parents, the change not appearing until the following generation); direct external (the environment changing the organism, the change being passed on to the next generation by a gemmule or gemmules); and hybridisation. All three were dependent on inducement by external (environmental) changes (Winther, 2000: 430-432).

<sup>40</sup> However, an additional problem arose when homology was used as evidence for common descent, despite common descent now being used as a criterion for homology. I will discuss this problem in the next section.

sometimes much obscured” (Darwin, [1859] 1985: 420). Darwin’s comments concerning the relevance of embryos for classification were picked up by the generation of morphologists spearheaded by T. H. Huxley, F. M. Balfour (1851-1882), E. Ray Lankester (1847-1929), Ernst Haeckel (1834-1919) and Carl Gegenbaur (Russell, 1916: 247). The implications were heavily explored and debated, and led to considerable work in comparative embryology, and from that into different ways of investigating embryos towards the last few decades of the nineteenth-century.

The incompleteness of the fossil record was a problem for Darwin, and it was also a problem for morphologists looking to classify species on the basis of degree of relatedness (Bowler, 1996: 84). Any new line of evidence which would allow biologists to make inferences concerning ancestral species would therefore have been extremely welcome. One possibility was that if embryos were less modified (by evolution) than adult forms, they would reveal the ‘archetype’ better. The pre-Darwinian conception of archetype was now reformulated in an evolutionary way as an embryological archetype or fundamental plan, and could therefore potentially provide indications about the structure of *ancestral forms* (Russell, 1916: 237).

The embryological criterion of homology was given considerable impetus by Darwin’s work, and seemed to provide a way to peer into the past. This window into the history of evolution could be used to infer phylogenetic relationships based on homologies revealing a common ancestor. It could also be used to infer the nature of that common ancestral form itself. When it was realised that embryology could lend itself in these ways to morphological and classificatory work, a boom in phylogenetic speculation ensued. Some of this was rigorous, some more fanciful. Before exploring this, we need to return to the study of germ-layers, and their significance for morphology.

In the late-1860s, the Russian embryologist Alexander Kovalevsky noticed that invertebrate embryos possessed the same primary germ-layers as vertebrates, and that the notochord (a flexible rod-like structure which forms in the embryos of all chordates, and exists in some adult forms) in the invertebrate ascidians (sea squirts) was specifically homologous to the notochord in *Amphioxus* and vertebrates. He found that in all of them the notochord formed from folds in the

ectoderm (Mikhailov and Gilbert, 2002; Russell, 1916: 271).<sup>41</sup> He reached this conclusion with an embryological comparison of the germ-layer origin of the notochord in these different species, thus establishing “a new way of detecting homologies between organs in different forms” (Bowler, 1996: 148). This seemed to make it possible, however different the adult structures are, “to see a common origin for organs in their mode of formation at this early stage” (ibid.).

The significance of any such homologies was fiercely contested by prominent embryologists.<sup>42</sup> However, despite contradictory claims, Kovalevsky’s findings were picked up enthusiastically by biologists of an evolutionary disposition (Oppenheimer, 1967: 266-269; see also Raff and Love, 2004). Among them were T. H. Huxley and Ernst Haeckel.

Haeckel was one of Darwin’s fiercest advocates.<sup>43</sup> Haeckel combined the germ-layer theory, his own interpretation of Darwinism and the old law of parallelism, into a new doctrine – the *biogenetic law*.<sup>44</sup> The first stage of this was the idea that in the development (or *ontogeny*) of so-called ‘higher’ organisms, the evolutionary history of the organism (*phylogeny*) was repeated, or *recapitulated*.<sup>45</sup> Ontogeny could therefore, for adherents of this approach, serve as a record of evolutionary history. Embryos of ‘higher organisms’ (like humans) would resemble the adults of ‘lower organisms’ (like fish).<sup>46</sup> This, in turn, provided a theory of ontogeny by historical causation, as opposed to more ‘proximate’ mechanistic causes of the production of form.

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<sup>41</sup> There were other observations and descriptions in the series of papers Kovalevsky (also spelled in the Polish form Kowalewski) published from the mid-1860s to the early 1870s on these matters. This is simply one important and instructive example.

<sup>42</sup> For example, Alfred Mathieu Giard, who argued “that homology does not necessarily mean an immediate common origin or close relationship” (Russell, 1916: 273).

<sup>43</sup> Richards (2008) argues that not only was Haeckel in his popularisations of Darwinism more faithful to Darwin’s own thinking than is commonly supposed by historians, but that his own work productively and creatively extended Darwinism in ways not all of which were to become discredited. This is not an uncontroversial position, cf. Ruse (2004).

<sup>44</sup> Richards (1992) has constructed a comprehensive and convincing argument that – contrary to the claims of other historians who put an ocean between Haeckel and Darwin – Darwin was indeed also a recapitulationist, and also a Progressionist (like Haeckel), conceiving of an overall progression over the course of evolutionary history, driven by external forces acting on populations, rather than internal forces acting within individuals (the Lamarckian version of Progressionism) (see Richards, 1992, esp. pp. 111-166).

<sup>45</sup> Haeckel actually invented, amongst many other words, the terms ‘ontogeny’ and ‘phylogeny’.

<sup>46</sup> As Richards (2008) points out, it was Haeckel’s concern to establish different kinds of biological individuality, and the relations between these different kinds that provided the background to this claim (Richards, 2008: 132-133).



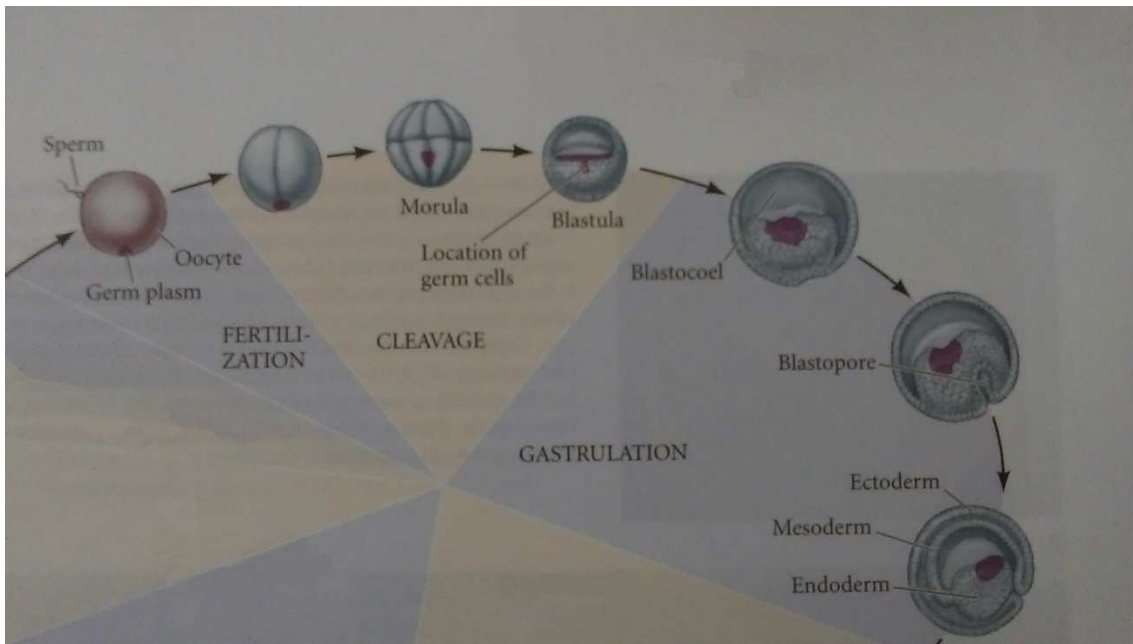
From this, Haeckel proposed that the examination of ontogeny would provide a guide to phylogeny. Despite acknowledging that ontogeny contracts the phylogeny by sometimes taking short-cuts through it (so not all adult stages in the evolutionary history of the organism were passed through during development, but ontogeny was an edited version of phylogeny), he proceeded along this line of reasoning with little caution. He constructed phylogenetic trees based on the different stages of embryonic development and from those stages posited hypothetical ancestral forms.<sup>47</sup>

One of the most notorious hypothetical forms, proposed in 1874, was the *Gastraea*, which was supposed to be the ancestral form of all metazoans.<sup>48</sup> The gastrula is an early stage of development in the vast majority of animals (see **Figure 6**). Haeckel claimed, crucially, that the gastrula was homologous across all forms (Nyhart, 1995: 190-191). All organisms possessing a gastrula had a unique common ancestral form, and this was the *Gastraea*. The *Gastraea* was supposed to be an organism which actually was a gastrula (see **Figure 7** for a representation of Haeckel's stages of development). The gastrula is a significant phase in development, as it is during gastrulation (or sometimes just after) that the germ-layers form. A methodological consequence of this view is that it was deemed pointless to study earlier stages of development than this. For those pursuing what has been called (e.g. by Baxter, 1977) the 'germ-layer doctrine' (these ideas, or slightly watered-down versions), it was the gastrula and the fate of the germ-layers and their products that were crucial – a basic, fixed point one might say – for morphological study and phylogenetic inference.

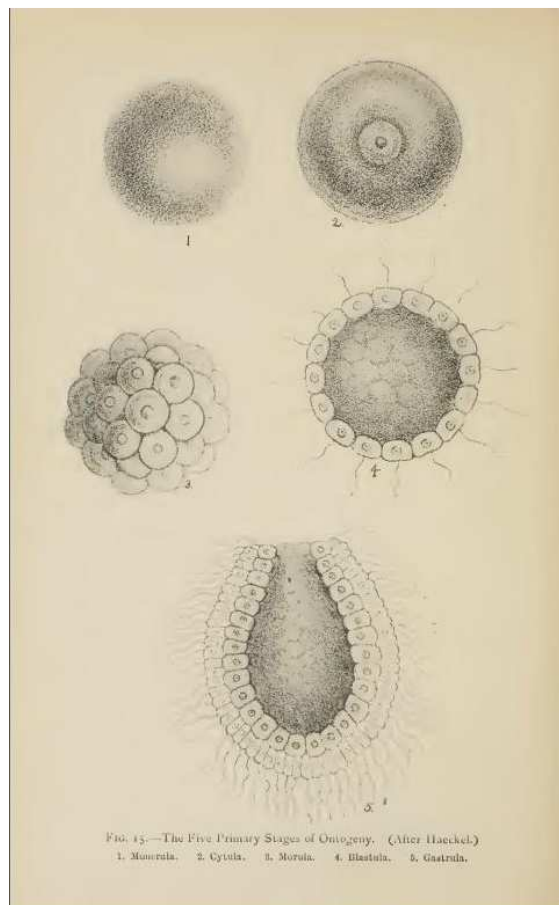
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<sup>47</sup> This is not unreasonable, and modern evolutionary developmental biologists have done this, albeit working from a far broader and deeper empirical base, and not extrapolating quite so far away from it.

<sup>48</sup> Other hypothesised forms corresponded to other stages of ontogeny, such as the *Synamoeba*, which was a proposed ancestral adult form of the embryonic stage known as the morula.



**Figure 6 – Diagram of the stages of development leading up to, and including, gastrulation. The embryo on the bottom right of the diagram is at the gastrula stage. Source: Gilbert, 2010: 7.**



**Figure 7 – Haeckel's five early stages of development, and supposed ancestral forms. The bottom is the gastrula/Gastraea. Source: Russell, 1916: 292.**

The root of the popularity of the biogenetic law lay in the ease of understanding it “in the simple mechanical terms of the reigning positivistic and deterministic science” (Churchill, 2007: 70).<sup>49</sup> It also offered the possibility of a combined approach to the problems of development, inheritance and taxonomy which didn’t threaten to fundamentally disrupt any existing disciplines, but merely to ‘Darwinise’ them, and in so doing establish stronger links between them (Rasmussen, 1991: 72). Its demise was replaced not by a different unifying theory, but by a fragmentation of those problems to be treated by different approaches (Rasmussen, 1991: 51-52).

Haeckel had problems accounting for the proposed third germ-layer, the mesoderm (Nyhart, 1995: 192). He was also forced to acknowledge that the ontogenetic record of phylogeny was not perfect, that the ‘true’ record of phylogeny (dubbed ‘palingenesis’) was ‘falsified’ by adaptations (labelled ‘cenogenesis’). Whether the germ-layer doctrine held or not depended upon the perceived relative significance of palingenesis and cenogenesis, and also the homology across the metazoans of the gastrula.

On the former point, in his history of the relationship between ontogeny and phylogeny in biology, Stephen Jay Gould observed that given the seemingly limitless number of observations that could be made and interpreted as ‘palingenetic’ or ‘cenogenetic’, there was no real way in which empirical results could have led to the downfall of the germ-layer doctrine. Exceptions were acknowledged, and seemingly damaging results accommodated within the system (Gould, 1977: 168-169).<sup>50</sup> Gould argues that the downfall of this method of phylogenetic speculation, which had occurred in practice if not in theory by the end of the nineteenth-century, lay in its eclipse by experimental biology.<sup>51</sup>

Gould argued that young researchers flocked from stale and sterile descriptive, comparative, phylogenetic research (dominated by the germ-layer doctrine) to

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<sup>49</sup> Excellent accounts can be found in Churchill (2007), Rasmussen (1991), Richards (2008) and Russell (1916).

<sup>50</sup> All that was needed in many cases was to label any problem a cenogenetic modification, and to assert that despite the presence of these, they were far outnumbered by palingenetic processes which preserved in the embryo the true record of evolutionary history.

<sup>51</sup> Not that it died out at the end of the nineteenth century. Gould in fact argues that it would only be destroyed *in theory* by the rise of Mendelian genetics (Gould, 1977: 202-206). Furthermore, Churchill (2007: 61-70) observes that, in a weak and diluted form, it still functioned as a useful heuristic, and hostile rebuttals into the 1930s indicate some continuing manifestations of the ‘strong’ form.

the more exciting and dynamic experimental embryology, which opened up a rich seam of research problems and questions, and seemingly the means by which to attack them (Gould, 1977: 186-202). In this view the germ-layer doctrine and its associated research programme were rejected as irrelevant and uninteresting, rather than incorrect. This view was influenced by the so-called 'revolt from morphology' thesis, the implications of which will be explored in the following chapter.

### **2.2.3. Methodological changes**

As the 1870s progressed, two contradictory movements became established in the biological sciences. On the one hand, there was the zenith of Haeckelian evolutionary morphology. On the other, there was the advent of a new way of conducting research in biology, and more specifically morphology. This was inspired by physiology, more precisely the physiology exemplified and promoted by Claude Bernard (1813-1878).

It is not the content of physiology that interests us here, but the methodology. In the beginning of the nineteenth-century, Xavier Bichat (1771-1802) established the basis for an analytical science of physiology, by establishing 'fundamental units' into which the organism could be analysed. For Bichat the 'fundamental units' were tissues. The advent of cell theory advanced the potential for analysis beyond the level of tissues. The idea of functional localisation, and the increasing success of the physical sciences in not just producing new knowledge but in producing knowledge useful for industrial production, led to the ideal of an analytical science based on physico-chemical explanations for physiological states and processes.

Bernard emphasised the importance of the analytical experiment and the need to establish the determinate causes of physiological phenomena of interest (Bernard, [1865] 1957). This was to be the work of the laboratory, of rigorously controlled conditions and variables. Only one variable was to be altered, and this was to provide a window into the phenomenon.<sup>52</sup> Such ideals deeply

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<sup>52</sup> The fact that Bernard's ideal matches up so neatly with the ideals of scientific investigation (as popularly understood) shows us not merely the success of such methods, but Bernard's success in advocating them. He was less successful in his disdain of statistical methods (see Morabia, 2006).

influenced Wilhelm His (1831-1904) and Wilhelm Roux, two embryologists who pursued, in different ways, the ideal of establishing a science of developmental mechanics. In the USA it was His who had more influence, particularly on Wilson's collaborator Charles Otis Whitman (1842-1910) (Maienschein, 1986). Roux's programme of *Entwicklungsmechanik*, based on prior mental analysis of an organism followed by experimental intervention, was to be taken up by his fellow German Hans Driesch. To say it led the men in different directions would be an understatement.

Roux envisaged a hierarchy of methods. The *naturalistic* methodology, of not interfering experimentally in or on the organism, but instead observing and comparing observations, was at the lower end, the higher end being experimental analysis. For Roux, a science first masters the descriptive method, which performs the important task of determining "in a definitive way the patterns of normal development against which experiments would have to be measured" (Churchill, 1973: 170). The next step on the methodological ladder is the comparative method, which enables the scientist to make worthwhile inferences. Then, higher still, is the descriptive experiment. This involves a significant degree of manipulation of the experimental object, but one that falls short of providing a causal analysis of development. This could be provided by the analytical experiment, which involves rigorous and artificial control of conditions and factors, and the manipulation of just one factor to ascertain its possible role. This, Roux believed, would contribute towards providing a causal-mechanical account of development (Churchill, 1973: 171-172).

Roux did not completely disparage these lower methods, which he believed a science must pass through in order to reach the heights then being achieved by the physical sciences. But they were regarded as necessary drudge work, an apprenticeship.

Roux was not an experimentalist noted for his experimental skill.<sup>53</sup> He can perhaps be seen more as a theorist than an experimentalist, but he was responsible for one significant experiment of his own. In 1888, he used a hot

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<sup>53</sup> Indeed, Churchill (1973) compares him unfavourably in this respect to the French biologist Laurent Chabry (1855-1894), who demonstrated tremendous technical abilities in his tragically short career. Ironically, Chabry was very much in the French teratological tradition which made use of 'natural experiments', in stark contrast to Roux's mantra of analysis and active intervention.

needle to kill one of the cells in a frog embryo at the two-cell stage of development. The purpose of this experiment was to test Weismann's hypothesis of qualitative division of germ-plasm at cell division (Maienschein, 1991a: 49). If Weismann's hypothesis was correct, Roux would have expected the result of further development to be a half-embryo, corresponding to the half derived from one of the two cells, the survivor. This is because each of the cells at the two-cell stage would only have half of the germ-plasm. This is exactly what Roux found in his experiment (Maienschein, 1991a: 50). How he interpreted this became known as the 'Roux-Weismann hypothesis' or the 'mosaic theory of development'. The mosaic theory postulated that the hereditary determining material is parcelled out to different cells as cell-division and development proceeds (Maienschein, 1991a: 49). The organism then was thought to be like a mosaic, in the sense that the different cells would have different parts of the germ-plasm in them. The fate of a cell and its descendants was therefore deemed to be independent of context. Roux's experiment suggested that this highly deterministic model of development could be seen in the earliest stages of development (Maienschein, 1991a: 50-51).

Inspired by Roux's experiment and the goal of establishing a causal-mechanical embryology in general, Hans Driesch decided to repeat the experiment with sea urchins (Maienschein, 1991a: 51). Rather than killing one of the cells with a hot needle, he violently shook them apart. Instead of the result which he had expected to get – a confirmation of mosaic theory – he got quite the opposite. Each of the cells went on to form a whole sea urchin, albeit smaller than normal. The same result sometimes occurred when he shook apart the embryo at the four-cell and eight-cell stages (Maienschein, 1991a: 52). This led to the formulation of what has been called the regulative theory of development. In the regulative theory, the developing embryo was considered to be a self-regulating whole, and the fate of an individual cell within that whole determined by its location. The fate of a cell and its descendants was therefore believed to be highly contextual. These two opposing theories provoked much embryological work in the 1890s, including Edmund Wilson's.

Roux's programme for an experimental embryology had its roots in the concerns of evolutionary morphology, more than he cared to admit. The key

step he made was to emphasise the importance of understanding the direct, proximate, causes of the different forms compared by morphologists. Towards this end, he developed a methodology which aimed to distinguish between aspects of form which have their origin in inherited factors (historical causes) and those which are due to adaptations, proximate or mechanical causes. The drive towards causal analysis and experimentation was therefore derived, in part, from the problematic established by Haeckel's biogenetic law – which type of cause was more prevalent and relevant, in the origination, reproduction and evolution of form and forms (Nyhart, 1995: 286-287). The example of the early experimental embryologists demonstrates a link between the establishment of a technical infrastructure to frame new epistemic objects and the need to simultaneously develop an analytical and conceptual framework concerning the nature of causation in the system of interest (including identifying candidate causes and types of cause). Without this, the isolation and manipulation of putative causes of interest could not occur, and results could not be clearly interpreted.

In the next chapter I will explore the historiography of the shift that occurred in the interests and practices of embryologists in the last decades of the nineteenth-century, and re-interpret it in terms of attributions of causality. To provide a context for examining their work, however, I need to establish what exactly the challenges are that faced (and still face) embryologists when studying the objects and processes of their science.

### **2.3. The nature and challenges of embryological research**

Research on embryos and developmental processes poses distinctive problems for biological researchers. As embryological investigation was at the heart of Wilson's research and morphological research in general in the era I am concerned with, an exploration of those distinctive problems and challenges is required. This section will outline some of these challenges, and how researchers, historical and modern, have tried to deal with them.

One of the key elements of embryological morphology was its comparative nature. In the Darwinian context, "comparative studies allow us to make

inferences about the evolutionary histories of both organisms” of different species being compared (Sanford *et al*, 2002: 834) and so the comparative method came to constitute the foundations on which the science of evolutionary morphology was constructed. Strasser and de Chadarevian (2011) have analysed the comparative method in biological research. For them the comparative approach consists of “the systematic comparison of a wide diversity of cases (or species in biology) that reveals regularities which are turned into universal claims” (Strasser and de Chadarevian, 2011: 320).

Conducting a comparison requires the elaboration and construction of stable reference points between comparators. This is complicated in embryological comparisons because it is not merely anatomy and structure that is being compared, but a process; one which also exhibits functions which need to be stabilised and isolated as well. The complexity of the comparative study of development has been attributed in part to the need for such a “5-dimensional analysis”, incorporating not just the three spatial dimensions but also one for the individual course of development and one for the evolutionary history (Richardson *et al*, 2001: 280).

Comparison of forms in development is further complicated by *heterochrony* (changes in developmental timing) and the transformation of “developmental characters” during key phases of development (*ibid.*).<sup>54</sup> These differences can occur not only between species, but also, critically, within species. Heterochrony makes it extremely hard to determine specific stages in development and to identify and delimit structures and processes to serve as a basis of comparison.<sup>55</sup>

Love (2008) observes that the “recognition of sameness for units and similarity of mechanisms in different species” necessary for such comparisons is, in fact, “a manifestation of the problem of homology” (Love, 2008: 231). Returning to the morphological research of the nineteenth-century, we can observe that the very thing researchers were trying to determine – homologies between

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<sup>54</sup> Heterochrony was yet another coinage of the prolific Haeckel (Gould, 1977: 221).

<sup>55</sup> Heterochrony within a species, which can confound or complicate the ability to determine specific stages, should be contrasted with the heterochrony between species, or the study of heterochrony as a way of drawing inference about evolutionary processes. In these latter two, heterochrony is an aid to investigation rather than a hindrance, even if concepts of heterochrony vary widely (Klingenberg, 1998).



organisms – was a precondition of the work they were themselves trying to perform. Morphologists were therefore faced with a ‘bootstrapping’ strategy, moving from and employing gross and obvious anatomical homologies, to less obvious homologies that could be established using finer anatomical or embryological investigation.

A related problem was the use of homologies to infer phylogenetic relationships, which post-Darwin formed a key part of the concept of homology. However, as Griffiths (2007) establishes, “operational criteria used to diagnose homologies were developed by the highly successful comparative embryological tradition of the first half of the nineteenth century” (Griffiths, 2007: 647). These criteria constituted (and continue to constitute) a way to establish homologies, independent of previously established evolutionary relationships. These criteria of homology were (and are) “the relative position of parts in the overall layout of two organisms...[:] the possession of ‘special qualities’, or shared features which cannot be explained by the role of a part in the life of the organism...[and] characters that cannot be homologised by the direct application of the first two criteria may nevertheless be homologous if they can be connected by a series of intermediates in other species such that each adjacent pair of characters can be homologised using the first two criteria” (Griffiths, 2007: 648). Griffiths urges that the establishment of homologies be considered independently of the explanation of homologies (Griffiths, 2007: 651). To invoke common descent as an *explanation* of a homology rather than a criterion of establishing a homology, allows one to use a homology or homologies to securely infer evolutionary relationships while avoiding problems of circularity (Griffiths, 2007: 648).

The establishment and justification of homologies was an important element in Wilson’s work up until the mid-1890s, and of course in morphological research in general in the nineteenth-century. Wilson’s attack on the embryological criterion of homology was significant enough to be cited in a modern discussion of it (Scholtz, 2005: 124). This modern work demonstrates that scientific debate over homology (and how it can be established) continues to this day.<sup>56</sup> Scholtz draws our attention to the consequences of the independence of ontogenetic stages; that certain stages of development can be altered while leaving others

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<sup>56</sup> The discussions in Bock and Cardew (eds.) (1999) also exemplify this.

unchanged (Scholtz, 2005: 127). The chief consequence is the “refutation of a special importance of any particular stage”, such as those found in embryonic development (ibid.).<sup>57</sup> No one stage (including the adult) is privileged over any other in the determination of a homology. The key insight we can draw from Scholtz, however, is that “the homology concept is in one way or another very much intermingled with...concepts, perceptions, and ‘laws’ of ontogeny and development”, which include how evolutionarily and ontogenetically independent different stages of development are (Scholtz, 2005: 135).

These issues and problems aside, the study of a process such as development can only be made tractable for comparative purposes by establishing definable and non-arbitrary stages of development. For morphological investigation, “development has to be considered as an orderly sequence of successive forms, not in its real nature as a process essentially continuous. Morphology has to replace the living continuity by a cinematographic succession of stages” (Russell, 1916: 168).<sup>58</sup> These stages can then be used as a basis for comparison across (and within) species.

Love picks up on this when he notes that “changes that occur in ontogeny are all physically continuous and thus the measures of time utilized must connect the “stages” represented” (Love, 2008: 231). Due to the intrinsic variability of development, chronological time (minutes and hours) is of no use.<sup>59</sup> Instead, embryologists sequentially order events and states (particular structural arrangements in early development, for example) in a series. This tension between the continuous process of ontogeny and the practice of dividing development into discrete stages is explored further in the following chapter, in the discussion on Wilson’s representation of cell-lineages and the formation of particular relations of cells in the early embryo.

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<sup>57</sup> Scholtz downplays the significance of phylotypic stages or zootypes. See Wagner (2014) for a defence of such concepts, which stress the significance of some relative invariance within a phylum for a defined period early in organismal development. Even if we were to accept the existence of a phylotypic stage, most ontogenetic stages can still be considered to be independent.

<sup>58</sup> A kinematograph or cinematograph was an early film (motion picture) camera. An interesting analogy, as the apparent movement or process observed in a cinema is in fact built up from myriad stages (frames) succeeding each other in quick succession.

<sup>59</sup> Though chronological staging is actually used in zebrafish.

In the early days of comparative embryology such *staging* (or the establishment of a *series*) was not standardised, and was constructed to work with a specific problem and method of comparison (Hopwood, 2007: 2-3). The impetus towards a standardisation of the normal stages would wait until the 1890s, when embryologists Albert Oppel and Franz Keibel pressed for and constructed normal plates and tables. These were intended to serve as a basis for systematic comparative investigation into the relationship between ontogeny and phylogeny, and ultimately to test the biogenetic law (Hopwood, 2007: 7-8).

What is the consequence of such staging? The pre-Darwinian comparative embryologists who conducted work on chicken embryos had such a large amount of samples that it “allowed abstraction from individual specimens and even some consideration of normal variation” (Hopwood, 2007: 3). Such abstraction and cognitive transformation of the observations to interpretations and representations to identify almost or actual transcendental types, was reinforced by the dominant ‘truth-to-nature’ mode of presenting biological findings (*ibid.*).<sup>60</sup>

Love observes that “developmental stages compose a ‘periodization’ that intentionally ignores variation associated with phenotypic plasticity” (Love, 2010: 681). Such periodization relies on idealisations which “involve ignoring types of known variation” in order “to depict a non-abstract typical case for various descriptive and explanatory purposes” (Love, 2010: 682). Such idealisations have their advantages, but they tend to persist rather than be undermined by subsequent observations and comparisons with them (*ibid.*), and the consequences of abstracting away variation can be a channelling of scientific observation and interpretation, to the exclusion of potentially relevant phenomena (Love, 2010: 684).

Two terms have been introduced here which require some clarification: idealisation and abstraction. Idealisations and abstractions are both simplifications, but can be distinguished by the result of the simplification. In the case of idealisation, it is a simplification which takes the form of a

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<sup>60</sup> Daston and Galison (2010) identify ‘truth-to-nature’, that is, idealised representations of the perceived reality behind appearances, rather than naturalistic depictions, as the dominant mode of representation in natural historical and biological work before the closing decades of the nineteenth-century.

misrepresentation, the “assertion of a falsehood” (Jones, 2005: 175). The “concrete object” or objects of interest must be changed in some way, “we mentally rearrange some of its inconvenient features” (Cartwright, 1989: 187). Abstraction, on the other hand, is a simplification which takes the form of an omission (Jones, 2005: 175), or a subtraction (Cartwright, 1989: 187), but *not* a misrepresentation (Jones, 2005: 175). Cartwright (1989), and following her, Jones (2005), argue that abstraction and idealisation are mutually exclusive.<sup>61</sup>

So is the stripping away of variation to produce normal stages of a normal development of a particular organism a strategy of idealisation or abstraction? If we consider normal stages, are they constructed by abstraction or idealisation? On the one hand, variation is, as Love puts it, “abstracted away” (Love, 2010: 684). It is subtracted, it is omitted. But it can only be said to be an abstraction if the omission does not constitute a misrepresentation. Whether normal stages and series constitute a misrepresentation is surely a matter of the use to which they, as tools, are being put.<sup>62</sup> The same normal stages could be construed as an idealisation in one context (one in which the variation omitted is highly relevant, such as evolutionary developmental biology) or abstraction in another (perhaps a biomedical context where a reference point of normal structure or function is required). We may also want to speak of models as more or less idealised or abstract (Jones, 2005: 192-199), which allows us to more fruitfully home in on *what it is* in the model that makes it more or less idealised, rather than simply label it as idealised or abstract and leave it at that. Already we can see that there are tensions between the representation of development, and the potential work which such representations might be used for.

Jones (2005) suggests that rather than focus on whether a particular model is an abstraction or an idealisation, we can focus instead on the process of idealisation or abstraction, and use this to highlight what it was that the scientist (or scientists) conducting it prioritised, and what they saw as rightfully omitted or abstracted away. In this way, we can analyse abstraction as an “epistemic

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<sup>61</sup> But these authors differ about how they are exclusive. For instance, Cartwright (1989) believes that idealisation pertains to models and abstractions to laws, but Jones (2005) argues that models can contain both idealisations and abstractions, and so can laws. Jones goes further in stating “That is not to say, of course, that a given representation cannot idealize some features of a system and abstract away from others.” (Jones, 2005: 176).

<sup>62</sup> And as tools, their representational capacity is not a key criterion of their successful deployment.

activity” which “emphasises the actions, choices, displacements, conceptual and physical transformations involved in the creation and use of biological models” (Leonelli, 2008: 509 and 527). From this point on, I shall refer to the process of omitting things from a model (such as variation) as abstraction rather than idealisation, as this does not imply a judgment on my part as to whether it forms a misrepresentation or not. Instead it allows us to focus on how the abstraction was conducted, and to what purpose.

It also allows us to consider not whether a particular representation is a misrepresentation or not, but rather how (and why) the representation came to be produced. Intermediate between the phenomenon and the particular image used in a paper or monograph are active and selective observation, and the selective representation of these observations. These can be of particular stages, states, or even processes of development. They are constructed in certain ways for certain purposes, and can influence the way in which not only the reader but the *producer* of the images is induced to think about development or aspects of it. Such representations constitute models, which initially are constructed with some reference to ‘the world’ or ‘nature’ and to ‘theory’, but which become autonomous, and take on a life of their own. In this way, they can function as ‘mediating instruments’ which can be used to help build or rebuild theories (Morgan and Morrison, 1999; in particular Morrison and Morgan, 1999). This will be explored in the following chapters with particular reference to the representations in Wilson’s work.

A classic example from the history of embryology of staging and arrangement into a series is the 1951 work of Hamburger and Hamilton, entitled ‘A Series of Normal Stages in the Development of the Chick Embryo’ (Hamburger and Hamilton, 1951). This work begins with the bold statement that: “The preparation of a series of normal stages of the chick embryo does not need justification at a time when chick embryos are not only widely used in descriptive and experimental embryology but are proving to be increasingly valuable in medical research” (Hamburger and Hamilton, 1951: 49).

The purpose of the paper is to present the results of the embryological investigation of the chick in a way that will be of direct practical relevance to scientific investigators. The aim of the authors was “to serve the practical

purpose of identifying and designating embryos on the basis of external characters” (Hamburger and Hamilton, 1951: 50) and to that end used “photographs and drawings [to] show most of the diagnostic criteria” (ibid.).

Recognising the variability of embryos, particularly in the tempo of development (globally or locally), they produced a series which was “independent of chronological age and of size of embryos” (ibid.). Different characters were used at different points in development to establish stages. This may be because a character was particularly prominent, or in one fascinating example, because it enabled the authors to provide the reader with little notations giving important information: “We have chosen intervals of three somites as “stages”; this makes it possible to designate embryos with intermediate numbers of somites by a + or – sign” (ibid.). For embryologists who need to identify the stages of many embryos, this is an economical way of conveying information about the features characteristic of particular stages.

To cope with the acknowledged “individual variation in individual characters”, Hamburger and Hamilton “tried to establish average or “standard” types by comparing a considerable number of embryos in each stage, and...selected for illustrations those embryos which appeared typical” (ibid.).<sup>63</sup> Hamburger and Hamilton, working with a large number of embryos, made a judgment about what variation to abstract away, and how to represent that for the embryological investigator reading the paper. The purpose of the paper was not to produce an exhaustive monograph on the embryology of the chick, accounting for all possible and actual variations exhibited, but to provide an idealised guide of diagnostic characters. An embryologist using this paper could use the stages

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<sup>63</sup> The first quote in this sentence (and this whole section, in fact) highlights an important point – that variation is itself a varied concept. While variation always implies comparison, what is being compared differs according to interest. At one level of resolution, a certain amount of variation may be observed, which at another would display a quite different amount of variation. For example, in studying genetic variation, we could study two populations of humans, to see what the genetic variation is between them. We could also study just one population, and see what the variation is within that population. We could study the genetic variation between many different individuals in different human populations. We could measure the genetic variation between a sample of humans and a sample of another species. We could also measure the genetic variation within a human, either the genetic variation of the microbiome (and perhaps compare this with the microbiomes of other humans) or the genetic variation between different human cells (and then see what the variation in the variation is between different humans, or different populations of humans!). We should also consider the different types of variation we might encounter when studying development, where one stage of development may exhibit a variation that other stages may not.

and series thus established in their own work, and most crucially, the communication of their work and results. The importance of stages is such, that “one of the earliest tasks to be mastered in one’s training as a developmental biologist is to learn to identify the stages of normal development using a stage series” (DiTeresi, 2010: 57). Referring to published canonical stage pictures of the frog *Xenopus*, Nick Hopwood recalls “internalizing these images”, which “became badges of membership in a community of researchers” (Hopwood, 2005: 1). However, as we shall see in chapter 4, the early experimental embryologists were not trained in such a way, and thus had to rely on their experience and growing familiarity with an organism to conceive of its normal development and normal stages.

As we have seen, the Hamburger and Hamilton paper began with a brief justification of the establishment of normal stages and series in the chick in particular. Why go to all this trouble for the chick and not a bat, or a woodlouse? Ankeny, in her work on the use of ‘case-based reasoning’ in developmental biology (Ankeny, 2012), observes that the “the chicken was clearly selected [for developmental work] for convenience and ease of experimentation” (Ankeny, 2012: 647). Von Baer used it to establish principles of development, and modern biologists use it to examine these and other principles (ibid.). It is not necessarily the best organism for this purpose, but as a case it is intensely studied in depth “with the goal of eventually elucidating norms or baseline patterns against which newly observed yet similar phenomena (e.g., in other species) can be compared” (Ankeny, 2012: 646).<sup>64</sup>

Cases can help ‘tame variation’ when the sheer weight of it threatens to make meaningful scientific work impractical, as it threatens to in developmental, and particularly *comparative* developmental, biology (Ankeny, 2012: 652). While Ankeny acknowledges that the ‘choice’ (or perhaps a term with fewer

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<sup>64</sup> In the case of the frog *Xenopus laevis*, which Ankeny examines, the process of metamorphosis which it exhibits is established as the example to which all other examples of metamorphosis can be compared. It even serves as the basis for establishing exactly what metamorphosis *is*, to identify whether certain processes in other organisms are in fact metamorphic. This brings to mind the early morphological innovation of Étienne Geoffroy St. Hilaire. Rather than accepting Man as the universal case, and comparing the structure of other organisms to human structure, he supposed that there were ideal perfect forms of organs and organ systems, and that for different organs, the most well-developed examples will be found in different species. For each organ or organ-system a series or scale of increasing perfection could be constructed, with one species possessing the nearest to ‘perfect’ manifestation of that organ to which the others could be compared (Russell, 1916: 54).

connotations of conscious decision-making) of an organism as a case can be due to the “similarity provided by the organism in question in relation to the process or issue under examination” (ibid.), factors such as “historic primacy or importance,...experimental tractability, [and] manipulability” are also critical (ibid.).

In the context of late nineteenth-century embryological work, understanding organisms as cases makes more sense than considering them as model organisms. Model organisms are highly constructed and standardised (Ankeny and Leonelli, 2011: 316), and are associated with the concentration of practical biological work on a small, narrow range of organisms.<sup>65</sup> Model organisms in this sense were not used in the embryological work in the late-nineteenth-century that I am focusing on. In late-nineteenth century embryology, instead of life-long commitment to one organism (with associated resources and community), there was a far more opportunistic approach to the selection and use of organisms, as we shall see when Wilson’s research is examined in more depth.

Bolker (1995) adds to “Historical accident and availability” some *biological* characteristics influencing the adoption and selection of model organisms. These include “rapid development and short generation time” (Bolker, 1995: 451), insensitivity to environmental conditions to ensure “minimal variation between individuals and between batches of embryos” (Bolker, 1995: 452), and “short generation times” (ibid.).

Bolker claims that the consequences of extrapolating from work conducted with organisms exhibiting such characteristics are that “we lack knowledge of the existing diversity in developmental patterns and processes” (Bolker, 1995: 453) and that this “ignorance of developmental variability and diversity leads to an overly deterministic view of development, and to a concomitant narrowing of focus to proximate, internal mechanisms” (ibid.). The problem identified here is the generalisation of results based on organisms that were not selected for particular purposes (such as the illustration of cases) but for practical and economic reasons.

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<sup>65</sup> Whether this association is necessary or contingent, I couldn’t say.



After discussing this, she notes that “Phylogeny is rarely or never a factor in the choice of model systems” (ibid.). This may be true to a significant extent in the present-day, but in nineteenth-century morphology, phylogeny was a significant factor in determining the choice of an organism to use as a basis for comparison, or as a case.<sup>66</sup> Organisms were chosen in part on the basis of their phylogenetic position because it was the problems of phylogeny, or more precisely the relations of ontogeny and phylogeny, that was the object of investigation.

## 2.4. Conclusion

In this chapter, I identified the concrete challenges facing embryologists and morphologists, which derived from the problems that were deemed to be paramount throughout the middle and latter decades of the nineteenth-century. After the publication of *On the Origin of Species*, a key problem was identifying and demonstrating evolutionary and genealogical relationships between different species. This led to a debate about the proper criterion (or criteria) that should be used to distinguish homologies from non-homologies, as these were in turn used to justify claims concerning common ancestry. Methodologically, the task for nineteenth-century morphologists and embryologists was to find some way to make valid comparisons between specimens, and between species.

Towards the end of the century, the advent of experimental methods in embryology, and a shift in the kinds of problems embryologists wanted to investigate, led to a debate about the methodology and purpose of embryological investigation. I will pick up on this debate in the next chapter. To enable me to develop the discussion, I have ended this chapter with a treatment of the ways in which embryologists have approached the challenges of investigating the complex process of organismal development. Chief amongst these are the processes of abstraction which allow them to divide the process of development into (normal) stages, to identify common features that can be used

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<sup>66</sup> Although I am generally in agreement with Bolker on these points, she did perhaps make the point too strongly about phylogeny not being a factor in modern biology, as phylogeny will at least be a factor in choice of organism in evolutionary developmental biology, even if ease of manipulation or the manifestation of a mechanism of interest may be more important factors.

as the basis for comparisons, and to abstract away the variation between embryos. In chapter 6 I deal with the processes of abstraction which manage variation, using the concept of typological practices concerning the production and use of 'normal development'. Normal development features in Wilson's work in his experiments on *Amphioxus* in 1892 that I detail in chapter 4. Experimental work such as this, which aimed at identifying processes responsible for the production of form, involved comparisons made between individuals of the same species, divided into 'normal' and 'manipulated' treatment groups. Although *Amphioxus* was chosen in part due to its phylogenetic position and relevance for assessing theories of vertebrate origins, the kind of intraspecific comparison employed was of no use for phylogenetic purposes. Such experimental work was thus an important shift in methodology from the practices associated with evolutionary morphology. The shift from evolutionary morphology to experimental embryology, and Wilson's role in this, is the focus of the next chapter.

## **Chapter 3 – From germ-layers to cell-lineage: morphology and the problems of development**

### **3.1. Introduction**

In the previous chapter I set the scene regarding late nineteenth-century biology, in particular morphology and embryology. In the late nineteenth-century, biologists increasingly believed that there were problems with the programmes of evolutionary embryology and comparative embryology. The challenges of embryological research I outlined in the previous chapter posed problems, but so did empirical results suggesting that the methods of those fields might not be as robust as previously thought, particularly with regard to ascertaining homologies, and therefore relations of descent.

In this chapter, I relate these factors to changes in how some biologists made attributions of causality concerning the process of embryonic development. I will show how this led to a decline in investigations that aimed to discover or use presumed historical causes of ontogeny. Instead, there was a shift towards the assessment of the role and weight of different proposed causal factors – historical and various proximate ones – and accompanying this, changes in scientific practices to more adequately address the new problems and questions.

I discuss the historical debates concerning some of these changes. This includes outlining the elaboration of, opposition to, and results of the so-called ‘revolt from morphology’ thesis that experimental embryology arose out of a reaction against the supposedly stale questions of evolutionary morphology. This historiographical debate eventually focused on two supposedly rival approaches to the study of life, naturalism and experimentalism, and the relationship between them.

It is in this context that I introduce Edmund Beecher Wilson, his training, early career and research interests. Picking up from the previous chapter’s reference to the decline in the germ-layer doctrine, I note Wilson’s supposed role in this as part of a review of some of the historical perspectives on Wilson and his work.

Informed by the historiographical stance I have adopted, I detail how Wilson's embryological interests changed, from the problem of assessing relations of descent, the history of forms (and how embryology can contribute towards that), to the problem of identifying the (relevant kinds of) causal factors and their relative weight in the production of form(s). In the former set of interests, the production of form is interesting insofar as the way it is produced (traced back to structures and events in early development) in embryogenesis can be compared between different species. In the latter set, the production of form by embryogenesis is the central topic of interest, and comparison plays a different role. For Wilson that role was the comparison of different phenomena in different organisms, and using these comparisons to posit a single process to explain the diversity of modes of development. There was therefore a shift from concern with the pattern of forms observed, to a greater interest in the processes responsible for those patterns. In outlining Wilson's shift in priorities and practices, this chapter sets the scene for future chapters where the outcome of this – already hinted at in the preceding sentences – will be assessed.

In this chapter I provide an account of Wilson's training and early research career. This was dominated by evolutionary morphological approaches, with a view to gaining some kind of insight into the genealogical relationships of particular organisms, but it provoked an interest in embryonic variation. Moving on from this, I analyse one key aspect of Wilson's early career, which occurred at what I have demonstrated to be a vital time for embryology – with a mass of data generated, and rival programmes in evolutionary morphology and more experimental approaches – from the late 1880s to the early 1890s. In these years Wilson began collaborating with, amongst others, Charles Otis Whitman and Edwin Conklin (1863-1952), travelled to Europe and then moved to Columbia University, which allowed him to focus more intensely on research.

Wilson's embryological work shifted over the course of 1887-1891 because he was trying to establish a solid basis for the embryological comparison of different species, to be able to establish homologies between them, and gain an understanding of the genealogical relationships and evolutionary history of key groups of organisms. A central plank of this programme, from the late 1880s

onwards, was the perceived need to establish whether the middle germ-layer, the mesoderm, was a layer independent of the other two germ-layers.

It is the thesis of this chapter that in following such threads of research, he sowed the seeds of fundamental changes in the way he conducted embryological investigation and conceptualised development. I detail how, in order to establish the homology of germ-layers across species, and therefore the homology of the structures arising from the germ-layers later in development, Wilson was forced to study ever earlier stages of development. This prompted the adoption of a new technique – cell-lineage research – and work with a new organism. As indicated in the methodological discussion in the introductory chapter, my approach is to reconstruct the route towards (and through) the cell-lineage research, tracing the internal logic of Wilson’s research as it proceeded from the late-1880s and into the 1890s.

As a result of this work Wilson became increasingly fascinated with the early stages of development prior to the formation of the germ-layers. This took the form of an increasing interest in the cleavage patterns of embryos. Cleavage, also known as segmentation, is the process in early embryonic development by which the egg divides into many smaller cells, called blastomeres, without an overall increase in size of the embryo. Cleavage produces various forms of symmetry in the early embryo. Different arrangements of the cells and symmetries produced constitute different discernible ‘cleavage-forms’. Wilson’s interest was piqued by the variability displayed by the cleavage forms, and his findings helped to undermine the Haeckelian framework of evolutionary morphology.

As a result of the challenges Wilson faced in finding new and better ways to frame the epistemic object – securing embryological grounds for making judgements concerning the homology of germ-layers and structures deriving from these between different species – his work threw up new questions and surprises concerning the nature of embryonic development, and in particular the causes of differentiation, determination, and production of certain cleavage-forms. This led him to become particularly interested in assessing the relative strength of two possible causes, mechanical conditions and what he called a “hereditary tendency”.

Later in the chapter, I draw attention to the fact that Wilson's growing mastery of embryological detail, and his talent for representation, led to ever more processual depictions and interpretations of his findings. Increasingly, Wilson became interested in the *process* of development.

### 3.2. Evolutionary morphology and Wilson

In 1894 Wilson delivered a lecture at the summer gathering at Woods Hole in Massachusetts, in which he detailed the problems with the embryological criterion of homology.<sup>67</sup> One of the key elements of this was the denial that germ-layers are homologous in their origin across all metazoans (Wilson, 1895a: 108-113). The zoologist (and Wilson's friend) Frank Lillie recalled Wilson excitedly declaring to him in 1891: "I believe I am going to destroy the germ-layer theory of development!" (Lillie, 1944: 124). But just a few years beforehand, Wilson had happily used the germ-layers as the basis for embryological comparative morphological investigation.<sup>68</sup> What exactly happened in the late 1880s and early 1890s to change Wilson's views on this matter?

Wilson was embedded within the context of an American morphology which "pressed for refinements in the determination of homologous structures" (Benson, 1985: 174) and which grappled with the question of "whether the origin of the germ layer revealed the evolutionary heritage, or whether it was the fate of the germ layer that was more important" (ibid.). The decline in adherence to germ-layer doctrine, as you will see in this section, has formed a key part of historical debates around the so-called 'revolt from morphology' and the supposed move from naturalistic to experimentalist modes of scientific investigation. Before I begin my discussion of Wilson's career, I would like therefore to bring in some other perspectives on Wilson, particularly as they

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<sup>67</sup> Curiously, though it is now referred to as Woods Hole, it was officially known from 1877 to 1896 as Wood's Holl. I retain the modern (and pre-1877) spelling (<http://www.nefsc.noaa.gov/history/stories/whistory.html> Last accessed 14.05.2015).

<sup>68</sup> In 1886, Wilson co-authored a textbook which contained the following section regarding the germ-layer theory: "Germ-layers like those of *Lumbricus*, and called by the same names, are found in the embryos of all higher animals; and it will hereafter appear that this fact has a profound meaning" (Sedgwick and Wilson, 1886: 150).

relate to the question of naturalism and experimentalism with respect to the development of germ-layer theory.

Gross (1985) sees Wilson as one of the leaders of a group of American biologists who in the course of their careers managed to bring “the revolution against nineteenth century natural philosophy, and the old spirits and specters, to a triumphant conclusion” (Gross, 1985: 70). This view would seem to corroborate the ‘revolt from morphology’ thesis proposed in its most notable form by Garland Allen (1978). In this view, a generation of biologists trained in morphology and embryology such as Thomas Hunt Morgan (1866-1945) and Edmund Wilson “became exasperated with the aims and practices of morphology.” In particular, they rejected the focus on evolutionary and phylogenetic questions, and the descriptive and speculative methods employed to answer them (Allen, 1978: 18-19). However, in response to other historians questioning aspects of this interpretation (Benson, 1981; Maienschein, 1981), Allen revised his thesis to focus on the adoption of (interventionist) experimental methods in embryology and the rejection of naturalistic methodologies (Allen, 1981). The debate had largely run its course by the mid-1980s, but it had the effect of focusing attention on exactly what had changed in those last decades of the nineteenth-century. What is now clear is that there was not a replacement of observational and descriptive morphology with a rigorous, exciting new experimental embryology, but a synthesis or integration of observational, comparative and experimental embryology. These men started as “observers and tracers of cell lineage, later experimenters, later synthesisers” (Gross, 1985: 70).

Starting off with descriptive and comparative work, Wilson moved towards experimental methods, and abandoned previous problems of evolutionary relationships. He replaced these with increasing emphasis on the problems of differentiation and determination of the adult from the egg, all the while moving in investigative focus further and further back in the course of development. Crucial to this evolutionary picture of Wilson’s move away from comparative studies of phylogenetic problems was the role of his cell-lineage studies as a bridge towards his new interests. These studies led Wilson to try and ascertain the interplay of internal and external factors in development. Starting from the

problem of homology, he ended up transitioning through the work which aimed to tackle that problem to a concern with the determination of development, and the sources of that determination (Maienschein, 1978, 1981).

At the beginning of Wilson's career he pursued "very traditional descriptive studies" and comparative work, and this continued until at least the mid-1880s (Maienschein, 1981: 99). Indeed, the evidence of Wilson's early work from his published papers and presentations made at University meetings points unequivocally to an emphasis on phylogenetic relationships, reached by means of detailed, painstaking descriptive and comparative work (see Wilson, 1882a, 1882b). On this matter, I am in agreement with Maienschein; the content of Wilson's research, if not necessarily the style of work, was in line with his mentor, William Keith Brooks (1848-1908) (Maienschein, 1987a: 779).

Baxter (1977: 366-367) ascribes Wilson's (almost passive) acceptance of the germ-layer doctrine to this tutelage by Brooks. The method of ascertaining homologies by tracing back organs to the germ-layers they derived from was employed by Brooks, who saw any attempt to track embryological structures and arrangements of cells prior to the gastrula, the first stage at which the germ-layers are apparent, as pointless (Conklin, 1968: 115).<sup>69</sup>

What is apparent in the changes which occurred in embryology in the late nineteenth-century is a shift from one regime of the attribution and assessment of (degrees of strength of) causality to another. The historiography that I have just briefly outlined indicates ways in which that might be characterised. Broadly speaking, there was a shift, among a certain influential subset of a generation of biologists, from more naturalistic research to more experimentalist approaches. This was a shift from a concern with the reconstruction and investigation of the evolutionary process to a concern with the immediate ontogenetic production of form, therefore from the invocation of historical (phylogenetic) causes of form to proximate (we might say, mechanistic) causes of form, and to a focus on the relative role of different kinds of proposed or apparent proximate causes. This led Wilson to consider a shift in the role of embryology; how it can and should be conducted, and what it is good for. What was the epistemic object for which

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<sup>69</sup> Specifically, in this particular anecdote related by Conklin, the cleavage stages. Other people in the laboratory labelled Conklin's studies of cleavage as mere "cellular bookkeeping" (Conklin, 1968: 115).



embryological investigation was relevant, and what technical conditions embedded in new and existing methods and equipment used by embryologists were appropriate to such new epistemic objects? This is why attempts to establish a firm basis for the embryological criterion of homology, and the failure of such attempts, mattered. It was at the nexus of many different issues concerning the attribution of causation, and this helps explain the shift from one regime to another. This shift was from a set of practices directed towards providing explanations of changes in form. In that regime, whether embryology was useful for answering these questions was contested. The shift was to sets of practices and experimental systems directed towards providing explanations of the origin or causes of the production of organismal form (Amundson, 2005). In this sense, there was not so much of a revolt from morphology, but rather a revolt *towards* morphology. In this regime, comparative and experimental methods combined were deemed more fruitful, rather than just comparative method alone, as we will see over the course of the rest of this chapter, culminating in the arguments made by Wilson himself to that effect.

### **3.3. Wilson's training and early research**

In examining the biological sciences at the end of the nineteenth-century, and also Wilson's career, it is vital to consider the rise of the graduate university. This rise went hand in hand with the massive expansion in the academic biology community. As Keith Benson observes, from 1875, when there were no graduate biology programmes in the US, and 1910, when such programmes were well-developed in the major universities, the number of graduate students increased twenty-fold (Benson, 1988a: 331). The rise of the graduate universities was not merely a quantitative phenomenon. These institutions provided the material basis for original scientific research, in terms of libraries, laboratories, and graduate students. They expected original research from their biologists, and specialised teaching. This was in stark contrast to the denominational colleges which previously dominated the hiring of biologists, and which burdened them with overwhelming, and extremely broad, teaching commitments, as well as religious constraints in some cases (Cravens, 1978: 19-20). They also provided little in the way of resources for research.

Established in 1876 as a private research university, Johns Hopkins University was to become notable for the eminence of the biologists who passed through its graduate programme in the latter decades of the nineteenth-century. It decided to concentrate on doing a few things very well, rather than trying to do everything and achieving only mediocrity. The priority was placed on physiology, in anticipation of the construction of the medical school and hospital. The Head of Department at Johns Hopkins, H. Newell Martin (1848-1896), was a physiologist and enthusiast for experimental methods. However, a morphologist, William Keith Brooks, was also hired, and the research programme he led did not just lie in the shadow of the physiological one in the department. Indeed, in terms of postgraduates trained, Brooks' programme in descriptive morphological zoology outperformed the rest of the department by a significant margin (Benson, 1981: 118, 1985: 168-169). It was on that programme that Wilson did his doctorate.

The two fundamental orientations in biology, morphology (a concern with structure or form) and physiology (an interest in function), became less distinct in the last decades of the nineteenth-century (Benson, 1985; Maienschein, 1981). Wilson received training in both orientations. Furthermore, in the 1890s he imbibed Whitman's urgings for a physiological morphology (Maienschein, 1987b: 189).

The influence of Brooks as a teacher at Johns Hopkins has been noted, with one historian highlighting the extent to which his "students exhibited many shared concerns owing to their joint exposure to the problems confronting embryological morphology" (Benson 1981: 118). His high quality research programme in morphology has also been recognised, as well as his rejection of Haeckelian recapitulationism in the mid-1880s (Benson, 1981: 122).

Additionally, the importance of Brooks' (and others') descriptive embryology in providing the empirical basis for the nascent experimental embryology has been stressed, as well as his support for experimental techniques (Benson, 1981: 124). In his programme of descriptive work and hypothetical modelling Benson sees Brooks as "representative of the embryological community at the end of the nineteenth century" (Benson, 1981: 122).

As a graduate student of Brooks, Wilson underwent training and conducted work concerning the problems of “vertebrate ancestry, the *gastraea-theorie*, and definitions of homologous structures” (Benson, 1985: 174). Wilson’s postgraduate training exposed him to both the morphological concerns of Brooks and the concerns and (experimental) methods of physiology. Brooks, notwithstanding his limited use of experimental methods and manipulations in his work, was a morphologist largely concerned with exhaustive descriptive and comparative work, and engaged in the establishment of phylogenetic relationships. He was also deeply interested in the problem of the origin of variation, an interest he shared with William Bateson (1861-1926), with whom Brooks briefly collaborated in the early-to-mid-1880s (Hall, 2005).

The products of Johns Hopkins University, such as Wilson, are interesting because of the supposed clash between the scientific approaches of the two key figures in the biology department. Their mentor, Brooks, was a morphologist who had reservations about the uses and scope of experimentalism. But they worked in a department led by a physiologist – H. Newell Martin – who impressed upon students the importance of experimental methods. Wilson’s Major was in morphology, but his Minor was in physiology.

Encouraged by his experimental training and the insistence by Brooks that his graduate students should be able to draw, Wilson became a talented artist, section-cutter and user of novel staining techniques. He had therefore mastered the new techniques generally acknowledged to have been pivotal in the transformation of biology in the late nineteenth-century – the improvement of microscopes and the use of effective sectioning, preserving and staining methods (Benson, 1988b: 71; Coleman, 1977: 22-24; Maienschein 1994a: 8-9). His artistic abilities allowed him to produce many of the diagrams and representations for his papers and books, some of which I shall analyse later in this chapter.

There is little scholarly work on Wilson’s early papers. This should not be a surprise, as this work was rooted in the methods and preoccupations of his mentor and his mentor’s generation of biologists, and therefore does not interest modern scholars as much as his later work on cell-lineages, experimental embryology and chromosomes. But Wilson’s early works are

important in establishing that the early parts of Wilson's career were rooted in descriptive and comparative methods. Wilson was at the cutting edge in terms of adoption of new techniques, but he employed these techniques as part of well-established wider methodologies to answer the research questions that were posed.

Wilson did not to spend his whole career using these methods, but it would be folly to think that he abandoned them in the late-1880s and 1890s. It was in using the germ-layers as the basis for an embryological criterion of homology to ascertain phylogenetic relationships that Wilson spent the bulk of his early career, involving himself in the problems and debates of the community of descriptive, comparative, evolutionary morphologists.

What most supports the thesis that in the 1880s Wilson's observations, descriptions and comparisons were explicitly made with traditional morphological questions in mind is that the conclusions he drew were almost exclusively phylogenetic. This occurred even when he made comments which made it clear that the same work might have led him to draw conclusions relating to completely different problems.

Wilson's work on *Renilla* – the sea pansy, a cnidarian which is a colony of polyps – in the early 1880s illustrates this (Wilson, 1882a). He observed “great variation in the earliest stages of development” with many different “modes of segmentation, belonging apparently to quite different types of development, yet bringing about the same result” (Wilson, 1882b: 247). But rather than draw conclusions or pose questions about differentiation or determination in development, about why different modes of segmentation were produced, he concluded that “little weight consequently can be attached to the early changes of the egg as a guide to the affinities [i.e. relatedness] of animals” (ibid.). He was therefore focused on how his embryological observations could guide investigators seeking answers to phylogenetic questions or problems. Wilson was seeking a firm foundation on which to base an embryological criterion of homology. As late as 1892, Wilson observed that the problems of evolutionary morphology could “only be solved by a study of the embryological history of the organism” (Wilson: 1892: 384). In 1882, Wilson simply reiterated the need to study a slightly later (though still early) stage of development, the formation and

fate of the germ-layers. In this respect, he was still completely in line with the mainstream of evolutionary morphological research.

The *Renilla* paper raises in nascent form two themes in subsequent Wilson's research career. These are the challenges associated with studying the process of development, and the problem of variation. These themes are intimately related. The following quote brings out some of Wilson's excitement at the protean sea-pansy:

The segmentation of the egg in *Renilla* is remarkable for the surprising amount of individual variation of which it is capable. So great is this variation that it is safe to say that no two eggs ever develop in precisely the same way; and although most of the variations may be arranged in a definite series, some of them are so irregular that they seem to follow no definite law. No one indeed without actually following the entire development of some of these eggs would suppose them capable of normal development. For a long time, in fact, I passed by some of the less usual forms as due to abnormal or pathological changes, and only after repeated and careful study was able to convince myself that these peculiar embryos gave rise to active larvae, differing in no visible respect from those which had developed along the more usual course.

...at least five or six well-marked modes of yolk-cleavage, with many minor variations, may occur as normal phenomena of development, that the segmentation may be at first equal or unequal, complete or partial, regular or irregular, and that a great amount of variation exists in the duration of the various stages of activity and quiescence.

Wilson, 1882a: 729-730

Wilson's early work on the sea-pansy therefore impressed upon him not only the great amount of variation that exists between organisms, but that even some of the more variant forms were capable of normal development. In order to ascertain the facts of the latter part of the quote, two other workers were involved in a painstaking effort which involved the separation and isolation of eggs and tracking of development to the free-swimming larval stage (Wilson, 1882a: 730). That the normal development encompassed forms exhibiting

variation in the pathways of development and of forms exhibited at pre-larval stages therefore made Wilson aware early in his career of the need to separately observe the full development of numerous individuals. He could not assume that studying a small number of samples, without regard to particular individual courses of development, would inform him about the nature of development for that particular species. Similarly, no assumptions could be made about the fate of seemingly unusual forms observed. Only by observing the whole developmental process for organisms exhibiting such unusual forms could one know whether it would develop normally. Interestingly, his case here, while not analysed in causal terms by Wilson, implies that whatever causes were responsible for early embryonic variants exhibited little specificity, if one was seeking the causes of larval or adult normality.<sup>70</sup> Conversely, any causes which were not thought to be responsible for the production of variants, but might be thought more specific in terms of producing larval or adult normality, might as a result of these observations be deemed to be more stable, as they held over a much wider range of conditions than had previously been thought. While this interest in variation would be somewhat suppressed in Wilson's publications for several years after the work on *Renilla*, it would be re-activated and accompanied by a new interest in the causes of that variation in the research described in section 3.5., especially subsection 3.5.2.

After Wilson left his fellowship at Johns Hopkins, and spent a happy spell working in Europe, the only academic employment in the USA he could find was at Bryn Mawr, a teaching institution. Although he was allotted time and resources for research, these were limited, as his published output in these years indicates.<sup>71</sup>

### **3.4. Wilson from the late-1880s**

Baxter claims that it was only when Wilson embarked on projects concerning the embryology of annelids (a phylum of segmented worms, which includes

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<sup>70</sup> But not necessarily for other effects, such as the fate of particular cells. Assuming the proportionality criterion holds, how specific or stable a candidate cause is course depends on the precise *explanandum* one is attempting to construct a causal account to explain.

<sup>71</sup> The list of publications included in Morgan's memoir of Wilson (1940), while incomplete, serves to illustrate this.

earthworms and leeches), between 1887 and 1890 (Wilson, 1887, 1889, 1890), that he systematically investigated the germ-layers, and sowed the seeds of his estrangement from the germ-layer doctrine (Baxter, 1977: 367). By 1890 he was starting to conduct 'cell-lineage studies', studying the origins of particular embryonic structures to particular origin cells, and tracing forwards the fate of the cells produced from successive divisions, starting with the egg. In the wider context of Wilson's career, the cell-lineage studies not only undermined his adherence to the embryological criterion of homology, but opened up suggestive new avenues of research.

For Baxter, it was the work on the cell-lineage of *Nereis* (a polychaete worm), published in full in 1892 (Wilson, 1892a), that undermined Wilson's adherence to germ-layer doctrine. In this work, Wilson extended the logic of the germ-layer doctrine – that homology was determined by common embryological origin – to the germ-layers themselves. He found that while a particular germ-layer, the mesoderm, could always be traced back to the same cell or blastomere within the same species, it could not be traced back to the corresponding cell or blastomere in different species. Rather, "corresponding cells in different species could have different prospective values" (Baxter, 1977: 370). What this meant was that the same cell – in a particular place in the cleavage at a particular stage, and descending in the same way from the segmenting egg – could give rise to a different germ-layer, and consequently different descendant tissues and cells. The mesoderm was therefore not homologous across the animal kingdom. If the germ-layers themselves were not homologous, then surely any homologies established on the basis of the universality of the germ-layers was untenable.

Baxter claims that Wilson's loss of interest in phylogenetic questions was due to "his exposure to the work of his German contemporaries", who revealed to him the more exciting possibilities of the new experimental embryology (Baxter, 1977: 374). However, neither of these claims fully captures what was going on. As a proportion of Wilson's work and interest, phylogenetic problems certainly faded over the course of the 1890s, but the lecture of 1894 (which Baxter cites as the key attack on germ-layer doctrine) if anything stands, not as a repudiation of the programme of comparative morphology, but an attempt to

clear the ground to allow it to continue on a firmer basis (Wilson, 1895a). Furthermore, as I will demonstrate, it was the progress of his own work and the problems and questions it threw up which led him to new questions and approaches, though the work and ideas of his contemporaries signalled possibilities that Wilson was receptive to as a result of the issues raised in his own research.

1891 brought with it three significant linked events. Hermann Muller, a prominent geneticist who studied under Wilson, located the start of Wilson's work on 'The Cell in Development and Inheritance' (Wilson, 1896) to 1891. As Muller knew Wilson and had little reason to distort the facts in this case, we can accept this claim and timeframe with some confidence. This means, as Muller explained, that in 1891 Wilson began the task of gathering the material needed for this wide-ranging text; editing, organising and integrating it. The basis for the book was subsequently laid out and developed in a lecture course delivered during 1892 and 1893. Muller believed that these tasks enabled Wilson to achieve a "rounded conception" of the cell and development that was lacking in many other biologists (Muller, 1943: 30).

Additionally in 1891, Henry Fairfield Osborn (1857-1935), late of Johns Hopkins, offered Wilson a position at Columbia University. This position was to provide Wilson with the resources of a research-oriented university and time to conduct research. Additionally, the job offer came with the opportunity of spending a year abroad before taking up the position. Wilson accepted the offer, having wanted to conduct research to the extent that he had enjoyed as a postgraduate, and to be able to make a return to Europe, which he had found scientifically and culturally stimulating on his previous visit in the early-1880s.

In Europe, he first went to Germany, then Italy. In Germany he not only indulged his cultural interests, but met up with his friend Theodor Boveri (1862-1915), who was to influence his work, not just then, but subsequently as well (Monroy and Groeben, 1985: 41). The timing of Wilson's stay in Germany coincided with a debate raging about the nature of the cell and its role in development. Through Boveri, Wilson assimilated the concepts of *Zellforschung*, the programme of experimental cell research that posited the cell as the centre of all biological phenomena (Dröscher, 2002: 364). Criticised by the likes of T. H.



Huxley for being preformationist and morphological, *Zellforschung* treated the cell as autonomous, and sought explanations for phenomena at a higher, multicellular level at the lower level of the cells and their interactions (Dröscher, 2002: 359-360). Against *Zellforschung's* emphasis of the role of the nucleus in directing development, Huxley outlined an epigenetic view of development which focused on the properties of protoplasm responsible for the transformation of the relatively homogeneous germ into a complex differentiated form (Richmond, 2000: 277).<sup>72</sup> The debate over the role of the cell in development centred on how the cell and particular constituents of it related ontogenetically and physiologically with other cells and the rest of the organism, as well as on questions of functionalist versus morphological and epigenetic versus preformationist conceptions of the cell and development.

The sojourn in Europe was to be critical in shaping the direction of Wilson's research. In Italy, Wilson travelled first of all to Naples, and the Stazione Zoologica. Some of the key morphological studies establishing the embryological criterion of homology were conducted by German workers at Naples in the 1860s and 1870s.<sup>73</sup> Through Brooks at Johns Hopkins University and Whitman at the Marine Biological Laboratory, this led to similar questions being pursued by similar means by the scientists trained at those institutions (Benson, 1988a: 338).

It was at Naples that many of the instruments and techniques that were to be used in cell-lineage studies were perfected. Most notably, these included "the Zeiss homogeneous oil immersion objective, which increased the resolving power of the microscope, and the rotary microtome from Leyer that allowed continuous or ribbon sectioning of embryonic material" (Benson, 1988a: 339). Additionally, stains became available with the development of the dye industry

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<sup>72</sup> Huxley also criticised what he thought were metaphysical assumptions underpinning *Zellforschung*, particularly on the powers attributed to the nucleus to direct the cell, the organism, and development (Richmond, 2000).

<sup>73</sup> It is clear that many of the threads that contributed to the change in American biology had their roots in German debates and work. The influence of Wilhelm His on American embryology – and Whitman in particular – is one such example (Maienschein, 1986: 86). Others include the role of the Roux-Driesch debate in focusing attention on the internal and external in development (Maienschein, 1986: 84). The British influence from Huxley cannot be ignored, and there is ample evidence of this throughout Wilson's work in particular – see the references, otherwise sparse, to Huxley's work in 'General Biology' (Sedgwick and Wilson, 1886) and also in the various editions of 'The Cell in Development and Inheritance', e.g. Wilson, (1896: 295 and 328).

in Germany in the nineteenth-century, in the 1880s in particular. These instruments and techniques made possible lines of research that had previously been impossible.<sup>74</sup> As well as being developed in Naples, such instruments and techniques migrated quickly to Johns Hopkins University and the Marine Biological Laboratory, the latter being a regular haunt of Wilson (*ibid.*).

The use of marine invertebrates as organisms of choice in evolutionary embryology was also pioneered at Naples. Countering Allen's (2007) claim that it was the establishment of marine laboratories themselves that made the use of marine invertebrates inevitable, Benson quotes Anton Dohrn, the driving force behind the creation and running of the Stazione Zoologica, who justified the establishment of marine biological research stations in terms of the usefulness of marine animals for evolutionary embryology research: "to get back to these ancestors, and to build up scientific genealogy, must lead to the investigation of the embryology of marine animals, must cause, in consequence, the desire of having laboratories near the coast" (Dohrn, 1872, quoted in Benson, 1988a: 338).<sup>75</sup> A further advantage of marine invertebrates for the scientific investigator was that "marine organisms were both more durable and less personable than higher animals, they were easier to manipulate while alive; they were, figuratively and sometimes literally, transparent to the sufficiently careful observer" (Pauly, 1988: 135).

If the nineteenth-century can be characterised as a period of globalisation, with qualitative improvements in means of communication and transport across the world, the Stazione Zoologica can be seen as a consequence of that. Certainly, scientists had previously travelled to different countries for study, or research trips. But the international community at the Stazione was something beyond that, something that has been described as "an international centre of scientific exchange" (Fangerau and Müller, 2007: 609). Such a centre provided a place

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<sup>74</sup> The availability and development of this equipment and associated techniques owed much to Dohrn's pioneering deal with the Zeiss company. In exchange for discounted instruments, Stazione scientists would make suggestions as to how they could be improved (Groeben, 1985: 12).

<sup>75</sup> Though Allen does detail the extent to which such organisms were wonderful for scientific research. Indeed, "Once biologists became familiar with the advantages of working with marine organisms...these groups became model organisms for the study of all manner of general biological problems" (Allen, 2007: 137).

where scientists could share suggestions, thoughts and techniques, and also critically discuss methods and problems (Fangerau and Müller, 2007: 612).

At Naples Wilson met Hans Driesch and Curt Herbst (1866-1946) and encountered their nascent employment of experimental methods and techniques, and the problems that they were using these methods to address. The Naples 'experience' was pivotal in bringing to the fore these methods and questions (Maienschein, 1985: 189; Monroy and Groeben, 1985: 41), and Wilson's first work in experimental embryology took place using *Amphioxus* in Sicily in 1892.<sup>76</sup> The paper that was to result from this work was published in 1893 (Wilson, 1893a).

### **3.5. The shift from 'traditional' morphology to cell-lineage work**

From the early-1890s Wilson conducted research on the earliest stages of development. This involved the tracing and tracking of cells, and their descendants or lineages, throughout the course of development.

There have been a number of reasons suggested for Wilson's adoption of cell-lineage work, including the fascination he held from his student days with the work of Edward Laurens Mark (1847-1946) on the very early stages of snail development (Maienschein, 1987a: 779).<sup>77</sup> Wilson's relationship with Charles Otis Whitman was more significant (Maienschein, 1990a: 368-369). Whitman himself conducted cell-lineage studies on *Clepsine* (a leech, also an annelid), which were published in 1878, 1886 and 1887. In this research, Whitman was attempting to test claims that cleavage produced "indifferent cells" which "have no more of a fixed relation to the postembryonic body than have snow flakes to an avalanche" (Stent, 1998: 237). The germ-layers would thus only be formed at gastrulation, and only after gastrulation would they "be destined to take on the tissue differentiation characteristic" (ibid.). Whitman found the contrary. In

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<sup>76</sup> That this is Wilson's first foray into experimental work is generally acknowledged, not least by Morgan and Muller in their obituaries-cum-biographies of Wilson (Morgan, 1940; Muller, 1943). The significance of this lies in the tendency in those accounts to emphasise Wilson as an experimental embryologist, to the exclusion of the rest of his work. The only exception to this is the work Wilson undertook on chromosomes in the 1900s, which Muller places even before the experimental embryology in importance, for obvious reason given Muller's work in genetics.

<sup>77</sup> Curiously, among his other accomplishments, Mark has also been recognised as the creator of the Harvard System of referencing! (Chernin, 1988).

tracking the fate of individual cells from the first cleavage to the formation of the germ-layers, he found that “a definite developmental fate can be assigned to each identified embryonic cell and to the clone of its descendent cells” (ibid.), suggesting that “the differentiated properties that characterize a given cell of the post-embryonic animal are causally linked with that cell’s developmental line of descent” (ibid.).<sup>78</sup> Crucial here is variation, or rather, the lack of it. Too much intraspecific variation in early embryogenesis would make the kind of *determinate development* Whitman discovered less likely.

Contrary to the views of William Brooks, Whitman came to see the investigation of these early stages as vital, still (as of the late-1880s) within the framework of an evolutionary comparative morphology that aimed to establish a definitive basis for ascertaining phylogenetic relationships (Maienschein, 1978: 136-138). Through the cell-lineage work Whitman came to see the importance of identifying the “distinction between the roles of internal and external factors” in development (Maienschein, 1978: 138). However, even this additional problem was related to the more traditional task of establishing homological relationships, by separating out the primary ancestral characteristics (palingenetic) from the secondary adaptations (cenogenetic) (ibid.). The cell-lineage work in the 1880s constituted for Whitman a pursuit of problems within the Haeckelian framework, while increasing his doubts about specific aspects of that framework (Maienschein, 1978: 137). In Whitman’s work in this period, he displayed an interest in the efficacy and role of different modes of causality. The question of the relative importance, role and nature of internal (historical) and external (proximate) factors became not just relevant for explaining the production of form, but also for explaining changes in form. This is also clear in the works of Wilson in the early-1890s, as we shall see.

Maienschein notes that, as well as Whitman, “To some extent Wilson had begun to recognize the inadequacies and confusions of tracing evolutionary relationships by 1890” (Maienschein, 1978: 139). The 1890 lecture Wilson delivered at Woods Hole entitled “Some Problems of Annelid Morphology” demonstrated that while “still operating within an essentially Haeckelian context, considering phylogenetic questions through germ-layer studies...at this point he

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<sup>78</sup> Both of these are quotes about Whitman’s work rather than by Whitman himself.

felt frustrated by the confusions of the search and sought the more stable ground of empirical detailed description of embryonic development” (Maienschein, 1978: 140).

This assessment, as we shall see, is partly correct. However, working within the Haeckelian framework and pursuing the problems of evolutionary morphology was not necessarily the same thing (a point also made in Guralnick, 2002). Furthermore, in Whitman’s cell-lineage research, Wilson did indeed have a model of how to pursue the tracing of evolutionary relationships unencumbered by the problems emerging with the Haeckelian approach.

A weakness in Maienschein’s 1978 account is that it relies too much on the 1894 lecture delivered at Woods Hole by Wilson (Wilson, 1895a) as the basis for a discussion of the significance of the cell-lineage work. Wilson’s views on the significance of germ-layers and the embryological criterion of homology changed in a short space of time. But the precise timing, and way in which this impacted on the rest of his research agenda in the months and years following the commencement of his cell-lineage work, is best dealt with in that period. To that end, I will examine the path to the cell-lineage work itself, and also trace the immediate consequences of it for Wilson’s research.

### **3.5.1. Before cell-lineage – working with *Lumbricus***

The 1887 paper entitled ‘The Germ-Bands of *Lumbricus*’ (Wilson, 1887) was the first research paper published by Wilson since 1884. At this time Wilson was still working at Bryn Mawr College. The work was conducted with two species of common earthworm, *Lumbricus rubellus* and *Lumbricus communis*. These had been the subject of works previously conducted by Kovalevsky and Kleinenberg. The paper is a work of comparative evolutionary morphology, with the aim being to “describe only the general structure and mode of growth of the germ-bands, reserving for a future paper an account of the early embryonic stages and a detailed description of the development of organs” (Wilson, 1887: 183). This he does in a paper which appears in the *Journal of Morphology* at the end of 1889 (Wilson, 1889). *Lumbricus* was chosen due to its close (phylogenetic) relation to organisms on which similar work had been conducted, such as the leeches of the genus *Clepsine* (Wilson, 1887: 183).

The 1887 and 1889 works constitute a distinct phase of Wilson's career, which ended with a paper published in October 1890 (Wilson, 1890). All three of these papers were published in Whitman's new *Journal of Morphology*, which also hosted the key papers he would publish in 1892 (Wilson, 1892a) and 1893 (Wilson, 1893a) detailing the results of his studies on cell-lineage and the experimental manipulation of development.

In comparing the derivation of the nervous and excretory systems of annelids and vertebrates from the germ-layers, the works are obviously meant to be a contribution towards testing the hypotheses of the so-called 'annelid theory' (for example, Wilson, 1887: 188-190). The annelid theory proposed that vertebrates (and arthropods) evolved from a "primitive" annelid, a type of worm (Russell, 1916: 274). Anton Dohrn was the primary advocate of the annelid theory. Central to this theory was the claim that the segmented structure (metamerism) of (modern) annelids and vertebrates was the result of common ancestry, and was therefore homologous. Consequently, rather than the lack of segmentation in invertebrate hemichordates being explained by the evolution of segmentation in the vertebrate lineage after they parted, it was explained by the hemichordates losing the segmentation, which nevertheless had been retained by the vertebrate lineage. Dohrn therefore proposed that degeneration – loss or simplification of parts or features – was more widespread in evolutionary change than had previously been thought (Dohrn and Ghiselin, 1994). While the genesis of the annelid theory "drew its main support from comparative anatomy" (Bowler, 1996: 157), embryological evidence was soon required to support its claims and deal with the difficulties presented (Bowler, 1996: 161).<sup>79</sup>

The annelid theory was a contribution to the efforts to account for the origin of vertebrates, a problem which "became a centrepiece of evolutionary biology" in the late nineteenth-century (Bowler, 1996: 141). Such a search was made possible by evolutionism's overturning of the conception of four distinct types of animal proposed by Cuvier in 1812 (*ibid.*). Vertebrates descended from invertebrates, but which, and how?

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<sup>79</sup> One difficulty arising from the idea that the vertebrate is simply an 'inverted' annelid "is that the relationship between the mouth and the brain does not correspond to what the hypothesis predicts" (Bowler, 1996: 158).

A competitor of the annelid theory, the 'ascidian theory' was based on work by Kovalevsky which demonstrated homologies between structures in the sea squirts known as 'ascidians' and the "vertebrate type" (Bowler, 1996: 150). While there were variants of the theory, the predominant version held that both ascidians and the 'lowest' vertebrates were derived from a common ancestor which was in fact a sexually mature version of the ascidian larva (Bowler, 1996: 153).

Despite his adherence to the ascidian theory, Brooks required his graduate students to read Dohrn's 1875 account defending the annelid theory, and considered it "one of the most important contributions to evolutionary morphology" (Bowler, 1996: 165). Wilson was therefore immersed in the debates over the relative merits of the annelid and ascidian theories.<sup>80</sup> Once he was at Columbia, Wilson taught his own students Dohrn's principle of the succession of function. This principle dictated that intermediates in a proposed succession of forms (for example, between his ancestral annelid and ancestral vertebrate) each had to be functional despite the changes in form hypothesised (Groeben, 1985: 16; Dohrn and Ghiselin, 1994).<sup>81</sup> In Wilson's 1889 paper there was serious engagement with previous work connected with the annelid theory by the likes of Balfour and Kleinenberg (e.g. Wilson, 1889: 391-393).

Wilson was also influenced by the work of the zoologist Adam Sedgwick (Wilson, 1889: 441), who proposed (in key papers published in 1880 and 1884) that the divergence of invertebrates and vertebrates was ancient, and consequently that the metamerism of both invertebrates and vertebrates were derived, so analogous, features and therefore not homologous (Bowler, 1996: 184). The relevance of annelids to the study of vertebrate origins was that they

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<sup>80</sup> A series of articles on the annelid theory by a British morphologist, John Beard, were published in *Nature* over the course of 1888 and 1889. They couldn't have inspired Wilson's 1887 work, but at the very least they reflect the importance of these issues in this crucial period. They also served to highlight the changes and transformations that occur in annelid development, and the consequent difficulty in detecting "traces of adult annelid structures in vertebrate development" (Bowler, 1996: 167-168).

<sup>81</sup> This was a functional morphological approach, which emphasised the role of changes in function in leading to transformations in the morphology of particular parts, or even the whole of the organism (e.g. Dohrn and Ghiselin, 1994: 34-37 and 45). Dohrn stressed that in the transformation of an organ the bearer of the function remained that same organ, though what was the main function was replaced by what was a subsidiary one (Dohrn and Ghiselin, 1994: 67). He claimed that this approach would "be of great use for morphology – and for the evolutionary history of structures, which, finally, are only the content and the process of functions projected as form, and cannot even be conceived of without functions" (Dohrn and Ghiselin, 1994: 74).

could be used to embryologically test hypotheses like this. At issue in particular for Wilson were the origin of the metameric structures, and the formation of nephridia (excretory structures in annelids) and rudiments of the nervous system. The former involved investigating their derivation from a particular germ-layer (the mesoderm or the ectoderm), and from this sprang the need for Wilson to establish the independence of the mesoderm as a primary germ-layer. The latter related to the comparative morphological work of Balfour on the relation of the annelids to vertebrates (Russell, 1916: 282).

The 1889 paper was vital in throwing up problems for Wilson in his attempt to come to grips with the relationship between annelids and vertebrates by using the germ-bands, their 'history' and the structures derived from them. In this paper, he addresses the origin of the mesoblast (mesoderm) which he briefly dealt with in the 1887 paper. Wilson aimed to establish that the mesoblast was not derived from either or both of the two other germ-layers, contrary to other accounts such as that of Kleinenberg (Wilson, 1889: 391-392). The purpose, as in previous work, was to use the mesoblast, and the structures which derive from it, as a basis for establishing homologies between *Lumbricus* species, *Clepsine* (Whitman's leeches) and vertebrates. Wilson found that "The entire mesoblast is derived from a pair of primary mesoblasts or teloblasts that lie at the posterior ends of the germ-bands, and no mesoblastic elements arise from the ectoblast overlying the germ-bands. The primary mesoblasts are differentiated in the course of the cleavage" (Wilson, 1889: 389). The mesoblast germ-layer therefore arose, not from pre-existing layers after gastrulation, but *before* the crucial process of gastrulation.

Variability in development caused problems for Wilson however. There was variation in both the developmental tempo and the cleavage (Wilson, 1889: 395 and 397). Wilson noted that such variability was an issue in other species as well. These problems led Wilson to confess that "I have had no better success than Kleinenberg in following the details of the cleavage process" (Wilson 1889: 397). He also admitted that "my account of the cleavage will be found unsatisfactory, owing to the impossibility of following continuously the development of the individual ova" (Wilson, 1889: 395).



Indeed, cleavage was to cause Wilson some problems. He observed that “the cleavage process varies greatly in the order of division, which after the first two divisions loses all appearance of regularity. On account of these circumstances the segmenting ova vary widely in appearance, and the process of cleavage thus acquires that apparent irregularity which other observers have found so perplexing” (ibid.). In the stage following the third cleavage, “There are in all thirteen cells, which do not perceptibly differ in the character of the protoplasm, and I am unable to say what is the precise relation of these cells to those of earlier and later stages; or to recognize the future primary mesoblasts, though it is possible that they are already present” (Wilson, 1889: 397). We see here the germ of problems concerning the nature and morphological significance of cleavage to which greater attention would be drawn in subsequent works. In particular, the problem of the *variation* of cleavage forms presented itself. Such variation in early developmental processes posed a challenge for the conduct of embryology. Given this variation, how were meaningful stages, cell-lineages and standards to be determined for the purposes of compiling data for representation and comparison? They also posed a challenge to the Haeckelian framework, which was based on the constancy and equivalence of early development across the animal kingdom. If this was seriously challenged, then the application of embryology for phylogenetic purposes was undermined. At the very least, the firmness of the basis of certain ways of embryologically-ascertaining homologies was undermined. This would trigger a search for other ways to do this, which animated subsequent work by Wilson.

For now, when dealing with the question of the origin of the germ-layers, Wilson located the origin of the mesoblast back to two “primary mesoblasts”, but he “failed to trace the origin of these cells in the process of cleavage, the original character of which has been so altered that it is impossible to determine the relation of the primary mesoblasts to the micromeres and macromeres of the typical unequal cleavage” (Wilson, 1889: 398). Once again, the nature of development in *Lumbricus* had prevented him from tracing the origin of the mesoblast.

Wilson considered the relation of the head and the trunk in annelids to be one of the most crucial in annelid morphology (bearing as it did on the development of

the ancestral form of annelids, and thus on key genealogical questions [Wilson, 1890: 62]), and in this was directly inspired by the ideas of Adam Sedgwick.<sup>82</sup> Relating his observations to this key question Wilson concludes that: “The essential agreement in the history of the mesoblastic bands between forms so different both in structure and in the conditions of embryonic development as *Clepsine*, *Lumbricus*, and *Polygordius*, is very strong evidence that mesoblastic concrescence has some ancestral meaning, and was not originally caused, though afterwards it was undoubtedly in many cases modified and rendered more conspicuous, by accumulation of food-yolk in the ovum” (Wilson, 1889: 437). By “ancestral meaning”, Wilson meant that this process was not a result of functional or adaptive modification or what we might call proximate causes, but resulted from a hereditary or historical cause.

However, he made “no conjecture as to the character of the adult ancestral form, except to state that the views suggested are reconcilable with the derivation of annelids either directly from Coelenterata, or from Platyhelminths, in accordance with the views of Balfour and Sedgwick, or Lang” (Wilson, 1889: 441). The purpose of the observations Wilson made, and the interpretations and discussions arising from them, was an elaboration of certain key aspects of the development of *Lumbricus*, with the aim of providing more data and evidence to help sort out the competing hypotheses about vertebrate origins, and how annelids related to this.

As Wilson moved towards the end of the paper he noted that “Our knowledge of the mesoblast in annelids appears at present to be in a very confused and unsatisfactory condition” (Wilson, 1889: 442). He continued: “It appears impossible at present to determine the primitive origin of the material now segregated in the primary mesoblasts, for the extreme condensation of development involved in their origin has completely masked the original mode of development” (Wilson, 1889: 445). Despite the monumental work that went into the 1889 paper, he was unable to definitively settle the matter, because of the intractability of the early stages of development for embryological study.

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<sup>82</sup> Indeed, Wilson stated that “as far as our knowledge goes, the development of *Lumbricus* can be most simply and clearly interpreted in accordance with Sedgwick’s hypothesis” before going on to outline an account of the development, using the framework of Sedgwick’s ideas (Wilson, 1889: 441).

He restated the problem at the beginning of his 1890 paper: “It is impossible to doubt the homology of the mesoblastic bands in *Polygordius*, *Eupomatus*, *Lumbricus*, *Clepsine*, *Lopadorhynchus*, and *Enchytraeides*—a series that includes representatives of the three modes of mesoblast-formation” mentioned by Wilson (Wilson, 1890: 206).<sup>83</sup> He believed that it must “be possible to reduce these modes of development to a common type” (ibid.) and considered it “a remarkable illustration of the elementary state of our knowledge of annelid development that no one, as far as I am aware, has made even a suggestion as to how this is to be done” (ibid.).

He mentioned a hypothesis that he raised in the 1889 paper, which he dismissed as “a somewhat unsatisfactory suggestion, which, however, had the merit of emphasizing the importance of a careful study of the relations between the germ-bands and the blastopore in the Polychaeta” (Wilson, 1890: 207).<sup>84</sup>

Wilson needed a means to establish the homology of mesoblast-formation. He believed that the only way to do this was to track the cell-divisions and fates of early stages of development, to determine whether there was a common mode of formation. In this way he would be following in the footsteps of Whitman’s cell-lineage research. The summer of 1890 brought with it a possible way of doing this. Wilson was able, “through the kindness of Dr. E. A. Andrews, to procure very abundant material for the study of the early stages of two species of *Nereis*...and the facts thus brought to light point the way, as I believe, to a solution of the problem” (Wilson, 1890: 207).<sup>85</sup> The eggs of *Nereis* “are

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<sup>83</sup> The three modes: “in some cases the mesoblast first appears in the form of a pair of large cells (teloblasts), by the proliferation of which the paired mesoblastic bands are produced. The teloblasts are often differentiated at a very early period, – sometimes even prior to the gastrulation, – arising near the region corresponding to the posterior lip of the blastopore. In no case do they arise from the ectoblast; in some cases they seem to arise from, or at least to be closely associated with, the cells of the archenteron. In still another class of cases the mesoblast appears to arise neither by delamination from the ectoblast, nor from teloblasts, but from a central mass of “mes-entoblast,” the lateral portions of which give rise to the mesoblast-bands, and the central portion to the entoblast” (Wilson, 1890: 205-206).

<sup>84</sup> The hypothesis was “that the walls of the coelomic cavities were originally formed as a series of gut-pouches, as in *Amphioxus*. The primary mesoblasts lie at the extreme posterior limit of the entoblast, and it is not difficult to picture the process by which a series of gut-pouches, successively formed at the posterior part of the archenteron, might be crowded further and further back in development, until the present complete segregation of the mesoblast in a single pair of the cells was attained” (Wilson, 1889: 445).

<sup>85</sup> *Nereis* is another annelid, in a different class (Polychaeta) to *Lumbricus* (Clitellata – though Wilson referred to its modern subclass, Oligochaeta). Andrews himself was an advocate of the annelid theory, and proposed his own version of it (Bowler, 1996: 167).

transparent, of comparatively large size, and they may be procured in abundance" (ibid.) so they were amenable to observation, and enough material could be found to conduct proper studies. Also aiding observation and the tracking of cell-lineages through development was 'self-marking', a technical condition produced by the organism itself: "The transparent macromeres contain large oildrops, which run together during the development, until, in the great majority of cases, only four are left" (ibid.). However, Wilson would also need to apply his own marks in order to track cell-lines throughout development. Here again though the properties of *Nereis* development would help. Wilson found, to his advantage, that the cells constituting the part of the embryo from which the mesoblast arose were not only distinctive in appearance ("larger, differently granulated" [Wilson, 1890: 208]) from other nearby cells, but also stained differently. Fortunately, they, "upon treatment with certain reagents (combinations of acetic acid, etc.), assume a brownish color that differentiates them very sharply" (ibid.).

Observations seemed to suggest that "The mesoblast...arises directly from a thickened bilobed ventral plate" and therefore "seems to arise from the ectoblast" (ibid.). The distinctive appearance and staining of the cells of the "thickened bilobed ventral plate" allowed Wilson to examine this possibility, as it made "it possible to trace their origin, cell by cell, from the beginning of development" (ibid.), in other words, to trace a cell-lineage. This work succeeded in demonstrating "that the mesoblast is completely segregated in the anterior part of the plate, while the posterior part alone gives rise to ectoblastic structures (neural plates, seta-sacs). Moreover, *each of the two divisions of the ventral plate may be traced back to a single cell (pro-teloblast), which is obviously homologous to a corresponding cell in the early embryo of Clepsine*" [Wilson's emphasis] (ibid.). All of these factors had thus enabled Wilson "to trace the origin of the mesoblast-bands from the beginning of development" (Wilson, 1890: 207).

Wilson depicted these early events in the three diagrams below (**Figures 8, 9, and 10**). These diagrams were, in Wilson's own words, "from camera [lucida] drawings, and are not schematized in outline, though slightly simplified" (Wilson,

1890: 208).<sup>86</sup> To say they were slightly simplified is something of an understatement, given that the cells were represented as nothing but outlines. Such representations, however simplified, do demonstrate several key pieces of information. They depict the relative positions of the cells in three dimensions, display which daughter cells form from the division of which parent cell, and highlight the ancestral cells from which particular structures (in this case the mesoderm) ultimately derive.<sup>87</sup> The diagram therefore displays some form of *activity*.

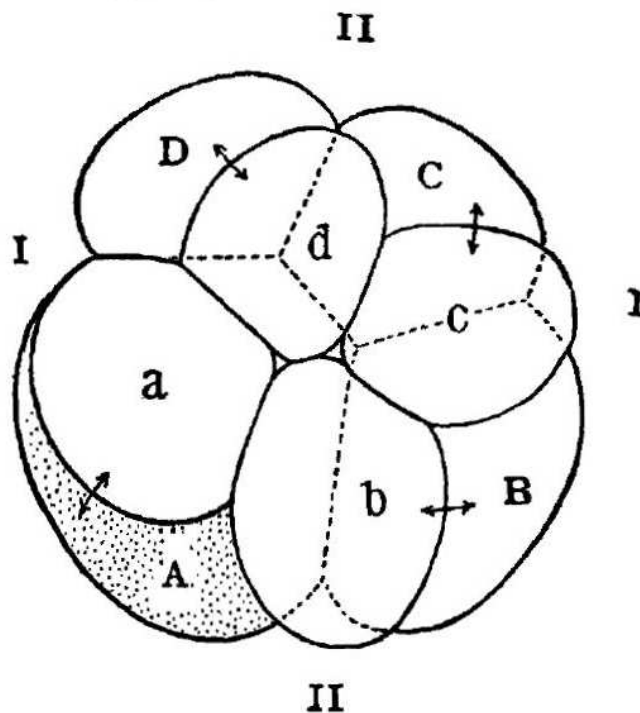


FIG. 1. — Eight-cell stage of *Nereis* viewed from the upper pole. I.-I., the first cleavage-plane; II.-II., the second; A, B, C, D, the four macromeres; a, b, c, d, the corresponding micromeres.<sup>1</sup>

**Figure 8 – Depiction of the cells in the eight-cell cleavage stage of *Nereis*. Note that the macromeres (large blastomeres formed due to unequal segmentation of the egg) are labelled with capital letters, and micromeres (small blastomeres formed due to unequal segmentation of the egg) are labelled with lower-case letters, the same letter belonging to ‘sister’ cells. The diagram displays three dimensions, and shows the generation of the particular form of cleavage. Source: Wilson, 1890: 208.**

<sup>86</sup> The *camera lucida* allowed the observer to view both the sample and a projection of it onto a drawing surface simultaneously. I discuss the *camera lucida* more in chapter 4.

<sup>87</sup> The technique of using dots, lines and arrows to indicate the three-dimensional and dynamic nature of development had been pioneered by von Baer. See Brauckmann (2011).

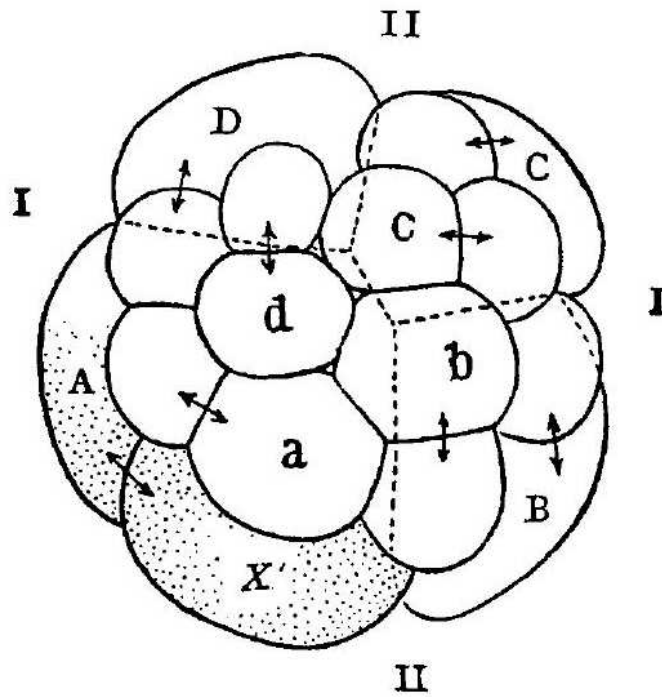


FIG. 2.—View from the upper pole of the sixteen-cell stage of *Nereis*. *X*, the first pro-teloblast which has been separated from *A*.

Figure 9 – Depiction of the cells in the sixteen-cell cleavage stage of *Nereis*. As in Figure 8, the diagram displays three dimensions, and shows the generation of the particular form of cleavage. In this one, however, the fourth cleavage division displayed shows the formation of new micromeres from the division of both macromeres and micromeres. It also shows the formation of the cell labelled 'X', which divides from the macromere labelled 'A'. X is large and granulated, and is called the "first pro-teloblast" by Wilson. Source: Wilson, 1890: 209.

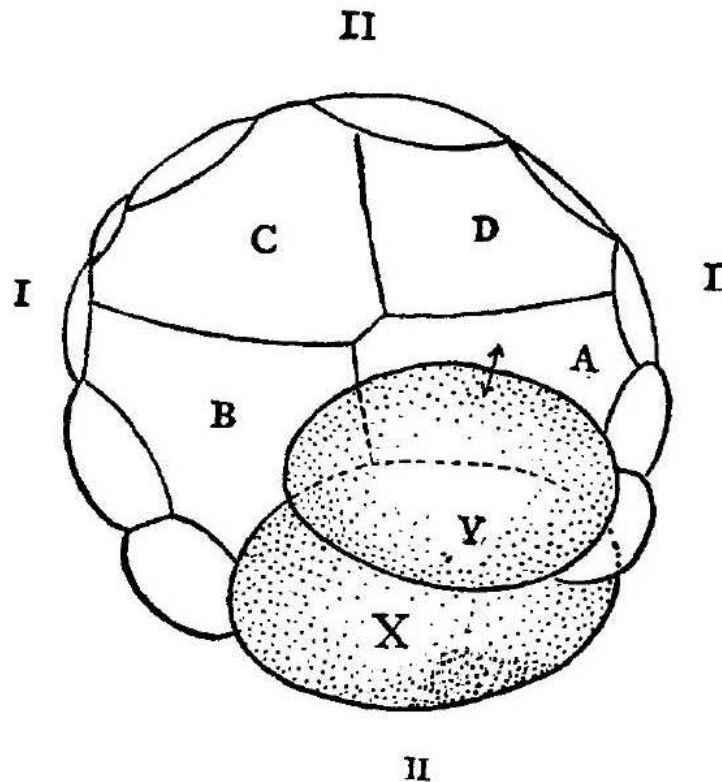


FIG. 3. — View of a later stage from the lower pole, showing the two pro-teloblasts, *X* and *Y*, the four macromeres, and the edge of the cap of micromeres.

Figure 10 – Depiction of the cells in the sixteen-cell cleavage stage of *Nereis*. As in Figure 8, the diagram displays three dimensions, and shows the generation of the particular form of cleavage. In this one, however, the fourth cleavage division displayed shows the formation of new micromeres from the division of both macromeres and micromeres. It also shows the formation of the cell labelled 'X', which divides from the macromere labelled 'A'. X is large and granulated, and is called the “first pro-teloblast” by Wilson. Source: Wilson, 1890: 209.

Wilson’s diagrams over the period 1896-1925 have been shown to increase both in their abstraction and the amount of specific information contained in them (Maienschein, 1990b). This is said to reflect his growing confidence in the diagrams serving as accurate interpretations of what is being presented. The later diagrams are deemed to be more abstract because they come to represent general types rather than particular individuals. This is how abstraction can accompany greater specific detail (Maienschein, 1990b: 235). Although Maienschein does not discuss depictions presented by Wilson earlier than 1895, it is clear from Wilson’s own words that the drawings are of specific

cleavage forms, rather than generalised depictions of a 'typical' cleavage form.<sup>88</sup>

One way of understanding these diagrams is as models, mediators between 'the world' or 'nature' and theory (Morgan and Morrison, 1999). This enables us to approach their role in a way which highlights not merely their genesis, but the possibilities they presented. They were intended by Wilson to represent particular, important aspects of the embryo at particular times, and the processes that were occurring. Such representations are not only representations, but by being separated from the world, can be used as tools for generating new hypotheses as well as new questions. In so doing they permit new ways of engaging with the world. In Maienschein's account of the transformation of Wilson's composition of diagrams, she observes that as Wilson gained greater confidence in the theory he was expounding, the diagrams he constructed moved closer to theory, and away from 'nature' or 'the world'. In the earlier period of Wilson's career that I am concerned with, the issue is rather the *lack* of theory, or at least its haziness. In this sense, the diagrams can be seen as emanating from, and closely corresponding to, 'the world', and in so doing providing Wilson with pointers to theoretical possibilities. In this way, the diagrams can be seen as a "descriptive model" which becomes ever more "distinct from the data set from which it has been generated" (Ankeny, 2000: S269). Crucially, "once these descriptive models have been established, they are used by scientists without regard to the particular experimental arrangements under which they were developed" (ibid.) and so can have a life of their own.

This mirrors the path from which an epistemic object of prior experimental systems is made into a technical condition (or part of a technical condition) of a new experimental system. The abstraction of the model from the concrete details which allowed it to be constructed in the first place allows it to be used in different contexts for different purposes. It constitutes a technical condition which shapes the expectations of researchers, as well as providing a material

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<sup>88</sup> Wilson's 'An Atlas of the Fertilisation and Karyokinesis of the Ovum', an exercise in 'mechanical objectivity' (after Daston and Galison, 2010) in which Wilson attempts to remove as much of his subjective presence from the atlas as possible, and allow the 'objective' photographs to present the states and phenomena of interest (Maienschein, 1990b: 229) (see Wilson, 1895b).



comparator or reference, providing the relative stability required of a technical condition. The background conditions of an investigation will be shaped in part by this model functioning as a technical condition, as ensuring that the experimental materials conform to the model will affect the construction and usage of the rest of the technical assemblage. The technical assemblage must contain means of identifying and controlling potentially relevant causal factors which might make experimental materials (e.g. embryos) diverge sufficiently from the model to compromise their usefulness as indicators of the effects of experimental manipulations. These factors must be identified and controlled as background conditions. Normal development functioning as a technical condition plays the kind of role indicated above, but at this stage in Wilson's research, his diagrams and his descriptions were not explicitly those of normal development. Normal development would be present in his experimental work, however, as I describe in chapter 4.

Wilson promised to furnish a more detailed account of his cell-lineage work in a later piece of work, which was to be the classic 1892 paper. The cell-lineage programme was now underway. It was prompted by problems with tracing the mesoblast-bands back to the earliest point in development, to establish a common mode of mesoblast development across the annelids and vertebrates, a task made important by the need to examine the basis of the 'annelid theory'. Wilson's move into cell-lineage work was as a result of problems with working with the germ-layers as the basis for investigation, but it did not constitute a rejection of the centrality of germ-layers for comparative evolutionary morphology. He was still concerned to establish whether certain germ-layers had common modes of formation, and could therefore be deemed homologous.

### **3.5.2. Wilson's cell-lineage research**

The problems associated with assuming the homology of germ-layers meant that the formation of the germ-layers themselves needed to be investigated:

It appears to me that the only course open to embryological investigation is to examine more precisely the origin of the gastrula itself; *to take as a starting-point not the two-layered gastrula, but the ovum*. The "gastrula" cannot be taken as a starting-point for the investigation of comparative

organogeny unless we are certain that the two layers are everywhere homologous. Simply to assume this homology is simply to beg the question. *The relationship of the inner and outer layers in the various forms of gastrulas must be investigated not only by determining their relationship to the adult body, but also by tracing out the cell-lineage or cytogeny of the individual blastomeres from the beginning of development; and I am convinced that many contradictions that appear under the ordinary germ-layer theory will disappear when thus examined.*

[italics in original] Wilson, 1892a: 367

Wilson made it clear at the very beginning of the 1892 paper entitled 'The Cell-Lineage of Nereis' that the work was undertaken "in the hope of clearing up certain perplexing problems involved in the origin of the germ-layers in annelids, especially those relating to the formation of the mesoblast in the polychaetous forms" (Wilson, 1892a: 362).<sup>89</sup> At the end of the paper the use of the study of cell-lineages as a research method to these ends was reaffirmed, as from it, "rightly applied, we may hope ultimately to attain a firm basis for an estimate of the different forms of gastrula and a comparison of the germ-layers" (Wilson, 1892a: 455).

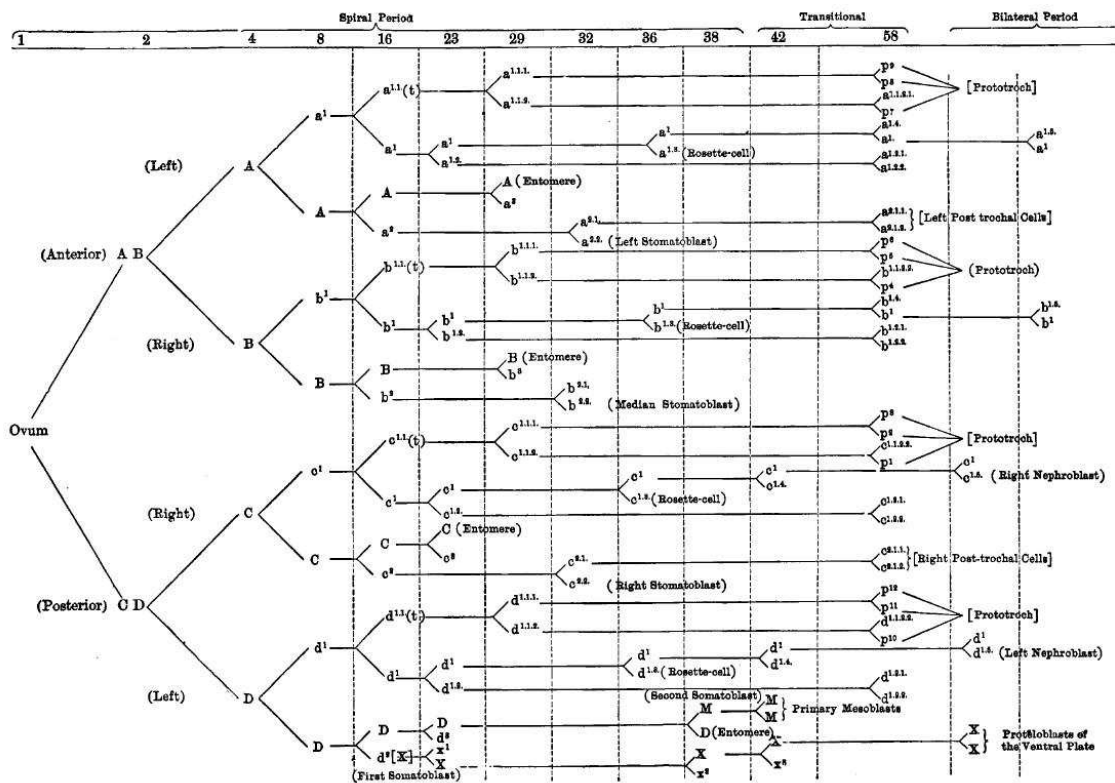
As has already been described, the eggs of *Nereis* were to prove extremely worthwhile, seemingly providing Wilson with "a form in which the detailed history of the mesoblast might be followed in the cleavage-process, and its precise relation to the other layers thus determined" (ibid.). It was precisely the ability to trace "the history of the individual blastomeres in the cleavage-process" that also made this particular work amenable to the study of the cleavage of the egg in its own right (ibid.). Observations about cleavage had been made by Wilson before, but they were largely of an incidental character. It was in this 1892 work (conducted from the summer of 1890 onwards) that the problems of cleavage came to assert themselves more forcefully.

Through his cell-lineage studies Wilson established a triploblastic conception of germ-layers, and was able to trace back the entire mesoblast to a single cell (Wilson, 1892a: 370). This is significant, as was the use by Wilson of a highly

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<sup>89</sup> Wilson is said to have coined the term 'cell-lineage' in this 1892 work (Guralnick, 2002: 541).

schematic representation of the process of development understood as ‘cytogeny’. In this, distinct cells arose in distinct stages in a determinate way (see Wilson, 1892a: 382), though beyond a certain “point the development of the embryo as a whole cannot be fully represented in the diagram, on account of increasing variations in the order of division of the individual cells” (Wilson, 1892a: 383) (see **Figure 11** below).



**Figure 11 – Wilson's cell-lineage diagram of *Nereis*.** The descent of the cells is presented in a genealogical fashion. The diagram combines the continuity of the lines with the discrete stages (marked by the vertical dotted lines) reflecting patterns of cell-division. Note also the division into three ‘periods’, labelled at the top of the diagram. Source: Wilson, 1892a: 381.

The diagram above was a considerable technical and observational achievement. How Wilson represented his observations was a departure from previous representations and accounts of cell-lineage. Both Wilson and Whitman's method was to “mentally mark the embryo in observation and physically mark a diagram to track a process of cell division leading from a determined state to a visible embryonic differentiation” (Griesemer, 2007: 402). But Wilson's genealogical representation was something novel. Considered as

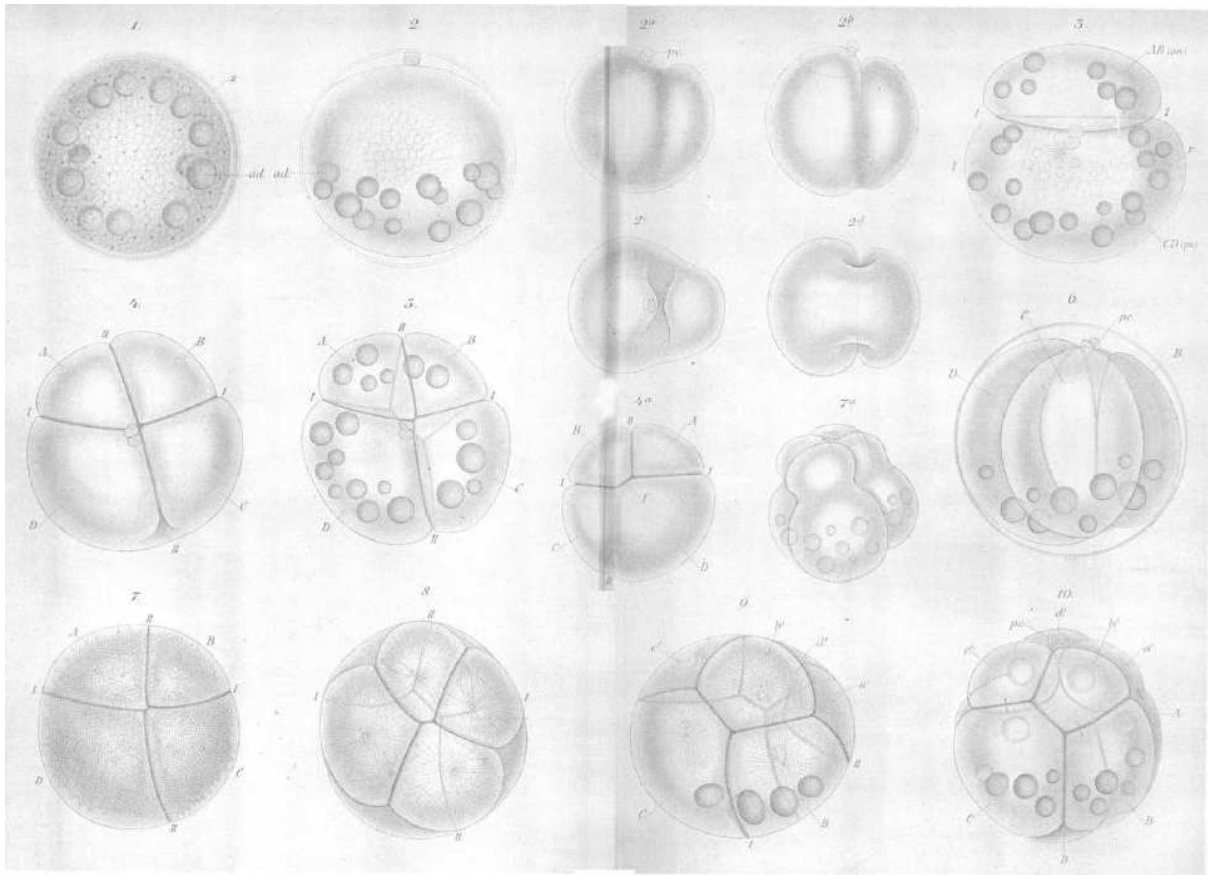
an abstraction from Wilson's raw observations, the diagram represents an overall process (early embryogenesis) over time, as well as individual processes, such as the formation of particular cells with particular fates as particular structures or organs. The original purpose of the diagram is betrayed by the attempt to superimpose discrete stages on the processes exhibited. The stages, divided by the vertical dotted lines, are defined by particular events of cell-division. The stages formed part of the three periods which Wilson divided early embryogenesis into: spiral, transitional, and bilateral. The cell-lineage programme, which originated in the need to trace back particular germ-bands to particular cells, now possessed a hybrid character. The division of the diagram into the three periods characterised by the form of the cleavage exhibited and the relation of the patterns of cell-division to those periods shows how important the phenomena (and problems) of cleavage became to Wilson. What the diagram does not depict is any sort of detail about the cells themselves, beyond their ancestry and, for some, their fate. Unlike the previous diagrams examined in this chapter, there is no indication of the form or position of the cells themselves.

While the diagram exhibits a great deal of (condensed) information relevant to Wilson's research interests, it is abstract enough to take on a life of its own. Griesemer contends that "abstraction of genealogical form from cytoembryological content through the history of cell-lineage diagrams facilitated an identification of the cell-lineage workers' findings on fate determination in embryogenesis with Weismann's doctrine of germ plasm continuity and somatoplasm discontinuity". He goes on to claim that "the working drawings of cell-lineage workers facilitated the theoretical abstraction of Weismannism and the conceptualization of Mendelism as the foundation for a modern causal theory of heredity" (Griesemer, 2007: 406).

Drawing parallels between Mendel's research programme and the cell-lineage programme, Griesemer notes that in both programmes, "the aim is inference about an earlier stage of the process on the basis of a distribution of progeny (organisms or cells) later on" (Griesemer, 2007: 404) and that the data produced "could be manipulated via further symbolic annotation, and new

diagrams...could be drawn to abstract features of theoretical interest”  
(Griesemer, 2007: 406).

One of the promises of a research programme which was concerned with tracing back structures further back in development, to the one cell that gave rise to an entire cell type, tissue, or germ-layer, is that it could then be used to trace forward from the early stages of embryogenesis, and ultimately from the egg. This tracing forward would allow researchers to identify which germ-layers and cell-types might derive from one blastomere in a particular position at an early stage. It promised the ability to predict the course of differentiation, and therefore to identify the causes of it. If the promise was to be fulfilled, the causes could be identified as existing internal to the cells, and acting in a highly specific and stable manner. Undoubtedly, Wilson came to take a strong interest in how the differentiation exhibited as one moves from left to right in **Figure 11** was actually caused. The following chapter discusses this issue, the problems encountered in trying to ‘trace forward’, and the role of his early experimental work in transitioning to new questions concerning the role of different causes in the process of differentiation.



**Figure 12 – ‘Realistic’ drawings of the early stages of embryogenesis in *Nereis*. The top row depicts the first cleavage, the middle row the second cleavage, and the bottom row the third cleavage. Source: Wilson, 1892a: 467.**

As already suggested, the 1892 paper was significant in pointing to new research directions and for its commentary on the nature of development. One of the new directions was Wilson’s interest in the cleavage of the egg (see **Figure 12** for Wilson’s naturalistic depictions of the first three cleavage stages), which he noted “takes place with a precision and regularity which oft-repeated examination only renders more striking and wonderful” (Wilson, 1892a: 377).<sup>90</sup> Wilson in the course of the paper placed great emphasis on the orderliness of development, sharing his “impression of a strictly ordered and predetermined

<sup>90</sup> Wilson outlined his method for the ‘naturalistic’ depictions before the plates section at the end of the paper: “All of the figures, unless otherwise stated, were drawn with the aid of the camera [lucida], but in many cases the finer details have been added free-hand to the camera sketch. Most of the figures were drawn from a single specimen, but in a few cases, in order to economize space, a single figure combines the sketches from more than one specimen” (Wilson, 1892a: 464). While generally individual instances were drawn, Wilson still had to select the specimen he believed to be most representative for his depiction, a process which was not dealt with by Wilson here.

series of events, in which every cell-division plays a definite *rôle* and has a fixed relation to all that precedes and follows it” [Wilson’s emphasis] (ibid.).

This orderliness allowed Wilson to divide the cleavage phases “into three very marked periods”, which he dubbed spiral, transitional and bilateral (Wilson, 1892a: 378). He observed that “[i]n the first period, [the spiral] which extends to the thirty-eight-celled stage, the germ-layers are completely differentiated. At the same time most of the individual blastomeres are differentiated into the parent-cells or protoblasts from which the future organs arise. The embryological material is, as it were, sifted out and arranged” (Wilson, 1892a: 377-378). Here the symmetry exhibited was not the bilateral symmetry displayed by the adult organism, but “a peculiar modification of radial symmetry which is best characterized as spiral in character, and *which cannot be reduced to the bilateral type*” [Wilson’s emphasis] (Wilson, 1892a: 378). It is at this thirty-eight cell spiral stage that the cell from which the entire mesoblast arises (the shaded  $d^4$  micromere) is separated from the macromere labelled D, as seen in the diagram on the following page (**Figure 13**).

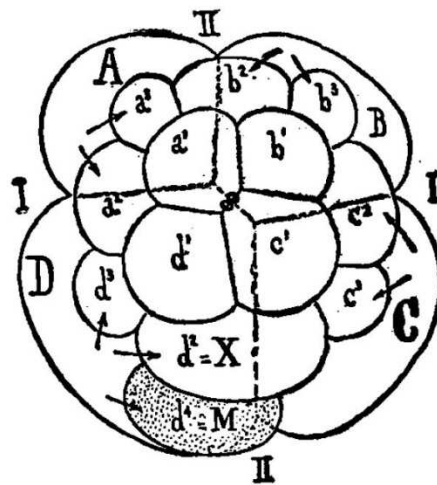


DIAGRAM I.

Figure 13 – Wilson's diagram of the thirty-eight-celled cleavage stage in *Nereis* (Wilson, 1892a: 378). The diagram shows the derivation of the micromeres in three stages from the correspondingly lettered macromeres. The macromeres are represented with capital letters (A, B, C, D). The micromeres are labelled according to the macromere they derive from (in lower case form) and the stage at which the division of the macromere gives rise to the micromere. So,  $b^2$ , derived from macromere B in the second round of formation of micromeres. Wilson used this diagram, and the related account, to explain how these early cleavage stages give rise to a spiral cleavage form: “The first four ( $a^1$ ,  $b^1$ ,  $c^1$ ,  $d^1$ ) are formed in a right-handed spiral, the second four ( $a^2$ ,  $b^2$ ,  $c^2$ ,  $d^2$ ) in a left-handed spiral, and the third set ( $a^3$ ,  $b^3$ ,  $c^3$ ,  $d^3$ ) in a right-handed spiral like the first set” (Wilson, 1892a: 378). The micromere  $d_4$ , which is the primary mesoblast that gives rise to the entire mesoderm, separates from macromere D after the three previous waves of micromeres (which constitutes the basis for the entire ectoblast) are separated from the macromeres (ibid.).

Figure 13 is a depiction by Wilson of the first cleavage stages of *Nereis*, which is consistent with the description contained in the 1890 paper. However, it differs in several respects. Less significantly, the importance of the ‘secondary mesoblast’ over the ‘primary mesoblast’ (to use the 1890 terms) was emphasised by the shading of just the  $d^4$  blastomere (‘M’) rather than both ‘X’ and ‘Y’ being shaded in the 1890 diagram (Figure 10). Also without much significance was that all blastomeres were now labelled. More significant is the fact that, although the outlines of the macromeres had been sketched in, there was less of an attempt to faithfully depict in three dimensions. Though there was no specific comment (as there was in the 1890 paper) on how the diagrams such as Figure 13 were constructed, the note on how the later figures were prepared suggest that once again Wilson drew from the *camera lucida*, though



not purely, as “in many cases the finer details have been added free-hand to the camera sketch” (Wilson, 1892a: 464). There was, then, the room for slight departures from the precise details of individual examples, and Wilson did indicate this for some of the later figures (*ibid.*). **Figure 13** therefore constituted a greater abstraction than **Figure 10**. The most significant change from **Figure 10** was the arrows. In **Figure 10**, the arrows were bidirectional and indicated that the cells thus connected were siblings. In **Figure 13**, on the other hand, the arrows were unidirectional and denoted descent. It therefore aligned with the genealogical depiction of cell-lineage (**Figure 11**) but also moved from a static depiction (**Figure 10**) to a *processual* one.

Wilson tellingly remarked that “It is impossible to reflect upon the complicated yet perfectly ordered events of the cleavage in *Nereis* without attempting to discover the nature of the causes by which their course is determined” (Wilson, 1892a: 443). Having become newly fascinated with cleavage-forms, Wilson assessed the significance of his findings with inferences concerning the roles of different causal factors in development, namely a “hereditary tendency” (or historical cause) and “mechanical conditions”. He gave an example of how the same micromeres give rise to cells in different germ layers in polyclades (flatworms) and annelids, and observed “that cells having precisely the same origin in the cleavage, occupying the same position in the embryo, and placed under the same mechanical conditions, may nevertheless differ fundamentally in morphological significance”. From this, he reached “the conclusion that the cell possesses a definite hereditary tendency upon which primarily its nature depends, however much its outward form or mode of division may be affected by the mechanical conditions of its environment in the body; and full weight must be given to this heredity in every attempt to interpret the origin and meaning of cleavage-forms” (Wilson, 1892a: 441). What is the significance of such a remark? Maienschein claims that “Cell lineage study, in fact, focuses on cells and cell fates and reveals a complex interaction of external and internal directive factors operating on development” (Maienschein, 1990a: 368). Baxter concurs: “Wilson’s study of *Nereis* was also significant because it was his first encounter with the question of internal versus external determination of development” (Baxter, 1976: 39).

Is this the case? It would certainly seem that the practical demands of cell-lineage work raised the problem of how determinate and regular within particular species the pattern of cell-lineage is. This provoked questions about the fates of the descendants of individual cells, and to what extent they can be accounted for by position, external influences (which can then be identified and controlled) and factors internal to the cell. In short, the broader question about the determination of development as a whole was raised. The work on cleavage-forms, which demonstrated that mechanical conditions alone could not account for the fate of particular blastomeres, therefore led Wilson to invoke a hereditary tendency which the investigator had to account for and give full weight “in every attempt to interpret the origin and meaning of cleavage-forms” (Wilson, 1892a: 441). Wilson’s preliminary conclusions concerning cleavage-forms and the developmental significance of the division of the egg into succeeding generations of cells generated further questions. Indeed, his preliminary conclusion would not apply to an organism which did not display determinate development, such as *Lumbricus*, which Wilson was aware of, having worked with *Lumbricus*. The problem was to find some way of explaining both forms of development, and the cleavage-forms manifested (and their variability) in both. The problem was to find some way of investigating the precise role each posited cause – hereditary and mechanical – had in development.

Although he dealt quite extensively with cleavage in this paper, he promised further work on “the internal phenomena of cleavage and a detailed study of the differentiation of the tissues and organs” (Wilson, 1892a: 371). He outlined the questions concerning cleavage that his work had suggested to him:

What is the significance of the spiral and bilateral forms of cleavage, and where lie the causes that determine the transformation of the one into the other? What determines the form and succession of the divisions of the individual blastomeres, which, as in the case of the first somatoblast, may have so complicated and yet so definite a history? Is the blastomere, like the ovum, a self-regulating mechanism that contains within itself the causes of its own transformations, that is wound up like a clock, as it were, and must of necessity run the course predetermined in

its own structure? Or are its successive phases of activity determined or guided by influences proceeding from without – by the interaction of the cell with its fellows in the cell-complex?

Wilson, 1892a: 444

Wilson's preliminary treatment of the origin of the three main types of cleavage-form (bilateral, radial and spiral) is striking and instructive.<sup>91</sup> Wilson was still interested at this point in what his researches into the cleavage stages could tell him about the embryological demonstration of homologies. He related that "*the spiral form of cleavage has no necessary relation to the homology of the blastomeres, and hence is without phylogenetic significance*" (Wilson, 1892a: 447-448) and concluded from this that "*exact equivalence of embryological origin is not a proof of homology, as far, at least, as the cleavage-stages are concerned*" [italics in original] (Wilson, 1892a: 448). Although Wilson's research demonstrated that adult homologies within the annelids corresponded to cell-homologies in the cleavage stages (ibid.; Wilson, 1892a: 436), he concluded that cleavage forms had no relation to the adult form, and that "precisely similar modes of cleavage may arise quite independently of the nature of the materials, upon which the cleavage operates" (Wilson, 1892a: 448). Although he found that the fate of a particular cell in a cleavage form differed between embryos of different taxa there was in fact little relation between the cleavage forms themselves and phylogenetic position. A hereditary tendency might be responsible for the fate of a cell within a given cleavage form, but a shared hereditary tendency (to employ Wilson's language) across related species causing a particular form of cleavage did not seem to exist.

Instead, to account for the cleavage forms, Wilson turned to the "mechanical conditions peculiar to the earlier stages of embryonic life" (ibid.). **Figure 14** is an example of one of Wilson's attempts to use mechanical conditions to explain differences and similarities in cleavage-forms. The most abstract diagram Wilson had yet constructed, it accompanied his argument that the difference between spiral and radial cleavage-forms lay in the timing of the mechanical conditions leading to an alternation of cells, so that new layers of cells straddle

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<sup>91</sup> These three kinds of cleavage-form, as well as another, had been identified by von Baer, see footnote 33.

previous layers, rather than a particular cell lying directly on top of another in an older layer.<sup>92</sup> Robert Guralnick highlights Wilson's interest in investigating the role of mechanical conditions and in outlining "what the perfect form of cleavage would look like based on physical or mathematical laws" (Guralnick, 2002: 545). Forms could then be assessed depending on whether they conformed to such a *mechanical ideal*, and deviations accounted for by processes such as precocious segregation (Guralnick, 2002: 546).<sup>93</sup> Precocious segregation is where later stages of development get pushed back to earlier stages.

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<sup>92</sup> A figure depicting the tessellation of hexagons was probably more abstract (Wilson, 1892a: 451), but this was not intended in any way to represent cells, even if it would be employed as a geometrical argument in his discussion of cells, and cleavage-forms.

<sup>93</sup> Although this mechanical ideal did not constitute an explicit normal development, it plays a similar explanatory role to the normative idea of the 'natural state' in Aristotelianism. The 'natural state' is the condition an organism or other entity should be in, and if it is not, this deviation must be accounted for by the action of 'interfering forces' (Sober, 1980). I discuss the Natural State Model more fully in chapter 6.

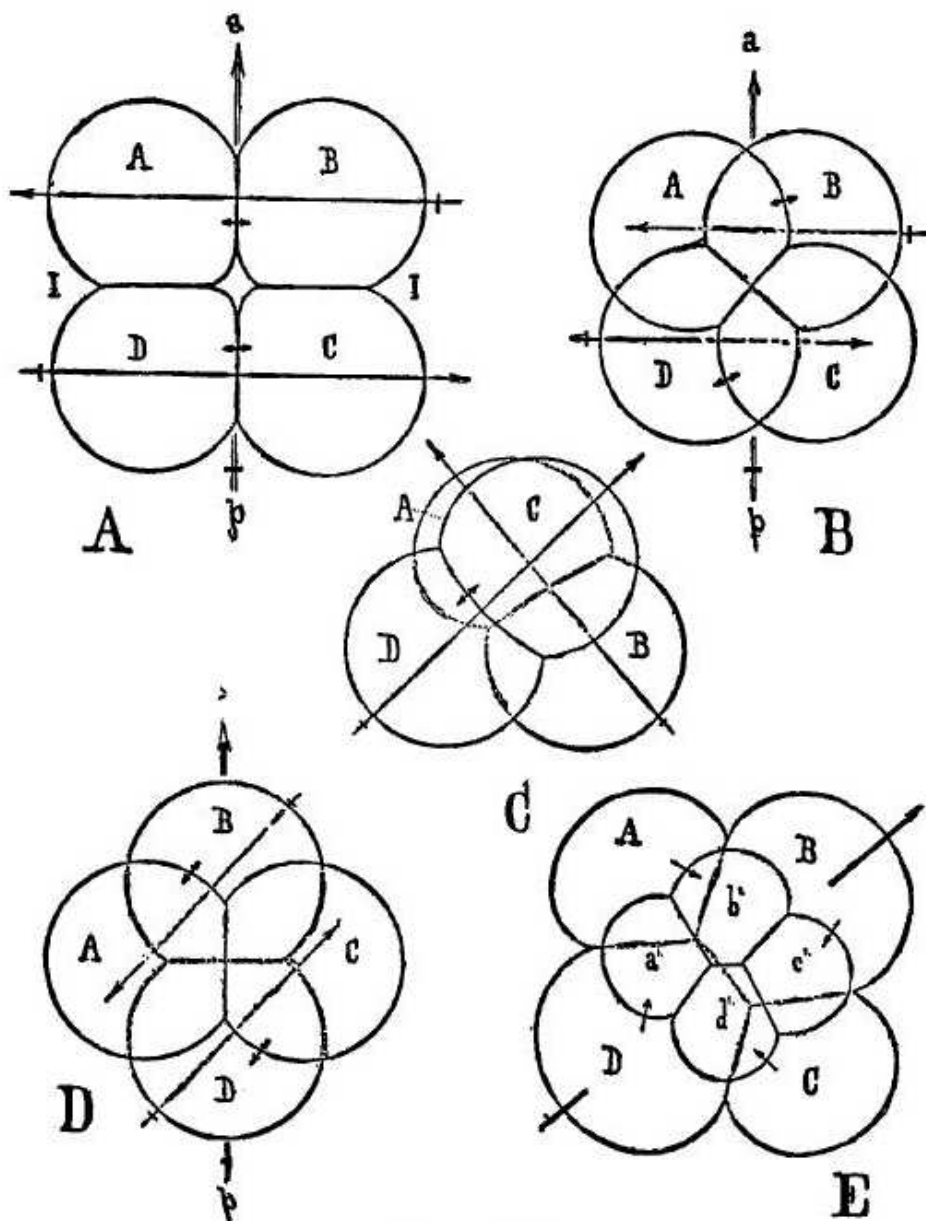


DIAGRAM VIII.

- A. Four-celled stage of true radial type (*Amphioxus, Synapta*).
- B. Spiral type (*Nereis, Crepidula*).
- C. Side-view of the last.
- D. Spiral type (*Discocalis*).
- E. Eight-celled stage (*Discocalis*).

Figure 14 – Highly abstract depiction of cleavage-forms at different stages and in different species. The only information remaining about the cells is their relative position, relative size, and genealogical relations. The diagram's purpose is to illustrate Wilson's mechanical argument that the spiral form of cleavage is distinguished from the radial by when the layers of cells alternate by a cell in a new layer lying on top of the border between the cells below, rather than on top of one particular cell (Wilson compared this to the tessellation of hexagons). In spiral cleavage-forms this alternation occurs early in development, in radial forms later on. Source: Wilson, 1892a: 452.

Guralnick is correct in suggesting that Wilson found mechanical causes to be primary, but not correct in asserting that Wilson in 1892 “has already rejected the use of embryology in reconstruction of phylogeny and in comparative sciences” (ibid.), a mistaken comment possibly resulting from a confusing skipping between Wilson’s works of 1892 and 1894.<sup>94</sup> It is *through* the cell-lineage work that Wilson comes to this view, concluding for example that “*exact equivalence of embryological origin is not a proof of homology*, as far, at least, as the cleavage-stages are concerned” [italics in original] (Wilson, 1892a: 448). The second (non-italicised) part of this quote reflects the process by which Wilson was trying to find secure grounds for an embryological criterion, but finding that it continued to elude him led him to greater scepticism about the use of embryological data. Wilson had embarked on his cell-lineage work to try and find a secure basis for establishing homologies between germ-layers, but had only found that when he traced lineages back to early stages – the cleavage stages – this left him with no grounds for homology. The hereditary tendency (a cause effected through a lineage of cells) Wilson spoke of was relevant to identifying the causes of different prospective fates of seemingly equivalent blastomeres, in the absence of a demonstration that identical mechanical conditions are associated with identical prospective fates. It therefore demonstrated that germ-layers derived from these cells could not be deemed truly equivalent, or homologous. Rather than demonstrating homology, ascription of a hereditary tendency instead removed the grounds on which an embryological demonstration of homology could be built.

Guralnick does admit that there was still some role for Haeckelian thinking in Wilson’s work in 1891 (Guralnick, 2002: 546 and 548). But he downplays the importance of such thinking, and opposes it to Wilson’s tendency to ascribe mechanical causes for cleavage-forms. For instance, he claims that the argument concerning the origin of bilateral cleavage is “not phylogenetic” because Wilson attributed the delay in bilateral cleavage being achieved in development to “a mechanical cause” (Guralnick, 2002: 551). But in Wilson’s own words, we see that at this point there was no mutually exclusivity concerning the causes. He argued “that *they must be the result of a throwing*

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<sup>94</sup> Guralnick seems to prefer to consider the findings of mechanical causes as reflections of prior belief.

*back or reflection of the adult bilaterality upon the early stages.* In some cases this influence has extended to the very beginning,...[but] In some cases, of which *Nereis* is a beautiful example, it has not extended so far; the early stages are still dominated by the mechanical conditions peculiar to them, and the bilateral form only appears when these conditions have been in a measure overcome” [italics in original] (Wilson, 1892a: 454). The mechanical conditions which give rise to the spiral form obscure the inherited bilateral form. So, for Wilson, in these early stages proximate (mechanical) causes prevent historical causes from manifesting themselves, and therefore inferences concerning the existence and operation of historical or hereditary causes could only be reached if the proximate causes were somehow controlled.

Guralnick’s (2002) account of the cell-lineage research programme deals admirably with Wilson’s work, and his focus on cleavage-forms in particular. However, in moving from the 1892 work to the 1894 lecture and back again, it cannot give us a clear account of the *immediate* effects of Wilson’s findings and interpretations. These are that Wilson had picked up on some very different modes of development, which indicated that for some organisms cleavage-forms are determinate, which was ascribed to an ‘hereditary tendency’, whilst for other organisms cleavage-forms were found to be less determinate (or indeterminate) and mechanical conditions were thus deemed to be more significant. This also seemed to apply to different stages of development, as Wilson’s explanation of bilateral and spiral cleavage exemplifies. Furthermore, Wilson perceived there to be no *definitive* phylogenetic pattern to these different modes of development, posing a further question mark against the Haeckelian framework.

Wilson came to associate these findings and puzzles with the nascent debate over the applicability of the mosaic theory of development, and alternative context-dependent models of development and the role and fate of cells within the embryo. He ended his landmark 1892 paper by stating that “How far this dependence [of individual cells on the embryo as a whole] goes, and how far the various blastomeres may be capable of replacing one another, is a question to be determined not by analogy, but by direct experiment” (Wilson, 1892a:

460). This experiment, and how it attempted to account for variation in early embryonic development, forms the basis for the next chapter.

### 3.6. Conclusion

Wilson's research from 1887 to 1891 posed problems that prompted the adoption of cell-lineage research. This research, which was intended to provide a sounder basis for comparative embryological work, raised new questions which provided a bridge to new research directions and methods.

Firstly, the search for a firmer basis for the embryological establishment of homologies had succeeded in producing much valuable material on the origin of the mesoblast, but had also undermined the germ-layer doctrine by finding that the origin of the mesoblast was not homologous across the annelids, because it did not share the same developmental origin and processes of formation. Additionally, if it was not homologous across the annelids, it was not homologous across the animal kingdom as a whole.

Secondly, as Wilson's observations of relations between different stages of development grew denser, just like the addition of frames to a movie reel, the possibility of the apprehension of development as a process grew. The way in which Wilson conducted his cell-lineage research, and represented the results, was to strengthen this tendency.

Thirdly, as Wilson travelled from Germany (his base when finalising the 1892 paper, submitted at the end of 1891) to Italy (where he was to conduct experimental work) in early 1892, he took with him a considerable interest in cleavage-forms, and questions about the extent to which development is determinate. As with Whitman, the interest in the relative importance (and nature) of internal and external causes of the development of organismal form (including embryonic forms) was intertwined with the question of what role embryology could have in evolutionary morphology – how could homologies be placed on a firm footing using comparative embryology?

As will be described in the following chapter, Wilson's work on *Amphioxus* in 1892 attempted to deal with such questions by adding an experimental



component, *in conjunction with* the comparative perspective. This was to produce some interesting and important outcomes for the direction of Wilson's research and thinking about the nature of development. It led, in that experimental work, to Wilson systematically observing the courses of individual development in as large a number of samples as possible, to construct a normal development, against which he could compare the effects of his experimental manipulation of the mechanical conditions experienced by blastomeres.

The shifts in Wilson's work and interests, occasioned by the resistances he encountered in trying to find firm bases for comparison and the identification of homologies, exhibit the productivity of even pre-experimental investigative systems for generating new questions. In Wilson's case, the new questions concerned the origin in early embryonic development of later, more differentiated structures. From this, questions arose concerning the causes and significance of the forms and processes of cleavage. Namely: to what extent and when did hereditary causes and mechanical causes operate, and which of these were stronger at particular stages of development? These were the questions which suggested themselves to Wilson, and from which he conceived of his 1892 experimental work. Like Roux, as I described in chapter 2, this led him to try to find a way to discern between the effects of historical causes and more proximate ones in embryonic development.

By moving from more traditional observational morphological work with embryos (such as the work with *Lumbricus*) to studying the cell-lineages of *Nereis*, Wilson attempted to find new assemblages of technical conditions to better frame an epistemic object of evolutionary morphology. Namely, finding a more secure embryological basis for identifying relations of homology between structures in organisms of different species, including between those we today consider to be belonging to different phyla. Wilson's work focused on trying to find a basis in early embryonic development to demonstrate the homology of germ-layers. He did not do this, but in the process of trying to frame the epistemic object, generated new questions and surprises concerning the nature of embryonic development. These new questions, part of the surplus of questions generated by the systems he devised but picked up by Wilson, led to a transformation of the epistemic object, which became now the causes of

differentiation and (level of) determination of development. This meant Wilson needed to devise a new set of technical conditions to frame the new epistemic object, and he did so by producing an experimental system incorporating normal development as a technical condition. At the heart of this new experimental system was a need to find a way to discern the roles and relative strengths of the causal factors he had invoked in his cell-lineage work, mechanical conditions and hereditary tendencies.

In 1894, Wilson set out an assessment of the embryological criterion of homology, in the light of the many efforts he had made to employ it in his work (Wilson, 1895a). In the lecture he delivered that year at Woods Hole, he made a plea for the reform of comparative morphology. However, he still wished to preserve a role for embryological factors in the determination of homology, albeit now in a subordinate role to comparative anatomy. He saw the addition of experimental methods to the armoury of comparative morphology as a way of saving it (Wilson, 1895a: 123).

In 1901, Wilson made the exuberant claim that “the introduction of experimental methods into morphology is the most momentous step in biological method that has been taken since the introduction of such methods into physiology by Harvey and Haller” (Wilson, 1901: 20). This did not imply a rejection of non-experimental methods, still less the comparative method. Wilson acknowledged that “our science is entering on a phase in which experimental methods seem destined, and rightly so, to take the leading rank” (Wilson, 1901: 21). However, this was a concession following an extraordinary passage in which he stated two key points. The first was that “Observation and experiment give us our materials, but it is the comparison and correlation of those materials that first build them into the fabric of science” (ibid.). Then, secondly, that he considered it to be “a reversal of the true standpoint to regard biological classification, in the broadest sense of the term, as no more than a preparation for experiment” (ibid.).

There are two key lessons to be learnt from these quotes. Firstly, he considered both observation and experiment as furnishing materials for comparison. Secondly, classification was still deemed important. Yes, he meant it here in a broader sense than specifically investigating the phylogenetic problems of

evolutionary morphology, but elsewhere in the piece he still affirmed that the sort of problems associated with classical evolutionary comparative morphology, such as “genealogical hypotheses...the origin of vertebrates, the origin of metamerism...still remain questions of very high interest” (Wilson, 1901: 16) even if the wider interest in them was now (in 1901, not 1892!) “beginning to wane” (ibid.).

Wilson emphasised the need for mutual support and exchange between the field naturalist and the experimentalist in the laboratory, and suggested that moves in that direction were already advanced: “The field naturalist came to realize that he could not attain right conclusions in the investigation of the larger problems before him without more thorough studies in anatomy and development. The laboratory morphologist learned better to appreciate the fact that his refined methods of technique are after all but a means toward the better understanding of the living organism and its relation to its environment” (Wilson, 1901: 19). Wilson’s work with *Amphioxus*, explored in the next chapter, neatly demonstrates the use of experimental methods to investigate problems generated through more naturalistic work.

## **Chapter 4 – Establishing ‘normal development’ as an embryological research strategy**

### **4.1. Introduction**

As he travelled from Germany to Italy in his year-long European sojourn, Edmund Wilson was also making a journey from the descriptive and analytical cell-lineage work he had recently finished, to the experimental manipulations he was to conduct. As I described in the previous chapter, the work with *Nereis* impressed upon him various phenomena of development that he wanted to explain, such as the cause and morphological significance of particular cleavage-forms. He believed that only by intervening in the early stages of development could he gather the data needed to provide such an explanation. He chose to conduct this work with the marine invertebrate *Amphioxus*.

While Wilson’s turn towards experimental work has been much commented on in scholarly literature, there has not been, to date, a detailed examination of that work.<sup>95</sup> In this chapter, I undertake to do this. I locate the origins of his work in the problems posed for comparative morphological work by the variety of cleavage-forms in early embryonic development. After explaining the rationale behind Wilson’s selection of *Amphioxus*, I then provide a full account of the methods he used in the 1892 experiment. Drawing on Wilson’s descriptions, as well as the methods of the likes of Hans Driesch and Berthold Hatschek, I detail the way Wilson collected and treated *Amphioxus*. Central to Wilson’s experiment was being able to compare the effects of his experimental manipulation – of shaking apart the cells at early stages of development – with the ‘normal’ development of *Amphioxus*.<sup>96</sup> Wilson split his samples of *Amphioxus* into two groups, one of which was to undergo this manipulation, the other was not.

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<sup>95</sup> For example, while Allen (1981) and Maienschein (1981 and 1986 in particular) cite the experiment, they refer to it only in broad terms. For the points they were making, it was the interpretation of the fact of Wilson’s adoption of experimental methods, not the analysis of the conduct of his experiment that was crucial.

<sup>96</sup> The relationship between the ‘natural’ and the ‘normal’ in Wilson’s experiment and paper will also be explored in this chapter.

Central to this chapter is an account of how Wilson constructed 'Normal Development' for experimental purposes, using it as a comparator against which the effects of the experimental manipulation could be determined. In Wilson's experiment, normal development can be understood as a technical object or concept which is produced by his experimental practice. Starting with my examination of the experiment, I describe the processes by which Wilson selected, observed, compared and represented his material. This description reveals the importance of Wilson's observation of actual samples in understanding how he produced normal development, in addition to the expectations generated by the study of previous accounts of the embryology of *Amphioxus*.

The experiment provides an excellent example of the role that introducing experimental practice into embryology played in establishing 'normal development' as a tool of the embryologist. The crux of this chapter is to establish that not only was this 'normal development' required as a necessary input to the experiment, but that 'normal development', or at least a certain understanding of what this entailed, was also *produced* by the experiment. Wilson integrated control experiments, in which he studied normal development, into his overall experimental set-up. It was through these control experiments, conducted with the expectations conditioned by study of other work on *Amphioxus*, that a normal development was generated. Wilson's normal development for this species was notably different from preceding (sometimes implicit) accounts of its normal development, for example in the work of Berthold Hatschek. The *Amphioxus* experiment conducted by Wilson therefore provides an excellent way of exploring material practices which resulted in the reconceptualisation of normal development. Later chapters will pick up on these practices and their consequences, by considering normal developmental as a technical condition. For now, we may note that the novel epistemic object which Wilson wished to explore entailed a new set of technical conditions, and that normal development was one of those conditions.

I conclude by considering four ways of interpreting the findings I present. I contrast Wilson's processes of generating normal development with the way in which, the year before, Driesch used normal development to deal with the

results of his experimental interventions on sea urchins. Then I explore how Wilson's experimental practices (and the constraints upon them) can be made sense of. I make observations concerning the conceptual language employed by Wilson, such as the terms 'mechanical' and 'inherited', which chapter 5 will explore in more detail. Finally, I point towards implications for the conceptualisation of normal development itself, which is the task of chapter 6.

The developmental psychobiologists George Michel and Celia Moore supply us with the insight that: "Intuitive definitions of normality maintain certain assumptions about the individual, the environment, and the types of processes that create the individual's behavioural repertoire (including the symptoms characteristic of abnormality)" (Michel and Moore, 1995: 411). This is certainly true of Wilson's definition of normal development by 1896 (Wilson, 1896). The task of this chapter will be to demonstrate that not only did prior expectations and assumptions guide Wilson, but that a deep engagement with the embryonic development of *Amphioxus* allowed him to produce normal development for the particular purposes of his experiment.

In teasing out how the normal was produced and used in Wilson's work, I provide the materials for the succeeding chapters, which *analyse* the role of normal development in embryological practice and theory, unmasking assumptions, background conditions and other factors that are implicit in the concept of normal development and its role within experimental systems.

## **4.2. Background to the *Amphioxus* experiment**

As I described in the previous chapter, Wilson's work on the cell-lineage of *Nereis* was meant to provide a more robust basis for the homologies of germ-layers across species. But instead, it presented Wilson with findings that prompted new problems and questions – which led to the formation of a new epistemic object requiring a new set of technical conditions. The two main (linked) groups of new problems concerned cleavage-forms and the determination of development. These included questions about the "significance of the spiral and bilateral forms of cleavage" and "the causes that determine the transformation of the one into the other" (Wilson, 1892a: 444). These questions

were embedded in the phylogenetic debates concerning the origins of vertebrates (including the rival annelid and ascidian theories) described in chapter 3. Wilson was also beginning to ask serious questions about the nature of development itself. This included engaging for the first time with concepts such as preformation and epigenesis – to what extent was the fate of the organism (and its parts) set at conception, or progressively determined over the course of development (ibid.)?

At this point, Wilson discussed these questions in broad terms of opposing an (internal) inherited tendency to (external) mechanical conditions, particularly in his assessment of his findings in the light of the fates of blastomeres he tracked from early embryonic development. The inherited tendency was the historical, phylogenetic causation. The mechanical conditions were the role of the yolk and the interactions between cells. Wilson observed that “We cannot escape the conclusion that the cell possesses a definite hereditary tendency upon which primarily its nature depends, however much its outward form or mode of division may be affected by the mechanical conditions of its environment in the body; and full weight must be given to this heredity in every attempt to interpret the origin and meaning of cleavage-forms” (Wilson, 1892a: 441). The point, however, was the *relative* weight of the two (sets of) causes, historical and mechanical, in the production of embryonic form. If the former causes could be shown to have much greater weight than the latter, then clear inferences could be drawn from embryological observations and comparisons for the solution of phylogenetic questions. If, however, the weight of mechanical or external causes were significant, this would pose serious problems for such inferences.

One related dichotomy to the internal and the external were the rival the mosaic and regulatory theories of development (Amundson, 2005: 144-148 and 170-175; Hamburger, 1997; Maienschein, 1991a; Sander 1991). The former proposed a view of development where the source of differentiation and change was internal to autonomous cells which operated largely independent of context. As a consequence, with each cell division, cells lose developmental potential or (to use a modern term) potency, and therefore become irreversibly differentiated. The regulatory view emphasised the influence of contextual factors (the whole, including sets of neighbouring cells) on the fate of individual

cells and their descendants (the parts). In the regulatory view, cells do not lose developmental potential or potency. Wilson started to engage with the mosaic theory of development (which was allied with ideas of internal sources of determination) associated with Roux and Weismann, noting its problems and the opposition to it. What was most perplexing for Wilson was that the nature of the development of the annelid *Nereis* seemed to differ so much from a previous organism he worked with, another annelid, *Lumbricus* (the earthworm). *Nereis* displayed determinate development, with early commitment of cells and their descendants to certain fates, whereas *Lumbricus* exhibited a less determinate development. How could these organisms – both annelids – have such different modes of development? Wilson now sought to account for these different modes of development, and at the same time assess whether the mosaic theory provided a basis to do so. Linking all these issues was the overriding question of variation.

It was increasingly apparent to Wilson that there was considerable variation in early embryological development. How this related to later development, and how the variation could be explained, were crucial problems. I will pick up on these issues in following chapters. For now I wish to stress the significance of early variation for theories concerning the determination of development. Considerable variation in early development preceding a less variable outcome of development would have posed serious problems for ideas such as the mosaic theory. If the source of determination was internal, how could this early variation be explained in the light of a convergence of forms in later development? How could this decoupling of earlier from later stages be accounted for in a theory which purported to explain the later state of an organism in terms of its development from an earlier state, without reference to anything *outside* of the organism?

Wilson began his 1893 paper by linking the question of cleavage, and variation in cleavage forms, to the “problems of embryological dynamics”, which included an assessment of the formation of particular cleavage forms in terms of their significance for the proximate, mechanistic understanding of the production of form (Wilson, 1893a: 579). But included in this “embryological dynamics” was still an interest in obtaining and interpreting data of consequence for the



programme of evolutionary morphology. The study of “the natural forms of cleavage” of *Amphioxus* was intended to form the basis for comparison for both “the cleavage of the chordates with that of lower forms” and the experimentally manipulated samples of *Amphioxus* (ibid.). He admitted that he “was led to examine the cleavage of *Amphioxus* primarily in order to determine the origin of the mesoblastic pole-cells described by Hatschek, and thus to find a definite basis for comparison with the annelids” (Wilson, 1893a: 597). Once again, the experimental work inspired by work in the new developmental mechanics was intertwined with questions deriving from debates on vertebrate origins. Even in this work, so methodologically different to his previous morphological investigations, there was still a concern with tracing the origin of particular cells forming precursors to later tissues. While this was motivated by comparative morphological concerns, the question as to what extent the fate of a cell (and its descendants) was determined at various points of development was highly pertinent to this.

Wilson ended his 1892 paper on the cell-lineage of *Nereis* with the following observation: “The facts seem to accord best with the hypothesis that the blastomeres [cells formed by the cleavage or segmentation of the fertilised egg] are capable within certain limits of pursuing their individual development, yet at the same time depend *in a greater or less degree* on that of the whole. How far this dependence goes, and how far the various blastomeres may be capable of replacing one another, is a question to be determined not by analogy, but by direct experiment.” (Wilson, 1892a: 460). The 1892 experiment and 1893 paper on *Amphioxus* was intended to be such an experiment, “with the main object of determining first, the *limit* of regenerative power, and second, its *form of action* as shown in the mode of cleavage of the isolated blastomeres.” (Wilson, 1893a: 587).

The purpose of the experimental manipulation was to vary the mechanical (that is, external) conditions experienced by *Amphioxus*. Such a variation in conditions in early development could then be mapped to the variations in the course and results of development. This would enable Wilson to observe the particular respective roles of mechanical and inherited conditions. If the Roux-Weismann version of the mosaic theory were true, then after each successive

division, (non-germline) cells would have progressively fewer inherited material factors to determine their own function and drive their descendant cells' future differentiation. Therefore, if the cells were shaken apart when the embryo was at the eight-cell stage, each non-germline cell would only have some of these inherited determinants, and could only produce the cells and structures which those determinants were responsible for. In other words, only parts could be produced, monsters. The work by Driesch on sea urchins in 1892 had tantalisingly suggested that this need not be the case (Driesch, [1892] 1974). If the separated blastomeres could develop to produce functional wholes, this would support Driesch's regulatory theory.

According to Maienschein, Wilson saw "experimentation as essentially a refined extension of traditional empirical methods, a move away from speculative science, from excessive theorizing and from what he regarded as the earlier pernicious intrusion of metaphysics into science" (Maienschein, 1986: 181). Maienschein also highlights how experimentation was not just used to help produce causal-mechanical explanations in the analytical and manipulative mode of the likes of Roux.<sup>97</sup> Wilson, and other American biologists, saw a different role for experiment, a creative role. Experimental manipulations created new phenomena that needed to be explained, and also helped to furnish clues for an explanation. Experimental methods and techniques therefore provided fruitful means of generating working hypotheses (as a means to guiding further experiments) and the creation of further new phenomena more refined, or perhaps broader, working hypotheses (Maienschein, 1991b: 422).

This explains why Wilson would want to conduct an experiment, manipulating the early stages of development. But why did he use *Amphioxus*?

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<sup>97</sup> A detailed account of Roux's approach to embryology can be found in Nyhart (1995: 278-305).

### 4.2.1. *Amphioxus*



**Figure 15** – *Amphioxus*, now known as *Branchiostoma lanceolatum*. Image courtesy of John Wahler.

The marine invertebrate *Amphioxus* (see **Figure 15**; now known as *Branchiostoma lanceolatum*) was a highly attractive organism for Wilson. Considerable work had already been done on the embryology of the organism, going back to the 1840s study by Martin Heinrich Rathke (1793-1860) (Rathke, 1841), and the landmark studies by Alexander Kovalevsky in the 1860s (in particular, Kovalevsky 1866 and 1877). What merited such attention, which was to intensify after Kovalevsky's work? Kovalevsky discovered a notochord in *Amphioxus*, making it a chordate. Although it is an invertebrate it therefore shares a key structure (and in modern taxonomy, belongs to a common phylum) with all vertebrates, but only with a small proportion of other invertebrates. A modern primer on *Amphioxus* informs us that “the morphological and genomic simplicity of amphioxus, together with its key phylogenetic position, make it an invaluable animal model for understanding the invertebrate-chordate to vertebrate evolutionary transition” (Bertrand and Escriva, 2011: 4820). It was precisely this position that led to intense interest in *Amphioxus* in the final decades of the nineteenth-century, when the origin of vertebrates was a question driving much embryological research, as described in chapter 3 (also, see Maienschein, 1994b). A contemporary writer observed that:

Probably no single group illustrates more beautifully the principles of transformism; for the Protochordates in their embryonic development exhibit remarkable reminiscences of past adaptations, and, in their adult development, the most varied present adaptations...[Amphioxus,] with its

resemblances to lower forms, gives us the connecting link between Protochordate and Chordate organisation.

Willey, 1894: vii-ix

The embryonic development of *Amphioxus* was therefore thought to provide an insight into past evolutionary changes, in particular those changes which occurred at the point at which the immediate precursors to vertebrates were coming into being.

Perhaps the most significant work since Kovalevsky's on *Amphioxus* prior to Wilson's work was that of the Austrian zoologist Berthold Hatschek, originally published in German in 1881 (Hatschek, [1881] 1893). Hatschek updated Kovalevsky's work without radically departing from it. Wilson cited Hatschek's work a great deal, and, while their accounts differed, Hatschek's methodology served as the basis for Wilson's work.

*Amphioxus* was valuable for Wilson because of its "plasticity" and "protean variability", and because its "development is capable in a very high degree of artificial modification through mechanical disturbances" (Wilson, 1893a: 579).<sup>98</sup> It was abundant in the Bay of Naples, the lakes of north-eastern Sicily and on sandy shores worldwide; and as a genus it is composed of only eight species, with little substantive difference between these species (Willey, 1894: 11). They could therefore be obtained in many locations across the world, allowing scientists in a number of countries to work with the organism, and build on, compare and verify the work of others. It is, however, an organism which even today is difficult to keep for more than one life-cycle outside of its natural habitat (Bertrand and Escriva, 2011: 4827). This was a particular problem for Wilson, who was only able to work for a few weeks at Faro in Sicily. This time constraint was compounded by the need to get to grips with the organisms and make the experimental set-up work. This produced practical difficulties that culminated in work that is somewhat rough around the edges.

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<sup>98</sup> It is difficult to believe, considering the scientific literature on *Amphioxus* predating Wilson's work, that he was aware of this while planning his experiment. More likely is that he acquired this knowledge as the result of his observations in that experiment.

### 4.3. The *Amphioxus* experiment – methods

Wilson did not provide a detailed account of his methods, or justifications for every decision he made. He did, though, give enough detail to provide us with some instructive information about his practices and aims. We can also use some of the sources he drew upon to flesh out the picture. These include Arthur Willey, Berthold Hatschek and Hans Driesch (Willey, 1890; Willey 1894; Hatschek, [1881] 1893; Driesch, [1892] 1974).<sup>99</sup> Willey and Hatschek's studies of the embryology of *Amphioxus* were based on work conducted in the same place as Wilson (Willey, 1890; Hatschek, [1881] 1893). Driesch worked on sea urchins in Trieste and Naples (Driesch, [1892] 1974).

Their work was similar enough to Wilson's to indicate (along with relevant citations) that Wilson took inspiration from large parts of their methodologies.<sup>100</sup> Willey and Hatschek, in particular, spoke at greater length about their methods of collection, storage, preparation, preservation and observation. Any inferences about the similarity of Wilson's procedures in these areas are strengthened by the fact that Wilson was not shy in making clear his differences with these men. For example, when Wilson described the release of "reproductive elements" or fertilised eggs, he contradicted Hatschek's account of what part of the female they are discharged from, and tartly noted that "It is difficult to believe that Hatschek's very explicit statements...rest upon erroneous observation, but I can suggest no other explanation of the contradiction unless the animals vary in habits from year to year" (Wilson, 1893a: 580).

Wilson collected adult organisms from the shore, allowed them to spawn and then harvested their eggs, which he kept individually (Wilson, 1893a: 579). He divided the eggs into two groups, one of which was to undergo development untreated, while the other was to undergo the manipulation. Wilson monitored and observed the development of the eggs, and stained and preserved them at particular stages of their development (Wilson, 1893a: 580). Fixatives used were picro-sulphuric solution, sublimate-acetic and Flemming's fluid (a nuclear

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<sup>99</sup> I have been unable to find the location of Wilson's laboratory notebooks. I am informed by Jane Maienschein that this is because, owing to Wilson's modesty and fastidiousness, they were not kept (personal communication, 2013).

<sup>100</sup> For example, the procedures outlined in Willey (1890: 81) are strikingly similar to those laid out in Wilson (1893a: 579-580).

fixative), and stains included Mayer's haema-calcium (a general reddish-violet stain, presumably intended to produce contrast) and osmic-carmin (which, according to a contemporary source, stained chromatin, and stained it a different colour depending on whether it was "resting" or "kinetic"; Lee, 1893: 100-101) (Wilson, 1893a: 586 and 597). The purpose of such staining was to identify which cells were dividing at particular points, and to distinguish between different types of cells (*ibid.*). With the manipulated group, he would shake apart the blastomeres at different stages (usually corresponding to the number of cells at the particular stage, so the two-cell, four-cell stages and so on) and then track their development (Wilson, 1893a: 587). Wilson aimed to compare the development of the non-manipulated (control) organisms with the manipulated ones. This was to ascertain the effects of interventions in early development, to change the mechanical conditions affecting the embryo, and to discover what effects, if any, induced variation (through experimental, external interference in development) had on the fate of the organism.

#### **4.3.1. The paper**

The 1893 paper which Wilson published detailing his work with *Amphioxus*, and outlining his conclusions based on it, was developed from autumn 1892 to spring 1893, and the final version submitted to the *Journal of Morphology* in April 1893, being published in August that year.

Wilson started this paper with a brief introduction, which (together with a footnote) outlined the purpose of his work and a sketch of his methods. He then described his observations of the non-manipulated *Amphioxus* in a section entitled "Part I.-Normal Development" (Wilson, 1893a: 580-586). This was organised into sub-sections pertaining to the different stages of *Amphioxus* (e.g. two-cell, four-cell). This was followed by a section entitled "Part II.-Induced Forms of Development", dealing with his observations of the results of his experimental interventions (Wilson, 1893a: 587-596). This was split into sub-sections, the first and last of which dealt with general observations, the other three with the cleavage forms observed after particular types of post-manipulation forms were generated (e.g. developed from isolated blastomeres or from fragments comprising two or more blastomeres still attached after

shaking). Part III of the paper began with a sub-section, entitled “A. Cleavage and Germ-layers in Annelids and Chordates”, in which Wilson compared the cleavage forms he observed in *Amphioxus* to those of other organisms (Wilson, 1893a: 597-598). He then moved on to “B. On Normal Cleavage-Types” where he discussed the three main types of cleavage form, how they might possibly be generated, and the significance of this for debates on the determination of development (Wilson, 1893a: 598-604). He dealt more fully with the latter question in the final part of the paper, entitled “Regeneration and the Mosaic Theory of Development” (Wilson, 1893a: 604-615).

#### **4.3.2. Collection and handling of *Amphioxus***

Hatschek observed that spawning occurs with greater frequency and in greater numbers when the weather is reliably warmer and recommended visiting from May onwards (Hatschek, [1881] 1893: 22). Wilson conducted his work in June and July (Wilson, 1893a: 579). He will not therefore have been restricted in the amount of organisms available, though the time required to store, process and record more samples was tight. Wilson was only in Sicily for six weeks, and *Amphioxus* eggs could not be artificially fertilised. In the light of this, he decided to devote most of his time to “the study of the earlier stages [of development] and to the preservation of material” (Wilson, 1893a: 586).

Willey revealed that he collected the embryos from a *pantano* (small lake or lagoon) which was connected to the sea by a canal. He recounted that the *Amphioxus* “embryos float on the surface, and are to be had by dredging on the surface at sunrise, but the readiest method of obtaining them in quantity is to take the adults in glasses and allow them to spawn there, if they will” (Willey, 1890: 81). Wilson followed suit, allowing him to maximise the number of samples at his disposal. He described how he obtained the animals and their eggs (“the reproductive elements”), transferring the eggs from the small vessel containing “clean water” to smaller vessels, also containing clean water and “a small quantity of freshly discharged spermatozoa” (1893a: 579-580).<sup>101</sup> Wilson claimed that the advantage of this method is that it obtains “perfectly clean”

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<sup>101</sup> One of the points of disagreement between Wilson and Hatschek was over the discharging of the egg, which Hatschek (and Kovalevsky) believed emanated from the mouth. Wilson observed it many times emerging from the atrial pore (Wilson, 1893a: 580).

eggs “in any desired quantity” (Wilson, 1890: 580). By clean, Wilson probably meant that the *Amphioxus* eggs are kept from potentially damaging influences. In their natural habitat these would include parasites. In the water in Wilson’s laboratory, this might have included microbial growth or the build-up of waste. Willey also spoke of the need for clean water. Following spawning, he believed that the resulting eggs “must be very carefully distributed among several glasses containing clean, but unfiltered, water from the *pantano*” [italics in original] (Willey, 1890: 81). Willey claimed that “If the water is filtered, or if sea water is employed, or if too many ova are place in one glass, they will certainly die or develop abnormally” (ibid.). There was thus already a judgement of normality (and how it would be ensured that *Amphioxus* developed normally rather than abnormally) underpinning the methods of collection and storage of *Amphioxus*, methods which Wilson was himself to employ. In Hatschek’s more extensive account of collecting in the *pantano* of Faro, he refers to the waters of the *pantano* as being salt water (Hatschek, [1881] 1893: 2). When Wilson described later in his paper how his manipulated samples were to be kept, he referred to them being “poured into a larger vessel of fresh water”, speaking of refreshed or new water, relatively free from contaminants, and not freshwater.

On the use of the vessels, while Hatschek distributed his samples into individual vessels to avoid overcrowding (which could have led to abnormal results), Wilson did not elaborate on this matter. However, Driesch emphasised the advantages of storing specimens individually in terms of being able to track the individual developments of organisms (Driesch, [1892] 1974: 42).

At various stages of development the embryos were “preserved” in a mixture of reagents. Each individual *Amphioxus* thus prepared served as a representation of only one particular stage of development. Comparing his preserved samples with live embryos and balsam-mounted samples at the same stage of development, Wilson observed that “specimens show that with proper precautions the only perceptible alteration is a very slight swelling, and even this does not take place if the ingredients of the mixture are used in exactly the right proportion” (Wilson, 1893a: 580).



### 4.3.3. *Manipulating Amphioxus*

Wilson employed Driesch's "ingenious shaking-method" to separate the blastomeres (Wilson, 1893a: 586). In essence, this involved gently shaking the eggs "in a small glass tube about half filled with water" and then pouring this "into a larger vessel of fresh water", as previously mentioned (Wilson, 1893a: 587). While inspired by Driesch, the shaking method was modified by Wilson, taking into account the greater ease with which the blastomeres can be separated in his organism compared to Driesch's sea urchins, and the disintegration of the *Amphioxus* blastomeres caused by violent shaking.

Following the shaking method of the Hertwig brothers, Driesch had put in water between 50 and 100 eggs which had already undergone cleavage in specified conditions after they had been artificially fertilised. Note that the conditions were merely stated rather than strictly controlled and standardised. Driesch referred to an *average* temperature in which they were kept, rather than a constant and uniform temperature to which all eggs were subjected.

There was clearly a 'knack' to the activity of vigorous shaking. Driesch detailed the consequences, from hard-won experience, of shaking too early (cleavage is "reversed") or too late (second cleavage has already occurred) (Driesch, [1892] 1974: 41). He observed that "It is therefore necessary to watch carefully for the right moment" (ibid.). He did this by microscopically inspecting them as "often as possible" during cleavage (Driesch, [1892] 1974: 42).

The advantage of *Amphioxus* over Driesch's sea urchins of the easier separation of the blastomeres was offset by the inability to artificially fertilise the eggs (Wilson, 1893a: 580). This, combined with Wilson's short stay in Faro to complete the work, necessitated a prioritisation of problems and tasks. Thus he paid most attention to the two-cell and eight-cell stages.

Wilson identified his "main object as determining first, the *limit* of regenerative power, and second, its *form of action* as shown in the mode of cleavage of the isolated blastomeres" (ibid.). This quote betrays the heritage of interest in cleavage-forms, and also the inspiration of Driesch's experiment revealing the regenerative power of his sea urchins. It also exhibited the comparative approach which Wilson brought to, and integrated with, his experimental

work.<sup>102</sup> Such an approach does not simply involve stressing and accumulating examples of the variability of biological phenomena across (and within) species, but within this approach “practices have also been used to uncover regularities and produce universal (or at least general) knowledge” (Strasser and de Chadarevian, 2011: 320). This was certainly an aim of the practices that Wilson exhibited throughout his research career. In knitting together the comparative with the experimental in his work with *Amphioxus*, Wilson stood out from other experimental embryologists such as Driesch and Roux, whose different backgrounds precluded such a union. Driesch and Roux’s backgrounds were experimental and physiological, not comparative and morphological. Their primary concern (at this time) was with the mechanics of development, and not with the variation exhibited in forms.

On the face of it, Driesch’s and Wilson’s works were extremely similar. They were, it is true, dealing with different organisms. This fact cannot be underestimated, as the literature on the significance of the selection of experimental organisms demonstrates (Burian, 1993; Bolker, 1995; Rheinberger, 2010a).<sup>103</sup> However, Wilson worked with a wide range of organisms, and was perfectly aware of the inter-specific variation in modes of development that were exhibited (Wilson, 1896 frequently displays this, e.g. 281-282, 313-320). Wilson wanted to *account* for such variation (exemplified in the seemingly contradictory results of Driesch and Roux) and bring it under a common explanatory framework, as the following chapter will demonstrate.

#### **4.3.4. Comparing and calibrating – the structure of Wilson’s experimental set-up**

As we saw in the previous chapter, for Wilson experiments and observations served to furnish the materials for the higher-order task of comparing. His

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<sup>102</sup> And, in combining these approaches, Wilson was able to bring together the natural historical and the experimental in his own work (see Strasser, 2010 for an argument on the combining of natural historical and experimental approaches in the twentieth-century), something which he would later argue for more broadly (Wilson, 1901).

<sup>103</sup> I use the term experimental organism rather than model organism, after the distinction drawn by Ankeny and Leonelli (2011). Model organisms, according to this perspective, are a very particular subclass of the broader class of experimental organisms. The criteria for model organisms outlined in that paper do not correspond with the nature and role of *Echinus* (sea urchins) or *Amphioxus* in the work of Driesch and Wilson.

previous comparative work required comparison of cell genealogies and germ-layers between different species. Previous work controlled and standardised the conditions in which organisms were kept, killed, prepared, marked and observed. In his 1892 experiments with *Amphioxus*, this was added to with a new group of samples – the ‘normal development’ – that formed what we might call a control, with which the other group exposed to a different treatment was compared.

Wilson used the terms ‘natural’ and ‘normal’ at the beginning of the 1893 paper when referring to his discussion of the samples which he did not shake. Part I is entitled ‘Normal Development’, and in the introduction preceding it, he promised that this section would deal with “the natural forms of cleavage”, in contrast to the “induced forms caused by the isolation or mechanical displacement of the blastomeres”, which he dealt with in the second part of the paper (Wilson, 1893a: 579). The account of ‘normal development’ therefore had at its heart a concern with natural forms generated in the course of normal development. After the introduction, the term ‘natural’ was not employed in the rest of the paper. Concern with the ontological status of the objects he was working with and creating were abandoned when he moved into the actual study itself. ‘Normal development’ was used as a term denoting the overall mode of development (i.e. normal in contrast to abnormal development). ‘Natural’ referred to specific forms that could be found at particular stages of normal development, for example “the natural forms of cleavage” (ibid.).

After the introduction, attributions of normality (through the use of terms such as ‘normal’ and ‘abnormal’) and not ‘naturalness’ were applied to forms existing at particular stages of development. However, having established a link between notions of normality and naturalness in the introduction, the assumption of the naturalness of the ‘normal’ forms was embedded in the subsequent descriptions of the uninduced and induced development of *Amphioxus*. Such an association is not unproblematic. Wilson’s strategy of establishing a normal development was not intended to be used to provide an account of the *natural* development of *Amphioxus*. If this had been the aim, Wilson would have compared his ‘laboratory normal’ samples at particular stages to ‘wild natural’ samples at the equivalent stages, as Hatschek did. However, the establishment of the normal

development was part of the experiment aimed at generating data concerning the natural *processes* of development in *Amphioxus*. These he could quite reasonably assume to be present in all three conditions (laboratory normal, induced, and wild natural), even if these natural processes of development generated different forms, depending on the different conditions the organisms were exposed to. While the normal development is produced as part of the experiment itself and did not refer to anything outside of the laboratory, the association of the normal and the natural allowed Wilson to associate his findings in the laboratory with what occurs ‘in nature’ itself outside of the laboratory. I will pick up on this observation shortly, and examine it in depth later in the thesis.

Two different types of comparison took place in Wilson’s work. The first was a conventional interspecies comparison, the second a novel intraspecies comparison. The former reflected Wilson’s background in comparative morphology, the latter his new experimental approach. In the intraspecies comparison, there was still a need for some kind of comparator. Therefore, the ‘normal’ *Amphioxus* set its own standard. The ‘Induced’ forms were measured against that very standard, and deviation from it was dealt with in a wholly different fashion to deviation exhibited by a ‘natural’ form.

In the opening paragraph of his work Wilson used this language of an *artificial* modification being attained through *mechanical* disturbances (Wilson, 1893a: 579). An example of the effect of the type of comparison engendered by the normal *Amphioxus* setting its own standard is how he dealt with the variation exhibited within the ‘normal’ samples that were not modified by artificial and mechanical disturbances. Such variation was acknowledged, but tucked away from the main body of text into a footnote describing the issues and problems he experienced in conducting the experiment (Wilson, 1893a: 587). He recounted the following as “sources of error”: “First, normal eggs and embryos vary considerably in size. Second, they do not develop precisely at the same rate” (ibid.). Results, which are of interest in themselves, do not form a central part of the discussion of the nature of the ‘normal’ forms. Instead, the deviations away from what were deemed to be the natural and the normal are relegated to the status of a footnote and abstracted away from the model of the normal that

Wilson was building.<sup>104</sup> While it might be argued that attributes such as size and rate were not central to Wilson's research questions, these attributes were definitely relevant for the form of the embryos which presented themselves to Wilson, and form was central. Given the relevance (recognised by Wilson, see Guralnick, 2002) of physical forces and interactions for the production of particular forms in early embryonic development, any variation in these forces and interactions due to variation in size at a particular stage would surely have been a relevant consideration. The rapid changes of form in early development also suggest that changes in the rate of development would also be a relevant factor. Wilson made a judgement about what kinds of variation he would ignore in producing a normal development, kinds of variation that could conceivably have played a role in this production, given their relevance for his main concerns pertaining to form.

A key part of the process of generating normal development was the selection of organisms. Wilson states in a methodological footnote that "a certain number of the eggs always develop abnormally, whether shaken or not" (Wilson, 1893a: 587). Yet the descriptions of these 'abnormal' forms are missing from the descriptive portion of the paper dealing with 'Normal Development' (Wilson, 1893a: 580-586). He therefore left out embryos which he deemed to be abnormal in his construction of an idea of the normal or natural. Then, although he gave quantitative details of, for example, the proportion of different cleavage forms at various (e.g. eight-cell, sixteen-cell) stages, he arrived at the 'normal' development through a *qualitative* process of abstraction.<sup>105</sup> He selected or removed certain embryos from consideration, and assimilated his observations (within stages using the various samples of *Amphioxus* preserved at those points, and between stages thus abstracted) to internalise a picture of normal development. To measure the effect of the varying of mechanical conditions that the blastomeres experienced, Wilson needed to observe not only the variation exhibited between manipulated (i.e., shaken) embryos, but also the variation exhibited by those that did not undergo this treatment. What was therefore being compared was the variation between the variations of two different populations of *Amphioxus*. Moreover, both of these populations were

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<sup>104</sup> A footnote which was not actually in the section dealing with the 'normal' forms!

<sup>105</sup> I shall deal fully with the role of abstraction in normal development in chapter 6.

kept and observed in artificial conditions. Wilson and Hatschek's collecting strategies differed in that, in addition to capturing mature forms for *in vitro* spawning and subsequent tracking of the development from the fertilised egg, Hatschek collected organisms at all stages of development from the *pantano* and compared their states at particular stages to the forms developing in the laboratory. Wilson only compared forms developing in artificial conditions, and did not compare these forms to those in the wild. There was thus a tension between the relatively naturalistic interpretation of Wilson's observations of *Amphioxus* development, in which he sought to encompass a wide range of observed variation within his normal development, and the less naturalistic conditions in which the *Amphioxus* developed and were observed.

While he described the different forms in quantitative ways (for example by enumerating the frequencies of particular variants at particular stages), what made the difference for Wilson's judgements was the qualitative assessment of data, through the process of calibrated observation, which I detail in the following section.

#### **4.3.5. Observing and representing *Amphioxus***

Wilson described how, and more pertinently with what combination or mixture of reagents, the embryos were preserved, and the stages prepared (Wilson, 1893a: 580). Wilson's language ("the best results being" [ibid.]) betrays, though does not explicitly state, the trials he went through to secure a combination of reagents to preserve the embryo, the yardstick being a comparison of the preserved embryos against living, unpreserved embryos. The preparation of the stages drew on his experience of working with annelids, and the materials that worked with those organisms (ibid.).

The observation of the formation of the 'natural' forms exhibited at different stages was to provide a basis for the experimental manipulation. Attempting to calibrate a 'basis' or baseline using extremely variable phenomena is a tricky task. What Wilson established for himself in the first part of his experimental work was what I call 'calibrated observation'. This did not involve an objective compiling and analysis of data (quantitative or qualitative) to provide some kind

of average figure. Instead it was a calibration of Wilson's own expectations of what constituted normal development.

Crucial to Wilson's construction of a normal development were the prior expectations generated by his reading of Kovalevsky and Hatschek, who he cited as precursors to his own work (Wilson, 1893a: 580). Hatschek's work presents an unequivocal account of the development of *Amphioxus*. It did not *acknowledge* variation at any stage of early development, not even to dismiss it as irrelevant or an artefact (Hatschek, [1881] 1893: 43-52).

These expectations were calibrated by repeated and focused observations, and the development through these of a keen sense of the organisms and their pathways of development. It involved establishing an intuitive sense of what happened in the normal development to generate expectations, empirically grounded to some extent (but not totally), which he could then take to the observation of the modified forms he created. The quote I included in the introduction to this chapter speaks of "Intuitive definitions of normality" (Michel and Moore, 1995: 411). I am describing the generation of such intuitions. As Michel and Moore suggest, assumptions are built into these intuitions (*ibid.*). I have already indicated a few of these, and will document more throughout the rest of this chapter and thesis.

How might this process of calibrated observation be conceptualised? Such a process does not conform to the regulative representational ideal of "mechanical objectivity" prevalent in late-nineteenth-century science. This ideal has been defined as "the insistent drive to repress the willful [*sic*] intervention of the artist-author, and to put in its stead a set of procedures" (Daston and Galison, 2010: 121). It was supposed to ensure the representation of actual instances rather than ideal types by a scientist working as a passive mediator (possibly using automatic or mechanical aids), rather than as an active constructor of representations (*ibid.*).

In the 1893 paper Wilson makes no reference to the details of the mechanics of his observational techniques. However, in previous work (e.g. Wilson, 1892a) he used the *camera lucida* to aid him in his depictions. The *camera lucida* is a device which uses a prism to allow the observer to view the image of the

specimen under the microscope superimposed onto an image of paper on the desk next to it. The figures in the 1893 paper, resembling in form many of those in the 1892 paper, suggest that a *camera lucida* was used to produce them. They were not naturalistic, but contained some deviations away from 'perfection'. This is characteristic of the style of depiction associated with the *camera lucida*. The *camera lucida* does not merely allow the image to be copied onto the paper. It does, however, save "the memorization step otherwise needed in the interval elapsing while turning from the object to the drawing can be spared" (Fiorentini, 2006: 33). Any "mental activity directed to the technical accomplishment of the drawing, thus, recedes in favour of an inspection of the observed in terms of its meaning" (Fiorentini, 2006: 34). This, combined with the ability of the observer to comprehend depth due to the ability to change the microscope focus (something a photograph could not achieve), will have allowed Wilson to assess the three-dimensional structure of embryos.<sup>106</sup>

Wilson's use of the *camera lucida* hints at mechanical objectivity, of the automatic (and therefore supposedly more objective) production of representations. However, some of his representations, particularly geometrical, suggest a kind of "truth-to-nature" representation style revealing an ideal form or type underlying the apparent variation. I suggest, however, that Wilson's method has more in common with the ideal of "trained judgement" by which the scientist – building on internalised experience – discerns patterns, rather than ideal types, through his or her own "interpretive eye" (Daston and Galison, 2010: 311). While this is associated with a rejection of mechanical objectivity occurring from the early-twentieth-century, it does seem to reflect what Wilson was doing in 1892-3. The *camera lucida*, for instance, requires that judgement be exercised in translating the reflected image into a drawing. As Fiorentini describes, "the mirroring surfaces of the prism guarantee the fidelity of the perceived image in relation to the chosen scene; however, the degree of congruence of the resulting picture depends on the process of selection performed by the observer after having perceived the virtual image conveyed by

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<sup>106</sup> In this way, the use of the *camera lucida* corrects a problem with microscopical observation – that "it is not possible to ascertain the relative place and form of an object by moving one's head" (Schickore, 2001: 137). This also applies to relative places and forms *within* an object. This causes observers "great difficulties in assessing particular details", particularly those pertaining to three-dimensional structural relations (ibid.).



the prism in his or her eyes” (Fiorentini, 2006: 35-37). Such selection, particularly selection leading to the successful apprehension and representation of the three-dimensional structure of embryos, suggests the employment of trained judgement.

As detailed in the previous chapters, representations, in the form of diagrams and figures, are extremely instructive in analysing the interpretation and the stress placed on particular results by the scientist. Wilson in particular used a considerable amount of carefully constructed diagrams to not only illustrate and demonstrate, but also to work through the material he observed to develop wider points. They therefore served a cognitive function as well as an expository one. In the 1893 paper, unlike previous papers, the diagrams are not a roughly even mixture of the abstract and the naturalistic. They are overwhelmingly abstract, and the depictions of the early stages of development are particularly so. There is a curious division in terms between the representations found at the back of the paper in the ‘Plates’ section, which were labelled as figures, and the one ‘diagram’ found in the main body of the text. The difference is that the figures are of actual specimens (a very few living, most preserved), however abstracted or idealised, whereas the diagram is an abstract representation of the three main types of cleavage shown by *Amphioxus* in its normal development, with some indication as to their possible formation.

**Figure 16**, taken from the back of the 1893 paper, depicts the first three cleavage stages of *Amphioxus*. It does so by depicting the first two cleavage stages (labelled as figures 2 and 3, respectively in my **Figure 16**), and then the different ways in which the third cleavage stage can proceed, to produce four different resulting eight-cell cleavage forms. Wilson employed only the cell outline, the ghosted cell outline of cells lying behind or beneath foregrounded cells, arrows, circles and bars. The arrows depict the division of cells. In the second cleavage stage the arrows are bidirectional, indicating that the division is equal. In the third cleavage stage the arrows are unidirectional, and depict the lineage of cells, with the smaller micromeres derived from the larger macromeres. The circles help to show how the cells move in relation to each other (for instance between figures 7 and 9 in my **Figure 16**). The bars (with circles at either end) provide information about the orientation, and relative

orientation, of cells. These simple symbolic representations, placed in and between outlines of cells, allow the reader to visualise the process of cleavage and the transition between stages, dynamically, as a *process*. In subsequent cleavage stages, the complexity of the divisions and cell movements meant that Wilson could not and did not depict all divisions and movements, but selected particular ones in an individual figure to give some indication of what must be occurring throughout the development of the embryo depicted in the diagram. They therefore demonstrate how abstractions, when skilfully conducted, can end up conveying more important information than a less abstracted depiction. This was enabled by Wilson's deep engagement with the individual development of *Amphioxus* embryos, together with the representational skill he had developed in years of research.

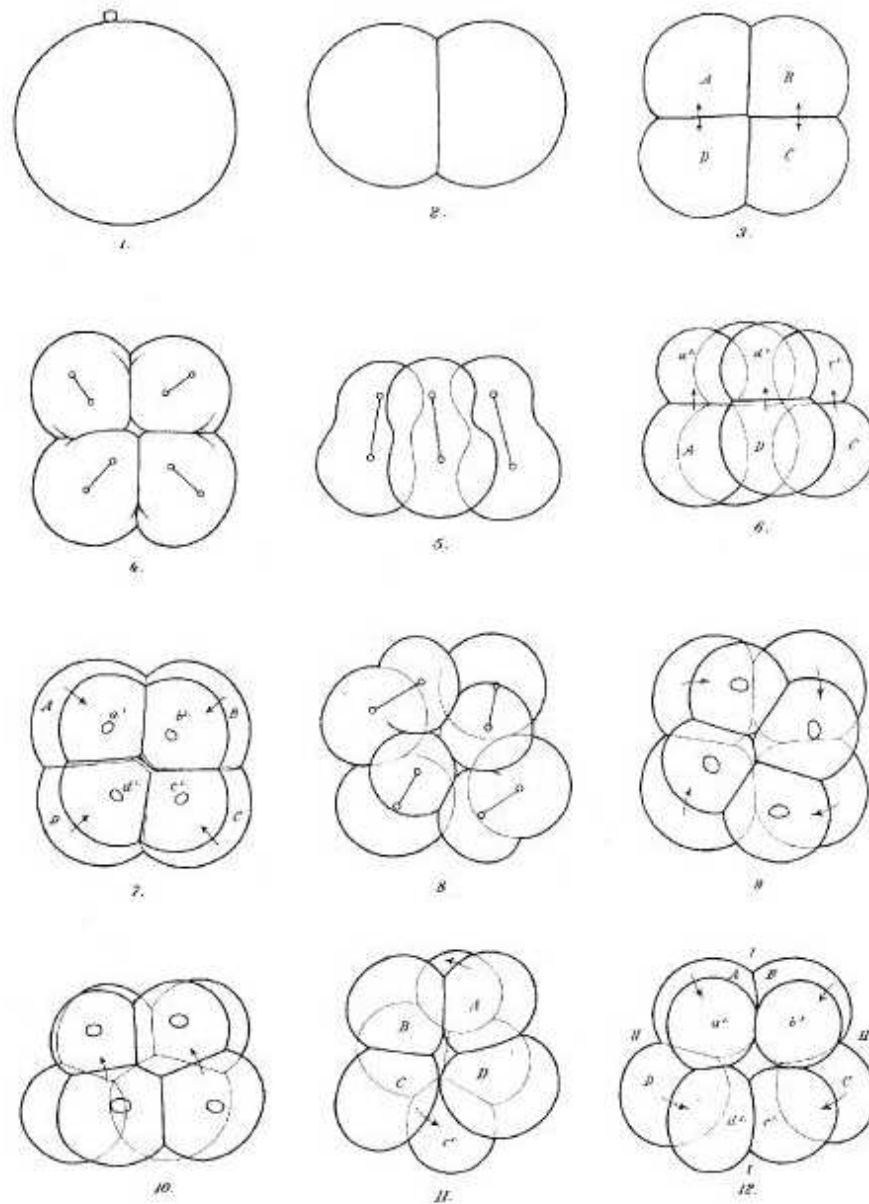


Figure 16 – Wilson's depictions of the early stages of embryogenesis. He represented the first three stages of cleavage, and the variation in forms exhibited in the third stage. Figures 2 and 3 correspond to the first cleavage (two-cell) and second cleavage (four-cell) stages. The next three rows represent the proposed formation of the three main cleavage forms in the third cleavage. Figures 4 to 7 represent the formation of the “pure radial form” (Wilson, 1893a: 620), figures 8 to 10 represent the formation of the spiral form, figure 11 a “mixed form” (ibid.) and figure 12 the bilateral form. Source: Wilson, 1893a: 621.

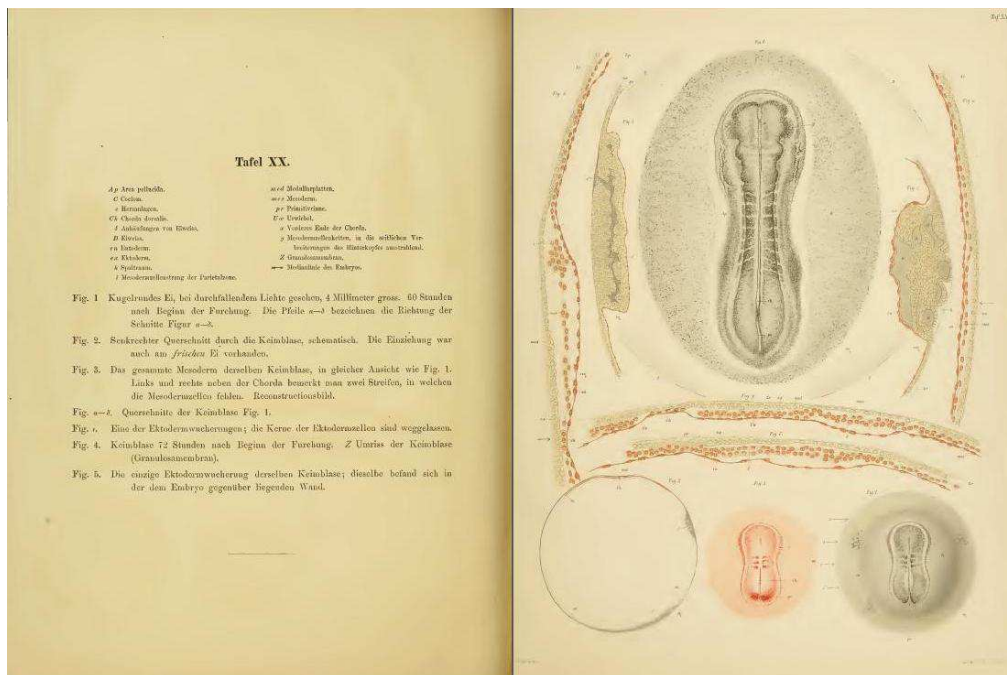
#### **4.3.6. The *Amphioxus* experiment – comparisons with Roux and Driesch**

Examining Driesch's work with sea urchins reveals a key difference with Wilson. Rather than using his own 'normal' or control group to serve as a comparator, Driesch instead used the books of the zoologist Emil Selenka (1842-1902). After describing his methods of keeping the sea urchins and intervening in their development, he began the description of his results with "a few words about the normal course of events as revealed in Selenka's excellent investigations" (Driesch, [1892] 1974: 42). Driesch does not state why he relied on Selenka's account rather than observing a control group of his own. However, he had faced trouble obtaining material which wasn't "almost exclusively useless" (as he referred to the samples which stymied his first week of research) and only a small number of samples (fifty) survived the vigorous shaking procedure (Driesch, [1892] 1974: 41). It would therefore not be unreasonable to suppose that Driesch believed that using all samples at his disposal to conduct the experimental treatment was a better use of his resources than setting aside some into a control group, particularly given the availability of Selenka's account. If Driesch assumed little or no variation in normal development, this decision would be unproblematic for him.

Selenka produced over sixteen volumes of 'Studies of the Developmental History of Animals', which were detailed accounts of the embryology of various animals of interest to zoologists.<sup>107</sup> Generally, the first half of these handbooks were given over to detailed textual descriptions of what can be found at different stages of development, with no illustrations. The second half then comprised of double-page plates ('Tafel') providing examples of different stages of development. The right-hand page would feature hand-drawn examples of particular stages and the left-hand page the written details of what each figure represents. **Figure 17** below is an example of one double-page (Selenka, 1886: 146-147):

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<sup>107</sup> The 16<sup>th</sup> volume is the highest number I could find in a search on archive.org. 'Studies of the Developmental History of Animals' is a translation of the original title '*Studien über Entwicklungsgeschichte der Thiere*'.



**Figure 17 – Example of a *Tafel* from one of the works of Emil Selenka, a key source of information for Hans Driesch (Selenka, 1886: 146-147).**

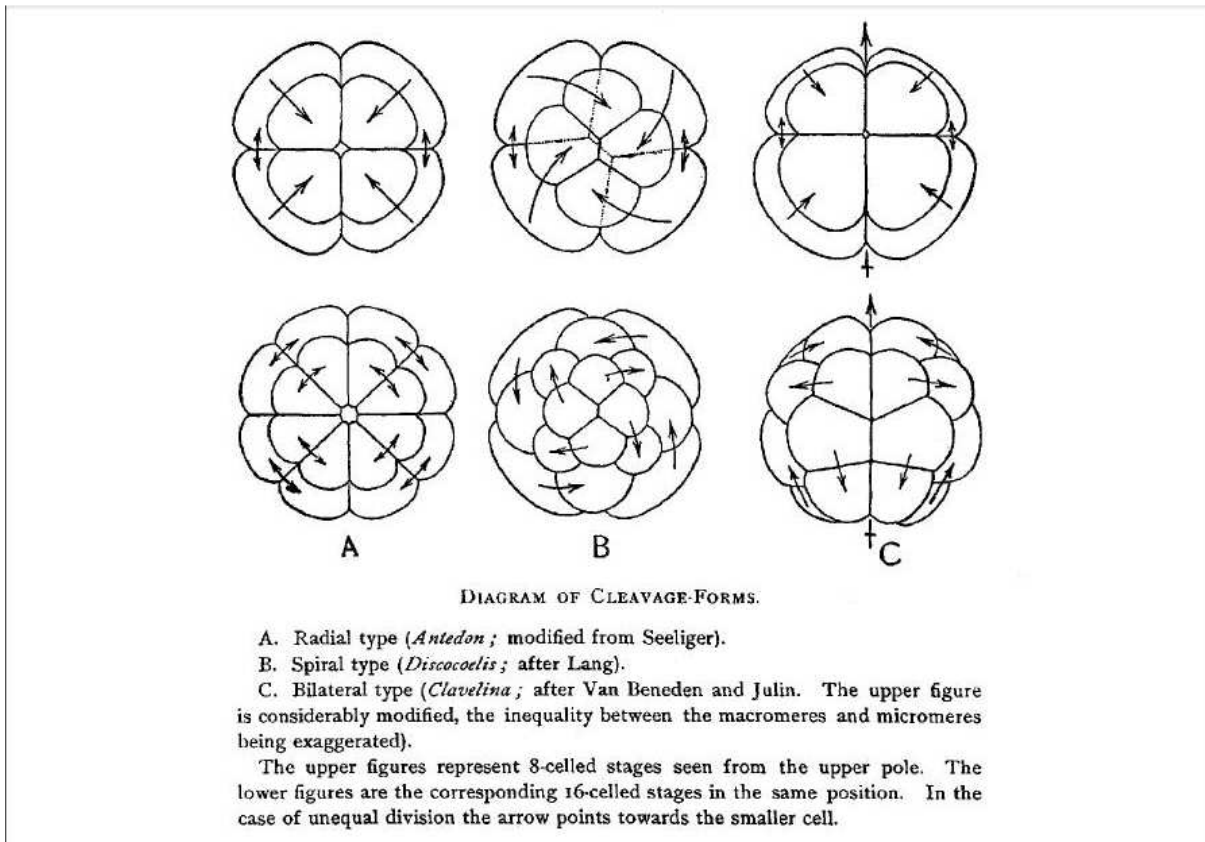
Driesch drew his conception of the normal course of development from such images. Wilson, while having initial expectations of what constituted normal development generated by the work of the likes of Hatschek, deepened, developed and fundamentally changed this view by directly observing the embryos which had not undergone his experimental treatment. The nature of Driesch's engagement with the 'normal' or undisturbed was indirectly mediated through the idealised view of Selenka, thus robbing him of the realisation (for sea urchins at least) of the variability that is exhibited by even uninduced forms. The two men may have been exposed to the same sorts of inputs, but Wilson's methods enabled a transformation of the product of these inputs (normal development) in a way that Driesch's could not. All Driesch could do was to map the differences between the sea urchins which underwent his experimental treatment and the normal development on the page. It was not possible for him to rework what was on the page. This is nicely illustrated by a figure depicting the (normal) sixteen-cell stage, which he tells us is "copied from Selenka" (Driesch, [1892] 1974: 44).

Unlike Driesch, in his key experiments and paper on the early stages of frog (*Rana esculenta*) development, Wilhelm Roux did use a control group of non-manipulated samples (Roux, [1888] 1974). Like Wilson, Roux spoke of normal development, and compared the observed forms in the manipulated group to those of the control group. However, unlike Wilson, Roux only introduced particular observations of the control group when discussing the results of the experimental manipulation, to determine (and usually, demonstrate) that the results are a consequence of his intervention (Roux, [1888] 1974: 9). There was no separate discussion of the observations and patterns displayed in the control group. Furthermore, while the establishment and description of the control was central to the generation of normal development within Wilson's experiment, it was not so for Roux. It is clear that for Roux, normal development (more specifically, the normal development of this particular species of frog) transcended the experiment, including the control and the manipulated arms. Roux spoke of cells which he repeatedly punctured "with a fine needle" developing "normally", without reference to unmolested cells in the control group. Shortly afterwards he deemed "malformations" to be exhibited in control eggs (ibid.). His standard of normal development was therefore external to the control group and the experimental set-up. I develop these points in the following chapter.

#### **4.4. The Amphioxus experiment – results**

In the paper, Wilson aimed to establish the normal or natural development and forms of cleavage (remember that normal and natural are interchangeable in this context for Wilson) and then deal with "induced forms [of cleavage] caused by the isolation or mechanical displacement of the blastomeres" (Wilson, 1893a: 579). The first part was therefore entitled 'Normal Development' and concerned the first four cleavage stages in particular, with brief summaries of the subsequent stages.

#### 4.4.1. 'Normal Development'



**Figure 18 – Diagram of the three main cleavage forms exhibited in the animal kingdom and in *Amphioxus*. Source: Wilson, 1893a: 599.**

Starting with the earliest stages, we may note that Wilson agreed with Hatschek in his depiction of the first two cleavage stages, though Wilson observed that despite four cells of equal size being the rule after the second cleavage, “slight variations exist in the position of the blastomeres” (Wilson, 1893a: 580). These were not without significance for Wilson, and he believed that they were “a key to the more considerable deviations of later stages” (Wilson, 1893a: 581). He attributed any “displacements” to the “mutual pressure” of the four cells, invoking a mechanical explanation for any variation. Wilson believed that the four-cell stage of *Amphioxus* was radial, “and that the departures from this arrangement are purely accidental”. The use of the term accidental to describe

such ‘departures’ from a “type” (a term used by Wilson in this respect) is suggestive, as we shall see in chapter 6 (ibid.).<sup>108</sup>

The third cleavage stage in the normal development of *Amphioxus* fascinated Wilson. In this stage, three distinct forms (see **Figure 18**) were found (and transitional forms between these), “each of which is a fixed type of cleavage elsewhere in the animal kingdom” (Wilson, 1893a: 581). Around three-quarters of samples exhibited radial cleavage, one-fifth spiral and only one sample bilateral (Wilson, 1893a: 582). The three main forms and their ‘intermediates’ are all, Wilson believed, “capable of complete and normal development” (Wilson, 1893a: 584). Having found them all exhibited at this stage of development, Wilson regarded all of the three different cleavage forms (radial, spiral and bilateral) to be *both natural and normal* in *Amphioxus*. Willey acknowledged this discovery as “an example of a polymorphic cleavage”, which contradicted the idea that cleavage “follows the uniform and stereotyped plan that has been hitherto supposed” (Willey, 1894: 108).<sup>109</sup> The mature work by Edwin Conklin on *Amphioxus* also acknowledged this, praising Wilson’s study of cleavage, and generally agreeing with his results (Conklin, 1932: 78-80). He noted “that the spiral character of the cleavage in *Amphioxus* is not as constant nor as prominent a feature as in annelids and mollusks” and that “the cleavage is pre-eminently bilateral” (Conklin, 1932: 80). While acknowledging the variation, Conklin tried to establish one type as ‘pre-eminent’, which is subtly different from Wilson’s treatment of relations between the three forms, as I will elaborate on in the next chapter.

One consequence of the ‘polymorphic’ cleavage was that Wilson’s idea of normal development was broadened – a considerable amount of variation of form in early embryonic development could be considered to be part of normal development, provided that the end result was functional. This meant that the adult stage was reached and that this had a ‘normal’ structure and functioning, even if it was smaller in size. The presence of the three main forms of cleavage in *Amphioxus* provided Wilson with a model which could be used to explore the

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<sup>108</sup> For now, I merely note the connotations of the term accidental with contingency, anomaly, and as an antonym of essential (and so relating to deviations away from essences).

<sup>109</sup> One can only assume that it was “hitherto supposed” by the likes of Hatschek, as in this particular section Willey includes many figures taken from Hatschek’s monograph, which was also the most recent comprehensive work on the embryology of *Amphioxus* before Willey’s book (Willey, 1894: 107-108).



formation of the different cleavage forms existing throughout the animal kingdom. There was the potential, therefore, for Wilson's experimental manipulations to provide an insight into key developmental mechanisms at early stages of development, as well as ascertaining their morphological and evolutionary significance. The value of results gained from experimentation using *Amphioxus* was therefore amplified owing to its natural properties.

The fourth cleavage stage also exhibited the three main types of cleavage form, and Wilson indicated that there were more transitional forms between them than in the third cleavage stage. He now spoke of "numerous transitional forms" rather than "Various transitional forms" (Wilson, 1893a: 582). Indeed, in the discussion of the radial forms exhibited, he admitted that the form he depicted only denoted two samples which corresponded in "the nearest approach to a true radial type" (Wilson, 1893a: 583). However, in this stage most forms exhibited bilateral cleavage (*ibid.*). Within the bilateral form he conceived of two varieties; both involving the equal division of the upper tier of cells, and the unequal division of the lower tier of cells. The difference between the two varieties was where two of the secondary macromeres (C2 and D2) were formed. Wilson observed that the less typical "form closely approximates to the cleavage of the tunicate *Clavelina*" (*ibid.*). Hence, as for the other cleavage-forms depicted in **Figure 18**, one of the variety of cleavage forms exhibited by *Amphioxus* was compared to that of another organism in the animal kingdom, even if the forms only approximated and did not completely correspond (Wilson, 1893a: 584).

Wilson also compared the spiral form found in variants of *Amphioxus* to fixed types of cleavage form in other organisms, in this case annelids. However, Wilson observed of the spiral form that the "pure form is very rare" (*ibid.*), and that in those spiral forms he was unable to track the origin of blastomeres and their changing relationships, meaning that his depictions of them were "hypothetical" (*ibid.*).

Beyond this cleavage stage Wilson no longer recorded or detailed the variation in cleavage form, "since they are even more numerous than those of the earlier stages" (*ibid.*). He did observe that from the sixteen-cell stage to the two-hundred-and-fifty-six-cell stage, the bilaterality in the upper half of the embryo

disappears. Moving away from an orderly division of planes, the “division in the micromeres comes to conform to no general law and appear to be determined by individual mechanical conditions of environment” (Wilson, 1893a: 585).

#### **4.4.2. ‘Induced’ embryos and assumptions about normality**

Wilson found that when he shook apart the blastomeres at the two-cell stage, the isolated blastomere obtained underwent “a cleavage identical with, or approximating to, that of a normal embryo” (Wilson, 1893a: 587). Furthermore, though it would be of roughly half the size of the non-manipulated organisms, it would lead to the production of a larva much like normal, albeit with an abnormally positioned tail. For the blastomeres isolated by shaking at the four-cell stage, such a fate was also possible, but less likely. They “may undergo a cleavage nearly or quite identical with that of a normal ovum, but often varies more or less widely from it.” Wilson found only one example of a larva being produced in this case, albeit one with no mouth or anus, and therefore unviable. If, however, the shaking of the four-cell stage produced two two-cell forms, it “may give rise to two perfect, half-sized dwarfs” (Wilson, 1893a: 588).

When he examined the results of his manipulations on embryos at the eight-cell stage, Wilson observed development to the gastrula stage on occasion, but attributed this to incomplete separation of blastomeres. The isolated blastomeres underwent cleavage “approaching that of a complete ovum but *never identical with it*” [italics in original]. But these forms only rarely reached the blastula stage, and never the gastrula stage. Of the ones which reached the blastula stage, they seemed to form *parts* of the normal gastrula. This suggested to Wilson “the view that the corresponding blastomeres have undergone a partial development – *i.e.*, as if they still formed part of a complete normal embryo” [italics in original]. Beyond this point, although some developed cilia and moved like normal non-manipulated forms, they did not progress beyond this point and died within a few days (Wilson, 1893a: 589). In modern terms, as development proceeded they progressively lost *potency*.

As with the cleavage-forms for the ‘natural’, uninduced embryos, Wilson did not go into detail about the fates of the embryos shaken apart at the sixteen-cell stage, though he noted the “immense variety of forms” (Wilson, 1893a: 590).

Like Driesch's work with sea urchins, once again the eight-cell stage seemed to be the ceiling for regulative capacity. The terms 'regulative' or 'regulatory' development – as opposed to 'mosaic' development – were not used by Wilson, and there was no alternative term used in the results or discussion sections of the paper, presumably because of the novelty of the perspective. Importantly, however, Wilson observed that "The isolated blastomeres undergo a cleavage that approximates more or less nearly to that of a normal ovum, but *the extent of divergence is nearly proportional to the age of the initial form*" (ibid.). I take age to mean the stage at which the development was at when the blastomeres were separated. In other words, the earlier in development the blastomeres were isolated, the more likely it was that the 'normal' course was pursued, and the 'normal' end result obtained, size being the only difference. Regulative capacity diminished with developmental time, and the clock started ticking when the egg was fertilised. It could not be rewound by reversion to a one-cell state by mechanical separation, or restoration of the original mechanical conditions of one cell not bounded by others.

Wilson concluded that mechanical conditions alone could not account for the cleavage-forms. If they could, blastomeres shaken apart at stages such as the sixteen-cell stage should exhibit the same regenerative power (the ability of a separated part to reconstitute the whole, which underpinned the regulatory theory) as ones shaken apart at the two-cell stage. This would have been because they faced the same mechanical conditions, in the sense of being isolated cells not exposed to different interactions from neighbouring and surrounding cells, regardless of the nature of the eventual processes triggered by the change in mechanical conditions and interactions between cells being altered or lost (Wilson, 1893a: 607-608).

Wilson did not find that the regenerative power (a term Wilson did use) at later stages was the same as for earlier stages. He discovered that the separated blastomeres from a two-cell embryo "may give rise to a half-sized dwarf larva exactly agreeing, except in size, with the normal larva up to the period when the first gill-slit is formed" (Wilson, 1893a: 588). However, for separations at the sixteen-cell stage, "isolated blastomeres continue to divide for some time, but as far as observed always give rise merely to flattened plates or shapeless

masses of cells” (Wilson, 1893a: 590). Other specimens which developed after manipulation at the eight-cell stage produced either parts or severely deformed organisms which did not survive past a certain stage of development such as the blastula (Wilson, 1893a: 589). These ultimately non-viable forms were for Wilson evidence of *abnormal* development.

Such findings led Wilson to the conclusion that “the unity of the normal embryo is not caused by a mere juxtaposition of the cells. They indicate that this unity is not mechanical but physiological, and point toward the conclusion that there must be a structural continuity from cell to cell that is the medium of coordination, and that is broken by mechanical displacements of the blastomeres” (Wilson, 1893a: 595). If it were purely mechanical, then an isolated blastomere shook apart from its fellow cells at any stage of development would be able to develop in such a way as to reconstitute a new whole organism, but this was not the case.

Wilson did not specify what this ‘structural continuity’ might be. If it was some form of hereditary substance it surely could not be the sort of static, morphological mosaic-work of hereditary particles envisaged by Roux and Weismann. That would not account for the phenomena Wilson was attempting to explain here.

#### **4.5. Conclusion – ‘Normal development’ as an input and output of experimental work**

The way in which I have presented Wilson’s work from the late-1880s to the mid-1890s highlights his transition from work belonging to the tradition of evolutionary morphology to experimental embryology. His previous work, with *Lumbricus* in particular, generated questions about the origins, and thus the determination, of later structures in embryonic development from earlier parts. This led to his adoption of cell-lineage research, which then threw up questions of its own relating to the causes and significance of the phenomena of cleavage and the variation he observed. It is intriguing to observe many of the facets Rheinberger described concerning the progress of experimental systems in what was, strictly speaking, non-experimental work. Initial resistances and

problems become epistemic objects in themselves. In Wilson's case, these epistemic objects led him to devise an early experimental system of his own, involving *Amphioxus* and some basic equipment and methods. Wilson's interest in the variation in early embryonic development was reflected in the variation found in the normal development that he produced as a technical condition as part of his experimental system.

The experimental design of Wilson's experiment called for the establishment of a 'normal development', against which the results of the experimental manipulation could be compared. 'Normal development' constituted both an input and an output of the *Amphioxus* experiment. It was an input, because some idea of what constituted 'normal development' needed to be in place for the experiment to occur at all. Reading the work of Kovalevsky, Willey and Hatschek, and studying the (abstracted) accounts and diagrams of the development of *Amphioxus* will have formed a significant part of that. During the course of his work, Wilson's own processes of observation, selection, exclusion, comparison, integration and recording, were guided by this input (a cultivated preconception) of what the 'normal development' of *Amphioxus* consisted.

As we have seen, the result of this re-calibration of expectations (the output) was a 'normal development' which included considerable variation, which was considered by Wilson to be 'natural'. For example, all three main cleavage-forms exhibited by *Amphioxus* in the early stages of development were included as part of the normal development. The effects of the experimental manipulation were measured by comparing the observed variation in the manipulated samples to the 'natural' variation established by the control samples. Wilson also set out to understand the significance of variation, and to explain its generation. Variation is therefore central to understanding the background, rationale, method and explanations in Wilson's experiment and paper. It will therefore be examined, in progressively more conceptual ways, in the next two chapters.

I will now try to make sense of some of the findings of this chapter. I believe that it is helpful to consider that normal development performed an active *heuristic* function for Wilson. A heuristic procedure can be defined (Wimsatt, 2007) as a rule or rules employed implicitly and/or explicitly, with the aim of simplifying the

collection and management of data.<sup>110</sup> Three key properties of heuristic procedures have been identified (Wimsatt, 2007: 68-69). A heuristic does not guarantee a correct solution, or even a solution at all. If it does produce a solution, however, it does so in less time and with less effort than an algorithmic procedure. Finally, a heuristic produces errors which are systematic, thus allowing the biasing effect (and working backwards, the existence) of the heuristic to be identified (ibid.). Using the notion of heuristics as a theoretical lens allows us to do two things. Firstly, to give us a way to analyse the decisions Wilson made, why he made them, and what the effects of them were. Secondly, it neatly distinguishes the practice of Wilson from that of Driesch and Roux, and therefore gives us a possible explanation for the differences that arise between Wilson's theorising and the theoretical frameworks of the other two men.

Considering the role of heuristic procedures in the establishment of normal development, we may consider the following observations. Wilson did not collect and incorporate every item of data about the samples he observed. He did not specify exhaustive rules for the selection (or discarding) of samples, for deciding what aspects of the ones which were selected were to be used, or for integrating these into an overall account of the normal development. There was no algorithm which simply needed to be applied to move from the preserved samples in the laboratory to the verbal and pictorial representations on the page. Instead, Wilson used his own rules to sort out the 'normal' from the 'abnormal', to select what was to be observed from the totality of observable properties, and to reduce the ranges of variation exhibited at each stage of development to the ranges expressed in the paper. Normal development for Wilson performed a heuristic function in a way that it couldn't for Driesch, who had to rely on the passive images on a page to compare the effects of his experimental intervention.<sup>111</sup> For Roux, any heuristic function of normal

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<sup>110</sup> Nickles emphasises the role of heuristics as "problem-solving methods", which is compatible with my definition, if one take a broad view of 'problem' (Nickles, 1987: 106).

<sup>111</sup> The insight of the artist Alexander Ecker cited by Wilhelm His in support of three-dimensional modelling of embryos is relevant to understanding the significance of this difference between Driesch and Wilson. Ecker held that "the pictures in the memory that have once made their way through the hand stick much more firmly in the head" (Ecker, 1886, as cited in Hopwood, 1999: 483). Although Wilson was engaged in two-dimensional representation rather than three-dimensional, Hopwood observes that according to this view, "If drawings were good, then drawing was held to be better" for appreciating the form of the embryo depicted (ibid.).

development was external to (perhaps even transcendent of) his experimental set-ups.

Wilson's establishment of a normal development which was an *abstraction from observed variation* was the aim of this heuristic activity, the end-result of calibrated observation. Such abstractions can themselves be considered to be heuristic tools, insofar as they are considered "as baselines to organize and structure our perceptions of the data in productive ways" (Wimsatt, 2007: 152). Given the function of normal development within Wilson's experimental set-up, this was exactly its role. One can say that, picking up again on the insight of Michel and Moore, the determination of a normal development had, through the process of its own generation, become intuitive through the development of empirically-mediated heuristics.

An analysis of normal development, what it is, what role it plays, how we can characterise its production and reproduction and how variable it is, will be undertaken in the following chapters. Central to that task is how normal development was, and is, produced and used to provide a means to manage, describe and explain variation.

## **Chapter 5 – Variation and conceptualisations of development**

### **5.1. Introduction**

In the previous chapter, I outlined how normal development was generated by Wilson's work with *Amphioxus*. Wilson's normal development was generated by him as part of his experiment (rather than relying on a table produced by someone else), and included a wide range of variation in early embryonic development. In this chapter, I assess the role and significance of variation in that work. The key thrust of this chapter will be to identify the relations between the use and explanation of variation and other key aspects of biological thought and practice. These include questions concerning differentiation and the determination of development.

I introduce variation as a theme of the chapter by detailing some of the conceptual changes in the biological sciences surrounding variation up to and including the 1880s and 1890s. Crucially, as well as variation becoming a major focus of biological research in the latter half of the nineteenth-century, how it related to other concepts in flux such as heredity and development was also shifting. The challenge for scientists in this period was to work out new ways to provide coherent accounts of these three problem areas (what these concepts actually refer to, how they are caused, and what effect they have on other questions) and the links between them. Variation became for Wilson an instrument as well as the very phenomenon he was trying to explain and take account of, as it was part of the experiments that sought to provide the empirical data for such explanations.

Moving on from this background, I explore the theoretical developments Wilson drew from the *Amphioxus* work, from the 1893 paper to 1896's *The Cell in Development and Inheritance*. This will illustrate the deep connections and reciprocal relations and accommodations between variation, normal development, and various theoretical and methodological stances. I detail in particular how Wilson tried to explain the variation in cleavage-forms that he found and how he interpreted his experimental results to provide a modified account of the mosaic theory of development. I chart how he tried to make



sense of the seemingly contradictory and confusing results that had been thrown up by his and his peers' experimental work.

The latter issue demands that a number of characteristics associated with particular conceptions of development, which were either identified at the time or can be distinguished analytically, should be considered. The parameters I use to capture these conceptions of development are: mode of differentiation, type of cause, source of causation, mode of transmission, type of cell division and metaphor of cell relations. An analysis such as this is not without its drawbacks. The terms I use in this analysis do not (and did not) have universally agreed meanings. Furthermore, though I consider the characteristics separately, they cannot be understood without reference to their context and relations with the other characteristics, and to explanations that use them. With this in mind, after separating them I have attempted to bring them back together, and in doing so reveal their inter-relations.

The analysis will show that seemingly logically related concepts that attempt to explain development (including variation in development, one aspect of this being differentiation), such as the link in the mosaic theory between the 'atomistic' mode of transmission and the 'inherited' type of causation, are only contingently associated. This is demonstrated by a comparison of Wilson's ideas to those of Roux and Driesch. Given the different ways in which Roux and Driesch conducted their experimental work compared to Wilson, this provides another key connection between normal development (which underpinned and shaped Wilson's research in a different way to the work of the other men) and the changing conceptions and use of variation in biological research. The connection is that normal development is a way of managing the variation in experimental set-ups. This theme will then be developed in chapter 6, when the exact nature of the relationship between normal development and variation is analysed.

## **5.2. Variation – Introduction and Historical Background**

As we saw in chapter 3, Wilson's morphological work was made difficult by the variation in early development which was exhibited to a greater or lesser extent

by the organisms he worked with. How could he unequivocally trace the origin of a particular germ-layer for a particular organism, when embryos differed so much at particular stages, particularly in the mode of cleavage? However, as we have seen in the preceding chapters, from being a factor which confounded Wilson, variation became both the object of and a tool for research. Variation in early embryonic development became a source of questions, which could also be used to tackle related questions concerning the determination of development.

How the variation exhibited within and between organisms was treated underwent a shift in the late nineteenth-century. One aspect of this was the transformation in its relationship to the concept of heredity.<sup>112</sup> Previously, the existence of both variation and heredity, while acknowledged (they were vital elements of Darwin's theory of evolution), was deemed to be problematic. How could offspring vary from their parents, and how could variation be maintained and generated given the existence of heredity? Darwin himself conceived of variation as resulting from external interference affecting the development of particular organisms, either directly, or indirectly by affecting the reproductive system (Bowler, 2005: 10). Such variations could then become part of the inheritance transmitted to offspring (*ibid.*). Additionally, Darwin observed that variability itself could be transmitted to future generations from exposure of populations or species to varied conditions (Hodge and Radick, 2003: 5). For Darwin, variations were not usually directed in any sense, as the later orthogenesisists were to insist. They claimed that the direction of variation was directed by the development of the organism, such developmental forces thus driving evolution, which led some of them to deny the role of natural selection and adaptation altogether (Bowler, 2005: 17). For Darwin, variation (as a source of difference even given "identical external conditions"), and heredity (as conservative given those same circumstances) were "capricious processes that did not necessarily lead to adaptation", though of course, given other conditions, they could (Müller-Wille and Rheinberger, 2012: 74-75).

August Weismann's theory of heredity and development supposedly led to the analytical separation of the processes of ontogeny and phylogeny, a

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<sup>112</sup> Heredity was also a concept in flux during this period (Müller-Wille and Rheinberger, 2012: 76-94).

reformulation of the relations between variation and heredity and between variation and development. Weismannism divided variations into those which were heritable and non-heritable. Those variations which directly affected the development of an organism through changes in somatic cells which occurred after their sequestration from the germ-line (reproductive) cells would not be heritable. Weismannism made use of the hypothesised 'idioplasm', the hereditary substance thought to contain a hierarchy of materials responsible for the determinate progressive differentiation exhibited in development. Rather than being generated by a plurality of processes (as proposed by scientists following Darwin), in Weismannism heritable variation was generated by changes to the idioplasm contained in the germ-line cells. The scope for the generation of heritable variation was considerably narrowed. At the same time, heredity and variation were now understood to be complementary concepts. Weismannism's 'harder' heredity accounted for the maintenance of variation, and his hypothesis of changes to the idioplasm (the inherited substance) accounted for the generation of variation (Churchill, 1987: 362). However, like Darwin, but not Weismannism as it came to be understood, for most of his career Weismann accepted that external circumstances were, in the final analysis, the means by which changes to the hereditary material in germ-line cells were effected, generating variation (Winther, 2001).

Peter Bowler attributes the breakdown of the "developmental" view of variation, which Darwin himself subscribed to in many respects, to a combination of factors. These included the rejection of the inheritance of acquired characteristics (and therefore the delinking of heredity and development) and the reconceptualization of variation as a property of populations rather than individuals.<sup>113</sup> A consequence was the reformulation of variation and heredity to be understood as complementary rather than antagonistic. 'Hard' Weismannian heredity (as opposed to a 'softer' heredity more intertwined with development) provided an explanation of how variation, once generated, was preserved. Finally, the view that variation was generated by "additions to development controlled by the existing process of development", Haeckelian recapitulationism, was rejected (Bowler, 2005: 11 and 17). Rather than the

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<sup>113</sup> Though, for Weismann, it was only the inheritance of acquired somatic characters that was ruled out – acquired changes to the germ-plasm could be, and were, inherited (Winther, 2001).

embryonic development of ancestors being preserved (but with the timing of various stages altered) with novelties added to the end of the developmental process (terminal addition), novelties and variants could manifest at any stage of development. This undermined the usefulness of studying the embryonic development of extant organisms to make inferences concerning the nature of ancestors. This had implications not only for phylogenetic research (including the debates over the rival annelid and ascidian theories of vertebrate origins), but also for what causes were relevant and therefore worth investigating in ontogenetic – i.e. embryological – research as well.

In Wilson's time, a variety of views concerning all these factors existed, indicating that the 1880s and 1890s in particular was an era of flux and contestation about how variation and heredity was seen and treated. At the point we examine his career Wilson did not conceive of heredity in the Weismannian sense, though he was aware of it. In fact he specifically rejected it. He was to for years to come, because the hypothesis of a qualitative division of the idioplasm did not in his view accord with the cytological, morphological or embryological evidence (Wilson, 1896: 306-311).

The 1880s and 1890s saw the advent of experimental investigation in embryology. Much of this work (particularly by the key actors examined in this chapter) centred on early embryogenesis, and took advantage of a picture of the cell which took shape in the second half of the nineteenth-century as entities which "possessed the capacity to escape the organism, to vary independently and to start a new life of their own under favourable conditions" (Müller-Wille, 2010: 231). Indeed, it was the individuality of the cell and its centrality to the problems of development and heredity that directed Wilson towards its study (Maienschein, 1990a: 369).

In this late-nineteenth-century experimental work, rather than merely taking account of variation and sorting it, the generation of variation became something to explain. The programmatic declarations of Wilhelm Roux, which justified and provoked such experimental work, helped to engender this. He made it clear that he believed that the development (and evolution) of organismal forms could be analysed into "the two components of variation and inheritance" which also needed to be explained, requiring analysis and

decomposition into their causally-efficacious components (Nyhart, 1995: 293-294).<sup>114</sup>

Experiment was not the only way in which this investigation could proceed, but Roux believed it to be the surest way. For Roux, some inferences as to the causes of variation could be made using naturally-occurring (i.e. not artificially-induced) variations and abnormalities (Nyhart, 1995: 294). But the generation of variation was understood to arise from a constellation of factors known and unknown. In Roux's programme, only a causal-analytical series of experiments which kept all factors (produced by analysis of a wider system into its components) except for one constant could identify the relevant factor or factors responsible for a particular phenomenon. In one such experiment, one factor would be varied to ascertain the effect of its variance upon organismal form and variation. This would provide an indication of the specificity of the varied factor in effecting changes to the organism, and also allow one to make judgements concerning the stability (against a range of changes to the varied factor) of non-varied factors that one might regard as causally relevant.

To conduct an experiment of this kind, an experimenter needs to be able to control the plethora of variables that exist inside and outside an experimental object, such as an organism. In the case of Wilson's experiment, though the control of variables was far from the rigour that would be expected in modern laboratories, the variable he wished to vary, and did, was the mechanical conditions impinging on the blastomeres in the early embryo. To measure the effect of this, he needed to not only observe the variation exhibited between forms that did and did not undergo this treatment, but also the variation *within* treatments. Following this, he needed to use his results to draw conclusions concerning how the observed variation was generated, and spell out the consequences of this for the process of organismal development as a whole.

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<sup>114</sup> William Bateson likewise wanted to explain the generation of variation, partly because of its intrinsic interest, partly to contribute towards explanations of evolutionary change. Like Roux and Wilson, Bateson rejected many of the methodological aspects of evolutionary morphology/embryology without abandoning many of the questions raised by that programme (Hall, 2005).

### 5.3. Consequences of the *Amphioxus* experiment

#### 5.3.1. Explaining cleavage forms and their significance

In a discussion on the different types of cleavage manifested in *Amphioxus*, Wilson detailed the other organisms in which those types of cleavage were found (Wilson, 1893a: 600). For example, he observed that in annelids, “the cleavage is strictly spiral up to the 32-celled stage, after which it becomes bilateral”, whereas in a nemertean (ribbon worm) species, the cleavage is “perfectly radial up to the 8-celled stage, and then assumes the spiral form”, while for “gasteropods the cleavage is at first strictly spiral; in cephalopods it is perfectly bilateral from the beginning” (Wilson, 1893a: 601).

He concluded from this that the cleavage forms or types “are obviously devoid of any great phyletic importance” (ibid.).<sup>115</sup> Interestingly, this was not justified on the basis that there seemed to be no clear relationship between community of descent and what we might call ‘community of cleavage form’. Rather, Wilson supported this statement with evidence of organisms (including *Amphioxus*) exhibiting different cleavage-forms at different stages of development (ibid.). Wilson turned to questions of developmental determination, as he saw that the cleavage-forms were “very important for an analysis of the factors that determine the form of cell-division” (ibid.).

Wilson was therefore moved by the unhelpfulness of his results for phylogenetic work to a greater focus on questions relating to developmental mechanics. Wilson presented two possible causes of the “form of cell-division” – mechanical conditions and an inherited character. These were presented as the only possibilities, with no mention of possible alternatives. Contradictory evidence was presented. On the one hand it was demonstrated that mechanical conditions alone could not account for the cleavage-forms. The power of regeneration (which as we saw in the previous chapter, Wilson associated with

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<sup>115</sup> Evidence that Wilson was still concerned with (and maintained some optimism about) such questions surfaces in remarks made in a letter to Hans Driesch in July 1894, where he tells Driesch that “I still think you are too nihilistic regarding [the] question of descent & of general morphology” (Wilson, 1894a).

mechanical causation) therefore existed, but became less powerful and effective with every cell division.<sup>116</sup>

Variation in cleavage-forms in *Amphioxus* also undermined the idea that the forms were inherited, as that would imply a constancy of cleavage-forms independent of external conditions, which was not observed (Wilson, 1893a: 600-601). Wilson was therefore denied an unequivocal mechanical or inheritance-based explanation for the variation in cleavage forms. Reflecting on this, he observed that “the variable cleavage of *Amphioxus* is a very interesting case; for we here observe, as it were, a conflict between an hereditary tendency not yet firmly established, and mechanical conditions that are, in a measure, opposed to it” (Wilson, 1893a: 603).

The use of the term “mechanical” by Wilson to describe an external factor relevant for the development of an organism requires some clarification. Driesch and Roux used the term “in the Kantian sense of law-bound causation” (Nyhart, 1995: 295). However, Wilson used the term in a sense which to our modern ears is far more literal – the effect of physical forces impinging on objects. This radical difference does not seem to be a mere case of a concept which is in a normal state of ambiguity and flux. As Lynn K. Nyhart elegantly observes, in the 1890s, “Researchers used the term in a bewildering variety of ways, and their discussions suggest the penumbra of confusion it wore at the time” (ibid.). In Wilson’s case, it concerned the physical interactions between a cell and its surroundings, including neighbouring cells (Wilson, 1893a: 607-608). He made use of Gottfried Berthold’s “principle of minimal surfaces”, to which he had been directed by Hans Driesch. This principle emphasised the reduction of surface area as determining the direction of the division planes of dividing cells (Besson and Dumais, 2014). Wilson used it to account for the production of spiral forms from radial ones as “an effect of mutual pressure among the blastomeres” (Wilson, 1893a: 601).

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<sup>116</sup> Wilson himself rejected the use of the term “regeneration” to describe this: “This certainly is not ‘regeneration’ – at least nothing is regenerated – but I believe nevertheless that it is one extreme of a series of which true regeneration forms the other” (Wilson, 1892b). As Wilson did not provide an alternative term to ‘regeneration’, for want of a more appropriate term I have used the term here, with this caveat.

The hereditary tendency he referred to was “a gradual shifting backwards in the ontogeny of the adult bilaterality, which thus became projected, as it were, upon the cleavage-stages”, a recapitulation (ibid.). He noted that this tendency “is often disturbed by displacements of the blastomeres”, which helped to produce the other cleavage-forms, and accounted for the independence of the variation in normal development in early embryonic development from the less variable normal development exhibited in adult *Amphioxus* (ibid.). After finding difficulties with the Haeckelian framework (of using *early* development as a means to gauge evolutionary relationships), it is curious to see this kind of Haeckelian process (of adult stages being moved to an earlier stage of development) being invoked. Crucially, Wilson had found that the normal or abnormal did not map onto the ancestral or environmentally-induced.

The notion of the shifting of stages of development to earlier or later parts of ontogeny (heterochrony) became a key tool for Wilson in his attempts to grapple with the seeming contradiction between mosaic and regulative modes of development.

### **5.3.2. Differentiation – discussion of the mosaic theory and its discontents**

Towards the end of the *Amphioxus* paper, Wilson moved towards discussing the theory of mosaic development. Mosaic development also formed the topic of his 1893 lecture at Woods Hole. Wilson advanced a modified version of the mosaic theory of development, radically different from those versions advanced by Roux and Weismann. Wilson's strategy in this section of the paper was to state the assumptions underpinning the Roux-Weismann version of mosaic theory, argue why these assumptions were untenable, and then engage with the opposing ideas of Driesch and Oskar Hertwig. At one point it seems as if Wilson was ready to endorse these ideas, based on a different interpretation of the idioplasm in which it divides quantitatively and is dynamically transformed physiologically, rather than dividing qualitatively as in the Roux-Weismann theory.

I have previously noted how crucial the experiments conducted – and interesting phenomena generated – by his friend Hans Driesch (Driesch, 1892 [1974]) were for Wilson's *Amphioxus* work. Wilson acknowledged the



“wonderful impetus to the study of all these question [sic]” provided by Driesch (Wilson, 1893b). It was from Driesch that Wilson borrowed (though not wholesale) the key technique to separate the blastomeres (cells formed by the cleavage of the fertilised egg) of the early embryo. Driesch was at that time attempting to further the mechanistic programme of embryology, driven in particular by Roux. Both Roux and Driesch wanted to establish causal-mechanical explanations of differentiation and the production of developmental form. Wilson’s interest in such a project will have been piqued by the results obtained, and conclusions drawn, by Driesch – which contradicted Roux’s theory of organ-forming germ areas, also known as the mosaic theory.

The central ideas of Roux were derived from his experimental work with the frog *Rana esculenta*. In his 1888 paper detailing these experiments and the conclusions he drew from them, Roux observed that “we can infer from these results that each of the two first blastomeres is able to develop independently of the other and therefore does under normal circumstances” (Roux, [1888] 1974: 25). He concluded from this “that developmental processes may not be considered a result of the interaction of all parts...We have instead of such differentiating interactions, the self-differentiation of the first blastomeres and of the complex of their derivatives into a definite part of the embryo” (Roux, [1888] 1974: 25-26). Thus, the key element of Roux’s mosaic theory was that differentiation occurred through processes internal to the blastomeres, and was produced by the division of blastomeres into separate lineages of cells independent of each other. Cell division was therefore of prime importance for the Roux-Weismann theory, but only secondary for Driesch and Hertwig. For Driesch and Hertwig the stress was on external causes of differentiation: the modification of the idioplasm effected by external factors, which were thought to be mechanical or chemical conditions surrounding the cell or cells. However, Wilson believed that Driesch and Hertwig’s rejection of the mosaic theory was “one-sided and premature” (Wilson, 1893a: 612).

Two separate theories thus purported to explain development, and to provide a framework for embryological investigation. Wilson was inspired by these dramatic and surprising results of experimental interventions in the developmental process (Maienschein, 1991a: 53). He saw his experiments as a

way of adding more empirical data to contribute towards a *reconciliation* of both theories, recognising that both said something meaningful about development, but that neither alone was able to account for the multifarious phenomena that embryologists were encountering. Wilson had the benefit of studying the early development of two organisms, *Nereis* and *Amphioxus*, which displayed very different characteristics in early development. He made this clear in a letter to Driesch. Justifying the promulgation of his “purely provisional hypothesis”, Wilson related to Driesch that he had “been forced to do this by the necessity of bringing under a common point of view my work on Nereis & that on Amphioxus – i.e. a highly specialized and a slightly specialized form” [Wilson’s underlining] (Wilson, 1893b). On this basis, Wilson argued that rather than reject the mosaic theory *tout court*, one must take account of at what point in embryogenesis mosaic development starts to hold, and the mosaic theory therefore becomes applicable. In some organisms, the mosaic theory would hold from a later stage of development, in others mosaicism would be apparent at much earlier stages. Wilson stated that, as a general rule, “*the ontogeny assumes more and more of the character of a mosaic-work as it goes forwards*” [italics in original] (Wilson, 1893a: 610). So there was no confusing mess of contradictory evidence from different organisms, nor was there universal applicability of the theories of either Roux and Weismann or Driesch and Hertwig.<sup>117</sup> Instead, these theories could be seen as explanations of different aspects of the same process – one that Wilson then endeavoured to explain.

If the transition from regulatory development to mosaic development was simply a question of the progression of development, and the differences in the modes of development between different organisms was merely one of the different time-frames in which this process started and reached its various stages, how could these differences be explained? Wilson concluded that “the difference depends on a difference of organization which, in turn, ultimately depends on the nature of the original germ plasm.” (Wilson, 1893a: 611).

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<sup>117</sup> Oppenheimer made the point, that is essential to bear in mind, that in these early years in the work of all the biologists concerned, the dogmatic schemes of later years had not yet appeared, and that Roux placed “strong emphasis on the interrelationship of parts” and Driesch exhibited a “remarkable materialistic analysis” (Oppenheimer, 1967: 78). This does not underplay the real differences between Roux and Driesch before they hardened, but simply recognises that it was simply two different models of development that were at stake at this point, even if they were not free from wider implications.

### **5.3.3. The further development of Wilson's theoretical perspective**

The next steps in Wilson's argument led him further towards the significant conclusion that differences in the type of development exhibited in two different organisms must be a result "of an original difference in the germ-plasm in the two ova" (Wilson, 1893a: 614). Furthermore, "The entire series of events [in ontogeny] is primarily determined by the organization of the undivided ovum that forms its first term, and, as such, conditions every succeeding term. The morphological value of the individual blastomere at any particular stage is the product of two factors, one of which (the embryonic environment) is external, while the other (the nature of the idioplasm) is internal" (ibid.). He noted that "in cleavage-forms that are identical up to a comparatively late stage, blastomeres may exactly correspond in position, mode of origin, and embryonic environment, and yet be of entirely different morphological value; and it is in this sense that we may regard cleavage-forms as controlled by a definite hereditary element apart from purely mechanical conditions" (ibid.).

To see how Wilson reached such conclusions, I have identified the key steps in his argument:

1. Ontogeny is "a connected series of interactions between the blastomeres in which each step conditions that which succeeds" (Wilson, 1893a: 613).
2. Therefore "The character of the whole series depends on the first step, and this in turn upon the constitution of the original ovum" (ibid.).
3. The mosaic character arises from an inequality in the division at a particular stage, "and this conditions the entire subsequent development through the peculiar inter-relations established by it" (ibid.).
4. "If such inequalities exist they must be determined by a definite cause" (ibid.) – this is supposed to be in the inequalities in the undivided egg, which "must in the last analysis be sought in the constitution of the original germ-plasm" (ibid.).

I have presented the argument in this way, because rather than representing clear-cut premises and conclusions, the argument became increasingly strong in its claims by degree, starting from a fairly weak statement that could brook no disagreement, and proceeding almost imperceptibly towards quite a

remarkable concluding statement. The implicit assumptions held by Wilson led him to follow a thread of causation further and further back in development, until even the regulative development of Driesch could be explained by resort to the germ-plasm in the ovum. The only difference between an organism exhibiting mosaic development and one exhibiting regulative development was the degree to which the inequalities established in the cells as a result of the activities of the germ-plasm were more or less well-established at certain stages of development. If sufficient well-compartmentalised inequalities were established at a sufficiently early stage then the embryologist would see the sort of development associated with *Nereis*. If this process took longer, development would be more like *Amphioxus* or *Echinus*. At no point did Wilson state that any one point of development completely determined the next and future stages. He used words like 'conditions' and 'depends', but then, as he followed one thread of causation, turned these into 'determines' and 'is determined by'. It was this slip that allowed the thread of causation to be traced back to the "constitution of the original germ-plasm" (ibid.). In Woodwardian terms, it seems that Wilson, having identified causes that were specific or stable *enough* to form a key part ('conditions' and 'depends') of a causal account for the phenomena he was trying to explain, then moved to judging them sufficiently stable or specific to be the predominant or only significant causes that needed to be invoked ('determines').

However, it must be stressed that Wilson still had a *physiological* interpretation of the idioplasm, and not a morphological one that would posit a fixed, localised hereditary material. For Wilson, the idioplasm changed over the course of development in a dynamic and responsive way, and was not merely divided into qualitatively distinct parcels to be passed down to daughter-cells. By this interpretation of the idioplasm, Wilson was able to explain differentiation and "physiological specialization" without invoking the qualitative division advocated by Roux, which he believed his research had discredited (Wilson, 1893b).<sup>118</sup> This is important, and in one respect places him more in the Driesch-Hertwig camp. However, while Driesch and Hertwig would locate the original basis for changes in the idioplasm not exclusively internally, with perhaps significant

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<sup>118</sup> Wilson was careful not to say too much about the idioplasm however. He admitted to "an intentional vagueness regarding the seat of the idioplasm" (Wilson, 1895c).

external influence, Wilson even at this early stage of his career saw the original conditions in the egg as responsible for the conditions which would modify the idioplasm in the course of development. Wilson's physiological idioplasm just added a few extra stages in the causal chain originating in the germ-plasm.

On the relation of the organism to the environment, or the internal sources of causation to external ones, *formally* Wilson advocated equivalence. But he exhibited greater concern for the internal rather than the external. For example, in a private letter to Driesch, he revealed that "the direction of my work has led me to give more thought to the inner factors...of cleavage" [Wilson's underlining] (*ibid.*). This was a consequence of the thread he chose to follow, and the fact that external conditions could be controlled in a way that was not possible for internal ones. This meant that an asymmetry was established in terms of which potential causes were assigned to the 'difference-making' category and which were assigned to the 'background conditions' category.

It was not just the research paper of 1893 that signalled a shift in Wilson's thought and work, but also his summer lecture at Woods Hole that same year. The paper was an indicator of what Wilson felt confident about declaring in the more austere forum of the journal, but the lecture perhaps betrayed the general direction of his thought more clearly.

The same criticisms that Wilson had of the mosaic theory in the 1893 paper were replicated here, though he once again refused to go over to the Driesch-Hertwig camp. In fact, he suggested that their choice of organism – the sea urchin – may have led them astray. That said, *Amphioxus* demonstrates comparable plasticity to the sea urchin, though against this Wilson also had experience of the more mosaic-style development of *Nereis*.

On the relation of the cell to the organism, Wilson accepted the claims of both camps, that on the one hand "the prospective value of a cell may be a function of its location" (Wilson, 1894b: 12) and on the other, that there exists "in some measure, an independent power of self-determination due to its inherent specific structure" (*ibid.*). These he integrated by emphasising the physiological specialisation of the cell, rather than the parcelling out of specific substances or structures to successor cells. This was contrary to the position of Roux and

Weismann. Whether development was seen as more regulative or more mosaic-like was a function of the timing of the physiological specialisation – before or after cell-division (Wilson, 1894b: 12-13).

The 1894 lecture at Woods Hole revealed some fascinating insights into Wilson's thinking on the relation of the organism to the environment. Speaking of the work conducted on the Pluteus-stage of sea urchin development, after accounting for the formation of the arms he pointed out that "In this case the necessary condition of development is a certain internal stimulus... This stimulus, itself, however, is directly dependent on external conditions (the chemical environment), and hence the formation of the arms is determined by both internal and external conditions" (Wilson, 1895b: 117).

This led Wilson toward two conclusions. One, that "it enables us in a measure to comprehend how a single property of the germ-plasm may involve a whole train or cluster of events in development..., each differentiation tending to become the parent of new differentiations. This conception does not in any manner set aside the necessity of assuming, for each species of animal, a specifically organized germ-plasm, nor does it conflict with the fact that the egg-substance may even show a certain amount of regional differentiation before development begins". Rather than a remodelled preformationism, Wilson considered this 'germ-plasm as the root of all developmental events' perspective to be "a rational conception of epigenesis" (Wilson, 1895b: 117-118).

The second conclusion that Wilson reached concerned "the vital part played in development by environmental conditions. We perceive that our attention has been focused so closely upon the germ-plasm regarded as the substratum of inheritance and development as to obscure our view of the essential relation in which it stands to the conditions under which development takes place. In other words our point of view has been too largely morphological while the physiological aspect of development has been thrown into the background". After discussing some of these physiological views, he identified two kinds of conditions: external to the embryo, and internal. The internal conditions, including chemical and physical factors as well as "physiological relations between the developing parts" are "progressively created by the activity of the

idioplasm itself” (Wilson, 1895b: 118-119). So although environmental conditions (external or internal) at any one particular point in development may play an equally important role as the idioplasm, the fact that a substantial portion of the conditions were created by the activity of the idioplasm sets up a primacy (in the sense of being the origin of chains of causation accounting for differentiation) for the idioplasm in development. This was stated quite explicitly for the first time in this lecture.<sup>119</sup> By 1896 he had come to speak about normal development and the role of the environment in the following terms:

*[N]ormal development is in a greater or less degree the response of the developing organism to the normal conditions*

[Italics in original] Wilson, 1896: 326

I explore the issues raised by this conceptualisation of normal development and the relationship Wilson perceived between the developing organism and its environment and analyse their significance in section 5.5.3. and chapter 6. For now, we may note the role played by the *Amphioxus* experiment in generating a conception of normal development in Wilson, and in providing him with the means to interpret it in terms of an opposition between active internal causes and passive external conditions. This opposition resulted from Wilson assigning primacy to internal causes in the chain of causation with which he sought to explain differentiation and the determination of development, and it reflected the modern distinction between instructive causes and permissive conditions.

#### **5.4. Drawing out the characteristics of different conceptualisations of development**

In the mid-1890s Wilson encountered and tried to evaluate two predominant conceptions of development, which attempted to explain the generation of later stages (larval and adult) through progressive cell differentiation.<sup>120</sup> These were

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<sup>119</sup> By 1897, Wilson finally acknowledged “the inadequacy of all mechanical theories of cleavage” and ruefully observed that “The more we study the problem of development, the more complex and difficult it appears” (Wilson, 1897).

<sup>120</sup> These two ways of conceptualising development (and inextricably, heredity and reproduction as well) and the differences between these ways were important to *Wilson* (and subsequent historical and philosophical treatments of the period). The differences between those ways were not always judged to

associated with the work of Roux and Driesch. Remember that the mosaic theory postulated that the fate of a cell and its descendants was independent of context, and determined by factors internal to the cell. The alternative theory of Driesch (later called regulative development) claimed that the fate of a cell and its descendants was shaped by contextual factors – the parts were regulated by the whole, and thus determined by factors external to the cell, or “mechanically”, to put it in Wilson’s terms. Neither of these men’s ideas was in any way static, but we can characterise them at the point in the mid-1890s after Wilson worked with *Amphioxus* and was thinking through the consequences of this work and how it related to the experimental results and theories of Roux and Driesch.

I will consider the two different conceptions by identifying them with a series of opposing characteristics, which reflected ideas about organismal development at the time. Such ideas, as I have noted, were in considerable flux at this time. Some of these were more explicitly advocated (i.e. mosaic vs regulatory) than others, and some of the characteristics (such as tree vs web) are purely analytic labels chosen by me. The separation of (and distinction drawn between) the organism and the environment allowed these characteristics to be generated, though it did not guarantee that they could or should be. The abstraction separating organism from environment has its roots in Darwinism (Pearce, 2010), but also more immediately, experimental practice, particularly that deriving from the causal-analytical tradition which Roux did so much to promote, and which Driesch and Wilson were to a large extent working within (Lewontin, 2001: 59-60). Neither the concept of the organism or that of the environment are unproblematic, nor divorced from scientific context.

The characteristics are:

#### *Mode of differentiation*

Does differentiation occur early, or late? In the case of mosaic development, the differentiation occurs early, and a given somatic cell, if detached from the organism, cannot reconstitute the whole. However, in regulatory development

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be significant by contemporaries, however. A 1903 text on heredity which attempted to classify various theories of generation actually placed Roux and Driesch’s ideas in the same category (“Organicistes”, with Descartes and von Baer as well), and effectively in a different ‘kingdom’ to the theories of Weismann (Delage, 1903: 437).



such differentiation (and hence, mosaic development) occurs later, meaning detached cells retain the capacity to regenerate to form a new whole organism under adequate conditions. As *patterns* of development, they are not mutually exclusive, as Wilson showed, but can follow each other successively over time.

#### *Type of cause*

This is the type of cause exhibited (or attributed) in development, or at least foregrounded in explanations, owing to some set of empirical, methodological and epistemic factors. The types of cause include attributing developmental patterns and phenomena to inheritance (that is, to some form of transmission, or historical causation, such as phylogenetic explanations for ontogenetic processes and events), to mechanical forces and interactions impinging on and between cells, and to cascades of (intra- and inter-cellular) chemical (physiological) reactions.

#### *Source of causation*

The distinction between organism and environment divides a living system into internal (the organism) and external (the environment) parts. As the distinction between the internal and the external may also pertain to the cell and its surroundings (including, or perhaps not including, neighbouring cells), it is better to consider this as a measure of what extent a conceptualisation of development prioritises context in discussing the causes of particular phenomena. An Internal approach will prioritise causes internal to the central object of inquiry (a cell, an organism, both), whereas an External approach will emphasise the ultimate role of the contextual environment.

#### *Mode of transmission*

The kind of inheritance or transmission exhibited by and within an organism can be characterised as physiological or atomistic/combinatorial. A physiological mode of transmission is dynamic: that which is inherited (e.g. from cell to cell) is subject to change as well as contributing towards it. Additionally, it is the whole which undergoes these changes, rather than just parts. On the other hand, in an atomistic mode of transmission, that which is inherited is not subject to change,

except being sub-divided in ways which do not affect the properties of the individual parts thus separated.

#### *Type of cell division*

This refers to the type of cell division exhibited, more specifically the division of substances or forces *relevant* to intra-organism heredity from parent to daughter-cells. Qualitative division is the unequal distribution of such substances and forces, quantitative division their equal distribution. It must be stressed here that qualitative division does not necessarily imply the unequal parcelling out of some hereditary material. However, the extent to which all or only part of such material was *relevant and active* in the functioning of cells and their descendants, rather than being merely passive and only playing a role in extraordinary circumstances, is the point of distinction in this category.

#### *Metaphors of cell relations*

The metaphors of tree and web describe two perspectives concerning the relation of cells after one or more rounds of cell division. To what extent do cells continue to interact in causally relevant ways for the development of organismal form? The tree metaphor suggests that cell relations are conceived vertically, with the diachronic relation of parent and daughter cells in a lineage more explanatorily important than synchronic horizontal relations between cells. The web metaphor stresses those horizontal relations more than the vertical relations.

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There are many connections and relationships which can be drawn between the different characteristics sketched above. For example, metaphors of cell relations seem to be closely related to the mode of transmission exhibited. If there are lateral relations affecting the constitution of hereditary materials or forces, as the physiological mode of transmission suggests, one would imagine that the relations between cells can be conceptualised more as a web than a tree. Conversely, if relevant hereditary materials are only altered as a result of cell-division (and so, vertically through lineages) the relations seem to be more

tree-like. More connections will be revealed (or tested) by the comparisons drawn below between the schemes of Roux, Driesch and Wilson.

## **5.5. Comparing Roux, Driesch and Wilson**

Up to this point, I have mainly focused on the debate over the mosaic theory against the regulatory theory as the key point of difference between the developmental theories of Driesch and Roux. However, this difference is only part of the story. Initially united by their mechanistic approach and embrace of experimental methods, they were divided on many issues as a result of their interpretations of series of experiments they carried out (most famously) on frogs (Roux) and sea urchins (Driesch). So that we may be able to compare these men further and examine how different elements of their thinking related to each other, I now detail other aspects of their theories.

### **5.5.1. Roux**

One of the clearest statements of Roux's views concerning organismal development is contained in his 1888 paper on the 'Developmental Mechanics of the Embryo' (*Entwicklungsmechanik des Embryo*). This paper described the results of various experiments carried out on embryos of the frog *Rana esculenta*, using a hot needle to kill blastomeres at various stages of development. More crucially, it contained the first clear articulations from Roux of his contribution to the so-called (by Wilson among others) "Roux-Weismann hypothesis" of mosaic development.

Summarised briefly, the results of the experiment showed that when a certain part of the embryo was destroyed by the needle (for example, one cell at the four-cell stage) the resulting development produced a form missing that part which it can be presumed was destined to be formed by the descendant cells and tissues from the destroyed blastomere. Among the "special inferences" Roux drew were "that the qualitative division of the cell body and of the nuclear material...can proceed properly without any influence from the neighbouring cells" and that "the nucleus reaches its proper position in the blastomere, so important for the correct arrangement of the separated materials, without being

affected by the vital activity of the neighbouring cells” (Roux, [1888] 1974: 27). These two quotes reveal several seemingly interlinked elements in Roux’s thinking. For Roux, the activity of the cells is largely autonomous and independent of context. This characteristic, of internally-driven self-differentiation, is guided primarily by the nucleus. The nucleus itself is divided unequally at every cell-division – the daughter cells receive different complements of determinants to guide their future development, and that of their own descendant cells. The most important cell-cell relations are therefore those of diachronic genealogy, not of synchronic interaction. The differential parcelling out of nuclear determinants is what causes differentiation. While certain caveats were later added to Roux’s scheme to take account of phenomena such as regeneration, in the normal course of events he did not believe the hereditary material to be dynamic or responsive to changed conditions.

With this in mind, it is easy to see why Roux’s scheme could be associated so closely with Weismann’s theory of development and inheritance. Deriving from exciting experimental results, and presenting such a powerful explanation for the complex phenomena of development (not just restricted to differentiation), Roux’s theory was an incredible impetus and reference point for future experimental and theoretical work, including most immediately that of his admirer Hans Driesch (Hamburger, 1997; Maienschein, 1991a).

### **5.5.2. Driesch**

In the seminal 1892 paper in which he expounded the results of his experiments on sea urchins, Hans Driesch declared that Roux’s “principle of organ-forming germ-areas is refuted for the observed species” (Driesch, [1892] 1974: 49). He also speculated that this principle may well be refuted for Roux’s own frog species if “those who are more skillful [sic] than I” were able to isolate (rather than kill) the blastomeres of that species (Driesch, [1892] 1974: 48).

What Driesch specifically rejected was the idea of qualitative nuclear division, whereby various nested levels of determinants were parcelled out to daughter nuclei during the process of cell division. Instead, in 1894 he proposed to replace this with a framework which purported to build explanations of

development – and differentiation in particular – upon “a broad base of demonstrable cellular reactions” (Churchill, 1969: 167). These reactions included physical forces impinging on and between cells, but also chemical processes occurring from, between, and in cells. Some of these chemical processes were so-called ‘biological releases’ which were cascades of chemical reactions, ensuring that “ontogeny, becoming an ever-expanding constellation of stimuli and responses, continued to progress” (Churchill, 1969: 169-170). Ontogeny was a progressive unfolding of various stages of chemical production, release, reaction and response. Despite the fact that Driesch saw a key role for the nucleus in directing this process, it differed from the sorts of suggestions made by Roux in a number of key respects. The progressive loss of potency experienced by a particular part of the embryo – the diminishing range of possible cell-types that could be generated – was not caused by any change in the nucleus. No, that structure remained with a full stock of whatever factors were relevant to development and heredity. It was progressive changes generated in the cytoplasm which reduced potency, and this resulted from progressive chemical changes brought about by the cascades of chemical reactions that had already occurred as part of the developmental process. As the cytoplasm acted as a mediator between external stimuli and the nucleus which had the capacity to act upon receiving a particular stimulus, the cytoplasm could determine whether any given stimulus elicited a response from the cell. This process was dynamic and multi-directional, as the nucleus could itself influence the chemical make-up of the cytoplasm by releasing various substances into it (Churchill, 1969: 172).

As a result of all these dynamic chemical interactive processes, the fate of cells could change, as a result of external stimuli. For example, the isolation of a blastomere could reset a cell which had already been set down one developmental path, towards being able to give rise to all types of cell (like an egg-cell is able to). If a cell were moved within an embryo from one location to another, its new position in the whole might stimulate a change in its developmental fate. However, Driesch was keen to stress that such changes in fate were, after a certain stage of development, not completely unbound, and there were often limits to the changes that could occur. Whole-part and part-part relations were crucial in Driesch’s explanation not just of how development and

differentiation could occur normally, but also in explaining the results of his experimental interventions. Cells did not just relate to each other in a vertical way, passing on determinants to descendants, but also in a horizontal way, interfering in the activities and fates of their cousins. The inheritance of certain characteristics of cells to its descendants was to be understood not by the differential distribution of nuclear components, but in the transmission of cytoplasm which had undergone differential cascades of ontogenetic chemical reactions.

**5.5.3. Comparisons and analyses of the differences between Wilson, Driesch and Roux**

The table below displays how the ideas of Roux and Driesch can be characterised in these previously described categories:

	<b>Mode of differentiation</b>	<b>Type of cause</b>	<b>Source of causation</b>	<b>Mode of transmission</b>	<b>Type of cell division</b>	<b>Metaphor of cell relations</b>
<b>Roux</b>	Mosaic	Inherited	Internal	Atomistic	Qualitative	Tree
<b>Driesch</b>	Regulative	Chemical	External	Physiological	Quantitative	Web

The disagreement in every category of the distinctions I drew suggests that each member of a set of characteristics entails the rest of the members of the set. We should perhaps examine this suggestion in the light of the discussion of Wilson's results and theoretical arguments. I have added a row including Wilson's 1893-6 positions:

	<b>Mode of differentiation</b>	<b>Type of cause</b>	<b>Source of causation</b>	<b>Mode of transmission</b>	<b>Type of cell division</b>	<b>Metaphor of cell relations</b>
<b>Roux</b>	Mosaic	Inherited	Internal	Atomistic	Qualitative	Tree
<b>Driesch</b>	Regulative	Chemical	External	Physiological	Quantitative	Web
<b>Wilson</b>	Mosaic (modified version)	Inherited, Chemical & Mechanical	Internal	Physiological	Quantitative	Web

This extremely schematic representation of the three viewpoints, while failing to do justice to the richness of the three men's ideas, does demonstrate that the concepts contained in the pairs of opposites *do not* in fact map onto one another; that is, there are not two exclusive sets of logically related concepts for each of the categories. One could not identify an entire conceptual framework from identifying one of the elements. The only association that is not broken (though not necessarily shown to hold in all circumstances) is that between Mosaic and Internal. Roux's inferences concerning the self-differentiation of cells and their independence from external (mechanical) factors underpin his attribution of a mosaic pattern, and his mosaic theory in general. However, as we have seen, Wilson saw a role for external mechanical factors, and furthermore proposed a physiological view of the mode of transmission. How is it then possible that Wilson came to the same pattern of development as Roux, and proposed a modified view of his theory? How is it that Wilson's views were so out of kilter with the sets of associations revealed by my schematic representation of Roux and Driesch's theories?

Part of the reason may be that while Wilson had warm personal relations with Driesch, he did not with Roux. Despite coming into increasingly serious epistemic disagreement with Driesch, his criticisms were couched very sympathetically. However, Roux's accounts were treated with disdain: "Roux's course has been a very devious one, and I think he will find it hard to clear

himself of the charge of not having been altogether candid; his writings are a terrible labyrinth through which [one] wanders in a state of mental stupefaction” (Wilson, 1897).

Beyond that possible reason, we are confronted with a key difference between Wilson and both of these men concerning the respective roles of normal development in their experimental work, and how this informed their views on development. Remember that in Driesch’s experiment, he relied on the highly abstracted tables of Selenka, and that Roux used a control group in which no abstraction was used in producing a normal development. In Wilson’s experiment, on the other hand, the establishment of a moderately abstracted normal development was integrated into the experiment as a whole. Just as much focused attention was placed upon the embryos which did not undergo manipulation as those which did. The consequences of that are relevant for understanding why Wilson departed from the associations between characteristics of theories that were exhibited in the table covering only Roux and Driesch.

The use of a normal development as a range of natural variation to compare the effects of manipulations (in terms of a range of variation exhibited in the results) will have provided a more fine-grained capacity to assess the role of the different causes (inherited or mechanical). One cause (mechanical) was varied in the manipulated arm and kept constant in the control arm. Within the normal development, the mechanical cause was kept constant (or at least as constant as possible, ‘accidents’ could happen and were suggested as reasons for particular phenomena), leaving open the possibility of data shedding some light on the role of inheritance as a cause. In so doing, Wilson was able to find evidence for both of these causes, and simultaneously the limitations of invoking any one of those causes as the only cause for the difference exhibited between his control and manipulated arms. The causes were therefore not incompatible in Wilson’s account; they were complementary, explaining in combination what any one alone simply could not. This was not inconsistent with Wilson’s prioritisation of the internal over the external, although this came to colour the relative significance allotted to the causes. Wilson’s more pluralist view did affect how he considered the question of cell-relations and descent.



Both the inherited and mechanical causes were reconciled by employing a physiological view of inherited substance and a web-like interpretation of the way cells relate to each other. Wilson's interpretation of the idioplasm posited it as an inherited substance, albeit one which can be changed and also which must be changed over the course of the cycle of cell divisions so that differentiation of cells and tissues can occur. Using this interpretation of the idioplasm, Wilson was able to incorporate the evidence which suggested a role for internal inherited factors and external mechanical factors into a common explanation for differentiation and variation. This interpretation of the idioplasm, combined with the role of normal development in his experimental system, therefore provided the means by which the specificity of both mechanical and inherited causal factors could be detected and assessed. Wilson had constructed an experimental system which was sensitive to the effects of variation in both of these candidate causes. This made it clear to Wilson that in constructing an explanation of differentiation and variation he could not rely on one causal factor alone.

When the focus is on the early stages of development, the difference between the mosaic and regulatory theories seems stark. The mosaic theory posited the narrowing of potency (the ability of cells to produce, upon subsequent divisions, different types of cells) with increasing cell differentiation whereas the regulatory theory claimed that potency is preserved throughout this process. However, beyond the earliest stages of development, the distinction between the two theories was one of degree rather than of kind, as Wilson observed when attempting to bring them both under the same explanatory framework. Driesch admitted as much in 1894 when he acknowledged that "as ontogeny progresses the prospective potency of all parts increasingly narrowed" (Churchill, 1969: 170). Unlike Wilson, however, Driesch sought to preserve the difference between the two theories, by emphasising the causal relevance of each and every stage of development in determining the fate of any particular part (and thus also the whole) beyond that stage. Potency might diminish over time, but rather than development being the mechanical "determined unfolding of set steps" through the division of particles in the nucleus from the egg onwards, the future was still an open book (Churchill, 1969: 173). For the organism, and parts of it, its "fate changed within the limits of the prospective potency at the time"

(ibid.). Series of chemical reactions and triggers helped change this fate, by working within and mediating between cells (Churchill 1969: 168-169). The difference between mosaic and regulatory theories was the extent to which, for any part at a particular point in development, the fate of that part and the parts to be descended from it was already determined. Mosaic theories were determinate, regulatory indeterminate.<sup>121</sup>

Driesch initially attempted to provide a mechanistic explanation for the different fates of isolated blastomeres which he found in his sea urchin experiments, and which Wilson found in *Amphioxus*. Driesch was soon to forswear the possibility of explaining (at least in terms acceptable to other embryologists) many of the phenomena he sought to account for in this way (Roth, 2011: 256; Churchill, 1969: 177). Driesch's continued belief in the constitutive and directive role of the environment in determining the fate of parts and the whole organism, coupled with his mechanistic ideal of explaining differentiation, localisation and accommodation in terms of cascades of ontogenetic chemical reactions (impossible, given the knowledge and technique available), led him to this conclusion. Wilson went in the opposite direction, attempting to find in the egg the sources (cytoplasmic or nuclear) of later differentiation. Unencumbered by the necessity of dealing with the sort of chemical ontogenetic complexity that Driesch envisaged, and having relegated the environment to a passive, permissive condition of development, in his investigations in the following decade Wilson was able to penetrate into realms which Driesch considered unknowable (Collier, 1997: 230-233).<sup>122</sup> Wilson's undoubted success suggests that Driesch was mistaken. These ways in which Wilson made a – cytological and embryological – study of development *possible* conditioned the ways in which development – and normal development in particular – could be conceptualised.

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<sup>121</sup> Regarding cleavage patterns, a key concern of Wilson in the 1893 paper, developmental biologists no longer speak of them being determinate or indeterminate, but variable or invariant (Pearson, 2003: 69). This use of more neutral descriptive language seems intended to avoid making judgements about exactly the sorts of issues I am discussing in this section.

<sup>122</sup> Roux noted the benefits of this approach in 1888. He claimed that "It has thus been shown that the development of the form of the fertilized egg...occurs without external formative forces. We therefore have to look for the formative forces in the egg itself, *which imposes a very pleasant limitation on further investigation*" [my italics] (Roux, [1888] 1974: 5).

## 5.6. Conclusion

In the conclusions which Wilson drew from his experiments with *Amphioxus*, he attempted to reconcile the contradictory theories of development advocated by Wilhelm Roux and Hans Driesch. By 1896, Wilson spoke in harsh terms about the 'Roux-Weismann theory', and seemingly accepted many aspects of Driesch's theory. However, Wilson adopted a similar approach to the internal/external distinction as Roux, and renovated the mosaic theory rather than rejecting it. Warm personal relations with Driesch (and hostility towards Roux) may explain part of this, as might Wilson's greater satisfaction with the empirical details of Driesch's scheme. That Roux's theory had ossified into something of a closed system seemingly impervious to opposing facts, while Driesch's ideas were still being worked out and closer to the experimental evidence, was also crucial in shaping Wilson's relative attitudes to the two sides. One key link I have found between Wilson's "provisional hypothesis", which seemingly rejects so many aspects of Roux's viewpoint, and the mosaic theory is in the relations of organism and environment.

Whatever the curiosities of Wilson's attitudes to Driesch and Roux, I have demonstrated that he did manage to provide an explanation for differentiation and determination which transcended their contradictory views, and brought into question links between particular sets of conceptualisations of the process of development, links which seemed to be necessary in Roux and Driesch's work. The role of Wilson's particular generation of normal development in this should not be underestimated. By appreciating the variation within normal development while abstracting some of it away from his control group, and incorporating the generation of normal development into his overall experimental set-up, Wilson was able to detect more sensitively the new variations generated as a result of his experimental intervention, without sacrificing tractability. In so doing, he was able to produce results which he interpreted in ways that partly reflected Driesch's ideas, partly Roux's, while producing an explanation which explicitly rejected both of them and forged a new working hypothesis. This working hypothesis situated the instructive causes of development within the organism, with the environment relegated to providing permissive conditions. This led, in

1896, to the explicit formulation of what normal development was, the theory now reflecting this methodology as well as ultimately deriving from it.

In 1896 he came to define normal development in a way which divided the factors involved in development into what have since been labelled instructive causes and permissive conditions (Wilson, 1896: 326). This distinction allows biologists to control certain (external, environmental, extra-organismal) conditions which are deemed to be permissive conditions, and manipulate internal, intra-organismal conditions to identify the causes of the phenomena they wish to investigate. This distinction was implicit in the causal-analytical mode of experiment promoted by Wilhelm Roux, and was a powerful conceptual tool allowing scientists to focus increasingly finer techniques on the cell to understand its structure and role in development. Wilson's experiments on the eggs of *Dentalium* and *Patella* (both are kinds of mollusc) in the early years of the twentieth-century were excellent examples of this (Wilson, 1904a, 1904b). Such work stood in contrast to Driesch's drift away from experimental biology, methodologically paralysed in the face of the overwhelming complexity and dynamic interaction he conceived between developing organisms and their environments. This demonstrates the importance of the methodological and theoretical aspects of normal development as a technical condition, in helping to successfully frame an epistemic object in order to generate a viable and productive experimental system. This is achieved by providing norms to identify and control certain factors which become background conditions, while also providing the means for assessing deviation from a normal development defined in terms of the response of the organism to changes in those background (permissive) conditions.

As I have shown, the background to so many aspects of the problems Wilson was trying to tackle in the *Amphioxus* experiment lay in the explanation of variation. In trying to explain variation, Wilson was forced to manage the variation in his own experiment. Part of this management was the incorporation of a range of variation into his normal development, another part the comparison between the 'normal' variation and the experimentally-induced variation. This was directed at explaining the variation in cleavage forms, which in turn offered Wilson pointers for trying to explain how variation is generated in

the course of development – differentiation. The nature of the experimental system which Wilson established allowed him to do this, by including as a comparator and norm a technical condition – normal development – which incorporated a wide range of variation itself. As I have shown, this provided his experimental system with the kind of sensitivity needed to detect specificity in the causal factors he was assessing. In the next chapter I use my study of Wilson’s work to explore how the treatment of variation can be conceptualised in a framework that interprets normal development as a kind of technical condition in experimental embryology.

## **Chapter 6 – Variation and strategies of abstraction**

### **6.1. Introduction**

In this chapter, I build upon the implications suggested by my analysis of Wilson's experiments with *Amphioxus*. Chiefly, I aim to conceptualise Wilson's generation of normal development as part of those experiments, by situating them in two approaches: that of experimental systems (already outlined in chapter 1), and that of a 'taxonomy of norms' produced by different ways of managing variation by methods of abstraction in experimental work.

I begin by revisiting and recapping Wilson's method of abstraction in the *Amphioxus* experiment. I reiterate the need to perform some operations of abstraction to take account of, and manage, variation.

Moving on from this reminder, I make sense of the connections between the establishment of norms (such as normal development) in biological research, theoretical and epistemic stances taken towards variation, and methodological strategies of abstraction. To do so, I use what I have termed a 'taxonomy of norms', which is based on explicit connections between various types of norms and the ways of abstracting variation that are associated with them. The taxonomy includes the essentialist normal, the average or statistical normal, and the reference standard normal. Following my discussion of the taxonomy, I build an account of the practices of abstraction, and relate this to the procedures of standardisation and the use of heuristics in experimentation and reasoning.

The previous two chapters illustrated how a particular set of experimental practices were made to work, and how they contributed towards a particular theoretical articulation of development. This was further demonstrated by way of a comparison with different articulations, which were arrived at using different experimental set-ups. My account has therefore foregrounded the role of practice in driving scientific agendas. In this chapter, I explore how Wilson's work and his experimental strategies can be fruitfully interpreted by an experimental systems approach. This is a way of conceptualising the progress

of research as an investigation into epistemic objects (objects of investigation) by directing various resources (technical conditions) to create the circumstances in which the epistemic object's contours can be traced.

I use this approach to highlight the role of normal development within a nascent experimental system. I argue that understanding normal development as a technical condition in an experimental system is a powerful way of understanding normal development's role in Wilson's work, and suggest that this is also the case for subsequent experimental embryology and developmental biology.

Regarding the taxonomy of norms, I find that previously identified norms do not encompass the norms and experimental strategies used by Wilson. In particular, Wilson's normal development cannot be regarded as a reference standard, and in fact this norm was not exhibited in the early period of experimental embryology that Wilson worked in. I therefore propose a renovation of the taxonomy, and use the previously introduced concept of heuristics to make sense of how the different kinds of normal are employed in the work of practising scientists.

Furthermore, using the example of Wilson's work with *Amphioxus*, I bind together the experimental systems approach and the taxonomy of norms. In doing so, I establish a link between the practical and conceptual aspects of normal development. This will help to form the basis of a discussion concerning developmental biology more generally. This, together with the analysis of causal relationships drawn from Woodward (2010), forms the basis of the discussion in the following chapter.

## **6.2. Wilson's method of abstraction to produce normal development**

In chapters 4 and 5, I detailed how Wilson produced normal development as part of an experimental investigation into the development of *Amphioxus*. Recapping this, and reframing it for the different purposes of this chapter, I consider in turn Wilson's attitudes to, and practices concerning, variation, abstraction, and normal development.

### 6.2.1. Variation

Wilson's attitude towards variation was remarkably liberal. Irritated by the variation in cleavage forms which stymied his morphological work before the *Amphioxus* experiment, rather than ignore the variation he decided to harness it and to try to explain its generation. *Amphioxus* was selected in large part for this reason, for its "protean variability" (Wilson, 1893a: 579). This variability had the implication that the embryos would vary with or without external interference. This presented an opportunity for Wilson to assess the significance of such variation for morphological and comparative purposes, but also a problem for his other aim of investigating the role of different factors (i.e. mechanical or inherited) in differentiation and development. He resolved this in part with a strategy of abstraction which discounted some of the observed variation by establishing a range of normal variation (his normal development), against which the variation observed in the manipulated samples could be compared. He managed to reduce the possible intractability of comparison between non-manipulated and manipulated embryos by comparing against a normal range of variation. Such an approach allowed Wilson to take account of the variation inherent in the differing forms of *Amphioxus*, and provided a powerful means of establishing whether a change had occurred due to the experimental manipulation, rather than some other factor responsible for producing normal variations. Taking account of variation made the sensitivity of the experimental set-up more acute – and the conclusions more robust – than if Wilson had set upon a particular morphology and its stages and determined that to be normal, and ignored all other variation.

Wilson considered all the three main cleavage-forms to be part of normal development in the early stages of the embryogenesis of *Amphioxus*, and recognised that these were similar to the kinds of cleavage exhibited in very different species. He concluded from this variation that for the task of assessing evolutionary relationships by identifying early embryonic homologies, the cleavage-forms were of no help. Instead, he used the results of his experiment to try and work out how the different forms were generated. He believed that this involved an interplay of mechanical forces (from outside and between the cells) and inherited factors (inside the cells), and a shifting of features of



particular stages of development to earlier stages. On this basis, he tried to explain the variation in the different modes of development that were exhibited between different organisms, and the differentiation of cells into cells of different types. Once again, the sensitivity of his experimental set-up aided by the comparison of manipulated embryos with a range of variation allowed Wilson to firmly define the level of influence mechanical factors (the variable in his experimental treatment) had on these processes. This sensitivity led Wilson to conclude that one factor or the other could not be found to act alone, which a less sensitive test might not have detected (cf. Roux and Driesch). He was thus able to come to a particular (and as the last chapter showed, distinctive) hypothesis explaining differentiation and the different modes of development in different species, simply by the fact that his experiment showed that neither mechanical conditions nor inherited tendencies alone could account for the phenomena he observed.

### **6.2.2. Wilson's method of abstraction**

Wilson's method of abstraction was one in which he directly apprehended the variation exhibited by the non-manipulated or control embryos, but discounted those he considered to be abnormal. In order for Wilson to judge some embryos as abnormal, he must have possessed a pre-existing conception or expectation of the normality of *Amphioxus* embryos. This was likely to have been conditioned by his study of previous accounts of *Amphioxus* development, but also involved him employing functional criteria concerning the activity and viability of the embryos as they proceeded through development. Keeping the embryos separate allowed him to track backwards from embryos which did not reach the larval or adult stage to the forms they exhibited during the earlier stages of development. He did not include acknowledged variation in size and rate of development in his account underpinning the picture of normal development, despite these factors surely being relevant in considering the form of the embryo. As abstraction goes, however, this was light, as it still allowed a considerable range of variation to be considered normal. Wilson was not merely a consumer of an abstraction already produced, such as a 'normal table' or a handbook, but the producer of the abstraction, the results of which he would use to ascertain the effects of his experimental manipulation. Later I discuss the

role of heuristic procedures in such abstractions. For now, though, we may recognise that Wilson, in observing the development of those embryos which he had deemed normal after his abstraction, was able to generate a picture of normal development which informed his observations of the manipulated embryos. His representations, I have argued, constitute a form of ‘trained judgement’, which will also be associated with the role of heuristics in observation and representation later in this chapter.

The abstraction was not just from observed variation to the variation deemed to constitute the range of the ‘normal’. It was from the experimental results to the “provisional hypothesis” he outlined. The experiment identified an interplay of inherited and mechanical factors in development. Over the next year or so, this resulted in a conceptualisation of the process of development as a series of stages through which an inherited substance is progressively transformed. The end result was a picture of development into which the internal factors are allocated the role of instructive causes, and external factors the role of permissive conditions. This led to a picture of normal development which is simply the development that occurs when the organism experiences “normal conditions” (Wilson, 1896: 326).

### **6.2.3. Normal development**

Wilson’s normal development, as we have seen, was quite different in form and provenance to other normal comparators used by experimental embryologists in the years immediately before the *Amphioxus* work. Rather than taking normal development to be a particular series of forms at particular stages, Wilson conceived of normal development as encompassing a range of variation. So he attempted to not just depict static stages, but the dynamic processes by which the embryo at any one stage transformed into the particular arrangement of cells at a succeeding stage. Even when he abstracted from the variation to identify the three main types of cleavage-form exhibited as part of the normal development, he was cautious to point out the many transitional forms that existed between them. While, as I have indicated, normal development came to take on a very different (and unlike 1893, specific) definition, as a product and component of Wilson’s work with *Amphioxus* it was a way of taking account of

much of the variation observed in the non-manipulated *Amphioxus*. It identified this range of variation with the sort of variation that might occur naturally, and this was incorporated into an experimental set-up. In turn, the experiments were intended to provide evidence to aid Wilson's attempts to explain how that variation itself occurred. In order to understand Wilson's experiments more fully, and the role of normal development in experimental systems, we therefore need to understand the nature and the role of variation in embryology and developmental biology.

### **6.3. Conceptualising abstraction and variation in experimental embryology**

Variation is absolutely central to the biological sciences. Variation is particularly important in developmental biology – variation in development can cause all sorts of problems in making comparisons, and therefore in making experiments tractable and meaningful. The inherent variability of the objects of biological study such as organisms, populations and species, is qualitatively different to those entities and processes studied by physicists or chemists. For example, it can be said that while it is in the nature of biological natural kinds (e.g. species) that there is variation *within* the kind (and for *new* kinds to be produced) this is rarer or a less important feature of the sorts of kinds dealt with in the physical sciences (such as elements, or fundamental particles).<sup>123</sup> The biologist therefore has to engage with the problem of managing variation, and of explaining it, in a way that the physical scientist does not.

Variation can exist within and between individuals and groups of individuals. There can be variation among the DNA of a population of cells within an organism, between two cells of different types, between two cells of the same type, between either side of an axis in a single organism, between two individuals, between two groups of individuals, between two species, and so on. What is being compared, over what time frame, how it is to be measured, and

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<sup>123</sup> And any such variation in physical sciences is either highly discrete (i.e. isotopes of elements) or highly constrained within certain limits which may not be transgressed. There are exceptions to this point, such as the variation in the relationship between absolute magnitude or luminosity of stars, and their effective temperatures, as depicted on the Hertzsprung-Russell diagram.

for what purpose, is up to the investigator working within various material, theoretical and technical constraints. There are, conceivably, unlimited ways in which comparisons between two (or more) individuals or groups can reveal variation.

Variation is a concept which links the interests of natural historical (or naturalistic) and experimental practices. Both seek to investigate variation, particularly the generation of it. Both also seek to abstract away variation as a methodological practice. In the case of natural historical work, variation is the object of inquiry insofar as the diversity of organisms and their classification is the goal.<sup>124</sup> Certain practices, particularly those that seek to establish types or to represent natural objects, involve the abstraction of the variation that is exhibited in nature, albeit an abstraction guided first by an appreciation, comprehension and synthesis of the variation discovered or revealed. In the case of Wilson's *Amphioxus* work, the fact that variation needed to be explained was the trigger for experimental manipulation. Generally in experimental practice, the generation of variation is understood to arise from a plethora of known and unknown factors. To make an experiment tractable, and its results meaningful, the variety of variation therefore needs to be reduced. The experimenter must control variation that is not an experimental variable, first by recognising it, then by reducing it as much as possible. This is where the establishment of a 'normal development' enters experimental embryology, as a *typological practice*, "a strategy for managing complexity and variation via a practice of categorization that proceeds not by applying definitional criteria but rather by comparison to some reference standard" (DiTeresi, 2010: 29). This perspective on typological approaches in biology takes inspiration from a reassessment of typological thinking and practice. Typological thinking was characterised – and rejected – by Ernst Mayr (1959) as tacitly invoking essentialism and metaphysically opposing the population thinking that was at the heart of post-Modern Synthesis biology. Recent work, however, has decoupled typological thinking from essentialism and demonstrated its potential compatibility with population thinking (Lewens, 2009). Additionally, the

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<sup>124</sup> The variation studied and worked with will of course be at a level relevant to the particular goal. So in many cases this will be at the level of species or variety, and variation below that level is then discounted.

epistemological role of typological thinking has been distinguished from metaphysical claims, inviting us to instead direct focus onto how typological practices (such as abstraction, approximation, and generalisation) are used tactically by scientists in the specific investigative contexts they operate in (Love, 2009). This is the approach taken in this chapter.

Central to this view of normal development is its role in an experimental system. This is a different focus to that of many biologists, who see normal development not as something to be *produced*, but something *given*. While they may acknowledge that certain conditions may need to be provided in a laboratory to enable normal development to be manifested, this simply allows it to be expressed, not to be actively created. We saw in Wilson's 1896 definition the importance of reproducing "normal conditions" to allow normal development to be manifested (Wilson, 1896: 326).<sup>125</sup> However, as we saw in chapter 4, to establish normal development is not quite as straightforward as simply allowing development to unfold unmolested by human intervention in 'normal conditions'. It takes active work by a scientist to construct the conditions to allow this to happen, and then abstract the observed results into a normal development which serves as a control or standard. Wilson was forced to use normal outcome to help establish quite what was normal in the first place.

Additionally, the term 'normal' encompasses a multitude of incompatible or overlapping concepts. Is 'normal development' a specific course of development, or a particular range of courses of development? How sensitive is this notion of normal to variation? How is it established? To explore this, some distinctions will have to be made between different types of normal, how they are established, and how they relate to other key concepts underpinning experimental embryology.

### **6.3.1. Three types of 'normal'**

The different ways in which development can be normal are different ways in which scientists and particular scientific communities treat and conceptualise

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<sup>125</sup> It is worth comparing this with Slack's definition of normal development, which I cited in the Introduction to the thesis. Slack defined normal development as "the course of development which a typical embryo follows when it is free from experimental disturbance". Quite what is meant by "typical" in Slack's definition is not stated.

variation. I add as a caveat that this section should not be read as an endorsement or rejection of any one way of conceiving the normality of development or of organisms in general, even if some are exemplified by and associated with (by me, and in the literature) ideas and practices rejected by most modern biologists and philosophers. The approach I take in this section steers away from normative comment, but it underpins my normative thrust in the following chapters.

Three different ways of conceiving of and producing normal development have been identified (I base my account on Christopher DiTeresi's version of them, 2010: 16-17). I label these three different types of normal a 'taxonomy of norms':

1. Essentialist/Natural State, that only a type or 'essence' has reality, and that variation is merely contingent or accidental;
2. Average/statistical, that the normal is the most common form;
3. Standard, that the normal is constructed by a given scientific community, in a non-arbitrary manner, but guided by particular scientific purposes.

The essentialist version of normal is most closely identified with the Natural State Model employed initially by Aristotle and described by Elliott Sober (1980). The essentialist normal views apparent variation as masking an underlying reality, and therefore variation can either be ignored as an obstruction to the true nature of the biological entity of interest, or as an indication that interfering factors are present. In the case of a process, there is a "natural tendency" which proceeds towards the attainment of the "natural state" of a particular object, and which, in itself, does not require explanation (Sober, 1980: 360). Departure (or 'deviation') from that course, however, *does* require explanation, in the form of "interfering forces" (ibid.).<sup>126</sup> What interpretations of

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<sup>126</sup> For Aristotle, the natural state need not be the most prevalent. In fact, in a very strict sense, it may not actually be present at all. Additionally, there may be some kinds which are by their very nature products of a divergence from a natural state, the result of events during development steering the organism away from its proper course. The mole is one such example, with its sightless eyes (Ransome Johnson, 2005: 173). James Lennox suggests "that Aristotle viewed an animal kind as 'deformed' *relative to some wider class in which it belongs*—the limbs of the seal or the subcutaneous eyes of the mole of

development are in accordance with this approach? Teleological ones, certainly. If there is a definite goal towards which the organism must strive, it can succeed or fail. Normal development is the organism more or less succeeding, abnormal development, more or less failing to achieve its goal or purpose. The source of this *telos* may be form imparted to the embryo from its male parent, a striving to participate in the perfection of transcendental forms, expression of a 'genetic blueprint' crafted by natural selection, or the existence of a tiny proportion of possible developmental routes to a tiny proportion of possible endpoints in some huge multidimensional developmental morphospace (an idea historically associated with idealistic morphology, today with varieties of structuralism). Note that these different manifestations of an essentialist normal type of development straddle the boundaries between very different conceptualisations of life – functional versus formal, historical versus logical. What they have in common is the idea that there is a narrow range of variation which can be deemed acceptably normal. This legitimates, and is in turn informed by, practices which reduce the variation of potential controls, standards, comparators, or models produced for experimental work.

The essentialist normal, reflecting the Natural State Model (Sober, 1980), posits a single end-point and trajectory towards that end-point. The explanatory task set by this norm is to identify what factors cause deviation from this end-point and trajectory. One advantage of the essentialist normal is that it reflects (probably because it helped to shape) our intuitions concerning development. It is therefore less demanding of the user. It is less transparent, however, and the basis for its formulation is also implicit and therefore lacks verifiability and accountability. It does not sit well with modern notions of objectivity, which requires something beyond the judgement of individuals or collections of individuals; it requires measurement and analysis to produce norms. The essentialist normal, however, can be conditioned and improved by experience and expertise. In this sense it can be understood using dual-process theories of cognitive processes. There are at least fourteen varieties of these theories, but they all posit the existence of two main systems of cognitive processing (Evans, 2008). Following Jonathan Evans and Daniel Kahneman (2011) I will use the

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deformed relative to the class of four-footed, live-bearing animals" [italics in original] (Lennox, 2001: 229).

labels 'System 1' and 'System 2' for them. System 1 cognitive processes are automatic, unconscious and relatively effortless. System 2 cognitive processes, on the other hand, involve effortful and conscious mental work. System 1 produces quick judgements based on heuristics, including noticing deviations from the normal. It is shaped by the conscious experience imparted onto it by System 2 cognitive processes (Evans, 2008; Kahneman, 2011). An example of this might be the shaping of expectations as to how embryonic development proceeds (to enable biologists to make quick judgements as to the normality of embryos, or perhaps the stage of development they are at) after much careful observation and recording of the structure of many embryos. A normal development produced in this way is difficult to transmit (and justify), but understanding it in this way means that when it has been produced and used by embryologists who have worked with and gained an appreciation of the embryonic development of a particular organism, it cannot be completely dismissed.

The statistical notion is simply that what is regarded as normal is the most prevalent manifestation (or range of manifestations) of the entity or process of interest, within a larger set of varying entities or processes. Note here that there may be more than one normal under this definition. This is not necessarily a more 'objective' measurement, as what is chosen as the parameter, and how entities and processes are demarcated into groups (particularly if the variation between forms and processes are continuous rather than discontinuous), is a practice requiring some judgment on the part of the investigator or investigators. The statistical normal is relative to a certain context, and in this sense is open to influence from the essentialist normal. The essentialist normal conditions decisions concerning where and when to divide up a range of cases, plays a role in circumstances in which the most common examples are not in fact 'normal' and helps to determine which contextual (environmental) conditions are appropriate. It might therefore be expected that given the proper ('normal') contextual conditions, the essentialist normal will find itself the most prevalent form. The context-relativity of the statistical normal also opens it to influence from wider culture and society. For example, when hospital laboratories were formulating "normal values" for physiological parameters in the United States in 1920s and 1930s, they predominantly (and disproportionately) used data



acquired from healthy white volunteers (Crenner, 2014). John Dupré has observed that “[i]t makes no sense to ask whether something is normal or abnormal without specifying what kind of thing of which it is supposed to be a normal or an abnormal instance.” As a result, “[t]axonomy must always precede judgments of normality and deviance. Conversely, to understand a judgment of normality correctly we must appreciate what taxonomic category is being applied to the subject of the judgement” (Dupré, 1998: 224-225). Whether an attribution of normality in a given circumstance is appropriate therefore depends on the identification and classification of kinds, and identification of the proper kind to which the target belongs, against which it will be assessed. What is a normal value or property of one kind of human, or one kind of organism, might not be so for another kind. For example, in Christopher Boorse’s influential naturalist biostatistical approach to defining health, in which “health is normal functioning, where the normality is statistical and the functions biological”, more than one standard for determining the normal is possible. This is because the judgement of investigators determines what parameter or parameters set the standard, and also how entities and processes are demarcated into groups (Boorse, 1977; Kingma, 2007).

Health and medicine are the areas where debate over the definition and use of the term normal has been most contested in the philosophical literature. They were also original sources of the term normal, although Ian Hacking has also identified “nonmedical routes to the normal” which centre on the growing importance of standardisation in an industrialising world (Hacking, 1990: 164-165). The search for human nature was replaced by the search for the normal human, and statistics was designed to facilitate that. The tension between the normal as a statistical measure (an average, a normal distribution) and the normal as a standard derives from the dawn of the normal (Hacking, 1990: 168). That tension can play out in the statistical normal becoming the standard normal (as in health and disease; Boorse, 1977), or the standard becoming decoupled from the statistical, as is seen in the case of many model organisms.

An advantage of the statistical normal is its apparent objectivity and neutrality. This is also one of the disadvantages, as this objectivity and neutrality is in fact coloured by judgements which may employ aspects of the reasoning associated

with the essentialist normal. If, on the other hand, a 'purer', more objective statistical normal were to be produced, it is difficult to see how it would be useful in scientific investigation, as it would include as part of the control or reference group an extremely wide range of variation (possibly continuous), which may include examples that are transparently abnormal.

The entanglement between the essentialist and statistical normals requires some comment. Canguilhem began his analysis by recognising that "[t]he ambiguity of the term normal has often been noted. Sometimes it designates a fact that can be described through statistical sampling; it refers to the mean of measurements made of a trait displayed by a species and to the plurality of individuals displaying this trait-either in accordance with the mean or with certain divergences considered insignificant. And yet it also sometimes designates an ideal, a positive principle of evaluation, in the sense of a prototype or a perfect form. The fact that these two meanings are always linked, so that the term normal is always unclear, comes out even in the advice we are given to help us avoid this ambiguity" (Canguilhem, [1965] 2008: 122). The normal organism is one which has the capacity to shape its milieu, to make it normal for itself, but the milieu itself must be somewhat normal in the first place to enable the organism to possess exhibit this capacity. Consequently, we are not able to determine whether an organism or its milieu are normal by considering them separately. Building on this observation that it is the relation between an organism and its milieu that allows us to make judgements concerning whether either is normal, Canguilhem argued that it is something other than a statistical sense of normal that allows us to identify whether anomalies – new variants, for example – are normal or abnormal. On the statistical measure, they are surely abnormal, yet the biologist or medical doctor's evaluation may deem it to be archetypally or prototypically normal. The archetypal normal may be based on a form of essentialist normal, though this need not necessarily be the case, as I will show when discussing how Wilson's normal development fits into the taxonomy. In the prototypical normal, as with the archetypal normal, "the normal must be called an instituter of the norm, or normative" (Canguilhem, [1965] 2008: 127). The archetypal normal was said to "underlie" the prototypical normal. Canguilhem did not specify precisely what this meant. If, however, we consider a prototype to be something like a standard

generated by scientists or medics, it need not be determined by an archetypal normal, but perhaps must not become too distant from it. It is to the standard version of normal that I now turn.

The standard normal is defined as a shared (community) research norm, based on an internalisation of normal development by researchers, as a result of their training, exposure to laboratory handbooks, and their own experience.<sup>127</sup>

Internalisation has been defined as “the internal reconstruction of an external operation” (Vygotsky, 1978: 55). It is the process by which the explicit becomes implicit, or tacit. Drawing on an earlier example, it is the process by which System 2 cognitive processes shape System 1 processes. I gave the example of the effects of System 2 concentration on observing and recording embryos, but one might equally stress the role of education and training, for example through learning how to use normal series, identifying normal stages for particular organisms, and practices related to the standardisation of organisms, abstraction of variation and use of standards. One consequence of this internalisation is the evidence in modern biology of variation being “systematically” ignored in highly standardised model organisms (Carlson Jones and German, 2005: 83). It seems likely that the ‘systematic’ nature of the ignoring of real variation has its roots in the internalisation of community norms through training and materials such as handbooks, which abstract away natural variation to make the contents tractable and helpful for laboratory use.

For the standard normal, rather than employing a natural state, embryologists can use a “reference state”, against which the effects (deviations from the reference state) of experimental manipulations can be measured (DiTeresi, 2010: 16). Given the need for a standard against which the effects of experimental manipulations can be compared and the difference measured, it is clear that the advent of normal development as a standard was made

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<sup>127</sup> Sabina Leonelli has identified the precise kinds of knowledge and skills that a scientific education and training is intended to introduce and develop in an individual. Both theoretical knowledge and embodied knowledge are required for “integrated understanding” (Leonelli, 2009: 205). Theoretical knowledge is access to “the articulated content of knowledge” such as “facts, theories, explanations, and concepts concerning phenomena that are available independently of specific procedures or ways of acting.” Embodied knowledge, on the other hand, “is the awareness of how to act and reason as required to pursue scientific research” (Leonelli, 2009: 196). As well as these two kinds of knowledge, there are also three kinds of epistemic skills that are vital for scientists to acquire: theoretical, performative and social (Leonelli, 2009: 201).

necessary by the introduction of experimental practices into embryology. DiTeresi goes further to say that it was the search for *mechanistic accounts* of development that led to the use of normal development as a standard (2010: 17-18, 66). However, as in this period American biologists used experiments creatively to 'generate working hypotheses' (something I believe that Wilson did, including with *Amphioxus*), it was not necessarily the search for mechanistic accounts of development that provoked the adoption of experimental methods and therefore the eventual adoption of normal development as a standard (Maienschein, 1991b: 420-423).

The reference standard normal solves many of the problems of the essentialist normal and the statistical normal. It transcends the tacit subjective judgement of individual scientists by being an explicit, well-defined community standard. It is produced in a form which can be transmitted, and can be accompanied by research materials including model organisms. It aids comparability between laboratories, and allows standardisation of training. Consequently, it permits scientists to move from one laboratory to another with greater ease. Finally, it allows the staging of samples and experimental work to proceed more smoothly and with less preparatory work, orientation and familiarisation with the material. The wheel does not have to be reinvented each time a new set of experiments begin. However, the reference standard, as we have seen, does have problems. In one sense, these problems are related to the narrowing of the range of organisms used, in another the amount of variation abstracted away to produce the standards – the series of stages deemed normal – in the first place. Once in place, the standards are difficult to reform or shift. In part this is because of their entrenchment in infrastructures of education, training, and material and technical resources. Crucially, they also shape what is regarded as normal in the first place, and the amount of variation deemed to be permissible within the range of the normal.

In experimental embryology (and experimental biology as a whole), attributions of normality are tied to the need in experimental designs to use a control against which the effects of the experimental intervention can be measured. Normal development is such a control. We saw in previous chapters how the notion of an experiment incorporating a control group was (allied to an analysis

of the living system into causally-relevant parts) introduced into embryological work by Wilhelm Roux. He was himself inspired to do this because of the method's use in physiology. Such methodology characterises much experimental practice today. However, the near-ubiquity of the usage of controls in experimental work in embryology and developmental biology does not imply a constancy of form and function of controls in all experimental set-ups. The linkage between controls and norms suggests that, if norms differ, then so do the controls. One way of ascertaining how (and giving an indication as to why) controls differ between particular experimental set-ups, is to ask the following questions: What is the control, how (when, where, and by whom) is it produced and enters into the experimental set-up, what role does the control have in the experiment, and how is the potential difference between treatment samples and control samples discerned?

I provide the following examples of controls, by way of answering those questions.<sup>128</sup> Once again, the focus is just as much on the process of production, as on the product. The first and second examples revisit Driesch's use of normal tables in his sea urchin experiments and Roux's use of controls in his experiments with *Rana esculenta*. The third example considers 'modern experimental embryology' as examined by DiTeresi. Each of these results in very different controls, with different roles, processes of generation, and relations to the experimental set-up and situation. In the case of Driesch's experiment, the control was the normal tables produced by Selenka. They were stripped of any indication of intraspecific variation at any particular stage of development, and were external to the experimental set-up itself. Roux's controls, on the other hand, were part of the overall experimental set-up, and he was able to compare in a qualitative way the difference between what he observed in the control group, and the group of organisms which underwent his experimental intervention. However, Roux's control was not the same as his normal development, which seemed to exist as a norm external to the experimental set-up itself. In modern experimental work, the control exists not just in the control group, but also forms part of the treatment group as well, insofar as some form of standardised organism is used. The standardised

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<sup>128</sup> I do not include here the control of conditions, though this will be examined in the following chapter.

organism, bred to minimise variation within strains or varieties (to minimise the variation of possibly causally-relevant factors), functions as a control in making sure that all factors are as far as possible kept the same, with the exception of the factor to be varied in the course of the experiment. Here, the controls are produced predominantly outside of the experimental set-up itself. The part that is in the experimental set-up (the established control group) is usually compared to the treatment group by averaging the values for particular relevant parameters and comparing these to the average of the values for those parameters in the treatment group.<sup>129</sup>

Examining the role of the creation of controls in experimental set-ups thus reveals not only the connections (but not 1:1 mapping) between the establishment of norms and controls, but also that the taxonomy of norms in which I have described the different ways in which normality can be discerned and attributed in biological practice is an analytic taxonomy. They are purified ideal types of ways in which normality can be established in and between organisms. In practice, there may be a mixing of different norm-establishment practices, at different points of the experimental process, or if only one type can be identified, instantiated in an 'impure' way. Later I revisit Wilson's experiment with *Amphioxus* with these thoughts in mind.

### **6.3.2. Abstraction**

Entailed by the practice of 'managing variation', all of these versions of 'normal' require, to a greater or lesser extent, processes of abstraction. As detailed in chapter 2, abstraction has been identified as a simplification which takes the form of an omission (Jones, 2005: 175), or a subtraction (Cartwright, 1989: 187), but *not* a misrepresentation (Jones, 2005: 175), which is instead characteristic of idealisations (ibid.).

Here, rather than worrying about whether such simplification constitutes a misrepresentation or not, I analyse abstraction as an 'epistemic activity' which

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<sup>129</sup> Sometimes, however, control experiments set up within the framework of a wider set of experiments (with the aim of discounting the possibility that certain varying factors confound attempts to clearly discern the role that a particular factor of central interest plays), may involve a qualitative judgement of the significance of the difference in output values of particular parameters between control and treatment (Weber, 2005: 126).

“emphasises the actions, choices, displacements, conceptual and physical transformations involved in the creation and use of biological models” (Leonelli, 2008: 527).

Leonelli defines the process of abstraction as “*the activity of selecting some features of a phenomenon P, as performed by an individual scientist within a specific context, in order to produce a model of (an aspect of) P*” [italics in original] (Leonelli, 2008: 521). Crucially, there are many different ways of doing this, with different end products. Two examples of processes of abstraction are “intellectual” and “material” abstracting (Leonelli, 2008: 521-523). The former is a theory-guided process of abstraction “requiring no physical interaction with the phenomenal properties to be abstracted” which is “geared towards explanation” and aims “to uncover ways in which a model can be *representative for* a given theory” (Leonelli, 2008: 521). The latter is a theory-informed (but not guided) process of abstraction “performed by physical interaction between the researchers and the phenomenon to be modelled”, to produce something that is “taken to be *representative of* a set of phenomena” (Leonelli, 2008: 523).

There are other ways of conceiving abstraction. Hans Radder has identified three ways of abstracting: of leaving out, setting apart and summarising. In the first way, “abstraction means that we leave out from the conceptual interpretation of the original process everything but the result” (Radder, 2006: 109). In the second way, the “result of an observational process is set apart, or separated, from the original process” (ibid.). The third way is manifested “by leaving out the particularities or idiosyncrasies and by mentally setting apart what is relevant and common, we abstract a general concept from its individual, spatiotemporal instantiations” (Radder, 2006: 110). Radder, while accepting the importance of the first and second ways, rejects the third way as an explanation of concept formation, as he had previously argued that “[t]he observation of particular situations is always conceptually interpreted right from the start” and so abstraction could not adequately be interpreted “as a kind of inferential procedure from directly given, uninterpreted particulars to their conceptual, general representations” (ibid.).

At different stages of scientific investigation, different abstractions may be performed and produced. Such abstractions will take the different forms so far

discussed, but also differ in their performers, producers, and users. The examples described by Leonelli (2008) and DiTeresi (2010) deal with what I shall refer to as 'community abstractions', which help to produce a norm and/or control, and which equip scientists with the particular means and heuristics with which to relate the treatment group in an experimental set-up to the control. It is a group of scientists or technicians (on a one-off or ongoing basis) who perform and produce the abstractions for internalisation, adaptation, and use by individual scientists. A distinction may be drawn between such 'community abstractions' and an 'individual abstraction' where the performer, producer, internaliser, adapter and user are one and the same individual scientist. The goals of such an individual abstraction may differ from those of a community abstraction, the latter of which is intended to be used as a community resource and must possess certain characteristics, such as being able to be scaled up or transmitted in some appropriate form or format. Indeed, the process of individualised abstraction may lead to a shifting of goals as a result of, and in response to, the process of abstraction itself.

Standardisation is a key process of abstraction in modern biology, particularly when model organism systems are used in research. Standardisation, however, is not synonymous with abstraction, but is merely one way of (or motive for) abstracting. The products of abstraction may be genetically homogeneous lines of mice, ecotypes of *Arabidopsis thaliana*, verbal descriptions in a monograph, diagrams of stages of embryonic development in a handbook, or the concept that there are stages of embryonic development. The particular ways in which abstractions are carried out by a scientist, and then used in their work, may differ. But what they all have in common is that they are ways for the biologist to take account of the variation inherent in their objects and processes of interest, while omitting or simplifying some of that variation in the production of a particular abstraction.

If we see the managing of variation as abstraction, we can therefore begin to see that the different processes of abstraction that may be employed by biologists correspond to the production of different norms; different normal developments, doing different work. Different kinds of epistemic processes or activities will produce different norms.



As suggested at the end of the fourth chapter, heuristics play a role in these processes of abstraction. Variation, as manifested by organisms, has to undergo abstractions to be transformed into a form which allows it to be conceived, represented, measured and compared in a manageable way. Heuristics are a 'low cost' (in terms of cognitive and other kinds of resources) way of doing this. Processes of abstraction affect how variation is represented and used in experimental situations. Three key ways in which it can do this are in terms of range, type and structure. The range of variation for any particular parameter is the total range of values which can be assigned to the members of a set depending on the parameter. The range of variation may be the heights of organisms, the numbers of bristles on a particular limb or appendage, or the networks of genes involved in a particular developmental process that is exhibited in many different species. The type of variation is what has been identified as the object or objects that may vary. For height it would be the whole organism, for number of bristles it is the limbs, for the developmental process it is the set of genes involved in it. Structure is the way in which the values are distributed, for instance, in terms of abundance and association with other values in the range. For height, the structure would probably be a continuous, normally-distributed bell-curve. For the bristles it would be discrete integers, but these may not be normally distributed, as there may be some developmental reason why there may only be a few bristles on the limbs of some species, multitudes on the limbs of other species, but no real range of intermediate values. For the genes, there may be several core genes which do not vary in their presence or role, there may be several that have specific and unique roles in only one species, then there may be a distribution of different types of other genes, which may be more or less prevalent across many or few species, and have constant or varying roles.

There is no a priori way in which we might identify the nature of the structure of variation just by knowing that variation is exhibited. Identifying and measuring biodiversity, by way of contrast, requires that the variation of the natural world be already partitioned into different (nested) types – species, genera, families, and so forth – which can then be measured in their relative abundance.

Variation in nature is structured, but it is structured in an indeterminate number of ways. It is up to the scientist's abstractive work to bring out a particular way in

which the variation of biological objects of interest are structured, and also to impose some structure on it. These two aspects are not antagonistic or contradictory. In fact the imposing of structure will often work with the structure brought out – lines will be sharpened, fuzzy groupings made less fuzzy and more concentrated, boundaries and limits drawn. In this way, the process of establishing types from variation is advanced, and the normal is distinguished from the non-normal. With all these ways in which variation can be abstracted different approaches may co-exist and help constitute the observed, measured, represented and compared variation.

Presented like that, the processes of abstraction of variation that are needed to bring the 'natural' into an experimental situation, and to compare two sets of variation in that situation, seem very complex. And they are. Yet, when they actually take place, they do not (and cannot, if any experimental work is to be done at all) approach the level of complexity one might think is involved. This is where heuristics come in. Heuristics are ways of dealing with complexity – to transform a difficult and expensive (in terms of time, energy, and resources) problem into an easier one. As indicated previously, they do not do this by providing an algorithm for transforming the raw variation into usable variation, but rather with a rougher 'rule of thumb' that can allow for quicker selection/exclusion and organisation/representation. Irrelevant variation (for the particular purposes of the scientist – though here the possibility of excluding *inconvenient* variation arises) can be excluded. The variation which remains can be structured (falling in particular clumps, or in a continuous distribution, with one or a few peaks) and then represented in accordance with that structure, to enable it to be measured and provide a basis of comparison. As we have seen, the various ways in which that can be done can vary greatly, and can therefore produce different models of variation with different ranges and structure.

Debate in the psychological literature on heuristics tends to focus on heuristics used generally by humans – the availability heuristic or the effects of anchoring, for example. There is disagreement on the value of heuristics for reasoning. Some psychologists (e.g. Kahneman *et al*, 1982) believe that the mind needs to be trained to override heuristics, which are regularly irrational in their products, albeit useful for reasons of minimising cognitive effort which might be directed

elsewhere. Other psychologists (e.g. Gigerenzer and Brighton, 2009) argue that heuristics often provide a more accurate result than the more time and energy-consuming processes of taking all data points into consideration, which presents the possible problem of ‘over-fitting’ the data. Intuition tells experienced users of such data that certain data points are anomalous and should be excluded – not an infallible judgement, but given their expertise, often a useful one. Wimsatt’s (2007) focus on heuristics tends more towards Kahneman *et al*’s view that heuristics introduce systematic bias, and provides ways in which these biases can be exposed and analysed, to find out the precise limits of their usefulness and the ways in which their results may be interpreted. Gigerenzer and Brighton’s approach might be fruitful in considering heuristics as intuitions that can be trained and their effectiveness improved. This approach would be fruitful even if we do not accept that they can be improved to exhibit better representational accuracy than more laborious approaches.<sup>130</sup> Increasing experience and familiarity with certain materials can be gained by training and working with those materials over a period of time.

The extent and nature of that experience will condition how well a heuristic works for a particular purpose. A greater availability of observations and engagement with particular organisms will provide a larger bank of memories and associations with which to make intuitive judgements concerning those organisms. This will in turn lead the scientist to be able to make observations which other scientists lacking this bank of experience may not be able to make.<sup>131</sup> The more appropriate deployment of heuristics, and greater availability of experience to inform them when deployed, may be the very essence of ‘trained judgement’ as a representational ideal (Daston and Galison, 2010).

Training may provide a concentrated form of this development, usually using proxy materials such as tables of normal stages, handbooks, demonstrations, and so on. If we consider that not only can an individual possess and develop

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<sup>130</sup> However, in transforming ‘natural’ variation into a form useful for the practising scientist, representational accuracy is not necessarily the only aim.

<sup>131</sup> A classic example of this is the work of the cytogeneticist Barbara McClintock. Her close engagement and observation of the chromosomes of maize enabled her to link her observations of the breakages of chromosomes with changes in the colouration of the seeds, to propose the existence and role of transposable elements. It took decades for her colleagues to accept this, in part (though not entirely) because they simply could not see what she saw, or make the conceptual connections she made (Keller, 1983).

the power of such heuristics, but also a community, we may consider such training (and reference) materials, and also objects (such as strains of model organisms, methods and techniques, and so forth), as inculcating a kind of community heuristic. This reduces the heuristic load on any individual scientist, but also locks them (entrenches them, perhaps) to a certain extent into the particular heuristics embodied in those materials and practices, and the interpretations that most naturally or easily follow from the employment of those heuristics.

#### **6.4. Wilson's normal development**

One lacuna of Rheinberger's account, identified by Weber (2005: 149-153), is the absence of a discussion of methodological norms in the generation and reproduction of experimental systems. Indeed, despite the concepts of normality and deviance having a resonance and significance in the biological and biomedical sciences not shared with other natural sciences, these are not dealt with by Rheinberger in his work on experimental systems. Weber observes that, as much as they have a life of their own and generate surprises and questions, experimental systems are reproduced by scientists, and are therefore imbued with some purpose, direction, or *telos*. Building on Weber's insight using the discussion of abstraction above, we might add to this that in foregrounding the experimental situation and its own dynamics, Rheinberger has left out the *theoretical background* which must either guide or inform the particular processes of abstraction at play in any particular experimental set-up. By theoretical background I mean nothing more than empirical knowledge and expectations relevant to the problem being explored by experimental set-up, as well as discipline-specific awareness as to what constitutes relevant and important questions, problems, results and interpretations. The theoretical background in this sense plays a role, regardless of whether the processes of abstraction are external to (and imported into) that experiment or series of experiments, or internal to them. The norms (and their theoretical background) should therefore play a part in the operation, interpretation and fate of an experimental system. I believe the taxonomy of norms provides us with a set of *methodological-material norms* which, in addition to the theoretical

backgrounds that scientists bring to experiments, can be integrated with the experimental systems approach to form the basis of an analysis of experimental practice in developmental biology. In this section, I use this combined approach to assess Wilson's work, its significance, and fate.

Questions of the relevance of the formation of particular structures at particular stages of development for evolutionary questions were touched upon in Wilson's 1893 paper, but were not central. Instead, increasingly central to Wilson were the *causes* of forms and structures. To that end, he was explicit about the use of functional criteria to inform his construction of normal development. He cited the ability to develop to later stages as a criterion for developing 'normally', though some degree of structural correlation to functional later stages of development was relevant. Despite the functional grounding, in his description Wilson ended up generating a new structure-based normal development. Due to the differing requirements of the normal development for comparative purposes as an arm of an experimental set-up compared to other contemporary or modern uses of normal development, the process of abstraction required to produce the normal development was different. In the process of abstraction, scientists need to make decisions about what is left in the final representation of the varied phenomena that present themselves. In the case of Wilson in 1892/3, the goal of the experiment demanded a process of abstraction that was more sensitive to, and more inclined to include, the variation that was exhibited during his observations, compared with an abstraction for comparative morphological purposes. Thus we have a conception of normal development which includes within it wildly different organisations of the early embryo. It was the cause, and significance, of those early embryonic forms that was the subject of Wilson's enquiry. He did not need to establish a single canonical form that early stages must take, and there was no prior theoretical reason why there must have been such a representation.

Wilson's method of producing normal development was to derive the normal from observations of many manifestations of forms already labelled 'normal'. The abnormal was then judged to be anything that diverged from the expectations established of the normal so constructed. It would seem then that

the abnormal was identified using an intuition of the normal, rather than the other way round.

‘Normal development’ was both an input and an output of the *Amphioxus* work. It was an input, because some idea of what constituted ‘normal development’ needed to be in place for the experiment to take place at all (for comparative purposes). The construction (or, we might say, reconstruction) of ‘normal development’ itself, through Wilson’s own processes of selection, exclusion, integration and recording, was guided by his own preconceived conception of what the ‘normal development’ of *Amphioxus* consisted of. These expectations guided Wilson’s interpretation of the forms he observed, but the different results he obtained compared with his predecessors showed that while the output was conditioned by the input, it was not fully determined by it. This is therefore an example of the third way that abstraction can be performed that Radder identified (2006). It evades the objections Radder has to the third way by summarising not from “directly given, uninterpreted particulars to their conceptual, general representations” but, using Radder’s first and second ways, by summarising from particulars interpreted using existing conceptions to produce new conceptual representations.

If we consider normal development as part of an experimental system, we can see that the particular form which normal development took for Wilson, that of a range of variation encompassing all three cleavage-forms (and their intermediates), is an example of something moving from the periphery of focus to becoming a key component of an experimental system by functioning as a technical condition. In the work preceding the 1893 experiments with *Amphioxus*, the very variation in early embryogenesis which came to constitute part of the normal development as produced and used by Wilson was seen as ‘noise’ causing problems in the embryological work he was conducting. This variation in normal development then became the question (or at least one of the most important of several questions) that he wanted to answer: what caused the different cleavage-forms in early development? The process of the development of normal forms therefore became an epistemic object. In the process of attempting to engage with this epistemic object, he produced normal development in the ways in which I described in chapter 4, and therefore

introduced normal development as a technical condition into his nascent experimental system.

The processes that generated the forms which constituted a normal development was the epistemic object. The establishment of the normal development itself, and the existence of the normal development as a comparator against which the effects of the experimental manipulation could be compared, served as a technical condition. However, the reciprocal relationship between the epistemic object and the technical condition just described (each was needed to help constitute the other) meant that in this particular experimental system, we might only describe the epistemic object and the technical conditions as a proto-epistemic object and a proto-technical condition. In conducting the various elements of his experiment, Wilson was able to progressively differentiate the proto-technical condition of normal development from the epistemic object. In the early stages of the experimental system, the technical condition was to a large extent dependent on the presumed contours of the epistemic object, what processes and forms constituted a normal development. The distinction between them was therefore more diffuse and porous, and the epistemic object and technical condition of normal development were less differentiated. As a result of Wilson's elaboration of normal development, through his observation of the individual developments of *Amphioxus* specimens, however, the technical condition of normal development became more distinct and differentiated, and less dependent, on the presumed epistemic object. The technical condition, by the process of the generation of a normal development, achieved some measure of independence from the epistemic object. It became more like a technical condition in a more mature experimental system; it increasingly fulfilled its function of framing the epistemic object, and was decreasingly affected in its own form and function by the epistemic object. There are thus differences to be drawn between experimental systems considered mid-stream (which even Rheinberger's example does, starting at a point where there is already a well-established tradition of experimental practice in that field of biochemistry) and those which are considered at early stages like Wilson's. In circumstances where the technical conditions themselves need to be generated, we would expect the initial stages of the experimental system to show the same sort of relationship between the

technical condition and the epistemic object as we have seen for Wilson's *Amphioxus* experiment.

We might also observe that in exhibiting variation, biological objects *qua* biological objects and not just as epistemic objects, are inherently vague. The process of framing and stabilising them, essential for the progress of experimental systems when one considers them as epistemic objects, may in fact end up concealing important aspects of their nature and relations rather than giving shape to them, when one considers them as biological objects. This was less of a problem in Wilson's work, as variation was taken into account and incorporated within the normal development, which was generated as a technical condition and integrated into an experimental system configured to deal with specific questions which included the significance and causes of variation. Was Wilson's way of generating normal development fundamentally different to other ways? If it was, it would mean that other ways of producing and using normal development would not necessarily evade the problem of how normal development as a technical condition deals with certain kinds of biological objects. To deal with this, we have to consider Wilson's normal development in the light of the taxonomy of norms outlined earlier.

Returning to the three types of normal outlined above, one would think that Wilson's normal development would pertain to the third sense of normal, that of being a reference standard. In assessing this, we must return to the intimate connection between norms and the processes of abstraction which give rise to them. The reference standard and Wilson's normal are both examples of material abstraction. They represent phenomena, and are produced "by physical interaction between the researchers and the phenomenon to be modelled" (Leonelli, 2008: 523). However, there are key differences. Firstly, the process of abstraction by which Wilson took his observations of the development of many individual specimens of *Amphioxus* was an *individualised abstraction* for specific, particular purposes. It was an individualised internalisation based on short-term experience, rather than a community abstraction intended to be a resource for a multitude of known and unknown purposes. While there were indeed shared research norms in play, in the sense of the proper conduct of scientific investigation in general, Wilson's normal



development was not a community resource produced to be mobilised and circulated throughout a scientific community. Furthermore, while he had access to and used the accounts of *Amphioxus* development provided by the likes of Hatschek, Wilson did not have handbooks of 'normal stages', or other community resources such as standardised (model or otherwise) organisms. Wilson was the performer, producer, and consumer of the material abstraction (and shaper of the heuristics and the experiential material used by them), rather than just the consumer.

The reference standard as a category in the taxonomy is based on an examination of the modern era of biology – with model organism systems, systematic training of experimental embryologists, and the presence of resources such as the normal stages of organisms in handbooks (DiTeresi, 2010: 65-74). I contend that this norm does not apply to the use of normal development at the dawn of experimental embryology. While there were initial stage series being produced at the time, they were used in comparative embryology and not Wilson's experimental study (Hopwood, 2007). Furthermore, there were neither model organism systems nor community organism standards at this time (Logan, 2002). There was a more opportunistic approach to the selection and use of organisms based on the problem at hand. This is related to the idea of organisms as cases, outlined by Rachel Ankeny (Ankeny, 2012). An organism used as a 'case' is intensely studied "with the goal of eventually elucidating norms or baseline patterns against which newly observed yet similar phenomena (e.g., in other species) can be compared" (Ankeny, 2012: 646).

Cases help 'tame variation' when the sheer weight of it threatens to make meaningful scientific work impractical, as it threatens to in developmental, and particularly *comparative* developmental biology (Ankeny, 2012: 652). While Ankeny acknowledges that the selection of an organism as a case can be due to the "similarity provided by the organism in question in relation to the process or issue under examination" (ibid.), factors such as "historic primacy or importance,...experimental tractability, [and] manipulability" are also critical (ibid.).

We therefore need to rethink the taxonomy of norms categories in the light of the differences I have identified. There seem to be two options. One is to keep the category of reference standard and add a fourth more appropriate to the era I have described. The other is to expand the existing category by watering down the definition of a reference standard to include both modern and historical contexts. I am inclined towards the former option, providing as it does a clearer distinction between the practices of embryology prior, and subsequent to, the changes it underwent in the early twentieth-century. This might allow us to see how previous practices fed into newer ways of organising embryology and conceiving of the process of development, and what was left behind. It might also help us to compare the two different eras. Finally on this point, I would like to propose a new approach to using the classification of types of 'normal'.

DiTeresi presents them as separate and exclusive, but it need not necessarily be so. There are multiple ways that the objects of biological study can vary, even within one tightly defined experiment. The argument has not been made that previous ways of conceiving of and treating variation have become obsolete. Often prior 'styles' of thinking and practice go out of fashion and fade in significance, rather than going extinct (see Hacking, 1992a and Pickstone, 2000). In one piece of work, two or more different means of treating variation may therefore co-exist. There is important future work to be done in ascertaining what the effects and significance are of the interactions between different types of 'normal' within a single piece of scientific research.

What served as the control in Wilson's work, and what was its relationship to the experimental set-up as a whole? The control was the normal development which he established as part of the experimental set-up itself. It was the range of variation exhibited in the control which served as the comparator for Wilson's observations of the manipulated samples. Like other controls, as previously noted, one of the key reasons why normal development becomes employed in experimental embryology is because of its use as a benchmark (I avoid the terms reference and/or standard here as I have used them in very particular ways in the preceding text), against which the effects of experimental manipulations can be measured. From this, the investigator can surmise what he or she believes to be the causes of the difference, and infer from this the cause(s) of the normal phenomena. Normal development functions by

structuring the expectations of the observer. By taking into account the variation which is included in the abstraction process, it allows them to then ignore that variation when it is exhibited by the various samples at different stages that have undergone the experimental intervention. Normal development is therefore used as a point (or series of points in a process such as development) against which *deviations* can be determined or measured. The word 'deviation', as well as carrying some normative load, has roots in the Latin *deviare*, and has its earliest recorded uses in English in the seventeenth-century, when it meant "turning aside from a path or track" (OED, [1989] 2015b). If we see the normal course of development as a particular path or track, what Wilson did was to expand the number of alternative paths open in the early stages of the journey of the embryo. He broadened out the 'point' to a range of variation deemed to be normal. He did not, however, change the notion of a specific destination towards which all valid routes must ultimately tend. In fact, by making the end of the journey the criterion for discerning which paths or tracks were valid (or 'normal') and which were not, he fixed the end-point of normal development by definition. While there was a broadening at one stage of development of what was considered to be normal, this was accompanied by a narrowing at the later stage.

How are we to integrate this analysis of the different type of normal exhibited by Wilson's work by considering it both as one norm in the taxonomy of norms, and as an experimental system? Precisely in the way suggested by Weber. Normal development is a technical condition, and the way in which it is produced, reproduced, transmitted, integrated into an experimental set-up and interpreted, involves methodological norms arising out of scientific practice itself. These methodological norms correspond to the different ways in which the normal can be produced and used in experimental embryology, that is, to the taxonomy of norms. In this way, the experimental system retains a life of its own, while also being guided by the problems prioritised by individual scientists and communities of scientists. Wilson's own *Amphioxus* experiments demonstrate this. They were directed towards (multiple) ends, but ended up resulting in quite a different weight attached to the question of the mode of development to the weight attached to that question going into the experiment.

To assess the significance of this observation for modern developmental biology, we must assess the fate of particular concatenations of technical conditions associated with normal development, and the role of certain methodological norms in its production, as these issues lie at the heart of understanding experimental systems in modern developmental biology.

## 6.5. Conclusion

In previous chapters, the relationship between normal development and the role of variation in an experiment or series of experiments was touched upon. The extent to which variation functions as part of an *explanans* or *explanandum*, the amount (and types) observed, represented and managed in an experimental situation, and the ways in which it is treated, were all considered in the light of the work conducted by Edmund Wilson with *Amphioxus*.

In this chapter, I have endeavoured to conceptualise further the nature of the relationship between the establishment of norms in scientific (more specifically biological, and embryological) practice, and the treatment and conceptualisation of variation. Integrating parts of the experimental systems approach introduced by Rheinberger and the taxonomy of norms I outlined, I have detailed a picture of normal development as a technical condition which contains within it a methodological-material norm conditioning the treatment of variation. To treat variation is to import it from a preceding setting ('nature', or from another experimental system), to detect and transform it, represent and distribute it by particular processes of abstraction, and use it as a control. Different methodological-material norms mean different technical conditions.

For Wilson, I have situated his normal development in a fourth category in the taxonomy of norms, his normal development therefore being a technical condition of a different kind to those in modern developmental biology in which the reference standard norm predominates. Different technical conditions mean different experimental systems. The principle of supplementation suggests that a new element may not only amend the experimental system, but transform it. Different experimental practices involve and require different ways of producing normality – normality understood as both a technical condition and a

methodological norm forming part of a technical condition. Variation as a central characteristic of living things (and between living things) is relevant to any experimental system in the biological sciences, and is relevant to the questions being asked, the answers sought and the answers (and surprises) given. Therefore a control and/or a norm which incorporates certain assumptions about variation means that it will affect the way that variation is dealt with in the experimental situation; how it is interpreted, conceptualised, and fed into future experimental systems. The example of normal development displays why this may be the case. As an important technical condition, it incorporates considerable theoretical and practical background concerning variation – its treatment and conceptualisation – which surely impinges on the experimental system as a whole.

Conversely, the system as a whole affects the parts. If an experimental system evolves to generate new questions regarding the nature of variation (for example, its causation, function and maintenance), the technical conditions incorporating methodological-material norms concerning variation and its management in experimental situations must surely come into question. There are many reasons why sometimes this is not the case; the dynamism and open-endedness of experimental systems must be measured against the entrenchment of certain experimental programmes. One key reason for this can be the reliance on a particular model system which provides resources such as specimens, online genomes and ontologies, support and – intellectual and material – exchange networks. Other reasons may include institutional and funding factors, and the canalisation of scientific focus encouraged by the long training into certain ways of doing science for certain purposes. I examine these in more detail in the following chapter. There are many reasons why often the conservatism engendered by these factors just listed must be exposed and resisted – an experimental system is not dynamic and productive just by being an experimental system.

There are many reasons why an experimental system can fail to reproduce or to run out of steam. It might do this if the latest manifestations of technical conditions, and the methodological-material norms which help to constitute them, are no longer appropriate to the investigation of the particular aspect of

the epistemic object under investigation. In that case, the system will cease to be productive.<sup>132</sup> The system will have found itself captured by the technical conditions which should only provide a stage.

To better appreciate this, we might consider how causal relationships are elucidated in biology. I have previously introduced the notions of permissive and instructive causation. These are related to the concepts of specific and non-specific causes in development. The former pair of terms (instructive and permissive) captures the prevalent belief that in development, only the genome (with perhaps also some cytoplasmic factors in the egg, which are often ultimately be attributed to the *maternal* genome) functions as an instructive cause of the generation and/or maintenance of particular structures, functions, or features of the organism. All other factors, partitioned from the category of the genetic into the category of the environmental, are deemed to be merely permissive. They are the background conditions that allow these structures and functions to develop, but have no directive or creative role in those processes. This view, which has been prevalent either implicitly (as background theoretical assumption) or explicitly in biology throughout the twentieth-century (Gilbert, 2003), has come under criticism both within and without the biological sciences in the last few decades (Lewontin 2001, Oyama 2000b, Griffiths and Stotz 2013). However, despite seeming philosophically, theoretically, and even empirically robust, many of these challenges have suffered from not seeming to be amenable to the advocacy of concrete changes in scientific practice, either through the suggestion of a particular experimental programme, or new methodological precepts or norms. Too often, the proposal of a new way of conceiving development and the relation of causes in a complex four-dimensional way, while seeming plausible in the abstract, has been viewed by many scientists as obscurantist once the problem of operationalising these visions becomes manifest. So I believe that a bridge must be built linking the conceptual with the practical and concrete. I will do this by linking the central role of norms and controls in the processes of abstraction lying at the heart of experimental practice to the way in which causal attributions concerning

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<sup>132</sup> New forms of epistemic objects in modern biology in particular, including the processes of development, and how they relate to variation in terms of its generation, maintenance, and form, are linked with increasingly prominent questions which blur the lines between the study of development, of heredity, and of evolution.

organismal development are made. I do this in the next chapter using Woodward's work on the three ways in which causes in the biological sciences are assessed: stability, proportionality, and specificity (Woodward, 2010).

## **Chapter 7 – Normal development, experimental systems and causation**

### **7.1. Introduction**

In the previous chapter I posited normal development as a technical condition (incorporating methodological norms) in experimental systems used to investigate organismal development. In this chapter I expound some consequences of this view. The task will be to establish a link between the nature of normal development as a technical condition within experimental systems, and more ontological conceptions of normal development and variation in development, which arise from and reinforce the methodological norm. I shall do so first by developing the Rheinbergerian approach I have adapted for my purposes throughout the thesis, by assessing the role methodological norms such as normal development have in experimental systems, and how such roles change in mutual adaptation to the changes occurring elsewhere in an experimental system. I then examine how methodological norms might not change in a way that ensures such mutual adaptation, due to conservative processes that counteract the dynamic changes in experimental systems identified by Rheinberger.

I then move on to the analysis of causation, by clarifying how technical conditions relate to the attribution of causal factors in development. I establish important links between the role of normal development in experimental systems and the sorts of empirical and theoretical products of such systems. This requires a discussion of how biologists assess candidate causal factors in the systems they study.

The ability to successfully identify the causes of phenomena is central to the scientific and social worth of the biological sciences. However, the phenomena biologists deal with – not least, the complexity of the development of organismal form – often means that factors in biological systems are not merely partitioned into the categories of cause and non-cause. Instead, different candidate causes are considered to have more or less weight. One influential way of assessing the extent to which a proposed cause is relatively strong or weak has been



proposed by James Woodward (2010), and I provided an account of this in chapter 1.

I use Woodward's work as a basis for examining the role of normality as a technical condition. It is useful partly because of its influence and its use as common ground for opposing sides in a debate concerning causal attribution (Waters, 2007; Griffiths and Stotz, 2013), but also because I am concerned with processes – such as the process of development – and Woodward's account centres on causal processes. By examining Woodward's analysis of causal attribution, I demonstrate the intimate reciprocal relationship between the epistemic and the ontological, and suggest how this relationship might be transformed in developmental biology by changing the approach to producing, distributing and using normal development in comparative and experimental studies of development. The three attributes of stability, proportionality and specificity are strongly linked to whether some factor is attributed to be instructive or permissive. They help constitute explanatory frameworks in which the various factors relevant to and concretely involved in development are partitioned in terms of the instructive-permissive distinction. How the three causal attributes are used is not given, or logically necessary, but structured by the way in which norms are produced and integrated into overall experimental set-ups. They therefore provide an indication of how this entire theoretical-material-practical system might be reformed, given changes to any one part of the system. This would be an example of a supplementation (Rheinberger, 1997: 4). My task will not be to dictate the changes to this system from the outside. Neither will it be to simply describe what is going on. It is to introduce into the discussion a way of conceptualising the relations between theory and practice, drawing on the historical case I have outlined and analysed throughout this thesis as well as matters arising in modern developmental biology. The aim is that this will provide the critics of certain dominant (gene-centric, reductionistic, context-blind) ways of conceptualising and investigating development with ways in which they can bridge the gap between their abstract accounts, and the practical demands of scientists who need to continue producing and reproducing productive experimental systems.

## **7.2. Normal development as a technical condition**

In the previous chapter, I outlined the role of normal development within experimental systems. Operating as a technical condition, together with others, as a methodological norm it helps to provide the stable context within which the unstable and uncertain epistemic object can be framed. How does it do this, and how does this change over time? The short answer to the first part of the question is that it does so by providing a stable, standardised comparator against which the outcomes of experimental interventions can be compared and measured. In this section I develop this short answer, and in the process detail how normal development as a technical condition also primes observation and interpretation within the experiment, to guide the shaping of the epistemic object before the experimenters, and also guide the process of question-generating in and from the experimental system. The short answer to the second part of the question is that, in a successful and productive experimental system, change occurs by epistemic objects becoming progressively clearer and more stabilised, and becoming worked into the technical conditions of succeeding manifestations of the system. When the experimental system changes like this (new questions being generated, some of these tackled; technical conditions and epistemic object in a state of flux) the parts of the system must change to maintain a state of mutual adaptation. The function towards which the system must be adapted is the ability to appropriately frame the new epistemic object (to properly answer the new questions generated by previous iterations of the system), to be sufficiently stable to do so, and to keep generating new relevant and productive questions. Furthermore, the system must be flexible enough to be able to continue to generate surprise.

### ***7.2.1. Normal development as part of the technical conditions, and relationship to epistemic objects***

Experimental systems centre on the relationship of technical conditions, “tools to produce answers about epistemic objects” (Green, 2013: 171) and epistemic objects, objects of investigation. In experimental systems, technical conditions (the technical assemblage) provide a relatively stable and controllable context for the investigation of the epistemic objects. As the epistemic object is by

definition “what one does not yet know” (though one knows there may be something interesting to know), they are less controllable and therefore less stable (Lenoir, 2010: xiv). In the previous chapter, I argued that in Wilson’s 1892 *Amphioxus* experimental system, the boundaries between epistemic object and technical conditions (especially the technical condition of normal development) were far more blurred and porous than in more mature experimental systems. This should not blind us to the reciprocal interrelationships between technical conditions and epistemic objects in more mature systems, nor to the dynamic process by which the epistemic objects of yesterday are sufficiently (though not necessarily completely or even adequately) understood and controllable enough to serve as the stabilised technical conditions of today.

I will discuss shortly a key aspect of the relationship between the technical assemblage and epistemic objects, the fact that the technical conditions which constitute a technical assemblage must operate and mutually adapt to each other and to the assemblage as a whole to frame a given epistemic object. Any changes to a technical assemblage, such as change to an existing technical condition, or the removal or addition of technical conditions, should therefore lead to a change in the technical assemblage as a whole, through changes to the other existing technical conditions, and the relations between them. We would expect the technical conditions (and the technical assemblage as a whole) to adapt in response. We might also expect such a response as a result of a change in epistemic object.

Wilson’s production of a normal development from scratch, albeit incorporating some knowledge of the embryonic development from Hatschek and other predecessors, was provided as an example of what I called a proto-technical condition. This is a technical condition in the making, one that serves as a technical condition by virtue of its relative stability compared to the epistemic object, rather than any absolute stability by a defined standard. Wilson’s normal development encompassed a wide range of early embryonic development, was functionally defined, but did not succeed in becoming part of other experimental systems, even if other embryologists such as Willey and Conklin acknowledged the polymorphic cleavage he found.

In the mid-twentieth century, the reference standard version of producing and using normal development, and the normal stages and standardised model organism strains associated with that, became a fundamental part of the technical conditions of modern experimental systems in developmental biology. Cheryl Logan has observed in her work on standardisation in experimental biology in the early-twentieth century, that “as procedures and instruments became more standard, the objects they measured had to be just as standard” (Logan, 2002: 354). Procedural standards, and standards such as normal series, demand standardised organisms which complied with those standards. The reference standards were and are external community-wide standards (and resources) to which the individual scientist must be initiated and accommodated, rather than being a control established by an individual scientist or team for the purposes of one or a series of experiments (Ankeny and Leonelli, 2011: 317-318). Normal development in its reference standard form is therefore able to travel further, and be incorporated into more experimental systems, in a way that Wilson’s normal development was not. It means results are broadly comparable between laboratories, and this enables communication and cross-fertilisation across developmental biology, and also between different disciplines and fields incorporated into various model organism communities (Ankeny and Leonelli, 2011: 318).<sup>133</sup>

### **7.3. Change in experimental systems – mutual adaptation and maladaptation**

Mutual adaptation of the parts (the individual technical conditions) of the technical assemblage is required to provide a coherent frame to investigate the epistemic object, given that the technical conditions interact and sometimes overlap. Like nature, a well-adapted, functioning experimental system does not arise purely by chance, nor by design. François Jacob memorably invited us to consider that Nature “works like a tinkerer who uses everything at his disposal to produce some kind of workable object” or *bricolage*, without there actually

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<sup>133</sup> Though the issues of comparability, reproducibility, and verification are extremely vexed, the community does all it can to standardise as many of the variables which could lead to failures in living up to those scientific virtues.

being a tinkerer, or *bricoleur* (Jacob, 1977: 1163). To produce the *bricolage* of an experimental system does involve *bricoleurs*, however, the scientists attempting to produce a successful experimental system. This process will involve modifying technical conditions, adding new ones, subtracting others, and relating them to each other (spatially and temporally) in different ways.

Hacking envisages an “interplay” of the “elements” of a laboratory science (which he divides into fifteen categories of “ideas”, “things”, and “marks”), a “mutual adjustment.” If we characterise the laboratory sciences as generating successive experimental systems, these elements constitute the technical conditions, or parts of them.<sup>134</sup> In the process of the operation and progress of an experimental system, these “plastic resources” can be reshaped to fit the changing requirements of the system, a change in the epistemic object for example (terms, but not translation into the language of experimental systems, from Hacking, 1992b).

Andy Pickering also speaks of “*plastic resources for practice*” [italics in original], and he argues “that experimental practice should be understood in terms of the deformation and moulding of such resources, with the objective of achieving a three-way coherence [involving material procedures, instrumental models and phenomenal models] in which facts are sustained.” The process of making an experimental system work, to produce a fact, or give shape to an epistemic object, is described as “interactive stabilisation”, a term which stresses “the interdependence of the three elements of practice, the mutual credibility that each element bestows on the others when coherence is achieved.” Coherence is the point at which the elements of the experimental system function so as to “hang together and reinforce one another”, to allow the system to do its work generating data, phenomena, surprises and knowledge. Coherences are hard-won however: “the end points of struggles against incoherences in experimental practice, and are always liable to come apart in future practice.” This is where the need to stabilise them originates, to accommodate them to the “*resistances arising in the material world*” [italics in original] which are aspects of nature or the material world, which to produce coherence must be discovered, controlled,

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<sup>134</sup> Hacking’s elements may form part of a given technical condition, be shared with another technical condition, or actually be such a technical condition.

eliminated, harnessed, or accounted for. Coherence is no guarantee that the elements of the system are indeed right, but only that they fit together in a way that engenders confidence in the knowledge produced by the system (Pickering, 1989). An apparently productive and successful experimental system is no guarantee of the correctness of any of the assumptions built into any one aspect of it.

Like the integrated organism, with parts mutually adapted by a tinkering process of evolution, the integrated experimental system, or the technical assemblage, is an integrated mutually-adapted whole which, nonetheless, is an open system amenable to external influence. It also possesses its own internal – developmental, one might say – drivers of change.

Consequently, when one element of the system changes – the epistemic object for instance, or one of the technical conditions – so must the whole change. As a result, the parts in turn need to change, needing to be tinkered to frame the new epistemic object, to be mutually adjusted to function as a technical assemblage as a whole. This is the source of the principle of “supplementation” which Rheinberger identified for experimental systems – that adding, subtracting, or changing one element would – or at least should – change the whole (Rheinberger, 1997: 4).

Rheinberger acknowledges that, as a result of the process of the continuation, bifurcation, and hybridization of experimental systems, “technical objects become integrated as stable subroutines into other, still growing experimental systems.” But as a consequence, this may generate “a historical burden” constraining the future development of experimental systems. However, he claims that these historical elements, if they begin to block the progress of experimental systems, are usually “completely replaced by subroutines that embody the actual stabilized knowledge in a subtler way” (Rheinberger, 1997: 80-81).

I wish to question that claim, at least insofar as it applies to aspects of modern biological research. Rheinberger’s account, and mine so far, has focused on the dynamic aspects of the process of changes in experimental systems. This focus is a strength of the experimental systems approach, but I wish to direct attention

instead to the potential role of what I term 'conservative forces'. These conservative forces (in contrast to the dynamic ones) may entrench certain technical conditions and leave them less able to mutually adapt to changes in the experimental system and technical assemblage as a whole. Such entrenchments would become a problem if they cause the system to stop generating surprises, as the use of an entrenched constellation of technical conditions would reduce the capacity of scientists to frame different epistemic objects.

Here I outline some of the conservative forces, with examples relating to normal development. These are 'sunk costs' and weight of infrastructure, resources, training, expertise, standards, and theory.

As we have seen, normal development is something of a composite technical condition. It overlaps with other technical conditions such as model organisms, normal stages and the 'human capital' of scientific research, the training, experience, and skills of scientists and technicians themselves, as well as their empirical and theoretical knowledge and commitments. In economic theory, 'sunk costs' – prior investment, for example to produce a piece of infrastructure such as a building – should be irrelevant in considering whether, for example, for particular purposes, the building should be renovated or torn down and a new one built in its place. The only consideration is the money to be spent now on that project, and the costs and benefits calculated to be associated with either option. In life, however, if not in economic theory, things are not quite so simple. The builders and users of the existing building may have very good (if intangible) reasons for preferring renovation over demolition, and the desire to retain things which took resources and effort to construct and maintain is understandable. Decisions are never devoid of context or consequences, and are seldom made on the basis of one criterion. For example, for environmental reasons, it may be preferred that no new building takes place, and that the old buildings should instead be renovated.

Similarly, in scientific research, sunk costs are not irrelevant. It takes time and effort to produce the infrastructure (material, communicative, intellectual and human) to produce the technical conditions that form part of experimental systems. It would take quite considerable effort and upheaval to abandon such

infrastructure, or change it sufficiently to accommodate the need to constantly transform technical conditions, in response to changes in the wider experimental system. The training of scientists takes many years, and the resultant skills and expertise are hard-won. Using them is both satisfying (to the individual scientist) and productive (Leonelli, 2009), so they should not be abandoned lightly. Tacit and embodied knowledge and skill is not easily learnt, nor can it be acquired by everyone exposed to new training.<sup>135</sup> Sometimes old dogs cannot learn new tricks (at least not very well, or quickly), and not everyone may have the talent or commitment to do so, even when young. Scientists are not an unlimited resource, funding for training is finite, and the skills, experience and knowledge that scientists have is not easily transferable or transmittable.

Whole industries are built around certain pieces of equipment, the production of particular strains of mice, or zebrafish, or *E. coli*. The development of new industries for new technical conditions cannot happen overnight. The drive towards standardisation had good reasons behind it, and it produced its own momentum, which is difficult to shift. Standards take time, effort and resources to produce, and to be agreed, accepted and disseminated. It is not clear that standards, or the resources and communities associated with them, can be, or should be, abandoned for new ones. Resources and institutions are often available and able to maintain and reproduce elements of a technical assemblage, but new elements require high initial start-up costs for which money, people and time may not be available. In the next section I deal with the role of empirical and theoretical entrenchment of technical conditions, and its consequences.

Furthermore, given the difficulty of making an experiment work – selecting the sort of epistemic object, and producing and maintaining the sort of technical assemblage which is productive – there is a push toward stabilisation of the system. As Hacking observes, speaking about the “elements” of an experimental set-up in laboratory science, all of them “and more can be

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<sup>135</sup> Burian (1993: 360) notes, along with Clause (1993) and Kohler (1994), the extent of the investment required to establish new organisms for research (particularly to produce a standard which is fit for experimental work in a number of different contexts), and also the accumulation of empirical knowledge, protocols and experience required to interpret results from these standardised systems.



modified, but when each one is adjusted with the others so that our data, our machines, and our thoughts cohere, interfering with any one throws all the others out of whack.” It is for this reason that fields “mature”, and stabilise. This occurs when “A collection of kinds of instruments evolves – an instrumentarium – hand in hand with theories that interpret the data that they produce.” A consequence of this is that “data uninterpretable by theories are not generated” and consequently, “[t]here is no drive for revision of the theory [or, indeed, the associated instrumentarium] because it has acquired a stable data domain” (Hacking, 1992b: 55). One need not accept this in full to realise that stability (or obstruction, or ossification) of an experimental system, or at least its technical assemblage, may occur due to the limiting of the type of data produced by a given assemblage. Similarly, this stability may limit the type of data thought relevant to forming the establishment of new epistemic objects, the stabilisation of old epistemic objects, and the reproduction of technical assemblages (Donaghy, 2014, makes a similar point concerning the use of data in building mathematical models of metabolic systems).

There are therefore plenty of good reasons why technical conditions may endure, and these reasons may confound their easy replacement or modification as part of the normal dynamics of the progress of experimental systems. The questions this poses are: Does this potential entrenchment matter? Might established technical conditions find themselves out of sync with the rest of the experimental system? Might they become out of sync with new epistemic objects, other technical conditions, certain theoretical backgrounds? Also, does this entrenchment occur, what forms does it take, and do we have good reason to counteract such powerful conservative forces and also advocate the forcible alteration of a technical condition, such as normal development? If the dynamic processes associated with experimental systems fail, then surely intervention from outside (to unblock the process of the replacement of subroutines) is necessary. This is an example of how the articulation of the experimental systems approach might lead to the generation of some means for scientists to assess the dynamics and progress of experimental systems, with a view to identifying potential entrenchments and problems, to enable them to selectively and purposefully intervene to reform the assemblage.

The engineering-evolutionary epistemology of William Wimsatt can guide us here. He has identified “generative entrenchment” as a key feature of evolving systems, and proposes that “[a] deeply entrenched feature of a structure is one that has many things depending on it because it has played a role in generating them” (Wimsatt, 2007: 133-134). Furthermore, different parts of a structure – or system – can be differentially entrenched. I have spoken of the evolution and progress of experimental systems throughout this chapter, but have so far not proposed that experimental systems undergo some form of selection process, or can be considered to evolve or adapt to forces outside of it.

My talk of adaptation thus far has been more that of a Cuvierian correlation of parts than a Darwinian adaptation to external conditions. In my account it has been the correlation, not adaptation, to external conditions that is important. However, this does not discount the possibility (indeed the probability) that much sense can be made of the progress (not necessarily in terms of improvement, but in terms of continuation with change) of experimental systems in this evolutionary sense of selection acting on systems with differential adaptation, robustness, stability and fecundity. The ‘environment’ would be the scientific community, which selects particular experimental systems, or succeeding experimental systems. One way it selects is by opting for those which seem to answer questions deemed relevant and important by sufficient numbers, although not all parts of the community have an equal role in this, the disbursers of funds and appointments being key actors. There are other features which may make an experimental system more amenable to being ‘selected’. One would be the greater capacity to generate surprises (a dynamic rather than conservative force). Another would be that it not require significant additional resources to continue, or to have an overwhelming justification for the production of new or modified technical conditions. Finally, an experimental system may be more likely to be ‘selected’ if it is productive and possesses a significant degree of internal adaptation – or in Pickering’s terms, coherence.

Wimsatt emphasises the importance of the robustness and stability of structures and systems. That arrangement and interrelation of parts (in spite of various changes that are impinged upon it) must be able to be maintained in roughly that form, or occur in the normal progress of the system. The system may be

adapted to external conditions, as well as possibly being internally mutually adapted (or maladapted). As Wimsatt relates: "Systems shaped by selection processes show significant degrees of adaptation, so things that become entrenched in them are commonly elements or parts of functional designs. If the system were not at least moderately well adapted, messing around with deeply GE'd [generatively entrenched] parts of it might not be so strongly selected against." He continues: "Robust or fragile, if many other things depend upon it, it is then "essential" or at least conditionally "necessary" for what it does, so structures that survive leave it unchanged or only very slightly modified" (Wimsatt, 2007: 134). If the external conditions have selected for internally coherent, adapted, and stable configurations of technical conditions, the other technical conditions will depend on the technical condition of normal development.<sup>136</sup> Changing it or removing it would occasion a transformation, or possibly a crisis, of the whole system. The only alternative to this picture is a more modular view of the technical assemblage, in which individual technical conditions may be changed or removed without having much of an effect on the other technical conditions, or the technical assemblage as a whole to any significant extent. However, the fact that normal development as a technical condition has co-evolved (and co-varies) with other technical conditions (such as model organisms, handbooks, and experimental designs) and that there is overlap between these technical conditions, suggests that experimental systems involving normal development are rather more entangled than modular.

This demonstrates how, if normal development becomes a problem in some way, as I intend to suggest it has, it will be difficult to reform or shift. But not impossible to reform or shift. Wimsatt's metaphors between the entrenchment in (natural) evolutionary processes and the processes by which elements become entrenched in cognitive and cultural (and architectural) structures can only go so far. The engineering approach, focused on tinkered fixes, which seems to be how natural evolution proceeds, also allows for the complete stripping down and re-construction of structures. If one element is no longer available, or desirable, a new structure or system can be designed to function without it. It may require

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<sup>136</sup> In the sense that because of mutual adaptation, all other technical conditions depend on any given one.

considerable toil to get the new system to work, but if it needs to be done, an engineer will probably manage it.

Wimsatt makes the wry but serious observation that “Scientists rarely do foundational work, save when their house threatens to come down about their ears. (Philosophers like to mess around with foundations, but preferably in someone else's discipline!)” (Wimsatt, 2007: 137). In other words, speaking in terms of the framework within which I have worked in this chapter, scientists will only radically transform a system when it is needed, because it is no longer productive of surprises or questions, for example.<sup>137</sup> The system may be producing inappropriate results, not generating the sorts of questions that the scientists can actually make much use of (the surplus yields fewer and fewer progressive leads we might say), but as long as it is still functioning to some extent it will be tolerated. The house may be riddled with damp, but to tolerate it is possibly the only option. Philosophers, on the other hand, are therefore in a position to observe and point out maladaptations, blocks, or epistemological obstacles. Scientists, because of their alternative enculturation and perspective, may not be able to see these in quite the same way.

There are many different ways in which any one technical condition or the technical assemblage as a whole can be a problem: obstructing discovery about the epistemic object, constraining questions that can be asked using experimental systems, being out of sync with the theoretical background, and being out of sync with the conceptual or material aspects of one element in the technical assemblage, or the rest of the technical assemblage as a whole.

#### **7.4. Empirical and theoretical consequences of the role of normal development**

The role of a technical condition is to “set the boundary conditions of experimental systems and in the process create the space in which an epistemic object can unfold” (Rheinberger, 2010a: 218). As a result, “technical conditions determine the realm of possible representations of an epistemic

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<sup>137</sup> I am using more of an organismal metaphor of interacting and interrelated parts, rather than the foundations and building metaphor of Wimsatt.

thing” or object (Rheinberger, 1997: 29). The technical assemblage therefore plays a key role in shaping empirical data, theoretical knowledge, and future technical conditions and subroutines. The nature and arrangement of the technical conditions and their mutual establishment of the space, stage, and boundaries is therefore crucial. Not only for future experimental systems, in terms of their technical conditions, the new epistemic object, the questions generated and chosen, but also for the theoretical background which informs all of that, and the interpretation of the products of an experimental system, such as the data and phenomena that is observed (and what is observable, of course).

Instantiations of normal development as a technical condition in experimental systems in modern developmental biology involve, as we have seen, an abstraction of variation at various points in its production. This includes the choice of a limited number of model organisms, the selective breeding of those organisms to produce strains possessing limited variation and insensitivity to environmental conditions, the theoretical background which is based on the instructive-permissive distinction, and the foregrounding of empirical results which confirm and extend such a distinction. This is not to say that generating and recording variation is not relevant to model organism-centred research. Indeed, often one of the first stages in the production of a particular variant or strain of a model organism is to identify the level of some type of variation it can be made to exhibit, often as a result of induced mutations. For example, in *Drosophila melanogaster*, workers in T. H. Morgan’s laboratory screened the myriad flies produced by the so-called “breeder reactor” for mutants (Kohler, 1994). In zebrafish, a useful model organism in developmental biology due to the range of mutations exhibited, mutagenesis screens were used to identify mutations and their relative frequency at certain loci (Meunier, 2012). However, such practices, which identify, map, and assess the significance of variation, are limited to a particular type of variation, namely genomic variation. One does not have to adhere to the thesis of causal parity or causal democracy (Oyama, 2000a) to acknowledge that to investigate and explain particular developmental events or phenomena requires reference to entities or processes, and the variation thereof, which do not refer back to the genome or relevant genomic variation. Even if one held that the genome was somehow causally special, by

exhibiting and possessing a higher magnitude of causal specificity, stability and proportionality, it would not always be practical to give a causal account solely in terms of the genome and its variation. There is therefore a need for the strategy of identifying and mapping variation in the production of particular variants or strains of model organisms to be generalised to other forms or types of variation, as well as genomic variation.

In chapter 4 I demonstrated that the particular way in which Wilson produced and conceived of normal development led to a different framing of the epistemic object – the processes of development – than Driesch and Roux. Key to this was not only his own role in generating it, but also the range of variation included within it. This provided him with a more sensitive test of whether and how his experimental intervention made a difference to the courses and results of the developmental processes. It also allowed him to assess the causes of the variation he saw in the embryonic development of *Amphioxus*.

For Wilson then, his technical conditions allowed him to embrace the variation in developmental processes revealed in his results. Conversely, the need to standardise and strictly control the technical assemblage mean that scientists are pressed to try and reduce variation in technical conditions, and also in the consequent observed data and phenomena which give shape to the epistemic object. Various procedures are employed to try and deal with variation – re-calibration, re-orientation and re-running of the technical assemblage, or manipulation of the results to remove the variation considered to be due to various possible sources of error. These kinds of experimental systems are therefore set up in such a way that when they do generate ‘surprises’ in the form of variation presenting itself when it ‘shouldn’t’, potentially posing questions about the source and significance of that variation, such surprises and questions are unwelcome, and are discarded by the experimenters along with most of the rest of the ‘surplus’ generated by the system. Furthermore, they are less likely to actually produce variation, or have as an epistemic object, some thing or process which instantiates variation or variability as a core property. It would not be chosen, nor would it be framed in such a way by the technical assemblage which has evolved from preceding iterations of the experimental system. This is not necessarily a problem. A surplus of questions

is always generated by experimental systems, and only a few can be pursued. Therefore even if only a small subset of generated questions may lead to the framing of an epistemic object which does instantiate variation or variability, it would be possible to explore these. If variation and variability are key concerns of some group or groups of experimentalists, however, such a system will not be productive of a high number of relevant questions.

There might be a further problem if the reproduction of the technical assemblage, as part of the progress of experimental systems, reproduces the assumptions and biases of it (in total, and of constituent elements) too faithfully, by re-confirming in the empirical results the material and intellectual background underlying them. This may occur, for example, through the processes of abstraction used in the production of normal development. The cycle of experimental practice from the production of an experimental system involves interpreting results and selecting new questions from the surplus generated and producing or reproducing succeeding experimental systems. This cycle raises the possibility of the transformation of a methodological precept into a theoretical or ontological one, through its framing of successive epistemic objects in such a way that it comes to colour (or, perhaps, solidify) the theoretical background and the technical assemblage. This would explain the slippage of normal development from methodological element to something more ontic.

But I need to demonstrate exactly how this process might occur. I do so in the next section, where I consider the establishment of causal accounts and attributions as a key product of experimental research. Such attributions of causality underpin many technical conditions, the relationship of these conditions and the technical assemblage to the epistemic object, the interpretation of results and the selection of problems. An analysis of causal attributions, and the role that aspects of normal development as a technical condition might have to play in it, is therefore an essential part of the argument in this chapter.

## 7.5. Assessment of causal factors in development

Woodward identified stability, proportionality, and specificity, as three interrelated attributes of causal relationships. Stability is the criterion which depends on a “relationship of counterfactual dependence” which holds against a range of changes in background conditions. A causal relationship can therefore be more or less stable depending on the amount of changes to background conditions that can occur while the relationship still holds (Woodward, 2010: 292). Proportionality is simply the criterion that the level of explanation or causal account is appropriate to a given *explanandum*. That is, it is not too broad and general, or too narrow and particular. Any posited causes must fit with their effects (Woodward, 2010: 298). Woodward identifies two notions of causal specificity in the biological sciences. The first is that a cause is specific if it has a fine-grained influence on the effect, the second “that a causal relationship is specific to the extent that a single (type of) cause produces only a single (type of) effect, and to the extent that each single type of effect is produced only by a (type of) single cause” (Woodward, 2010: 308). Woodward frames the second sense of specificity by asking whether it is “the case that within the specified range of kinds of effects, a particular kind of cause produces only one kind of effect from that range and is it the case that for a given effect, it is (capable of being) caused only by a single kind of cause within some pre-specified set of alternatives?” (Woodward, 2010: 311). He answers this by stating that “C will be a more (rather than less) specific cause (in the one to one sense) to the extent that it causes only a few different kinds of effects within a pre-specified range” [*italics in original*] (ibid.).

In chapter 1 I delineated the connections between the three criteria. But as well as their more logical interrelation, one must also acknowledge that they are not assessed separately when a potential cause or causes are considered.

Together they form part of the more or less intuitive apparatus with which biologists (and non-biologists considering biological work or systems) approach a particular proposed causal mechanism, or the design of experiments, or a wider programme of work to examine the causal mechanisms at play in a particular biological system of interest. In the next section, I examine how these criteria link the ontic (attributions of causality) with the practical, with a view to



assessing the ways in which such criteria are (implicitly, or explicitly in different ways from that in which Woodward detailed them) conceived and employed in the generation of questions, experimental situations, observations, interpretations, and the communication of new biological knowledge.

In previous chapters, I gestured towards Woodward's account, and linked it with the idea that the processes of ontogenesis can be (and are) partitioned into instructive *causes* and permissive *conditions*. Specifically, when a factor is labelled instructive, it is because it possesses the linked attributes of biological causation in a stronger sense than other comparable factors. It is deemed to be more specific and more stable. Permissive conditions are deemed to be less specific, and less stable. However, although, as Woodward argues, "a concern with whether causal relationships are specific, stable and so on arises in a very natural way in many biological contexts" (Woodward, 2010: 288), I argue that the way in which causal relationships are investigated and framed are dependent on the particular context or set of contexts in which the investigator or investigators are operating. That is, the experimental system. I therefore establish a link between the epistemic nature of normal development as a methodological norm operating as a technical condition within experimental systems, and an ontological conception of normal development and variation in development, which arises from, and reinforces, the methodological norm. Of course, experimental systems are not hermetically sealed, and they generate surprises. There are, therefore, possible countervailing forces to the process of entrenchment just sketched.

The criteria of specificity, proportionality, and stability can only be assessed relative to a given context. The way in which a causal relationship is deemed to be stable, proportional, or specific, depends on the system, relations of interest, and experimental set-up. For example, Woodward acknowledges that in the event that a causal relationship cannot be assessed against a complete and exhaustive range of "background conditions", "we rely on (i) subject matter specific information to tell us which sorts of changes in background circumstances are most "important" for the assessment of stability and/or (ii) attach particular importance to stability in background circumstances that (again perhaps on the basis of subject matter considerations) are regarded as "usual"

or “normal” (Woodward, 2010: 292-293). More pragmatic considerations of what background conditions can be identified, controlled, recorded and measured may also affect which background conditions are used to assess the stability of causal relationships.

These considerations are present when assessing proportionality. Woodward observes that “which level (or levels) is (are) most appropriate will be in large part an empirical, rather than a priori matter – empirical in the sense that it will depend on the causal structure of the situation under investigation.”

(Woodward, 2010: 297). Furthermore, Woodward emphasises that “the investigator’s purposes, and in particular what it is that the investigator wishes to explain or understand should also influence the choice of level” (ibid.).

Therefore, the question that the investigator wants answered, the problem solved and the *explanandum* sought, sets the level at which the criterion of proportionality then determines whether a putative cause is a ‘good fit’.

The role of the investigator in establishing the level at which an explanation is sought is also crucial in considering how specific a cause is. The disagreement between Waters and Griffiths and Stotz hinged on the different effect they used as an example. For Waters the effect was the sequence of nucleotides in the precursor m-RNA, and therefore only DNA had any causal specificity. For Griffiths and Stotz, considering a polypeptide or a functioning protein as the effect of interest means that, alongside DNA, factors other than DNA can be deemed causally specific. Woodward notes that, for the second notion of causal specificity, specification of a restricted range is required. He observes that “it will often be intuitive enough what sort of range is reasonable and non-artificial in particular cases.” (Woodward, 2010: 311). This “intuitive” sense requires unpacking, and linking to the way in which norms are generated, reproduced and used by scientists, working with particular experimental systems.

To start with, it harks back to the discussion of normal development by Michel and Moore cited in previous chapters, that “[i]ntuitive definitions of normality maintain certain assumptions about the individual, the environment, and the types of processes that create the individual’s behavioural repertoire (including the symptoms characteristic of abnormality)” (Michel and Moore, 1995: 411). This can be extended to encompass other sorts of assumptions. Given the role

of the management of variation in normal development, assumptions concerning the extent and significance of biological variation in objects and processes of interest are likely to be central. It will not be crucial here to establish the precise processes by which such assumptions underpin an intuition of normality in scientists, merely to note that such an intuition is present, and the form in which it currently takes. That said, it is important to note that there may be multifarious means by which assumptions and intuitions concerning normality are transmitted, generated, internalised, and reproduced. These may range from: the wider sociological context (the concept, with normative load, of normality engendered by State bodies in the nineteenth-century for example, see Hacking, 1990); the exigencies of scientific communities (the need for reproducibility and the establishment of 'objectivity' driving efforts to standardise scientific objects such as reagents, strains, and so forth, see Porter, 1995); the reciprocal relationship between epistemic activities and ontological principles (identified by Chang, 2009); the greater ease of controlling 'environmental' conditions than internal, particularly genetic, conditions; and other reasons suggested in the course of this thesis so far.

As established by DiTeresi (2010), a current intuition concerns normal development as a reference standard – researchers are trained to work with particular model organisms (or, more precisely, particular strains of certain organisms) for which normal stages have been compiled. These model organisms come in standardised forms, with as much variation being bred out of them as possible (that is, within strains – there may be considerable variation between strains of the same model organism, as different strains are needed for different sorts of work). There is then a canonical reference form which represents the normal, and becomes internalised as the intuitive idea of the normal. Intellectually and materially, variation has been abstracted away. The experimenter will, with these organisms, change one or more variables, and observe the effects of the change against the reference standard, the normal development.

Given that the set of causal relationships (assessed to a significant extent by pre-existing norms and assumptions concerning normality) presumed to be strong support the elements and configuration of the technical assemblage, the

interpretation of the results generated by the experimental system, and the decisions made concerning succeeding epistemic objects and technical assemblages, the nature of one particular technical condition – normal development as a reference standard, for example – will play a key role in entrenching certain theoretical norms, and also methodological and epistemic norms.

In Wilson's research in the early-1890s, he became concerned with finding a way to ascertain the roles and relative significances of mechanical and inherited causes in differentiation and the production of particular cleavage-forms in early development. This led him to devise an experiment in which at different stages of development he manipulated the mechanical conditions experienced by blastomeres, and observed the effects of these manipulations on the pathways and outcomes of development. I have described how he created this experimental system, producing a proto-technical condition to frame his proto-epistemic object. He started not from a bifurcation of a prior experimental system, and was not working in a mature discipline. But he still brought theoretical norms (expectations as to the nature of development, and of the development of *Amphioxus* in particular) and methodological norms to the system. Both of these can be seen in the way in which Wilson designed the experiment around the two kinds of cause he expected to play a role, and in terms of which he interpreted the results to produce a modified version of the mosaic theory. Wilson's experimental system was nascent, not mature, and the causes he invoked were broad, opaque and abstract. Modern experimental systems exist in a mature field, and the causes they invoke are more concrete and well-defined. Despite this difference with my main case study, in modern experimental systems candidate causes are still investigated to ascertain their role in developmental processes; are assessed in terms of their specificity and stability. My case study demonstrated how normal development can come to be produced and used as a technical condition as part of an experimental system. It grounded my analysis of how normal development functions as a technical condition more generally, and finally it shows us that normal development can be construed and used differently. Modern experimental systems need to successfully frame their epistemic objects as much as Wilson's needed to, and did, at the dawn of experimental embryology.

## 7.6. Conclusion

I have established that normal development, as it is currently constituted as a technical condition, may in many cases be a block on the further progress of experimental systems. I have suggested that this might be the case where investigators seek to focus on biological variation and variability, which requires that the technical assemblage work to frame an epistemic object which might have an additional dimension of variability. This builds on my previous analysis of the role of normal development in managing variation, and the different ways in which different versions of normal development may lead to different strategies for abstracting variation. In the concluding chapter, I outline some burgeoning areas of research where the focus on biological variation suggests the need for a technical condition more sensitive to, representative of, and capable of representing and framing, epistemic objects involving a consideration of variation.

The main conclusion is therefore that even though many forces act against the change of entrenched technical conditions, such as normal development, in certain circumstances it may be necessary. How it might be done is quite another question, and it is beyond the scope of this thesis to provide a detailed and programmatic answer, but the case study of Wilson provides us with some possible indications. There are some additional indications that I would like to suggest. Firstly, there are already attempts to develop standards which encompass a considerable – more naturalistic – range of variation. One such example is the Standard Event System pioneered by Ingmar Werneburg (2009), which involves the identification of developmental characters, allowing scientists to identify which are present or not at various points in development, allowing intraspecific variation to be revealed within a standardised framework.

Technical developments in imaging and processing large numbers of embryos and new computational tools to automate the process of observation, measurement and analysis of samples, will enable scientists to better apprehend the level of variation present in nature or standardised strains. Additionally, it will allow them to collate enough results to allow comparison

between the variation of control treatments and experimental treatments, while having enough samples to ensure it is statistically significant.

The history and philosophy of biology has the potential to offer much towards this reconfiguration that I propose. Firstly, it is able to apprehend and identify the sort of epistemological obstacles that entrenched technical conditions, such as normal development, constitute. Secondly, it is able to bring a historically-grounded philosophical approach to key methodological problems by asking – and attempting to answer – new questions. I detail some of these new questions in the concluding chapter.

More concretely, my case study of Wilson has shown that normal development can incorporate a wide range of variation, and still successfully work as a tractable technical condition framing an epistemic object. It shows us that a different way of producing normal development is possible, for instance, by using a functional criterion.

The question now posed is to what extent should and can we, in modern developmental biology, take variation seriously methodologically, epistemically, and ontologically. This is the natural point at which this thesis leaves off, and the future work will begin, as I detail in the concluding chapter.

In the final chapter, I describe and suggest new ways of conceiving of normal development, and new ways of treating, abstracting and conceptualising variation, building on the lines of argument and approaches established in this and previous chapters.

## **Chapter 8 – Conclusion**

### **8.1. Key findings**

In my analysis of the assessment of causal factors identified as relevant to biological processes, I have elaborated on existing debates by discussing the role of normal development. I have been allowed to do so by the role allotted by Woodward to background conditions in attributing strengths or magnitudes to particular candidate causal factors. Background conditions are not external to the experiment, but a part of it. Technical conditions which serve to frame the epistemic object are there in part to background (and thus control and manage) certain conditions, and foreground (and thus manipulate and vary) others. This is the link between the Rheinbergerian part of my analytical framework and the Woodwardian part. The role of technical conditions in defining and managing (by excluding as well as controlling) the background conditions, helps us to understand how normal development affects the theoretical aspects of developmental biology by shaping how causal attributions are made. Critically, using my case study on Edmund Beecher Wilson, I have assessed how biologists form normal development as a technical condition in the experimental systems they devise, to allow them to make experimental manipulations in the processes of development, and to be able to make comparisons between embryos.

I have also demonstrated how causal attributions can be shaped by normal development in a particular direction, such as recapitulating the instructive-permissive distinction. Furthermore, I have shown how those causal attributions can lead in turn to the entrenchment of certain technical conditions, such as normal development. It is on the role of normal development as a technical condition, which I have considered to be in part a methodological norm (after Weber, 2005), that I focus in this conclusion.

In this thesis I have identified how (and why) a version of functionally-defined normal development comprising a wide range of early embryonic variation was generated by Edmund Wilson (1893), and what the effects of this were. I went on to compare Wilson's normal development to other manifestations of normal

development in the work of Hans Driesch and Wilhelm Roux, and also to other modes of normal development that have been identified more generally. As indicated above, I have analysed what role normal development plays in experimental systems and in attributions of causality.

In this concluding chapter, I identify some possible implications of this in the light of some new developments in the biological sciences, and end by pinpointing what questions are opened up by my work.

One of these implications centres on the distinction between instructive causes and permissive conditions, which was implicit in Wilson's 1896 definition of normal development. The instructive-permissive distinction was a crucial conceptual component of experimental systems in developmental biology from the twentieth-century onwards (Gilbert, 2003). It was complicated somewhat by the discovery of induction by Spemann and Mangold ([1924] 1974) and related work, but was raised again to prominence with the rise of genetics, and the advent of developmental genetics. This is a simplification of a rich historical picture of course. But what is not in doubt is that by the end of the twentieth-century, something approaching a theory of development had arisen in which differentiation (as the central organising principle of development) was driven by differential gene expression. In principle, if not in practice, organismal development could be reduced to the genomes of an organism and its mother.

It is on this role of DNA and the genome that some of the analyses of biological causality that I have described and used in this thesis have been elaborated. Empirical, theoretical and philosophical problems with the instructive-permissive distinction have instead led to the identification of biological specificity as the key criterion establishing DNA as a special type of cause in biological explanations. This has animated discussions concerning the attribution of causality, and strength of causality, in biological systems. Woodward's manipulationist theory of causation has been used as a battleground, initially between causal selection and causal parity, and also for more finely-tuned debates concerning the location and distribution of biological specificity (Griffiths and Stotz, 2013, Waters, 2007; Weber, 2013). Many of these arguments, though dealing with processes such as the expression of DNA, RNA editing, and folding of proteins, seem to exclude temporality as a dimension or factor of



interest. They focus on processes which occur at unspecified times in an organism with no given history. While the implications for an understanding of development are apparent (and are sometimes made so), the examples provided are not explicitly *developmental* processes. They are not located in time, or assessed with reference to the production of a structure, or the ongoing processes involved in a structure. Additionally, they do not give any indication of the types of causal scenarios exhibited in more macro-level processes: in other words, the particular combination and timing of different types of causal specificity that might be involved. Producing a catalogue or taxonomy of causal motifs encompassing these different types of causal specificity might enable us to make progress in this endeavour.

In my assessment of normal development, I detailed what I called a taxonomy of norms, which I expanded by adding the individualised standard based on functional criteria used by Wilson. This demonstrated that in the early days of experimentation in embryology, there were different ways of managing variation. More than this, though, it allows us to detail explicitly the advantages, disadvantages, and biases associated with each of the norms. In this way, it provides us with the possibility of developing a resource along the lines of Wimsatt's catalogue of reductionist heuristics (2007). This would recognise their importance in scientific work, but seek to make explicit what role they play in shaping investigation and interpretation. Like those heuristics, they are only analytically separate; in practice two or more norms are likely to coincide in any one use of normal development as a technical condition.

The three prior versions of normal – essentialist, statistical, and reference standard – all found a place in scientific practice in embryology or developmental biology. The final normal, the one I identified, did not. The individualised abstraction of Wilson had the advantage of including within it a wide range of variation, defined as normal as a result of functional outcomes. It was therefore more sensitive to the exact effects of experimental manipulations. Producing the normal development himself allowed Wilson to really appreciate what was and was not important in the changes he observed. As an individual abstraction, however, it suffered from some of the same disadvantages as the essentialist normal. Furthermore, as a normal incorporating a wide range of

variation it was less tractable for further transmission and easy use in laboratories, unlike the reference standard. It was, to a large extent, a local standard which was labour-intensive to produce.

It is important to recognise, however, that although the taxonomy I have detailed provides four norms with certain characteristics, each of those norms is historically-situated and conditioned by contexts of use and production. The essentialist normal has a long history, but still has a history. The average or statistical normal derives from particular State and medical practices in the nineteenth-century. The reference standard normal relates to the rise and use of normal stages and model organisms. And finally, the functional normal arose in the context of Wilson's entry into experimental work and his recognition of the variability of *Amphioxus* development, which was an advantage for the particular questions he wanted to answer.

To be clear, the norms to which I have referred throughout the thesis are norms of a special type. That is, they are not broad, science-wide norms like Mertonian (and related) norms of science (Merton, [1942] 1973). They are activity-specific. These kinds of norms with which I have been concerned have been defined as "action-oriented prescriptions" (Alegre, 2013: 3229) or "an abstract principle that guides action" (Smokler, 1983: 129). Crucially then, the norms are guides (of a material and conceptual nature), or heuristics, which allow the scientist to focus on what conduct and information is necessary to achieve a particular goal. The norm, the guide to action or prescription, is designed for a particular goals or intended outcomes. The production and transmission of the successful norm must therefore ensure that it incorporates the right kind of guidance (but not too much) to ensure the scientist can use it. It is a tool, a technical condition, and one which, in the case of normal development, incorporates social (their formulation and dissemination, including education and training) as well as material (organism strains and normal stages) aspects and methodological prescriptions. I have focused on the latter two aspects, but also on the conceptual consequences of them. Just as the norms themselves must be understood in the contexts of their origin, production, and use, so must the advantages and disadvantages associated with them. These relate to the social and economic organisation of science, methodological and epistemic norms,

and material and technical infrastructure. There is therefore the possibility that new combinations of these norms, produced and operated in different ways, may preserve or amplify the advantages of existing or prior norms, and ameliorate some of the disadvantages. I explore this possibility in the following sections.

## **8.2. Implications for the analytical framework**

I now explore the implications of my work for the elements of the analytical framework I used in this thesis. Firstly, I have built on Rheinberger's experimental systems approach by taking it into previously unanalysed areas. Previously, the approach has been used to assess and characterise already mature fields of experimental endeavour. I have used it, instead, to focus on the advent of an experimental system in which the scientist – Wilson – brought techniques, questions, observations and experience from prior non-experimental work, rather than evolving his experimental system from a prior one. In many respects, Wilson's work with *Amphioxus* was an attempt to 'bootstrap' an experimental system. One of the key technical conditions, the normal development of *Amphioxus*, was generated as the experimental system itself was. Consequently, while the technical conditions of Wilson's experimental system were relatively stable compared to the epistemic object, in absolute terms they were altogether less stable than technical conditions in more mature fields, and the lines between his technical conditions and the epistemic object were considerably blurrier. A further development of Rheinberger's account was the discussion of the conservative forces which serve to entrench certain technical conditions in particular assemblages. I gave an account of how this could occur, and how it relates to other – theoretical – entrenchments as a result of bias in the sorts of questions generated by experimental systems and their filiations.

It was at that point that I was able to draw together the two main elements of the framework, and in so doing link the practices of biological research with the theory deriving from it and guiding it. The latter is the interpretation of the nature and specific details of the causal structure (including assessment of candidate

causal factors and relations) of biological processes of interest.<sup>138</sup> Woodward's work on causation is intended to be sensitive to the actual way that causes and causation are invoked and used by scientists. It is not, however, centred on the practical aspects of creating an experimental system and drawing conclusions about the relative weight of causal factors by interpreting the less than clear results of a series of experiments.<sup>139</sup> Conversely, while Rheinberger's deep engagement with exactly those practical details does yield a new understanding of theoretical developments in the biological sciences, it is not related to the causal aspects of biological theory. My thesis has attempted to use each approach to close lacunae in the other. By focusing on how processes of management and abstraction of variation in the practices and resources of normal development help create background conditions, we can more clearly assess how causal attributions are made in biology. Likewise, a focus on causal attributions can help us to further understand the consequences of what is produced by experimental systems. The practical and experimental turns in philosophy of biology have served to provide a counterbalance, a corrective, against the tendency to focus too much on theory. My work has aimed to analyse the relation of theory and practice using the intersection of the two main elements of the analytical framework of this thesis.

### **8.3. Implications for biological research**

In this section I identify two changes to the biological sciences that suggest that, in some cases, the technical condition of normal development needs reformulation and reintegration into new experimental systems. Firstly, I point to a shift in the organisation of some important new areas of research in the biological sciences towards a more naturalistic mode. The way in which biological research is being reorganised in this way undercuts many of the

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<sup>138</sup> The biological processes mainly being those of organismal development, the processes being of varying granularity in space, time, structure and function.

<sup>139</sup> Though, characterising his approach as a functional account of causation, he does claim that “[o]ne of the attractions of the functional way of thinking about causation is that it recognizes an important place for methodological considerations in thinking about causation” (Woodward, 2014: 701). This is undoubtedly true, and has allowed me to “evaluate methods of testing and reasoning, and concepts we employ in terms of whether they help us to realize scientific goals” by drawing upon elements of Woodward's work, but it is reasonable to say that it is still not central to Woodward's own work on causation (ibid.).

philosophical and practical objections to a more naturalistic mode of experimentation. Such a naturalistic mode would greater reflect natural variation in investigations.

Secondly, changes in the problems tackled in key areas of the biological sciences dictate that greater attention should be paid to biological variation. I provide examples such as evolutionary developmental biology (evo-devo) which show a greater interest in variation as something which investigators wish to explain, and examples where certain research questions demand that the experimental set-up itself be more sensitive to biological variation.

Following the discussion of these two changes, I outline the opportunities provided by various theoretical, empirical, technical and material developments in the biological sciences. These can be exploited and developed in taking variation seriously as part of an altered set of practices concerning normal development. To achieve this is not unproblematic, so I follow this by discussing the various obstacles that such an approach may face. I conclude by suggesting ways in which such challenges can be met, or at least begin to be tackled, and also outline the work that History and Philosophy of Biology can undertake to contribute. This includes, but is not restricted to, developing a programme of work to tackle various conceptual and practical issues concerning the nature of biological variation and its investigation.

### **8.3.1. A new naturalism?**

From the beginning of the twentieth-century, biologists have rigorously reduced the variation of factors present in the experimental systems they set up and use. When variation presents itself, it is often viewed as a source of error, and therefore identified and removed from future experimental runs, or removed in the process of post-experimental calculation, analysis, and interpretation (Carlson Jones and German, 2005). Such treatment of variation has been consistently criticised since the beginning of the twentieth-century, particularly by those adhering to the 'naturalistic' or natural historical orientation in the biological sciences (Mayr, 1982: 540-550; Michel and Moore, 1995: 383-392). By 'naturalistic' (and 'naturalist'), I mean the opposition to (and opponents of) conducting science in highly controlled artificial laboratory conditions, and

advocacy of working in less tightly controlled conditions more reflective of the context in which objects of study normally exist 'in nature'.

These naturalists argue that if objects and phenomena in the laboratory are managed in such a way that they do not reflect the conditions in nature outside the laboratory, no inference can be made between results obtained in the laboratory and what 'really happens in nature'. Ian Hacking has advanced a powerful argument against the naturalist objection to the stripping away of the richness and complexity of life to produce controlled artificiality in the laboratory. This is that "mature laboratory sciences are true to the phenomena of the laboratory", phenomena that may only be produced in the specially controlled conditions of the laboratory (Hacking, 1992b: 60). There is no easy inference from the findings of the laboratory to those of nature, and such an inference is not really the point.<sup>140</sup>

One way in which the results of laboratory investigations can help to understand and intervene in the world outside the laboratory is to "remake bits of our environment so that they reproduce phenomena first generated in a pure state in the laboratory," which, if the aim of knowledge is ultimately use-oriented, poses fewer problems in terms of translation from the laboratory to 'nature' (Hacking, 1992b: 59).<sup>141</sup> Furthermore, though in the laboratory we cannot replicate the complexity of nature nor produce general laws with applicability in natural situations, we can export from laboratory systems "somewhat invariant causal principles", which can be used to successfully understand and intervene in the world outside the laboratory (Waters, 2008: 717). This seems to blunt the criticisms of those such as Bolker (1995, 2012, 2014) and Love (2010), who inveigh against the use of a narrow range of highly standardised model organisms which are bred to exhibit as little morphological and ontogenetic inter-organismal variation as possible.

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<sup>140</sup> Though Ankeny and Leonelli (2011) would argue that research centred on model organisms is precisely aimed at gaining a comprehensive understanding of the workings, processes, and mechanisms of a single organism, which can then be used to approach more specific problems and questions in other organisms.

<sup>141</sup> We might observe the changes that have occurred in the natural environment resulting from the adoption of certain modes of agricultural production as an example of this.

New fields of research, however, particularly those concerning human health, have arisen from the realisation of the importance of variation in shaping outcomes. The discovery of the role of variants of different genes in influencing response to a potential pathogen (for instance, through the Human Leukocyte Antigen immune system genes) is one example of a set of findings that have led to the recognition that understanding the scope and effects of natural variation should be an important part in biological research (Davis, 2014). In this respect, such research therefore needs to be ‘closer to nature’ and take account of (and include) variation and some of the complexities and relationships exhibited in the objects and processes in which researchers wish to intervene and control.<sup>142</sup> Here the inference from laboratory to nature (or field, or body) matters.<sup>143</sup> The variation which exists in ‘nature’ – in and between organisms, between environments – now matters greatly. For example, in personalised medicine, the aim is to identify certain factors in particular groups of people which can affect the efficacy of a particular treatment, or inform treatment options by providing insight concerning the prognosis for a particular condition. To use a sample population in laboratory or epidemiological studies that has had considerable amounts of natural variation extracted from it seems to be foolhardy in the context of such research. Another area of burgeoning research concerns the microbiome (philosophical research as well as biological, see Dupré 2012; O’Malley 2013). Researchers examine the microbial flora present in organisms, and the role of different varieties of microbotic flora and their relations with the host in developmental and physiological phenomena of interest (Blaser *et al*, 2013; Cho *et al*, 2012). There is a particular interest in the diversity of microbotic communities living in, and interacting with, macrobes, and the significance of variation in this between individuals at particular stages of development, and between different stages of development within individuals (Gritz and Bhandari, 2015; Schloissnig *et al*, 2013; The Human Microbiome Project Consortium, 2012; Turnbaugh *et al*, 2009). The need to take account of naturally occurring variation is central to this research.

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<sup>142</sup> It seems that Woodward’s interventionist account of causation is even more suited to this kind of research than more ‘traditional’ research.

<sup>143</sup> We may observe here that rather than labourising nature, the impetus is towards naturalising the laboratory.

### **8.3.2. Explaining variation**

There are also new developments in the biological sciences which stress the importance of variation as part of the *explanandum* as well as the *explanans*. This may be because this *explanandum* is crucial to providing part of the *explanans* of another explanation (in some cases linking this concern with variation with the concern with variation presented in the previous section). But all the same, a renewed interest in studying the causes and biological significance of variation has emerged in parts of the biological sciences.

This is not a new thing. In the early twentieth-century, prominent scientists such as William Bateson, Nikolai Vavilov and Theodosius Dobzhansky saw the investigation of the nature of variation as central to their studies of heredity and evolution. Similarly, the whole field of population genetics can be seen as interested in variation, or more precisely the inheritance of genetic variation. The point is, however, that there is a renewed interest in variation, in fields (i.e. outside of genetics) which had not previously been concerned with it, such as biomedical science and developmental biology.

In burgeoning fields such as evo-devo and developmental evolution (devo-evo), ascertaining the origin of novelty (through new variants being generated) is central to many research programmes. In evo-devo, the aim is to enhance or extend the neo-Darwinian theory of evolution (also known as the 'Modern Synthesis') by accounting for the generation of novelty through studying the developmental mechanisms which produce such novelty and allow it to be inherited (Pigliucci and Müller, 2010). The origin and nature of variation is therefore central. Yet, in evo-devo at least, criticism has been levelled that in its own research practices it fails to take account of much organismal and ontogenetic variation, as a result of using standardised model organism strains (Love, 2010). Very few researchers take variation seriously in the organisms they use, or incorporate a range of variation in organisms (or at least, variable organisms) into their work, with some notable exceptions (e.g. Hall, 2014; Hallgrímsson *et al*, 2012).

Love's critique makes clear that this is problematic for evo-devo because the question of phenotypic plasticity is often a central part of investigations in that



field. If (non-hereditary or non-genomic) variation is abstracted away, phenotypic plasticity (phenotypic variation generated by developmental changes), which ordinarily would present itself, would do so to a far lesser extent. His proposed solution is to use a greater range of model organisms and create alternative periodisations or stagings, based on using different characters to those currently used in normal stages. This would ensure that the periodisations thus established could not be collapsed into a single periodisation. Consequently, variation would be revealed rather than abstracted away (Love, 2010). I return to these two suggestions shortly.

There are other problems besides those identified by Love. One is that even though the production and distribution of strains of model organisms aims at standardisation and a reduction in inter-organismal variation, there is evidence that a considerable (and, probably, biologically relevant) amount of variation remains (Carlson Jones and German, 2005). This should not be a surprise. Even genetic clones kept in ostensibly identical environments would experience some difference in microenvironment, such as position in the uterus, or place in the laboratory. They may possess different epigenetic markers or inherited maternal RNA affecting gene expression, or will simply develop in a (slightly) different way due to stochastic variation in early development.

As well as the practical implications of a renewed or greater focus on variation, I close this section by suggesting that it may also lead to a re-alignment of central theoretical and conceptual parts of the apparatus of developmental biology. One of the central problems in developmental biology is differentiation, and one of the main ways of explaining differentiation is through differential gene expression (Love, 2014: 41-47). In one respect then, this suggests that variation is central to developmental biology. Variation in cellular environment between cells affects variation in gene expression between cells, which causes the variation in the types of cells observable in more mature organisms. This basic story, augmented by other developmental processes (such as cell migration and adhesion as well as induction), is of course true, and is a triumph of twentieth-century developmental biology and genetics. But it is only central if one wishes to interpret those types of variation, and the processes associated with them, as central. Alternative ways of formulating principles of developmental biology may

be possible, and are indicated by certain empirical findings. Associated with this is the need to consider different ways in which variation can manifest itself and prove itself to be biologically – causally – relevant. The three sets of empirical findings I would like to discuss are developmental plasticity, transdifferentiation and the role of the microbiome in macrobiotic development. These phenomena call into question the idea that there is a set mode and temporality to the developmental process in any given type (such as, but not restricted to, a given species or variety) of organism.

Developmental plasticity is defined as “the ability of an organism to react to an external or internal environmental input with a change in form, state, movement, or rate of activity”, and we might add, developmental fate (West-Eberhard 2003, 33). It thus creates and responds to variation. Plasticity is conceived in opposition to differentiation, each process constraining the other (Bateson and Gluckman, 2011). Developmental plasticity is the ability of the organism, as part of its normal development, to vary in outcomes measured at particular stages of development (multifinality), and of routes towards certain outcomes at certain points.<sup>144</sup> The phenomena of developmental plasticity suggest that organisms exhibit variation in outcomes and pathways towards outcomes. This can include different neural and vascular connections and networks, the different phenotypes exhibited by the planktonic crustacean *Daphnia* depending on early exposure to chemicals indicating the proximity of predators (Gilbert and Epel, 2009), the formation of the different castes of social insects (Rajakumar *et al*, 2012), or the responses of plants to environmental conditions.<sup>145</sup> Developmental plasticity is dependent upon the capacity of the organism to use cues from the environment as signals to be interpreted by developmental processes. The

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<sup>144</sup> A plasticity of an altogether higher order is the plasticity of the modes of development themselves, as a result of the interaction of evolutionary and developmental processes which shape the very nature of development, and more specifically, the type of life cycles which constitute development (Minelli, 2014, 2015). I have tried to use language which avoids a bias towards adultocentric conceptions of development, or mistaking the direct development characteristic of mammals as paradigmatic of even vertebrates, let alone other creatures.

<sup>145</sup> These are just some examples, relatively simple ones at different ends of the granularity scale, in which environmental signals are causally efficacious in selecting between limited numbers of possible phenotypes. What is important about them is that there is not a *default* phenotype. Other examples with a less limited number of possible phenotypes would include angiogenesis and the formation of the integrated vascular network, and the equivalent processes in the formation of the nervous system, in which the developing system is in constant interaction with the new environments it encounters at every stage. There is no predetermined plan, but the eventual networks are the result of that ongoing reciprocal interaction.

range of relevant variation (internal or external) which can produce functional organisms at a given end-point is therefore widened – a wider range of variation becomes relevant for understanding the variation between forms of a given type.

Similar to developmental plasticity, the phenomenon of transdifferentiation leads one to focus on the multifinality of developmental processes. Therefore the variation in outcome and processes of development, as well as the variation in different factors and processes (internal and external) which affect these, is central to understanding development. Sometimes these varying factors present in the life cycles of organisms in a reliable and stable way, other times not so. The variation in that reliability may be worth investigating in itself.

In standard accounts, the central process of differentiation in development is described as hierarchical and irreversible. Germ-layers are specified, then tissues within them, then cell-types within them. Cells become ever more differentiated, and with the exception of stem-cells, this is a one-way process. However, the “transformation of one *differentiated* cell type into another” [italics in original] (Slack, 2009), or transdifferentiation, calls into question the hierarchical and one-way process of differentiation, or indeed the idea that a cell is even differentiated when it seems to be.

Transdifferentiation invites us to consider that rather than this phenomenon being an exception to the ‘normal’ model of differentiation, it may in fact be one process or tendency amongst many that interact, counteract, or act as part of the developmental process as a whole with other tendencies. This may include the role of stochasticity in development (Kupiec, 2014). Indeed, the maintenance of a differentiated state is itself an active process – the need to faithfully transmit epigenetic marks through DNA replication and cell-division (Bateson and Gluckman, 2011, 58) – and therefore not a spontaneous or default condition.

Transdifferentiation directly challenges the central principle of differential gene expression. The observed variation in the various cell types at any one time in an organism’s development can be attributed to the active stabilisation of that variation (e.g. Minelli, 2014), and the source of that variation can be attributed to

a wider set of causes than the genealogical pathway of a particular cell. A wider range of causal factors therefore become relevant for understanding the existence, persistence and nature of differentiated cell types.

Microbes are increasingly thought to play an instructive role in the development of the organism, and in differentiation and other countervailing processes (Blaser *et al*, 2013; Cho *et al*, 2012). The need to take naturally-occurring variation into account is relevant to the investigation of the developmental and physiological function of dynamic interactions between developing macrobiotic organisms and more or less closely associated microbial communities. The microbiome contributes external signals (if one does not consider the microbiome to be part of the human organism itself) shaping developmental 'decisions' made at various stages. In understanding the ongoing dynamic variation in and between microbial communities in different developing organisms, scientists can make sense of the reciprocal, iterative relationships between the organism and succession of microbiotic communities that it hosts and interacts with. Monogenomic differentiated cell-lineages are not just 'there' in the first place to interact with the microbiota (developing an insight in Dupré 2012).

Given the key role of the microbiome and the phenomena of transdifferentiation and developmental plasticity, the way that variation is managed and the causal relevance of certain types of variation for given outcomes of interest are assessed should depend on a more explicitly articulated justification for dividing systems up into potentially relevant causes and background conditions. More varying factors would therefore be incorporated into the realm of potentially relevant causes and there would need to be more explicit reasons within the context of the research situation for making certain potentially varying factors invariant. Putative ways of *measuring* causal specificity offer ways to do this that can be explored and developed.

### **8.3.3. Opportunities and prospects**

One problem with a greater focus on variation is that if experimenters were to measure more variation, and use this to divide up samples, they will be left with very small sub-samples, below the numbers needed for statistical significance.

One way of getting round this is to systematically analyse what variation is relevant. Another way is to increase the number of samples. Robert Kohler's (1994) account of Morgan's fly laboratory emphasised the importance of generating a large number of flies for inspection. The large number of flies allowed even rare mutations to become apparent. Once an observation of a new mutant was made, investigators were mentally prepared to observe it when it appeared again, as they did. Awareness of variation permits the detection of it. Large numbers may reduce the variance exhibited in a given population of samples, but they increase the number of variants observed. Methods of dealing with large numbers of samples have been slow to enter parts of developmental biology (excepting much research involving yeast), but they are being developed (Tills *et al*, 2013). We increasingly have the means to produce, analyse and interpret large amounts of data concerning embryonic development, in an increasingly automated way. This has the potential to reshape our perceptions concerning the extent and significance of variation in development. We also increasingly have the computing power and the statistical tools to deal with multivariate complexity, which will be essential in dealing with the larger number of varying factors and assessing causal relationships between them.

Finding and elaborating new methods to deal with greater amounts of variation could (and should) generate new ways of producing and using normal development, ones that encompass all variation deemed to be normal. The question that should guide the abstraction process to produce new normal developments should be: does the organism show the requisite plasticity to remain functioning at an appropriate level? The new standard would therefore take its lead from the criteria used by Wilson as far back as 1892. This new standard would make functionality the basis of standards of the normal.<sup>146</sup> Developing such a standard would be challenging, as attributions of functionality are often dependent on context and mode, rather than an overall level of functioning (Amundson, 2000). Here, the insights of Michel and Moore

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<sup>146</sup> Robert Wachbroit has demonstrated that both goal and etiological theories of function appeal in some way to what he calls the "biological concept of normality", which would seem to pose a problem for defining the normal in terms of the functional (Wachbroit, 1993). However, as his "biological concept of normality" incorporates functional criteria itself, this is less significant and problematic than is implied.

concerning the equifinality and multifinality of development can help clarify that a functional standard would not be restricted to specific modes of existence, or specific routes between two modes. Instead of being concerned with particular functions, metrics of functional level could be produced.<sup>147</sup> These would identify the overall level of functioning exhibited by the organism (or part thereof), and then derive the normal from that. Marcel Weber (2013) suggests a further constraint, arguing “that the relevant counterfactuals that guide causal selection in biology are counterfactuals that describe interventions that are *biologically normal*” [italics in original]. Such interventions are identified as being those “that could naturally occur as part of the normal biological functioning of an organism.” This would still require a judgement to be made by investigators, but rather than the implicit and intuitive judgement of normality that Michel and Moore rejected, this would be explicit, and open to critique (for one possible model, see Hall, 2014).

Emerging model organisms provide an opportunity to produce standards more appropriately suited to research concerned with the role of context and variation in development (Bolker, 2014).<sup>148</sup> New periodization methods, with some of the attributes called for by Love, are being developed. Examples include the Standard Event System (Werneburg, 2009). The Standard Event System (SES) explicitly rejects the use of terms such as “normal stages” and “normal development” as unacceptably typological. It works by identifying the time at which certain developmental characters (for example, the presence of a certain number of somites) appear. Each of these characters is assigned a “Standard Event Code” (SEC), with associated description and illustration. The investigator, observing the embryos, fills out an SES-formula. This lists the SECs below a section where they enter (amongst other information) the species, breeding temperature, and age in days. They may then add other forms which include drawings or photographs of the specimens. The SES reveals heterochrony, interspecific variation and intraspecific variation in a way

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<sup>147</sup> This is an important point to clarify: I am focusing on a global criterion of function and functionality, not on individual sub-organism functions, and therefore most of the debates concerning function are not relevant here.

<sup>148</sup> These new model organisms may even include microbes, which have been proposed as models for specific developmental mechanisms (rather than developmental phenomena), and which may have their representational worth as models improved by synthetic biology or natural engineering methods (Love and Travisano, 2013).

in which standard staging systems do not. The SES presumes no set stages, order of stages and characters associated with those stages. It instead allows the observer to record what is and what is not there at any particular point in time, in a form which is easily digitised, comparable, and extendable. Another example is the proposed use of 'developmental steps' (Scholtz, 2012). A developmental step is defined as "a describable and comparable (homologisable) *pattern* at any moment of development" [italics in original] (Scholtz, 2012: 147). Like the SES, using developmental steps would allow developmental variation to be recorded rather than being resolved into highly abstracted stages.

Automation and *in silico* methods offer new possibilities, but should be approached with caution. Automated processing of embryos could allow a greater number of embryos to be assessed, but also incentivises standardisation and reduction of variation to make samples uniform enough to be efficiently processed.<sup>149</sup> One solution would be to automate only part of the process, such as the videoing of samples and computerised three-dimensional morphometric analysis. Other aspects of the process would involve human eyes and interpretation. Some limited level of automation does pose the possibility of getting round some of the problems raised by the human staging of embryos, such as focusing on one feature as a primary criterion and assuming that all others follow from this at a particular stage.<sup>150</sup> This is a habit encouraged by the need to stage many embryos quickly, but inhibits the apprehension of variation, for example of the timing of the appearance of particular structures.

*In silico* methods offer a possible way around the problems associated with producing contextually-relevant normal development, which implies the use of local standards, which has practical problems as well as causing problems of translation, commensurability and reproducibility. There will still be the requirement for high-quality data to be inputted into computer systems however, and data produced *in silico* will no doubt require *in vivo* validation to satisfy community standards after results have been produced. To deal with the possible problems associated with the production of local standards, some

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<sup>149</sup> An important point made to me by Jennifer Cuffe.

<sup>150</sup> I owe this insight into the realities of staging embryos at the bench, and the shortcuts (or perhaps heuristics) used by practising scientists, to an illuminating and helpful discussion with Brian K. Hall.

inspiration might be found in efforts to develop tools to integrate different ontologies (in the computational sense of the word; Leonelli, 2010): in particular, families of related ontologies encompassing small datasets produced in different contexts for different purposes. This is an acute issue in ecology, and part of the solution is to ensure that certain standards are formulated and used. These would concern data collection, the recording of the “structure, content and appropriate usage” of data, and the development and use of software to ensure that data are able to travel outside their particular context of production (Madin *et al*, 2008).

#### **8.4. Open questions**

Given that variation is a constitutive feature of living things, biological variation must be taken account of in experimental biology. Furthermore, the practical and conceptual problems and questions raised by this should be confronted by philosophers of biology. In experimental practice, I propose that the normal development incorporates a wider range of variation, and that the experimental set-ups themselves must incorporate more variation into experimental designs. In my ongoing and future work, I aim to explore the implications of ‘taking variation seriously’, conceptually and practically.

In the conceptual sense, I would like to develop my nascent analysis into the place of normal development in the practical-theoretical framework of modern developmental biology. This will entail an examination of the conceptual and/or theoretical structure of developmental biology, a task which has already begun (Minelli and Pradeu, 2014). In particular, the concept of differentiation in development, how this relates to normal development, and how it is also relates to the concept of specificity, needs to be explored further. The effects of current shifts in the practice and theory of modern biology (not restricted to developmental biology) on the concept of biological specificity are under-analysed.

A task inextricably linked with this is to detail exactly how variation is dealt with (practically and conceptually) by developmental biologists, and what factors are implicated in variation in this treatment. This would involve a systematic study of



literature, the design and distribution of questionnaires and analysis of the results, and close study of several laboratories. The ways in which the introduction of *in silico* methods, the ability to generate large amounts of data, and the drive towards more naturalistic mode of research have changed experimental practices concerning variation are of extreme interest.

I have already identified some of the problems associated with a programme for a variation-sensitive developmental biology. As a start to the philosophical part of that programme, I suggest several areas for future research. On a more conceptual level, we require a clarification on exactly what biological variation is, how it relates to other concepts of similarity and difference in biology, such as (bio)diversity, and how it relates to various ways of producing and conceptualising 'types'. We also need to identify how the ways in which biologists work affects their attitudes concerning the extent and relevance of biological variation; how they apprehend it, observe it, measure it, and integrate it into their ongoing experimental and theoretical work. Going to the heart of how a variation-sensitive developmental biology might work are questions concerning how one determines what variation is to be included in the normal development, what functional level is and how it might be defined. Finally, the question is posed that if the programme is successful, and experimenters aided by technological developments produce normal developments incorporating the range of variation that they deem appropriate for their own experimental programme, therefore producing their own local standards, what implications does this have for the notion of standards, for the production, export, and integration of data, and for commensurability in general?

Developing research projects that speak to these questions will entail close discussion with developmental biologists themselves, and close analysis of their work. The task of this thesis has been to assess the role of normal development in embryology and developmental biology. I have identified new ways of thinking about critiques of certain aspects of modern biology, and in doing so have endeavoured to identify ways in which those critiques can be harnessed to suggest practical changes to the way that experimental work in developmental biology is conducted.

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