

Lenny Moss
(The University of Exeter)
Stuart A. Newman
(New York Medical College)

THE GRASSBLADE BEYOND NEWTON: THE PRAGMATIZING OF KANT FOR EVOLUTIONARY-DEVELOPMENTAL BIOLOGY

Introduction

Kant's practice as a philosophical investigator involved a kind of intimate and productive interpenetration between the sciences and philosophy that few contemporaries, conditioned as we are by ever-increasing divisions of intellectual labor, are likely to fully fathom, let alone emulate. Kant brought metaphysics to bear on basic problems in mathematical physics, weighed in on contested questions concerning preformationism versus epigenesis in biology, as well as questions about human racial diversity, and conversely drew upon all of the above in formulating his own metaphysical epistemology. Questions about ultimate origins, and our ability to address them, streamed through his entire oeuvre as did the challenge of securing both the rational grounds of causal "mechanistic" explanation and of free will. Might there be a value in revisiting Kant's style of intellectual/scientific practice and the legacy of his contributions to addressing problems of understanding life in the light of on-going scientific advances? The present paper will explore exactly that.

While it would be fair to say that Kant scholarship has blossomed in the English-speaking world over the past several decades, it is nonetheless the case that bringing Kant's legacy to bear as a resource and critical partner in the furthering of biological understanding in a contemporary context has hardly been broached. Only a small fraction of Kant scholarship has concerned itself directly with Kant's engagement with a natural science and where such work has been done (and brilliantly so), for example

by Michael Friedman¹ and Eric Watkins², it has been largely partitioned to the side of the physical (as opposed to life) sciences although two recent anthologies suggest that this is the process of changing³. Interest in Kant's *Third critique* in general, and especially on the biological side of this work, has been late in coming and even where a recognized philosophical expert has emerged, e.g., Hannah Ginsborg, it has been largely on the basis of a philosophical practice outside of any detailed engagement with the empirical life sciences⁴. The record is rather different when it comes to those working more in an historical/interpretive than in a problem-solving vein. More will be said about this below. First we will sketch the basic framework bequeathed by Kant to subsequent investigators into the nature of "organized beings".

Simply stated, Kant recognized a very basic dilemma in understanding living organisms. Kant referred to living organisms as "organized beings" precisely because as creatures of nature they exhibit a kind of organization which requires a special explanation. Said organization entails an ability to self-sustain, often to grow and develop, to reproduce and to take-up and incorporate non- or less-organized matter into that organization that allows for all of the above. Kant characterized an entity that performs as such to be a "natural purpose". The problem for Kant was that from the point of view of the physics of his time such organization could only have come about contingently as there was no physical principle on the basis of which the arrival of such organization could be accounted for as a necessary consequence. To view "organized beings" solely on the basis of physical mechanisms was thus inadequate, if not absurd, inasmuch as it meant proceeding as if that organization that enabled them to function as "natural purposes" could have come about through pure chance. Alternatively, "organized beings" could be reckoned by way of our understanding of "purpose" but if we were to understand all life-activity as inseparable from purposeful intention at any and every level

¹ M. Friedman, *Kant and the exact sciences*, Cambridge MA, Harvard University Press, 1992.

² E. Watkins, *Kant and the metaphysics of causality*, Cambridge, Cambridge University Press, 2005.

³ See I. Goy - E. Watkins (eds), *Kant's theory of biology*, Berlin, De Gruyter, 2014 and P. Huneman (ed), *Understanding purpose: Kant and the philosophy of biology*, Rochester NY, University of Rochester Press.

⁴ Siegfried Roth is a notable exception whose highly detailed scientific discussions have attempted to defend the implicit relevance of Kant's views if not, albeit, to renew them for productive purposes. See for example his "Kant, Polanyi, and molecular biology" in I. Goy - E. Watkins, *Kant's theory of biology* cit.

then we would either have to posit an immanent mind in nature «all the way down» or ascribe all the activities of life to the intended acts of a transcendent designer. Kant's best solution to this dilemma was to find a way to compromise, to formulate a «methodology of teleology» that would best empower the explanatory sciences, as he understood them, to take natural explanation as far as they could go. Kant reasoned that:

If, therefore, the investigator of nature is not to work entirely in vain, he must, in the judging of things whose concept as natural ends is indubitably established (organized beings), always base them on some original organization, which uses that mechanism itself in order to produce other organized forms or to develop its own new configurations (which, however, always result from that end and in conformity with it)⁵

What gave Kant the optimism that granting the prior existence of some form of «purposive organization» could then provide for a productive course of research was the observation that different life forms bore family resemblances that suggested principles, or mechanisms, of transformation that could well be amenable to empirically lawful characterization.

It is commendable to go through the great creation of organized natures by means of a comparative anatomy in order to see whether there is not to be found therein something similar to a system, one indeed, regarding the principle of their generation, without which we would have to settle for the mere principle of judging (which provides no insight into their production) and would have to give up claim to insight into nature in this field. The agreement of so many genera of animals in a certain common schema, which seems to lie at the basis of not only their skeletal structure but also of the arrangement of their other parts, and by which a remarkable simplicity of basic design has been able to produce such a great variety of species by the shortening of one part and the elongation of another, by the involution of this part and the evolution of another, allows the mind at least a weak ray of hope that something may be accomplished here with the principle of the mechanism of nature, without which there can be no natural science at all.⁶

Beginning with his efforts to provide a model of human racial diversification, consistent with a monogenist (what we would now term «monophyletic») theory of the human species, Kant brought

⁵ I. Kant, *Critique of the power of judgment*, ed. by P. Guyer, Cambridge, Cambridge University Press, 2000, p. 287.

⁶ *Ibid.*

together both preformationist and epigenesist concepts, postulating the idea of some «pre-established», «purposeful», stock of potential (*Keime und Anlagen*) that may give rise, by mechanical means, to a spectrum of organismal forms. This was in effect Kant's Teleological Method put to work in biological problem solving⁷. The explanation of life-process by way of the explanatory laws and mechanisms at our disposal become no longer impossible if one can assume an "original" organization of components that can vitiate the problem of contingency. The assumption of an original purposive organization of components, which is the crux of the teleological heuristic, provides for a kind of pragmatic "bracketing"; pragmatic in the sense that it enables the explanatory pursuit of some biological phenomena while setting aside others. In theory, whether Kant imagined this or not, heuristic teleological bracketing can flex and recede in tandem with new explanatory capacities to account for at least aspects of living processes as direct causal implications and not merely highly contingent outcomes.

Following this line of thought, some degree of enabling teleological bracketing would be retained so long as life itself could not be reinvented from non-living matter. Inasmuch as life, two-hundred and twenty-five years later, has still not been reinvented from non-living scratch (as in the perennially perplexing "origin of life" research agenda), there are many questions that can be asked about the extent to which some form of teleological bracketing has been put to use, explicitly or implicitly, in the subsequent history of biology and to what extent some form of teleological bracketing continues to be the most apposite approach to a productive and reflectively coherent, bio-scientific research program. The present paper will both detail an updating of our ability to go beyond overwhelming degrees of contingency in accounting for life processes in dynamic physiochemical terms as well offer a novel approach to even further reducing the need for teleological bracketing. *En passant* we will also be making the case for the continued inevitability of some form of bracketing in biological science and for the superiority of teleological bracketing to Neo-Darwinian *bracketing*. We will thus be making the case for the continuing centrality of Kant's problem-solving agenda.

⁷ Id., *On the use of teleological principles in philosophy*, in *Anthropology, history and education*, Cambridge, Cambridge University Press, 2007.

Neo-Darwinian bracketing and bracketing upon bracketing

We have suggested that some form of bracketing has been and continues to be an unavoidable (if not always acknowledged) device in the elaboration of biological theory. In his seminal and brilliant, but also controversial, account — *The strategy of life: teleology and mechanics in nineteenth century German biology* — the historian Timothy Lenoir attempted to demonstrate how the further extension of the use of teleological bracketing, or «teleomechanism» enabled nothing less than the entire foundations of modern biology, i.e., developmental morphology and the understanding of development in terms of the interaction of discrete germ layers, the discovery of the human ovum, the rudiments of functional morphology, the foundations of cell theory and physiology and the origins of cytopathology. Be this as it may with respect to historical precision (more on this in the conclusion) it should not be difficult to see how teleological bracketing can be adapted to serve as a flexible placeholder for successive steps in our advancing but incomplete ability to understand the origins of purposive form and function, not as contingent in relation to physiochemical processes, but as expressions of such (even if contrary to Kant's expectations).

An entirely different style of bracketing emerges with Darwin, and assumes a decisive shape with the neo-Darwinian synthesis of Darwinism with Mendelism on the basis of population genetics. The gist of this is handily expressed by Patricia Kitcher in her recent review of Hannah Ginsborg: «But Darwin offered an alternative: the proper way to understand the contingent (with respect to basic laws) is in relation to the contingent – a whole series of accidents». So conceived, the idea of natural selection can (and arguably did) become a far more totalizing bracket than Kant's teleology. The positing of hypothetical gene-based variants, conceived as frozen accidents, could become indefinitely bracketed from any accountability to questions about the contingency of purposive function, through the mere incantation of *Natural selection*.

This biological strategy was reinforced with the disciplinary separation of embryology from transmission genetics in the early 20th century. This division pertains especially to the particular character of multicellular development. Unlike single-celled organisms, which are generated by essentially identical progenitors and for which species-characteristic goals are manifest from the

start of their lives, the embryo is at every stage a different kind of being from the animal or plant it will eventually become. While it changes in a directional fashion according to a species-specific routine, the “goal” of this process is not simply the maintenance and propagation of the organism, but rather the sequential construction of its mature form. For biologists of the period these developmental routines (later called “programs” with the rise of computer science) were increasingly conceived as the embryo-stage expression of an organism’s “genes”. Genes thus in effect become surrogates and indefinite substitutes, for actual physico-chemical developmental process.

Moreover, with the Mendelian-Darwinian «Modern Synthesis» in ascendancy it became nearly unquestioned to assume that the clearly goal-directed development of a species-specific body form was (despite appearances of having an internal logic of its own) exclusively in the service of regenerating a suite of characters that had been originally brought about by natural selection acting on adult organisms. This assumption permitted another bracketing, this time not of the integrated, holistic character of the mature organism, but of the developmental processes by which a structurally and functionally competent body is created in every generation. The bracketing of development is encapsulated in the assertion by the population geneticist Brian Charlesworth, a prime contemporary exponent of this view, that «[u]ntil we have a predictive theory of developmental genetics, our understanding of the molecular basis of development – however fascinating and important in revealing the hidden history of what has happened in evolution – sheds little light on what variation is potentially available for the use of selection»⁸.

This second level of bracketing insulated Modern Synthesis studies from exposure to developmental propensities and constraints that could have shaped evolutionary trajectories and thereby challenged purely adaptationist accounts. Such bracketing, in stark contrast with, for example, developmental morphology rooted in teleological bracketing, serves only to obscure, rather than disclose, actual phylogenetic history rooted in the developmental process. This strategy has turned out to be scientifically inadequate for reasons that will be described below.

⁸ B. Charlesworth, *Evolution: on the origins of novelty and variation* (Review of *The plausibility of life: resolving Darwin's dilemma* by Marc W. Kirschner and John C. Gerhart), «Science» 310 (2005), pp. 1619-1620.

From Newtonian mechanics to excitable soft matter

Because embryos are composed of complex materials, their development is ultimately a problem of physics and chemistry. The mechanical paradigm formulated by Isaac Newton, which dominated scientific thought throughout the 18th century, held that matter was inert and inertial, changing its form and position in a linear/continuous fashion, and only when acted on by external forces. Although physical science was itself undergoing changes during this period, opening the way to chemistry, thermodynamics, electricity and magnetism, the “unmechanical” behaviors of the new objects of study, which exhibited qualitative transformations, irreversibility and action-at-a-distance (also a property of Newtonian gravity) elicited skepticism in some scientifically conservative circles. In fact, the dynamics of chemical and other mesoscale systems have greater relevance to biology than clockworks and other devices constructed according to classically mechanical principles. An acknowledgement of the explanatory possibilities inherent in the new chemistry and physics can begin to be seen in the work of thinkers less committed to Newton’s mechanicism than Kant, or perhaps even Darwin⁹. Lamarck, for example, described living tissues as being suffused by «contained» and «subtle» fluids (discussed in Newman and Bhat¹⁰), and rational morphologists like Geoffroy Saint-Hilaire, Lorenz Oken and Richard Owen, inspired in part by J.W. von Goethe, speculated about natural «laws of form»¹¹. But the new physical science had made few inroads into biology at the time experimental embryology (which followed the invention of the achromatic lens and formulation of cell theory) and evolutionary theory began to emerge, despite hints of the continuities between nonliving and living matter such as Luigi Galvani’s electrical stimulation of muscle twitching in a dead frog in 1780 and Friedrich Wohler’s test tube synthesis of urea in 1828.

⁹ D.J. Depew, B.H. Weber, *Darwinism evolving: systems dynamics and the genealogy of natural selection*, Cambridge MA, MIT Press, 1995.

¹⁰ S.A. Newman, R. Bhat, *Lamarck's dangerous idea*, in S. Gissis, E. Jablonka (eds.), *Transformations of Lamarckism: from subtle fluids to molecular biology*, Cambridge MA, MIT Press, 2011, pp. 157-169.

¹¹ G. Webster, B.C. Goodwin, *Form and transformation: generative and relational principles in biology*, Cambridge-New York, Cambridge University Press, 1996.

Darwin's conventionally materialistic conception of organismal transformations was in keeping with the manufacturing wisdom of the Industrial Revolution. His notion that trial and error acting on incremental change could arrive at a functionally optimal outcome echoed the experience of his maternal grandfather, the pottery magnate Josiah Wedgwood, who tested several thousand different earthenware formulations before arriving at the one that made his fortune. But the major advances in the chemistry and physics (including thermodynamics and fluid mechanics) of meso-scale matter was due to scientists active in the early 19th century such as John Dalton, J.-L. Gay-Lussac, C.-L. Navier, and Sadi Carnot, who established scientific foundations for understanding qualitative transformations in the composition and organizational state of materials (reviewed in Newman and Linde-Medina¹²). Such changes are of course precisely what occur during the development of a multicellular animal or plant.

By the mid-twentieth century physics was profoundly different from that of Kant's era. The most famous theoretical advances were relativity and quantum theory, but these pertain to phenomena on larger, smaller and faster scales than those on which biological systems exist. More relevant to the life sciences was the rise of physics of the middle scale. Among the phenomena that characterize this scale of matter are nonlinear chemical oscillations (with concentrations of molecules changing periodically with time) and multistable dynamics (with the material composition settling on one or another alternative value depending on the system's initial composition). Also included are transitions between, and separation of, phases (particularly immiscible liquids like oil and water), and viscous flow (characterizing differences between honey, say, and alcohol). Another exotic phenomenon at the mesoscale (studied theoretically by the mathematician Alan Turing) results from coupling between chemical reaction and diffusion leading to the spontaneous breaking of spatial uniformity of composition, leading to standing waves of chemical concentration.

Mathematical, and later, computational tools were becoming available that enabled formulating theories of matter that was "soft" (viscoelastic) and "excitable" (capable of storing chemical or mechanical energy that was releasable upon stimulation), or both.

¹² S.A. Newman, M. Linde-Medina, *Physical determinants in the emergence and inheritance of multicellular form*, «Biological Theory» 8 (2013), pp. 274-285.

Organisms and the embryos that give rise to them consist of such materials (typically in complex amalgams operating on multiple scales), but soft or excitable materials (even nonliving ones) can change in abrupt ways, are responsive to environmental influences, and typically assume preferred, though not limitless, forms (e.g., waves and vortices in water, wrinkles and cracks in dried paint)¹³. While it is understandable that Kant despaired of finding a material basis for purposeful behavior, and Darwin and Alfred Russel Wallace envisioned evolutionary processes that advanced in small increments, with no jumps or preferred outcomes the same cannot be said for 20th and 21st century life scientists. We have suggested that by the lights of a properly understood method of teleological bracketing, new formulations with diminished needs for bracketing would and should follow from advances in our ability to see the purposiveness of living processes as no longer merely contingent in relationship to, for example, the new physics and chemistry of the mesoscale.

Physico-genetic mechanisms of the origination and development of biological form

Developmental biology has in recent decades begun to incorporate the physics of excitable soft materials, but not without resistance. The dominant conceptual framework from mid-20th century was structured by the concept of a “genetic program,” which constituted the continuation of the type of Neo-Darwinian bracketing discussed above. The rise of cybernetics and the temptation to assimilate the long linear sequences of DNA embedded in chromosomes to the software script of a Universal Turing machine led to tendencies to reify and ossify the idea of the genetic program, to treat a regulative bracketing device, a placeholder, as itself as a bona fide entity.

Genomes of course are essential to the life of cells and to all multicellular activities, including embryogenesis. They harbor, amongst other things, templates for the sequences of RNA and proteins, two major categories of molecules of organisms. The composition of the embryo, including its complement of DNA-templated molecules, changes during development, partly due to prior changes in gene “expression” (i.e., the initiation of processes of “transcription” and “translation” resulting in the *de novo* synthesis

¹³ G. Forgacs, S.A. Newman, *Biological physics of the developing embryo*, Cambridge, Cambridge University Press, 2005.

of peptides and proteins) but also partly due to chemical, mechanical and electrical changes in the cell mass occasioned by changes internal and external to it. None of this however is tantamount to justifying the reification of the notion of a genetic program for development, however¹⁴. But the fascination with computers beginning in the 1950s, the superficially apt circumstance of DNA's encoding sequence information in a linear fashion as on the cards and tapes of the early cybernetic era, and the requirement of the Modern Synthesis for a medium that stored heritable variation autonomously from the organism's other life activities, locked the field into this misleading paradigm for several decades.

At the same time, another research agenda more open to physicalist explanations began to emerge. This can be illustrated with three examples. One set of studies involved mixing cells derived from different embryonic tissues and observing that they sorted out, first into homotypic "islands" of one cell type surrounded by "lakes" of the other, and then into two distinct phases, one (the more cohesive), becoming engulfed by the other (less cohesive) one. This was interpreted as resulting from differences in the affinity (adhesiveness) of cells of the same and different type, the same reason that droplets of immiscible liquids, oil and water, for example, separate into distinct phases¹⁵.

This "liquid-tissue" model was influential in moving developmental biology away from the genetic-program paradigm, and its primary exponent, Malcolm Steinberg, explicitly referred to the thermodynamic-driven self-organization of developing tissues as providing an alternative basis for «goal-directedness» of embryogenesis¹⁶. These morphogenetic effects are now understood to be not simply the outcome of relative cell affinities, but to depend as well on tension exerted on the surfaces of cells from their interiors¹⁷ and production by certain cells of molecular signals that repel other cells¹⁸.

¹⁴ L. Moss, *What genes can't do*, Cambridge MA, MIT Press, 2003.

¹⁵ M.S. Steinberg, *On the mechanism of tissue reconstruction by dissociated cells, I. Population kinetics, differential adhesiveness, and the absence of directed migration*, «Zool.» 48 (1962), pp. 1577-1582; M.S. Steinberg, *On the mechanism of tissue reconstruction by dissociated cells, III. Free energy relations and the reorganization of fused, heteronomic tissue fragments*, «Proc. Natl. Acad. Sci. USA.» 48 (1962), pp. 1769-1776.

¹⁶ Id., *Goal-directedness in embryonic development*, «Integrative Biology» 1 (1998), pp. 49-59.

¹⁷ G.W. Brodland, *The differential interfacial tension hypothesis (DITH): a comprehensive theory for the self-rearrangement of embryonic cells and tissues*, «J Biomech Eng.» 124 (2002), pp. 188-197; M. Krieg, Y. Arboleda-Estudillo, P.H. Puech, J. Kafer, F. Graner, D.J. Muller, C.P.

The mechanisms that generate the multilayered initial stages (gastrulae) of animal embryos¹⁹, pancreatic islets, and tetrapod limb buds, are therefore not entirely «generic» in that they are not precisely the ones driving similar-appearing outcomes in non-living systems. They nonetheless can be considered «biogeneric»²⁰ in the sense of employing generic physical mechanisms to organize biological materials (e.g., aggregates of cells) in novel ways. The example of tissue phase-separation and boundary formation suggests that the physically explicable emergence of goal-directedness at a higher, and thus later-evolved, level of organization (e.g., multicellularity) can occur in a medium of earlier-evolved basic units (e.g., single cells) whose own origins and organizational principles are less transparent.

A second example of the new physicalist embryology involves the mechanism for the generation of somites, paired blocks of tissue that emerge in a sequential head-to-tail direction during vertebrate embryogenesis. The English biologist William Bateson, in the 1890s proposed that repetitive tissue elements, like flower petals, the digits of tetrapod limbs, and the somites, which give rise to the vertebrae and ribs, were determined by an underlying oscillatory or «vibratory» process akin to that causing ripples on sand or water²¹. This idea was ridiculed by promoters of the neo-Darwinian Modern Synthesis such as Ernst Mayr²², who considered it inconsistent with the tenet that genes and genetic programs were exclusively responsible for the inheritance and generation of forms. In the 1970s, using advanced mathematical models, the developmental biologist Jonathan Cooke and the mathematician Christopher Zeeman proposed a mechanism for somitogenesis that (unlike Bateson) postulated molecular components interacting in plausible ways (as a “clock” and “wavefront”), al-

Heisenberg, *Tensile forces govern germ-layer organization in zebrafish*, in «Nat Cell Biol.» 10 (2008), pp. 429-436.

¹⁸ R. Winklbauer, *Cadherin function during Xenopus gastrulation*, «Subcell Biochem» 60 (2012), pp. 301-320.

¹⁹ M. Krieg, Y. Arboleda-Estudillo, P.H. Puech, J. Kafer, F. Graner, D.J. Muller, C.P. Heisenberg, *Tensile forces govern germ-layer organization in zebrafish* cit.

²⁰ S.A. Newman, *Physico-genetics of morphogenesis: the hybrid nature of developmental mechanisms*, in A. Minelli, T. Pradeu (eds.), *Towards a theory of development*, Oxford, Oxford University Press, 2014, pp. 95-113.

²¹ Id., *William Bateson's physicalist ideas*, in M. Laubichler, J. Maienschein (eds.), *From embryology to Evo-Devo: a history of evolutionary development*, Cambridge MA, MIT Press, 2007, pp. 83-107.

²² E. Mayr, *The growth of biological thought: diversity, evolution, and inheritance*, Cambridge MA, Belknap Press, 1982.

though the identity of the putative molecules was still completely unknown²³. Then, in the late 1990s, Olivier Pourquié and his colleagues presented compelling experimental evidence for a mechanism for somitogenesis, involving a demonstrable intracellular biochemical oscillator within the cells of the segmentation-competent tissue, and a wavefront consisting of a gradient of a known «morphogen» with its source at the embryo's tail tip²⁴. Others provided plausible biochemical dynamics for the underlying oscillation²⁵. This turned out to be complex biogeneric processes based on the regulated transcription and translation dynamics of gene expression and protein synthesis rather than the simpler generic feedback circuitry that can produce periodic effects in certain simple chemical systems²⁶.

Fish, amphibians, birds, reptiles and mammals all have different characteristic ranges of somite numbers, which are typically 30-50, but can rise to more than 300 in snakes. Experiments have suggested that the increase in number of somites in snakes occurred by evolutionary alterations in the ratio of parameters characterizing the interaction of the clock and wavefront²⁷. We can now revisit the Kantian concept of a stock of potential, a stock of «germs» (*Keime*) and «proclivities» (*Anlagen*) in light of current science. The clock-and-wavefront system in effect constitutes a stock of *Keime* and *Anlagen* capable of giving rise to a wide spectrum of forms adaptively contingent upon the life needs of particular organisms. To insert the physics and chemistry of the clock-and-wavefront model into the generic placeholder space of the stock of *Keime* and *Anlagen* is not to terminate any role for teleological bracketing but it is to resize and reconfigure and incrementally diminish the size and scope of the “bracket” in relation to the further elaboration of the physico-chemical dynamics which are

²³ J. Cooke, E.C. Zeeman, *A clock and wavefront model for control of the number of repeated structures during animal morphogenesis*, «J Theor Biol.» 58 (1976), pp. 455-476.

²⁴ I. Palmeirim, D. Henrique, D. Ish-Horowicz, O. Pourquié, *Avian hairy gene expression identifies a molecular clock linked to vertebrate segmentation and somitogenesis*, «Cell.» 91 (1997), pp. 639-648.

²⁵ J. Lewis, *Autoinhibition with transcriptional delay: a simple mechanism for the zebrafish somitogenesis oscillator*, «Curr Biol.» 13 (2003), pp. 1398-1408; N.A. Monk, *Oscillatory expression of Hes1, p53, and NF-kappaB driven by transcriptional time delays*, «Curr Biol.» 13 (2003), pp. 1409-1413.

²⁶ E.g. M.P. Orbán, P. De Kepper, I.R. Epstein, *An iodine-free chlorite-based oscillator. The chlorite-thiosulfate reaction in a continuous flow stirred tank reactor*, «J. Phys. Chem. A.» 86 (1982), pp. 431-433.

²⁷ C. Gomez, O. Pourquié, *Developmental control of segment numbers in vertebrates*, «Journal of Experimental Zoology Part B» 312B (2009), 6, pp. 533-544.

by no means merely contingent in relation to the aspect of “purposive” development it elucidates.

The third example of emergent developmental pattern formation based on a physical process unknown prior to the 20th century pertains to skeletogenesis of the tetrapod limb. Turing’s reaction-diffusion mechanism, alluded to above, published in a paper titled «The chemical basis of morphogenesis»²⁸, showed that a balance of positive and negative feedbacks in an open chemical system (essentially identical to networks that generate temporal oscillations like that in the somitogenesis model), coupled with differences in the rates of diffusion of the key reactive molecules (i.e., morphogens), could produce stable patterns consisting of multiple peaks and valleys of molecular concentration. (Ironically and regrettably, Turing’s earlier pre-biological computation-theoretic concepts established a strong influence in biological development decades before his more biologically apt theories began to be appreciated). Because the vertebrate limb skeleton is arranged in a quasi-periodic fashion (e.g., the single humerus bone of the forelimb, followed by the radius and ulna pair, the rows of wrist bones, and then the digits), it lends itself to a natural interpretation in terms of a Turing-type mechanism sustained in the excitable medium of the limb bud mesenchyme, with the molecular peaks inducing skeletal tissue²⁹. Key aspects of the skeletal patterns of mutant and fossil limbs can be accounted for by the assumption that the limb pattern is formed by a reaction-diffusion type mechanism³⁰. As with the phase-separation of adjoining tissues during gastrulation with both «reaction» and «diffusion» being realized in more complex biological fashion than the chemical versions discussed by Turing³¹.

More generally, the production of the basic morphological motifs of animal body plans and organs can be understood in

²⁸ A.M. Turing, *The chemical basis of morphogenesis*, «Phil. Trans. Roy. Soc. Lond. B.» 237 (1952), pp. 37-72.

²⁹ S.A. Newman, H.L. Frisch, *Dynamics of skeletal pattern formation in developing chick limb*, «Science» 205 (1979), pp. 662-668.

³⁰ J. Zhu, Y.T. Zhang, M.S. Alber, S.A. Newman, *Bare bones pattern formation: a core regulatory network in varying geometries reproduces major features of vertebrate limb development and evolution*, «PLoS One.» 5 (2010), e10892.

³¹ *Ibid.*; T. Glimm, R. Bhat, S.A. Newman, *Modeling the morphodynamic galectin patterning network of the developing avian limb skeleton*, «J Theor Biol.» 346 (2014), pp. 86-108; J. Raspopovic, L. Marcon, L. Russo, J. Sharpe, *Modeling digits. Digit patterning is controlled by a Bmp-Sox9-Wnt Turing network modulated by morphogen gradients*, «Science» 345 (2014), pp. 566-570.

terms of «dynamical patterning modules» (DPMs): associations of the gene products of the interaction toolkit and the novel physical effects they mobilize (toward novel and emergent ends) in the context and on the scale of cell aggregates³². In modern animals the DPMs are biogeneric components of the self-organizing processes – adhesion and differential adhesion, cell polarization (e.g., making one end different from the other), lateral inhibition (making adjoining cells assume different states), gradient formation (making different regions of the cell cluster experience different chemical influences), and so forth – that drive embryonic pattern formation and morphogenesis. Moreover, although the physical processes and forces embodied in the DPMs are features of the natural world that are independent of the emergence of animals or any other life form, the particular molecules that first mobilized these processes in holozoan multicellular aggregates had specific origins in time and space. These molecules and the DNA that preserves their sequences (the DPM-associated «interaction toolkit»³³), furthermore, are so entrenched in the developmental repertoire of the animals, that they are essentially interchangeable in organisms as evolutionarily divergent as fruit-flies, round-worms and humans³⁴. The findings and concept of DPMs allow for both a revisiting and further articulation of the neo-Kantian perspective. DPMs can be thought of as a new stock of *Keime* and *Anlagen* albeit with a difference inasmuch as a major transitions in life-forms can begin to be analyzed in terms of continuities and discontinuities in DPMs and the space of possibilities that they introduce. DPMs are always already contained within a cellular, i.e., «organized» context of which they are not the source, so are still within the framework of a teleological bracket, and yet can be seen to be providing the resources for the *de novo* appearance of whole spectra of new life forms.

The self-organizational mechanisms that mold and pattern the bodies and organs of animals and other multicellular organ-

³² S.A. Newman, R. Bhat, *Dynamical patterning modules: physico-genetic determinants of morphological development and evolution*, «Phys. Biol.» 5 (2008), 15008; id., *Dynamical patterning modules: a "pattern language" for development and evolution of multicellular form*, «Int J Dev Biol.» 53 (2009), pp. 693-705.

³³ S.A. Newman, R. Bhat, N.V. Mezentseva, *Cell state switching factors and dynamical patterning modules: complementary mediators of plasticity in development and evolution*, «J Biosci.» 34 (2009), pp. 553-572.

³⁴ S.B. Carroll, *Endless forms most beautiful: the new science of evo devo and the making of the animal kingdom*, New York, W.W. Norton & Co., 2005.

isms (typically combinations of DPMs) in some cases represent originating biogeneric physical processes that remain active in present-day forms. Most often, however, embryogenesis of extant organisms is driven by «hybrid» mechanisms, in which processes that were active in ancestral forms have become reinforced by subsequent evolution, but have left traces of their origination, particularly in terms of morphology³⁵. Because the earliest ancestors of Metazoa (the organismal kingdom that contains all extant and extinct animals) were just clusters of cells, the most primitive developmental mechanisms were likely more exclusively based in the physics of soft, excitable materials (to which the clusters would have been inescapably subject) than are the highly evolved mechanisms of present-day development.

The mid-20th century developmental biologist C.H. Waddington referred to developmental processes as «canalized» if they embody fail-safe mechanisms that keep morphogenesis on-track to a species-specific outcome even when perturbed³⁶. Thus, while ancient cell clusters may have been caused by self-organizational biogeneric effects such as phase separation, oscillation, and reaction-diffusion coupling to become multilayered, segmented and otherwise patterned, these earliest prototypes of animal bodies and organs were still to be transformed by canalizing evolution into modern, stable organismal “types,” each generated by a purposeful (in the sense of the end-state being embodied in the material and its dynamics) developmental process.

Just how far can we now push back the teleological bracket toward the origins of “organized beings”? The fossil record suggests a relatively sudden emergence of primitive animals during the late Precambrian and early Cambrian periods³⁷. Sheet-like and hollow spherical forms³⁸, and budding and segmented tubes³⁹ are

³⁵ S.A. Newman, *Physico-genetics of morphogenesis: the hybrid nature of developmental mechanisms*, in A. Minelli, T. Pradeu (eds.), *Towards a theory of development*, Oxford, Oxford University Press, 2014, pp. 95-113.

³⁶ C.H. Waddington, *Canalization of development and the inheritance of acquired characters*, «Nature» 150 (1942), pp. 563-565.

³⁷ C. Larroux, G.N. Luke, P. Koopman, D.S. Rokhsar, S.M. Shimeld, B.M. Degnan, *Genesis and expansion of metazoan transcription factor gene classes*, «Mol Biol Evol.» 25 (2008), pp. 980-996; A. Rokas, D. Kruger, S.B. Carroll, *Animal evolution and the molecular signature of radiations compressed in time*, «Science» 310 (2005), pp. 1933-1938.

³⁸ L. Yin, M. Zhu, A.H. Knoll, X. Yuan, J. Zhang, J. Hu, *Doushantuo embryos preserved inside diapause egg cysts*, «Nature» 446 (2007), pp. 661-663.

³⁹ M.L. Droser, J.G. Gehling, *Synchronous aggregate growth in an abundant new Ediacaran tubular organism*, «Science» 319 (2008), pp. 1660-1662.

seen in Precambrian Ediacaran deposits beginning about 630 million years ago. Within a 10 million year period beginning around 575 million years ago (the so-called Avalon explosion⁴⁰) the sponges and diploblastic (body plans consisting of two tissue layers) cnidarians (corals, hydroids) and ctenophores (comb jellies) arose, and essentially all the triploblastic (three-layered body plans) metazoans followed within a space of no more than 20 million years, beginning about 535 million years ago (the well-known Cambrian explosion⁴¹). Fishes with paired fins emerged more than 500 million years ago, giving rise to lobe-finned fish (including tetrapods) beginning roughly 80 million years afterwards. We now understand (in principle) the DPMs and related processes responsible for the origination of each these morphological motifs, which constitute, in their generic predictability, the *Keime*, and in their parametric variability, the *Anlage*, of animal body plans and organ forms.

Conclusion: teleological bracketing today, and the purposes of Kant

Kant provided a template for the productive mutual interpenetration of philosophy and the empirical investigation of living phenomena that has remained underappreciated, despite the recent flourishing of Anglophone interest in the philosopher. In large measure this is due to the contemporary disciplinary landscape, where a problem-solving orientation in the life sciences *and* a familiarity with Kant exist as two independent variables that are seldom united. The salient exception to this was the remarkable effort of the historian Timothy Lenoir to carve out an appreciation for a distinctively Kantian biological methodology and the role it played in the monumental advances made in nineteenth-century German biology⁴². Whether or not Lenoir entirely succeeded in reconstructing a coherent Kant-inspired «teleomechanist» research program originating in the 1790's and extending through the first half of the 19th century⁴³, the history we have presented

⁴⁰ B. Shen, L. Dong, S. Xiao, M. Kowalewski, *The Avalon explosion: evolution of Ediacara morphospace*, «Science» 319 (2008), pp. 81-84.

⁴¹ S. Conway Morris, *Darwin's dilemma: the realities of the Cambrian 'explosion'*, «Philos Trans R Soc Lond B Biol Sci.» 361 (2006), pp. 1069-1083.

⁴² T. Lenoir, *The strategy of life: teleology and mechanics in nineteenth century German biology*, Dordrecht, Holland - Boston, U.S.A., D. Reidel Pub. Co., 1982.

⁴³ See K. Caneva, *Teleology with regrets*, «Annals of Science» 47 (1990), pp. 291-300; R.J. Richards, «Stud. Hist. Phil. Biol. & Biomed. Sci.» 31 (2000), pp. 11-32; J.H. Zammito, *The Lenoir*

above of the pragmatic bracketings that have accompanied the pursuit of scientific biology in the last two centuries amply confirm Lenoir's main insights.

We have been arguing in this paper for the benefits of a flexible appropriation of Kant's «methodology of teleology» for use in a philosophically reflective and informed biological problem solving practice. From this perspective the fact that the understanding of the teleological aspect of the program underwent reconsiderations and changes in tandem with new developments in microscopy, organic chemistry, enzymology, thermodynamics and rheology (and in our time the nonlinear physics and chemistry of mesoscale, soft, excitable matter and molecular biology) is not only *not* an impediment to the argument but exactly what one would hope and expect. In its earliest formations the status of that ostensibly purposive organization that Kant suggested we had to take, *heuristically*, as a given, was subject to alternative interpretations. Originally referred to as a *Bildungstrieb* by Blumenbach, and later more generally as a *Lebenskraft*, this was sometimes understood as the source of a novel "force" (and where a *Lebenskraft* had occasion to be posited as a real force which was itself responsible for living organization *de novo*, then there would be justification for seeing the demarcation between Kantian teleomechanism and *Romantische Naturphilosophie* as having become blurred). To the extent that such "slippage" from the Kantian ideal may have influenced the thinking of the likes of von Baer and Müller it did not however prevent them from the most outstanding problem-solving successes measured in the most materialist of terms. But even more to the point, the fact that forty to fifty years after Kant's formulations, explicit further self-reflections and clarifications of the meaning of a the *Lebenskraft* in light of ongoing advances in the physico-chemical sciences attests to the vigor and durability of Kant's formulations.

In the 1830's these ambiguities in the conception of the *Lebenskraft* became a source of concern, a primary result of advances in organic and physiological chemistry. A principal advance in establishing the meaning and limits of the notion of *Lebenskraft* was made by Berzelius and Liebig. Their work reinstated the importance of conceiving *Lebenskraft* as the expression of a complex interrelation of material parts incapable of further analysis but inseparable

thesis revisited: Blumenbach and Kant, «Stud. His. Phil. Biol. Biomed. Sci» 43 (2012), pp. 120-132. But also P. Sloan, *Buffon, German biology, and the historical interpretation of biological species*, «British J. Hist. Sci.» 12 (1979), pp. 109-153.

from the order and arrangement of matter. Lebenskraft was to be understood as the expression of this state of affairs rather than its sustaining cause, and the object of physiology was understood to consist in the investigation of the lawlike effects of this state of organization.⁴⁴

In the Neo-Darwinian picture, which we have argued is oblivious to Kant's central insights, programs for multicellular embryogenesis and homeostasis are produced exclusively by random mutation coupled to opportunistic adaptation and written in the language of genes. In contrast, in the physico-genetic paradigm we propose to replace it with, there are purposeful routines and processes of development and function, but no "genetic programs" per se. In the newer view, the elaborate, highly integrated and canalized mechanisms that shape and pattern present-day animals (and the analogous ones in plants and fungi), which mediate the purposeful trajectories of development, emerged over time, having their origins in physically generic, self-organizational effects acting on ancestral cell clusters. These effects were harnessed, stabilized and canalized by these clusters utilizing specific gene products (different in the different kingdoms) that happened to be available at the time. The understanding informed by these new findings and concepts is of an evolutionary process that has gradually turned the outcomes of material and efficient (generic and biogeneric) causes into the formal and final causes of present-day organismal development.

As we turn from an increasingly discredited view of evolution based upon the accretion of random frozen mutational accidents to an evolutionary-developmental perspective, informed by the latest work in the physics and chemistry at the mesoscale, we have good reason to resume our conversation with Kant about the benefits of employing a method of flexible and responsible teleological bracketing in our philosophically informed, biological problem-solving practice.

⁴⁴ T. Lenoir, *The strategy of life: teleology and mechanics in nineteenth century German biology*, Dordrecht-Boston, D. Reidel Pub. Co., 1982, p. 160.