

Transcendental Biology

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ABSTRACT: This essay shows how Conrad Hal Waddington is at the very center of divergent genealogies of theoretical biology: he is at once remembered for his contribution to epigenetics and complex systems biology (in its current formation) and largely forgotten for the debt that he owes to Alfred North Whitehead's philosophy of organism. The essay traces Waddington's debt to Whitehead and demonstrates the way in which this conceptual lineage challenges the transcendental conditions of biological knowledge presupposed by the reigning paradigm of complex systems biology.

KEY WORDS: epigenetics, complex systems, process philosophy

The perspective that we advocate in biology differs then from the physical cases, and takes care of dynamics where the possible outcomes, as defining properties of biological observables, cannot be entailed from the knowledge of the system.—Giuseppe Longo and Maël Montévil (2013)

The work of Conrad Hal Waddington (1905–1975) is foundational for contemporary theoretical biology. Not only did Waddington coin the term “epigenetics,” an area of research that has proven to be a game changer for the contemporary biosciences, but he is also cited as one of the early promoters of complex systems biology, a paradigm that now dominates the theoretical culture of biology (Tronick and Hunter 2016; Bard 2008). Despite the central role that Waddington played in the formation of contemporary theoretical biology, his debt to the process philosophy of Alfred North Whitehead (1861–1947) is almost never mentioned in the scientific literature, despite the fact that Waddington himself attributes the development of his groundbreaking work in epigenetics to Whitehead's metaphysics (Waddington 1957, 1975). And while this little recognized genealogy of theoretical biology (from Whitehead to Waddington) has gained modest traction in the history of

science and process philosophy,¹ it has been all but eclipsed from the dominant discourse of theoretical biology.

This essay shows how both formulations of Waddington's legacy reveal a much deeper set of commitments to and assumptions about the transcendental conditions of knowledge in theoretical biology. By tracing the various ways in which Waddington has been appropriated by biologists in the twentieth and twenty-first centuries, the article demonstrates how his work lays the groundwork for two opposing conceptions of the transcendental, even though only one of them has gained traction in mainstream theoretical biology. Within this frame, it becomes possible to understand how the disavowal of Waddington's debt to Whitehead is a consequence of this conceptual genealogy (Whitehead-Waddington) challenging the forms of transcendental knowledge presupposed by complex dynamical systems. And while an alternative conception of transcendental biology is already implicit in Whitehead-Waddington, as well as in certain strains of theoretical biology, the central provocation of the essay is to develop it along more empirical and materialist lines, together with the transcendental empiricism of Gilles Deleuze and the "culture of interstices" promoted by Whitehead and Isabelle Stengers.

To make this case, I begin by tracing the deep connections that exist between Waddington's work on epigenetics and Whitehead's philosophy of organism. This will set the stage for a more detailed consideration of how Waddington figures prominently in twenty-first century genealogies of theoretical biology (in the wake of reductive molecular genetics and certain versions of neo-Darwinianism), but with little to no mention of Whitehead or the process metaphysics that were foundational to Waddington's work. By the end of the essay, we will be in a position to diagnose this omission by showing how the overly Kantian relation to the transcendental conditions of knowledge that dynamical systems theory presupposes cannot accommodate the "culture of interstices" that Whitehead-Waddington make possible; we will then remedy this exclusion by speculating about the history and future of an alternative conception of the transcendental within theoretical biology—one that requires a different genealogy of Waddington's relevance for contemporary theoretical biology.

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Despite the fact that Whitehead referred to his speculative metaphysics as a "philosophy of organism," he has relatively little to say about actual organisms. Organism, for Whitehead, is cosmic in scale, and biological organisms are merely one aspect (a dense web of "social" relations) of a much wider and dynamically evolving whole. Nevertheless, the organic view of the cosmos, which, as Whitehead explains in *Process and Reality*, is "mainly devoted to the task of making clear the notion of 'being present in another entity'" (50), is also responsible for

his trenchant critique of mainstream evolutionary theory: “Evolution on the materialistic theory,” he explains, “is reduced to the role of being another word for the description of the changes of the external relations between portions of matter. There is nothing to evolve, because one set of external relations is as good as any other set of external relations. There can merely be change, purposeless and unprogressive” (Whitehead 1967: 151–52).

This criticism of evolutionary biology did not go unheard in the early twentieth century. Waddington is perhaps the most well known biologist who espoused Whitehead’s organic philosophy. Though there were numerous biologists in the early twentieth century who endorsed organicist views,² it was Waddington who found in Whitehead a metaphysical foundation for his work on epigenetics (see Squier 2017; Bono 2005). In fact, as early as 1929, when Waddington was still an undergraduate at Cambridge, Whitehead’s *Science and the Modern World* would prove to be transformative for Waddington. Leaving his study of geology behind for biology after reading Whitehead’s early metaphysical treatise (Peterson 2011: 306),³ Waddington wrote a prize-winning essay titled, “Philosophy and Biology,” in which Whitehead’s organic philosophy figured prominently: what we normally think of as objects, wrote the young Waddington, are in reality “possibilities of realization of certain qualities, which are realized when the objects have ingressed into events” (Waddington 1929: 39).

Although Waddington would come to be known for his work on epigenetics and his trenchant critique of the modern evolutionary synthesis, Whitehead’s thought would remain deeply influential to Waddington. The central importance of “canalization” (a concept borrowed from Whitehead—see below) in Waddington’s epigenetics is a case in point. During his time at Thomas Hunt Morgan’s famous “fly lab,” Waddington became fascinated with how the developmental pathways of *Drosophila melanogaster* were determined and would introduce the notion of canalization in 1942 to explain it (Waddington 1942, 1953). After exposing fruit flies to heat shock, a number of them developed the crossveinless phenotype. The crossveinless trait was then selected for and the phenotype was reproduced even when the environmental stimulus was no longer present. Waddington (1953) then used this experiment, along with his research on other developmental modifications, such as the persuasion of “biothorax-like” modification through the use of a chemical stimulus, as the basis for his theory of canalization, or the tendency for robust inheritance to occur under changing environmental conditions.

Canalization is one of the cornerstones of Waddington’s epigenetics: it expresses the way in which “developmental reactions, as they occur in organisms submitted to natural selection . . . are adjusted so as to bring about one definite end-result regardless of minor variations in conditions during the course of the reaction” (Waddington 1942: 563). In other words, canalization accounts for how organisms develop along specific developmental trajectories (over successive gen-

erations) despite environmental perturbations.⁴ However, as Susan Merrill Squier notes, “[t]his same principle [canalization],” not only accounts for evolutionary stability, but it “also explain[s] evolutionary changes: if the environmental perturbations were sufficiently great,” Squier continues, “they could push a population out of the canalized course of its development into a wholly new trajectory. In some instances, an abrupt and large-scale deviation from the canalized path of development could even be necessary for evolutionary survival” (2017: 29).

Waddington famously represents the epigenetic landscape as a river delta with many branching paths. At the top of the diagram, a ball represents a developing system (an undifferentiated cell) that starts its descent down the hill with a variety of possible paths (representing developmental pathways). Waddington refers to this possibility space of development as “multidimensional phase space” (using systems theoretical vocabulary), but then adds that such a mathematical conception is “not very easy for the simple-minded biologist to imagine or to think about” (1957: 27). As the ball rolls down the hill, it is able to roll in and out of pathways or “creodes” early on, but is then further constrained as it rolls down the hill—which is illustrated by the steepness of the slope, corresponding to the degree to which a system is canalized—toward an end state, an eye or an ear, for instance (see Waddington 1957: 29; Peterson 2011: 310). A second diagram represents the “underside” of the epigenetic landscape where genes (the pegs) and the chemical forces they exert (the guy ropes) affect, but do not wholly determine, “the course and slope of any particular valley” (Waddington 1957: 35).

In general, epigenetics offers a conceptual frame that counters the mechanistic, gene-centered view of evolution and development advanced by the neo-Darwinian synthesis. For Waddington, genetic materials do not wholly determine the developmental and evolutionary trajectory of the living system, as the architects of the modern synthesis believed. Even if Waddington was unaware of the material basis of the gene, he realized that it could only be one among other factors determining the developmental pathway or creode of an organism. What’s more, he also realized that characteristics acquired from an organism’s interactions with its environment—cytoplasmic gradients, gaseous substances, etc.—could be canalized and passed on to future generations.⁵ As Waddington writes, “[w]e certainly need to remember that between genotype and phenotype, and connecting them to each other, there lies a whole complex of developmental processes. It is convenient to have a name for this complex: ‘epigenotype’ seems suitable” (Waddington 1957: 30). The “epigenotype” is a neologism that captures the way in which developing organisms grow together through complex gene-environment relationships. In this non-dualistic frame, “organism and environment,” explains Waddington, “are not two separate things, each having its character in its own right, which come together with as little essential inter-relation as a sieve and a shovelful of pebbles thrown on to it” (1957: 189).

But if Waddington's theory of epigenetics offers a non-dualistic alternative to the neo-Darwinian view of development and evolution (which I discuss in more detail below), then this is because it is largely framed in terms borrowed from Whitehead's process philosophy. Indeed, the notion of canalization, which Waddington introduced into theoretical biology in 1942, is a concept that Whitehead employs variously throughout his metaphysical works. In *The Function of Reason* (1978), canalization defines the way in which thought "sinks into a stationary stage" and is "canalized between the banks of custom" (18). But in *Process and Reality*, Whitehead deploys the notion in a way that resonates more explicitly with Waddington's use of it a couple decades later.⁶ There, canalization expresses the coming together of heterogeneous materials (conrescence) into a definite unity of organizational togetherness. Something that has been canalized displays enough robustness that it can withstand environmental perturbation (Whitehead 1978: 107).

In fact, Whitehead uses canalization to describe biological organization in particular: canalization is what allows "life"—or what Whitehead will call "the name originality" (1978: 104)—to survive and endure.⁷ "Apart from canalization," Whitehead explains, "depth of originality [life] would spell disaster for the animal body." And "[w]ith it," he continues, "personal mentality can be evolved, so as to combine its individual originality with the safety of the material organism on which it depends. Thus life turns back into society" (1978: 104). In this context, canalization functions as a form of "social" cohesion (in Whitehead's terminology) that provides enough shelter for the pure, anti-social novelty (life)⁸ introduced into a social order to reproduce itself across successive generations.⁹ Whitehead continues: "even in the lowest form of life the entirely living nexus is canalized into some faint form of mutual conformity. . . . The survival power, arising from adaptation and regeneration, is thus explained" (1978: 104). This early conception of biological canalization in Whitehead helps to scaffold Waddington's own theory of biological organization that explains the preservation of a phenotypic novelty over successive generations in a changing environmental landscape.

Whitehead's theory of "conrescence" also plays no small part in Waddington's conception of the developmental pathway. For Whitehead, conrescence is defined as the process by which a diversity of elements (past occasions) grows together to form a definite unity of subjective feeling (Whitehead 1978: 104, 23). Although Waddington never defines development as a "subjective feeling," in *The Evolution of an Evolutionist* (1975) he admits that what he had been calling a creode in the epigenetic landscape is another name for Whitehead's notion of conrescence (Waddington 1975: 9–10). As he writes in *The Strategy of the Genes* (1957), the term *creode* is a combination of "two Greek roots, it is necessary" and "a route or path" and designates a "pathway of change which is equilibrated in the sense that the system tends to return to it after disturbance" (Waddington 1957: 32). He then

adds that a creode is a “trajectory in phase space . . . characterised by the property that the system, if constrained to move slightly away from the creode, will tend to return to it” (Waddington 1957: 32).

But notice: if the creode is one of the possible pathways or trajectories in phase space that attracts a system despite the disturbances it may experience, then in order for it to be a concrescence in Whitehead’s sense, the nature and quality of the attraction cannot be determined in advance of the system following the path or route.¹⁰ In other words, the trajectory of the concrescence is determined in the very process of the concrescence unfolding. This is a feature of the creode that Waddington seems to notice by 1975: “If I had been more consistently Whiteheadian,” he remarks, “I would probably have realized that the ‘specificity’ involved does not need to lie in the switch at all, but may be a property of the ‘concrecence’ and the ways in which it can change” (Waddington 1975: 9–10).¹¹ Although Waddington does not examine what “specificity” means in terms of concrescence, and how this would map onto the essential “privacy” of every occasion of experience (Whitehead), he at least seems to recognize the value of theorizing it, as well as the importance of the concrescence determining its own meaning and significance.

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Although Waddington’s thought may have been appealing to organicists in the mid-twentieth century (Peterson 2017; Haraway 1976), it was slow to gain acceptance in the twentieth-century life sciences. Within an epistemic culture of biology largely under the rule of a hardened neo-Darwinian paradigm¹²—which asserted that the development and evolution of phenotypes remained under the strict control of genetic mechanisms—Waddington’s views were viewed as still too Lamarckian and seemed to incorporate the models of soft-inheritance that the explanatory frameworks of the modern synthesis were supposed to eliminate (see Scarfe 2013a). While Ernst Mayr, one of the principle architects of the modern synthesis, was encouraged by Waddington’s ideas early on (see Peterson 2011: 313), he would end up harshly criticizing Waddington’s attempt to fuse Whitehead and evolutionary theory to “find something intermediate between Darwinism and Lamarckism” (Mayr to Daniel Polikoff, July 28, 1981; in Peterson 2011: 312–13). As Erik L. Peterson notes, the disapproval of Waddington’s processualism was pervasive in mid-twentieth-century evolutionary biology and it was considered by some, especially Mayr, to have a “European” audience in mind when it used esoteric metaphysical notions to anchor its theories of embryology (Peterson 2011: 315; Mayr to Waddington, July 20, 1959). In short, Waddington’s processualist views were especially unwelcome in a climate dominated by a mechanistic paradigm that sought to fuse Darwinian natural selection and Mendelian genetics into one coherent frame.

Despite the general hostility toward Waddington's thought for much of the twentieth century, contemporary attitudes towards it seem to be changing. Today, Waddington is often regarded as a pioneering, and even a proleptic biologist, rather than an obscure, metaphysical, and anachronistic one. This turn of favor is not easy to characterize. But at least part of this shift has to do with the importance attributed to epigenetic mechanisms in recent years,¹³ as well as the attendant need to piece together a holistic framework for evolution and development that can incorporate these findings without resorting to the molecular reductionism that reigned supreme for half a century (see Jamniczky et al. 2010; Boogerd et al. 2007: 6; Tanay et al. 2005).

To appreciate how these methodological and epistemological transformations have changed attitudes toward Waddington's work, it is essential to note how the massive accumulation of data from high-throughput genome-wide experimentation (genomics and other-omics research programs [Boogerd et al. 2007: 6; Tanay et al. 2005]), as well as the associated discovery that gene expression does not occur in isolation of wider molecular and cellular environments (Gissis and Jablonka 2011; Gilbert and Epel 2009), has shifted the priorities of many researchers.¹⁴ Indeed, scientists are discovering that epigenetic mechanisms—such as DNA methylation, histone modification, and non-coding RNA¹⁵—are essential for the regulation of gene expression (see Zhang et al. 2006; Gilbert and Epel 2009). Much of the urgency felt among researchers to comprehend these regulatory systems stems from the biomedical sciences and their discovery that epigenetic factors are responsible for a wide variety of human diseases and developmental disorders (see Laugesen 2014; Barker 1995). The identification of epigenetic aberrations is crucially important to the epigenetics of cancer, for example, and is leading to important discoveries about how bioactive phytochemicals can correct these aberrations (Tollefsbol 2018: xiii).

What's more, within the last couple of decades researchers have also realized that phenotypic modifications induced by epigenetic mechanisms can be inherited (see Champagne et al. 2003). With these findings, old questions about "hard" and "soft" inheritance have begun to resurface in life science research, albeit in revised form (see Gissis and Jablonka 2011; Jablonka and Lamb 2005, 2008). While neo-Darwinians had well and truly discredited any attempt to smuggle the inheritance of acquired characteristics into biology, and moreover thought they could account for any instance of environmentally induced gene mutation within their overriding framework of genetic mechanism (see Dobzhansky 1982), experimental evidence continues to lend support to the idea that gene mutation is not alone sufficient to account for the intergenerational transmission of traits (see Champagne et al. 2003; Champagne 2010; Tebbich, Sterelny, and Teschke 2010; Grant 1986). Even with these findings, most epigenetic researchers are still unwilling to take the next step and grant that the environment actually induces change in the nucleotide

sequence itself (see Scarfe 2013a: 377–78). Researchers therefore seem willing to accept that epigenetic factors influence gene expression, and these can be passed on (there is more than one heritable code), but they will not permit them to be encoded in the DNA sequence (Tollefsbol 2018; Henikoff and Matzke 1997). Such reciprocal causality would not only undermine divisions between soft and hard inheritance (something that most epigeneticists at least tacitly endorse), but it would also open the door to legitimizing notions of organic selection, also known as the “Baldwin Effect” (see below; also see Scarfe 2013a, 2013b).

However, researchers are quick to note that there are still significant gaps in their understanding of epigenetic mechanisms. This means that many of the hard questions about development and evolution remain unanswered (including soft and hard inheritance). As the biologist Brian K. Hall notes, the real challenge is that “[k]nowledge of many levels of biological organization and integration across those levels will be required to document and then decode the epigenetic code and the epigenotype” (2013: 356). And according to Hall, as well as growing number of researchers, epigenetic mechanisms are far more “complex” than the ones identified in the central dogma—the unidirectional causation of DNA, RNA, and protein—and so cannot be studied using the well-worn experimental methods of molecular genetics. Epigenetic regulatory systems involve mechanisms of non-linear self-organization that are impossible to grasp in terms of the individual components that make them up. Consequently, sophisticated methods of data collection need to be paired with mathematical models that can accommodate the distributed and causally circular forms of self-organization—operating far from thermodynamic equilibrium—that epigenetic systems display (see Érdi 2008; Ringrose 2017). Epigenetic regulation is therefore increasingly conceived of as a complex dynamical system, which “recognize[s],” Hall continues, “that understanding the nature of development and evolution, indeed of life itself, will entail a comprehension of far greater degrees of complexity than previously thought” (2013: 356).

The wager is that complex dynamical systems, which gained traction in mathematics, physics, information theory, engineering, economics, and other domains throughout the late nineteenth and twentieth centuries (see Érdi 2008), provide an adequate theoretical frame for quantifying the various and ongoing interactions between the genome and epigenome (see Ringrose 2017). As Leonie Ringrose writes in the introduction to her 2017 edited collection, *Epigenetics and Systems Biology*, epigenetic regulatory systems are all: “*complex*, comprising multiple molecular components that regulate many genomic targets”; “*dynamic*, allowing flexibility in reaction to environmental, developmental, or disease signals”; and finally, they are “*stochastic processes*, such that the output of a given epigenetic regulatory event can vary from cell to cell, over time, and from individual to individual” (2). Ringrose then adds that the challenge to making progress in the quantification of regulatory systems is twofold: the aversion that many experimen-

tal biologists have to mathematics on the one hand, and the lack of experience that theoretical scientists have with wet and unruly systems on the other (*ibid.*: 3). However, complex systems biology requires that both domains (systems of differential equations and methods of experimental verification) collaborate to build verifiable models of molecular and non-molecular components entering into relationships of circular causality to produce self-organizing systems that steer the development and evolution of organisms (Rohlf et al. 2012; Steffen, Fonseca, and Ringrose 2012). At stake is the design and deployment of computational models that allow researchers to predict when, where, and how epigenetic mechanisms operate in living systems (Steffen, Fonseca, and Ringrose 2012).¹⁶

It is here, at the intersection of epigenetics research and complex systems biology, that Waddington's work is most frequently referenced today. He is cited as a progenitor of contemporary epigenetics, although generally with the proviso that epigenetics is now studied in a more restricted sense than Waddington had in mind, i.e., as "molecular epigenetics" (Allis and Jenuwein 2016; Hall 2013). However, research by Eva Jablonka, Marion Lamb, and others continues to push the boundaries of inheritance systems—by suggesting that behavioral and symbolic systems can be inherited—and insist that the environment may very well be able to modify the DNA sequence (Jablonka and Lamb 2010; Scarfe 2013a). Waddington is also regularly referenced in connection to early applications of dynamical systems theory to biology (Tronick and Hunter 2016; Bard 2008; Hall and Laubichler 2008). As Ed Tronick and Richard Hunter argue, Waddington's notion of the epigenetic landscape, and the associated concepts of canalization and the creode, is closely related to the notion of "state space" in dynamical systems theory, or the representation of all possible states of a system. "Attractor states," they write, "are deep canals that are hard to leave, like the mature phenotype, whereas other states are shallow troughs, easy to get into and out of, like the early organization of the developing phenotype" (Tronick and Hunter 2016: 2).

Waddington would have likely agreed with this characterization given that he had already thought about his epigenetic landscape diagram as a multidimensional phase space (see above), and the creode as "trajectory in phase space" (1957: 32). What's more, Jeremy Gunawardena from the Department of Systems Biology at Harvard Medical School insists that, "Waddington's intuitive conception [of state space, attractors, and dynamical robustness]," which he depicted as an "epigenetic landscape," was later "formalized by the French mathematician René Thom, in what became known as 'catastrophe theory,'"¹⁷ and this has been mathematically developed in Shinar and Feinberg's theorem for "absolute concentration robustness," and successfully applied in the context of bifurcation enzymes (Gunawardena 2010a: 581; Shinar and Feinberg 2010). It is for this reason that Waddington's "epigenetic landscape," Gunawardena writes elsewhere, "continues to provide a conceptual basis for thinking about biological dynamics in high dimensions . . .

and dismantl[ing] some of the barriers between biology and mathematics” (Gunnawardena 2010b: 32–33).

But if contemporary references to Waddington are most often framed in terms of how he anticipates molecular epigenetics and dynamical systems theory, then they only pay tribute to a portion of his contribution to theoretical biology. The other aspect of Waddington’s thought, which was largely dismissed by his contemporaries, and still seems to escape the notice of mainstream biologists, is the debt that it owes to Whitehead’s process philosophy. But then the question becomes: if Waddington’s theoretical biology is fundamentally rooted in Whitehead’s philosophy of organism, then what explains the fact that process metaphysics does not also appear in the conceptual genealogy of epigenetics and complex systems biology? In other words, why don’t concrescence and the subjective form/aim sit alongside of canalization and the epigenetic landscape as a part of the conceptual genealogy of twentieth-century theoretical biology?

In what follows, I argue that there is much more at stake in the elision of process philosophy (and Whitehead in particular) from the archives of theoretical biology than cleaning up what may seem like dated and esoteric metaphysical vocabulary to contemporary biologists. (Whitehead’s difficult language has proven to be a barrier to his acceptance in contemporary philosophy circles as well [see Gaskill and Nocek 2014]). This exclusion reflects a much deeper set of commitments held among theoretical biologists that rests upon the (implicit) disqualification of an epistemic culture of life exemplified by Whitehead’s process philosophy, expressed in certain aspects of Waddington’s epigenetics, and shared by a small number of biologists and philosophers in the twentieth and twenty-first centuries. What I propose to examine in the second half of this essay is how this disqualification is clarified by the way in which the transcendental conditions of knowledge are framed in mainstream complex systems biology. Ultimately, my contention is that a divergent conception of the transcendental underwrites the Whiteheadian strain in Waddington’s thought, which is why it is barred from the dominant epistemic and discursive culture of theoretical biology; but its cultivation is vital to advancing a non-reductive materialist frame for evolutionary and developmental biology.

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Today, there are a handful of philosophers of biology and theoretical biologists who draw on Whitehead (and Waddington), in conjunction with other process-based theories, to conceptualize the developmental and evolutionary pathways of living systems. These theorists tend to hail from outside of mainstream theoretical biology and philosophy, although their work is no less significant for understanding the possibilities and limitations of epistemological practices in these domains. Spyridon Koutroufinis (2014, 2013), Adam C. Scarfe (2013a,

2013b), Philip Clayton (2013), Brian Henning (2013), and James Bono (2005), among others, have taken to engaging in debates in theoretical biology (dynamical systems theory, epigenetics, biosemiotics, organismic selection, etc.) in order to secure a conceptual space for Whitehead's contribution to biological thought. In their work, it is precisely those "Whiteheadian" dimensions of Waddington, which have largely been disqualified, ignored, or considered too "European" by mainstream biology (Mayr), that are showcased and deemed to be especially rich conceptual resources for contemporary biology.

At the most general level, Whitehead's work offers a robust theoretical basis from which to resist all attempts to isolate genetic materials from their wider environments, phenotypic or otherwise (see Bono 2005). His speculative metaphysics undoes the well-worn habits of modern thought indebted to substance-based ontologies and its many attendant binaries: between subject and object, mind and matter, organism and environment, and so on (see Whitehead 1978). These essentialisms are undercut by Whitehead's assertion that all human and nonhuman entities *just are* the perspectival integrations (or prehensions) of their wider environments, where each of these perspectival integrations has a definite and singular relation to every other integration. With this, Whitehead gives philosophical expression to some of the latest and most radical work in epigenetics that demonstrates how phenotypic development is an expression of gene-environment relations that extends well beyond the cytoplasm, and even the cell, to language and culture (Jablonka and Lamb 2005; Gissis and Jablonka 2011). What this means is that there is both an empirical and theoretical basis for not excluding or abstracting out those elements within the overall environment of a system that seem tangential to its development. The developing organism is the growing together of a multiplicity of environments (from molecular to the cultural) into a uniquely coordinated (living) society over a finite period of time; and given the right conditions, portions of the coordination can be passed on to the next generation (inherited) (Whitehead 1978: 104).

But perhaps the most compelling contribution that Whitehead makes to biology—which will prove to be especially difficult for contemporary theoretical biologists to accommodate—is his conception of *self*-organization. If theoretical biologists largely agree that the organism is a complex self-organizing system, then Whitehead not only confirms this intuition but he also grasps what it means to be a *self* in the distributed organization of living matter. For Whitehead, if the concreating (developing) entity is an integration of its environments, then it is also a singular integration of them: each entity feels or prehends its environments in its own way. As Whitehead puts it, what is over "there" is experienced and privately enjoyed over "here" (1967: 69). Each entity is a wholly unique and therefore privately *enjoyed* integration of its surroundings (no matter how inconsequential

that novel integration is); otherwise, it would be a bare mechanistic reproduction of what has been (Whitehead 1978: 85).

At the scale of the developing organism, this means that the system must have a real, if minimal and pre-conscious sense of self that exemplifies the manner in which the organism incorporates its environments into a determinate constitution of itself (as relevant or irrelevant datum that is positively or negatively prehended respectively [see Whitehead 1978: 41, 221]).¹⁸ This seems to be the sense of “privacy” and “internal relationality” that Waddington may have intuited when he conceived of the creode as a concrescence whose specificity is a “property” of the concrescence itself. Koutroufinis contends that Whitehead’s sensitivity to the internal dynamics of self-formation (subjective form and subjective aim) is invaluable to the theorization of self-organization of “real organisms” (Koutroufinis 2014: 9), and I would argue that Waddington also asks us not to prescribe the course of development in advance of its unfolding. While this view is far from mainstream in today’s theoretical biology, and for reasons that will become clear shortly, suffice it to say that a premium is placed on the organism’s basic freedom to determine how it responds to its immediate and mediate environments: the organism *decides* what and how environments are meaningful to its formation.¹⁹

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There is a rich, if undervalued, conceptual genealogy in twentieth- and twenty-first-century evolutionary and developmental biology that shares this concern for the autonomy of developing organisms. Although this is an archive that I cannot fully exploit here, it’s worth highlighting certain features of it in order to expose the range of conceptual terrain that it covers. For instance, the evolutionary psychologist, James Mark Baldwin (1861–1934), intervenes in the causality of natural selection, and his work has once again become important to those for whom development follows the creative and experimental behavior of organisms, rather than the mechanistic forces of selection. Baldwin realized that organisms are not the passive recipients of natural selection, but rather, selection often follows the unpredictable experimentation of organisms in their habitats. He discovered that when not-selected-for phenotypic behaviors (or functions) are advantageous they are often passed on to subsequent generations (see Baldwin 2005). This is what has come to be known as “organic selection” (or the Baldwin Effect), and lends support to the idea that functionality is determined by the “value-selective” activity of the organism; hence: the organism is not simply the “object of selection” (Scarfe 2013b: 264).²⁰

The idea that form does not determine function also anchors Stephen Jay Gould and Richard Lewontin’s argument in their classic 1979 paper, “The Spandrels of San Marco and the Panglossian Paradigm: A Critique of the Adaptationist

Programme.” This position is further developed by Gould and Elisabeth S. Vrba (1982), who demonstrate that not-selected-for phenotypic traits, or “exaptations” (deepening Darwin’s notion of pre-adaptation), can have new and unanticipated functions that later become primary adaptations. Their work forcefully demonstrates how the function and evolutionary success of a phenotype cannot be determined in advance of its unfolding. Similarly, Stuart Kauffman’s notion of the “adjacent possible” empty niche resonates with this work as well: it shows how it is impossible to pre-state all the functions of a phenotype, which implies that the opportunities for evolutionary becoming cannot be determined in advance of their emergence (2016: 71; Longo, Montévil, and Kauffman 2012).²¹

There are many other scientists and theories that belong in this genealogy. For example, there are strains of biosemiotics, especially those drawing on the semiotics of C.S. Pierce and the ethology of Jacob von Uexküll, that are likely to be a part of this conceptual history (Hoffmeyer 1997). Likewise, Humberto Maturana and Francisco Varela’s autopoietic systems theory (1980), Gregory Bateson’s notion of the “soma” (1963), and perhaps even the “mind in life” work advanced by Evan Thompson (2007) are all likely to figure prominently in this genealogy. However, what’s at stake here has less to do with elaborating an exhaustive history of ideas and has much more to do with sketching a conceptual through-line that exposes a shared commitment to the idea that the trajectory of phenotypic development and evolution cannot be determined in advance of its emergence. This is a form of “strong emergence” that often makes scientists and analytical philosophers uncomfortable (since its causes are “mysterious”), and so it tends to be dismissed or explained away in favor of “weaker” notions of emergence (Chalmers 2006; Bedau and Humphreys 2008; Bedau 1997; Deacon 2003).

But of course Whitehead already understood the need for a strong conception of emergence when he theorized the subject’s formation in terms of the decisions it makes in the privacy of its own emergence. These decisions cannot be anticipated, gleaned from other entities, or even shared, since they are heterogeneous to all other decisions and are therefore irreducible to all that has been given.²² And although the biologists assembled in this genealogy are not all Whiteheadians *sensu stricto* (and certainly not in the way that Waddington was), they are a part of an epistemic culture that resists the temptation to derive the conditions of phenotypic development and evolution from other events. What is at stake, then, is preserving what I would call the *radical alterity of the developing organism*. Thus, if Whitehead speaks of “life” as “interstitial” (“Life lurks in the interstices of each living cell” [Whitehead 1978: 105]), and Isabelle Stengers, following Whitehead, insists on cultivating a “culture of interstices” in the sciences (Stengers 2011: 328), then I think we have a preliminary sketch of what this “interstitial culture” within biology might look like.

However, the central challenge to promoting this epistemic culture is that it runs counter to today's dominant theoretical paradigm in biology: complex systems biology. In what follows, I contend that the complexity sciences, which have well and truly taken hold of theoretical inquiries into evolution and development in the last decade or so, cannot accommodate the modes of knowing promoted by the interstitial culture of life. Drawing on the work of Giuseppe Longo, in close collaboration with Maël Montévil, Kauffman, and others, I demonstrate how the complexity sciences presuppose a relation to the transcendental conditions of biological knowledge that forecloses what is most essential to the marginalized knowledge practice we been examining: the alterity of organismic development. Ultimately, this will leave us searching for alternative knowledge practices and transcendental frameworks for biology, as well as with a much clearer sense of Waddington's ambivalent relationship to the history of theoretical biology, and an answer to why his "Whiteheadianism" has been largely disavowed by contemporary theoretical biology.

* * *

According to Longo and his colleagues, in order to construct an adequate theory of biological systems (which does not yet exist [see Longo and Montévil 2014; Longo, Montévil, and Kauffman. 2012]) it is essential to identify the assumptions and limitations of physico-mathematical modeling, especially in complex dynamical systems. For physicists working with differential equations, the first step is to choose the appropriate phase space (Longo, Montévil, and Kauffman 2012). Physical phase spaces, they explain, are not already given, like "absolutes underlying phenomena"; rather, they are the physicists' "remarkable and very effective invention in order to make physical phenomena intelligible" (9; Bailly and Longo 2011). Longo and Montévil write that inventing a phase space amounts "to construct[ing] a mathematical space which contains all the required ingredients for describing the phenomena and to understand[ing] the determination of its trajectory, if any" (Longo and Montévil 2014: 188). In order to generate this mathematical space, the physicist must first discover what the "pertinent observables" of a trajectory are. Pertinent observables are determined from invariant preserving transformations or symmetries in a trajectory (e.g., for Poincaré momentum is preserved in dynamics, and so on [see Longo, Montévil, and Kauffman 2012: 9]). And in both classical and quantum physics these symmetries express "conservation laws" that make it possible to "compute the trajectories of physical objects" (Longo and Montévil 2013: 65). Once theoretical symmetries have been generated from the relevant equations, it is possible to construct a phase space that is a reference system for the possible trajectories.

Longo and his colleagues take great pains to show how the construction of phase space is the *sine qua non* for physics to be done. Even before the so-called

invention of phase space in the late nineteenth century, Newton was working within a Cartesian space; thermodynamics had to invent its own mathematical phase space from its pertinent observables, namely, temperature, pressure, and volume; and quantum physics, likewise, had to set up another space (out of Hilbert space of probability densities) to understand the wave function (Longo, Montévil, and Kauffman 2012: 9). As Longo and Montévil explain in their co-authored book, *Perspectives on Organisms*, these and other instances of phase-space construction amount to discovering the right *a priori* conditions of intelligibility. “Since Newton and Kant,” they continue, “physicists consider the construction of (phase) space as an *a priori* of the very intelligibility of any physical process” (Longo and Montévil 2014: 193; 2013). In short, phase spaces, which represent all possible trajectories of a physical system, are the transcendental conditions of possibility for knowledge about systems in both classical and quantum physics. These spaces are the physicists’ analogues to Kant’s transcendental conditions in the sense that the conditions of a physical system’s intelligibility must be externally set.

We begin to see the limitations of physico-mathematical modeling for biology when we look more closely at how symmetry changes and random events are understood in these transcendental spaces. In physics, symmetry changes describe those situations where symmetry is broken and “something is not preserved”; although generally, there is a transition from one “coherence structure” to another, and a new “non-trivial” symmetry is established (Longo, Montévil, and Kauffman 2012: 10). Now, random events are usually correlated to symmetry changes. Longo and Montévil define a random event as one in which “the knowledge about a system at a given time does not entail its future description” (Longo and Montévil 2013: 70). However, there is a catalogue of every possible outcome given in the initial measurement of the system and their probability of occurring is then determinable using probability theory (Longo and Montévil 2013: 70). Thus, random, symmetry-breaking events “occur within a perfectly pre-given space of possibilities” (Longo, Montévil, and Kauffman 2012: 15).

What concerns us is that this model cannot accommodate how biological systems develop and evolve. If we take the pertinent observable of a biological system to be the phenotype of the organism,²³ then this observable cannot be regarded as a mathematical invariant in a trajectory. “In contrast to this core perspective in physics,” explain Longo and Montévil, “we propose that biological objects do not have such stable symmetries, and, thus, that their trajectories are not specific: there are no sufficiently stable symmetries and corresponding invariants, as for phenotypes, which would allow to determine the evolutionary dynamics of the object” (2013: 68). What this means is that phenotypes do not have theoretical symmetries from which you could construct a pre-given phase space. Koutroufinis makes a similar point, but underscores the fact that the possibility space of a developing organism, unlike a physical system, cannot be externally set (in parameters) since the space

of its intelligibility is constantly transforming according to its own internal dynamics (2013: 323–24). In other words, we cannot pre-determine the transcendental “background space” that would be able to make sense of a phenotypic trajectory.

If this is true, then biology confronts us with a very different understanding of randomness: one that is non-probabilistic (Longo and Montévil 2013). This is because the probabilities for an event occurring cannot be measured due to the fact that the field of possibility defined by the phase space is continually changing. Unlike in physical and chemical systems, there is no pre-defined transcendental field of possibility that would be capable of calculating all possible trajectories using probability theory. If Longo and his colleagues are right, then developing phenotypes are *strongly* emergent systems, and this brings complex dynamical systems face-to-face with the limits of its descriptive power. As Koutroufinis puts it, biological organisms are anti-entropic systems whose mathematical calculation would require the “simulation of a *self-constraining dynamic*,” but this is simply “not conceivable within contemporary dynamic systems theory” (2013: 327). What biological systems challenge us to think then are modes of organization where the possible field of action is continually evolving and therefore cannot be externally set. This is a notion of transcendental possibility that dynamical systems are not equipped to compute, although it was already conceived by Whitehead in his conception of the concreting subject; it was then intuited by Waddington with his elaboration of canalization and the creode; and then pushed in new directions by Baldwin, Gould, Kauffman, Longo, and others.

* * *

If this essay has demonstrated that the dominant conception of the transcendental within theoretical biology cannot adequately capture organismic development, then what would it mean to develop a conception of organismic possibility that resists being coopted by the transcendental framework of complex systems? Rather than abandoning the notion of the transcendental altogether, I propose that we deepen our conception of what transcendental could mean for biology, and thus expand our frame for grasping the conditions of organismic intelligibility. What this means is that we conceive of different permutations of the transcendental within the theoretical sciences.

On the one hand, there are those possibility spaces that are more Kantian in nature: they are externally set, and are thus adequate for capturing the possible trajectories of complex physical systems. But then on the other hand, there are the possibility spaces that emerge along with the materiality of the developing system. The latter are spaces of potentiality that living systems construct as they develop and that cannot be stated in advance of them unfolding. These are spaces of potentiality that are much more closely aligned to what Gilles Deleuze meant by the

transcendental field (i.e., transcendental empiricism) than what Kant meant by the transcendental conditions of knowledge. As Deleuze explains in *Difference and Repetition*, he is interested in the transcendental conditions of *real* instead of *possible* experience (1994: 154). Where Kant sought to define the conditions of all possible knowledge (they are fixed in advance and abstract), Deleuze realized that transcendental conditions can be no wider than what they condition; and for this reason, these are the transcendental conditions that are much better equipped to frame the actual spaces of potentiality that unfold with living systems (1994: 135; 1990: 102).

While this perspective on the transcendental requires further development, and is nothing more than a provocation at this point, it gestures toward a conception of organismic potentiality that breaks out of the transcendental straightjacket that complex dynamical systems impose on living systems. Transcendental empiricism, writes Deleuze, “forms an intrinsic genesis, not an extrinsic conditioning,” and it is precisely this internal genesis that cannot be expressed using the transcendental framework presupposed by dynamical systems theory (1994: 154). The latter’s Kantian impulses are not a problem *per se*; rather, they only become an issue when they are extended beyond their domains of relevance, and therefore exemplify what Whitehead called “The Fallacy of Misplaced Concreteness” (see Whitehead 1967: 51). It is just this overextension that is on full display in contemporary theoretical biology, which is why new attention needs to be paid to the “intrinsic genesis” of potentiality within biological systems and the cultivation of an alternative conception of transcendental biology. This new conception would also open the door to a different intellectual genealogy of theoretical biology: it would not only pass through the work of Whitehead, Waddington, Kauffman, Longo, and the others discussed in this essay; but it would also dig deep into the archives of Continental philosophy, including the work of Friedrich Nietzsche, Henri Bergson, Deleuze, Georges Canguilhem, and even Jacques Derrida, as well as work by any other thinker who directly engages the conditions of organismic intelligibility outside of a Kantian frame.

But if Waddington figures prominently in this genealogy of theoretical biology then it is because his work is central to the history of the transcendental that I have been sketching. Waddington is at the very center of divergent conceptions of the transcendental in biology: he is at once remembered for his contribution to epigenetics and complex systems biology in its current form, and he is also forgotten for the debt that he owes to Whitehead’s philosophy of organism (at least in mainstream theoretical biology), as well as his important intuition that developmental trajectories cannot be stated in advance of their unfolding. It is perhaps for good reason then that Waddington’s debt to process philosophy has been largely disavowed: it represents an onto-epistemological challenge to the comprehension of living systems using the conceptual and computational tools of complex systems biology. But what’s especially striking is that the germ for opposing complex systems biology is borne out of one of the most important sites of its emergence: namely,

Waddington's epigenetics. It is for this reason that Waddington appears Janus-faced in this history: pointing us to two different conceptions of the transcendental at once. Perhaps the challenge, and even the importance, of reading Waddington in terms of this history is to hold these two versions of Waddington together, and thus resist the temptation to reduce one version to the other (as Whitehead would say). The clear advantage is that we gain insight into Waddington's ambivalent relationship to the history of theoretical biology, and how his work is vital to opposing the transcendental biology that it was also instrumental in shaping.

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NOTES

1. In the history of science, see Bono's exceptional reading of Waddington's debt to Whitehead (2005). For a more recent take on the relation between Waddington's epigenetics and Whitehead's method and practices in particular, see Squier 2017. Additionally, Peterson's (2011) article, "The Excluded Philosophy of Evo-Devo?" engages many of the assumptions pervading the neo-Darwinian paradigm in biology during the twentieth century and how this put a strain on any attempt to introduce Waddington's Whiteheadian conceptions into biology. In this context, also see Peterson's (2017) important book, *The Life Organic*. In philosophy and theoretical biology, see Henning and Scarfe's (2013) tremendous edited collection which paves the way for a philosophy of biology that is Whiteheadian in spirit, and so is deeply sympathetic to Waddington's work. See for example, Scarfe's (2013a) essay in the collection.
2. For a more detailed discussion of organicism in twentieth-century biology, and Whitehead's influence on this movement, see Peterson 2017, as well as Haraway's (1976) important reading of organicist biology in *Crystals, Fabrics and Fields*.
3. While in his article, "The Excluded Philosophy of Evo Devo," Peterson discusses how influential Whitehead was on the young Waddington, and how *Science and the Modern World* is what persuaded "Wad" to study biology (2011: 306), in his more recent work, he notes that Waddington's friend, Gregory Bateson, also played no small part in luring Waddington away from geology (2017: 100–01).
4. As Squier puts it, canalization "was the evolutionary principle central to epigenetics that explained why, over the course of generations, a population tended to remain consistent" (2017: 29).
5. It's important to note that originally epigenetic influence did not extend beyond gene products. However, once Waddington discovered "genetic accommodation" then epigenetic control extended to the wider environment; epigenetics thus became a more holistic conception. See Hall 2013. Also, see Hall and Laubichler 2008 as well as Janniczky et al. 2010.
6. Whitehead notes that his particular use of the notion actually comes from Henri Bergson. See Bergson 1998.
7. I address Whitehead's conception of life in "Imaginative Chemistry" (Nocek 2014).

8. Whitehead contends that, “Life is a bid for freedom” (1978: 104). He also notes that life “is the name for originality, and not for tradition,” and it is fundamentally “anti-social” (104). See Stengers’s (2011) discussion of the anti-social nature of life in *Thinking With Whitehead*, Chapter 19.
9. As Whitehead puts it, life is not a “defining characteristic,” and not the name for “tradition,” or that which is inherited across successive generations (Whitehead 1978: 105). Rather, life is “robbery” (105); it is pure anti-social “immediacy” that “lurks in the interstices of each living cell, and in the interstices of the brain” (105–06).
10. This is absolutely essential for Whitehead: every occasion, no matter how insignificant, is a *novel* integration of its environments. This idea strictly follows from Whitehead’s “Category of the Ultimate.” “‘Creativity,’” explains Whitehead, “is the universal of universals characterizing ultimate matter of fact. It is that ultimate principle by which the many, which are the universe disjunctively, become the one actual occasion, which is the universe conjunctively. It lies in the nature of things that the many enter into complex unity. ‘Creativity’ is the principle of novelty. An actual occasion is a novel entity diverse from any entity in the ‘many’ which it unifies. Thus ‘creativity’ introduces novelty into the content of the many, which are the universe disjunctively” (1978: 21).
11. Waddington continues here by noting that René Thom’s catastrophe theory fits well with the notion of the creode-conrescence: indeed, “the catastrophe need not be in what precipitates the catastrophe, but could reside only in the possible stable regimes [i.e., creodes] . . . into which the system could be flipped” (1975: 10). In other words, “specificity” resides in the unfolding conrescence itself, and not in what is external to it, i.e., an external “switch.”
12. While neo-Darwinianism was around before the modern evolutionary synthesis, in the twentieth century it became associated with a gene-centered view of evolution made possible by synthesizing Gregor Mendel’s genetics and Darwin’s theory of natural selection in one framework. See Huxley (1942). In this view, genetic material is the sole source of heredity and leaves no room for the inheritance of acquired characteristics *à la* Lamarck, also known as, “soft-inheritance.” See also Scarfe (2013a).
13. According to Bateson, “[t]he growth in interest in epigenetics has been extraordinary. In 1960, four papers included the word ‘epigenetics,’ according to the web of science. By the year 2000, 415 papers were published in that year alone with Waddington’s word in their titles. In 2010, only a decade later, an astonishing 3,577 papers used ‘epigenetics’ in their titles” (2014: 198).
14. In my forthcoming book, *Molecular Capture*, I discuss how the inundation of molecular data in the post-genomics era has forced researchers to adopt a more systems theoretical perspective in order to understand how molecular and cellular components work together.
15. It is important to keep in mind that epigenetics tends to be studied in a much narrower sense than Waddington had intended. Today, most researchers are interested in “molecular epigenetics,” which designates those interactions within nuclei that regulate gene expression and that are heritable, but do not change the DNA sequence. See Henikoff and Matzke 1997.
16. In his critical assessment of recent trends in epigenetics, Scarfe notes that, in the main, “molecular epigenetics is just as reductive and mechanistic as the neo-Darwinian paradigm that it seeks to overcome” (2013a: 381).

17. “Catastrophe Theory” is a branch of dynamical systems theory that was developed by the French mathematician René Thom in the 1960s. In the most general terms, catastrophe theory studies how abrupt transformations in system behavior (or bifurcations) are made possible by relatively small changes. See Thom 1989.
18. It is worth noting that Whitehead has been wrongly criticized for promoting subjectivist metaphysics (advocating a universe filled with self-interested atomized subjects), and hence reintroducing all the old problems that his metaphysics is supposed to overcome (Schindler 1983: 121). However, a number of scholars have shown how this critique is based on a fundamental misreading of Whitehead, one that misses the “ecstatic” nature of actuality that underwrites his metaphysics. See for instance Halewood 2011 and Henning 2005.
19. Koutroufinis characterizes the self-determination of environments in terms of Jakob von Uexküll’s notion of the *Umwelt* (see Koutroufinis 2014: 18).
20. Scarfe (2013b) provides a range of experimental examples of Baldwin Effect in an effort to respond to critics who claim that the theory cannot be empirically verified.
21. Although the notion of the “adjacent possible” was first coined by Kauffman in the 1990s, in his most recent work, Kauffman insists that within the evolving biosphere, where natural selection exerts its force on a phenotype within a niche, there is no way to pre-state the functionalities selected and fed into the future evolution of the biosphere (Kauffman 2016: 71; Longo, Montévil, and Kauffman 2012). Kauffman frequently cites the evolution of the swim bladder—which makes neutral buoyancy possible—as a potent example of the production of “adjacent possibles” within the biosphere. As he explains, natural selection exerted its force on the fish to evolve a swim bladder in order to control buoyancy, but it did not “act” (*sic*) to forge a new empty adjacent possible niche for worm and/or bacterium habitation. Indeed, if a bacterium and/or worm were to find the swim bladder a suitable niche and could generate fit offspring, then the swim bladder is what enabled, rather than caused, a new opportunity for evolutionary becoming through the discovery of new and emergent functions that could not have been pre-stated (see Kauffman 2016: 72–74).
22. As Whitehead writes: “The concrescence, absorbing the derived data into immediate privacy, consists in mating the data with ways of feeling provocative of the private synthesis. These subjective ways of feeling are not merely receptive of the data as alien facts; they clothe the dry bones with the flesh of a real being, emotional, purposive, appreciative” (1978: 85).
23. In a co-authored piece with Perret, Longo writes that the material organization of the living system is the only “observable” possible for biology. In an attempt to correct any reduction of the organism to “information,” the authors write, “biological dynamics radically depend on their materiality, and this is far from the independence of matter proper to digital information theories. Moreover, DNA or RNA are not ‘rigid’ and this is essential to biological processes. . . . [T]he proper biological observable is ‘material organization.’ From the structure of DNA to neuronal dynamics, biological activities exist solely in their highly organized physical, chemical and biological materiality. Quite the opposite of information, the polyvalent use of a given material is a core property in biology” (Perret and Longo 2016: 13).

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