

On the Different Ways of “Doing Theory” in Biology

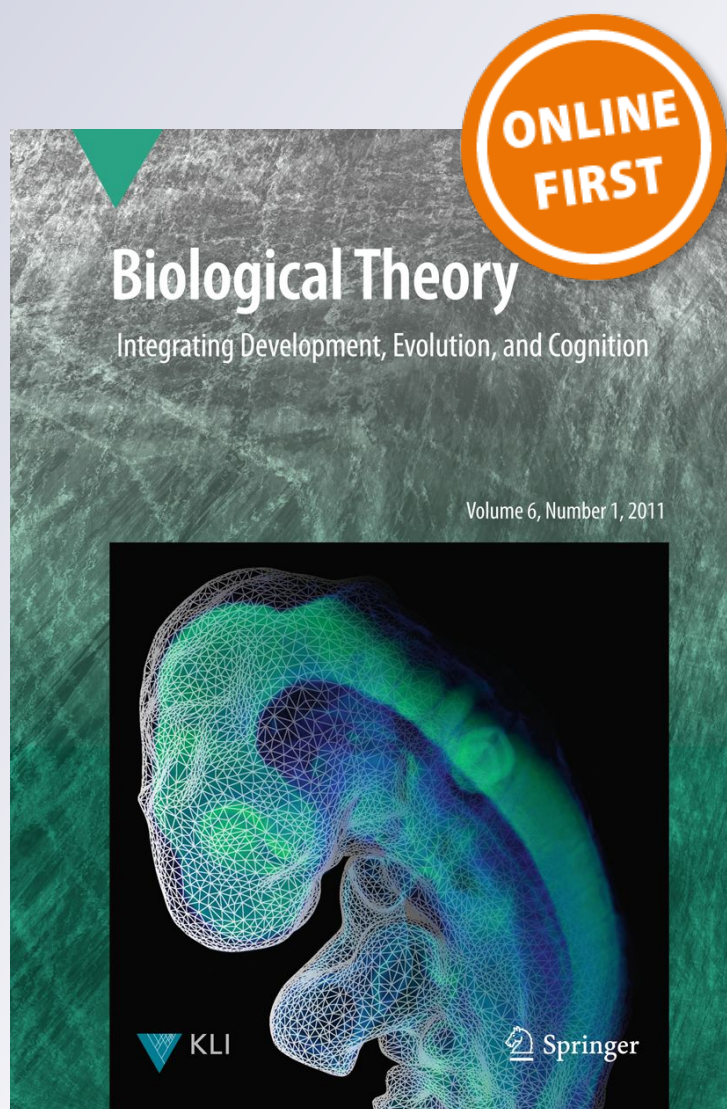
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On the Different Ways of “Doing Theory” in Biology

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Abstract “Theoretical biology” is a surprisingly heterogeneous field, partly because it encompasses “doing theory” across disciplines as diverse as molecular biology, systematics, ecology, and evolutionary biology. Moreover, it is done in a stunning variety of different ways, using anything from formal analytical models to computer simulations, from graphic representations to verbal arguments. In this essay I survey a number of aspects of what it means to do theoretical biology, and how they compare with the allegedly much more restricted sense of theory in the physical sciences. I also tackle a recent trend toward the presentation of all-encompassing theories in the biological sciences, from general theories of ecology to a recent attempt to provide a conceptual framework for the entire set of biological disciplines. Finally, I discuss the roles played by philosophers of science in criticizing and shaping biological theorizing.

Keywords Computer simulation · Mathematical modeling · Philosophy of science · Theoretical biology · Verbal arguments

It is often said in the hall of biology departments that biologists suffer from physics envy (I have never asked a physicist about this). If true, this may in part be a leftover effect from the heydays of logical positivism, when philosophers of science truly did think of physics as “the queen of the sciences” (Uebel 2011). It is also somewhat ironic, considering that the very first confrontation between

biology and physics—the famous dispute between Darwin and Lord Kelvin about the age of the earth (Burchfield 1974)—was handily won (after a mere 5 decades) by the biologist.

Be that as it may, clearly biology as a discipline, and biological theorizing in particular, has come a long way from whatever model physics may have offered in the very beginnings.¹ Indeed, the differences between biology and physics, and even the conceptual and methodological heterogeneity within biology itself, have been advanced as evidence for a fundamental disunity of “science” (Dupré 1983), treating the latter as a Wittgensteinian family resemblance concept (Magnus 2011). This thematic issue of *Biological Theory* explores several aspects of what it means to do theory in biology, and in this essay I will briefly survey the field both in terms of its conceptual history and as far as some recent developments are concerned. I will begin by commenting on the oft-proposed

¹ There are, of course, dissenting views. Consider for instance what Carl Woese—a microbiologist, not a professional historian—has had to say about the role of physics in shaping twentieth century biology: “It is instructive to catalog some of the changes that fundamental reductionism wrought in our perception and practice of biology. Chief among these is that the biologist’s sense of what is important and what is fundamental was retooled to conform to the classical physicist’s perception thereof. From this followed changes in the biologist’s concept of organism, in his or her view of what constitutes an explanation, in what constitutes a “comprehensive” understanding of biology, in what biology’s relationship to the other sciences is, in what biology can tell us about the nature of reality, in what biology’s role in the society is, and in what biology’s future course will be. These in turn produced changes in how biological knowledge is organized—the structure of academic curricula, the nature and purview of biological disciplines and text books, the priorities of biological funding agencies—and an overall change in the perception of biology by the society itself. All has by now been set in stone” (Woese 2004, p. 174).

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idea of laws in biology (a clear link to the above mentioned physics envy) and a related trend toward broad, all-encompassing theories. I will then examine several distinct ways of doing biological theorizing, from analytical to statistical approaches, and from computer modeling to verbal argumentation. I will conclude with a brief examination of the role of philosophy of science in biological theorizing.

Laws in Biology?

If there is anything that characterizes physics as a science it is its unending quest for universal laws, from Newton's mechanics to the current (and highly controversial) string theory (Smolin 2007). This is the case despite the fact that influential philosophers of science like Van Fraassen (1989) and Giere (1999) maintain laws play a marginal and mostly didactical role, even in physics. Regardless, it is not surprising, that discussions of general laws in biology are a recurrent staple of the literature and—interestingly—one that provides a good example of positive interactions between theoretically inclined biologists and philosophers of science. This is certainly not the locus for an in-depth examination of proposed biological laws, but it will be instructive to consider a few examples, particularly in view of the connection between laws and the topic of the following section, on broad biological theorizing.

In a number of cases authors draw a direct parallel between physical laws and proposed biological equivalents. For instance, Elgin (2003) argues that the “epistemic functions of a priori biological laws in biology are the same as those of empirical laws in physics” (p. 1380). Elgin begins by acknowledging the (almost) universal agreement among philosophers who subscribe to the concept of laws that these must be both universal and empirical in nature, though he hastens to say that these conditions are necessary but not sufficient to distinguish laws from “accidental” generalizations. He then discusses Sober's (1993) proposal that the Hardy–Weinberg principle in population genetics is an example of a biological law, even though it is universal but not empirical.

There are several problems with this proposal, chiefly the fact that Hardy–Weinberg cannot meaningfully be thought of as a “zero force law” analogous to, say, the law of inertia (as Elgin suggests), as well as the above mentioned lack of empirical content. Pigliucci and Kaplan (2006, Chap. 1) have discussed in detail why the various evolutionary mechanisms that can cause a population to deviate from Hardy–Weinberg equilibrium are not conceptually equivalent (in particular natural selection and genetic drift), and should not be thought of as “forces” characterized by intensity and direction. Moreover, it

simply seems strange to suggest that a scientific law can have no empirical content and instead simply be true a priori (as Hardy–Weinberg surely is, mathematically speaking). This risks embarking philosophy of science down the slippery slope of considering logical and mathematical principles themselves as “laws,” a usage that clearly does not accord to scientific practice at all. Apparently, however, this point is not at all clear in the minds of some biologists, since it is possible to find statements like the following: “The global-optimum model is not so much a predictor of nature as a definition of nature. It must be true that a perfectly adapted organism leaves the most possible offspring!” (Nonacs and Dill 1993). Or: “The existence of a global-optimum point is a ‘*deep axiom*’: a tautology that guarantees logical consistency at the core of a theory” (Stearns and Schmid-Hempel 1987). This is surely one area where more communication between theoretically minded biologists and philosophers of science would be welcome.

Elgin tried again a few years later, this time beginning with a discussion of the difference in the literature between strict laws (allegedly, like those found in physics) and *ceteris paribus* laws (seemingly, the kind common in biology) (Elgin 2006). While I think Cartwright's (1983) suggestion that all laws are, at bottom, *ceteris paribus* ought to be considered seriously, it still does not follow that there are no philosophically interesting differences between physical laws and biological generalizations. One of the most common objections to the idea of laws in biology is that biological organisms are complex and multiply realized, and therefore that one simply has to invoke a (very large) number of *ceteris paribus* conditions to make any sense of talk of laws. Elgin (2006) acknowledges this, but suggests that “if pendulums are multiply realized and yet still have laws, why should the fact that biological or psychological states are multiply realized be a reason to think that these sciences don't contain laws?” (p. 121). The analogy strikes me as so forced that it is hard to take it seriously, at least if one is even vaguely aware of the degree of biological diversity and the number of emergent behaviors of biological systems. In the end, Elgin has to resort to either examples of logical (but not empirical) “laws” like the above mentioned Hardy–Weinberg principle, or to generalizations that are better understood as being the direct result of underlying physical laws, as in the case of the famous scaling of metabolic rate with $3/4$ of body mass.²

² According to West et al. (1999) the $3/4$ scaling is a result of basic physical constraints imposed on organismal metabolism, which is why it is universal, transcending the particular evolutionary history of those organisms.

Besides appeals to Hardy–Weinberg as an example of biological laws, the next most popular area of discussion concerning this topic is perhaps the possible existence of laws in ecology. For instance, Mikkelsen (2003) makes a case for moving ecology from an idiographic (historical) mode of explanation to a nomothetic (law-based) one. He maintains that—contra to what he perceives as the practice among ecologists—generalizations should be interpreted in terms of law-like generalizations because functional kinds (such as “predators”) and structural kinds (like the various community types) correlate better than taxa (historical kinds) with fundamental ecological patterns and processes. As Mikkelsen (2003) puts it, “Imagine being dropped at a random spot on the land surface of the Earth. Which would allow you to predict the density of plant species around you—that is, the number of species per 10,000 square kilometers—most precisely: knowing the climate, or knowing the landmass on which you stand? Answer: climate wins, hands down” (p. 1395). Well yes, but it is arguable that such predictions are the result of “laws” in any way like those that physicists are after, and it is telling that Mikkelsen is in fact cautious enough to talk about “law-like generalizations.”

Lange (2005) presents a nuanced treatment of the issue, interestingly authored by a philosopher but published in a major ecology journal. Lange correctly points out that asking whether there are laws in ecology (or biology more generally) implies asking a logically prior question: “What would an ecological relationship have to be like in order for it to qualify as an ecological law?” (Lange 2005, p. 394). Unfortunately, the answer is not at all straightforward, nor is there a consensus among philosophers, though Lange himself admits that “some philosophers would argue that the best way to avoid this problem is to avoid using the concept of a natural law in the first place” (p. 396). The discussion hinges on the degree to which any proposed ecological law underwrites counterfactuals or, which amounts to the same thing, the degree to which a generalization in ecology can be thought of as an “accident.” Lange brings up the standard example of discussions about laws in philosophy: as far as we know there are no gold cubes larger than a cubic mile. This, however, is not the result of a law of nature, as the possibility of such cubes is compatible with the laws of physics. It is just that the proper conditions never arose. But an equally sized cube of Uranium-235 cannot be formed because the laws governing nuclear chain reactions prohibit it. So the latter is not an accident. The question is whether ecological “laws”—such as the species–area relationship—concern cases that are more like the gold cube or the uranium cube. Lange, who is sympathetic to the idea of there being laws in ecology, admits that the species–area relationship holds only as a *ceteris paribus* generalization, and that even so it is bound to be inexact. Moreover, he states that, “There

are counterfactual suppositions under which the laws of physics would still have held, but under which the ‘area law’ would not still have held” (p. 399). Why, then, insist in calling these generalizations laws, if not because of a misplaced case of physics envy?

Interestingly, the issue of physics envy also shows up explicitly in yet another author’s recent treatment of the issue of laws in ecology, Lockwood (2008). In this case, however, it is an ecologist who takes on the matter, and comes down rather negatively on the possibility of laws in his discipline. Lockwood discusses two frequent suggestions as examples of ecological laws: Malthusian growth and the logistic equation. He quickly finds them inadequate to the task, as they do not support counterfactuals, are not temporally universal, and in fact repeatedly fail empirical tests. In the end, Lockwood agrees with Wimsatt’s (1997) suggestion that “aggregative systems” (those typically studied by physics) do follow robust laws, while emergent systems (like those studied in biology) do not. This does not mean that biologists cannot generalize their empirical findings (within certain limits), and that such generalizations cannot be used to make reasonable predictions about the behavior of the systems of interest to them. And that, after all, is what actually matters.

The debate about laws of nature in general will likely go on in philosophy of science (Carroll 2011), and it will continue to inform the more specific discussions within biology and ecology. To date, the heartening thing to notice is that biologists interested in these topics are becoming significantly more savvy about the abundant philosophical literature pertinent to their discussions, and even directly engage philosophers in their own disciplinary journals.

General Theories of Biology?

Theodosius Dobzhansky (1964) famously said that “nothing in biology makes sense except in the light of evolution” (p. 449). Adding that to Richard Dawkins’ (1976) quest for “universal Darwinism” and to Daniel Dennett’s (1995) contention that Darwinism is a “universal acid” of sorts that cuts across disciplines, extending the idea of Darwinian evolution well beyond biology itself, one would think that biologists have settled on their version of a theory of everything long ago. One would be surprised. A perusal of the recent literature shows quite a bit of activity in this department, again largely on the side of ecologists (whose relationship with evolutionary theory has always been somewhat vague and at times even problematic, in my experience). I will briefly comment on three such attempts: Hubbell’s unified neutral theory of biodiversity, Scheiner and Willig’s general theory of ecology, and Scheiner’s conceptual framework for biology.

Stephen Hubbell's (2001) unified neutral theory of biodiversity and biogeography attempts to do precisely what its name implies: to propose a combined theoretical framework for biodiversity (measured by species–abundance curves) and biogeography (measured by species–area curves), where the “neutrality” consists in assuming that the differences among species that belong to the same trophic level within a given ecological community do not matter for the dynamics of that community. Hubbell's theory draws from explicit parallels with the neutral theory of molecular evolution (Kimura 1985) and from the Hardy–Weinberg equilibrium in population genetics (Hardy 1908; Weinberg 1908).

The unified theory has generated a significant literature, including a number of critics and empirical tests (a conservative Google Scholar search yields 2,850 hits). It is important to realize a couple of things, however: first, that the scope of the theory is crucially limited by the clause that it applies to species of similar trophic level within a given community, which makes it quite a bit more narrow in scope than its name (and some of the discussion that has followed the publication of Hubbell's book) might otherwise give the impression. Moreover, the theory is notoriously difficult to test, because while it does make distinctive predictions when compared to, say, niche assembly theories (which are non neutral), the predicted differences are very small, and easily lost in the noise characteristic of ecological data sets. This is not the place to get into an in-depth discussion of Hubbell's theory, but I can hazard a prediction based on the similar history of the neutral theory of molecular evolution (Hey 1999): in that case more than a decade of discussions led to the conclusion that a modified “quasi-neutral” theory was the best bet. Which basically means that stochastic as well as selective processes affect the outcome of evolution, just as it would be reasonable to expect.

Scheiner and Willig's (2008) ambitious attempt at providing a general theory of ecology is notable because it explicitly incorporates a large number of notions and references to the philosophical literature, even though both authors are biologists. Indeed, the authors directly link their quest for a general theory to ecologists' discussions about laws, which I have briefly addressed above. Scheiner and Willig (2008) maintain that the elements of a general theory of ecology have been around for half a century, but that ecologists simply have not recognized them because “we have misunderstood the nature and form of a comprehensive theory” (p. 21). We are told that seven “fundamental principles” are jointly necessary and sufficient for a general theory of ecology (p. 25). These principles are:

- (1) Organisms are distributed in space and time in a heterogeneous manner.

- (2) Organisms interact with their abiotic and biotic environments.
- (3) The distributions of organisms and their interactions depend on contingencies.
- (4) Environmental conditions are heterogeneous in space and time.
- (5) Resources are finite and heterogeneous in space and time.
- (6) All organisms are mortal.
- (7) The ecological properties of species are the result of evolution.

If you feel a bit let down once you go through this list, I share your reaction. Then again, the joke among evolutionary biologists has always been that ecology is the elucidation of the obvious (which, ironically, I have personally heard Sam Scheiner saying). The seven principles turn out to be basic observations about the world, except for the last one, which essentially links ecology with (and would reduce it to?) evolutionary biology.

Scheiner (2010) made an even more ambitious attempt—along similar lines—at a general theory of biology. There Scheiner makes clear (2010, p. 294) that his and Willig's general theory of ecology is meant to be the ecological equivalent of Darwin's theory in evolutionary biology, and it is on these two (and more) that a broader theory of all biology can be built. As before, the author proceeds to list ten principles that are necessary and sufficient for an all-encompassing biological theory. These are:

- (1) Life consists of open, non-equilibrium systems that are persistent.
- (2) The cell is the fundamental unit of life.
- (3) Life requires a system to store, use, and transmit information.
- (4) Living systems vary in their composition and structure at all levels.
- (5) Living systems consist of complex sets of interacting parts.
- (6) The complexity of living systems leads to emergent properties.
- (7) The complexity of living systems creates a role for contingency.
- (8) The persistence of living systems requires that they are capable of change over time.
- (9) Living systems come from other living systems.
- (10) Life originated from non-life.

There are several problems here. As in the case of the fundamental principles of ecology, some of the entries are straightforward observations about actual states of affairs (nos. 1, 4, 5, 9). No. 2 is simply not true, though cellular life is certainly dominant. No. 3 is interesting, though it remains open whether information transmission is

necessary for life or just a property of life on earth, and certainly non-living systems can also be characterized by transmission of information. No. 6 is problematic because of ongoing disagreement about what exactly counts as an emergent property.³ No. 7 is, again, not necessarily the case, as plenty of physical non-biological systems are also affected by contingency. No. 8 seems more an observation of factual reality than a logical (or even empirical) necessity. And no. 10 at face value flatly contradicts no. 9, though of course the way to resolve this is simply to stipulate that living systems usually, but not always, come from other living systems.

It seems fair to me to conclude that—despite these latest attempts—the only broad, truly general theory in biology remains the Darwinian one, modified first in the guise of the Modern Synthesis of the 1930s and 1940s (Mayr and Provine 1998), and currently undergoing further modification and expansion (Pigliucci and Müller 2010). That said, Dobzhansky's famous statement is perhaps a bit too grandiose, as there is quite a bit of research that has been done, and continues to be done, in biology that is simply not informed by evolution (because it takes evolution as a background condition). For instance, most of molecular biology since 1953, and much of transmission genetics before that, has proceeded with little or no reference to evolutionary theory. While this changes as soon as we get into cross-species comparative studies (as in the case of comparative genomics), the large degree of independence of some areas of biology may indicate that biology as usually conceived is a hybrid field, resulting from the confluence of physico-chemistry and organismal-historical biology. It is worth, then, reflecting on why ambitious attempts like those of Hubbell and Scheiner do not seem quite to deliver the same punch as, say, the general theory of relativity, or quantum mechanics in physics. I suspect the reason has much to do with why proposals concerning the existence of fundamental laws in biology also fall short of their models in physics (say, $E = mc^2$, or the Pauli exclusion principle, to name but a couple). As a number of both biologists (Gould 2007) and philosophers (Beatty 1995) have pointed out, we need to take seriously the role of contingency in shaping the history of living organisms, and therefore in affecting our understanding of that history and our ability to infer generalizations from its study.

Quite apart from fundamental discussions about determinism (i.e., whether there truly is such a thing as contingency, at a metaphysical level), in terms of human epistemic access to the world it is simply plainly the case that fundamental physics

³ I do not mean to imply that there are no such things as emergent properties, only that the concept is far from being clear (O'Connor 2006). And of course there are several physical but non-biological systems that also display emergent properties under at least some definitions of the term.

describes phenomena that behave in a largely non-historical, law-like fashion, while biology does not. It should not be surprising, then, that formulations of general laws and theories in biology come across as clumsy attempts to constrain the discipline and its objects of study so that it fits the pre-determined mold provided by theoretical physics.

The Four Modalities of Theoretical Biology

As I mentioned at the onset, it seems clear that “theoretical biology” is a highly heterogeneous type of enterprise, not only because it applies to widely divergent sub-fields of investigation—from genetics and molecular biology to ecology and evolution—but because it proceeds via the application of a panoply of methods, which in some cases yield contrasting insights or highlight fundamental conceptual differences in the ways different theoretical biologists think of their subject matter.

Even a cursory look at the literature allows one to distinguish four modalities for theoretical biology (though similar distinctions can also be found in, say, physics, especially if one considers the entire discipline, and not just specific subsets like particle physics). I refer to these as analytical modeling, statistical modeling, computer modeling, and conceptual analysis. I will briefly discuss each, commenting on their nature and their interrelationships.

The classic example of analytical approaches in theoretical biology is represented by much of the body of works that makes up population genetics theory, beginning with the above-mentioned Hardy–Weinberg principle and arriving at more recent advances such as coalescence theory (Hartl and Clark 2007). The basic approach here is to use mathematical formalism to arrive at analytical (i.e., precise, non-statistical) solutions of sets of equations describing the behavior of idealized populations of organisms. Population genetics theory has always had somewhat of a hard time squaring with the complexities of actual biological populations (perhaps in a way analogous to, say, the difference between equilibrium and non-equilibrium thermodynamics in physics). Crow (2008) has made the point that population genetics has been characterized by a number of high-level controversies throughout the twentieth century (his paper concentrates on the middle part of it), controversies that were not resolved because of the difficulty to relate the theory with the empirical evidence. Rather, what happened was that a particular controversy faded out of fashion only to be replaced by another one, while progress was being made on the new empirical ground of molecular genetics, for the simple reason that the data were easier to come by and the theoretical issues more limited in scope.

Despite these limitations, there is no doubt that theoretical (analytical) population genetics has represented the

mathematical core of the Modern Synthesis, and as such has played (and continues to play) a fundamental role. Just how fundamental, however, remains a debatable topic. Lynch (2007) has made a strong case that “nothing in evolution makes sense except in the light of population genetics,” a provocative reference to Dobzhansky’s phrase. In that paper Lynch openly scorns much of the new conceptual discussions about post-Modern Synthesis issues, from evolvability and robustness to biological complexity, and even gives a primer (presumably to his colleagues, not the general public) about “common misconceptions about evolution and complexity.” He concludes his paper by stating that “this stance [of biologists interested in those topics] is not very different from the intelligent-design philosophy of invoking unknown mechanisms to explain biodiversity,” attributing his colleagues’ allegedly misguided approach to the “well known fact that most biologists abhor all things mathematical”—though he rather astonishingly hastens to add that “this tone of dissent is not meant to be disrespectful” (p. 8603; it is hard to imagine what he would have written had he actually meant to be disrespectful!). As I pointed out to Lynch (Pigliucci 2008a) this sort of intellectual arrogance worn on one’s sleeve is both unhelpful and demonstrably misguided, given the fact that many of the people who have produced work on evolvability and allied concepts are as knowledgeable of population genetics theory as anyone else, and it is precisely because of that knowledge that they find the classical theory to be limited and insufficient for (though foundational to) the broader project of theoretical biology.

Indeed, one obvious way to convince oneself that population genetics is far from being everything needed for a theoretical population biology is to look at a related—and yet entirely independent—approach to analytical theorizing in biology: game and optimization theory. Popularized initially by John Maynard-Smith (1982), it has yielded intriguing insights into evolutionary population dynamics, particularly in the realm of competing behavioral or phenotypic “strategies” that natural selection may favor given certain environmental circumstances or others. Interestingly, however, optimization and game theory makes no reference whatsoever to the underlying genetics of the traits under investigation, essentially relegating population (and quantitative) genetics to background conditions. Indeed, a major source of insights into the nature of evolutionary constraints has come precisely by the comparison of the (independently achieved) results of game theoretical-optimization and population-quantitative genetics approaches applied separately (e.g., Charlesworth 1990). So much for the alleged “centrality” of population genetics.

The second general type of approach to biological theorizing is statistical in nature, beginning with Fisher’s ([1930] 1999) famous “fundamental” theorem of natural

selection, which was proposed as explicitly equivalent to one of the most solid pieces of theory in classical physics, the second principle of thermodynamics. Fisher laid the foundations for statistical genetics, which—when reconciled with the apparently discrepant Mendelian genetics—resulted in the Modern Synthesis of the 1940s (Mayr and Provine 1998). One way of thinking about the relationship between population and quantitative genetics is as particular examples of the general relationship between analytical and statistical treatments, which finds analogs also in physics (consider the contrast between the precise equations of quantum mechanics and the statistical ones of thermodynamics). Specifically, population genetics’ domain extends to simple systems (few loci, few alleles, low levels of interactions) that are amenable to being described by equations that can be solved analytically. Anything more complicated (i.e., more realistic) than that has to move to the realm of statistics, and especially of multivariate statistics.

Of course standard quantitative genetic textbooks (e.g., Falconer and Mackay 1996) do make a formal link between population and quantitative genetic theories, but after that all quantities relevant to the development of the theory become statistical in nature: variances, covariances, heritabilities, selection vectors, and so on. The standard example of one such statistical entity is G , the genetic variance–covariance matrix that plays a fundamental role in the modern theory of how constraints and natural selection shape evolution, since the introduction of the multivariate version of the breeder’s equation by Lande and Arnold (1983).

The entire quantitative genetic program in evolutionary biology has come under criticism in terms of inflated claims and insufficient attention to crucial (and usually empirically false) assumptions made by biologists pursuing the program (Pigliucci 2006), but a particularly interesting example has appeared in print recently because of Jonathan Kaplan’s (2009) criticism of a paper by Estes and Arnold (2007) claiming to have solved the classic problem of evolutionary stasis (Eldredge et al. 2005). Specifically, they maintain that stabilizing selection is the only reasonable explanation for stasis across time scales.

Estes and Arnold (2007) examined a number of potential explanations for stasis, a persistent problem that has often been presented as symptomatic of the Modern Synthesis’ narrow conceptual arsenal. These included: protracted periods of stabilizing selection; genetic and developmental constraints; selective constraints due to coevolution; canceling of positive and negative evolutionary trajectories over time; mathematical artifact; habitat selection; and complexities involved with evolution in metapopulations.

Kaplan (2009), however, points out that Estes and Arnold’s models—though they are in fact incompatible with some classes of processes—are not causal models, and

do not therefore warrant the alleged conclusions. In particular, Kaplan rejects Estes and Arnold's conclusion in favor of stabilizing selection as the explanation for stasis, for the simple reason that what they take to be “stabilizing selection” is a (re)description of a pattern (i.e., of stasis), and not a process or set of processes producing said pattern. Notice that Kaplan does acknowledge that Estes and Arnold have advanced the debate, though not quite in the way they think. Essentially they have managed to refine our understanding of what we need to explain when it comes to debates about stasis (somewhat ironically, this sort of refinement is precisely philosophers of science's bread and butter, and it is often treated as mere hair splitting by practicing biologists).

The reason Kaplan thinks that understanding the difference between what Estes and Arnold have actually done and what they think they have done is crucial to point out (besides the immediate implication that the problem of stasis has not, as yet, been solved) is that this confusion between pattern and process is actually common in evolutionary quantitative genetics, and the root of much disagreement on the very nature of explanations in evolutionary biology. While this certainly does not mean that one should stop doing quantitative genetics (just like the considerations mentioned further above do not imply that population genetics is useless), it certainly does point to significant limitations of the approach when it comes to causal explanations (as opposed to its more legitimate role in pattern description and quantification).

The third way of doing theoretical biology that I wish to briefly consider is based on computer modeling, and it is in a sense a continuation of the trend described above: when things get too complicated even for a quantitative genetic approach (let alone for a population genetic one), researchers move toward computationally intensive simulations of biological populations. There are several examples of this, some of which are continuous with the population-quantitative genetic type of issues just discussed, some having to do with broader questions concerning the evolution of evolutionary mechanisms (evolvability), and some concerning the relationship between structural biology and evolutionary dynamics.

A by now classic example of the first group is the work by Gavrilets (1997) and colleagues on so-called “holey” adaptive landscapes. Expanding on Dobzhansky's original model of evolution of geographic isolation (using a standard two-loci, two-allele population genetic model) and on Wright's metaphor of adaptive landscapes as multidimensional surfaces describing the dynamics of evolutionary change, Gavrilets explored the consequences of truly (and realistically) highly dimensional landscapes. This was simply not possible before the invention of computers capable of running complex and calculation-intensive

simulations, as the problem is not treatable either analytically (population genetics) or statistically (quantitative genetics), though for different reasons. One of Gavrilets' most important findings is that—contrary to common wisdom—the dynamics in highly dimensional landscapes are qualitatively different from those in lower dimensional landscapes, which had dominated biologists' theorizing on the topic for several decades. This is a nice example of how the same problem will look very different not just as the theory gets better (after all, Wright already clearly realized that actual adaptive landscapes are highly multidimensional, he just could not do the appropriate calculations), but as entirely new approaches to theory come along.

Another major application of intensive computer modeling to the cutting edge of evolutionary theory concerns the idea of evolvability, the ability of evolutionary mechanisms to evolve, whether by natural selection or other means (Pigliucci 2008b). Consider, for instance, the study by Crombach and Hogeweg (2008) on the evolvability of genetic networks. The authors used a computationally intensive approach to simulate the evolution of a number of genomes (defined as linear chromosomes of genes with binding sites) in a population, evolving toward given targets in a changing environment. Genetic networks arising from each genome via a Boolean threshold were allowed to change in response to the resulting selective pressure. At each step in the simulation the networks could respond by updating the expression of their respective genes, thus causing both genome and network topology to change over time. The process generated different categories of genes: those that were always expressed, those that were never expressed, and those that were expressed conditionally.

The results were spectacular, tracking the populations while they minimized the Hemming distance from a given target, in the process evolving a new genotype–phenotype mapping function that increases the likelihood of occurrence of beneficial mutations. This is no violation of standard Darwinism, but rather the result of the fact that the networks structure themselves around a series of “hub” genes whose dynamics make the networks sensitive to the rare beneficial mutations while maintaining neutrality in the face of the majority of the other possible mutations. Crombach and Hogeweg (2008) were able to document their networks eventually switching attractors, i.e. going from one to another stable configuration, by differentially silencing and activating subsets of the full network. As they put it: “The genotype–phenotype mapping from genome to network had evolved such that a small class of mutations was adaptive and therefore repeatedly observed. This demonstrates a clear example of mutational priming and hence of evolution of evolvability” (p. e1000112).

My last brief example in this category is a review by Cowperthwaite and Meyer (2007) on the effect of

mutational networks on evolutionary trajectories. The authors use models of RNA structure, where the genotype–phenotype map is relatively simple and predictable. The fitness of these molecules depends on their three-dimensional shape and can be modeled accordingly. Unlike similar models of fitness in mainstream evolutionary biology, those discussed by Cowperthwaite and Meyer are based on known properties of molecular folding, and do not require assumptions about statistical distributions. (However, because of computational limitations, the RNA models use the shape of the molecule as a proxy for its function, and do not actually model the function directly.)

Cowperthwaite and Meyer (2007) discuss simulations charting the mutational paths connecting distant genotypes across the fitness landscape of the RNA molecules, which allows researchers to understand patterns of mutational connectivity at a landscape-level scale. One of the intriguing results discussed in the paper shows that evolving populations of RNA molecules typically go through periods of stasis followed by “punctuations” rapidly leading to new molecular structures. This stasis—eerily similar to the one famously discussed by Eldredge and Gould (1977) in paleontological data—was not caused by stabilizing selection (contra the above-mentioned Estes and Arnold paper criticized by Kaplan) but by the interaction of directional selection for a target molecule and the characteristics of the genotype–phenotype mapping function of RNA molecules themselves. In practice, the simulated population of molecules was subdividing into groups that were phenotypically equivalent and yet genetically different—which allowed a partitioned exploration of the fitness landscape by the standard means of mutation and natural selection. Again, no spooky mechanisms anywhere in sight, but rather surprising dynamics emerging from the very structure of the genotype–phenotype map in a way that simply could not have been predicted by standard quantitative genetic models.

The above examples, and a rapidly increasing number of others in the theoretical biological literature, show what I think is a long-term trend: we are witnessing a shift from analytical and statistical models to statistical-computational ones, in a sense analogous to the explosion of so-called “experimental mathematics” (not an oxymoron) over the past several decades (Baker 2008). The idea is that modern theoretical biology is concerned with systems that are far too complex to be amenable to classical population genetic-style analytical treatments, and that even quantitative genetics can only provide statistical snapshots of coarse level phenotypes, not a credible analysis of long-term evolutionary dynamics. Computational approaches—while no panacea in themselves—are opening vast new horizons of biological theorizing similar to what has been going on for a number of years in other scientific disciplines, from structural chemistry to atmospheric physics.

The danger of this approach, however, has been pointed out by Gavrillets (1999) when he remarked that in evolutionary biology models should increasingly be thought of as playing the part of useful metaphors, rather than of providing specific predictions. This is a rather novel way of thinking about modeling, but the exploration of the potential implications of this suggestion would bring us too far from the scope of the current paper.

The fourth and last modality of biological theorizing I wish to briefly discuss is based on the articulation of verbal-conceptual models, and obviously comes closest to what philosophers of biology themselves engage in when they analyze the concepts deployed by working biologists. Verbal-conceptual models in science have the reputation of being second grade when compared to “rigorous” mathematical modeling, even though of course both the original work by Darwin and much of the work done during the Modern Synthesis (except for the part that was explicitly population-genetic) fall into this category. Indeed, there seems to be a resurgence of this approach as a necessary complement to increasingly “experimental” mathematical treatments like the ones discussed above.

Verbal-conceptual models include a broad category of biological theorizing that is particularly popular in molecular biology and biochemistry, where many papers present the results of complex experiments on the structure of genetic networks or biochemical pathways in the form of conceptual diagrams that are meant to both summarize the current status of knowledge and provide food for thought for the developing of new hypotheses and subsequent empirical tests (e.g., Kleffmann et al. 2004, Fig. 4; Honjo and Furukubo-Tokunaga 2009, Fig. 6).

Of course, there is also a long and influential tradition of this type in organismal biology, for instance when G. G. Simpson (1944) adopted Wright’s idea of adaptive landscapes (whose original graphic representation was not supposed to replace the mathematical modeling) and applied it to discussions of phenotypic evolution during geological time. More recently, very effective examples of coupling computational approaches with verbal-conceptual models (often rendered as diagrams of one sort or another) are offered again by research on the evolvability of genetic networks (Crombach and Hogeweg 2008, Fig. 6). More speculative theoretical explorations are also often done by way of this modality, as seen for instance in Newman and Müller’s (2000) work on character origination via epigenetic mechanisms.

The Many Ways of Theorizing in Biology

The term “speculation” has a rather bad reputation in science, often associated with the much-dreaded accusation

hurled at philosophers that they engage in “armchair theorizing.” But of course all theory is armchair speculation, and unless one thinks of mathematics in a special Platonic fashion, mathematical approaches are simply continuous with, and complementary to, all the other ways of doing theory in science.

Which brings me to the role of philosophy of science in all of this. I have suggested before (Pigliucci 2008c) that philosophy of science itself is characterized by different modalities, some of which have little to do with helping scientists and reflect instead on the logic of scientific theories, the epistemology underlying scientific claims, and so on. Indeed, philosophy of science itself is continuous with the history of science, since it would be difficult to attempt generalizations about the nature of science while focusing only on currently ongoing (and therefore far from being settled) scientific research.

To begin with, then, classic philosophy of science is concerned with the study of the logic of scientific discovery, as exemplified by the well-known names (even among scientists!) of Popper, Kuhn, and—to a lesser extent—Feyerabend and Lakatos (and, of course, a number of contemporary scholars, too many to mention). This type of philosophy of science is, arguably, of very little direct relevance to scientists themselves (except insofar as they are curious about how outsiders see and analyze their own activity). It is perhaps this sort of philosophizing that has brought a number of physicists (Steven Weinberg, Stephen Hawking, and Lawrence Krauss come to mind) to claim that “philosophy is dead” on the ground that, of late, it has not managed to solve any scientific problem with which physics is concerned. In so arguing, these scientists are committing an elementary category mistake prompted by a combination of intellectual hubris and a surprising amount of ignorance.

Philosophy of science, however, also functions in modalities that are (or ought to be) of more direct interest to practicing scientists themselves—whether the latter realize it or not. One such modality is represented by always necessary (if prone to annoy the targeted scientists) external criticism of socially relevant scientific claims (e.g., concerning race, gender, or the validity and application of certain types of medical research; Kaplan 2000; Kaplan and Winther 2012). I hesitate to use the label “science criticism” for this activity—even though it is arguably the most appropriate one available—because the term has been possibly irreparably tainted by much post-modern-inspired nonsense at the height of the so-called “science wars” of the 1990s (Koertge 2000). Regardless of what we end up calling it, it is the sort of philosophical inquiry that actually has practical implications, analogous to the better known ones usually associated with, say, business ethics, medical ethics, and bioethics, and one that

should develop into an earnest dialogue between philosophers and scientists about the social implications of science itself.

The third and last modality for philosophy of science is in even more close symbiotic relationship with science, one that seems to be welcome by scientists themselves. Indeed, recent years have seen an increasing number of philosophers of physics, biology, and other disciplines who have been publishing conceptual papers on a large variety of topics that are hard to distinguish from theoretical physics, biology, etc. This is, I think, a much welcome development, and a small (but, hopefully, growing) number of scientists have started to collaborate with philosophers and/or to publish in philosophical journals, as the case of debates about laws in biology discussed above exemplifies. As I pointed out elsewhere, this is along the lines of what Hasok Chang (2004) called “the continuation of science by other means”:

Complementary science [based on history and philosophy of science] is critical but not prescriptive in relation to specialist science....Complementary science identifies scientific questions that are excluded by specialist science....The primary aim of complementary science is not to tell specialist science what to do, but to do what specialist science is presently unable to do. It is a shadow discipline, whose boundaries change exactly so as to encompass whatever gets excluded in specialist science....The second dimension of the critical stance is more controversial....On examining certain discarded elements of past science, we may reach a judgment that their rejection was either for imperfect reasons or for reasons that are no longer valid. (pp. 249–250)

From this perspective, then, philosophy of biology represents a fifth type of theoretical biology, albeit one that is practiced from the outside looking into the core discipline. Because of that, it is uniquely positioned, I think, to perceive the threads connecting the other four modalities, as well as the advantages and limitations of each. The idea, of course, is not to make philosophers the ultimate arbiters in theoretical biology (or in anything else, for that matter). Rather, it is a recognition that it does take some distance from the nitty gritty of the specialized literature to be able to perceive the broad picture that is necessary for the advancement of broadly construed theoretical biology. Accordingly, it is not by chance that when biologists themselves step back to contemplate a more inclusive level of analysis (e.g., Scheiner mentioned above) they begin to sound like philosophers, despite the fact that even then they simply do not seem to be able to resist the occasional dig to philosophy here and there. Perhaps, however, ongoing cross-fertilization—like the one fostered by this special

issue—will bring less distrust and more fruitful collaboration between the two disciplines.

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