Holistic Biology: What it is and Why it Matters

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Introduction

The basic idea behind the series of articles in this special issue can be stated relatively simply. There are a number of features of biology that are problematic for those who are wary of the project of trying to reduce everything in biology to physics. For such people, biology has become over-mechanistic, over-deterministic, over-reductionist, and associated with the presumption that it cannot be reconciled with theistic views.

However, in recent years, there have been developments in biology that seem to weaken the grip of such a deterministic, reductionist, mechanistic approach. These approaches to biology can be called, holistic, organismal or systemic. In as far as they make biology less mechanistic, deterministic or reductionist, they can be regarded as welcome scientific developments for many who hold religious views (though that doesn't apply to all who hold religious views, nor only to religious people).

We do not intend to suggest that there is anything radically new about these developments. To some extent, they represent a recovery of older traditions in biology that were for a time largely eclipsed by the conspicuous success of molecular biology. In part the present return to a more holistic biology is just a turning of the tide, and the fact that it is sometimes presented as radically new arises in no small part from the rhetorical need to present biology as doing something new in order to garner funding, and similar extrinsic reasons. Most significantly, there are new empirical as well as conceptual developments that are increasingly driving a more holistic way of doing biology. The history of holistic biology is the focus of the next article in this special issue, by Michael Ruse.

It is difficult to even state the simple idea of the opening paragraph (i.e. that there are significant philosophical and religious advantages in holistic biology), without starting upon the numerous caveats and qualifications that need to be entered. In this introductory article we will indicate some of these complexities, and then assess what remains of the simple idea of the above paragraph. To anticipate, we will argue that something significant remains, though it is more subtle and nuanced than might originally be supposed.

One problem that is already apparent is that it is hard to know what are the best terms to use. We have mentioned three possible ways of indicating what may be problematic in biology from a religious point of view (i.e. deterministic, reductionist, mechanistic) and we have also used three different terms for the recent trends in biology that seem to counteract those problematic features (holistic, organismal and systems biology). There are common features in these approaches to biology, but also significant differences, and we will need to clarify the issues that arise about these different modes of biology. However, we will first probe what is meant by determinist, reductionist and mechanistic biology.

Concerns about Biological Theorizing

We will now consider features of biological theorizing that have caused concern in some religious and philosophical circles, i.e. that biology is too mechanistic, determinist or reductionist. Our general line in each case will be that there are strong forms that are potentially problematic, but that there are weaker and more nuanced forms that are not. The value of holistic biology is that it leads towards these more nuanced forms. There have been several philosophical efforts to resolve the tension between reductionism/determinism/mechanistic thinking and the religious worldview. The attraction of holistic biology is that it helps to deal with this problem from within science.

Determinism

The first point to be made about determinism is that it is a background philosophical assumption rather than a conclusion from scientific inquiry. Science has not proved determinism to be correct; it simply assumes it. Some might claim that science necessarily presupposes determinism, and could not proceed on any other basis. However, that is not obviously correct, and reflects a rather dated view of science. Isaac Newton, for example, was not a determinist in any obvious sense (at least not a naturalistic determinist); for example, he allowed for God acting outside the causal pathways studied by natural science to adjust the planetary motions. However, his lack of deterministic assumptions did not prove a barrier to his conducting scientific inquiry and making, to understate the point, major contributions to scientific understanding.

What science does presuppose is a degree of predictability, or lawfulness, in the phenomena it is studying. There is no theological problem with that assumption. Indeed, it has sometimes been argued, with some plausibility, that Christian theology implies a degree of predictability, and furthermore that is one of the key reasons why science has flourished in Christian civilization. However, determinism goes further than assuming a degree of predictability, and assumes that *all* phenomena are *completely* predictable from their causal antecedents, and that complete explanations can be offered for them.

Complete explanations and exact predictions are relatively rare in biology, at least at the macroscopic level. Most biological processes are affected, directly or indirectly, by such a complex network of causal factors that exact predictions are impossible. Biological predictions tend to be probabilistic rather than exact. Indeed that may one of the key differences between the physical and life sciences, though it is only a difference of degree, as exact predictions can be found in biology (e.g. all organisms die), and probabilistic ones in the physical sciences (e.g. radioactivity, the Uncertainty Principe). Physicists might say that biological systems are mostly *chaotic*, though that is not language that is widely used in biology.

It is hard to settle the question of whether or not formally chaotic systems, i.e. systems that are too complex to be predictable, are still deterministic. The lack of predictability creates an epistemological barrier to settling the matter. Some argue, as John Polkinghorne does, that it is a reasonable conjecture that systems that are not predictable are also not deterministic (see Saunders, 2002). Others point to the fact that systems modeled by deterministic mathematics can actually be chaotic and unpredictable. We suggest that neither position settles the matter conclusively. How systems are modeled doesn't finally settle how they actually operate. There is a gap between the underlying reality (ontology) and our understanding of it (epistemology) that may not be bridgeable; indeed, the two may not necessarily be aligned.

However, what can be said with confidence is that exhaustive mono-causal accounts are rare in biology. Most systems with consequences for macrobiology are influenced by such a wide range of factors that exact prediction is rarely possible. Genetic determinism has been one of the most pervasive forms of mono-causal determinism to be proposed in modern biology. However, as every geneticist knows, the genotype interacts with a wide range of factors to reach the phenotype; and in most cases the pathways by which genes exercise their effects are incompletely known. Even if and when we do possess such knowledge, this does not mean that determinism will reign.

Issues to do with genetic causation take us to the significance for holism of epigenetics, broadly understood. At the heart of epigenetics is the recognition that genes interact with other factors. Indeed one of the key forms of interaction is that contextual factors switch genes on or off. This is more than saying that they exercise their effects through complex pathways in which they interact with other factors; it is saying that whether they even begin to have effects at all is influenced by contextual factors.

For present purposes we propose to set aside general issues about determinism in biology and to focus on mono-causal determinism. There is an obvious convergence between the striking absence of mono-causal determinism in macrobiology and the assumptions of holistic and systems biology. For most purposes it is possible to remain agnostic about whether or not biological systems are actually deterministic, or just too complex to predict.

Reductionism

Turning to reductionism, it is important to distinguish between problematic and unproblematic forms of reductionism. Almost everyone recognizes the need to make some such distinction. Daniel Dennett (1995), for example, makes a distinction between *good* and *greedy* reductionism; in the latter, people "underestimate the complexities, trying to skip whole layers or levels of theory in their rush to fasten everything securely and neatly to the foundation" (82). The behaviorism of B. F. Skinner is one of his main examples of greedy reductionism.

Though almost everyone recognizes that some reductionisms are greedy, there are probably different views about how ubiquitous this is. Because holistic biology emphasizes the complexity of biological systems, they are likely to be highly sensitive to the tendency of greedy reductionism to underestimate the complexities. So, from the perspective of holistic biology, a lot of reductionism may look greedy. However, this doesn't rule out the possibility that holistic biology may still be reductionist in a more helpful sense of reductionism.

One important issue here is whether or not an explanation is *complete*. It is only when we have complete explanations that the reduction can be used to justify elimination. Without complete explanation, reduction cannot be justified. Given how rare complete explanation is in biology, elimination also ought to be very rare. However, there is a disturbing tendency to assume, usually on ideological grounds, that complete explanations will be possible in the end, even though they have not yet actually been achieved, and to proceed to elimination on account, as it were, in anticipation of the complete explanations that are anticipated.

The best known example of this is in neuroscience, where Patricia Churchland (1986) has been an enthusiastic advocate of the elimination of folk psychology, or *mentalese*, on the basis of the anticipated complete explanation of mentalese to neuroscience. It doesn't hold her back that we don't yet have that complete explanation; she assumes it will eventually be achieved, and proceeds on that basis.

In fact there has been a growing recognition that fully-fledged inter-theoretic reduction is seldom achievable. Gregory Bock and Jamie Goode (1998) concluded, after a review, that there were only two cases where it was widely accepted by experts in the field that reduction from biology to chemistry was possible, the bacteriorhodopsin receptor and muscle contraction. However (and we accept, of course, that the number of cases rises over time as knowledge accumulates), this has not led to the abandonment of reductionism in biology, but to a refinement of what form it should take, sometimes known as *neo-reductionism* (Rosenberg, 2007).

One of the key issues here is that reductionism seems to assume that all causal processes are ones in which the parts influence the whole. Unlike holistic biology, it does not recognize that the whole can also influence the parts. That raises the question of whether holistic assumptions are compatible with any kind of reductionism, which in turn depends on the scope of what is included in reductionism. Neo-reductionism rejects the possibility of top-down causation and assumes that causation is entirely bottom-up (Rosenberg, 2007). It assumes that people operate rather like automata such as *The Writer*, built in the 1770s, in which the writing is driven entirely by bottom-up mechanical causation. Such exclusively one-way reductionism is not compatible with holistic assumptions.

However, if you allow for two-way reductionism, there is more scope for reconciliation between reductionism and holism. One of the main advocates of two-way reductionism in the human sciences has been Michael Arbib (1985). Two-way reductionism may seem a radical extension of the concept of reductionism but, if the assumptions of holistic biology are correct, it is a necessary extension. Holism leads *either* to the conclusion that reductionism should be abandoned, except for certain simple cases, *or* to the view that it should be broadened to include two-way reductionism.

Though *top-down* and *bottom-up* is the most widely-used terminology, it is not entirely satisfactory, as the assumptions about levels that it embodies are controversial. After many years of using the concept of top-down causation in discussing topics on the interface of theology and science such as divine action, Arthur Peacocke (1999) eventually abandoned top-down terminology and spoke instead about *whole-part constraint.* This is clearer terminology that arises directly from holistic assumptions. Following Peacocke's lead, rather than talking about top-down causation, we would rather say that whatever reductionism is adopted should allow for the influence of wholes upon parts.

However, it needs to be noted that there is an ambiguity about what counts as *the whole.* It would be unwieldy to operate with the largest possible whole and, in any case, it would be hard to know what ought to be included in that. For all practical purposes, biology needs to operate with sub-wholes, to make the task of understanding the relation between parts and wholes manageable. The decision about what wholes to select is a pragmatic one, influenced by the objectives of a particular scientific inquiry.

Mechanism

The issues raised by mechanism in biology are also complex. As with reductionism there are issues about how broadly *mechanism* is to be defined. It might be argued, from a holistic perspective, that mechanistic explanations cannot possibly be adequate in biology. Objections have also been raised on theological (Mackay, 1965) and philosophical (Polanyi, 1968) grounds to mechanistic models, especially for humans. However, much depends on what is meant by biological mechanisms.

On the face of things it is puzzling there have been two concurrent developments in 21st century biology. One has been the widespread enthusiasm for systems biology which, as we will see, has been said to be *holistic;* the other has been a new focus on biological mechanisms (e.g. Craver and Darden, 2013). At first sight, these trends might seem contradictory, and that has led to a discussion about the role of explanatory mechanisms in systems biology (e.g. Mekios, 2015). The general response to this challenge has been to increase the scope and sophistication of explanatory mechanisms, so that they capture the complexity of biological processes more adequately.

Though it is standard practice among empirical biologists to try to formulate the mechanisms by which particular processes come about, we suggest that by mechanisms they usually just mean detailed explanatory models, and that biological mechanisms need not be machine-like. A good deal of confusion has been caused by a misunderstanding of what is meant by mechanism, but there seems a reasonable consensus that biological mechanisms need not be, and probably should not be, seen as machines. Rom Harré (1972) suggests that mechanism has two quite distinct meanings: one is a "mechanical contrivance", the other is "any kind of connection through which causes are effective" (118). Mechanisms in science, he suggests, are the latter but not the former.

Carl Carver and Lindley Darden (2013) are equally forthright in saying that "biological mechanisms are often quite unlike machines" in the sense of being "contrivances, with pre-existing, organised and interconnected parts" such as clocks, pumps, internal combustion engines or computers (15). Biological mechanisms are "tinkered together under mutual constraints through evolution by natural selection" and "their parts may be synthesized on the fly" (15). The result is that the "blueprint for the typical biological mechanism is decidedly messier than the blueprint for even complicated machines" (15).

However, even after clarifying that biological mechanisms are not machine-like, there are questions about how far the search for mechanisms can take systems biology or other more holistic approaches to biology. Constantinos Mekios (2015), for example, accepts that mechanisms can provide useful explanations in systems biology, but questions how far the search for mechanisms is able to carry through "the comprehensive explanatory integration demanded for the holistic understanding of complex biological systems" (47). In practice, however, biology generally tries to formulate what we might term *fine-grained mechanisms* that elucidate quite specific processes. The search for a mechanism often starts with an observable linkage between A and B. The search for the relevant mechanism is the search for a causal explanation of the linkage.

There are normally no constraints on the complexity of what is allowed as a mechanism. Mechanisms can be holistic in the sense that wholes can influence parts, we well as vice-versa. The operation of mechanisms can be determined by the environmental context of the organism. Mechanisms can be formulated in a way that explicitly adopts the assumptions about mutual interaction that are prevalent in systems biology, and there is no necessary conflict between systems biology and the search for mechanisms in the general sense of detailed causal models (Braillard and Malaterre, 2015).

It is important to bear in mind that the mechanisms that scientists propose are models. Modeling is at the heart of the scientific processes, and all models unavoidably draw on broad metaphors, i.e. a likeness is assumed between the actual biological process and the model, but models are not themselves exact descriptions. Even if mechanistic models represent biological processes adequately for predictive purposes, that does not demonstrate that the biological process actually *is* machine-like, only that it can be modeled mechanistically. It seems likely that systemic mechanisms are likely to be seen as less and less machine-like as they try to model the feedback-rich interactional complexity of biological processes.

Michael Ruse (2010) sees mechanism and organicism as having been the two dominant metaphors in western science. Historically, they have been regarded as alternatives. However, as holistic biology tries to understand the non-machinelike mechanisms that underpin holistic processes in biology, it may be that we are moving towards a hybrid that integrates features of both traditions. It is perhaps too soon to judge whether such a hybrid is possible, or whether the attempt to reconcile mechanism and organicism is fundamentally incoherent. The current search for so-called mechanisms that are explicitly not machine-like could be taken as a worrying pointer to how people are currently trying to maintain incompatible assumptions side-by-side. On the other hand, resolving this may just call for the kind of clarification of what is meant by mechanism in biology that we have set out here.

Summary

With each of the three topics we have considered in this section we have distinguished broad and narrow meanings of the terms concerned. In each case we suggest that legitimate concerns can arise when terms are used in a narrow way, but not when they are used more broadly. Specifically, there are potential concerns about mono-causal determinism, but fewer about multi-causal determinism; there are also potential concerns about reductions that are uni-directional and exclusively bottom-up, but fewer about reductions that allow for top-down or whole-part influences. Finally, there are concerns about the search for biological mechanisms if it is assumed that they are like machines, but not if mechanism just means a detailed explanatory model that sets out how causes achieve their effects.

Holistic Modes of Biology

Holism in biology has an identifiable origin in J. C. Smuts *Holism and Evolution* (Smuts, 1926), which proposed that systems should be viewed as wholes not just as collections of parts. This is basically an ontological proposal, i.e. that the universe fundamentally consists of a set of wholes rather than a set of parts. However, in weaker versions, it is just a causal or explanatory proposal, i.e. that parts are to be explained to some degree in terms of the action of wholes on them, and that causal processes are not exhausted by considering how parts affect wholes. We will not duplicate here Michael Ruse's fuller exploration of the holistic tradition in biology in the next article in this special issue, but will explore how far organicist biology and systems biology are holistic.

Organicism

In clarifying the distinction between holism and organicism, it will be helpful to anticipate here the formulation set out by Michael Ruse in the next article. He suggests that a holist is someone who sees everything as interconnected and that things make sense only if parts are considered in relation to wholes. An organicist, in contrast, is someone who sees the organic model, i.e. one based on life, as the basic or root metaphor in science.

It may help to clarify the relationship between holistic and organicist biology to make use of the classic distinction between denotation and connotation. We suggest that the kinds of biology that can be identified as holistic and *organismal* are largely the same. To put it another way, you can't find a kind of biology that is holistic but not organismic, or vice versa. Nevertheless, these terms have different histories, come from different metaphysical backgrounds, and have different connotations. They may refer to the same biologies, but their *sense*, as Gottlob Frege would have said, is quite different. Different authors in this special issue focus mainly on different terms.

Organismal biology has rather different origins from holistic biology. In part the organismal approach is just a preference for studying biological structure and function in whole organisms. The equivalent in medicine is *whole-*

person medicine. However, organicism also depends on a distinctive set of metaphors or models for scientific inquiry. As Michael Ruse (2010) has discussed, it is the main source of non-mechanistic explanatory models in science*.*

Organicism can be applied to any area of science. It is possible to argue, as Lovelock has done in his Gaia hypothesis (Ruse, 2013) that the biosphere should be thought of as a living system. In stark contrast, it is possible to use the kind of mechanistic models that come from physics to understand living systems. However, if organicism is to find an accepted place in science at all, it will probably be in biology that it comes into its own. One possibility is that there is a distinctive mode of organicist explanation that applies to living systems. That is a proposal to which Richard Gunton and Francis Gilbert are sympathetic in their article in this set.

There are more significant philosophical sources of organismal biology than of either holistic or systems biology. As Michael Ruse (2010) indicates, German Romanticism was one important influence. A. N. Whitehead was another, with his proposal that entities should be regarded as *structures of activity*. The concept of *fields* has been important in organicist biology. In at least some versions there is an ontological proposal that the universe (or at least the living world) consists of fields rather than entities, and that causal explanations are to be framed in terms of the action of fields. The transition from the metaphysics of early modern science, which required all theories to be corpuscularian in form, to one that allowed field theories as well, was a major transition point in the metaphysics of science (Harré, 1972).

Organicism in biology also tends to frame explanations in terms of developmental pathways. Indeed, developmental biology has long taken a more organismal approach than most other areas of biology. An early influence in this line of theorizing was Paul Weiss in his *Principles of Development* (Weiss, 1939). In similar vein, C. H. Waddington (who coined the term *epigenetics*) developed the concept of a *chreode* for the developmental pathway that an organism follows as it develops, as it is canalized towards certain necessary endpoints (Waddington, 1975).

The approach to evolution that Simon Conway Morris (2005) has developed around the phenomenon of convergence seems to be a rather similar idea, applying to evolution an equivalent of what Waddington called chreodes. For Conway Morris there seems to be something that has *canalized* evolution along certain pathways (convergences) and towards certain end goals (self-aware humans). For a philosophical discussion of the use Conway Morris makes of convergence, see Ruse (2008).

The problem is about how chreodes actually work, and how canalization actually arises. Neither Waddington nor Conway Morris has much to say about that, though Waddington's general metaphor is of a 3D landscape where the genes are symbolized by pegs and the epigenetic dimension is represented by cables or ropes that are attached to the pegs and hold the ravines/valleys and peaks forming the canals/chreodes. However, that leaves open the question of whether there could be a mechanistic answer to that question, or whether it necessarily requires a non-mechanistic answer. The general assumption in this special issue is that there is no reason why a mechanistic answer should not be sought. The alternative is to take the vitalist route, perhaps to invoke what Driesch (1908) called *entelechy,* some non-physical causal factor.

Conway Morris often seems ready to consider something akin to supernatural entelechy to explain evolutionary convergence. We do not rule that out, but it is the task of empirical scientists to seek the natural explanations. We also suggest that an explanation of chreodes or canalization in terms of mechanism should not necessarily be seen as an alternative to explanation in terms of entelechy, or some other non-physical causal factor, but rather as an account from a different perspective of the same underlying process.

The apparent choice between mechanistic and non-physical explanations of developmental and evolutionary pathways may be unnecessarily stark. Field theories provide an alternative non-corpuscularian way of theorizing, and one that is sometimes more helpful and appropriate. There is usually scope for mutual translation between mechanistic and field theories. As Wolfhart Pannenberg (1993) has pointed out, field theories can be coordinated more easily with theological interpretations in terms of *spirit.* That is not to say that fields and spirit are identical or equivalent, just that there it is easier to co-ordinate them.

Systems Biology

Systems biology, some have claimed, builds on holistic assumptions but extends them by using general systems theory and mathematical modeling. A significant precursor of modern systems biology was the development of General System Theory by the biologist Ludwig von Bertalanffy . Another key early influence was Alan Turing's work on *The Chemical Basis of Morphogenesis* (Turing, 1952). Specific quantitative models of biological systems then began to develop, an early example being Denis Noble's computer model of the heart pacemaker, and Noble has remained one of the most significant proponents of systems biology (Noble, 2006).

The claim that systems biology is holistic is often made in the literature, though it is harder to know is exactly what is meant by that claim, as systems biology is not obviously holistic in the sense meant by Smuts. Though few practising biologists have subscribed to holism in the sense that Smuts meant it, the concept of holism in a rather general sense has been quite widely accepted within systems biology. Systems biology is often contrasted with molecular biology, which has been castigated by many systems biologists as being too narrow and reductionist; systems biology has also been hailed as a paradigm shift in biology (Markum, 2009).

Not everyone is convinced by the claim that systems biology is holistic (see Gatherer, 2010). Some object that systems biology is not actually as holistic as it should be (Cornish-Bowden, 2006). Others see no need for systems biology to depart from standard reductionism. As Gatherer puts it, systems biologists are "holists by declaration rather than practice" (9). At present it seems that systems biology holds out the promise of becoming holistic, but this very much depends on which particular sense of holism one has in mind. Systems biology might be more hospitable to some kinds of holism than to other senses of the term, more broadly construed.

There is a need for clearer proposals about what would be involved in systems biology becoming more genuinely holistic. One possible approach that probably deserves more attention than it has received is Robert Rosen's *Relational Biology* (Rosen, 1991). He proposed that biology is about relations rather than things; this is akin to the more general shift in thinking that we mentioned above from corpuscles to the fields that connect and influence them. Rosen also inverted the usual hierarchy of the sciences, claiming that biology, with its focus on complexity, is the lowest level in the layer model, and that physics is a special case.

A particular issue raised by a systems approach to biology is the relationship between structure and function. Which determines which? Structure may underpin and constrain functioning but, equally, sustained patterns of functioning may influence structures. In as far as there is plasticity of structures, a pattern of functioning may lead to changes in structure which in turn creates new functional possibilities. There has recently been much interest in the plasticity of the nervous system in this connection. Some systems approaches to biology, and it is worth noting that there are many forms, would probably suggest that influences go in both ways.

The strong emphasis on mathematical modeling in systems biology means that it does not really make much use of either the machine or the organism metaphors, the dominant metaphors of Western science (Ruse, 2010). In that sense it seems to rise above the debate, but there is a real question about how much mathematical modeling has the verisimilitude to help us to really understand how biological processes work. The key issue is perhaps what the relationship is between the whole and the parts, and systems biology does not consistently grapple with that key question. Indeed, some forms of systems biology, particularly the so-called *omics* approach, look all too much like an intensified form of mechanism simply rewritten at the system scale rather than at the molecular scale. Other metaphors are possible, and the network metaphor suggested by Gregersen in this special issue also, in a different way, rises above the debate between mechanism and organicism.

The term *systems biology* actually seems to cover a range of rather different approaches. In particular, it seems to include two very different things. One is holistic only in the sense that it tries to include measurement of all relevant variables in order to make better predictions; such biology may aspire to comprehensiveness, but is not holistic in any philosophically interesting way, and does not have its main focus on mechanisms. There is another kind of systems biology, which pays close attention to the ways in which systems (often quite small-scale systems) work, and how the various component processes interact in a feedback-rich way; such biology often moves beyond simple bottom-up reductionism because it is very aware of top-down and whole-part processes.

The nature of systems biology is explored more fully by Harris Wiseman in this special issue, where he identifies four key features: a set of empirical methodologies that lead away from some of the greedy forms of reductionism mentioned above; an integrative, multi-scientific ethos; a reliance on data-aggregation and computational analytics (in its dominating "bioinformatics" form at least); and a focus on predictive assessments for producing translational advances in numerous fields, such as medicine and agronomics. Systems biology is also consistent with the DICI approach (developmental, integrative, complementary, interactionist) set out by Denis Alexander in his 2012 Gifford Lectures.

Summary

There are strong resemblances between holistic, organismal and systems approaches to biology, though also significant differences. We have suggested that holistic and organismal approaches differ more in their conceptual background than in which kinds of biology are being referred to. Though it is claimed that systems biology is more holistic (perhaps more by commentators on the field rather than by the practising biologists themselves), there is a significant ongoing debate about how holistic it is, or should be. However, for the most part, each of these modes of biology, in their different ways, avoids the problems identified in the previous section of simplistic mono-causal determinism, equally simplistic uni-directional reductionism and biological mechanisms that are specified in over-mechanical ways.

Applications to Specific Fields of Biology

In this section we consider the implications of the more holistic approach we have discussed above for specific areas of biology. There is no single branch of biology that is holistic biology, nor should there be. Holism in biology is an approach that takes into account the effects of the whole organism and the environmental context in every field of biology. It would be a large enterprise to consider the full range of implications of a holistic approach for every field of biology, and we do not attempt that in this article. However, in this special issue four varied topics are considered that together raise a range of issues: evolutionary theory and the *modern synthesis* (David Depew and Bruce Weber), genetics and epigenetics (Ilya Gadjev), neuroscience (Harris Wiseman) and ecology (Richard Gunton and Francis Gilbert).

Evolutionary Theory: The Modern Synthesis

The modern synthesis emerged in the 1940s and 1950s as a bringing together of genetics and natural selection, with an emphasis on natural selection as the creative driving force of evolution, with cumulative effects that went far beyond just deciding whether or not individual mutations should be retained. The modern synthesis evolved a good deal itself in the latter half of the twentieth century, and the question Depew and Weber tackle is whether it can continue to absorb challenges (as it absorbed challenges such as punctuated equilibria) or whether the challenges it currently faces require a more radical solution.

Depew and Weber focus particularly on challenges from developmental biology, which has always been more organismic than most fields of biology. A key question is whether evolutionary developmental biology (*evo-devo*) can be assimilated into the modern synthesis, or whether it calls for some new kind of synthesis. Depew and Weber argue that the modern synthesis can absorb the perspective of organismal development; given the track record of the history of the modern synthesis, that seems a reasonable claim.

However, the Darwinism that is emerging is not a narrow or strict one in which everything can be reduced to mutation and natural selection; it is one in which a more complex set of causal factors is operating than was envisaged when the modern synthesis was first formulated. There are several points that are worth making clear about this broadening of the modern synthesis. In as far as there are legitimate theological concerns about Darwinism, we suggest that they do not relate to *all* forms of Darwinism, but only to those forms that want to reduce absolutely everything in evolution, in a simplistic way, to random mutation and natural selection. It is also important here to be clear that we are not proposing causal factors of a non-scientific kind, but a broadening of the range of scientific factors that can be considered within evolutionary theory. *It is an expansion of the modern synthesis, not a departure from it.*

The modern synthesis has become increasingly emancipated in the range of factors that it is willing to assimilate, and has already moved on to the kind of broad Darwinism that is less likely to raise concerns about an overly simplistic kinds of evolutionary reductionism. S. J. Gould was one key figure in this development, something on which Conway Morris agreed with him, despite their disagreements about the role of pure chance (Morris, 1998). Conway Morris' focus on evolutionary convergence can probably also be assimilated into the modern synthesis, rather than requiring it to be abandoned (Morris, 2005; Ruse, 2008).

It is also worth making clear that this is not a case of science being distorted by religious concerns. Darwinism has become broader because scientific considerations have pushed it in that direction. However, fortuitously, developments that have been driven by science have also made Darwinism more congenial theologically. In this sense, a happy convergence is emerging between scientific and religious approaches to evolution.

Genetics and Epigenetics

One of the most serious challenges to have emerged recently to simple forms of reductionism in biology is epigenetics, something considered in this special issue by Ilya Gadjev. There is now abundant evidence that genes do not have inexorable consequences for organisms regardless of circumstances. On the contrary, numerous genes can be switched on or off in response to environmental conditions. So, for an effective response to a changing environment, it is not necessary to wait for genetic mutation, since the selection of which genes are currently operating can be modified more immediately. What emerges is an interactionism between genes and environment, rather than either genetic determinism or environmental determinism.

As Gadjev points out, this is not a radical change to how geneticists understand things; interactionism is nothing new. However, it does have important implications for the public understanding of biology where simplistic genetic determinism is rife, though it is sometimes now replaced by a rhetoric that suggests an equally simplistic environmental determinism. Sometimes biologists who understand the complexity of biological processes perfectly well can lend support to misleading and simplistic popularizations. The challenge facing the public understanding of biology is how to popularize a complex multi-factorial interactionism rather than reducing everything to either genes or environment. The challenge here is to win the argument for complexity against the allure of simplistic forms of reductionism or determinism. Once again, good science is pointing in a direction that is congenial theologically, not against it.

Predictive Neuroscience

Wiseman examines how systems biology echoes recent trends in predictive neuroscience, which are themselves modules of a larger project of data-integration and analytics across all of the sciences. Wiseman explores some of the pitfalls and advantages of these trends. There is now growing interest in P4 medicine (predictive, preventive, personalized, and participatory) which explicitly recognizes the complexity and contextuality of the phenomena concerned, integrating multiple factors that contribute to causal predictions. The challenge of making passably accurate predictions about the future of brain and behavior makes it necessary to abandon simple forms of mono-causal determinism and uni-directional reductionism. Nevertheless, such a change in mind-set can help persons rethink their health and sickness in broader, less mono-reductive terms (the problematic sense that every human ailment has a single specific and locatable biological cause). Equally, there are potentially worrying new forms of reductionism that arise when treating persons as systemic aggregates of data. Indeed, Wiseman raises questions about whether the conceptual revolution in predictive neuroscience is as radical as it needs to be; sometimes it seems to consist just of aggregating data across more systems, without an adequate recognition of the need for multi-directional causality.

Neuroscience has long been a rather reductive area of biology, and protests against that have been relatively rare (but see Rose, 2005), despite scientific data supporting a more contextual approach to brain function. The tendency to see the brain as determinative of behavior is now being balanced by an emphasis on the effect of context on how the brain itself functions. The structure of the brain itself depends on how it is used, as is illustrated by the well-known research showing how the demands on spatial processing of learning to be a taxi driver in London affects the structure of the brain (Maguire et al., 2006). There is also a growing emphasis on the effect of context on cognition, with a recognition of the importance of the *4 E*s, i.e. that cognition is enacted, embodied, embedded, and extended. All such effects are, of course, mediated through the physical brain. This emphasis on the contextuality of cognition is quite congenial theologically (e.g. Watts, 2013), and is closely parallel to the points that are being made by epigenetics about the contextuality of genetics.

Ecology

It might be imagined that ecology is an area of biology that always takes contextual and environmental factors into account. However, as Gunton and Gilbert point out, ecology can proceed at several different levels of analysis, and some levels of analysis are more contextual than others. In particular, Gunton and Gilbert distinguish at least four different paradigms in contemporary ecology: population, macroecology, trait and ecosystem ecologies. It is in the last that particular prominence is given to environmental causes and effects are especially prominent, with a focus on the ecosystem as a whole rather than just interactions between specific organisms. This is where scientific ecology becomes most closely associated with what are popularly known as ecological values or ecosystem services.

Gunton and Gilbert also advance the philosophical view that in every domain of science something that can properly be called *laws* can be found, and that there are ecological laws that are not reducible to laws in other domains. This approach allows for a complex form of determinism, but one that has no aspiration of carrying through a program of inter-theoretic reductionism. Gunton and Gilbert follow the philosophy of Herman Dooyeweerd, which emerges from the Reformational tradition, and which sets out a complex ontology in which there are multiple domains, each with its own laws, and no one reducible to another. Dooyeweerd's approach allows an interesting form of determinism without reductionism.

Other Applications

Other implications of a more holistic biology for public policy are explored by Reiss and Ruse (in preparation). For example, an exclusive focus on the effects of medicinal and surgical interventions can sometimes lead to a neglect of the equally powerful effects of environment conditions on medical prognoses. A holistic approach to biology lends support to the whole-person tradition of medicine. A holistic perspective is also relevant to genetic engineering. Without disputing the potential benefits of genetic engineering, enthusiasm for them has sometimes failed to consider adequately the effects of environmental context on the effects of genes, and has also neglected the sensibilities of consumers (an instance of the importance of social context).

Reiss and Ruse (in preparation) also draw attention to the problems of integrating genetic and physiological factors on the one hand, and social, cultural and environmental factors on the other. Nature-nurture debates are frequently polarized into an either/or form, when what is required is a recognition of the complexity of the interactions that occur, and that how each factor operates is dependent on other factors. Some of the issues this applies to are quite sensitive, and a worry about being excoriated or a concern for political correctness has made it harder to develop a fully contextualised holistic approach to such varied questions as the effects of general intelligence on cognitive performance, and the effects of race on athletic performance.

Theological Implications

Finally we explore how holistic biology might be fruitful for theology, something considered by Niels Gregersen in the final article in this special issue. To anticipate we suggest that there are at least three implications. First, holistic biology steers away from the crude and simplistic reductionism and determinism that has been the point of greatest tension between biology and theology. That has been the main theme of this article, and the theological threads can be gathered together with much more ado. Second, holistic biology suggests a more subtle view of divine action in which God's purposes are carried forward through engagement with the complex systems of creation rather than by discrete interventions. That is the principal focus of Niels Gregersen's article, and it will suffice here to introduce his fuller treatment of it. Third, holistic biology invites us to connect the inter-dependence that is increasingly evident in nature with the inter-dependence that is assumed to be central to the nature and purposes of God. That will call for rather more unpacking.

Implications for Ontology and Divine Action

Why do reductionism and determinism raise theological issues? There are two potential concerns. One focuses on the ontological conclusions that might be drawn on the basis of strong reductionism. The concern is that *if* (and it is a big *if*) it can shown that humans and other creatures are fully explicable in terms of low-level physical processes, then it can reasonably be claimed that the higher-level features that are of particular religious interest (i.e. moral, relational and spiritual capacities and sensibilities, or *soul* qualities) are *nothing but* the product of genes, neurons or other some other basic part of the human body.

These would be unwelcome conclusions for most religious people, as for many humanists. Against such views there is a wish to assert the reality and significance of the higher properties of humans and other creatures. In fact, people have perhaps been over-fearful of strong forms of reductionism, as there are many philosophical problems with drawing strong reductionist conclusions. For example, as already indicated, the strongest forms of reductionism trade on the belief that *complete* biological explanations will be forthcoming for all higher human qualities, and that is likely seldom the case, if ever, to be the case. Also, as we have already pointed out, the project of inter-theoretic reductionism has been widely abandoned in biology, and largely faded away in the 1970s.

However, it is not our purpose here to re-tread this well-worn philosophical territory but to add the scientific point that has been the major focus of this article, that the holistic direction in which biology is moving, which has increasingly been driven to recognize the importance of context, and the influence that wholes have on parts, undercuts this reductionism program, and stops it before it can make any headway.

The other religious concerns are about causal influences, both human action and divine action and, strictly, these concerns arise more from determinism than from reductionism. *If* it can established (and again it is a big if) that humans and other creatures are completely determined by low-level biological processes, then there seems to be no room left in the universe for intentional action of any kind, either human or divine. If the biological mechanisms that enable humans and other creatures to function are purely mechanistic, some might be tempted to conclude that humans really are just mechanical, and have no freedom or capacity for purpose, beyond that of any gene-based organism.

There are, of course, various ways of trying to avoid that uncomfortable conclusion. One is the *compatibilist* view that languages about determinism and free action can be run in parallel, with no conflict. However, even if it is allowed that there are two such epistemological perspectives, it seems that a high price needs to be paid, in terms of admitting that they are not referring to the same real world, for the two discourses to avoid running into conflict with each other.

There are particular issues that arise for divine action, and various ways of trying to reconcile it with a scientific worldview (Saunders, 2002). One approach is the Thomist device of saying that God is a *first cause*, and that is so radically different from the discourse about *secondary causes*, with which scientific determinism is concerned, that no conflict arises. It is also possible that a Calvinist or conservative Reformed theological position can live with scientific determinism more easily than can most theologies. As James Moore (1981) has pointed out, Calvinists are able to live with natural selection much more easily than those of other theological persuasions, and the theological determinism of Calvinists, formulated in terms of predestination, enables them to go in a different direction from most theologians when it comes to issues about action and determinism.

Our concern here is with the implications for these issues of fully recognizing the systemic complexity of biological processes, and that is the focus of Gregersen's article in this special issue. Gregersen is concerned with factors that lead to extending or supplementing the modern evolutionary synthesis. He concurs with Depew and Weber that there is nothing that makes such an extension impossible, though he thinks that the extensions called for are significant. One driver for this is the evolutionary trend towards increased self-organisation (see Gregersen, 2006). Another is the way in which organisms and groups interface with their environment, for example in the phenomenon of niche construction, creating habitats that influence future evolutionary trends.

This has implications, Gregersen maintains, for how we should understand biological explanation, which he suggests should be seen neither as a matter of timeless laws, nor in terms of genetic or any other kind of reductionism. He suggests rather that we should think of a network of overlapping biological explanations, serving different explanatory purposes. The suggestion is that holistic biology leads us, not just to a different kind of biological explanation, but to a new structure of biological explanations in which different kinds of explanation co-exist in an explanatory network.

In this context, Gregersen raises the question of whether explanations in terms of the presence and purposes of God could have a place within such a network of explanations. This is akin to, but develops further, Peacocke's formulation of divine action in terms of *whole-part constraint.* Gregersen is careful to distance himself from the view that God is literally the whole to which the parts of creation, so-called, relate. Rather he draws an analogy, suggesting that the causal influence of wholes to parts provides a helpful analogy for how God influences creation.

It is widely thought that holism is more religion-friendly than reductionism and mechanism. However, as Michael Ruse points out in this special issue, things can go in the other direction. We suggest that it depends partly on whether a particular religious person is more alarmed by the specter of pantheism or of atheism. If pantheism is the main fear, holism will appear too dangerous to be regarded as a friend. If atheism is the main fear, holism may seem a useful ally. Which fear predominates depends on general theological outlook, perhaps with conservatives tending to be more concerned about pantheism, and liberals about atheism. It also depends on historical period, with the early modern period being more anxious about pantheism, and the late modern period being more concerned about atheism.

Interdependence

Finally, we will consider the theological significance of the interdependence in the natural world that is emerging from recent holistic trends in biology. Again, it is important to emphasize that there is no wish to allow a religious perspective to distort what arises from science. The theme of interdependence is something that emerges from biology itself as Kriti Sharma argues (Sharma, 2015), though a religious lens may provide a sensitizing perspective that focuses interest on the significance of interdependence.

Sharma accepts that there has already been widespread acceptance of interactionism, but wants to press beyond that to the more radically organicist view that she calls *interdependence*. She thinks there is a good deal of misunderstanding about this, and that what many biologists have in mind when they talk about interdependence is really just a set of independent objects influencing each other by mutual interaction. Her more radical view, as she summarizes it in her final chapter, is that there are no “referents independent of terms”, no “objects independent of perception”, no “essences within things”, no “causal powers between regularities”, no “subjects independent of experience and actions”, no “laws independent of concepts and cognitive consonances”, and no “gaps between subjects and reality independent of the experience of such” (99). This is a radically revisionist ontology.

Interestingly, the area of biology that Sharma chooses as the core of her scientific argument is from microbiology. She focuses down in chapter 3 on signal transduction, giving a full and detailed history of how and why our current views about signal transduction evolved, and came to prominence in the 1970s and 1980s. Her point is that how you formulate the responsiveness of cells (i.e. their "reactivity, activity, irritability, dynamism, behavior" etc.) depends on your basic conceptual assumptions. It is a compelling example of how metaphysical assumptions influence scientific theorizing.

Sharma argues that the standard way of talking about signal transduction depends on some contingent, unnecessary and undefended assumptions about what is a cell, and what is inside and outside it. She suggests that we have slipped into a way of thinking about the cell as like an animal-agent, a way of thinking that she maintains is misleading, and which she wants to see replaced by a more radical ontology of interdependence. The problem is analogous to the common-sense assumption that the physical world is composed of particles of hard matter, an assumption that physics has been forced to abandon. Similarly, she wants to see biology abandon the idea that the living world is composed of discrete entities called *cells.*

Sharma has a Buddhist perspective on interdependence, but interdependence can also be approached from Christian and other religious perspectives. Stephen Verney (1976), in a Christian theological reflection on the evolutionary context of current human challenges, suggests that achieving a sense of interdependence is the evolutionary leap that humanity now needs to achieve, taking humanity beyond the present alternatives of, on the one hand, excessive individualism that leads to a breakdown of social cohesion and, on the other, the subjugation to authority on which totalitarian regimes are based.

Once one starts looking at reality through the sensitizing perspective of interdependence, one can discern something analogous to the perichoresis of the Trinity in the living world of cells, plants and animals (as the new more holistic biology is making clear). You might also argue that humanity is being challenged to achieve a degree of social interdependence that parallels the interdependence manifest elsewhere in the living world. Interdependence would thus become central to a theology of creation.

Conclusion

The issues about holistic biologies are complex, as will be apparent by now. Scientific data are requiring a return to some more holistic form of biology than was prevalent in the early heyday of molecular biology. However, there are many different forms that might take, and it is not yet clear which will, or should, predominate. Whichever it is, it will probably provide a counter-balance to the more unwelcome forms of mono-causal determinism, uni-directional reductionism and over-mechanistic mechanisms. At the same time, the complexities are such that this needs examining carefully in one area of biology after another, and this set of articles includes a detailed consideration of four sample areas of biology. There also seem to be potentially rich implications of the more holistic biology for various areas of theology, such as how we understand God's presence in the world, and what God reveals of God's character and purposes through nature.

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