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Introduction

Interdisciplinary reflections: The case of physics and biology

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The first recorded use of the word ‘biology’ in English was by William Lawrence, a fellow and professor of the Royal College of Surgeons in London. In lectures first delivered in 1816 and expanded in subsequent years, Lawrence asked how one should designate a ‘division of natural science [that] has for its object the various forms and phenomenon of life, the conditions and laws under which this state exists, and the causes which are active in producing and maintaining it’. He turned to Germany for his answer: ‘A foreign author [identified as G. R. Treviranus of Bremen in a footnote] has proposed the ... term “biology,” or science of life.’[1]

Lawrence went on to provide a thoroughly interdisciplinary discussion of the scope and methods of this new science. On the one hand, he recommended ‘a close alliance between the science of living nature and physics and chemistry’. (p. 66) On the other hand, he freely admitted that the application of physics and chemistry to biology was severely hampered by a lack of reliable data and the interrelatedness of life processes.

The dramatic uncertainties engendered by the lack of physical data were illustrated by a contemporary application of hydraulics to cardiac physiology: ‘One [author] estimated the force of the heart as equal to 180,000 lbs; another reduced it to 8 oz.’ (p. 62) When it came to chemistry, the more serious problem was the complex interrelatedness of living processes: ‘Thus, as the successive undulations of water spread wider and wider as they recede from the point first agitated, our chemical examination of a single excretion, by virtue of the mutual influences which bind together all parts of our system, expands at last to considerations embracing the whole economy.’ (p. 65) Lawrence therefore counselled against a simplistic reductionism that equated biology with nothing but physics and chemistry, warning us to ‘guard against ... partial and confined views.’ One example of such blinkered vision was a ‘chemical sect’ that would reduce zoology to ‘nothing but an assemblage of chemical instruments.’ There was also ‘a medico-mathematical doctrine, which explained all the phenomena of life by the sciences of number and magnitude, by algebra, geometry, mechanics and hydraulics.’ (p. 66)

Nevertheless, Lawrence thought there was compelling reason for biologists (not his term) to attend to physics and chemistry, since they ‘have their foundation in experiment, as physiology and medicine have in observation.’ (p. 67) The main contrast is that ‘in the latter case we are obliged to take our subjects in all the complexity of their natural compositions, while in the former it is in our power to regulate the conditions of the operation, and to reduce them, by successive analyses, to the greatest simplicity.’ (p. 67) Thus, physics and chemistry are ‘governed by strict method, and guarded against error by the severe rules of inductive logic,’ which Lawrence lyrically praised as ‘incorruptible sentinels.’ (p. 67) In other words, physics and chemistry provided the methodological ‘gold standard’ for biology.

Lawrence’s lectures, standing self consciously as they did at the birth of the new science of biology, serve admirably to introduce the papers of this special issue, which originated in a symposium organised to mark the end of a two-year project funded by the Templeton Foundation entitled ‘*Why “Why?”—Philosophical and methodological issues at the physics-biology interface*’. The project was motivated by the experience of two physicists (Wilson Poon and Tom McLeish) working at the interface with biology. They were struck by the apparent reluctance of many biologists to ask or answer questions starting with ‘why’, while physicists seemed quite addicted to asking just such questions. One example must suffice.

The author was once working on seeds, which were evolved to store nutrients for germination. Interestingly, soybeans are packed with *two* main storage proteins, glycinin and β-conglycinin. An obvious question is ‘Why two (and not just one)?’ While glycinin contains more sulphur-bearing amino acids than its counterpart, it is not clear that this alone explains why a single ancestral storage protein has diverged into two. A ‘physics’ surmise is that their

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[1] Lawrence applied for an injunction to stop unauthorized printing of his lectures. The Chancellery Court, however, ruled his work blasphemous (for its materialistic explanation of life and mind), and did not grant the injunction. I use a ‘legal pirate edition’, *Lectures on Physiology, Zoology and the Natural History of Man*, Third edition, ‘Printed for James Smith, 163, Strand, London’ in 1823. For further discussion, see *Life Before Darwin*, Heidi Y. H. Poon, Ph.D. thesis, The University of Edinburgh (2005), Chapter 4. ‘Biology’ was first used on p. 52, and then again on p. 58. Subsequent quotations are identified by page numbers in brackets.

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different sizes could give better packing (with the small ones filling the 'holes' left by the big ones). The author once raised precisely this question with a botanist specialising in seeds, 'Why are there two, rather than one, main storage proteins in soybeans?' He received an immediate, and angry, answer, 'I don't want to talk about God with you!'

This and subsequent experience of a similar kind (but without the theological vehemence) on the parts of the author and his colleague Tom McLeish led directly to the Templeton project, which they jointly ran with Alexander Bird and Greg Radick, and which funded the work of Darrell Rowbottom. The Edinburgh conference, at which all but one of the following papers were first presented, was organised to draw together some of the research themes that emerged during the project, and to open up dimensions that we did not have time to explore.

While we must, as always, guard against anachronism, it is nevertheless striking how many of Lawrence's interdisciplinary concerns reappear in the following pages. We open with two papers that consider precisely *how* physics and physicists have contributed to biology at two fateful junctures of the subject. Kersten Hall takes us back to the birth of the modern love affair between physics and biology—the discovery of the DNA double helix in 1953. He reconsiders the puzzle of why the physicist William Astbury failed to make this discovery two years earlier, even though at that stage he already possessed a diffraction photograph remarkably similar to the one that Watson and Crick analysed later. One of the issues is whether Astbury's failure was due to an overly physics-oriented view of biology, an accusation that biophysicists regularly attract from biologist critics. Greg Radick takes us further back to investigate the role of physics in the birth of Mendelian genetics. By tracking the diverse influence of physics on the work of Francis Galton, W. F. R. Weldon and William Bateson, Radick demonstrates that generalizations about what happens when 'physics meets biology' need to be treated with caution. Heeding Lawrence's advice to bring physics into biological research does *not* lead to a monolithic enterprise called 'biophysics'; it all depends on who takes what physics to do what kind of biology! Both Hall and Radick's papers highlight the opportunities for historical research in the variegated relationship between physics and biology.

One of Lawrence's central concerns was with the extent to which a 'reduction' of biological phenomena to physics and chemistry could produce genuine insights into living phenomena. Perhaps not surprisingly, the majority of the papers in this special issue have something to say about this topic. The discovery of the double helix in a Cambridge physics laboratory ushered in half a century of hard reductionism in biology—the only explanations that counted were *molecular* ones. Lawrence would likely have felt uncomfortable in this climate. Happily, there are signs that the limits of molecular reductionism in biology are now being recognized. Michel Morange's paper considers how such recognition opens up a host of 'niches' for novel modes of interaction with physics. Morange highlights the fact that the complex nature of the physics-biology relationship, already portrayed in Radick's historical study, continues today.

Interestingly, reductionistic molecular biology came of age at a time when physics was emerging from its own half century of hard reductionism to discover (some would say rediscover) higher-level 'emergent' properties that could not be trivially 'read' from the laws governing the behaviour of lower level (typically, smaller) entities.[2] Indeed, some higher-level properties can be understood even when certain lower-level details are neglected. For instance, for some purposes, globular proteins may be considered simply as colloidal particles with 'sticky patches' without resorting to chemical and structural details.[3] Such 'coarse grained' description is often essential in computer simulations—even the simplest biomolecules can only be studied at the atomistic level of description using the biggest of today's computers.[4] Biologists have traditionally been suspicious of such coarse graining. Lawrence himself stands in this tradition: biologists 'are obliged to take our subjects in all the complexity of their natural compositions'. Darrell Rowbottom reports in his paper the results of his field work studying the interaction between physicists and biologists in two UK universities, exploring the uneasiness felt by biologists in the use of coarse-grained models in physics-led computer simulations.

This uneasiness does not mean that today's biologists eschew the computer. On the contrary, computation is seen by many as the future of biology. The embarrassing lack of data that Lawrence complained about is now remedied by 'high throughput' laboratory (or 'wet') experiments. Such data, generated under the rubric of various 'omics' (genomics, proteomics, metabolomics, ...), form the 'input' for 'dry', or *in silico*, 'experiments' in the computer, where the response of living systems (from molecules through cells to whole organs) may, in principle, be simulated under many more conditions than 'wet' experiments could ever hope to do. This is the vision of 'systems biology', the subject of Calvert and Fujimura's contribution. Drawing again upon field work, they found that many systems biologists understood their mission as 'making biology more like physics' (remember Lawrence's 'incorruptible sentinels') by taking it in the direction of quantitative predictions. The newly emergent discipline of 'synthetic biology' is then the ultimate manifestation of this research programme.[5] However, other systems biologists interviewed by Calvert and Fujimura argued that total quantification and predictability was unrealisable because of the irreducible complexity of life. Lawrence's metaphor of spreading ripples comes to mind.

Interestingly, some of Calvert and Fujimura's interviewees thought that systems biology was less reductionist than the molecular biology that it was superseding. But it could be argued that systems biology is in fact the logical end point of reduction. The coarse graining favoured by some physicists is no longer necessary because of the vast amounts of data made available by the 'omics' revolution. Rowbottom reflects on this topic in his paper, concluding, however, that it is inappropriate to see the systems paradigm as an alternative to coarse graining.

[2] The classic statement is P. W. Anderson's (1972). More is different, *Science*, *177*, 393–396. Anderson compared the then relatively new science of molecular biology with the most reductionist of all branches of physics—high-energy particle physics. Anderson seems to suggest that the 'reductionistic turn' in biology has something to do with a misplaced 'particle physics envy'. Anderson shared the 1977 physics Nobel Prize for work on 'emergent properties' of disordered systems.

[3] See further Poon, W. C. K. (2006). Coarse graining in biological soft matter. In W. C. K. Poon, & D. Andelman (Eds.), *Introduction to soft condensed matter physics in molecular and cell biology*, New York: Taylor and Francis.

[4] Indeed, biology drives developments in computing. One of IBM's flagship supercomputer systems is 'Blue Gene', developed partly to 'solve the protein folding problem' on an atomistic level. The architecture of Blue Gene was built upon that of QCDOC and QCDOD, supercomputers developed specifically to study the behaviour of quarks (quantum chromodynamics, or QCD). This provides another interesting glimpse of the relationship between particle physics and biology.

[5] Borrowing the terminology introduced by Amos Funkenstein, biology then joins physics and chemistry to become 'ergetic' knowledge—knowledge by doing (Greek *ergein* = to do). 'Synthetic physicists' demonstrate that they understand the Big Bang by recreating its conditions in particle accelerators. The chemist's understanding of molecules is proven by synthesizing them in the test tube. Now, biology can show that it, too, understands its subject matter by synthesizing life itself. See *Theology and the Scientific Imagination from the Middle Ages to the Seventeenth Century* (Princeton, 1986). In Chapter V, Funkenstein argues that the transition from contemplative (passive) to ergetic (active) knowing gave rise to modern science. The 'ergetic' drive in biology, however, is not new. See Pauly, P. J. (1987). *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology*, New York.

A problem facing the reductionist's 'divide and conquer' approach is to know *how* to analyse apparently seamless complexity (recall again Lawrence's metaphor of spreading ripples) into manageable chunks. At first sight, this should be easy for biology: the living world is 'modular'—species exist within ecosystems, each species is made up of individuals, while each individual organism has organs made up of tissues, themselves constituted by cells bearing organelles. Steven French in his paper draws on the work of John Dupré to suggest that dividing up the wholeness that is life into discrete components *is* in fact problematic, even in something as 'obviously' modular as a phylogenetic tree. He argues that considerations of this kind point towards a 'structural realism' in biology, a stance that hitherto has been elaborated typically for physics, where 'structures' in the form of equations are plain to see.

Hot on the heels of their 25th April paper announcing the double helix, Watson and Crick followed with another note in the journal *Nature* (on 30th May 1953) explaining the genetic implications of their discovery: 'It ... seems likely that the precise sequence of the bases is the code which carries the genetic information.' Just five years previously, Claude Shannon had published a paper in the *Bell System Technical Journal* entitled 'A mathematical theory of communication', which single-handedly created the science of 'information theory'. From the moment of their almost contemporaneous birth, these 'two new sciences' have been closely intertwined.[6]

Traditionally, the information discourse of biologists has accepted a distinction that was at least implied in Shannon's original paper, that between software and hardware. In this kind of discourse, information and matter remain clearly distinct, the embodiment of information in bits of matter (whether a computer memory or a piece of DNA) being merely incidental. In her contribution, Evelyn Fox Keller sketches out a new discourse of 'informed matter' (the terminology is Jean-Marie Lehn's), which understands information as *inherently* embodied. Given the increasing prominence of 'information technology' in modern biology—witness the centrality of computation in systems biology—a shift in the epistemology of information as proposed by Keller and others will likely have serious repercussions for the life sciences.

Our collection started with a reminder of the role played by physics in the discovery of the DNA double helix, which in turn started the molecular biology revolution. In our final paper, Otávio Bueno considers two examples where molecular biology 'pays its debt' to physics by supplying physicists with 'toys' in the nanotechnology playground. Through cases studies of physicists using DNA to build nano-scaffolds of various kinds and to engineer a conducting nano-wire, Bueno is able to highlight just how different the methods and values of physicists and molecular biologists are.

The papers in this special issue do not by any means exhaust the range of possible investigations into the multifaceted relationship between biology and physics, either diachronically or synchronically. The publications of our Templeton researcher, Darrell Rowbottom, explore various aspects not discussed in this special issue, including the contrasting role of models in physics and biology[7]. A particularly interesting issue that arose towards the end of the project was the role of hypotheses. It appears that biologists give a much more explicit role to formulation and testing of hypotheses than physicists, a claim that is supported by close reading of a collection of biomechanics papers[8]. There is much room for further field work and philosophical reflection along these lines. Other possible avenues of research are not touched on at all either during the project or at the Edinburgh symposium. We will close by briefly outlining three.

Lawrence recommended 'a close alliance between the science of living nature and physics *and chemistry*'. We have so far left chemistry almost entirely out of the picture (but see comments in Rowbottom's paper). Evidently, a parallel investigation into the relationship between chemistry and biology is equally fascinating. Less obviously, studying the interface between chemistry and physics may also throw light on the physics-biology relationship. At the turn of the twentieth century, a number of scientists started to use the then new quantum and statistical mechanics to explain molecular properties and reactivity. The laboratory chemist engaged in synthesizing new molecules had little sympathy for or use of this esoteric, highly mathematical discourse. In the end, a new independent discipline, physical chemistry, emerged[9]. Interestingly, synthetic chemists do have a kind of 'folk physical chemistry' to enable them to rationalise their work in terms of the movement of electron pairs and the relative disposition of energy levels, but 'real' physical chemists by and large eschew this kind of 'creole'. One may wonder whether the developing relationship between physics and biology is substantially retracing this route: are we in the middle of a process that will end in the creation of a physical biology as an independent discipline, and the emergence of a 'folk physical biology' discourse in mainstream biology?[10]

Next, we return to the title of our Templeton project: 'Why "Why?" ...' Nothing in our work or in the Edinburgh symposium has addressed directly the question of why biologists seem to be reluctant to ask 'Why?' questions. But we did make some progress in understanding the question itself. Early on in the project, we began to think that the absence of 'Why?' questions in much of biological discourse, with its heavy bias towards molecular biological investigations, might be functionally equivalent to the strange silence of Darwin in mainstream biology. In the half century of biology ushered in by Watson and Crick's double helix, Theodore Dobzhansky's dictum that 'nothing in biology makes sense except in the light of evolution' was largely forgotten.[11] 'Making sense' of living organisms within the framework of evolutionary theory took a back seat in the euphoria of long last being able to plug the molecular data gap (recall Lawrence's lament). But the sequencing of the genome of organisms and the proliferation of the various 'omics' are bringing evolutionary concerns back into the mainstream. Physicists, especially those with a mathematical bent, have had a long history of being fascinated by evolutionary theory.[12] It should be fruitful to study this area of physics-biology interaction, especially in the light of the recent resurgence of interest in evolutionary discourse in biology and medicine.

A third potential avenue for future reflection comes from recalling the wider context of our project. It formed part of a Templeton Foundation funding round on 'Emergence of Biological Complexity'. One of the three sub-themes was 'biochemistry and fine tuning', exploring the 'extent to which arguments analogous to "fine tuning" in physics and cosmology can be applied to chemistry and biochemistry'. 'Fine tuning' arguments in physics and cosmology are well known and uncontroversial—the constants of physics

[6] See further Lily E. Kay (2000). *Who wrote the book of life?*: *A history of the genetic code*. Stanford.

[7] Rowbottom, D. (2009). Models in Physics and Biology: What's the Difference? *Foundations of Science, 14*, 281–294.

[8] Rowbottom, D., & Alexander, R. McN. (in press). The role of hypotheses in biomechanical research.

[9] See further John W. Servos (1990). *Physical Chemistry from Ostwald to Pauling: The making of a science in America*. Princeton.

[10] Interestingly, the classic text by Alfred J. Lotka reprinted by Dover as *Elements of Mathematical Biology* (New York, 1956), was originally published as *Elements of Physical Biology*. Chapter V of this book, entitled 'The Program of Physical Biology', is directly pertinent to our discussion. Indeed, the relevance extends to beyond biology proper. Lotka's programme included the use of mathematics in what we would now call the social sciences.

[11] Dobzhansky, T. (1973). Nothing in biology makes sense except in the light of evolution. *The American Biology Teacher, 35*, 125–129.

[12] R. A. Fisher read mathematics at Cambridge, and taught physics and mathematics at Rugby and other English public schools for a time. See also Radick's paper.

(e.g., those controlling the strength of the four fundamental forces, etc.) seem to adopt (very) precisely those values needed for carbon-based life to evolve on an earth-like planet.[13] This area of discourse relies heavily on 'counterfactual' discussions—e.g. *what if* the ratio of the strong to weak nuclear forces were to increase by just a little bit? (Answer: the only atoms in the universe would have been hydrogen and helium, and not the 92 of our periodic table.) Counterfactual questions are less familiar in chemistry and biochemistry, though a recent book (again based on a Templeton-sponsored symposium) gives a taste of such investigation by considering how water is 'fine-tuned for life'.[14] Counterfactual questions are rare, and controversial, in biology; many of these involve posing 'what if' questions to the evolutionary process. What if a meteorite did not strike and destroy the dinosaurs? Lurking behind specific counterfactual questions of this kind is that ultimate 'what if': what if we were to re-run the 'tape of life', as Stephen Jay Gould would put it. He suggested that the course would be so different as to be unrecognizable from anything that happened the 'first time round'.[15] Simon Conway Morris, however, argues[16] that evolution is so heavily constrained by the laws of physics and chemistry (and possibly other general laws) that the 're-run' would demonstrate very substantial similarities—hunters of fast-moving prey, for example, almost certainly would have to have 'camera eyes' (like ours or those of octopi), because the laws of optics leave little room for manoeuvre. A study of the history and philosophy of counterfactual questions in physics, chemistry and biology would be fascinating, especially in the light of what has already been said about opportunities for new research at the biology-physics interface mediated by resurgent evolutionary concerns.

[13] The standard text remains Barrow, J. D., & Tipler, F. J. (1988). *The anthropic cosmological principle*. Oxford. For a brief introduction, see Davies, P. D. (1982). *The accidental universe*. Cambridge.

[14] Lynden-Bell, R. M. et al. (2010). *Water and life: The unique properties of* H_2O. Boca Raton.

[15] Gould, S. J. (1989). *Wonderful life: The burgess shale and the nature of history*. New York.

[16] Conway Morris, S. (2003). *Life's solution: Inevitable humans in a lonely universe*. Cambridge.