



What Future for Evolutionary Biology? Response to Commentaries on “The Illusions of the Modern Synthesis”

Denis Noble¹ 

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Abstract

The extensive range and depth of the twenty commentaries on my target article (Noble, 2021) confirms that something has gone deeply wrong in biology. A wide range of biologists has more than met my invitation for “others to pitch in and develop or counter my arguments.” The commentaries greatly develop those arguments. Also remarkably, none raise issues I would seriously disagree with. I will focus first on the more critical comments, summarise the other comments, and then point the way forward on what I view as a necessary and long-overdue transition in the foundations of biology.

Keywords Evolutionary biology · Modern synthesis · Neo-Darwinism · Central dogma · Weismann barrier · Selfish Gene Theory

Responsibility for the use of Language

I wrote: “all parts of the Neo-Darwinist discourse encourage the use and acceptance of the other parts” (Noble, 2016). I repeated this in the target article because it expresses the difficulty of trying to “break out from its attractive simplicity” as it is still routinely taught in schools and universities. Full documentation of the omissions in the textbooks and popularizations has just been published (Shapiro & Noble, 2021). There are many, and the effort to maintain a restricted gene-centred account of evolution is doing real harm to progress. Students are not being taught about some of the important discoveries made outside the scope of today’s version of the Modern Synthesis. Specifically, they are being taught incorrectly about DNA replication, the Central Dogma, Lamarck’s contributions to evolutionary biology, and communication between the soma and the germ-line. This is a serious and

✉ Denis Noble
denis.noble@dpag.ox.ac.uk

¹ Department of Physiology, Anatomy & Genetics, University of Oxford, Oxford OX1 3PT, UK

unnecessary situation that urgently needs rectifying. It is far from being just a matter of language; the misuse of language is a symptom of what has gone wrong.

Louise Westling (2021) writes “attention to the language one uses is necessary for responsible expression, whether by scientist, poet, or philosopher.” Nowhere is that better illustrated than in the way the misuse of metaphors and similes in biology leads the unwary astray. It is necessary not only to expose the Central Dogma as an illusion based on thinking, incorrectly, that DNA replicates like a crystal (Dawkins, 1976, 2016), but also to admit that, in consequence, the replicator-vehicle distinction has to be abandoned. Selfish Gene theory is then empty (Noble, 2011a) since the “vehicle” itself, the complete living cell, is the only possible self-replicator. Without it, faithful replication is impossible. There is no empirical prediction to be tested.

The theory’s emptiness would also explain why in the Afterword to the 2016 edition of *The Selfish Gene* Dawkins openly muses: “In some ways I would quite like to find ways to recant the central message of *The Selfish Gene*.....” (Dawkins, 2016, p 345). But this is only a prelude to there being no recantation. An author cannot recant a statement on the basis of new empirical discoveries if the theory is empty of empirical content. You can only apologize for using misleading language. Nor is a statement like “They [genes] created us body and mind” (Dawkins, 1976, p 21) excused by inventing the term “memes” (Dawkins, 1976, chapter 11) to recognize that our mind is created by much more than genes. The consequential cultural damage to economics (Lee et al., 2019), sociology (Bliss, 2017), and many other fields is already done by the first, apparently categorical, assertion.

I also agree therefore with Smocovitis (2021) when she writes “Nothing is more frustrating to intellectual and cultural historians of biology who focus on discourse, than claims by biologists that “x is just a semantic argument,” as though language didn’t matter...”.

I am also delighted that Smocovitis has insisted on the importance of a historical perspective in evolution. Neglect of that history has been partly responsible for the errors in relation to Lamarck, and this is the point at which to acknowledge the historical contributions of Ernst Mayr’s (1982) magisterial *The Growth of Biological Thought* and Stephen Jay Gould’s mammoth and impressively detailed history of evolutionary biological thought, *The Structure of Evolutionary Theory* (Gould, 2002).

Perspectives

The most fundamental commentary on my article is that of Chen et al (2021). It is fundamental in a *philosophical* sense for it calls for spelling out the precise epistemological tenets of my viewpoint. I am pleased to respond, for the epistemological tenets have already been spelled out. The *general* principle of relativity is precisely the abandonment of an unjustified privileged viewpoint (Nottale, 1998, 2019, Noble, 2016, chapter 1). From an epistemological viewpoint that is all one can ever do (Noble, 2016, chapter 9, The Relativity of Epistemology).

That is also why I insist that my case does not simply rest on the misuse of metaphors, or on an arguable perspective. As I will now outline in this response, there

are serious *factual* errors in the textbooks and popularizations of evolutionary biology. From any perspective, correcting factual errors is a fundamental requirement of scholarship, particularly since those errors concern the *central postulates* of the Modern Synthesis, as outlined in Futuyma and Kirkpatrick (2018, p 18). I will also show why those corrections are necessary for biological science to provide the basis on which we can tackle major and urgent medical problems.

Evolutionary Biology's Factual Errors

70 years ago my biology teacher, using the highly popular *Animal Biology* (Grove & Newell, 1944), provoked a class of 14-year-olds to raucous laughter at the “sheer stupidity” of Lamarck. The memory of that misplaced schoolboy hilarity still haunts me 70 years later, now that I know that Lamarck drew a tree of life showing descent of living organisms from a common ancestor 28 years before Darwin’s famous notebook sketch (Noble, 2020). Lamarck’s tree diagram in his 1809 book (Lamarck, 1809, p 649 in 1994 reprint) is even more detailed than Darwin’s sketch. No-one taught me that fact as a student, nor is it taught today.

Lamarck was the “justly celebrated naturalistwho upholds the doctrine that all species, including man, are *descended from other species*” (my emphasis in Darwin’s praise of Lamarck in the introduction to the 4th edition of *The Origin of Species*). That praise was correct since Lamarck argued for descent from other species 50 years before Darwin, and against very strong critics in Paris led by Georges Cuvier.¹ Yet a major textbook (Futuyma, 2013, p 10, Fig. 1.5) still incorrectly and incomprehensibly attributes to Lamarck the cyclical (multiple origins) creation theory which is actually that of Lamarck’s arch-rival, Cuvier! Cuvier also penned the famous speech that trashed Lamarck’s reputation at his pauper burial. Lamarck needs to be reinstated as a brilliant thinker on evolution and incidentally also the inventor of the term “biology” (*biologie*) for our discipline.

Illusions and Intentions, and Further Factual Errors

Volk (2021) is rightly concerned to know why I use the term “illusion”, particularly since I also write “This is not an accusation of intended illusion.” Am I nevertheless making any conclusion at all concerning intentions? The conclusion of this reply will show that intention does play a major role, but not in the form of the four illusions analysed in my article. It is rather the more general intention to exclude purpose in scientific explanations.

¹ Lamarck did however think that there could have been many, even continuous, *origins* of life. This qualification does not detract from his 1809 Tree of Life diagram, justifying Darwin’s praise for him. Furthermore, Darwin also countenanced this possibility in his famous quote on life “having been originally breathed into a few forms or into one.” (Darwin, 1859).

An important reason why I chose the word “illusion” is that I myself experienced it as such. From the first formulation of the Central Dogma by Crick in 1958, the year I graduated from UCL, to the later 1970 reformulation, nearly everyone took it as a straightforward fact that DNA replicates like a crystal. I am old enough to have met and interacted with many of the originators and popularizers of the Modern Synthesis, including J B S Haldane, John Maynard Smith, Julian Huxley, Richard Dawkins, William Hamilton. I believe they, and many others, were genuinely convinced that they were conveying factual truth about biology: that the genetic material replicates itself like a crystal, and that the Weismann Barrier was necessarily correct.

It therefore came to me as a surprise to find half a century later, in interaction around 2009 with James Shapiro, Lynn Margulis, Eva Jablonka and other “Third Way” thinkers, that what I had assumed was established molecular biological confirmation of gene-centred ideas in biology was simply factually incorrect. That is what prompted my research for my target article, going all the way, from Weismann, through Schrödinger to Huxley, then Crick, to piece together for myself how the idea of the genetic crystal could have developed and become so apparently convincing. I must be one of the first to unravel that incredible story in a detailed historical way to ask how so many brilliant scientists could have been “taken in” by what they took to be established truth.

From that research I have come to a conclusion concerning their intentions. What unites them all is the conviction that science must eliminate purpose from its study of life. For some that was an implicit methodological necessity to guarantee the purity of science. For others it was quite explicit. Thus, Jerry Coyne, famous as the author of *Why Evolution is True*, is explicit about the impossibility of genuine agency when he writes.

“The illusion of agency is so powerful that even strong incompatibilists like myself will always act as if we had choices, even though we know that we don’t. We have no choice in this matter. But we can at least ponder why evolution might have bequeathed us such a powerful illusion.” (Coyne, 2014)

Whether that exclusion of agency is implicit or explicit, it *is* intended. Rather than admit that agency may have evolved, he chooses to say that evolution evolved an illusion in us. I prefer to wonder how he is able to write cogently without genuine agency and to admit that we, and many other species, were bequeathed genuine agency by evolution. I will take this issue further in my concluding paragraphs.

Agency and Semiotics

Tønnessen (2021) writes that “From a biosemiotic point of view (reviewed in Tønnessen, 2015), not only are all conscious organisms endowed with semiotic agency – any organism is.” This is an important extension of my arguments and I think it must be correct since consciousness evolved (Ginsburg & Jablonka, 2019) and it must have done so from targeted behaviour that does not require

consciousness. As an example, the behaviour of the immune system is highly targeted cognitively, but we are not aware of that happening.

De Mul (2021) clarifies this idea even further by distinguishing between the syntactic aspect of biological sequences and structures, and their semantic aspect. Thus DNA sequences in themselves can be regarded as information in the sense introduced by Shannon, involving just syntax. In contrast, “From a biosemiotic perspective, information can be understood as a sign, i.e. as a phenomenon which has a *syntactical*, *pragmatic* and *semantic* dimension.” I agree. It is life itself that gives meaning to sequences.

Schaetzle and Hendlin (2021) characterise my position as “no privileged level of semiotic interpretation.” I had not myself thought of the principle of biological relativity as including such an extension, but it is important. Meaning, rationality and other non-physical factors clearly influence behaviour, which means they have physical consequences, but they cannot themselves be physical causes. Rather, “reasons do not determine actions in the way that the dynamics of molecular interactions perform their role in causation.” (Noble & Noble, 2020).

Further insights concerning meaning are provided by Bolshoy and Lackova (2021) who extend my approach to the illusions of the genetic code. They list four such illusions:

- Both DNA texts and human texts were misinterpreted through Jakobson’s schema of communication
- There is no sticking of a word/ a text to its meaning
- Language is not a frozen synchronic structure.
- Language is not explainable thanks to mathematical logic

and conclude that “The mutual illusions of linguistics and computational biology emerged in a great extent from the digitalization sin—the metaphor of computer program.” There is, of course, no computer programme in the genome. The equivalent of IF–THEN–ELSE statements necessarily involve more than DNA (Noble, 2016, p. 147).

From all of these developments supporting and extending the illusory nature of central aspects of the Modern Synthesis Kull (2021) draws the correct conclusion that the facts imply “the existence of evolutionary mechanisms that do not require natural selection for the origin of adaptations.”

Magnani (2021) extends the arguments to the role of the brain in cognitive niche construction. Environmentally-induced novelties “may have greater evolutionary potential than do mutationally induced ones. They can be immediately recurrent in a population; are more likely than are mutational novelties to correlate with particular environmental conditions and be subjected to consistent (directional) selection; and, being relatively immune to selection, are more likely to persist even if initially disadvantageous” (West-Eberhard, 2003).

Delafield-Butt (2021) draws attention to the possibility that “mind and matter co-exist as two sides of the same coin, and it does very well in answering some fundamental problems with the logic of how experience and intentional agency

can come about in the first place (Delafield-Butt, 2008; Strawson, 2006). We must work hard not to make the same mistakes identified in others, ourselves.”

Gontier (2021) strikes off in yet another direction of thought, in which she pleads for us to recognize “evolution as the outcome of a myriad of mechanisms and processes that go beyond reductionist and “one-way” causal views and require a “nested view of organization”, which is a view that links to hierarchy theory (Gontier, 2018; Pattee, 1973; Simon, 1962; Tëmkin & Eldredge, 2015) and with which I most certainly and wholeheartedly agree.” I strongly endorse her placing of the principle of biological relativity within this plurality.

Camacho (2021) has a very different reaction to my article. He wonders whether “there may be alternative grounds for accepting the plausibility of the Central Dogma *and also* the illusion it perpetuates.” He argues that illusions like the Central Dogma “have *both* impeded and facilitated scientific inquiry.”

Witzany (2021) identifies an important omission in what I wrote, which is that “he does not mention that all gene regulatory elements, which are part of the genome also, represent both the driving force in evolutionary novelty and an essential contradiction to the central dogma.” To this I plead guilty as charged. He therefore concludes that my review “could be usefully extended to integrate some crucial features of RNA networks and viruses.” I agree and I look forward to seeing that kind of extension.

Jablonka (2021) focuses on the first of the four illusions by highlighting the importance of her work with Ginsberg (Ginsburg & Jablonka, 2019) supporting the role of selection through conscious choice. It is important to note that this process may have been the major driver of evolutionary novelty through and beyond the Cambrian explosion.

Sharov (2021) concludes: “The main advantage of the biosemiotics framework is that it leads scientific explanation beyond mechanisms – to those complex processes, where mechanisms are easily redirected or replaced based on the context of signs. I believe that notions of semiosis and agency will become incorporated into the theory of evolution and then mechanisms discussed by Denis Noble will be evaluated from the position of biosemiotics.” I hardly need to add to this. The big question then is how can non-physical entities like signs and concepts influence organism mechanics. This is the question my brother and I are now tackling (Noble & Noble, 2020).

The Molecular Biological Facts

Shapiro (2021a, b) analyses why the Modern Synthesis founders ended up in a dogmatic position, that became stronger the more evidence was found to discredit it. He lists four key facts:

- Discovery of mobile genetic controlling elements by McClintock
- Discovery of DNA sequence elements that establish control networks across the genome

- Discovery of repetitive and largely non-coding DNA whose amount tracks organismic complexity better than protein-coding DNA
- The ENCODE project showing functional transcription of non-coding elements

He concludes that “Contemporary genomics has turned evolutionary theory upside-down.” and has fully documented these discoveries in other recent articles (Shapiro & Noble, 2021; Shapiro, 2021a, b).

Gare (2021) also focuses on the inability of dogmatic forms of the Modern Synthesis to explain firm molecular biological discoveries, showing how replacement of the substance ontology by an ontology of processes provides a much better semiotic view of evolution (Gare, 2011).

Organism-Level Facts

Bacigalupi and Alexander (2021) cite some fascinating examples in their exploration of illusions 1 and 4 to show “that causal constraints can emerge based on relevant analogical and associative phenomena, which are about both the agent’s internal and external milieu. A small range of variations in initial and boundary conditions can result in a large increase in higher-dimensional patterns of behaviour” so that life can “create *effectively infinite* possibilities from which adaptive solutions can *fit* problem *templates* via interpretation, or some kind of *comparator*.”

Also favouring an organism-level view of evolution, Winters (2021) argues that “the shift towards a developmental view would help resolve some of the issues discussed in Noble’s identification of the first illusion of MS, in which it would highlight how organisms can intentionally participate in their own development (and subsequently the development of the natural environment).” We disagree though on whether “conscious processes evolved because they serve a purpose”. That is a serious point, which I will be addressing in future work. There isn’t space to do that here.

The Issues at Stake Cost Money and Lives

It matters enormously whether people really think that we ourselves are mere vehicles for our genes. Such thinking, by confusing conceptual and empirical questions, costs money and lives. Why else are we still investing billions in yet more extensive cohorts for genome-wide association studies, based as they are on the conviction that genes cause the organism’s states of disease and health in a one-way bottom-up process? We already know that, with the exception of rare genetic outlier diseases (which we knew about anyway even before genome sequencing), the only outcome of ever larger genome sequencing projects will be greater statistical significance for what is already clear: the association levels are, as a matter of empirical fact, so low as to be poor predictors of health and disease. Boyle et al. (2017) conclude

“detailed mapping of cell-specific regulatory networks will be an essential task for fully understanding human disease biology.”

Physiology Explains the Low Gene Association Scores

My own discipline, physiology, perfectly well explains the low association scores since it investigates and models those regulatory networks. As my research team discovered more than 30 years ago, critical physiological processes necessary for survival, like the heart’s pacemaker (Noble, 2011b), are so well-buffered *against* genetic variation that they continue to function well regardless of which particular set of gene products they use to achieve the goal of the organism, i.e. survival. Far from genes driving organism reactions, “cellular phenotypes, not genes, must be Mendel’s units of inheritance.” (Baverstock, 2021).

I wrote “goal”, precisely because that is also why it was a huge mistake for biologists to eschew teleology. All functions in living organisms serve the imperative of life, which is to maintain itself. *The tiny association scores are therefore very interesting.* They cannot reveal causation because even a zero score for association between a gene and a disease state does *not* mean absence of causal role. A gene with an almost negligible association score may be the template for a product that has much larger causal significance. In the case of the cardiac pacemaker the difference can be as large as 15% for association and 80% for causation (Noble, 2011b). Attributions of physiological causation require a rigorous causal hypothesis (Noble & Hunter, 2020). Hypothesis-free science is a mirage (Felin et al., 2021a, b).

How the Modern Synthesis Went Wrong

The low gene association scores are also further proof that the secret of life cannot be found at the level of DNA molecules. Life is, put simply, what can actively maintain itself as an open system despite the constraints and challenges of its environment, and of its storehouse of molecular templates called genes. It does so in open interaction with its environment, notably including other organisms. Indeed, life created today’s environment on earth and is still doing so, possibly even destroying it for our own species. Life is therefore necessarily social, and the study of the signs that facilitate that sociality is central to further progress.

Where then did the Modern Synthesis go astray? Historically, it did so in two stages.

First, it uncritically accepted Weismann’s Barrier dogma in order to exclude the inheritance of acquired characteristics. There was no evidence for such a tight barrier when Weismann first proposed it, and there was no evidence for it in Julian Huxley’s 1942 book *Evolution: The Modern Synthesis*. Some later modern adherents admitted as much. John Maynard Smith (1998) summed it up: “It [Lamarckism] is not so obviously false as is sometimes made out.” Huxley (1942, p 29) was also quite critical of Weismann, but still inexplicably went along with the complete exclusion of the inheritance of acquired characteristics.

Second, following Crick's formulation of the Central Dogma and the growing conviction that, in the absence of other experimental proof, it vindicated the Weismann Barrier, the Modern Synthesis became even more restricted. That was a tragedy. Careful analysis of Huxley's 1942 formulation of the synthesis shows that it actually contained the seeds of a more open flowering of evolutionary biology. Many of the processes omitted in modern popularizations and textbooks, as described in Shapiro and Noble (2021), were *already* present or at least hinted at in Huxley's book! All of those processes became eliminated during the hardening from 1970 onwards. There isn't space to document that history here. But if evolutionary biologists had followed Huxley's more nuanced multi-mechanism approach, all that would have been required to bring it into line would have been to admit two factual errors, which had been undermined by molecular biology: the Weismann Barrier and the Central Dogma. That would have re-aligned the Modern Synthesis with Darwin's own multi-mechanism approach.

The Way Forward

Where then do we go now? We have reached a critical turning point in evolutionary biology and it is high time for a major repair initiative. That is the aim of THETHIRDWAYOF EVOLUTION (www.thethirdwayofevolution.org). I see my own discipline of physiology as central to how that may be achieved. The rigorous computational tools of the Physiome Project (www.physiomeproject.org) are ready with many of the physiological models needed to do the job. That is exactly how the comparison between genetic association and functional causation was demonstrated for the cardiac pacemaker and could be demonstrated for many more of the low genotype association scores. The difference between association and causation is an important measure of the extent to which the functional physiological networks buffer the organism from genomic variation. We need to have that measure to make progress, because it underlies the purposiveness of life. The empirical measurement of that difference is also one form of evidence for purposiveness in organisms.

Physiology is also the way forward in following up the demise of the Weismann Barrier. Indeed it is already doing so in extensive research over many years on trans-generational maternal and paternal effects and on the molecular and other processes by which they occur (Gluckman & Hanson, 2004; Noble, 2013).

Through identifying and analyzing causation, physiology is therefore a natural ally of biosemiotics. The effectiveness of signs in the social interactions of organisms implies a causal role for those signs. Once we know that an organism uses intentional diversionary behaviour to escape a predator, we also know that the predator's movements are influenced by the signs communicated by the prey's behaviour. The ability to interpret signs is an important part of anticipatory behaviour in social interactions. This use of signs by organisms is also a measure of associative learning. When it becomes unlimited associative learning we also have a marker of intentional consciousness (Ginsburg & Jablonka, 2019; Jablonka, 2021).

That conclusion concerning animal consciousness and flexible goal-directed behaviour is the primary dividing line between the Modern Synthesis and its

opponents. It is an unbridgeable gap since to admit purpose in life would destroy the fundamental ethos of the Modern Synthesis, built as it was on the pared-down neo-Darwinism of Wallace and Weismann, the very purpose of which was to exclude Darwin's idea of sexual and, by implication, any other forms of agency-driven social selection. It is ironic that purpose in organisms was itself purposefully excluded by organisms (humans) from any scientific analysis of life. Yet those humans denying purpose in other species had themselves evolved from those other species! The Modern Synthesis has taken us on a wild goose chase, only to end up with a modern form of Descartes' dualism. Dawkins says it all when he writes:

“This book is mainly intended to be interesting, but if you wish to extract a moral from it, read it as a warning. Be warned that if you wish, as I do, to build a society in which individuals cooperate generously and unselfishly towards a common good you can expect little help from biological nature. Let us try to *teach* generosity and altruism, because we are born selfish. Let us understand what our selfish genes are up to, because we may then at least have the chance to upset their designs, *something which no other species has ever aspired to.*” (Dawkins, 1976, *The Selfish Gene*, p. 3)

The final emphasis is mine. In principle, that is all I need to do to make my point. But I feel compelled to spell the conclusion out since it is also clear that this paragraph must have been read by millions of readers without seeing the point.

It all has to do with purpose, intentionality, and the signs by which we indicate those to others.

First, the paragraph makes a wholly unjustified assertion that “we are born selfish”. Whether that is true or not, it cannot be because genes are selfish in the sense in which we can be. We can, literally, act selfishly. If we do, there are clear empirical consequences, the signs for which we can all observe. For genes the sense is purely metaphorical. However much we may study a DNA sequence, there can be no sign of literal selfishness.

Second, the purpose expressed is the wish to foster a society of the common good by educating our children.

Third, the text claims that only our own species can aspire to this admirable purpose. Yet, there are abundant signs of this nurturing in other species, including dogs and monkeys that foster the exclusion of uncooperative individuals (Brosnan & De Waal, 2003; Essler et al., 2017). This behaviour is not unique to our own species. That mistake goes back four centuries to the philosophy of Descartes when he asserted that animals are automata, whereas only humans have mental powers.

The *intended* illusions are not therefore the four specific illusions of my article, based on incorrect interpretation of the facts of molecular biology, even though we now know that those interpretations *are* incorrect and the associated concepts are therefore illusory *in that sense*. The *intent* was rather to instill the more general idea that purpose in biology is itself an illusion. Somehow the idea that science cannot analyse purpose took hold. That is the *intended* illusion and is what I and innumerable other students were taught.

We need a better future for evolutionary biology than reverting to Cartesian exceptionalism for just our own species. That would require an evolutionary innovation for just one species for which there is no evidence. It is surely more in keeping

with evolutionary biological thought to think that conscious intentionality involving genuine selfish and cooperative forms of behaviour have evolved, genetically, epigenetically and culturally (Ginsburg & Jablonka, 2019). Physiologists have no difficulty in identifying empirical criteria for such behaviour.

As I have shown in this response, correcting the errors in the textbooks and popularizations of evolutionary biology has become urgent and of great practical importance. It is no longer an academic argument.

Acknowledgements I acknowledge valuable comments on my target article from Geoffrey Bamford who noticed that the quotations from Crick's 1958 and 1970 formulations of the Central Dogma are the same, apart from italicized text. The 1958 formulation, of course, was simply the one-way transmission DNA → RNA → protein with no reverse transcription.

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