

CORRECTION

Evolution beyond neo-Darwinism: a new conceptual framework

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There was an error published in *J. Exp. Biol.* **218**, 7-13.

The quotation from a *Nature* 2010 editorial on page 10 of the article does not appear in the final published version of the editorial. The correct quotation is given below.

‘But for all the intellectual ferment of the past decade, has human health truly benefited from the sequencing of the human genome? A startlingly honest response can be found on pages 674 and 676, where the leaders of the public and private efforts, Francis Collins and Craig Venter, both say “not much”.’

We apologise for any inconvenience this may have caused.

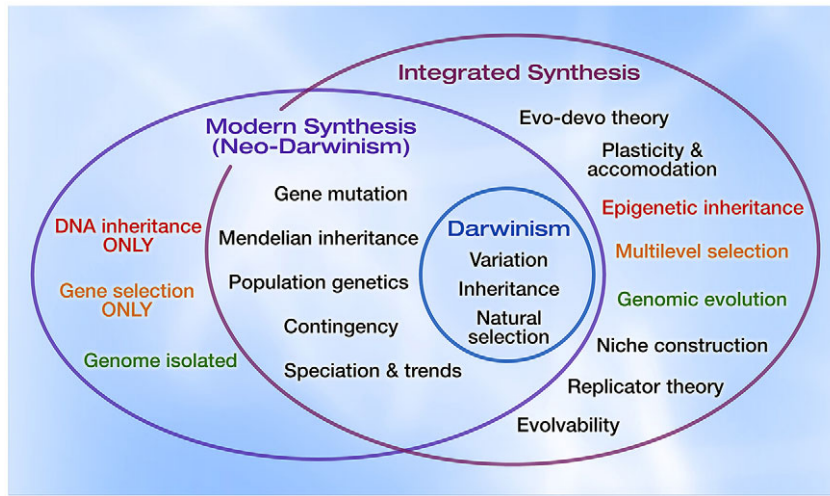


Fig. 1. Diagram illustrating definitions of Darwinism, Modern Synthesis (neo-Darwinism) and Integrated Synthesis. The diagram is derived from Pigliucci and Müller's (Pigliucci and Müller, 2010) presentation of an Extended Synthesis. All the elements are also present in their diagram. The differences are: (1) the elements that are incompatible with the Modern Synthesis are shown coloured on the right; (2) the reasons for the incompatibility are shown in the three corresponding coloured elements on the left. These three assumptions of the Modern Synthesis lie beyond the range of what needs to extend or replace the Modern Synthesis; (3) in consequence, the Modern Synthesis is shown as an oval extending outside the range of the extended synthesis, which therefore becomes a replacement rather than an extension.

let alone question incoherences or identify flaws. Many scientists see it as merely a description of what experimental work has shown: the idea in a nutshell is that genes code for proteins that form organisms via a genetic program inherited from preceding generations and which defines and determines the organism and its future offspring. What is wrong with that? This article analyses what I think is wrong or misleading and, above all, it shows that the conceptual scheme is neither required by, nor any longer productive for, the experimental science itself.

I will analyse the main concepts and the associated metaphors individually, and then show how they link together to form the complete narrative. We can then ask what would be an alternative approach better fitted to what we now know experimentally and to a new more integrated systems view. The terms that require analysis are 'gene', 'selfish', 'code', 'program', 'blueprint' and 'book of life'. We also need to examine secondary concepts like 'replicator' and 'vehicle'.

'Gene'

Neo-Darwinism is a gene-centred theory of evolution. Yet, its central notion, the 'gene', is an unstable concept. Surprising as it may seem, there is no single agreed definition of 'gene'. Even more seriously, the different definitions have incompatible consequences for the theory.

The word 'gene' was introduced by Johannsen (Johannsen, 1909). But the concept had already existed since Mendel's experiments on plant hybrids, published in 1866 (see Druery and Bateson, 1901), and was based on 'the silent assumption [that] was made almost universally that there is a 1:1 relation between genetic factor (gene) and character' (Mayr, 1982). Of course, no-one now thinks that there is a simple 1:1 relation, but the language of direct causation has been retained. I will call this definition of a 'gene' $gene_J$ to signify Johannsen's (but essentially also Mendel's) meaning. Since then, the concept of a gene has changed fundamentally. $gene_J$ referred to the cause of a specific inheritable phenotype characteristic (trait), such as eye/hair/skin colour, body shape and mass, number of legs/arms/wings, to which we could perhaps add more complex traits such as intelligence, personality and sexuality.

The molecular biological definition of a gene is very different. Following the discovery that DNA forms templates for proteins, the definition shifted to locatable DNA sequences with identifiable beginnings and endings. Complexity was added through the discovery of regulatory elements (essentially switches), but the basic cause of phenotype characteristics was still thought to be the DNA sequence as that forms the template to determine which protein is made, which in turn interacts with the rest of the organism to produce the phenotype. I will call this definition of a 'gene' $gene_M$ (see Fig. 2).

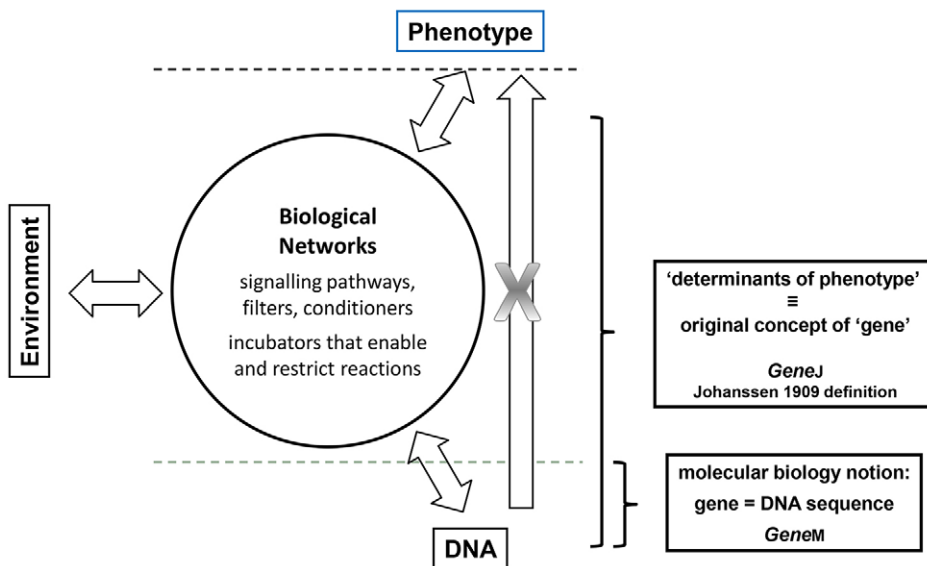


Fig. 2. Relationships between genes, environment and phenotype characters according to current physiological and biochemical understanding. This diagram represents the interaction between DNA sequences, environment and phenotype as occurring through biological networks. The causation occurs in both directions between all three influences on the networks. This view is very different from the idea that genes 'cause' the phenotype (right-hand arrow). This diagram also helps to explain the difference between the original concept of a gene as the cause of a particular phenotype ($gene_J$) and the modern definition as a DNA sequence ($gene_M$). For further description and analysis see Kohl et al. (Kohl et al., 2010).

But unless all phenotype characteristics are attributable entirely to DNA sequences (which is false: DNA does not act outside the context of a complete cell), $gene_M$ cannot be the same as $gene_J$. According to the original view, $genes_J$ were necessarily the cause of inheritable phenotypes because that is how they were defined: as whatever in the organism is the cause of that phenotype. Johanssen even left the answer on what a gene might be vague: 'The gene was something very uncertain, "ein Etwas" ["anything"], with no connection to the chromosomes' (Wanscher, 1975). Dawkins (Dawkins, 1982) also uses this 'catch-all' definition as 'an inheritable unit'. It would not matter whether that was DNA or something else or any combination of factors. No experiment could disprove a 'catch-all' concept as anything new discovered to be included would also be welcomed as a $gene_J$. The idea becomes unfalsifiable.

The question of causation is now an empirical investigation precisely because the modern definition, $genes_M$, identifies them instead with DNA sequences alone, which omits reference to all other factors. To appreciate the difference, consider Mendel's experiments showing specific phenotypes, such as smooth or wrinkled surfaces of peas. $Gene_J$ was whatever in the plant caused the peas to be smooth or wrinkled. It would not make sense to ask whether $gene_J$ was the cause. That is how it was defined. It simply is everything that determines the inherited phenotype, i.e. the trait. (Of course, different questions of an empirical nature could be asked about $genes_J$, such as whether they follow Mendel's laws. Some do; some don't.) By contrast, it makes perfect sense to ask whether a specific DNA sequence, $gene_M$, is responsible for determining the phenotype. That question is open to experimental investigation. $Gene_J$ could only be the same as $gene_M$ if DNA alone determined the phenotype.

This difference between $gene_J$ (which refers to indeterminate entities that are necessarily the cause) and $gene_M$ (whose causation is open to experimentation) is central and I will use it several times in this article. The difference is in fact large as most changes in DNA do not necessarily cause a change in phenotype. Organisms are very good at buffering themselves against genomic change. Eighty per cent of knockouts in yeast, for example, are normally silent (Hillenmeyer et al., 2008), while critical biological oscillators like the cardiac pacemaker (Noble, 2011a) or circadian rhythm (Foster and Kreitzman, 2004) are buffered against genomic change through extensive back-up mechanisms.

The original concept of a gene has therefore been adopted, but then significantly changed by molecular biology. This led to a great clarification of molecular mechanisms, surely one of the greatest triumphs of 20th century biology, and widely acknowledged as such. But the more philosophical consequences of this change for higher level biology are profound and they are much less widely understood. Fig. 2 summarizes the difference.

Some biological scientists have even given up using the word 'gene', except in inverted commas. As Beurton et al. (Beurton et al., 2008) comment: 'It seems that a cell's enzymes are capable of actively manipulating DNA to do this or that. A genome consists largely of semi stable genetic elements that may be rearranged or even moved around in the genome thus modifying the information content of DNA.' This view is greatly reinforced by the fact that gene expression is stochastic (Chang et al., 2008) and that this itself opens the way to an extensive two-way interaction between the organism's functional networks and the structure and function of chromatin [e.g. figure 10.5 in Kupiec (Kupiec, 2014)].

The reason that the original and the molecular biological definitions have incompatible consequences for neo-Darwinism is that only the molecular biological definition, $gene_M$, could be

compatible with a strict separation between the 'replicator' and the 'vehicle'. As illustrated in Fig. 2, a definition in terms of inheritable phenotypic characteristics (i.e. $gene_J$) necessarily includes much more than the DNA, so that the distinction between replicator and vehicle is no longer valid (Noble, 2011b). Note also that the change in definition of a gene that I am referring to here is more fundamental than some other changes that are required by recent findings in genomics, such as the 80% of 'non-coding' DNA that is now known to be transcribed (The Encode Project Consortium, 2012) and which also might be included in the molecular biological definition. Those findings raise an empirical question: are those transcriptions as RNAs functional? That would extend $gene_M$ to include these additional functional sequences. The difference I refer to, by contrast, is a conceptual one. The difference between $gene_J$ and $gene_M$ would still be fundamental because it is the difference between necessary and empirically testable causality, not just an extension of the definition of $gene_M$.

'Selfish'

There is no biological experiment that could distinguish between the selfish gene theory and its opposites, such as 'imprisoned' or 'co-operative genes'. This point was conceded long ago by Richard Dawkins in his book *The Extended Phenotype*: 'I doubt that there is any experiment that could prove my claim' (Dawkins, 1982). A more complete dissection of the language and possible empirical interpretations of selfish gene theory can be found in Noble (Noble, 2011b).

'Code'

After the discovery of the double helical structure of DNA, it was found that each sequence of three bases in DNA or RNA corresponds to a single amino acid in a protein sequence. These triplet patterns are formed from any combination of the four bases U, C, A and G in RNA and T, C, A and G in DNA. They are often described as the genetic 'code', but it is important to understand that this usage of the word 'code' carries overtones that can be confusing. This section of the article is not intended to propose that the word 'code' should not be used. Its purpose is rather to ensure that we avoid those overtones.

A code was originally an intentional encryption used by humans to communicate. The genetic 'code' is not intentional in that sense. The word 'code' has unfortunately reinforced the idea that genes are active and even complete causes, in much the same way as a computer is caused to follow the instructions of a computer program. The more neutral word 'template' would be better. Templates are used only when required (activated); they are not themselves active causes. The active causes lie within the cells themselves because they determine the expression patterns for the different cell types and states. These patterns are communicated to the DNA by transcription factors, by methylation patterns and by binding to the tails of histones, all of which influence the pattern and speed of transcription of different parts of the genome. If the word 'instruction' is useful at all, it is rather that the cell instructs the genome. As the Nobel-prize winner Barbara McClintock said, the genome is an 'organ of the cell', not the other way round (McClintock, 1984).

Representing the direction of causality in biology the wrong way round is confusing and has far-reaching consequences. The causality is circular, acting both ways: passive causality by DNA sequences acting as otherwise inert templates, and active causality by the functional networks of interactions that determine how the genome is activated.

'Program'

The idea of a 'genetic program' was introduced by the French Nobel laureates Jacques Monod and Francois Jacob. They referred specifically to the way in which early electronic computers were programmed by paper or magnetic tapes: 'The programme is a model borrowed from electronic computers. It equates the genetic material with the magnetic tape of a computer' (Jacob, 1982). The analogy was that DNA 'programs' the cell, tissues and organs of the body just as the code in a computer program causally determines what the computer does. In principle, the code is independent of the machine that implements it, in the sense that the code itself is sufficient to specify what will happen when the instructions are satisfied. If the program specifies a mathematical computation, for example, it would contain a specification of the computation to be performed in the form of complete algorithms. The problem is that no complete algorithms can be found in the DNA sequences. What we find is better characterised as a mixture of templates and switches. The 'templates' are the triplet sequences that specify the amino acid sequences or the RNA sequences. The 'switches' are the locations on the DNA or histones where transcription factors, methylation and other controlling processes trigger their effects. As a program, this is incomplete.

Where then does the full algorithmic logic of a program lie? Where, for example, do we find the equivalent of 'IF-THEN-ELSE' type instructions? The answer is in the cell or organism as a whole, not just in the genome.

Take as an example circadian rhythm. The simplest version of this process depends on a DNA sequence *Period* used as a template for the production of a protein PER whose concentration then builds up in the cytoplasm. It diffuses through the nuclear membrane and, as the nuclear level increases, it inhibits the transcription of *Period* (Foster and Kreitzman, 2004). This is a negative feedback loop of the kind that can be represented as implementing a 'program' like IF LEVEL X EXCEEDS Y STOP PRODUCING X, BUT IF LEVEL X IS SMALLER THAN Y CONTINUE PRODUCING X. But it is important to note that the implementation of this 'program' to produce a 24 h rhythm depends on rates of protein production by ribosomes, the rate of change of concentrations within the cytoplasm, the rate of transport across the nuclear membrane, and interaction with the gene transcription control site (the switch). All of this is necessary to produce a feedback circuit that depends on much more than the genome. It depends also on the intricate cellular, tissue and organ structures that are not specified by DNA sequences, which replicate themselves via self-templating, and which are also essential to inheritance across cell and organism generations.

This is true of all such 'programs'. To call them 'genetic programs' or 'gene networks' is to fuel the misconception that all the active causal determination lies in the one-dimensional DNA sequences. It doesn't. It also lies in the three-dimensional static and dynamic structures of the cells, tissues and organs.

The postulate of a 'genetic program' led to the idea that an organism is fully defined by its genome, whereas in fact the inheritance of cell structure is equally important. Moreover, this structure is specific to different species. Cross-species clones do not generally work. Moreover, when, very rarely, cross-species clones do work, the outcome is determined by the cytoplasmic structures and expression patterns as well as the DNA (Sun et al., 2005). In this connection it is worth noting that the basic features of structural organisation both of cells and of multicellular organisms must have been determined by physical constraints before the relevant genomic information was developed (Müller and Newman, 2003; Newman et al., 2006).

As with 'code', the purpose of this section is to warn against simplistic interpretations of the implications of the word 'program'. In the extended uses to which the word has been put in biology, and in modern computing science where the concept of a distributed program is normal, 'program' can be used in many different ways. The point is that such a 'program' does not lie in the DNA alone. That is also the reason why the concept of a 'genetic program' is not testable. By necessarily including non-DNA elements, there is no way of determining whether a 'genetic program' exists. At the limit, when all the relevant components have been added in, the 'program' is the same as the function it is supposed to be programming. The concept then becomes redundant [p. 53 of Noble (Noble, 2006)]. Enrico Coen (Coen, 1999) put the point beautifully when he wrote: 'Organisms are not simply manufactured according to a set of instructions. There is no easy way to separate instructions from the process of carrying them out, to distinguish plan from execution.'

'Blueprint'

'Blueprint' is a variation on the idea of a program. The word suffers from a similar problem to the concept of a 'program', which is that it can be mistaken to imply that all the information necessary for the construction of an organism lies in the DNA. This is clearly not true. The complete cell is also required, and its complex structures are inherited by self-templating. The 'blueprint', therefore, is the cell as a whole. But that destroys the whole idea of the genome being the full specification. It also blurs and largely nullifies the distinction between replicator and vehicle in selfish gene theory.

'Book of life'

The genome is often described as the 'book of life'. This was one of the colourful metaphors used when projecting the idea of sequencing the complete human genome. It was a brilliant public relations move. Who could not be intrigued by reading the 'book of life' and unravelling its secrets? And who could resist the promise that, within about a decade, that book would reveal how to treat cancer, heart disease, nervous diseases, diabetes, with a new era of pharmaceutical targets. As we all know, it didn't happen. An editorial in *Nature* spelt this out:

'The activity of genes is affected by many things not explicitly encoded in the genome, such as how the chromosomal material is packaged up and how it is labelled with chemical markers. Even for diseases like diabetes, which have a clear inherited component, the known genes involved seem to account for only a small proportion of the inheritance...the failure to anticipate such complexity in the genome must be blamed partly on the cosy fallacies of genetic research. After Francis Crick and James Watson cracked the riddle of DNA's molecular structure in 1953, geneticists could not resist assuming it was all over bar the shouting. They began to see DNA as the "book of life," which could be read like an instruction manual. It now seems that the genome might be less like a list of parts and more like the weather system, full of complicated feedbacks and interdependencies.'

(Editorial, 2010)

The 'book of life' represents the high watermark of the enthusiasm with which the language of neo-Darwinism was developed. Its failure to deliver the promised advances in healthcare speaks volumes. Of course, there were very good scientific reasons for sequencing whole genomes. The benefits to evolutionary and comparative biology in particular have been immense, and the sequencing of genomes will eventually contribute to healthcare

when the sequences can be better understood in the context of other essential aspects of physiological function. But the promise of a peep into the ‘book of life’ leading to a cure for all diseases was a mistake.

The language of neo-Darwinism as a whole

All parts of the neo-Darwinist forms of representation encourage the use and acceptance of the other parts. Once one accepts the idea that the DNA and RNA templates form a ‘code’, the idea of the ‘genetic program’ follows naturally. That leads on to statements like ‘they [genes] created us body and mind’ (Dawkins, 1976; Dawkins, 2006), which gets causality wrong in two ways. First, it represents genes as active causes, whereas they are passive templates. Second, it ignores the many feedbacks on to the genome that contribute to circular causality, in which causation runs in both directions. Those mistakes lead to the distinction between replicators and vehicles. The problem lies in accepting the first step, the idea that there is a ‘code’ forming a complete program.

The distinction between the replicator and the vehicle can be seen as the culmination of the neo-Darwinist way of thinking. If all the algorithms for the processes of life lie in the genome then the rest of the organism does seem to be a disposable vehicle. Only the genome needs to replicate, leaving any old vehicle to carry it.

The distinction, however, is a linguistic confusion and it is incorrect experimentally (Noble, 2011b). The DNA passed on from one generation to the next is based on copies (though not always perfect). The cell that carries the DNA is also a copy (also not always perfect). In order for a cell to give rise to daughter cells, both the DNA and the cell have to be copied. The only difference between copying a cell and copying DNA is that the cell copies itself by growing (copying its own detailed structure gradually, which is an example of self-templating) and then dividing so that each daughter cell has a full complement of the complex cell machinery and its organelles, whereas copying DNA for the purpose of inheritance occurs only when the cell is dividing. Moreover, the complexity of the structure in each case is comparable: ‘It is therefore easy to represent the three-dimensional image structure of a cell as containing as much information as the genome’ (Noble, 2011a). Faithful genome replication also depends on the prior ability of the cell to replicate itself because it is the cell that contains the necessary structures and processes to enable errors in DNA replication to be corrected. Self-templating must have been prior to the development of the relevant DNA (Müller and Newman, 2003; Newman et al., 2006).

My germ line cells are therefore just as much ‘immortal’ (or not) as their DNA. Moreover, nearly all of my cells and DNA die with me. Those that do survive, which are the germ cells and DNA that help to form the next generation, do not do so separately. DNA does not work without a cell. It is simply an incorrect playing with words to single the DNA out as uniquely immortal.

I was also playing with words when I wrote that ‘DNA alone is inert, dead’ (Noble, 2011b). But at least that has a point in actual experiments. DNA alone does nothing. By contrast, cells can continue to function for some time without DNA. Some cells do that naturally, e.g. red blood cells, which live for about 100 days without DNA. Others, such as isolated nerve axons, fibroblasts (Cox et al., 1976; Goldman et al., 1973) or any other enucleated cell type, can do so in physiological experiments.

Genes_M are best viewed therefore as causes in a passive sense. They do nothing until activated. Active causation lies with proteins, membranes, metabolites, organelles, etc., and the dynamic functional networks they form in interaction with the environment (Noble, 2008).

Notice also that the language as a whole is strongly anthropomorphic. This is strange, given that most neo-Darwinists would surely wish to avoid anthropomorphising scientific discovery.

An alternative form of representation

The alternative form of representation depends on two fundamental concepts. The first one is the distinction between active and passive causes. Genes_M are passive causes; they are templates used when the dynamic cell networks activate them. The second concept is that there is no privileged level of causation. In networks, that is necessarily true, and it is the central feature of what I have called the theory of biological relativity, which is formulated in a mathematical context (Noble, 2012).

I will illustrate the second point in a more familiar non-mathematical way. Take some knitting needles and some wool. Knit a rectangle. If you don’t knit, just imagine the rectangle. Or use an old knitted scarf. Now pull on one corner of the rectangle while keeping the opposite corner fixed. What happens? The whole network of knitted knots moves. Now reverse the corners and pull on the other corner. Again, the whole network moves, though in a different way. This is a property of networks. Everything ultimately connects to everything else. Any part of the network can be the prime mover, and be the cause of the rest of the network moving and adjusting to the tension. Actually, it would be better still to drop the idea of any specific element as prime mover. It is networks that are dynamically functional.

Now knit a three-dimensional network. Again, imagine it. You probably don’t actually know how to knit such a thing. Pulling on any part of the three-dimensional structure will cause all other parts to move (cf. Ingber, 1998). It doesn’t matter whether you pull on the bottom, the top or the sides. All can be regarded as equivalent. There is no privileged location within the network.

The three-dimensional network recalls Waddington’s epigenetic landscape network (Fig. 3) and is quite a good analogy to biological networks as the third dimension can be viewed as representing the multi-scale nature of biological networks. Properties at the scale of cells, tissues and organs influence activities of elements, such as genes and proteins, at the lower scales. This is sometimes called downward causation, to distinguish it from the reductionist interpretation of causation as upward causation (Ellis et al., 2012). ‘Down’ and ‘up’ here are also metaphors and should be treated carefully. The essential point is the more neutral statement: there is no privileged scale of causality, beyond the representation of scales, perhaps. This must be the case in organisms, which work through many forms of circular causality. A more complete analysis of this alternative approach can be found in the article on Biological Relativity (Noble, 2012), from which Fig. 4 is taken. One of the consequences of the relativistic view is that genes_M cease to be represented as active causes. Templates are passive causes, used when needed. Active causation resides in the networks, which include many components for which there are no DNA templates. It is the physics and chemistry of those dynamic networks that determine what happens.

In certain respects, my article reflects some of the points made over 30 years ago by Ho and Saunders (Ho and Saunders, 1979), who wrote: ‘The intrinsic dynamical structure of the epigenetic system itself, in its interaction with the environment, is the source of non-random variations which direct evolutionary change, and that a proper study of evolution consists in the working out of the dynamics of the epigenetic system and its response to environmental stimuli as well as the mechanisms whereby novel developmental responses are canalized.’ Their ideas also owe much to those of Conrad Waddington – the term ‘canalised’ is one that he often used.

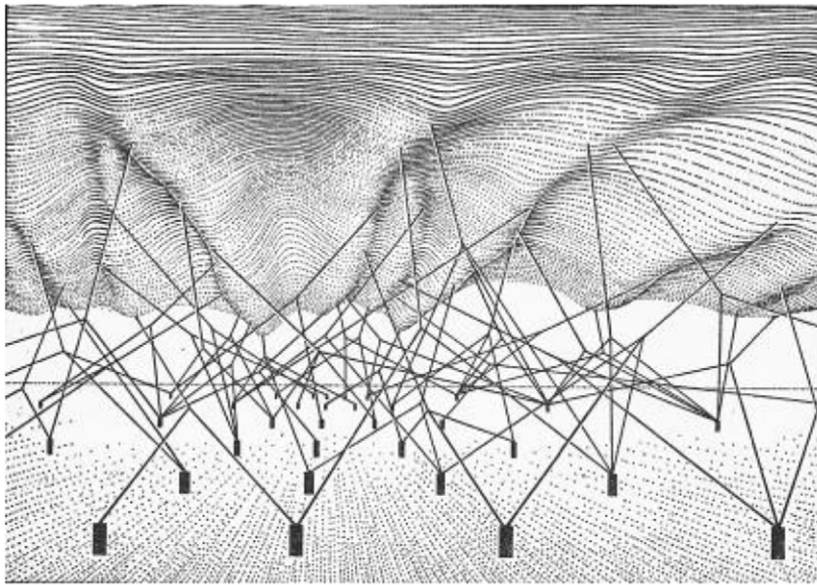


Fig. 3. Conrad Waddington's diagram of the epigenetic landscape. Genes (solid pegs at the bottom) are viewed as parts of complex networks so that many gene products interact between themselves and with the phenotype to produce the phenotypic landscape (top) through which development occurs. Waddington's insight was that new forms could arise through new combinations to produce new landscapes in response to environmental pressure, and that these could then be assimilated into the genome. Waddington was a systems biologist in the full sense of the word. If we had followed his lead many of the more naive 20th century popularisations of genetics and evolutionary biology could have been avoided. Image taken from *The Strategy of the Genes* (Waddington, 1957). Reprinted (2014) by Routledge Library Editions.

An important linguistic feature of the alternative, relativistic, concepts proposed here is that most or all the anthropomorphic features of the neo-Darwinist language can be eliminated, without contravening a single biological experimental fact. There may be other forms of representation that can achieve the same result. It doesn't really matter which you use. The aim is simply to distance ourselves from the biased conceptual scheme that neo-Darwinism has brought to biology, made more problematic by the fact that it has been presented as literal truth.

Conclusions

The extent to which the language of neo-Darwinism has dominated biological thought for over a century since George Romanes invented the term in a letter to *Nature* (Romanes, 1883) is remarkable. It is a tribute to the inventiveness and persuasiveness of many biologists and to their ability to communicate the original idea and its subsequent formulation as the Modern Synthesis to a very wide public. The integration of the early discoveries of molecular

biology also contributed great momentum, particularly as the Central Dogma of Molecular Biology (Crick, 1970) was perceived (incorrectly as it subsequently turned out) to confirm a central assumption, which was that the genome was isolated from the lifestyle of the organism and its environment.

In retrospect, neo-Darwinism can be seen to have oversimplified biology and over-reached itself in its rhetoric. By so conclusively excluding anything that might be interpreted as Lamarckism, it assumed what couldn't be proved. As John Maynard Smith (Maynard Smith, 1998) admitted: 'It [Lamarckism] is not so obviously false as is sometimes made out', a statement that is all the more significant from being made by someone working entirely within the Modern Synthesis framework. His qualification on this statement in 1998 was that he couldn't see what the mechanism(s) might be. We can now do so thanks to some ingenious experimental research in recent years.

Nevertheless, the dogmatism was unnecessary and uncalled for. It damaged the reputation of Lamarck, possibly irretrievably.

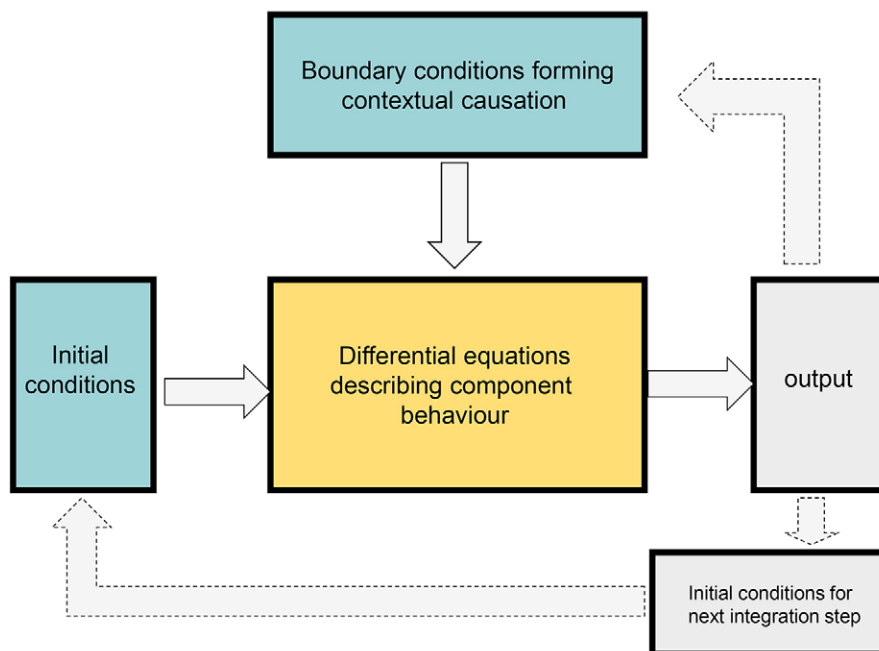


Fig. 4. Many models of biological systems consist of differential equations for the kinetics of each component. These equations cannot give a solution (the output) without setting the initial conditions (the state of the components at the time at which the simulation begins) and the boundary conditions. The boundary conditions define what constraints are imposed on the system by its environment and can therefore be considered as a form of contextual causation from a higher scale. This diagram is highly simplified to represent what we actually solve mathematically. In reality, boundary conditions are also involved in determining initial conditions and the output parameters can also influence the boundary conditions, while they in turn are also the initial conditions for a further period of integration of the equations. The arrows are not really unidirectional. The dotted arrows complete the diagram to show that the output contributes to the boundary conditions (although not uniquely), and determines the initial conditions for the next integration step. Legend and diagram are reproduced from Noble (Noble, 2012).

Lamarck should be recognised by biologists generally as one of the very first to coin and use the term ‘biology’ to distinguish our science, and by evolutionary biologists in particular for championing the transformation of species against some very powerful critics. Darwin praised Lamarck for this achievement: ‘This justly celebrated naturalist... who upholds the doctrine that all species, including man, are descended from other species’ (preface to the 4th edition of *The Origin of Species*, 1866).

Many others were damaged too, Waddington included. A little more humility in recognising the pitfalls that beset the unwary when they think they can ignore some basic philosophical principles would have been a wiser strategy. The great physicist Poincaré pointed out, in connection with the relativity principle in physics, that the worst philosophical errors are made by those who claim they are not philosophers (Poincaré, 1902; Poincaré, 1968). They do so because they don’t even recognise the existence of the conceptual holes they fall into. Biology has its own version of those conceptual holes.

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Competing interests

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Supplementary material

Supplementary material available online at <http://jeb.biologists.org/lookup/suppl/doi:10.1242/jeb.106310/-DC1>

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