Mathematics and biology*

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From the well-known saying, 'All chemistry is physics and all biology is chemistry', one might be tempted to conclude that because physical laws are most compactly expressed in the language of mathematics, biology too can, or should, be 'mathematized'. On the other hand, in popular perception, mathematics and biology are as far apart as is possible for any two fields of enquiry to be. Mathematics is believed to be analytical and deductive whereas biology is thought of as largely descriptive and based on induction. Admittedly, this oversimplifies a complex issue. Nevertheless, the fact stands out, that on the whole the practice of biology – as reflected in teaching programs and research publications – is free of mathematical language and symbols to an extent that would be unthinkable in contemporary physics or chemistry. The reasons for this are many. An important one is that biological systems confirm to the laws of physics but are not *necessary* consequences of the laws. Mathematics can illuminate aspects of the structure or function of a living system and can also be used to make sense of the statistical consequences of dealing with large aggregates of genes or cells or organisms. All the same, it is difficult to conceive of a living creature, taken as a whole, as being reducible to mathematical formalisms such as those that embody the laws of physics. The difficulty stems from the manner in which evolution has shaped the history of life on earth. Historical contingencies, the random nature of mutations and evolutionary opportunism all make it difficult to encompass biology within a mathematical framework.

IN a famous article, the physicist Eugene Wigner expanded on what he called 'The unreasonable effectiveness of mathematics in the natural sciences'. According to Wigner, it was extraordinary that mathematics – a set of formal rules for manipulating abstract symbols and a creation of the human mind – could explain the messy and complicated real world[1]. Others have drawn attention to the astonishing fact that a simple algebraic equation that a schoolchild can understand, the inverse-square law of gravitation, holds within it the key to 'the motions of the planets, the comets, the moon, and the sea' (Newton, from the first edition of the *Principia*). The present essay aims to make the point that the term 'natural sciences' in Wigner's title is inappropriate in the context of biology, almost certainly so in the case of biological entities that are at least as complex as a cell[2].

Reductionism and determinism

In what follows, by *reduction* I mean explaining something in terms something else, the 'something else' usually consisting of entities at a lower level of organization than what is sought to be explained. An outcome is said to be *determined* if, given a certain initial condition, it is inevitable. Inevitability implies that it is the consequence of a 'law', rule, or set of rules. A rule may be expressed in ordinary language or it may be put tersely in the form of a mathematical expression. Roughly speaking, reductionism is equivalent to the assertion that the whole is explainable in terms of its parts, and determinism is equivalent to saying that a specified initial condition leads unambiguously to a particular end result. A system that is determined (in this sense) is often, but not always, predictable. Chaotic systems are well-known exceptions: in their case, seemingly insignificant differences in initial conditions can lead to major differences in the outcome. In principle, reductionism is always valid. If an object is composed of structurally or functionally distinct parts, the object must be fully explicable in terms of the properties of those parts and their interactions. But reduction may or may not be useful; consider for example the case of a painting.

One can think of three roles for mathematics in biology. The first is an extension of its role in physics or chemistry. It would follow as a consequence of the reduction of biology to either of those two sciences, were such a thing possible. The second role is a modern one. It originates in the expectation, fuelled originally by the success of Mendel's principles and more recently by the discovery of the genetic code[3], that living creatures are essentially informational entities. The underlying hypothesis is that biological information – the information required for making a plant or an animal – is encoded in terms of a set of rules, sometimes referred to as a program. The program is said to determine the organism. A reliable set of procedures, an algorithm, leads one from the program to the organism. For example, the development of a multicellular organism from a fertilized egg has been compared to an algorithmic process. The third role for mathematics, including of course computational mathematics, is more conventional. Mathematics is an aid to organized thought and a bridge between empiri-

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cal knowledge and theoretical models. Similarly, the computer is an invaluable tool when it comes to handling large masses of data or carrying out many intricate logical operations at great speed. The first two roles are the more interesting ones, and their validity depends on whether it is useful to think of biology in deterministic or reductionist terms. An old-style biologist (say a biologist of the 19th century or earlier) would have questioned both, most likely on the grounds that organisms exhibit emergent properties that cannot be reduced to the properties of their constituent parts. However, the biology of the latter half of the 20th century and since has been characterized by an approach, known as molecular biology, in which the themes of reductionism and determinism are deeply embedded.

Molecular biology

The announcement of the double helical structure of DNA set the seal on a notion that was already gaining acceptance, namely, that heredity had a chemical basis: Mendel's particulate units of inheritance (genes) turned out to be molecules of DNA[4]. Today we know that the proteins that characterize living cells are synthesized on the basis of certain rules of correspondence relating sequential subsets of DNA (base triplets) to sequential subsets of proteins (amino acids). In parallel, we have discovered that development, the transformation of an egg into an adult, is accompanied by changes in the patterns of activity of DNA. The patterns differ from one cell to another and are altered when the DNA undergoes heritable changes. Thus the same chemical, DNA, is central to both heredity and development.

The interesting thing about the chemistry involved in making proteins from DNA is that it depends solely on interpreting the information contained in DNA; the DNA itself remains unchanged. In consequence, a DNA sequence can be thought of as an encoded or symbolic representation of a particular protein. This realization unleashed a burst of research in biology and set in motion an approach to understanding living forms, still going strong, known as molecular biology. Fuelled by the rate at which new facts came to be accumulated – on the whole, facts that were entirely unexpected, the field acquired unprecedented prestige and an ethos of its very own[5]. At its heart, molecular biology was, and even now to some extent is, driven by an assumption and a hope. The assumption is that the (known) relationship between one DNA molecule and the protein it encodes offers a clue to the (unknown) relationship between all the DNA molecules in an organism, the genome, and the organism itself. The hope is that this assumption can be shown to be correct – in other words, that the genome can be demonstrated to be an implicit, symbolic representation of the organism. Because both computers and molecular biology began to take hold of peoples' imagination at about the same time, it became popular to compare the genome to a computer program written in chemical language. The program was believed to reside in sequences of DNA and the organism was thought of as the output of the program. Salvador Luria, one of the pioneers of molecular biology, has put it pithily: 'Like the computer, the programmed organism has a tape containing the instructions (genes, DNA) and the machinery to implement the instructions on the tape'[6].

In short, molecular biology contains within itself both reductionist and determinist aspirations. These are, respectively, that life can be explained in terms of its molecular constituents, and that the properties of an organism are deducible from its DNA. The reductionist hypothesis remains unquestioned in principle. But in practice, and this is true of reductionism in general, the hypothesis is not useful beyond a particular level of organization. Once one starts looking at an entity sufficiently removed from genes and proteins, say the cell (let alone the organism), new attributes may emerge and entirely new explanatory concepts may be called for. To take a simple example, water is made up of hydrogen and oxygen atoms and water 'finds its own level'. But it would be a waste of time to try and explain the latter observation in terms of the former. Similarly, it is not so much that a reductionist approach to biology is wrong. Rather, and especially if the object of interest is the whole organism, it provides little insight. What about the second possibility? Increasingly, the prospects for genetic determinism too look dubious[7]. In both cases the reason has to do with the nature of life, and in particular, with the role played by evolution in shaping living forms.

The nature of life

It is notoriously difficult to give a crisp definition of life. Taken together, however, living creatures exhibit features that stand out from those of non-living entities. One might summarize them by saying that being alive is a property possessed by temporary, open, organized forms of matter that can store and transmit information and evolve by natural selection. Briefly, what this means is as follows.

Living matter exists far from equilibrium

To sustain life, organisms must constantly renew themselves. Both organisms and their constituent parts can maintain themselves only temporarily. Cells are re-modelled so rapidly that hardly any of the molecular components of our physical body is more than a few weeks old (which makes it interesting that we retain a continuous and unbroken sense of ourselves)[8].

Even temporary upkeep requires an input of energy and information

This process, known as metabolism, involves the chemical transformation of the air we breathe and the food we eat.

Metabolism creates new structures in the body and repairs or discards old ones. Besides exchanging matter, the organism continually scans the environment and extracts useful information from it. Both literally and metaphorically, we feed on our surroundings.

Life involves organization at various levels in a hierarchy

To begin with there is molecular organization. DNA, RNA, proteins, lipids and sugars are gigantic molecules made up of anywhere from a hundred to a million atoms. At the next level, the cells that are built from them are organized into distinct compartments that subserve (in part) different functions. Organized networks of production, distribution and disposal coordinate metabolism. Cells form bodies made up of specialized tissues and are arranged in a recognizable fashion. Lastly, the reception, storage and retrieval of information, both between cells and between the body and the external world, exhibits an intricate organization.

Life continually evolves

Species change through a process whose underlying basis is haphazard and undirected. Despite the randomness that lies at the core of evolution, living forms give the impression of having been designed to fit an end. But the impression is misleading: order results from randomness because randomness is filtered by evolutionary opportunism[9,10].

The implication is that an organism is best viewed as a special-purpose device that has been shaped by a series of opportunistic responses to the conditions encountered by it in its evolutionary history. It is this 'special- spect of organisms that leads to serious difficulties when we try to reduce biology to physics and chemistry.

Evolution and reductionism

Opportunism is inherent in the explanation of evolution by natural selection, first put forward by Darwin and Wallace almost 150 years ago. Natural selection begins with a random change, a mutation, in a DNA sequence. The change can spread through a population if, on the average, it leads to an improvement in the individual in whom it occurred. Here 'improvement' means one thing and one thing only. It means that the individual is more likely to have offspring (who inherit the changed DNA molecule) than the average individual in the population[11].

What one might call a unit evolutionary episode begins with a mutation, continues through the fate of the altered DNA sequence over generations and, on occasion, concludes with the establishment or elimination of the mutant gene. A mutant or variant version of a gene becomes established or 'fixed' if it replaces the pre-existing variety. The enormous number of independent mutations that can occur in the genome of a species within a single generation makes the occurrence of any one of them at a particular time unpredictable in advance. Besides, the likelihood of a mutation is independent of whether it leads to a particular outcome or not. A mutation can be judged to be beneficial or harmful only *post facto*. The judgement depends on the consequence of the mutation, which in turn depends on a host of circumstances. A mutation that happens to be successful builds on an earlier mutation that happened to be successful. The complex organism that results is put together via unforeseen steps and has not come about as the result of planning. Thus, the course of evolution is indeterminate and therefore unpredictable[12].

As if that were not bad enough, life on earth has been affected by catastrophic accidents that disrupted and re-set the course of natural selection. The accidents led to major changes in the composition of living forms. During each change the relative abundance of forms was drastically altered; a large number even went extinct. As a result, it is impossible to account for what happened after any of the catastrophic episodes as a logical extension of what was going on before. Taken together with the basic randomness that is inherent in evolutionary change, this means that nothing makes it *necessary* that a particular species of plant or animal should have existed in the past, or exists at present (including our own species, *Homo sapiens*).

To sum up, living creatures are entities in their own right and, as such, obey the principles of physics and chemistry. But because they have an evolutionary past, they are also products of history. They have been shaped by a series of random steps that resulted in successful responses to contingencies that were faced by their ancestors; therefore they are endowed with a substantial element of arbitrariness in the way they are put together. This makes it difficult, if not impossible, to think of them solely as products of physics and chemistry. Physics and chemistry set limits within which evolution can take place but cannot specify in advance either its course or its end.

Evolution and determinism

A cell contains encoded information within itself in the form of genes: every protein is the decoded version of some gene. Might not a living creature also be a decoded entity, the encoding being carried out by the genome as a whole? If the answer is yes, one could say that genes determine organisms. Then it would make sense to look for a theoretical underpinning of biology in the set of rules, the genetic program, hidden behind the organism. The programmatic view of development is that the genome has an algorithmic structure, that it is put together logically, as we would put together any set of instructions designed to ensure a desired end, for instance a cookbook recipe, a play or a computer program. However, many findings point to the lack of a rule-based, logical structure to the genome as a whole[7,13].

Algorithmic operations generally lead to unique outcomes, whereas the output of genomes can be highly flexible

The same genome, or very similar genomes, can be consistent with creatures that look drastically different. Sometimes this is because of environmental influences, sometimes because of differences in life stages and sometimes because the link between the genome and the organism has an intrinsically indeterminate component to it. Turtle and crocodile eggs develop into males or females depending on the temperature at which they are incubated; the caterpillar and the butterfly, in appearance so different, are genetically identical; bacteria that are members of the same clone and are raised in the same environment can differ in their ability to metabolize sugar.

Conversely, very different genotypes can be consistent with very similar organisms

South and North American mammals, or molluscan and vertebrate eyes, are textbook examples. Thus the relationship between genomes and organisms is not one-to-one. Chimpanzees and humans, different in so many respects, are said to share 98% of their DNA sequences. 'Sibling spe frogs share a much smaller fraction of DNA but require an expert to tell apart.

The same gene or DNA sequence can contribute to seemingly unrelated traits

Genes that mediate sexual differentiation in the fly also function in the development of their nervous system. In albino cats, a gene that encodes an enzyme in the pathway responsible for the synthesis of a skin pigment, melanin, also affects the manner in which the eye and brain are connected.

In short, genomes are organized very differently from plays, recipes or computer programs. DNA sequences and their functioning reflect the opportunistic fashion in which organisms have evolved. If there are rules that lie behind the ways in which plants and animals are built, the rules are not logical consequences of the ways in which genes are copied or gene activity is regulated (no more, for instance, than the functioning of human societies is a logical consequence of human biology).

The role of mathematics in biology

Undoubtedly it should be possible, and indeed is possible, to treat a living system as one does any other physical system, so long as one does so within a suitably restricted framework. The narrower the focus, the likelier it is that a physical or chemical, and therefore mathematical, approach will be useful[14]. Many aspects of the functioning of cells and tissues can be subject to mathematical treatment quite successfully. Metabolic networks can be modelled as linked cascades of chemical reactions, signalling in the nervous system is similar to electrical conduction through a network of wires and the flow of blood depends on hydrodynamic principles. Population genetics, a highly mathematical branch of biology, deals with the spread and distribution of genes in populations. Population geneticists aim (among other things) to show that measurable changes in the distribution are consistent with known or assumed evolutionary forces. None of these cases constitute counter-examples to the point I have been trying to make. As an illustration of precisely why not, let me take the case of something that has long been a popular subject among mathematically minded biologists.

Fifty years ago, in a publication that has been accorded the status of a classic, the logician and computer scientist Alan Turing constructed a mathematical model for the spontaneous origin of biological form. He began with what he thought was a formless structure such as a newly fertilized egg[15]. Turing's model was 'global': he looked at the embryo as a whole, and assumed that it could be compared to a bag with chemicals that were transported by diffusion and reacted with one another. The model was elegant and plausible. From it, Turing showed that depending on the chemical reactions and rates of diffusion, thermodynamic fluctuations alone could lead to a variety of long-term outcomes. Under some conditions there was a high concentration of chemicals at one place in the embryo and relatively low concentrations elsewhere. Under other conditions the chemicals became distributed in spot-like or stripe-like regularities, which mimicked the pattern of tentacles in a *Hydra* or arms in a starfish. Under yet other conditions the concentrations oscillated in a clocklike, and sometimes wavelike, manner.

Turing thought that his scheme could exemplify global or system-wide mechanisms for the genesis of developmental patterns. After an initially cool reception, the model began to evoke a great deal of interest. Later, stripe formation was shown to be ubiquitous in early embryogenesis. For example, even a fly embryo exhibits patterns of gene activity that resemble a zebra's stripes; one could think that they were Turing patterns. Unfortunately, subsequent experiments showed otherwise. Indeed, it appears that there is no global rule behind stripe formation in the fly embryo. Rather, the manner in which the fly makes stripes is bizarre and confounds expectations. The stripes turn out to depend on distinct genetic regulatory interactions that lead separately to the appearance of each stripe, and not even in serial order at that[16].

How can one account for the existence of such a non-intuitive stripe-forming system? A possible answer comes from the hypothesis that global schemes such as the Turing model tell us something about the evolutionary antecedents of present-day patterns – antecedents dating from a period when evolutionary embellishments were minimal and the link between genes and development was not as intimate as it is today[17]. According to this proposal, global systems for patterning, based on physics and chemistry, may have existed in the past. Inevitably, their outcomes would have been 'noisy', meaning subject to large variations, and so unreliable. The gene-based patterning mechanisms that we see today could have come about in the course of evolution because they buffered the variations and ensured that the patterns were produced reliably[18].

Stripe formation illustrates a case of a theory not standing up. More glaring is the absence of any theory. To realize this, one has only to see that whereas a series of findings have extended our knowledge of how genes, cells and organisms function, the bulk of the new knowledge has been in the form of one surprise after another. Consider some striking examples: the discovery that not all DNA codes for proteins; the fact that genes can consist of discontinuous segments of DNA; the observation that when mutated, some genes seem to leave the organism unchanged; and the absence of any correlation between genome size and gene number. Testifying to the absence of a theory of living systems, let alone a logical theory, none of these major findings were anticipated.

Summing up

Unlike physical objects, which can be accounted for as the necessary consequences of the operation of natural laws, living entities are products of an essentially ad hoc process known as evolution. They have been moulded by natural selection in a manner that has preserved a succession of minor, randomly caused changes that turned out to be successful. The properties that they exhibit demand evolutionary explanations. An answer to the question of just what constitutes an evolutionary explanation falls outside the scope of this article, but there are at least two respects in which it is very different from what would be called an explanation in physics or chemistry. First, in evolution the environment, including the ancestral environment, plays a central role in defining the organism. Second, the basic unit of change in evolution is not the individual organism. Instead, it is a collection of entities known as the species. Because of evolution, living creatures are products of history. They make sense, that is, are capable of being understood, *only in the context* of their history. Evolutionary explanations would be out of place in the case of purely physical objects. For example, no one would think of saying that to understand the hydrogen atom, all the hydrogen atoms in the universe had to be studied, in addition to how they got that way. Of course observation, description, experimentation, logical analysis and the construction of testable hypotheses – what is sometimes called the method of science – are as much a part of biology as of the other natural sciences. But there is something that makes biology special, and that is the history of change undergone by living matter and the manner in which the change has come about. It is because of this that one must doubt whether biology can ever have a mathematical structure in the way that theoretical physics does. The evolutionary biologist Theodosius Dobzhansky put it in the form of a maxim: 'Nothing in biology makes sense except in the light of evolution'. Coming back to Wigner, mathematics is unlikely to be 'effective' in biology, let alone 'unreasonably effective', because of evolution[19].

Notes and references

1. Wigner, E. P., *Communications in Pure and Applied Mathematics*, New York: John Wiley & Sons, Inc, 1960, vol. 13. One might paraphrase Wigner by saying that a game invented by human beings for their pleasure and amusement happens, just by chance, to explain features of the real world. Wigner acknowledges later that he is referring to the physical sciences alone ('The miracle of the appropriateness of the language of mathematics for the formulation of the laws of physics …'), but this qualification tends to be ignored. In *Conversations on Mind, Matter, and Mathematics* (edited and translated by M. B. DeBevoise; Princeton University Press, 1998), Jean-Pierre Changeux and Alain Connes argue whether mathematics is a creation of the mind or reflects the external world. It is worth noting that biology has influenced mathematics in the past, and the influence is likely to get stronger in the future. But the present article does not deal with this issue.
2. A second aim is to question, if only indirectly, the implicit assumption that a product of the mind can be analysed as if it need not carry an imprint of the forces that shaped that mind. From the viewpoint of evolutionary biology, a theory of knowledge must be embedded in the evolutionary history of the mind. The ethologist Konrad Lorenz gave the clearest explanation of evolutionary epistemology. See Donald T. Campbell, *Evolutionary Epistemology* In *The philosophy of Karl R. Popper*, edited by P. A. Schilpp, 1974, pp. 412–463. LaSalle, IL: Open Court.
3. With some exceptions that we can ignore, a gene is something that formally is defined by the following properties: it is a molecular polymer belonging to the general class known as DNA; it is found inside the nucleus of living cells; it can be passed *in toto* from a father or mother to a child; and it can change, in which case some traits are also changed (thereby making it appear that traits are passed down from parents to offspring whereas actually only the genes are). The link between a gene and a trait is via a protein. The units that make up a DNA polymer, taken in sequence, specify – via certain rules of correspondence – the sequence of units that make up a protein polymer. The rules are known as the genetic code. Taken together, the set of DNA molecules inside a cell constitute the genome. Because not all DNA molecules encode proteins, the genome has both genes and non-coding DNA. For a nuanced discussion of the philosophical complexities lurking behind these definitions, see *Genetics and Reductionism* by Sahotra Sarkar (Cambridge University Press, 1998). In *A New Biology for a New Century* (*Microbiol. Mol. Biol. Rev.*, 2004, **68**, 173–186), C. R. Woese distinguishes between 'empirical reductionism', a methodological tool, and 'fundamentalist reductionism', which is exemplified by the reductionism of 19th century classical physics.
4. J. D. Watson gives a racy account of the discovery in *The Double Helix* (Athenaeum, New York, 1968). *The Path to the Double Helix* by R. Olby (University of Washington Press, Seattle, 1974) is the more scholarly history. Curiously, even though molecular biology benefited enormously by the entry of physicists, and was built on the experimental tools devised by physicists, physics as such has played only a minor role in molecular biology (a prominent exception being the role of X-ray crystallography). Rather, what physicists contributed to the field was a 'physics way' of looking at problems, of getting down to essentials. Initially they were inspired by the hope raised by Erwin Schrödinger that 'we must be prepared to find a new type of physical law prevailing in it [living

matter]' (*What is Life?*, Cambridge University Press, 1944), but that hope gradually faded away.

5. Morange, M., *A History of Molecular Biology*, Harvard University Press, Cambridge, 2000.
6. See page 4 of *36 Lectures in Biology* by S. L. Luria (MIT Press, Cambridge, 1975). *DNA: The Secret of Life* by J. D. Watson and A. W. Berry (Knopf, 2003) adopts a similar viewpoint. A forceful rebuttal can be found in *Unravelling the Secret of Life* by Barry Commoner (*GeneWatch*, 2003, **16**, 1–8).
7. Nijhout, H. F., Metaphors and the Role of Genes in Development. *BioEssays*, 1990, **12**, 441–446. The phrase 'phenotypic plasticity' expresses the observation that genotypes and phenotypes do not have a one-to-one relationship. *Morphogenesis and Pattern Formation in Biological Systems* (eds Sekimura, T. *et al.*), Springer Verlag, Tokyo, 2003 and *Origination of Organismal Form* (eds Müller, G. B. and Newman, S. A.), MIT Press, 2003 contain more on the same theme. *Visual pathways in albinos* by R. W. Guillery (*Sci. Am.*, 1974, **230**, 44–54) contains a striking example of the complex relationship between genes and traits. Also see Marks, J., *What it means to be 98% Chimpanzee*, University of California Press, 2002.
8. Once life departs, decay can be extraordinarily rapid. It has been pointed out that after ten years a discarded automobile can still be found where it was left; an animal that dies in a forest vanishes in a matter of months if not weeks or days.
9. The contention of evolutionary theory is that inanimate nature and blind chance are sufficient to engineer outcomes that seem to be designed with a prior purpose (Dawkins, R., *The Blind Watchmaker*, Penguin, London, 1989).
10. Excellent accounts of evolutionary opportunism can be found in *The meaning of evolution* by G. G. Simpson (Yale University Press, New Haven, 1967) and *The Possible and the Actual* by F. Jacob (University of Washington Press, Seattle, 1982).
11. Natural selection is the only inanimate agency that we know of that is capable of mimicking conscious design. But all evolutionary change need not be because of natural selection. See for example *Ever Since Darwin* by S. J. Gould (W. W. Norton, New York, 1977).
12. Thereby resembling, albeit for entirely different reasons, what happens in systems that exhibit chaos. A mathematical equation may be deterministic in the sense that the outcome is exactly predictable once the starting situation is precisely specified. But if infinitesimal variations in initial conditions lead to large variations in the outcome, for all practical purposes the outcome is unpredictable.
13. For a contrary view of pattern formation in biology, see *A New Kind of Science* (Wolfram, S., 2002, Wolfram Media). Following the tradition established by D'Arcy Thompson. Wolfram is explicitly anti-selectionist: 'What I have come to believe is that many of the most obvious examples of complexity in biological systems actually have very little to do with adaptation or natural selection'. Apart from telling us how to go about creating an interesting but imaginary world, the relevance of his automata-based approach for understanding biological form is unclear.
14. This is true of fields ranging from literary studies to sports. There is of course a purely utilitarian role that mathematical or computer-based approaches serve. No one questions the usefulness of statistical analysis whenever quantitative measurements are carried out. But we are asking whether a mathematical or algorithmic structure might explain biology in the way that it seems to explain the physical universe.
15. Turing, A. M., In *The Chemical Basis of Morphogenesis. Philos. Trans. Roy. Soc. London*, 1952, **B52**, 14–152. For a discussion of the history of Turing models see *Alan Turing and the Chemical Basis of Morphogenesis*, Nanjundiah, V., In *Morphogenesis and Pattern Formation in Biological Systems* (eds Sekimura, T. *et al.*), Springer Verlag, Tokyo, 2003, pp. 33–45.
16. Akam, M., Making stripes inelegantly. *Nature*, 1989, **341**, 282–283. The point is not that a Turing mechanism is impossible; nor is it that no such mechanism exists in any organism. The point is that the same outcome can be reached by what is presumably an ad-hoc evolutionary process.
17. See Newman, S. A., Is segmentation generic?. *BioEssays*, 1993, **15**, 277–283. Multicellular development, including pattern formation, has to do with the behaviour of groups of cells. It demands, therefore, a 'sociological' approach. The same point has been made with regard to aberrant development in *The Society of Cells: Cancer and control of cell proliferation* (C. Sonnenschein and A. M. Soto, Springer-Verlag, New York, 1999).
18. C. H. Waddington made the concept of reliability or buffering the defining element his way of looking at development and coined the word 'canalisation' to describe it.
19. This calls into question the attitude that an area of study can be called a science only if it supports a mathematical framework. The mathematics-in-biology story has many other angles, among them sociological ones, that are not considered here. The intellectual prestige associated with mathematics, and at one step removed, of theoretical physics, has sometimes tended to overawe biologists. In *The Growth of Biological Thought* (Harvard University Press, 1985) Ernst Mayr offers an acid comment on this tendency: 'Physics envy is the curse of biology'. As to human and other reasons why mathematical biology has not been welcomed by many biologists, see Evelyn Fox Keller in *Making Sense of Life* (Harvard University Press), 2002.