Kauffman’s ‘Origins of order’


In 1993, Stuart Kauffman’s The Origins of Order: Self-organization and Selection in Evolution was published by Oxford University Press. It is an ambitious book that covers much territory, from general points about the dynamics of the evolutionary process to a proposed scenario for the origins of life. Given the scope of the book, and its controversiality, BioEssays commissioned two reviews. The first reviewer, Brian Charlesworth, is a population geneticist. The second reviewer, Peter Schuster, has worked on origins-of-life problems from the perspective of Manfred Eigen’s group.

Review 1
Making evolution seem complicated
By Brian Charlesworth

At the conclusion of Chapter 6 of The Origin of Species, Charles Darwin wrote: ‘It is generally acknowledged that all organic beings have been formed on two great laws – Unity of Type and the Conditions of Existence. By unity of type is meant that fundamental agreement in structure which we see in organic beings of the same class, and which is quite independent of their habits of life. On my theory, unity of type is explained by unity of descent. The expression of conditions of existence, so often insisted on by the illustrious Cuvier, is fully embraced by the principle of natural selection.’ Darwin added that ‘the law of the Conditions of Existence is the higher law; as it includes, through the inheritance of former adaptations, that of Unity of Type.’

Most contemporary evolutionary biologists would agree with these statements. The application of genetic principles to the study of the population processes which cause evolutionary change has demonstrated the power of even weak selective pressures to fix favorable genotypes in populations of moderate-to-large size. Forces such as mutation and random sampling of alleles due to finite population size (genetic drift) are likely to be of minor importance in causing the evolution of ‘interesting’ characters, although mutation and drift are probably very significant factors in evolution at the level of nucleotide substitutions of little functional significance. Of course, apart from the most extreme retailers of adaptive Just-So Stories, it is acknowledged that the range of possible variant phenotypes available to a species at any one time is limited by the potentialities of the current developmental system, so that selection is not omnipotent.

But a fully explanatory theory of phenotypic evolution requires two kinds of knowledge that we currently lack: knowledge of the spectrum of possible phenotypes that can be produced by the genetic variability available to a given evolving lineage, and an understanding of how fitness is related to phenotype over the duration of the lineage. As Darwin clearly understood, detailed information of the second kind is denied to us by the enormous complexity of the physical and biotic components of the environment that affect the reproductive success of organisms. It is, however, tempting to suppose that the first kind of knowledge can be provided by developmental biology. A predictive theory of the phenotypes which can be realized by mutation would supplant our current reliance on the empirical study of natural genetic variability for determining the nature of the raw material for evolution.

There has been a long history of attempts to integrate developmental and evolutionary biology, but the net results of these efforts have, for good reason, had little impact on the thinking of most evolutionary biologists. A major reason for this has been the more or less overt hostility of the proponents of these theories to Darwinian concepts of stepwise adaptive evolution, from Richard Goldschmidt and D’Arcy Thompson in the 1940s, to Pere Alberch, Stephen Gould and Brian Goodwin in the 1980s. This school of thought asserts that selection simply discriminates among a limited set of possibilities thrown up by the ‘laws of form’ laid down by the fundamental processes of development, which are not themselves the product of selection. Unity of type then does not necessarily reflect common descent: a particular outcome of development could be produced quite independently in different lineages, by fixation of the appropriate mutations.

The Origins of Order is an ambitious attempt to provide a detailed theoretical underpinning for the view that the role of selection in adaptive evolution is highly constrained by the possibilities for self-organisation inherent in the dynamics of complex systems of interacting components, such as the network of regulatory genetic switches involved in the development of multicellular organisms. While Stuart Kauffman recognises the role of selection in controlling the fate of variants thrown up by mutation, his primary interest is in establishing that complex systems have important properties that are not the product of selec-
tion. At a certain level, of course, this is a fact acknowledged by even the most die-hard neo-Darwinist. The properties of all components of living matter are the outcome of physical and chemical laws, and the nature of the phenotypes accessible by mutation and selection necessarily reflects this. But it is hard to make non-trivial predictions about the nature of the limitations on such phenotypes, and about the resulting constraints on the ability of selection to control the outcome of evolution.

Kauffman's thesis is that the generic properties of complex genetic and developmental systems can be successfully deduced, and enable such predictions to be made. He argues that, as the number of interacting components in a multi-dimensional space of phenotypes increases, the fitnesses of phenotypes that depart slightly from a given optimal phenotype become so close to the fitness of the optimum phenotype that selection has great difficulty in holding the population close to the optimum, against the pressure of mutation. As a result of this impotence of selection, 'the population does not remain tightly clustered around single peaks of high fitness but instead wanders within some larger volume of the ensemble' (p. 35). It follows that the properties of most members of the population reflect the possibilities allowed by the ordering processes that generate the phenotypes, rather than the properties of the phenotypes favoured by selection.

Furthermore, even if selection is capable of holding the population close to a particular selective optimum, there may be numerous alternative multi-dimensional phenotypes which are local optima with respect to fitness, so that a population may be trapped at a local optimum with fitness below the maximum possible. This is a point that was repeatedly emphasised by Sewall Wright (who is given only the briefest of acknowledgements by Kauffman). If the number of components which interact to determine fitness is very large, Kauffman claims that the relative fitnesses of the different optima become ever closer to that of randomly assembled phenotypes, and a greater proportion of the space of possible phenotypes is filled by fitness optima. 'Thus even when selection is very powerful and can hold populations on any accessible peak, the peak almost certainly exhibits properties typical of the entire space of possibilities' (pp. 35-36).

These two, allegedly generic, properties of complex systems constitute what Kauffman calls 'complexity catastrophes'. He claims that 'one or other must ultimately occur as the complexity of entities under selection increases.... As the complexity of entities increases, one or the other basic mechanism ultimately limits the power of selection.' (p. 36). These ideas are introduced in the context of the 'NK model' of Chapter 2, and applied to various special cases in later chapters. Under this model, a haploid genome of N loci (or a protein sequence consisting of N amino acids) is assumed to undergo evolutionary change as a result of the incorporation of new mutations at distinct loci, one at a time. Only two alternatives, 1 versus 0, are allowed at any locus in the simplest version of the model. The contribution to Darwinian fitness from a given locus is affected by epistatic interactions with K other loci. These are described by drawing $2^{K+1}$ random numbers between 0 and 1 from a uniform distribution (to represent the effect of the locus in question, together with the K loci with which it interacts). The fitness contribution of the 0 or 1 state of the $n$th locus is assigned by a random draw from this set of $2^{K+1}$ numbers, and the fitness of an N-locus genotype is determined by averaging the fitness contributions of each of the N individual loci. The case of K=1 corresponds to the case of completely additive fitness contributions from each locus, and in this case there will be a single optimum genotype. As K approaches N, the scope for epistatic interactions increases, and the number of possible fitness optima becomes extremely large. Furthermore, the heights of individual fitness peaks fall toward the mean of the fitnesses of all possible genotypes. This is the fundamental limitation to the power of selection (the second type of complexity catastrophe) that Kauffman believes to be an inexorable consequence of complexity.

While Kauffman presents these deductions as very general properties of complex systems, in reality they depend on specific assumptions about the way fitness is affected by the individual components of the systems. In particular, the assumption that the fitness of an N-locus genotype is obtained by averaging over the effects of each locus, so that each individual locus contribution tends to zero as N tends to infinity, is open to challenge. This assumption is critical for the occurrence of the complexity catastrophes: if it is relaxed, the whole edifice collapses. Many models of multi-locus genetic systems have been studied by population geneticists (but are not mentioned by Kauffman); none of them include this property. A moment's thought should, in fact, convince one that it is not obvious that it has the slightest justification. There is no reason a priori why a change to a single component of a complex system should not have just as big an impact on fitness as a change in a much simpler one: after all, λ phage, E. coli, Drosophila and people are all liable to lethal mutations due to single amino-acid changes at single loci.

Furthermore, evolutionary geneticists have long been used to the idea that an equilibrium between selection and mutation to deleterious alleles at many loci will generate a distribution within the population of the numbers of deleterious mutations per individual. Much work has been devoted to predicting and measuring the properties of this distribution. It does not follow, however, that selection fails
to adjust the mean of the population to the optimum with respect to a trait or set of traits, but merely that there is variability around this mean as a result of mutation, the deleterious alleles at each locus being held at low frequencies by selection.

The literature on molecular evolution, which Kauffman regards as a paradigm for the NK model, also provides strong evidence against Kauffman’s assumptions. The conservation of the sequences of functionally important protein or RNA molecules, or parts of such molecules, is compelling evidence for the ability of selection to maintain their specificity over millions of years. Indeed, there seems to be no limit to the ability of gene duplication, mutation and selection to develop ever-increasing varieties of new gene functions, with a corresponding increase in organismal complexity.

Kauffman discusses many other topics in this lengthy book, including the behaviour of Boolean networks of numerous interacting on/off elements (which he regards as a model of cell differentiation), the emergence of a self-replicating metabolic network in the absence of any genome, and the generation of biological patterns via Turing-style reaction-diffusion systems. Kauffman is certainly grappling here with important and interesting questions, and he displays great ingenuity in constructing models of complex processes. I lack the expertise to judge the utility of his approaches to this very diverse set of topics. Some of his ideas seem useful as a guide to thinking, such as the notion that different cell types may reflect different steady states with respect to the patterns of activities of many genes which can turn each other on and off. He concludes that this implies that there is a strictly limited number of possible alternative stable states in a Boolean network consisting of a large number of genes, when each gene is regulated only by two others, and that these stable states correspond to differentiated cell types.

The problem is that the generality of this idea means that it makes few specific and testable predictions. Furthermore, certain applications of it seem very strained. For example, on pp. 483-484 he uses it to explain the logarithmic relation between the cell cycle length and genome size of a species, on the basis of a calculation of the average time a Boolean system takes to cycle through a steady state path. But it is clear that cell cycles are under the control of a highly specific system of genes, which are only a small subset of the genome. He also ignores the fact that the largest genomes, such as that of Trillium, contain huge quantities of non-coding, highly repeated sequences, which are extremely unlikely to be involved in regulatory circuits. No alternative hypotheses to explain variation in cell cycle length are discussed, nor are ways of testing alternatives discussed.

Similarly, his account of early embryonic development in Drosophila in Chapter 14 stresses the possibility that the spatially periodic patterns in the expression of gap and pair-rule genes are self-generated by reaction-diffusion mechanisms. But the current view is that they are the result of responses of hierarchies of genetic switches to gradients of positional information which are ultimately of maternal origin (remarkably, this section of the book has few references to the primary literature on Drosophila development after 1988). This lack of respect for the facts, which is also apparent in some of the other examples that I have described, is unlikely to convince the majority of biologists to pay more attention to theoretical approaches to their subject.

How should one evaluate the claim that The Origins of Order provides important new insights into the mechanisms of development and evolution? This is no easy task. The book consists of 645 closely printed pages of text (substantially longer than the The Origin of Species). Kauffman has an inordinate love of detail, and of terminology borrowed from mathematics and physics. Combined with a prolix style (the fact that the Boolean network model produces 317 stable cell types in a genome of 100,000 loci is repeated at least five times), this means that the reader has to work excessively hard to extract the essence of Kauffman’s arguments from the superabundant raw material.

I have already given reasons why his claim that complex systems impose severe limitations on the power of selection is probably false. His other substantial claim is that complex networks of interacting components may have an inherently limited number of stable potential outcomes. Selection is forced to choose among these, for example when a novel cell type is being evolved. This is a non-trivial claim, and may well have some truth in it, although Kauffman ignores the fact that differences among cell types may arise from different specificities of gene products (e.g. by the use of different splice sites), rather than by on/off switches in activity. But in essence it is nothing more than yet another version of the ‘laws of form’ argument. It is thus not novel or challenging for the neo-Darwinian evolutionist, unless it can be shown that substantial limits are, in consequence, placed on the range of possible phenotypes realised in evolution. The astonishing diversity of life forms on this planet, and the numerous examples of the near-perfection of complex adaptations, suggests that this is unlikely to be the case. The products of evolution seem to me to be much more akin to the kind of ‘Rube Goldberg’ contraption-building criticised by Kauffman than the ‘ emergent order honored and honed by selection’ (p. 644) which he proclaims.

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