Book Review

At Home in the Universe: the Search for Laws of Complexity. By STUART KAUFFMAN. Viking 1995. viii + 321 pages. Hard cover. Price £20. ISBN 0 670 84735 6.

Considering how complicated they are, living organisms are remarkably orderly and well-controlled. The nature of the controls is a major preoccupation of modern biology, and molecular analysis has revealed and continues to reveal a host of integrative mechanisms – mostly controls of gene activity and pathways of signal transduction – linked together in networks and cascades, with switches and feedback loops. What makes the whole control system such hard work to analyse, and so difficult to grasp conceptually, is that all its components are special, each one separately crafted to perform its own specific job. One can understand the feeling that there must be some simplifying higher principle or law to keep the complex living system in order, but nobody as yet has been able to show what this might be. Stuart Kauffman, controversially, believes that he knows where to look for the answer. *At Home in the Universe*, a slimmed-down and somewhat popularized successor to his earlier *The Origins of Order*, addresses a broad range of problems: the origin of life, the 'mystery of ontogeny', difficulties with natural selection, the problem of extinction, and even the optimisation of the economy. I shall concentrate here on what he has to say about two topics of central biological interest: development and evolution.

Kaufmann views the organism as a network of interacting components, and thus far he is certainly correct. He considers, as a model, an array of N Boolian elements (he pictures light bulbs) each of which can be switched 'off' or 'on' in response to the on/off states of K others. With N set at 100,000, the approximate number of human genes, the total number of possible states of the network is thus unimaginable large – 2 to the power of 100,000. Starting from any arbitrary state, the system will shift constantly from one state to another. If it ever gets back to a state that it has been in before, thereby completing a cycle, that cycle becomes an 'attractor' and is reiterated indefinitely. Unless K is a very small number, the number of alternative attractor cycles, and the average number of steps in each one, are both enormous, and the system is effectively in chaos – no order emerges on any realistic time scale. On this side of chaos, however, Kauffman finds refuge in $K = 2$, which he thinks (surely much too conservatively) is the number of controls to which a gene is normally subject. It turns out that the number of alternative cycles, and the average number of steps in each, now both boil down to the square root of N, or approximately 317 – an extraordinary simplification! Moreover, a number around 317 is just about what Kauffman needs to explain the number of cell types in the human body (256, he says), or the time taken by the cell cycle, assuming that each step in the gene activation cycle takes a few seconds or minutes. He evidently sees this as his show-piece result, and he is ecstatic about it. 'Order vast, order ordained, order for free!', he exclaims (apparently discounting any expense arising from the assembly of all those specific connections and switches in the first place). He believes that this kind of attractor-driven simplification, which he calls 'self-organization', is a universal property of complex systems, and can occur without the detailed 'tinkering' of component parts that Francois Jacob saw as the essence of evolution.

But how does all this connect with reality? Can we really believe that cells are held in their various differentiated states by repetitive cycling through hundreds of different patterns of gene activity? And developing organisms are surely never cast adrift in a vast Boolian state-space, needing rescue by some friendly attractor. They each start from a rather precisely defined position, and proceed from there step-by-step, each step secured by the kind of self-organization with which molecular biologists are familiar – the specific fitting together of precisely 'tinkered' macromolecules.

Kaufmann's modelling seems no more realistic when he comes to consider the difficulties of natural selection. He concentrates on the predictions of a class of N–K models in which N genes each interact with K others. Each gene is considered to contribute to the organism an additive measure of fitness which can vary between 0 and 1 depending both on its own allelic state and on those of the other genes with which it is interacting. The key assumptions are, firstly, that each gene has only two alleles, and, secondly, that any single allelic substitution within a group of interacting genes will randomise the fitness values of all of them. Consequently, if every gene interacts with every other ($K = N-1$) selection can hardly make progress, since each allelic replacement will, on average, increase the fitness values of half the genes and decrease those of other half. And even in K is substantially less than N, selection leads only to one or other of a number of local sub-optimal fitness peaks from which all possible single steps lead downhill.

But surely, in this model, selection is being unfairly and unrealistically handicapped. In real life, genes are not restricted to only two alleles but can mutate in many different ways with effects both varied and subtle, offering natural selection a wide range of choices. Nor does an allelic substitution within a set of interacting genes necessarily throw all their previously evolved joint functions back into the melting pot. But it is on the basis of these more than dubious assumptions that Kauffman concludes that natural selection by itself cannot account for evolution, and needs help. That help may come, he thinks, from the 'principle of self-organization', which is evidently what Hoyle and Wickramasinghe overlooked when they scorned the possibility of a tornado in a junkyard assembling a Boeing 707! He admits that he cannot yet explain how this apparently teleological principle works. 'We are seeking', he says, 'a new conceptual framework that does not yet exist'.

This is a book of scope and originality. Many will be impressed by it and it has, indeed, already been enthusiastically reviewed in the columns of *Nature*. The trouble is that it hardly connects with biology as we know it. Kauffman comes over less as a biologist than as a prophet, with visions veering between the comforting and the apocalyptic. On the one hand, he would like to feel that we really are 'at home in the universe', occupying a welcoming niche preordained in the laws of complexity. On the other hand he is haunted by the idea ('An Hour upon the Stage' – chapter 10) that one further addition to present complexity – one more chemical, gene or species – may at any time and quite unpredictably take us over the edge of chaos and down to extinction.

Meanwhile, molecular biologists, relatively unconcerned about these higher matters, continue to unpick the living network piece by piece, trying, with some success it must be said, to understand how the marvellously integrated whole emerges from the precise interactions of its parts.

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