



MICROFOSSIL — glassy opal skeleton of a unicellular marine organism, taken from *On the Nature of Things* (Aperture, \$40). This beautiful volume commemorates the work of the influential science photojournalist Fritz Goro (1901–1986), most famous for his 50-year collaboration with *Life* magazine. The book's 159 technically brilliant images are accompanied by comments from eminent scientists who worked with Goro.

Kauffman appears to abandon parallel-processing ensemble models either by marginalizing most of their effects through the interesting device of “forcing structures” (leaving only a small subset of genes actually responsible for pattern regulation) or by introducing gene-independent Turing-style reaction-diffusion models. When he holds up *Drosophila* development as an example of such phenomenology, he is forced to recognize that there is little that is not under the sequential control of small numbers of genes acting in very local patches of cells in bizarre, combinatorial and often redundant operations that can be explained as much by history as by ensemble or gene-free ‘field’ theory.

For example, Kauffman maintains that most genes are regulated by only a few other genes ($K=0\rightarrow6$) via canalizing Boolean functions. If, for example, there are half-a-dozen *trans*-acting controlling factors, any one of which can be missing to turn a gene off, then the system is canalized. The Boolean ‘Or’ function is clearly canalized. Hence most genes (the house-keeping genes?) fall into chains of command structure in which genes are fixed in either active or inactive states. These represent the “frozen cores” by which each cell type supposedly becomes uniquely different. But to provide flexibility, a few genes, by virtue of their low connectivity ($K=1$), fall into “independent feedback loops” with alternative states, which through a “binary combina-

torial epigenetic code” can also give rise to novel cell types. Then (we’re nearly finished), if the products of a subset of genes can diffuse between cells (as they do), the tissue as a whole can settle down to being an “overall dynamic attractor”. By tweaking the parameters in such ways, Kauffman is dangerously close to simply restating in cyberneticspeak what we actually know is going on in, for example, the hierarchy of regulatory decisions, from *bicoid* to the segment-polarity genes that control segmentation during early *Drosophila* embryogenesis. Similarly, having shown that the original Turing models of ‘standing waves’ (the result of local differentials in rates of reaction and diffusion) are insufficient to account for embryogenesis, Kauffman ends his account of the origins of order by proudly wheeling on his and Brian Goodwin’s ‘Four Colour Wheels Model’ by which cells take their cues from phase differences of gene-encoded morphogens having progressively shorter wavelengths.

This is not the place to examine the extent to which the local protein and RNA gradients produced by the maternal, gap, pair-rule and segment-polarity genes can be squeezed into the bifurcating system underlying the Four Colour Wheels. The irony lies more with the point that all such diffusing molecules are *gene-controlled*. Morphogen concentrations and locale take their cues from the intimate and increasingly bizarre local interactions

involving redundant *cis*-acting binding sites, differential concentration-dependent binding affinities and intimate cell-cell interactions, and not obviously from the global dimensions of the tissue, as required by field models. Once we ‘reduce’ morphogens and pattern demarcation lines to the combinatorial genetic processes (the ‘syntagmata’ of Garcia-Bellido) of a finite number of genes whose products diffuse or signal to neighbouring cells, then we end up, after 700 pages, treading the same realistic stomping ground beloved of Earth-bound developmental geneticists. Such finite regulatory networks and local cell autonomy do not necessarily require the spontaneous self-organization of Boolean systems or pattern-generating morphogenetic fields but, rather, with their bolt-on modularity, are more easily understood as the accidental but functional products of an incessant process of evolutionary molecular Lego.

With its imagery of adaptive landscapes, morphogenetic fields and restrictive canalizing functions, this attempt at computerized biology is strangely old-fashioned. Importantly, it does not embrace the evolutionary consequences of genetic and functional redundancy and genomic flux. Such features impart a degree of internal tolerance and the facility for molecular coevolution in combinatorial regulatory systems that is far removed from the hard lock-and-key imagery of fixed adaptive landscapes and canalizing K connectivity. Landscapes of evolved organisms are more akin to the heaving surface of the ocean due to genomic and ecological turbulence, being both adaptive and nonadaptive, but functional for all that. Designing life through ensemble theory is as cosy as designing a jumbo jet on a computerized drawingboard. The real trick of *Life* is the gradual evolution of a jumbo from the first wire-and-wood contraptions while the bloody things are still flying in the air! This requires the internal tolerance governing evolving molecular interactions that is provided by modular and redundant systems.

It may be that Kauffman is not so much ahead of his time as that most of us are behind ours. *NK*, as an explanatory model for the origins of order, may come to signify Not Korrekt or Nobel Kauffman. My head, full of awkward biological knowledge, tells me the former might be the outcome, but my heart, incessantly fighting the vulgar Darwinism of solitary selfish genes, would settle for the latter.

*This is Ground Control to Major Tom
You've really made the grade
Now it's time to leave the capsule if you dare.* □

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