Book reviews

Evolution of Catalytic Function. Cold Spring Harbor Symposia on Quantitative Biology LII. New York: ISBN 0 87969 054 2. Cold Spring Harbour Laboratory. 1987. 952+xix pages. $150.

There are two points of view I would like to offer about this book. The first is the simplest. This massive volume offers a thorough and up-to-date survey of the greater part of those areas of molecular biology which deal with the specific physico-chemical behaviour of nucleic acids and proteins. For reasons which will appear, the book concentrates on RNA, and there is very little about protein/nucleic acid interactions, but otherwise most of the liveliest areas of study of macromolecular structure and function are dealt with. These include structure prediction of RNA and protein, 'engineering' studies of proteins, catalytic antibodies, molecular mechanics, molecular evolution, the theory of catalysis and the very early history of life.

There are more than 100 papers in the collection; to say that the contributors include Eigen, Gilbert, Jencks, Karplus, Klug, Orgel, Perutz, Knowles and Wittman will give an idea of the breadth and depth of coverage. Of course, very little of the material is completely new. Only those who are known to have a good story to tell, polished by rehearsal elsewhere, are invited to contribute to this sort of conference. Weiner says, in an excellent Summary, that the book is unsummarizable; it is also unreviewable. The volume will be in every library; it would also be a welcome addition to the bookshelf or bedside table of most molecular biologists.

The second point of view arises from the fact that it was not the intention of Jim Watson, in designing this Symposium, merely to provide a sort of Earl's Court Show of the best of this year's high-performance bandwagons. The thesis is that the discovery of catalytic RNA molecules represents a breakthrough in understanding of the origin and early history of life. RNA has pushed aside not only DNA but also protein as the central molecule of biology. Understand RNA and you understand Life.

It used to be fairly easy to dismiss any effort to deduce the properties of the first living systems, on very general grounds. Study the personal computer on your desk. Then compare it with the multi-access system you use at work and deduce what you can about the engineering design of the first electronic computers. Even after only 40 years and four 'generations' of development the machines have little in common. Features of the fundamental logical structure are preserved, but almost all the detailed engineering is not just new, but has been renewed several times. A few old buffers still refer to 'main memory' as 'core' in vestigial tribute to a device which appeared quite late in computer development, flourished for a few years, and has now disappeared without other trace. How likely is it that you could look at an 8086 chip or a hard disk and deduce the existence of the thermionic valve or the punched paper tape? How much less likely is it that engineering features of the first living things should have been preserved through 4 billion years of evolution, or that we should recognize them if they have been preserved? Evolution cannot be run backwards; there is no hope of ever finding any DNA which is more than, say, 10,000 years old.

However, the present volume shows that molecular biologists, whatever the philosophical difficulties, are not now deterred from constructing apparently robust arguments which lead to conclusions about the course of evolution from the very earliest times.

For example, Gilbert puts forward the following proposition: (*a*) introns are found at the end of structural units of proteins, and their positions are highly conserved amongst eukaryotes; (*b*) the natural explanation is that introns provide the mechanism by which complete complex proteins are assembled from small structural units; (*c*) prokaryotic genes, lacking introns, are homologous to eukaryotic 'split' genes; (*d*) therefore the presence of introns in genes is a primitive feature, which has been lost in prokaryotes.[1]

[1] This argument is very similar in structure to Thom's argument for megalithic astronomy. Surveys of stone circles show such a high proportion of alignments of astronomical significance that their builders must have been sophisticated mathematical astronomers. The length unit employed is identical at sites from the north of Scotland to France, so this advanced culture must have extended over a large area. Archaeologists have always realized

https://doi.org/10.1017/S0016672300028032 Published online by Cambridge University Press

Since introns can catalyse splicing, and the splicing chemistry could be used for replication, this argument can be extended to become the central thesis of this book, that the first living systems were based solely on RNA. DNA and protein were only added after prolonged evolution in the RNA world.

A complete living system might be a single molecule of RNA which was a substrate for an RNA replicase; the replicase (and any other necessary enzymes) are formed by (self-)splicing from the same RNA. This is a very neat and powerful idea, since it suggests for the first time how a single molecule system can provide both the storage for a genetic message and the physical articulation of the same message. Neither the chicken nor the egg came first; it was the nest which engendered both.

Evolutionary arguments have to be constructed with care to avoid, for example, teleology. One of the virtues of this Symposium is that several papers (e.g. those by W. F. Doolittle, and by Benner *et al.*) show how to do this with great clarity, both by precept and by example.

But the real problem with evolutionary arguments is that any feature of contemporary biological systems may have either of two evolutionary explanations. It may never have been adaptive (a 'frozen accident'), or there was a time and environment in which it directed evolution because of its greater fitness. If you *know* that the latter is true, you can deduce something about the nature of the biological world in which it arose. Conversely, if you understand enough about the genetic environment in which a feature appeared, you may be able to say whether it significantly enhances fitness. But if you have neither point of entry into the loop, the possibility of a frozen accident remains open.

It is often said that the key difference between prokaryotic and eukaryotic cells is that the latter have organelles; this gives them the functional flexibility to allow the construction of multi-tissue organisms. Gilbert would presumably say that the key difference between prokaryotic and eukaryotic cells is that the latter have retained the intron mechanism; this gives them the functional flexibility to allow the construction of multi-tissue organisms. If evolution theory meant that these two possibilities were incompatible, then a coherent account of early evolution would have to decide between them. But either (or both) might be a frozen accident – and therefore of no fundamental significance.

For me, the absence of the discipline provided by a series of events which *must* have a causal chain of explanation gives evolutionary arguments, including those in this book, a peculiar, unsatisfying, take-it-or-leave-it quality.

For example, Benner *et al.* argue that if the fact that so many co-enzymes (NAD, SAM, GTP, etc) are related to RNA is used to support the idea of a solely-RNA-biology, then this RNA world would have had aerobic metabolism, and therefore would also have mastered photo-synthesis. Faced with such an argument, I want to say that if it is true that such sophistication is possible with RNA alone, it seems surprising that a *universal* DNA-and-protein biology should then have taken over. Why are there no lineages in which there are significant differences in the genetic code? But these arguments never have to be forced to resolution, because even if it is not plausible to suppose that every feature of the code is adaptive, it is always possible to argue that the DNA-and-protein mechanism only arose in one lineage, or that it passed through a bottleneck of a single species, before it overran the world. In any case, Benner's original argument itself depends on several steps, each of which could lose substance in the same way.

The central problem seems to be that we never know which features of molecular biology are essential and which are casual. It would help a lot, of course, if we could survey a cross-section of biologies. What a pity that this part of the universe is so sparsely populated.

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that the point of weakness of this argument, if it has one, must be the accuracy of the site surveys. Surveying is tedious and laborious, and not many bright young archaeologists are interested in repeating other people's work if the maximum outcome is a negative result. The weakness, *if there is one*, in the intron argument must be in the two statements in (*a*), and there are the facts which ought to be tested. There is a certain vagueness about what exactly is proposed to be reassorted – for Gilbert, the unit is the exon, of mean length 50 residues; for Go it is a module of length 20 residues; for Blake the 'unit' can be anything up to at least an entire domain. Blake is clear that the boundaries of introns are the boundaries of supersecondary structure; Go's module boundaries appear to be *within* secondary structure elements. These ambiguities suggest that in this case also some independent re-surveying would be worthwhile.

Vaccines '88: *New Chemicals and Genetic Approaches to Vaccination. Prevention of AIDS and other viral, bacterial and parasitic diseases.* Edited by H. Ginsberg, F. Brown, R. A. Lerner and R. M. Channock. New York: Cold Spring Harbor Labortory. 1988. 396 pages. Paper $95·00. ISBN 0 87969 210 X.

This latest volume in the series of Cold Spring Harbor Symposia on vaccine development more than lives up to the high standard set by its predecessors. Its format follows the tried and tested methods of previous volumes, containing sections on Immunology, Parasitology, Bacteria and Bacterial Diseases, Virology and AIDS. This inter-disciplinary approach involving the study of a wide range of organisms and viruses as well as the differing practical disciplines of chemistry, molecular biology and immunology results

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