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

https://doi.org/10.1017/S0016672300028044 Published online by Cambridge University Press

in a unique overview of the field of vaccine design and development.

There are enough subject specialities covered in this book to keep most people happy. As a molecular parasitologist acutely aware of the lack of any recombinant vaccine to date against any parasite, it is particularly encouraging to see how far the virologists have progressed and to keep in touch with new developments in basic immunology. The section on AIDS is of use to non-specialist and specialist alike, documenting the latest developments in this rapidly expanding field. In addition to specific articles such as the mapping of protective epitopes and the recognition of a role for T-cell immunity in AIDS patients, there are also good general articles on the molecular biology of HIV including an excellent account of transcriptional regulation of HIV I by Peterlin *et al.*

If there is a dominant theme within this book, it is perhaps that of the T helper cell epitope. Such epitopes are reuired to stimulate the T helper cells which are responsible for the boosting of antibody production upon subsequent exposure of the immune system to an appropriate antigen. The importance of these epitopes is well illustrated by the tortuous progress being made towards developing a vaccine against the sporozoite stage of malarial parasite, *P. falciparum*. Synthetic peptides known to represent B-cell epitopes of the circumsporozoite protein have proved ineffective as a vaccine. This has subsequently led to the immunological dissection of circumsporozoite protein so that T–cell epitopes may be identified. The latest twist in this story is described in this volume by Michael Good and his colleagues. They find that although the circumsporozoite protein is highly conserved between different strains of the malarial parasite *P. falciparum*, the few areas of variability that exist appear to coincide with T-cell epitopes.

Another aspect of T-cell epitopes of relevance to vaccines is the host-based phenomenon of genetic restriction, where individuals differ in their ability to recognize given T-cell epitopes. This phenomenon is illustrated by Francis *et al.* in the opening article. These authors were able to overcome genetic restriction in mice to a Foot and Mouth Disease Virus nonadecapeptide by coupling T-cell epitopes from foreign heterologous proteins such as ovalbumin and sperm whale myoglobin to the peptide. Interestingly, different T-cell epitopes resulted in antibodies being raised to different regions of the FMDV peptide.

Studies of these types show how subtle our understanding of the immune response must become in order to design subunit vaccines utilizing peptides or recombinant proteins representing only a small portion of an important antigen. To overcome this one must put efforts into obtaining bacterial expression of full-length, protective recombinant immunogens, which is not a simple task. Even when these are available, a problem exists for human diseases in that there is a severe lack of safe, suitable adjuvants. This area of adjuvant research is a severely neglected area of vaccine development. Other approaches to this problem are described, however. Immunologists have tried to overcome the adjuvant problem by using 'natural' immunological stimulators such as the Interleukins and Interferons. Molecular biologists have tried to overcome the problem by inserting cloned DNA into surface protein genes of infective viruses, e.g. vaccinia, or bacteria. An interesting development related to this area is the work of Clarke *et al.* on the formation of chimeric proteins based on the Hepatitis-B Core Antigen. These proteins automatically self-assemble into virus-like core particles that are highly immunogenic. The trouble with these examples, once again, is that often only a limited size of recombinant protein can be expressed.

The most successful vaccines to date are undoubtedly those of the 'Jennerian' approach where 'attenuated' viruses or organisms are used to induce a protective immune response. Interestingly, molecular biology techniques are now being used to identify the mutations giving rise to these 'attenuated' forms with a view to developing new vaccines and modifying old ones. In many ways this work has brought us full circle in our approach to vaccine design.

Our increased understanding of the immune system and the immunological properties of antigens, and the availability of new chemical and genetic tools, is allowing us to develop rational approaches to vaccine design. Vaccines '88 must be recommended reading for anybody wishing to keep abreast of the latest developments in this exciting field of study.

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Genome Analysis: A Practical Approach. Edited by K. E. Davies. Oxford: IRL Press Ltd. 1988. 192 pages. $27·00/US$54·00. ISBN 1 85221 109 1.

Another winner for the 'Practical Approach' series! We have been fans and avid users of several earlier volumes of these technical tracts in our laboratories and the magpies are ready to swoop on my reviewer's copy should I leave it lying around. Luckily it is the more expensive spiral version which is very easy to xer...–oops, too many of life's pleasures are illegal.

Having said how keenly we espouse the latest technology, I will compound the conceit by suggesting that this volume in particular is aimed at the *cognoscenti* in the field of genome analysis. There are excellent chapters on genome transfer (which I loosely call somatic cell genetics), contig mapping, pulsed field gel electrophoresis (with a lovely trouble-shooting appendix of gel photographs which never get published), chromosome jumping, detection of single base changes in DNA, polymerase chain reaction (almost better known as PCR), fingerprinting and linkage