

Book Review

Cold Spring Harbor Symposia on Quantitative Biology, vol. 52: *Evolution of Catalytic Function*. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory, 1987. Pp. xix+955. \$150.00.

Cold Spring Harbor Symposia volumes come in two forms, those which deal with well-defined topics, such as the genetic code, biological clocks, and tumor viruses, and those which do not. The 1987 tome, entitled *Evolution of Catalytic Function*, belongs to the second category. Thus, despite a sincere effort to provide a unifying theme (Koshland, Orgel) and a most ingenious attempt at "summarizing the unsummarizable" (Weiner), the reports vary widely in scope, usefulness, and depth. A 955-page publication containing 101 articles written by 344 authors, this volume predictably lacks consistency and stylistic uniformity, containing review articles, scientific reports, methodological recipes, and speculative essays in unequal proportions.

The first five articles deal with the "soupist" theory of prebiotic evolution. An inventory of organic compounds thought to have either existed in the primordial soup or to have played a role in the origin of life (Miller) is followed by a devastating account of the state of the art (Ferris). It seems that the gaps in our understanding have essentially remained as wide as they were in the 1940s following the work of Bernal, Miller, and Urey. A laconic introduction into the "RNA world" (Schwartz) precedes a discussion on nonenzymatic replication of biological information (Joyce), and the section ends with an original and evidently productive attempt to devise "research strategies" for dealing with prebiological catalysts and with the reconstruction of "functional phylogenies" of proteins (Benner).

The next section deals with the "Essentials of Catalysis." We are first introduced to biological catalysts and their properties in an article that proves only too clearly that we know very little about how catalysts work (Jenks). The problems seem less distressing, however, after we become acquainted with an ingenious approach to understanding enzymes through the study of simple artificial "mimics" (Breslow, Bartlett). A new and exciting field of study, antibodies as catalysts of chemical reactions, is presented in a pair of articles (Tramontano, Pollack). These works demonstrate that the binding specificity of antibodies can also be used for catalytic purposes. Some theoretical foundations on which catalytic processes can be described and quantified are also presented. An article on engineered manipulations of antibodies, manipulations made possible by the increase in our understanding of three-dimensional structures of proteins (Pluckthun), closes the section. The only annoying part in this section is the tiresome descriptions of laboratory methods, which sometimes include elaborate lists of commercial sources.

The section entitled "RNA Anatomy" starts with a pair of papers (Dock-Bregeon, Turner) dealing with methodological questions pertinent to the construction of secondary structures. The third paper (Tinoco) contains an excellent review on the multitude of RNA structures. This survey manages in an enviable manner to be exhaustive, informative, and innovative, while at the same time remaining accessible and readable.

The existence of catalytic RNA was predicted by Francis Crick already in 1968, and its discovery constitutes one of the most exciting events of the 1980s. It is thus little wonder that the section dealing with this subject provides many of the redeeming reasons for publishing this volume in the first place. The section contains systematic surveys on all known types of RNA-mediated reactions, as well as in-depth characterizations of these systems. I was particularly impressed by some very clever attempts (Doudna) to create RNAs that would catalyze template-dependent RNA polymer-

ization. As autocatalytic reactions involving RNA seem to constitute a most promising area of inquiry, these trials are bound to result in major improvements in our knowledge of prebiotic evolution.

The section entitled "Templates" deals almost exclusively with RNA viruses, presumably as relics of a now defunct "RNA world." Despite the fact that the word *evolution* is mentioned frequently (Priano, Paul), most of the articles deal with purely enzymatic, structural, and kinetic facets of RNA replication. Only one article takes evolution seriously. The report on Brome mosaic virus and its relatives (Marsh) documents several processes affecting their evolution, and the discussion of interspecific recombination is one of the most interesting parts in this volume.

Empirical evidence strongly suggests that the primary sequence of a protein unambiguously determines its three-dimensional structure. However, the rules of the game remain elusive. I was thus enlightened to read about the major strides that have been made in this area (Karplus, Shoemaker). In particular, I would like to mention a new approach that combines powerful algorithms and experimental manipulations of proteins (Ponder). The most original part in this work is that instead of struggling with deciphering the tertiary structure of a polypeptide, given its primary sequence, an attempt is made to define a "space" of all sequences compatible with a given three-dimensional structure. Since the former approach has yielded little progress, one can only hope that this reverse attack will succeed.

The section dealing with proteins is the most heterogeneous part in the book. A considerable number of papers are devoted to descriptions of three-dimensional structures of particular proteins or of domains within proteins. Others deal with more universal features, such as repetitive structures (McLachlan) and the binding of prosthetic moieties (Quiocho). Few articles discuss the structural evolution of genes belonging to mutigene families. It is not surprising that one of the best in this series concerns hemoglobins (Perutz). My personal favorite is a creative approach of relating sequence evolution to changes in the structure of proteins (Chothia). Given both the veritable avalanche in the production of DNA sequences and the existence of an industry devoted to comparative studies of such sequences, it is essential to develop methods for studying nonlinear structures. Several articles (Creighton, Carrell, Laskowski) deal with evidence for positive Darwinian selection in proteinase inhibitors. The claim that these findings are "irritating to neutralists" (Weiner) is incorrect. Neutralists do not deny adaptation. The evidence for advantageous selection in the case of proteinase inhibitors, however, may not be as powerful as claimed.

It is odd that only seven of the 101 articles in this volume deal with the evolution of catalytic function, the official subject of the *Symposium*. It seems that site-directed mutagenesis is the most fashionable method employed to characterize catalytic sites of enzymes. Powerful applications of this method are used in the study of triosephosphate isomerase (Hermes, Alber) and two serine proteinases (Higaki, Wells). An idiosyncratic account of the evolution of enzyme specificity and accuracy (Ninio) uses DNA replication and mismatch repair to illustrate spatial and temporal constraints on enzyme function and control. It is an important contribution since, in addition to original interpretations, it contains many heterodox historical perspectives.

The section devoted to ribosomes constitutes the most systematic compilation in the *Symposium*. A historical overview of the functions of ribosomal RNAs and proteins (Nomura) opens this section. Appended to this prologue is a short note on GC content in bacteria (Nomura), tentatively showing that the genomes of prokaryotes may possess a degree of compositional heterogeneity similar to that in mammals. One can only wonder why such a significant finding was printed as a dangling and unindexed appendage. Four articles (Nierhaus, Oakes, Moore, Yonath) are devoted to the three-dimensional architecture, model of assembly, function, and sequence of interactions of the ribosome. Our only glimpse into the evolution of RNA sequences is provided

by a somewhat laconic presentation (Gerbi), followed by an updated account on secondary structures (Noller). These articles clearly show how constraints imposed by inter- and intramolecular interactions result in a process of coevolution at the molecular level.

A short section entitled "Protein Synthesis and the Genetic Code" contains six articles, half of which deal with evolutionary inferences derived from genetic systems of organelles (Jukes, Osawa, Ozeki). The prologue (Maizels) puts forward an intriguing hypothesis according to which the first protein-synthesizing apparatus produced homopolymers. The best article in this section (Fitch) uses phylogenetic reconstructions of tRNA sequences to provide a scenario for an increase in the specificity of translation during evolution. Unfortunately, tRNA molecules are quite short, and ambiguities cannot be avoided even if one uses the most rigorous methodology of statistical analysis.

The section entitled "Evolutionary Trees" starts with a well-documented account of the origin of cells (Cavalier-Smith). Four articles (Olsen, Lake, Li, Penny) deal with questions of tree reconstruction, each advancing a different method. Comparative studies in the future will undoubtedly sort out the conditions under which each of these methods performs best. An elegant study of evolutionary rate differences between male and female germ lines (Miyata) and a note on parallelism at the molecular level (Stewart) illustrate the power of molecular biology to unravel unexpected evolutionary phenomena. It is sad to note, however, that these articles also show how short of data we are and how empirical evidence is chronically lagging behind evolutionary theory. The chapter ends with specific applications of tree-building methods to several protein families (R. F. Doolittle, Goodman).

The last 30 pages are dedicated to "Exons and Introns." All authors agree that introns are primitive features and that intronlessness is a derived character. The chapter opens with a grand exposition of the "exon theory" (Gilbert), followed by a careful argument on the dos and don'ts of neo-Darwinian evolutionary theory as applied to exon shuffling and gene assembly from "miniexons" (W. F. Doolittle). Finally, the major empirical support for the exon theory (i.e., that a correspondence exists between exons and protein domains) is presented in an updated form (Go, Blake).

It would be superfluous to either recommend or deprecate the *Symposium*. Libraries will buy this volume as long as they can afford the price, but only a few individuals will be able to do so. Nor will I volunteer a prediction on the lasting value of such a volume. Most of the topics are either established orthodoxy or are in their speculative infancy, and it will take a long time to decide what their contribution to scientific progress will be.

DAN GRAUR
Tel Aviv University