BOOK REVIEWS

Life Before DNA

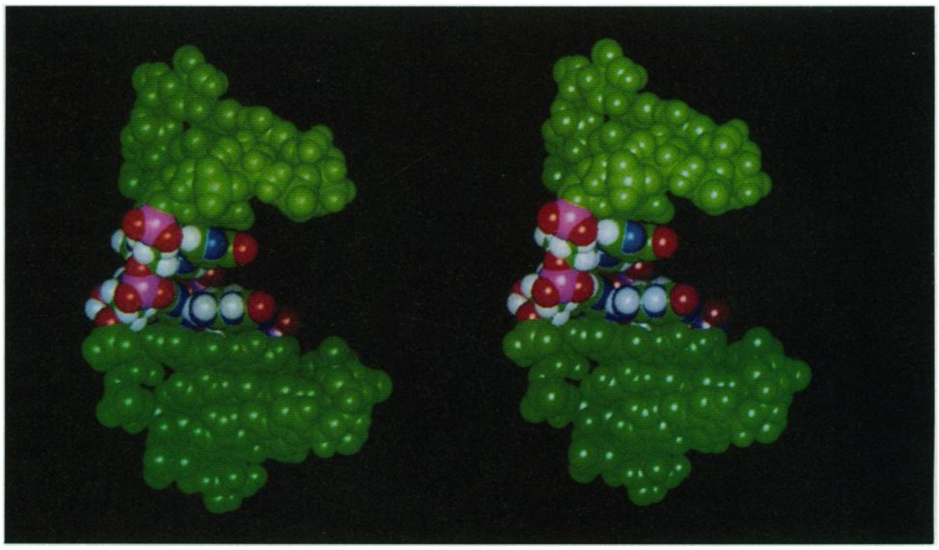
The RNA World. The Nature of Modern RNA Suggests a Prebiotic RNA World. RAYMOND F. GESTELAND and JOHN F. ATKINS, Eds. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1993. xxvi, 630 pp., illus. $95. Cold Spring Harbor Monograph 24.

"The RNA world" refers both to a time and to a place, first glimpsed in the late 1960s by Francis Crick. Since then, the discovery of RNA catalysis, ribozymes, and the extraordinary correlations of structure and function in RNAs and ribonucleoproteins has created numerous believers in a time when the Earth was populated by biologically active, self-replicating RNA molecules, aided and abetted in the later stages by the first crude polypeptides. How long this time may have lasted, how we got here from there, and the study of the RNA world's remnants today are the major themes of this opus. Twenty-three chapters are devoted to topics related to the RNA world, and it is safe to say that many of them will be required reading for some time to come for RNA biochemists, molecular biologists in general, and those interested in evolution. The most memorable parts of this book deal with the fascinating question of when the RNA world could have existed, and for how long; the two-part problem of how to relate primitive RNAs destined to become ribosomes to transfer RNAs and other molecules that may have arisen before them; and the fundamental suitability of ribonucleic acid for the many functions now heaped upon it by RNA world devotees.

The original harbingers that brought wide attention to the RNA world are, of course, the ribozymes—or RNA enzymes—whose discovery in the early 1980s began a new chapter in biochemistry. In this volume T. Cech reviews several of these activities, speculating on how primitive RNA polymerases may have been related to the cleaving and splicing ribozymes known today. RNA catalysis further expands its boundaries in chapters by M. Moore, C. Query, and P. Sharp and by S. Baserga and J. Steitz. These authors speculate that present-day RNA/protein structures known as "spliceosomes" may continue to carry out RNA-catalyzed steps, despite their many protein components. Elsewhere in the book this line of thought is applied to additional RNA/protein structures, including the ribosome.

Although there appears to have been tacit agreement on the part of the authors to avoid speculation on the origin of the genetic code, there are illuminating essays on how protein synthesis and ribosome translocation may have arisen. Though, as outlined by H. Noller, it is now common to assume that peptide bond formation was and is RNA-catalyzed, there are a number of mysterious facts about polypeptide synthesis that need to be addressed. The chapter by R. Weiss and J. Cherry succeeds in focusing our attention on some of these mysteries. These authors argue that ribosomes evolved from RNA-polymerizing RNA enzymes that attached oligonucleotides to the 5′ ends of growing chains. In making this suggestion, they highlight a central theme of protein synthesis: "a ribosome moves from the *5′ to 3′* end of its template strand, whereas RNA and DNA polymerases elongate from the *3′ to 5′* end of their template strand." Thus the issue of how protein synthesis became "turned around" with respect to its RNA template is introduced. In addition to unanswered questions about the code, this conundrum remains a central concern.

Like ribosomal RNA, the other major RNA now used for protein synthesis—transfer RNA—is assigned unexpected roles in the pre-protein RNA world. Likewise RNase P, the ribozyme-based activity characterized by S. Altman, which creates mature 5′ ends of tRNAs, must also have existed in a purely RNA world. Thus tRNA, long assumed to be an adaptor relating RNA to protein, could have been a primer for new RNA synthesis, reflecting its modern role in priming reverse transcriptase in modern retroviruses (J. Atkins); or a 3′ terminal "genomic tag" in the now-familiar hypothesis arguing that ancient motifs can be discerned by examining the tRNA-like 3′ ends of modern RNA bacteriophages and RNA viruses (N. Maizels and A. Weiner). Finally, several authors, including E. Blackburn and B. Bass, suggest that tRNA-like molecules may have acted as templates for RNA synthesis, by analogy to the highly structured RNAs used in modern telomerases or the guide RNAs used in RNA editing.



"Model of the duplex $\begin{matrix}GGC^{GA}GCC\\CCG_{AG}CGG\end{matrix}$ based on NMR data (SantaLucia 1991). Base pairs are colored green and the GA mismatches have traditional colors for atoms (O = red, H = white, C = black, N = blue)." The model "suggests even a small internal loop can provide a useful recognition element." [From Turner and Bevilacqua's paper in *The RNA World*]

In a way, it is a shame that those concerned with roles for tRNA—especially with regard to polymerase primers and templates—did not team up with those analyzing the development of ancient ribosome-like RNAs from such polymerases. What might have emerged was the suggestion that RNA, and not just protein, could be synthesized "backwards"—that is, with the template read *and* the product elongated from 5′ to 3′. This development could have been augmented by "adaptors"—forebears

Vignettes: Overseers

Managers make many mistakes. More often than not these hurt the people they manage, rather than themselves.

—*Peter J. Feibelman,* in *A Ph.D. Is Not Enough! A Guide to Survival in Science* (Addison-Wesley)

An example of the paranoia that had been creeping into the place was characterized by the plastic and tape sculpture that was hung in one of the stairwells by one of the inventive staff members. Certain members of the administrative staff felt so unloved that each believed independently that he had been hung in effigy. It seemed like a good idea, but that was not the intent.

—*Robert C. "Jack" von Borstel,* in *The Early Days of Yeast Genetics* (Michael N. Hall and Patrick Linder, Eds.; Cold Spring Harbor Laboratory Press)

of the first tRNAs—which would each have donated their 3′-terminal nucleotide to the growing RNA chain. Such a process could also have allowed critical parts of RNAs (such as those with enzymatic activity) to be amplified selectively in the absence of full replication. Protein synthesis could then be viewed as a further step along this path leading to the divergence of enzyme synthesis from genome replication.

That the RNA world must have had many complexities is evident, but a number of this book's authors believe that its time was very brief—limited to the period between the cooling of the Earth to life-sustaining temperatures and the date of the oldest fossils containing conventional DNA organisms. P. Moore argues that it must have lasted less than 100 million years, and that "when one starts thinking along these lines, one must consider the unthinkable, i.e., that the length of time that RNA-based organisms bestrode the earth might actually be zero." In a foreword, F. Crick addresses this issue by invoking "Directed Panspermia," by which life is viewed as having been "sent here" in several different forms, all "likely to have evolved originally from a common ancestor (on another planet) that existed some billions of years before the origin of our solar system." Such thinking may be necessary, especially in light of the arguments, presented by G. Joyce and L. Orgel, that getting from zero to RNA would seem even more difficult and time-consuming than getting from RNA to the present state of affairs.

Standing in opposition to such cries for a *deus ex machina* are three outstanding chapters that underscore RNA's inherent fitness for a dual role as template for life and catalyst thereof. As D. Turner and P. Bevilacqua argue in their illuminating discussion of RNA thermodynamics, "The many functional groups, high charge density, and strong interactions of RNA provide thermodynamic advantages for RNA in initial stages of evolution." The reader's confidence in RNA's abilities is further enhanced by its clever use of divalent metal ions to improve folding and catalysis, as discussed by T. Pan, D. Long, and O. Uhlenbeck, and by the revealing analysis by J. Wyatt and I. Tinoco of how familiar and unfamiliar secondary and tertiary structural elements blend to give RNA an almost protein-like complexity. In chapters such as these, but also in those more aimed at review or speculation, the reader can readily see the value and timeliness of this volume, and can anticipate further excitement to come from explorers of the RNA world.

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A Theory of Everything

The Quark and the Jaguar. Adventures in the Simple and the Complex. MURRAY GELL-MANN. Freeman, New York, 1994. xviii, 392 pp., illus. $23.95.

In the late '50s, when I was a graduate student at the California Institute of Technology, the two senior professors in elementary particle theory were Richard Feynman and Murray Gell-Mann. The modernist Man Ray once remarked that when he came to Paris as a young painter the other painters he met were Picasso and Braque; he decided to switch to photography. We Caltech grad students understood his feelings perfectly.

We idolized Feynman, with his dazzling style and his radical originality, but we went to Gell-Mann when we wanted a research problem. Gell-Mann was at the center of particle theory; he had been there for almost a decade and would remain there for over a decade more. The long road from the rebirth of quantum electrodynamics in the late '40s to the construction of the standard model in the early '70s is marked by monuments with Gell-Mann's fingerprints all over them: strangeness, the renormalization group, the V-A interaction, the conserved vector current, the partially conserved axial current, the eightfold way, current algebra, the quark model, quantum chromodynamics—and this is the short list.

At Caltech Gell-Mann was almost as famous for his erudition as for his physics; he was enormously learned in subjects most of us didn't even know existed. A story is told about a physicist, much bothered by this, who decided to become expert in some obscure corner of human knowledge, so that, just once, he could trump Gell-Mann. Of course, for the plan to work the subject had to be one that could be introduced naturally into conversation. He knew that the dining room of the Caltech faculty club was decorated near the ceiling line with the heraldic shields of universities; he decided to learn blazonry, the technical descriptive language of heraldry. When next he had lunch with Gell-Mann at the faculty club, he allowed his gaze to drift upward. "How interesting," he said (and here I must make up babble, for I know no blazonry myself), "gules rampant on sable argent." Gell-Mann looked up. "No," he said. "No, it's sable rampant on gules argent."

In recent years Gell-Mann's interests have shifted from particle theory to what he sometimes calls plectics, "the emerging science of complexity." Ten years ago he helped found a research center devoted to the study of complex systems, the Santa Fe Institute, where he is now a professor, having taken early retirement from Caltech.

The Quark and the Jaguar is an attempt to describe a Theory of Really Everything (my terminology, not Gell-Mann's), a theory not just of quarks but also of jaguars and economies and bacteria, a general theory of how complex systems develop from simple elements and of how they behave after they have developed. I say "describe" rather than "construct" because this theory does not yet exist. More precisely, it exists only in hints and fragments, but Gell-Mann believes it is emerging from research on complexity, especially from the sort of research being done at the Santa Fe Institute. Indeed, the very SFI concept of complex