BOOK REVIEWS: MOLECULAR BIOLOGY

# In the Beginning Was the Word

R. C. Lewontin

It seems impossible to do science without metaphors. Biology since the 17th century has been a working out of Descarte's original metaphor of the organism as machine. But the use of metaphor carries with it the consequence that we construct our view of the world, and formulate our methods for its analysis, as if the metaphor were the thing itself. The organism has long since ceased to be viewed *like* a machine and is said to *be* a machine. The ways in which the metaphors of biology have molded the concepts and experiments of the science have been a preoccupation of the historian of molecular biology Lily Kay. In *Who Wrote the Book of Life?* her most recent and unfortunately final book (she died of cancer in December), Kay asks how the view that DNA is "information" that is "written" in a "language" whose "words" are in "code" has driven the research program and claims of molecular biology.

**Who Wrote the Book of Life? A History of the Genetic Code**
*by Lily E. Kay*
Stanford University Press, Stanford, CA 2000. 470 pp. $60, £45. ISBN 0-8047-3384-8. Paper, $24.95, £17.95. ISBN 0-8047-3417-8.

Kay's analysis of the history of molecular genetics is poststructuralist. That is, while not denying the objective reality of genes, proteins, and cellular elements, it is "grounded in the conviction that once a commitment to a particular representation of life is made—material, discursive and social—it assumes a kind of agency that both enables and constrains the thoughts and actions of biologists." Unfortunately, the outline of this claim in the early part of the book makes a formulaic use of the special jargon of poststructuralist theory, a jargon that will be impenetrable to any biologist not possessed of a considerable education in literary theory. But the biologist should persist, because the central chapters on "Genetic Codes in the 1950s" and "Writing Genetic Codes in the 1960s" present a compelling case for the ways in which the purely theoretical analysis of DNA as a code led to the determinative experiments that demonstrated the mechanism by which amino acid sequences are specified and constructed.

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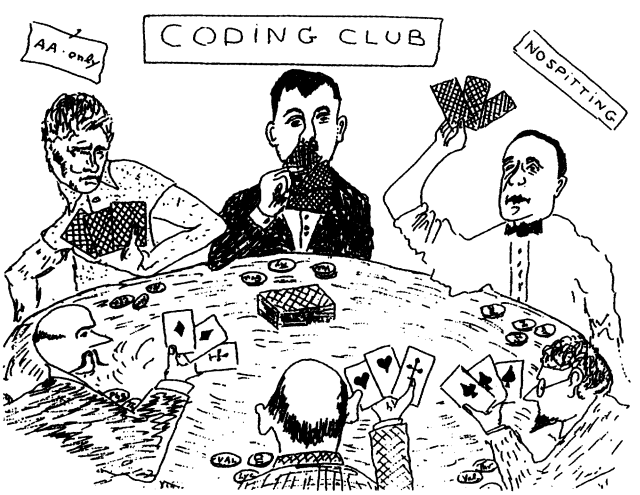
**Decoding club.** Gamow established his RNA Tie Club to facilitate communication among a group of physicists, chemists, mathematicians, and biologists who were drawn to the coding problem. Along with their tie, each of the 20 members had a tiepin carrying the abbreviation of an amino acid. Crick (Tyr), Rich (Arg), Orgel (Thr), and Watson (Pro) posed (left to right) for this photograph circa 1955.

Many biologists in the late 1950s (I among them) regarded with a certain contemptuous hauteur the attempts of renegade physicists to illumine the relation between gene and protein by engaging in the sort of cryptanalysis that became so romantic as a result of the wartime triumphs of Bletchley Park. But Kay shows quite convincingly that, although these code-breaking techniques could not in themselves provide the right answer, the view of DNA as code and amino acid sequence as plaintext was absolutely essential in the very conception of the critical experiments at the beginning of the 1960s. The brilliant paper by Crick, Barnett, Brenner, and Watts-Tobin, which demonstrated so elegantly that the DNA sequence was processed from a fixed starting point using each successive non-overlapping triplet to determine the next amino acid in the chain, and Nirenberg and Matthaei's path-breaking demonstration that poly-U RNA in an in vitro synthetic system resulted in the construction of a polypeptide consisting solely of phenylalanine, would have been conceptually impossible without the metaphor of the code. This, then, raises the problem of the counter-factual conditional that plagues all attempts to understand history: What if? What would have happened had the language metaphor never taken hold in molecular genetics? Would we now be ignorant of the details of the relation between DNA and protein? Would we have a different understanding? Would we know more about the world? or less?

Some contradictions surface in Kay's attitude toward the metaphors. At first, "code" always appears in inverted commas, but as the argument proceeds Kay herself uses the concept of code unproblematically. While claiming that we cannot really dispense with metaphors, she herself tries to do so by repeatedly saying that the DNA triplet–amino acid relation is merely a correlation. But that is surely wrong. DNA and amino acid sequences are not simply correlated, they are connected by a causal mechanism. And in the causal pathway, DNA sequence appears before the amino acid sequence.

A good deal of discussion in the book is devoted to showing why the metaphors of "code," "language," and "information" can be so misleading if taken as isomorphic with the phenomena of molecular genetics. This is especially a problem if these nonbiological notions are taken in their modern analytic and scientific contexts. If "information" is the information of Shannon-Weaver information measures; if "language" is what Jakobson, Chomsky, and other linguists take it to be; if "code" is what the Enigma machine was meant to




**Club games.** In Gamow's drawing of the "card game of life" played by members of the RNA Tie Club, the four suits represent the four nucleotide bases and poker chips serve as amino acids.

CREDIT: (TOP) ALEXANDER RICH; (BOTTOM) GAMOW PAPERS, MANUSCRIPT DIVISION, LIBRARY OF CONGRESS

create; then as Kay so clearly shows, we are badly misled by applying these measures to DNA. But, as she says, "code," "language," and "information" are themselves metaphors, terms appropriated by science and technology and given special content for special purposes. For an old-fashioned epistemologist, to say that DNA contains determinative information about amino acid sequences is simply to say that a knowledge of the DNA sequence is sufficient to provide knowledge of the amino acid sequence but not vice versa. The best way to protect ourselves against the damage of metaphors is to allow the models on which they are based to have as little specific content as possible while still allowing them to serve a constructive purpose. As Arturo Rosenblueth and Norbert Wiener once noted, "The price of metaphor is eternal vigilance."

The real damage done by the idea of DNA as "The Book of Life" is laid out in the last chapters of Kay's book. It is the elevation of DNA to the status of a master molecule, one which determines in some autonomous way the very nature of living organisms. The erroneous description of DNA as "self-replicating," as "making" proteins, and as "determining" organisms is repeated over and over in service of the hegemony of the gene. But DNA is not self-replicating any more than a letter put into a photocopier is self-replicating. DNA sequence does not specify protein, but only the amino acid sequence. The protein is one of a number of minimum free-energy foldings of the same amino acid chain, and the cellular milieu together with the translation process influences which of these foldings occurs. (Even Kay sometimes writes "protein" when she means "amino acid sequence.") And organisms are not determined by their DNA but by an interaction of genes and the environment, modified by random cellular events. Kay ascribes most of the fetishism of DNA as the ultimate information on which life is built to the tremendous prestige that technology acquired during World War II, to the immense amounts of money poured into biological research by technology-oriented government agencies, and to the impetus given to technology by the appearance of Sputnik. I would add that the notion of the primary role of the DNA "blueprint" and the merely mechanical, secondary role of the cell machinery that uses that blueprint for production is another form of the deep cultural prejudice (characteristic of modern capitalism) that mental labor is superior to mere physical labor, a prejudice that is replicated in the entire structure of laboratory life.

Biologists skeptical of the poststructuralist theories of a mere historian like Lily Kay might do well to consider the opinion of François Jacob on the matter:

> But science is enclosed in its explanatory system, and cannot escape from it. Today the world is message, codes and information. Tomorrow what analysis will break down our objects to reconstitute them in a new space? What new "Russian doll" will emerge? [*The Logic of Life*, (Pantheon, New York, 1973).]

But then again, what can you expect from a Frenchman?

BOOK REVIEWS: GENETICS

# Communication Breakdown?

**Sean B. Carroll**

> And it's whispered that soon
> If we all call the tune
> Then the piper will lead us to reason
> – *Led Zeppelin, "Stairway to Heaven"*

Framed by the rediscovery of Mendel's studies in 1900 and the determination of the sequence of the human genome in 2000, the 20th century, it can be argued, was "the century of the gene." Over its span, genetics rose from obscurity to form a cornerstone of evolutionary biology's Modern Synthesis, and the physical and chemical bases of inheritance and mutation were explained, the genetic code deciphered, the riddle of antibody diversity solved, a several hundred billion dollar industry born, and new tools invented that have revolutionized fields from forensic science to paleoanthropology.

**The Century of the Gene**
***by Evelyn Fox Keller***
Harvard University Press, Cambridge, MA, 2000. 190 pp. $22.95, £15.95. ISBN 0-674-00372-1.

Now seems a fitting time to look back upon this parade of great achievements and to ponder what the future may bring. In her new book, noted science historian Evelyn Fox Keller ventures in both directions; she covers a few highlights in the history of genetics and offers a bit of crystal ball–gazing. But *The Century of the Gene* is less a celebration of the triumphs of genetics than an appeal to biologists to shed their gene-centric mindset so as to usher in a new "Cambrian Period" of biological reason.

Keller explains that one major impetus for the book was "the call for functional genomics," a recent buzzword for the functional analysis of genes defined by genomic sequencing instead of classical genetics. In this new era, Keller sees "at least tacit acknowledgment of how large a gap between genetic 'information' and biological meaning really is" and "an acknowledgement of the limitations of the most extreme forms of reductionism that had earlier held sway." In a fairly short, very readable text, Keller develops the theme that both current genetic parlance and the reductionist approach are inadequate for explaining our expanding biological knowledge. She finds that they threaten to limit the future intellectual growth and public understanding of the discipline. And she suggests that new concepts, terms, and ways of thinking will be necessary to loosen the grip that genes have held on the imaginations of life scientists.

Keller perceives "ever-widening gaps between our starting assumptions and the actual data that the new molecular tools are now making available." For starters, she tackles no less than "the gene" as an outmoded term and concept. She alleges that the "prowess of new analytic techniques and the sheer weight of the findings they have enabled have brought the concept of the gene to the verge of collapse." Yet we are never really told which techniques and what mass of findings have precipitated this supposed crisis. To be sure, the analysis of eukaryotic genes has revealed that more structural features (introns, dispersed cis-regulatory elements, alternative splice sites) are involved in the regulation of the transcription and processing of RNA transcripts than for typical bacterial genes. And, in multicellular organisms, genes do encode products that function in more than one place and at more than one time (although pleiotropy, a perfectly well-understood term and concept, is not mentioned). But structural complexity or multifunctionality do not disable the term "gene" anymore than the range of architectural complexity or variety of uses of "buildings," from shacks to palaces, renders that noun obsolete.

"Genetic program" is another term that draws Keller's fire. She traces its origin to the pioneering work of Jacques Monod and François Jacob in the early 1960s, which extrapolated from the principles of enzyme induction in bacteria to metazoan development. Keller objects to the notion that there is a program contained within the genome. She rejects model descriptions such as a "genetic switching network" on the grounds that this phrase "harbors a potentially treacherous ambiguity" that fails to distinguish between genes as the source of the program

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