BOOKS: GENOMICS

A Private-Sector Perspective

Michael A. Goldman

In the introduction to this insider's review of the early years of the genomic revolution, Gary Zweiger recalls a guest lecture that Maynard Olson delivered to Stanford University's genetics department in the late 1980s:

> Olson used our attention-filled hour to drone on about a scheme to determine the nucleotide sequence of enormous segments of DNA.... The speech was a bore because it had to do with various laboratory devices, automation, and costs. He described technicians (or even graduate students) working on what amounted to an assembly line. He analyzed the costs per technician, as well as costs per base pair.... It all seemed so inelegant, even mindless.

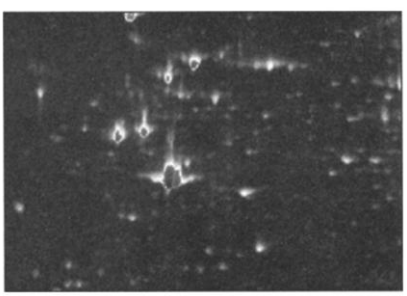
A few years earlier, I had fallen asleep while listening to Lee Hood give the same sort of forward-thinking talk. The idea of a brute-force, big-science sequencing project, which would produce reams of data we couldn't interpret, seemed as ridiculous in 1985 as Celera's shotgun method for sequencing the human genome seemed last year. Now, with the benefit of hindsight, we can look at the events leading up to this impressive achievement and consider the controversies surrounding it from a fresh perspective.

Transducing the Genome joins the rapidly growing list of books that seek to explain why genomics matters to researchers, the corporate world, and the general public. But this interesting account stands out in two ways: Zweiger views the genome sequencing efforts as a revolutionary convergence between biology and information science. And the author, formerly a scientist and executive with Incyte Genomics and now with Agilent, presents the story without the usual preconceptions that mark views from academe on the one hand and Celera on the other.

Transducing the Genome
Information, Anarchy, and Revolution in the Biomedical Sciences
by Gary Zweiger
McGraw-Hill, New York, 2001. 287 pp. $24.95. ISBN 0-07-136980-5.

Zweiger's explanations of the relevant concepts are usually clear, but some are confusing. For instance, he defines pharmacogenetics as the study of the effect of gene variants on drug response, and he casts pharmacogenomics as a large-scale study of drug effects on gene expression. But conventionally, the latter term is used for studies that simultaneously relate drug response to many gene variants—as in associations between single nucleotide polymorphism profiles and drug response. Because pharmacogenomics is so critical to industrial applications and may be one of the most obvious benefits of genome sequencing, it deserves a more precise treatment.

Although written long before the February 2001 publications in *Science* and *Nature*, Zweiger's description of the structure of the human genome rather accurately describes the findings they reported—an indication that the findings were really a quantitative increase in data that support a previously known picture rather than a radically new view. One point that he didn't anticipate was that humans appear to have fewer than 45,000 genes (he estimates upwards of 100,000), but this "fact" is probably premature.



Signature pattern. These spots from a 2D gel electrophoresis reflect the relative abundance of proteins in the source cells.

In the course of describing the race to sequence the human genome, Zweiger takes a perplexing detour into the idea of anarchy in science. After noting the free flow of ideas and materials between public and private sequencing efforts to discover genes and gene functions, he remarks that the youthful genomics industry received little guidance from "the laws of the land." He then jumps to consider whether anarchy is "an apt description of the social system in which genome discoveries have flourished." He distinguishes between a "maligned meaning" of the word ("disorder, chaos, or violence") and the absence of authoritative structure. But one is still left with the impression that he might believe anarchy is what we've got when patent law falls slightly behind.

The chaotic situation that Zweiger describes, however, does not seem that unusual. Since the scientific revolution, science has usually benefited from the absence of authoritative guidance. And to the extent that the development of genomics has been guided by National Institutes of Health grants panels, Zweiger points out the shortcomings of these efforts to steer research. Scouring the literature for the underpinnings of today's genomics industry, he weaves a nice story about fringe investigators in the 1960s who laboriously blotted random RNA and DNA samples on filter paper. Their approach didn't seem promising enough for federal funding at the time, but it eventually led to the conceptual basis for "gene chips" and modern gene expression profiling. The author also delights in telling us the history of Craig Venter's encounters with the more conservative scientific establishment. Marginalized by publicly funded science, Venter had no choice but to turn to corporate support. The irony of the response of public science to Venter's resulting for-profit motivation is clear. Time and again we see the loss of opportunities for revenue by a government science establishment too conservative to take the financial or political risks.

One of Zweiger's objectives is to tell us about the new fusion of information science and biology, but he does not establish that a revolution is currently upon us. He believes that the central dogma does not take account of complex gene interactions. This is not enough, however, to make the concept of a comprehensive sequence-based genome map revolutionary. Early in the 20th century, T. H. Morgan imagined a vast map of *Drosophila* genes; had he known DNA is the genetic material, he would have insisted on mapping with that level of accuracy. Nor are the ideas that multiple genes affect a trait and that interacting genes affect multiple traits revolutionary. These concepts were in the textbooks by the 1970s. The emphasis, to date, on single-gene science occurred not because we didn't think the broader picture was important, but because we didn't have the experimental and analytical techniques to tackle more complex interactions. Zweiger suggests that we are on the verge of a Kuhnian revolution that will replace the old paradigm of genetic determinism, but what he really describes in its place is poly-genetic determinism. What genomics has delivered is not a revolution but a sharp quantitative increase in our database.

In an informative appendix on the patent system, Zweiger clearly outlines the usefulness of, the conventional requirements for, and the procedures for obtaining patents. He repeatedly cites "the tragedy of the anticommons" (*1*), which holds that if too many parties have the patent rights to exclude other users, then there is no incentive left for anyone to develop a useful

The author is in the Department of Biology, San Francisco State University, San Francisco, CA 94132–1722, USA. E-mail: goldman@sfsu.edu

product. This argument is especially germane to discussions of the patentability of DNA sequences of unknown function. Because proprietary information and patenting have been very controversial aspects of genomics research, it is unfortunate that the author does not address these issues more directly.

For a new perspective on the scientific and commercial importance of genomics from an industry viewpoint, *Transducing the Genome* offers nonspecialists an excellent and enjoyable introduction. Readers interested in more history or requiring clarification of basic genome science will find Kevin Davies's account of the race for the human sequence (*2*) a good alternative. Nonetheless, just as there is still much to be learned from the human genome, there remains room for a thorough and analytical overview of the field.

References

1. A. M. Heller, R. S. Eisenberg, *Science* **280**, 698 (1998).
2. K. Davies, *Cracking the Genome* (Free Press, New York, 2001).

BOOKS: ECOLOGY

Beautiful Reef Builders

Stephen D. Cairns

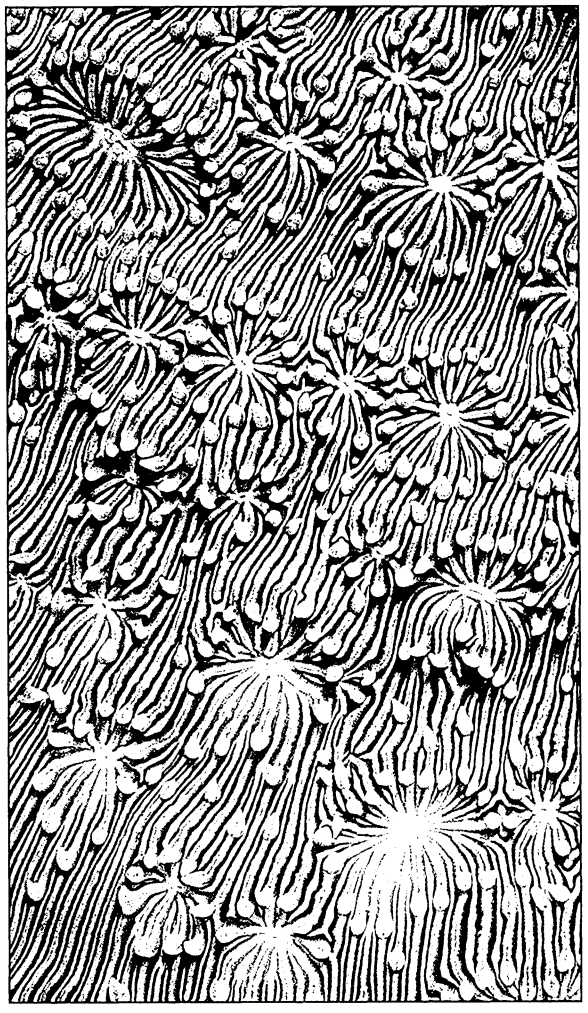
This three-volume set is the culmination and synthesis of 30 years of research by John Veron on the biology of reef corals (order Scleractinia), and it is a remarkable achievement. For the first time, all 795 known species of extant reef corals are treated in one publication. Every species is briefly described and compared with similar taxa. Species' distributions are depicted in thumbnail maps, and their colonies are illustrated in color. The remarkable aspect of *Corals of the World* is that Veron not only managed to obtain one to six in situ photographs of 790 species, but that these pictures are exquisite. They are supplemented with numerous shaded drawings and color paintings by Geoff Kelley, which beautifully and accurately illustrate the skeletal microarchitecture. And throughout the work, Veron and his editor, Mary Stafford-Smith, have scattered spectacular photographs—some covering two full pages—of coral reefs, coral assemblages, and simply stunning corals.

Corals of the World
by J. E. N. Veron

Australian Institute of Marine Science, Townsville, Queensland. 2000. 3 vols. 1410 pp. $175, $A265. ISBN 0-642-32236-8.

The author is in the Department of Systematic Biology–Invertebrate Zoology, National Museum of Natural History, Smithsonian Institution, Washington, DC 20560–0163, USA. E-mail: cairns.stephen@nmnh.si.edu

Veron begins with short introductions to observing corals, coral reef ecology, fossil corals, geological history, and coral morphology. The taxonomic accounts, which consume over 90% of the three volumes, describe the appearance, habitat, and distribution of each species. The author has previously described many new species of reef corals, and here he adds another 102 species and two genera to the world list (probably the largest number of new coral taxa ever introduced in a single publication). His taxonomic decisions increase the number of reef coral species by about 15%. Veron concludes with brief overviews of coral biogeography, the species concept in reef corals, and the evolution of coral species. Much of the material on these more academic topics has been abstracted from the author's earlier book *Corals in Space and Time* (University of New South Wales Press, Sydney, 1995). The third volume also includes an identification key to all genera and species of reef corals.



Colonies without walls. In members of the family Agariciidae, such as this *Pavona explanulata* from Australia's Great Barrier Reef, walls between the loosely packed polyps are poorly defined and prominent septa are continuous between adjacent corallites.

CREDIT: J. E. N. VERON/AUSTRALIAN INSTITUTE OF MARINE SCIENCE

Although lavishly illustrated and a pleasure to browse, the work has some technical faults. The title *Corals of the World* implies that Veron surveys all species of stony corals, but he has largely restricted his attention to the stony corals with symbiotic algae, which are primarily inhabitants of modern shallow-water reefs. These zooxanthellate scleractinians constitute only about 50% of the stony coral species. The author only briefly alludes to the azooxanthellate taxa, of which over 650 species occur in deep or cold waters. Second, the new species that Veron names here are not validly described according to the International Code of Zoological Nomenclature, because type specimens are not designated for any of them. For each new species, the author simply includes a reference to a forthcoming monograph. But it is nomenclaturally awkward to have created so many nomina nuda, which will become valid only in a subsequent publication. Finally, Veron's brief lists of selected taxonomic references (and, occasionally, identification guides) are no substitute for good synonymies—complete lists of the names that have previously been applied to each species. He states his aversion to synonymies; he believes they are likely to "include 'fuzzy' species boundaries and thus...arbitrary decisions." But in their absence, it is impossible to know what he has done with all the junior synonyms. As a result, Veron's recognition of species in this work is one of taxonomic fiat.

Thus, the audience for *Corals of the World* is probably not the taxonomic purist. Nonetheless, the book will certainly appeal to a wide range of readers: anyone with an eye for beauty in nature, marine biologists and divers, and those that strive to identify living reef corals. Indeed, Veron states early on that the work is intended to facilitate the identification of corals in their underwater habitats. In a broader sense, as noted in an advertisement for the book, it is for "all who appreciate the beauty of coral reefs and who want to know more about the organisms that build them." Even as a taxonomic purist, I can value that.