Book Reviews

The Recombinant DNA Debate

The Ultimate Experiment. Man-Made Evolution. NICHOLAS WADE. Walker, New York, 1977. x, 162 pp. $8.95.

Biohazard. MICHAEL ROGERS. Knopf, New York, 1977. xiv, 210 pp. $8.95.

Playing God. Genetic Engineering and the Manipulation of Life. JUNE GOODFIELD. Random House, New York, 1977. xvi, 220 pp. $8.95.

The controversy over research involving recombinant DNA molecules in vitro is a major and continuing event, which will undoubtedly provide legitimate employment for historians and philosophers of science for many years to come. With various bills now making their way to the floor of the House and Senate, the appearance of these three books is timely. Their analyses of the early stages of the debate are exemplary for their lucidity and accuracy.

The "recombinant DNA" story will be familiar to readers of *Science*, who will have followed it through Nicholas Wade's score or so of articles. His book draws this material together and presents a crisp narrative for the lay reader: the nature of the biochemical techniques; the excitement of the basic questions to which these techniques may hold the key; the conceivable hazards and potential practical benefits; the self-imposed moratorium, leading to Asilomar and the National Institutes of Health guidelines; the passage of the debate from within the scientific community into the arena of local and federal politics. Wade's book is the only one of the three to possess the twin virtues of a bibliography and an index.

Michael Rogers covers essentially the same ground, but at somewhat greater length and with a much more vivid writing style. His application to cover the Asilomar conference for *Rolling Stone* was initially unsuccessful. After winning the 1974 AAAS Westinghouse Science Writing Award, he gained a last-minute press space and went on to write an insightful piece that was, I think, the best account of that meeting. Rogers presents the science colorfully yet accurately. One minor transgression, which I mention in the obligatory spirit of reviewer's one-upness, is an occasional confusion between plasmids (tiny circlets of bacterial DNA) and bacteriophages (viruses that infect bacteria). Rogers is a keen and sensitive observer of people; through his eyes "science becomes more humorous, scientists more human, portrayed with the freshness of Norman Mailer's *Of a Fire on the Moon*, but without the oppressive egotism" (*1*).

June Goodfield's account is the most personal. Reviewing the three books elsewhere, Goodell (*1*) has characterized Wade's as a superhighway and Rogers's as a scenic tour, while Goodfield's is a "complicated rotary intersection, a book spinning with ideas." Compared to the other two books, Goodfield's account ranges a bit more widely (touching, for example, on cell fusion and on "test tube babies") and is more unevenly paced as a result of its emphasis on the author's own experiences and reflections. Thus instead of an abstract description of the biochemical techniques whereby DNA molecules are snipped apart and spliced together, Goodfield describes her difficulties and excitements in actually performing such an experiment in the laboratory, thereby giving the reader a much more immediate sense of what is going on. The first half is headed The Science and the Scientists; the second half, The Scientists and Society, becomes more philosophical. Goodfield does not hesitate to raise questions to which she has no answer. If one quotation may capture the engaging honesty of this second part of the book it is, "The problem is that it is so hard to produce a *rational* argument for one's moral qualms about DNA research" (p. 169, Goodfield's italics).

One of Goodfield's themes is that "the scientific profession has a relationship with society quite unlike that of any of the other professions" (p. 78). In professions such as medicine, she argues, services are provided to a client, who engages in a contractual relationship with the physician. The scientist, on the other hand, is seen as taking funds from a disinterested society to pursue his interests whither they will, with no accountability. Goodfield feels that these times are passing and that the recent DNA controversy reflects a more general need for scientists to explain and justify their work to the larger society that finances it. Although this opinion is widely held, I think it is an overly simple view, both of science and of the medical and other professions. It is increasingly apparent that the overall system of health care in the United States is complexly governed by the medical profession itself, which is in the curious position of effectively regulating both demand and supply. Conversely, scientists have had to justify their claims for support in a world that was competitive even when the federal money flowed freely and that is harshly competitive today (to cite a possibly extreme example, only about 20 percent of NSF grant applications in chemistry are successful). Nor does the federal support for basic science derive from a Medici-like patronage of the intellectual enterprise; rather it stems from the realization, born of World War II experience, that basic researchers are a national resource, bringing practical results. A detailed study (*2*), for example, has suggested that technical innovations that are directly attributable to advances in knowledge are "second only to labor supply increases as a major source of economic growth over both short and long periods since 1929." Admittedly, Goodfield's attention is focused more on ethical than on financial accountability, but the latter is relevant.

All three books end their story sometime before last summer. Again, most readers of *Science* will be familiar with the subsequent events: the growing body of experimental results, including documentation that shows that "nature has been conducting experiments prohibited under the NIH guidelines" (*3*); the mainly reassuring message coming from the group convened in June in Falmouth, Massachusetts, to evaluate the current evidence and to plan further experiments aimed at quantitative risk assessment (*4*); the endorsement of the general approach embodied in the NIH guidelines by "the leaders, and in some cases the full membership, of more than two dozen scientific groups with some 500,000 members" (*5*); the withdrawal of the Kennedy bill, which would have created a new federal bureaucracy and which had a general air of regulating some inherently criminal activity.

The surprising thing is that all three books are confined almost entirely to the

U.S. scene, and narrowly to the history of the recombinant DNA controversy as such. It would seem that any treatment of the larger issues, such as is attempted by Goodfield, would need to grapple with a lot of other questions. Why has there been no analogous public dispute in other countries? Why have other potentially biohazardous areas of research not come under attack? How does this controversy relate, if at all, to other public movements, such as that to legitimize laetrile?

It may be argued that the public debate in the United States simply reflects the superior virtues of its decentralized, participatory political system. But consider what happened in Britain. First, the Ashby Committee considered general questions; then the Williams Committee formed guidelines; finally the latter committee in turn withered away and gave place to a body to administer the rules. Although I think the British guidelines are technically inferior to the NIH ones (they freely trade one level of physical containment against one level of biological containment, which seems odd when one step in physical containment offers nothing like so large a safety factor as the step EK1 to EK2, and is moreover subject to large variations depending on the experimenter), they have the advantage of governing all equally. In contrast, the NIH guidelines in the first instance governed only those people whose work was funded by the NIH. The combination of intense discussion of the need for and the form of the guidelines and the initial limitation of their applicability to one kind of government-sponsored research, with no restrictions on private ventures, seems tailor-made to provoke just the sort of efforts toward local regulation that have occurred, and that still might lead to an anarchic patchwork of local ordinances.

Drawing attention to inconsistencies in public reaction, James Watson has observed that work on tumor viruses is considerably more dangerous than anything involving recombinant DNA is likely to be. The same could be said of research on various slow viruses and of other areas of biomedical research (*6*). The NIH guidelines ban some experiments lest they help pathogens acquire resistance to antibiotics, yet this process is probably facilitated by the practice of feeding antibiotics to pigs, cattle, and fowl. Although banned elsewhere for years, this practice has elicited little outcry in the United States, and only under Donald Kennedy's leadership has the Food and Drug Administration moved to stop it. More remarkable is the absence of excitement about, or even significant attention to, conventional research on infectious viruses and bacteria. Work on such pathogens is carried out under guidelines promulgated by the Center for Disease Control; the various levels of physical containment specified in these regulations provide the basis for the corresponding parts of the NIH guidelines. This work on known pathogens involves the same sort of people as work on recombinant DNA, and the regulations are largely self-enforced, without bureaucratic oversight or draconian sanctions. Consistency would seem to require assuming either that recombinant DNA researchers will behave as honorably as conventional microbiologists or that both sets of people need to be watched night and day. Rogers, however, is the only author to give significant attention to the parallels with the situation of the CDC guidelines. Part of the reason recombinant DNA research has been singled out may be that it offers a tool for the direct exploration of questions in human genetics. This has made it an item on the agenda of organizations (*7*) such as Science for the People, a well-intentioned group ("some of my best friends . . .") noted both for its apparent view that all research on human genetics should be abandoned because it is liable to perversion to ugly political ends and for its stridency in public debate.

As anyone who has attended a public meeting on this subject knows, another thread that runs through the discussion is a wistful, whiggish longing for an arcadian past (*8*). The complexities and anomies of the modern world oppress many people, and the recombinant DNA issue is a fine metaphor for these wider ills. Sometimes this thread unravels into a vague vitalism ("the evolutionary wisdom of millions of years"[*9*]), at other times it assumes darker shades of outright anti-intellectualism. One is reminded afresh that the issues debated between Huxley and Wilberforce, settled over a century ago in Europe, still are alive in the United States (*10*). The title of Goodfield's book is unfortunate.

All these factors roil together to make sober discussion difficult. It would help if the technical worries about health hazards could be clearly separated from the larger philosophical questions of the use and abuse of knowledge. The former pertain specifically to this issue, at this time, in this place; the latter arise not only in science but in all areas of human inquiry, at all times, in all places. Moreover, while public health questions are amenable to regulation, the larger issues are not; indeed, Lewis Thomas has argued (*11*) that the main justification for basic research in the life sciences is the hope that it may produce the self-understanding and "wisdom which our kind of culture must acquire for its survival." Wade thinks that the distinction has usually been made: "the controls imposed on gene splicing have been justified solely by concern for safety and not by any ideological consideration" (p. 153). I think that the question is more subtle and that much of the public discussion at every level has blurred these distinctions, often invoking safety as an argument of convenience in support of conclusions reached on ideological grounds.

In this fog, it is easy to lose sight of the fact that the entire recombinant DNA fracas was born of a unique act of social responsibility on the part of the scientists involved, when they voluntarily halted their work and tried to evaluate its potential risks to public health. The later "feckless debate which has offered outlets for anti-intellectualism and opportunity for political misbehavior while making dreadful inroads on the energies of the most productive scientists in the field" (*12*) has created a climate in which it is hard for people to continue to evaluate the risks in a dispassionate manner. Yet there remain technical questions that need to be answered in the light of evolving experimental knowledge (*13*), and related technical questions of potential risk will undoubtedly arise in other fields of biological research. It is important that members of the scientific community continue to address these questions, without putting on the white or black hats—"for" or "against"—that the news media keep thrusting upon them. It is crucial for all of us that the thoughtful and precautionary spirit that led to Asilomar be kept alive.

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References and Notes

1. R. Goodell, *Washington Post*, 11 September 1977, p. E1; reprinted in *Manchester Guardian Weekly*, 2 October 1977, p. 18.
2. W. D. Nordhaus, in *Research and Development in the Federal Budget*, D. I. Phillips, C. C. Cleare, M. Patterson, Eds. (AAAS, Washington, D.C., 1977). Specifically, according to E. Denison as quoted by Nordhaus, the percentage contributions to economic growth in the United States over the span 1948–1969 are 36 percent from labor supply increases, 34 percent from advances in knowledge, and 22 percent from increases in capital stock, leaving 8 percent in all other categories.
3. L. P. Elwell and S. Falkow, *The Sciences* **17**, 8 (1977); see also C. L. Gyles, S. Palchaudhuri, W. K. Maas, *Science* **198**, 198 (1977).
4. P. H. Abelson, *Science* **197**, 721 (1977); R. Curtiss III, letter to D. Frederickson, director of the

National Institutes of Health, 12 April 1977.
5. *Chronicle of Higher Education*, 1 August 1977.
6. Recommendations for the Conduct of Research with Biohazardous Materials at Princeton University, 6 December 1976; Report to the Canadian Medical Research Council, from its Ad Hoc Committee on Guidelines for Handling Recombinant DNA Molecules and Animal Viruses and Cells, January 1977.
7. In their book *Who Should Play God?* (Delacorte, New York, 1977), T. Howard and J. Rifkin, of the People's Business Commission, put recombinant DNA research squarely in the tradition of "Eugenics: The ideology behind genetics research" (chapter 2). They see this tradition running from Victorian England through Nazi Germany to modern genetics research.
8. See, for example, the proceedings of the March 1977 National Academy of Sciences forum, *Research with Recombinant DNA* (National Academy of Sciences, Washington, D.C., 1977).
9. E. Chargaff, *Science* **192**, 938 (1976).
10. Support for this statement is given in correspondence under the heading "Evolution and Education" in *Science* **187**, 389 (1975).
11. L. Thomas, *Daedalus* **106**, 163 (1977).
12. P. Handler, in his annual report to the National Academy of Sciences; reprinted in *Chem. Eng. News* **55** (No. 19), 3 (1977).
13. See, for example, the questions raised about the spread of "nontransmissible" plasmids from *Escherichia coli* K-12 to other host bacteria within the gut: B. R. Levin and F. M. Stewart, *Science* **196**, 218 (1977).

A Phyletic Analysis

The Origin and Early Evolution of Animals. EARL D. HANSON. Wesleyan University Press, Middletown, Conn., 1977. x, 670 pp., illus. $35.

The origins of self-replicating living systems, of eukaryotic cells, and of multicellularity were pivotal events that profoundly affected the whole subsequent course of organic evolution. Hanson's opus focuses on the origin and evolution of unicellular and simpler multicellular animals, organisms that progressively lost crucial biosynthetic capabilities while evolving the ability to ingest organic compounds and other organisms to meet their material and energy needs.

This book primarily expands and elaborates on two earlier papers by the author. Hanson's goal is "the elucidation of evolutionary history and of the biological innovations that have emerged within the course of that historical development." His approach is to develop objective methods of evaluating the phyletic informational content of extant organisms, to examine and analyze the surviving descendants of supposed primitive animals within as rigorous a phylogenetic framework as possible, and to infer the major evolutionary trends leading particularly to the modern protozoans, sponges, cnidarians, and flatworms.

The origin and phylogeny of the simpler multicellular animals present a set of old and perhaps unanswerable questions that continue to evoke interest, largely because pertinent evidence continues to accumulate. How does Hanson's book stand in presenting new relevant facts, original theory, incisive analysis, and critical synthesis? Are new trails blazed through forests of phylogenetic trees? Are any phylogenetic hedges pleasingly pruned?

Most of the descriptive factual material derives from standard monographs on protozoology and invertebrate zoology. The book must have been inordinately long in production, because the review of original literature largely ends at 1971, unfortunately missing a number of subsequent studies relevant to the author's arguments. Examples are documentation of the presence of syncytial digestive tissue in acoel flatworms and of one cilium per cell in some pseudocoelomate worms (E. N. Kozloff, *Trans. Am. Microsc. Soc.* **91**, 556 [1972]; R. M. Rieger *et al.*, *Zool. Scr.* **3**, 219 [1974]). And photoreceptor ultrastructure, a subject of extensive comparative analysis and controversy regarding its phyletic importance in lower metazoan groups over the last decade, is totally ignored.

Because its theoretical content also derives entirely from earlier studies (perhaps all possible ideas of the origin and early evolution of animals have already been proposed), the success of the book depends on the quality of its critical synthesis. This rests on: (i) Hanson's concept of the *seme*, the unit of phylogenetic information; (ii) adoption of Remane's criteria for detecting homologies; and (iii) a primarily cladistic approach, following Hennig, emphasizing the branch points of evolutionary trees over other aspects of change in time.

"A seme is an information-containing entity in an interbreeding population of organisms, but it will be most commonly used in reference to a structural or functional part of an organism, starting at the molecular level" (p. 89). A list of phyletically important structural, functional, developmental, and molecular semes is provided. Lack of information often precludes the use of more than a few. In each phyletic analysis where knowledge is judged adequate, Hanson employs about 12 semes. Examples are size, shape, and symmetry, feeding and digestive apparatus, skeletal structure, and pattern of ontogeny. All semes used are weighted equally. Each is coded as a qualitative multistate character, and an original generalized distance measure (R) is calculated from them. The value of R for a pair of taxonomic units increases with the number of neosemes (n; new character states) and aposemes (a; derived character states) and decreases with the number of plesiosemes (p; shared, primitive character states) according to the weighting indicated in the formula

$$R = [-p + (2a)^2 + (3n)^2]/t + 1$$

where t is the total number of semes compared. This measure is operationally defined, but arbitrary. The author's arguments would have been strengthened by comparison with other possible weightings and with unweighted methods and by comparison, and particularly demonstrated congruence, with other distance functions used in such analyses (discussed at length in Sneath and Sokal's *Numerical Taxonomy*, Freeman, 1973).

Hanson considers available knowledge adequate to permit determination of R values only within acantharian and ciliate Protozoa and turbellarian flatworms. Relationships between taxa generally regarded as classes and phyla are of necessity less rigorously presented. Hanson reiterates his earlier conviction that the turbellarian flatworm arose by cellularization of a ciliate. The sponges and cnidarians are derived from zooflagellates by colony formation and considered evolutionary dead ends. The evidence supporting these theories remains only as strong as in the earlier literature.

Hanson adheres rigorously to Remane's strong, objective criteria for determining homology, less so to Hennig's criteria of cladistic relationships. For example, "synapomorphy" (similarity because of shared, derived character states) is important in Hennig's methodology but does not enter the formula for R.

The three components of Hanson's synthesis listed above all have merit. His original contribution, the seme concept, guides selection of phylogenetically relevant characters. As Hanson points out, Remane's criteria of homology and Hennig's of cladistic relationships can be blended into a more inclusive theory and methodology for phyletic analysis. However, in my opinion these are more thoroughly treated by Sneath and Sokal in *Numerical Taxonomy*, evidently published after the completion of Hanson's manuscript, for it is not cited.

Hanson's general approach does clarify and increase objectivity in phyletic analysis, and it emphasizes the total biology of the organisms. However, the data base has not permitted a major breakthrough in our level of understanding the third evolutionary milestone.

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