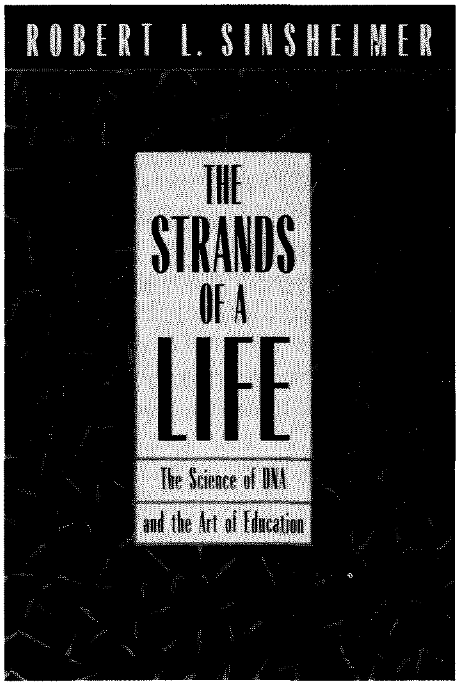
# Books




**University of California Press, 1994**
**$30.00**
**318 pages**

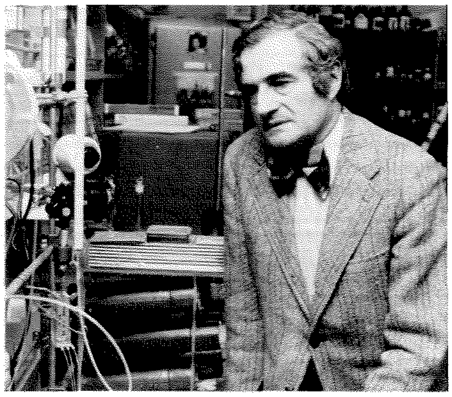
**by Clyde A. Hutchison III**

This autobiography of Robert L. Sinsheimer is the latest in the Science Book Series commissioned by the Alfred P. Sloan Foundation to foster public understanding of science. It will, of course, be of particular interest to readers of *Engineering & Science* because Sinsheimer spent 20 years at Caltech as professor of biophysics (from 1957 to 1977), and as chairman of the Division of Biology (1968–1977). It will also be of value to those concerned with the roots of molecular genetics. Sinsheimer's research on the bacterial virus $\phi$X174 (known affectionately as $\phi$X) pioneered many of the approaches we take for granted today. The book chronicles his contributions to science and to education, eloquently presents his philosophical viewpoint on these endeavors, and gives some glimpses into personal factors that have shaped a uniquely creative and productive career.

Sinsheimer describes his research on $\phi$X as "the centerpiece of my scientific career." The best known result of those studies was the discovery that the DNA of this virus is single-stranded, announced in 1959 in a startling paper in the first issue of *The Journal of Molecular Biology*. At the time, the discovery was as astonishing as "finding a unicorn in the ruminant section of the zoo." It is not, however, the unusual characteristics of $\phi$X, but rather the universally applicable features of the research that constitute his enduring legacy.

"Initially, we had only the rudimentary knowledge that $\phi$X was probably small and could grow in certain strains of *E. coli*. At the end of our research, we knew the complete sequence of its DNA and the details of its genetic structure . . ."

$\phi$X was selected as a research subject because of preliminary evidence that it was very small, even for a virus. In Sinsheimer's hands $\phi$X was the first bacterial virus to be purified to chemical homogeneity. Consequently, its DNA was the first viral DNA available in pure form for detailed physical and chemical analysis. This gave $\phi$X a unique position, which persisted for some 20 years, at the forefront in the development of molecular genetics. Many of the fundamental tools to link genetics and DNA chemistry were established using $\phi$X as the model of choice, first in Sinsheimer's lab at Caltech and then elsewhere, as $\phi$X and people trained to use it migrated around the globe. At Caltech, Fiers and Sinsheimer provided the first demonstration of a covalently closed circular DNA molecule—$\phi$X, of course. In Fred Sanger's laboratory in Cambridge, the $\phi$X genome was the first DNA to be completely sequenced. In 1978, the year after Sinsheimer decided to close his laboratory to accept the position as chancellor of the University of California at Santa Cruz, the first oligonucleotide-mediated, site-directed mutagenesis experiment was published, again using $\phi$X. The $\phi$X genetic system was ideal for this crucial step in the emergence of the new field of protein engineering. It is hard to overestimate Sinsheimer's central role in the birth of molecular genetics—through his establishment of the $\phi$X system, the many important



**Robert Sinsheimer in 1974, when he was chairman of the Division of Biology.**

discoveries made in his laboratory, and his influence on the many scientists that he trained.

I was particularly intrigued by the descriptions of the non-$\phi$X facets of Sinsheimer's scientific career and educational background. For example, his work during World War II on radar at the Radiation Laboratory at MIT occupies more space than the $\phi$X story. This early experience with "Big Science," before his graduate studies, stimulated his role in initiating the organized effort to sequence the human genome some 40 years later. I was also happy to have my memory refreshed concerning his fundamental contributions to nucleotide chemistry and the effects of radiation on nucleic acids.

When it was announced in 1968 that Robert Sinsheimer would become chairman of the Division of Biology at Caltech, those of us working in his laboratory were taken completely by surprise. He had previously appeared to be single-mindedly devoted to his research and teaching, with no apparent interest in administrative matters. In the mid-1970s when he publicly advocated a very cautious stance with respect to possible hazards of recombinant DNA research, I was even more puzzled. It was no surprise that he had a deep interest in the impact of modern biology on society. But his earlier writings, beginning in 1967, had seemed to view the prospect of mankind taking charge of evolution in a more positive light. By 1977 when he accepted the chancellorship at Santa Cruz, I was beyond being surprised. One reason I was eager to read *The Strands of a Life* stemmed from the hope of gaining some insight into these unexpected career transitions. It remains a bit mysterious, but I certainly learned a lot of interesting things about the circumstances of these events—about half the book is devoted to the Santa Cruz years.

One thing that comes clearly through the whole book is his love and respect for the scientific endeavor, only intensified by his encounters with the political arena of university administration:

> "Unlike anthropologists or economists, authors or poets, theologians or politicians, we natural scientists have the luxury of a single truth. There is only one proton mass, one periodic table, one genetic code. In consequence, science, during my career, has been essentially egalitarian. Nature is the only source of ultimate authority. Before nature, a world outside of man, a reality independent of human design or desire, we are all equal."

He concludes: ". . . I would love to return in a century or two to see where science stands and to learn what questions they are asking in the Sinsheimer Laboratory [at UC Santa Cruz]." When the technology to realize this dream becomes available, he certainly deserves to be high on the waiting list.

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