ROBERT L. SINSHEIMER—
A Concerned Biologist

At Caltech, and in all of science we have been, in a sense, children, spewing change into society with scant thought for the consequence. We in science are growing up now. Our toys become more potent. The little games we play with nature are for great stakes, and their outcome moves the whole social structure. We must accept our responsibility.

With these prophetic words Robert Sinsheimer, professor of biophysics and chairman of the division of biology since 1968, concluded his talk, "The End of the Beginning," at Caltech's 75th Anniversary Conference—Scientific Progress and Human Values—on October 26, 1966. A landmark speech at the conference, it summed up what is a dominant and recurring theme with Bob Sinsheimer: that a scientist is accountable to the society of which he is a part not only for seeking out knowledge but for doing so thoughtfully, humanely, and with due regard for possible consequences.

In a sense, the talk was a turning point in the life of Robert Louis Sinsheimer—or at least in some of his colleagues' views of him. Ray Owen, professor of biology and chairman of the division from 1961 to 1968, recalls having recommended that Sinsheimer be asked to make the speech; and he dates an accelerating change in Sinsheimer's outlook from that time. "The degree to which he's changed over the past few years is amazing," Owen says. "When he first came to Caltech, I saw him as a highly specialized kind of biophysical scientist. He was—and still is—a very guarded, thoughtful, and self-critical person, and much of his concern for social, moral, and ethical problems simply didn't show then."

Whatever the significance of "The End of the Beginning" in Sinsheimer's career, it was a moving statement of his philosophy. ("His way with words is almost Isaian," says Owen.)

Robert Sinsheimer was born in Washington, D. C., in 1920, but he grew up in Chicago. He was the second of three brothers and somewhat removed from both of them—from the older by a gap of six years in age, and from the younger by very different interests. Always an excellent student, he was eventually in a number of advanced classes in school, and handled some of the problems that went with being ahead of his age group scholastically by finding outside interests. For about a year he attended classes at the Chicago Art Institute ("My hand-eye coordination was inadequate for the artistic expression standards of the time."), and he did extensive reading. Some of the books that impressed him belonged to his older brother, who was attending the University of Chicago by the time Bob was in high school. *The Science of Life* by H. G. Wells, Julian Huxley, and G. P. Wells made him realize for the first time that one could talk about living processes in scientific terms.

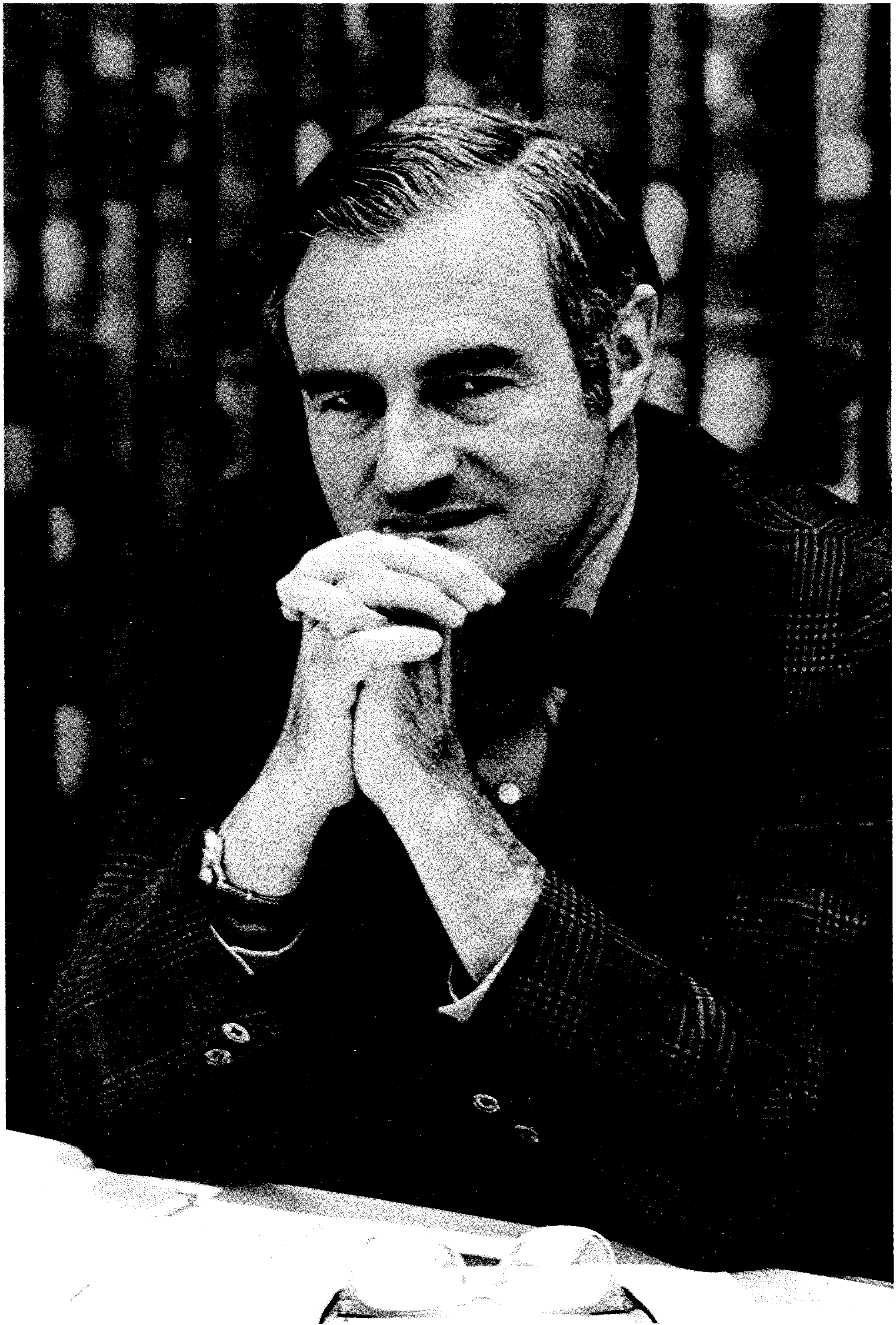
He went in for sports—particularly tennis and golf. He was captain of his high school chess team, which won the city championship. During the summers of 1933 and 1934, he spent a lot of time at the Chicago World's Fair—a good deal of it, predictably, in the Hall of Science. By the time he graduated from high school in 1936, he knew definitely that he wanted to go into science.

Sinsheimer had been stimulated by an excellent high high school chemistry teacher, and he wanted to become a chemist. But there had never been a scientist in the family, and his father didn't see how anyone could hope to make a living being one. In the depression economy of the thirties this judgment was a potent deterrent. When he enrolled at MIT, Sinsheimer designated chemical engineering as his option—a compromise between his real interests and practicality.

At that time all freshmen at MIT took the same basic course, so it was not until he was a sophomore and actually introduced to chemical engineering that Sinsheimer realized it was not for him. Quite coincidentally, just at that time MIT was overhauling its old, public-health-oriented biology curriculum. In a manner unique for the time, the new approach to biology was biology combined with physics—and it looked fascinating to Sinsheimer. Fascinating is just what it turned out to be. He happily remembers taking a course in atomic physics one hour and human physiology the next, and delighting in the mental agility it took to leap from one subject—and one mode of thought—to the other.

"There is an enormous difference," he says, "between learning how something works, theoretically, and the kind of diagnostic thinking it takes to find out why something is not working. In physics you end up reading a meter or adjusting something. In biology you end up with a complicated set of slides to try to make sense out of. You have to ask yourself what kind of measurements you should make to give yourself a clue to what is wrong."

MIT's new biology course took five years, so Bob Sinsheimer received his SB in 1941. His SM was awarded



The imminent intrusion of biological engineering in human life makes you question every value you have.

in 1942, just as World War II broke out, which made the problem of what to do next fairly simple. He followed one of his professors into MIT's Radiation Laboratory and spent the next four years designing and testing airborne radar—a lot of it actually in planes or at military airports. He recalls the job as socially isolated, restrictive, anomalous, and not very interesting. The bright spot of those years was his marriage in 1943 to Joan Hirsch.

Deciding what field of biology to study after the war took a good deal of thought, but he finally made what he calls a "good guess about what would turn out to be important"—research on nucleic acid. With PhD in hand, in 1948 he became a research assistant at MIT for a postdoctoral year, meanwhile looking around for a permanent job, which turned out to be a firsthand learning experience in some of the problems associated with being a pioneer. No university seemed to be offering molecular biology or biophysics, so Bob Sinsheimer had to find a school that wanted to hire an innovator. He finally went to the physics department at Iowa State College—and spent the next eight years in a frustrating attempt to build a biophysics program there.

George Hammond, chairman of Caltech's division of chemistry and chemical engineering, has known Sinsheimer since they were both junior faculty members at Iowa State more than 20 years ago, and he considers him "one of a handful of people who can legitimately be called a scientific pioneer . . . Even as a physicist at Iowa State he did things that physicists weren't supposed to have anything to do with.

"When Sinsheimer talks about the philosophy or the future of science," Hammond says, "he shows enormous imagination—and his mode of expression is truly poetic. Yet, at the same time, he is something of a scientific puritan about what constitutes intellectually decent scientific activity. For instance, I think some of the environmental research doesn't excite him very much—at least as science."

At Iowa State, Sinsheimer continued his personal research on nucleic acids, but largely in the chemistry and physics of the subject—the photochemistry of nucleic acids and their components, for example. Eventually, to make further progress, he had to do some biological work on a bacterial virus. The exciting place to do this, in 1953, was at Caltech with Max Delbrück, and the six-month leave of absence Sinsheimer spent here then as a senior research fellow greatly enhanced his understanding of genetics. (He is also appreciative of Delbrück's successful efforts to have this appointment funded—something that various restrictions at Iowa State made impossible.)

"Back at Iowa after that experience I really felt isolated from many aspects of life," Sinsheimer recalls, "and it continued to be literally impossible to get a sensible program in biology going there. So, when the opportunity to come to Caltech permanently arose, making the change should have been easier than it turned out to be. Academically and scientifically there was no question, but for eight years we had made our lives up out of other people, and they were very hard to leave."

At Caltech in 1957 and working for the first time permanently in a biology department—and with a good deal of the basic work in purifying the virus Phi X 174 already accomplished at Iowa—Sinsheimer's research began to move more quickly. He found then (and, according to his graduate students, still finds) that work always goes more slowly than he anticipates. What he is trying to do is to understand viral growth in molecular terms, and he is making progress.

In 1967, using methods developed by Sinsheimer, Arthur Kornberg and Mehran Goulian at Stanford succeeded in making a perfect copy of the DNA of the natural virus Phi X 174—the virus Sinsheimer had isolated and purified back in the late 1950's. Kornberg and Goulian made a number of versions of their synthetic DNA and shipped each one to Sinsheimer so he could test its ability to replicate the complete virus. The final version displays the full biological activity of natural DNA in living organisms; it can infect bacteria and reproduce itself just as the natural virus does.

This is probably as close as anyone has yet come to creating life in the laboratory, and the news media reported it widely. The research was, in President Johnson's words, "an awesome accomplishment." Sinsheimer, however, deplores the oversimplified view the public often gets of DNA research. "Scientists don't really understand the basic processes yet," he says. However, in 1968 at The Far Reach of Science symposiums sponsored by Caltech and *Life* magazine, Sinsheimer did say that this century is likely to be the one in which, for the first time, a living creature will understand its origin.

"We are the heirs of Icarus," he said. "We have become the latter-day Prometheus. But even in the ancient myths men were men and the gods were gods, and man could not rise above his nature to chart his destiny. Now we can begin to confront that chance and choice; soon we shall have the power consciously to alter our inheritance, our very nature. Not even the Greeks had a word for DNA."

The words for Sinsheimer in 1968 were "in demand," and he began getting offers of administrative positions outside Caltech. "How much he was tempted to accept any of them I'm not sure," Owen recalls, "but I wanted out of the biology chairmanship, and I wanted to hold onto Bob against outside enticement. I always felt that the last successful move a division chairman could make would be to arrange for the smooth succession of someone who wanted the job and would be acceptable to the rest of the division. And this worked out perfectly with Sinsheimer."

As a division chairman, Sinsheimer turned out to be "an extraordinarily gifted administrator—wise in the vision of future needs and very sensitive at the same time to the personal needs of the person for whom he was responsible," according to Robert Edgar, now provost of Kresge College of UC Santa Cruz and formerly professor of biology at Caltech.

Sinsheimer's one-word summary of the job of the division chairman is "endless." Though he has reduced the size of the research group he supervises and has a new executive officer to assist him in the administrative work of the division, time (or the lack of it) is still a major problem in his life. He is constantly torn between feeling obliged to accept administrative jobs—both at the Institute and for national committees and organizations—and personal preference for study, research, and leisure to think. He is, for instance, a member of the council of the National Academy of Sciences and recently completed a term as president of the Biophysical Society. "I'm asked to do things outside my immediate sphere," he says, "and I usually end up saying yes more than I probably should."

The results are, of course, continuous dilemmas and choices—alleviated somewhat by his ability to plan ahead. Geraldine Cranmer, secretary to the last three biology division chairmen, testifies to Sinsheimer's sense of organization. "Whatever needs his immediate attention gets it," she says, "and we never have last-minute mad rushes to meet deadlines."

Under Sinsheimer's chairmanship the major thrust of the biology division is in behavioral biology—that is, in trying to understand how the central nervous system functions and how this in turn affects and is responsible for behavior. He sees the advances that are being made in molecular biology as containing within them the potential for large medical advances, and he feels this is something Caltech should be involved in. He also thinks there are great potentials in the application of advanced forms of engineering and systems analysis to medical problems. He would like to see biology develop a more extensive interaction with engineering and information science than it has had in the past, and he suggests that systems analysis also has major contributions to make to the understanding of basic biology. After all, he points out, when you talk about biological components, you talk about systems—the nervous system, the endocrine system, the vascular system, for instance—and their full understanding really requires applications of systems analysis.

"I think there could be a kind of engineering that was derived from biology," he says, "in much the same fashion as it has traditionally been derived from physics at Caltech. In fact, I think it would be sensible—looking ahead 50 years—for biology and biological applications to come to occupy a significantly larger portion of the total activities of the Institute."

Right now a problem that is occupying a lot of Sinsheimer time and thought is how to do a better job of combining education in science and technology with humanities. "We get very intelligent students here," he says, "and we don't damage them too much. We give them a good technical education, but many of them come out untrained to think in areas where value judgments enter in. I think it's our responsibility to try to do something about that. And somehow the teachers in the sciences have to get involved in it; we can't leave it all up to those in humanities."

Something about which Sinsheimer has very deep convictions indeed is that of the imminent intrusion of biological engineering in human life and the gravity of its moral implications. "It's coming on us," he says, "and it makes you question every value you have. Everywhere we are suffering the consequences of the thoughtless introduction of new knowledge and technology into our society, and many of those consequences are grievous and becoming more so. With similar lack of forethought, the consequences of the introduction of the knowledge that is at hand in biology and psychology can be disastrous. It's equally disastrous to take the attitude that we can stop where we are. We have to make a responsible choice about the extent to which we want to design our existence."

He was, of course, saying just that back in 1966 at the 75th Anniversary Conference:

> *After two billion years this is the end of the beginning. It would seem clear, to some achingly clear, that the world, the society, and the man of the future will be far different from that we know. Man is becoming free, not only from the external tyrannies and caprice of toil and famine and disease, but from the very internal constraints of our animal inheritance, our physical frailties, our emotional anachronisms, our intellectual limits. We must hope for the responsibility and the wisdom and the nobility of spirit to match this ultimate freedom. . . . We must ask that the changes we introduce be orderly and with humanity aforethought.*

—Jacquelyn Hershey