PASADENA REVISITED

by WARREN WEAVER

IT WAS THIRTY-NINE years and a few months ago that a young assistant professor of mathematics walked into the entrance of the main building of Throop College, stepped up to the desk of the college book store (which was then just to the left of the entrance), and asked the attendant what textbook was to be used in calculus. She said, perfectly reasonably, "I would suggest that you wait until tomorrow and ask that question of your teacher." I must, at that moment, have looked very young and green.

Life in those days for the fledgling professor was rather different from what I imagine it is now.

Physically speaking, Throop College consisted of the chemistry building now known as the Gates Laboratory, the central building now known as Throop Hall, and a few assorted sheds spotted around in the rear. Will Lacey had joined the staff the year before, Stuart Bates two years before, Howard Lucas three years before. Earnest Watson was to come the next year.

There are not many of us left of that vintage. Linus Pauling was a senior in high school that year, and George Beadle, if I calculate correctly, had just graduated with honors from the seventh grade. Biology at CIT was, at that moment, not even a gleam in father's eye.

In the basic sciences, there then were, of professorial rank, one in physics, two in mathematics, and three in chemistry. We were so small in numbers that faculty meetings were held in President Scherer's office—a small room which has now become part of President DuBridge's present office. But it was entirely clear, even at that early moment, that something strange and wonderful was astir here.

"Pasadena Revisited" has been adapted from a talk presented at the dedication of the Norman W. Church Laboratory of Chemical Biology, November 15, 1956. Mr. Weaver, who is now vice president for the Natural and Medical Sciences of the Rockefeller Foundation in New York, was assistant professor of mathematics at Caltech from 1917 to 1920.

We had an early and clear vision of a new and special sort of institute which would be intellectually compact; which would be imaginative, flexible, and superb in quality; which would be dedicated not to size or noise or to the routine levels of technological training, but rather to outstanding quality and to the supreme adventure of advancing basic knowledge about nature.

Most important of all, we had the leadership that could not only dream such dreams, but could turn them into reality. I count it one of the great good fortunes of my life that I had the privilege of knowing Dr. Millikan, Dr. Noyes, and Dr. Hale. It is a tradition of American academic life to speak with deserved reverence about Mark Hopkins at one end of a log and a student at the other. When, a hundred years from now, there is talk about the development in this country of graduate education in science, I suspect there will be even more frequent reference to those three unselfish and inspired men who created and made manifest the concept of this great institution.

It may have occurred to some of you that I have, at this point, created a dilemma of explanation. If this institution, just then at its chrysalis stage, presented so challenging and so attractive an opportunity, why didn't I stay here?

I could claim that I never have officially left. For I treasure a handwritten letter from Dr. Millikan in which he said that he couldn't restrain me from leaving, but that the Institute could and did refuse to accept my resignation; that I would continue indefinitely to be a member of the faculty, and that I needed only to inform them when I wished to return. I have, on several occasions, warned Lee DuBridge and the trustees that I still hold this document.

But the real reason for my departure is one that Caltech people can understand. I went back to Wisconsin, and then to the Rockefeller Foundation, because Max Mason asked me to. I am sure that there are many persons here who have fallen under Max's spell, and who realize just why I have considered it one of the major joys and excitements of my life to be a friend and a working colleague of Max Mason. The more detailed reason for the shift to the Rockefeller Foundation is, moreover, closely related to our proper subject here.

For Max Mason and I, although both trained in the physical sciences, shared an enthusiasm for the biological sciences, and both had certain articles of faith and conviction concerning the interrelationship of the biological and physical sciences. It seemed clear that the century from 1825 to 1925—the century from Ampère and Oersted to Einstein and Schrödinger, from the first laws of the electric current and of electromagnetism to relativity and quantum theory—had been a great century of upsurge for the physical sciences. One was not so foolish as to think that this rate of progress would necessarily decrease; but it was surely evident that the physical sciences had developed a tremendous momentum; that support for the physical sciences was in general assured from federal, industrial, and other sources; and that, perhaps most important of all, our knowledge of physical laws and our capacity to control physical nature were advanced far beyond our knowledge of the mechanisms of behavior of the living creatures who held all this power in their fumbling hands.

It also seemed evident that the physical sciences—chemistry most notably, but physics and mathematics as well—had developed many experimental procedures and many techniques of theoretical analysis which could undoubtedly be applied with profit to biological problems —and which had, as yet, not been generally so applied.

Thus it was our shared privilege to help develop, in the Rockefeller Foundation, a program which, though labeled "Modern Experimental Biology," was in essence a program of attack on basic biological problems using all the theoretical and experimental armament of the physical sciences, it being of course absolutely essential that this effort be dominated by the biological viewpoint —by a constant recognition of the essential complexity, the essential subtlety, and the essential wholeness of living organisms.

Merger of the sciences

When one compares the status today of the interrelationship of the physical and the biological sciences with what the situation was 25 years ago, the change is substantial. It would of course be ridiculous to suggest that the Rockefeller Foundation is in any large measure responsible for this change. But one may, I think, take reasonable satisfaction in the fact that we were privileged, over that period, to give modest aid to many of the productive scientists who have done the real work.

Some early aspects of this development occurred in Europe, with the Bohr-Hevesy-Krogh-Rehberg group in Denmark; the Kluyver-Ornstein-Milatz group in Holland; with Astbury, and later the Randall group in England; with the Hammarsten-Svedberg-Tiselius-Theorell-Caspersson-Engstrom galaxy in Sweden; with the organic chemists devoted to natural substances, the enzyme chemists, the biochemical geneticists, the physical chemists concerned with macromolecules, the X-ray crystallographers, the virus experts, the submicroscopic anatomists—one cannot even hint at the range and excitement of the old fields which were brought to new life, and of the new fields which were opened up.

Rather than attempt any detailed technical discussion I would like to suggest in rather general terms what has been involved in this grand merger of the physical and biological sciences.

It would be entirely unfair to the great record of biology to intimate that it suddenly got smart, some quarter of a century ago. The earliest Italian anatomists realized the importance of, and bravely served, the experimental method. The bewildering variety of plant and animal life clearly made it necessary for biology, over long patient years, to describe, to classify, and to invent unambiguous terminology. A knowledge of form naturally precedes a knowledge of function—and an *explanation* of function quite inevitably comes later. The systematic and morphological approach to the living world has led to great triumphs of insight and interpretation, as illustrated by the theory of evolution itself.

A new viewpoint

But it remains true that the time had now come when biological phenomena could be analyzed on a new and more detailed and deeper level. To a great extent this resulted from the growing and releasing intellectual conviction that vital processes were not necessarily and inescapably mysterious, that one did not need to speak in terms of an *élan vital*, that the happenings in a cell and eventually even important aspects of the behavior of man are analyzable, are understandable, are describable, in the same sort of dependable and precise terms that has served so well for the atom and the star.

To an important extent, also, this new viewpoint was made feasible by a variety of new experimental techniques. I will speak of these, in general terms, under the heading of *new ways of seeing* and *new ways of separating*.

Until the microscope was invented, some 350 years ago, man had to observe nature only with his unaided eyes. Until the turn of the present century, there occurred only improvements in the power of the optical microscope, finally resulting in the fact that today one can usefully examine in that way objects whose dimensions are as small as about one-half a micron—that is to say, about five one hundred thousandths of a centimeter. But this is, for inescapable theoretical reasons, about as small as one can usefully see with ordinary light: and this leaves totally unexplored the world of the smallest bacteria, the still smaller animal viruses, and the still, still smaller plant viruses, to say nothing of the macromolecules, the molecules, and even the atoms with which the modern biologist must deal.

Ultraviolet microscopy has helped materially, as has phase contrast and fluorescent microscopy. But it was the electron microscope, a quite new device developed by the physicists, which decreased the size of observable objects by a factor of 100 or even, under specially favorable circumstances, by a factor of 500.

New kinds of seeing

Even this, however, is but a small part of the gain we have made in seeing. For there are new *kinds* of seeing—methods which are broadly analogous to seeing because they reveal the details of form and structure, and which are often better than ordinary seeing because they also give some evidence concerning constitution. There is the whole range of methods in ultraviolet and infrared spectroscopy, and the newer magnetic resonance methods, which give information about the details of chemical structure and about the mechanisms of chemical reactions. There are the cytochemical methods which permit the exploration of the detailed chemical organization within single cells. There are—which should be mentioned with special pride and emphasis here at CIT—the methods of X-ray and electron diffraction, which permit examination and analysis down to the actual level of individual atoms.

Coupled with these new ways of *seeing*, there are powerful new ways of separating. From one point of view any living organism—a single-celled protozoan as well as a man—is an almost incredibly and intolerably messy affair. It is a conglomeration of a vast number of exceedingly complicated substances and structures, all pretty thoroughly interdependent (which is almost a defining characteristic of an organism), and all thoroughly and subtly mixed up. To an old-fashioned physicist, used to a few variables and six-figure accuracy, or to an old-fashioned inorganic chemist, used to the purity of crystalline compounds, a bit of living protoplasm is more or less a shovel-full of guck.

So it has been of the greatest value that there have emerged, over the last quarter or third of a century, new and delicate methods of separating, out of messy mixtures, components which are relatively homogenous and thus suitable for study. The ultra-centrifuge of Svedborg, and the electrophoresis apparatus of Tiselius; column chromatography, to which Professor Zechmeister here at CIT contributed in so critically important a way, and the powerful later developments of paper chromatography; the newer Tiselius methods of charged carbon and starch; the Moore-Stein refinements in experimental procedures; counter-current methods; the employment of enzymes to break up and deliver desired fragments of molecules, the use of specially trained microorganisms which can report the presence or absence, in a messy mixture, of certain substances: all these are, in a broad sense, separation tools, most of which the physical sciences have furnished to the biologist.

This problem of separation is a very special one with biological material. On the one hand the chemical details of an organism may be very delicately characteristic. There are, for example, sub-species of snails that are so completely alike in all their morphological characteristics that not even the leading world experts can tell them apart. Yet one of these two sub-species is an intermediate host for the parasite which causes schistosomiasis, whereas the other is not. And these two sub-species do differ in certain details of their internal chemistry, and one can be told from the other by chromatographic techniques. There are of course numerous other instances in which biochemistry furnishes the only satisfactory discrimination between creatures which, on ordinary taxonomic criteria, are alike.

On the other hand, it is one of the remaining mysteries of biology that a vast variety of mixed-up material may be fed into an organism without in any way disturbing the basic and massive fact that this organism keeps on, so to speak, being itself. As Walter de la Mare remarked in "Peacock Pie":

"It's a very odd thing—
As odd as can be—
That whatever Miss T eats
Turns into Miss T."

In addition to these new methods of seeing and new ways of separating, there have been new ways of measuring. Perhaps most important of all, there has been a developing sense of active intellectual unity and comradeship between all the sciences, and a healthy emphasis on problems rather than on the compartments of the classical disciplines.

A fruitful union

I wish finally to relate the present situation at CIT to these remarks about the new partnership between the physical and the biological sciences: and I think that it should be clear to you that I have, up to now, been talking of the play without mentioning Hamlet. For in the fruitful union of chemistry and biology, the California Institute of Technology stands quite clearly in the very front rank. Nowhere else in the world, at least to the best of my knowledge, is there combined leadership such as is furnished here by George Beadle and Linus Pauling.

The wonderful new laboratory which is now being dedicated represents an act of inspired and unselfish faith on the part of the donor. It is a structure which, intellectually speaking, rests on a solid foundation of past and proved performance. It will, we are all confident, reach up into new heights of future activity.

To the Trustees, to the Associates, and to the Administration of CIT I say that it is your great opportunity and your great duty to see to it that there is kept preserved here the vision of Millikan, Noyes, and Hale.

Your heritage from the past is clear. Your faithfulness to that heritage has been superb. It is up to you to keep CIT compact, flexible, and imaginative. It is up to you to continue your marvelous record of providing a climate for leadership.