ESSAYS ON SCIENCE AND SOCIETY

A Life in Science

H. Gobind Khorana

I have met people who believed they knew at a very young age what they wanted to do in their lives. I envied them, but my own life was not like that. At age 18, when I sought admission to the Punjab University in Lahore, I applied to two departments, English Literature and the honors course in Chemistry. Admission into the latter was restricted and required an interview. My shyness kept me from the interview, but they saved a place for me anyway, and thus I became a chemist. At the end of World War II, I was awarded a studentship by the Government of India to study insecticides and fungicides in England. However, the Indian High Commissioner's office in London could only get me admitted into the Chemistry Department at Liverpool University, and I began to study Organic Chemistry. After I received my Ph.D. in 1948, I was eager to spend some time in a German-speaking part of Europe, and I managed to do this at the Eidgenössische Technische Hochschule in Zurich, Switzerland. I worked with Vladimir Prelog. He was inspiring and so was the institute, with its long tradition of excellence in organic chemistry. I spent a great deal of time studying the German chemical literature. It was then that I came across Fritz Zetzsche's work on carbodiimides. Serendipitously, carbodiimides became important in my synthetic work later.

After a year in Switzerland, I returned to India. However, in the aftermath of partition of my province, Punjab, I could not find a job. In fact, many of my old friends and teachers were now refugees in Delhi without jobs. Fortunately, a postdoctoral fellowship in Alexander Todd's laboratory in Cambridge (England) turned up, for work on peptides related to the newly discovered adrenocorticotropic hormone. Cambridge was a uniquely exciting place at that time. Todd's own work was at the climactic point of defining the chemical structures of the nucleic acids. Frederick Sanger was sequencing insulin, the first protein to be so tackled. At the Cavendish laboratory, Max Perutz and John Kendrew were embarked on the first x-ray structures of myoglobin and hemoglobin, and soon the Watson-Crick structure for DNA was to emerge from the same laboratory. Molecular biology was in the making.

At the end of 1952, the offer of a nonacademic research job took me to Vancouver, British Columbia. The scientific stimulation I had received in Cambridge sustained me in the first years in Vancouver. My first aim was to use carbodiimides in the synthesis of nucleotide coenzymes and related compounds. Biochemistry was experiencing its golden age in elucidating metabolic pathways and the biosynthesis of macromolecules. At almost every turn, new nucleotidic cofactors were being discovered. I also began to work on the synthesis of short oligonucleotides with precise chemical linkages as in DNA. I hoped that, in analogy with the synthesis of peptides started by Fischer in the early 20th century, this work could be significant.

In retrospect, my success in applying carbodiimides to the synthesis of nucleotides of interest to biochemists came astonishingly rapidly. The methods I developed attracted attention, and a number of established biochemists began to visit my small emerging group during the summers. In 1956, Arthur Kornberg and Paul Berg's visit provided my first intimate exposure to biochemistry and biochemical thinking. I decided to spend some time in Kornberg's laboratory to learn the practice of biochemistry from this great master. In the subsequent years, work in my laboratory became increasingly interdisciplinary.

The one gene–one enzyme hypothesis of Beadle and Tatum in 1941 had been important in christening the field of molecular genetics. By the early 1950s, genes were shown to be made up of nucleic acids. Therefore, nucleic acids directed the synthesis of proteins. During the same period, an in vitro system for protein synthesis was developed, culminating in 1961 in the electrifying experiment by Nirenberg that demonstrated the synthesis of polyphenylalanine under the direction of polyuridylate. Subsequently, biochemistry took the center stage in further definitive work on the genetic code. The most exciting experiments in my laboratory started with synthetic DNA polymers of defined nucleotide sequence and arrived at polypeptides of defined amino acid sequence. We prepared our high-molecular-weight DNA-like polymers by using short synthetic DNAs with specific sequences as templates for Kornberg's DNA polymerase. Fortuitously, reiterative copying resulted in size amplification and multiplication of the products.

The 1960s were the golden age of molecular biology. Scientists from a variety of disciplines came together and gave a unique momentum to the new field. However, many of my friends, with whom I had shared the most exciting period, felt that after the elucidation of the genetic code and the chemical basis of heredity, an era had ended. The new frontier had to be the brain. An exodus of scientists to neurobiology began. In my own work, I pursued the challenge I had posed in the late 1950s, namely, the total synthesis of genes. In the late 1960s, the necessity to amplify synthetic genes became clear and principles for their amplification, later rediscovered and named PCR, were worked out.

Making a radical switch in the mid-1970s, I became interested in biological membranes and in bacteriorhodopsin, the light-driven proton pump. This in turn led to interest in light transduction in the mammalian photoreceptor, rhodopsin, and in the photoreceptor cells in the retina. The transductions carried out by these cells—conversion of photons to chemical energy to drive biochemistry and conversion of chemical energy to electricity, the language of the brain—are extremely complex. This undertaking is very different from my earlier projects. In organochemical syntheses, the total synthesis of genes, and proton translocation by bacteriorhodopsin, I had been lucky to find answers at least in outline. In contrast, understanding of the sensory system, in particular, sensitization and desensitization, still lies far in the future.

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was born in 1922 in Raipur, Punjab, India (now Pakistan). He trained as an organic chemist, and was awarded the Nobel Prize for Physiology or Medicine in 1968, together with Robert W. Holley and Marshall W. Nirenberg, "for their interpretation of the genetic code and its function in protein synthesis."

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