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Special Issue Preface

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Biography of Harold A. Scheraga

Harold Scheraga was born in Brooklyn, New York, on October 18, 1921, and obtained his elementary and high school education, first in Monticello, New York, and then in Brooklyn. His undergraduate work was carried out at the City College of New York (1937−1941), with extensive training in Chemistry, Physics, and Mathematics, including research in the phase rule and in X-ray diffraction. With the aid of an Assistantship, he embarked on graduate work at Duke University in September 1941 to use electrical birefringence to determine anisotropic polarizabilities of organic molecules. He studied electrodynamics with Lothar Wolfgang Nordheim, atomic and molecular spectroscopy with Hertha Sponer, and quantum and statistical mechanics with Fritz London. With the attack on Pearl Harbor, and the entry of the U.S. into World War II, Harold divided his efforts between graduate research and work for the Air Force to develop a system to train the gunners in B-17 bombers to protect their aircraft against enemy fighter planes during bombing raids over Germany.

During this period, he married Miriam Kurnow, and completed his Ph.D. research in 1946, shortly after the birth of their first child, Judith. Later, Harold and Miriam had two more children, Debby and Danny, and all three children attended Cornell University. In subsequent years, they produced five grandchildren, Jonathan, Rebecca, Alexandra, Dana, and Jeffrey, all of whom have now finished college and are embarked on their own careers.

With a chance observation of a new book in the Chemistry library at Duke, *Peptides, Amino Acids, and Proteins*, by Edwin Cohn and John Edsall, with chapters by George Scatchard, Larry Oncley, and John Kirkwood, Harold was lured into Protein Physical Chemistry in 1946. With a one-year ACS postdoctoral fellowship, he worked with John Edsall in the Physical Chemistry Department at Harvard Medical School on flow birefringence experiments to determine the size and shape of an asymmetric blood plasma protein.

In 1947, Harold obtained a position as instructor in Chemistry at Cornell University, and spent his whole career there, with sabbatical leaves at the Carlsberg Laboratory in Copenhagen in 1956−57 with Kai Lindstrøm-Lang and at the Weizmann Institute in Israel in 1963 and in 1970, as a guest of Ephriam and Aharon Katzir and Michael Sela with collaboration also with Shneior Lifson. In alternate years in the 1970s, Harold was a visiting professor at the Weizmann Institute where he taught a course on the helix−coil transition. From 1960 to 1967, he served as Chairman of the Cornell Chemistry Department. In 1990, Harold taught a course on protein folding at the University of California in San Diego, as a guest of Murray Goodman. Since 1992, Harold has spent brief periods at the Scripps Research Institute in La Jolla, California, interacting with Charles Brooks, Jane Dyson, Jeffrey Skolnick, and Peter Wright.

In 1950, Harold was awarded his first research grant (from ONR) and, in subsequent years, he received both NIH and NSF grants to support his research in protein chemistry. His research initially involved experimental and theoretical studies of the size and shape of protein molecules. Simultaneously, he embarked on an experimental study of the mechanism of the thrombin-induced conversion of fibrinogen to fibrin, part of the blood clotting process, a subject on which he continued to work for many years.

With the publications of Sanger on the amino acid sequence of insulin and of Pauling on the α- and β-structures of the backbone of the protein molecule, Harold turned his attention to the helix−coil transition in polyamino acids and polynucleotides, and then to the interactions involving the side chains of proteins, initially to hydrogen bonding and subsequently to hydrophobic interactions. These studies focused on the role of these interactions in determining the three-dimensional structure and folding pathways of, first, bovine pancreatic ribonuclease A (RNase A) and, then, a ribonuclease homologue, onconase. The structural study of RNase A identified three Tyr···Asp interactions that motivated his development of a molecular mechanics approach to compute protein structure. Initially, a hard-sphere potential was used but this evolved into the more detailed all-atom force field, ECEPP (empirical conformational energy program for peptides), and later into a coarse-grained model and force field, UNRES (united residue).

The all-atom force field is now being used, together with density functional theory calculations, to use $^{13}C^{\alpha}$ chemical shifts to validate ensembles of NMR structures, and X-ray structures, and the UNRES force field is being applied to biological problems such as Aβ, PICK1, and Hsp 70 chaperones.

At age 90, Harold is continuing his active research career in developing and applying new approaches to provide an understanding of the intricacies of protein structure, dynamics, and reactivity.

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