Charles Tanford was born in Halle, Germany in 1921. He and his family left Germany in the 1930s and spent several years in England until immigrating to the United States in 1939. He attended New York University and graduated with honors in chemistry in 1943. He then went to Princeton University where he earned his M.A. in 1944 and his Ph.D. in 1947. His Ph.D. thesis was in physical chemistry and focused on the mechanism of combustion of gases in a burner flame, resulting in the “Tanford-Pease theory of burning velocity” (1). During his last year at Princeton, Tanford met Walter Kauzmann, a new assistant professor and protein physical chemist. Kauzmann, who had an infectious enthusiasm for proteins, introduced Tanford to Edwin J. Cohn and John T. Edsall’s treatise, *Proteins, Amino Acids and Peptides as Ions and Dipolar Ions* (2). Some of Cohn and Edsall’s work on the physical chemistry of proteins was the subject of a previous *Journal of Biological Chemistry* (JBC) Classic (3).

Soon Tanford found himself contemplating a career in protein research. “I had lucrative job offers from the industrial sector on the basis of my thesis,” recalls Tanford (4). “But the prospects of research into proteins, which I naively equated in my mind with some romantic notions, as a sort of physico-chemical exploration into the vast mysteries of life, outweighed any question of salary and I decided to join Cohn and Edsall’s laboratories if they had a place for me—which they did, as a ‘postdoc,’ with a stipend less than half of what I could have had in industry.”

Tanford worked with Cohn and Edsall at Harvard University Medical School for 2 years. He then became an assistant professor in physical chemistry at the State University of Iowa, where he remained for just over 10 years, being promoted to associate professor (1954) and then professor (1959). In 1960, Tanford joined the faculty of Duke University as a Professor of Physical Biochemistry and eventually became the James B. Duke Professor of Biochemistry (1970).

Shortly after arriving at Duke, Tanford became interested in hydrophobic interactions in proteins, thanks again to Kauzmann. At that time, most protein chemists believed that intramolecular hydrogen bonds provided the dominant energetic driving force for protein folding and that hydrogen bonds between amino acid side chains represented a significant
portion of that force. Tanford recalls, "Kauzmann made us realize that side-chain hydrogen bonds could not be energetically comparable with the hydrophobic force. To quote him directly: 'it does seem unlikely that hydrogen bonds other than those involving peptide linkages can make a major contribution to the stability of most native proteins'" (4).

Intrigued by this statement, Tanford began to investigate protein denaturation and the solubility of amino acids in various solutions. This is the subject of the two JBC Classics reprinted here. Tanford began by looking at the effects of aqueous urea (5, 6) and aqueous ethylene glycol solutions (7) on protein denaturation. He measured the solubility of amino acids and two glycine peptides in the various solutions and water and then calculated the free energies of transfer of amino acid side chains and backbone peptide units from water to the solutions. He and his colleague Yashuiko Nozaki repeated these experiments using guanidine hydrochloride, as reported in the first JBC Classic reprinted here. Nozaki was a superb experimentalist and long time research associate with Tanford first at Iowa and then at Duke. The pair discovered that guanidine hydrochloride and urea have similar solubilizing effects, but guanidine hydrochloride is 2 to 3 times more effective than urea at the same concentrations. They also concluded that urea solutions were better at solubilizing aromatic side chains, particularly phenylalanine and tyrosine groups, whereas guanidine hydrochloride solutions were especially powerful in solubilizing peptide units and histidine and glutamine side chains.

In the second JBC Classic reprinted here, Tanford and Nozaki extended the solubility experiments to include aqueous ethanol and dioxane solutions. The ethanol and dioxane experiments not only helped to provide a rational explanation for the ability of various solvent media to promote protein denaturation, but they also served a broader purpose: to provide a semiquantitative estimate of hydrophobic interactions inside a native protein molecule relative to the interaction of the same moieties when exposed to water. This estimate was possible because 100% ethanol could serve as a “model” for the hydrophobic conditions that exist inside a protein. From the results of these experiments they were able to construct a hydrophobicity scale for the amino acids, which measured the tendency of a particular side chain to be located in the interior of a native protein molecule. This work eventually led to Tanford’s publication of the book The Hydrophobic Effect in 1973.

In 1980, Tanford transferred to the Department of Physiology at Duke and became the James B. Duke Professor of Physiology. He retired in 1988. He now lives in England where he writes books about science for lay readers. His recent publications include Ben Franklin Stilled the Waves: An Informal History of Pouring Oil on Water with Reflections on the Ups and Downs of Scientific Life in General and Nature’s Robots: A History of Proteins.

In recognition of his contributions to science, Tanford has received many awards and honors including the Alexander von Humboldt prize (1984) and the American Society for Biochemistry and Molecular Biology’s Merck Award (1992). He is also a member of the American Academy of Arts and Sciences and the National Academy of Sciences. Tanford has served on the editorial boards of several journals, including that of the Journal of Biological Chemistry, and was the president of the Biophysical Society from 1979 to 1980.1

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1 Biographical information on Charles Tanford was taken from Ref. 4.
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