The author of this book holds a Chair in Biology at Florida Atlantic University and has been a longtime teacher of animal physiology. He has felt the need to provide some historical background on this subject especially for life science and medical students. This he has done (as stated in the Preface) by providing the "merest sketches" of the "origin and tortuous history of the science of biological function." These include "highlights of the evolution of the science of Biology" and a variety of topics that are of particular interest, and even amusement, to him.

The 20 chapters (most are about eight pages long) are organized mainly by historical period. Starting with the earliest cave art depictions of animals, this eminently readable and succinct survey ends with the atrocious abuse of physiology in the name of evolutionary genetics and social expression that reached its climax in the Holocaust during the Second World War of 1939–1945. A variety of interesting quotations and amusing (even bizarre) anecdotes maintain the attention of the reader. The four longest chapters (about twice the length of most) are those that deal with The Birth of Science (*i.e.* the 15th century), the Enlightenment (*i.e.* the 18th century), The Consolidation of Experimental Biology (*i.e.* the 19th century), and Physiology Abused (*i.e.* the 20th century). Because about one-third of the text pages are taken up by more than 100 black and white illustrations each chapter can be read surprisingly quickly. Some of these illustrations are also reproduced in color. An unnecessary duplication, at the end of the book, is the complete listing of all illustrations and their accompanying legends. Five pages of References and six of Index complete the contents.

The deep interest of the author in the history of science is reflected clearly in this attractive book. However, I could not help feeling that, because there is no indication of the current understanding of the scientific topics the author has selected, it will be most appreciated by readers who are already knowledgeable about experimental biology, human anatomy and physiology, and medicine. There is an excessive number of errors by the printer and several sentences that I found unintelligible. This said, the engaging simplicity of the presentation and the intriguing illustrative material make this sketch of the history of experimental biology accessible to a wide readership.

Frank Vella
18 Leyden Crescent, Saskatoon, Saskatchewan, Canada S7J 2S4

REFERENCE

[1] K. Maruyama (2002) β-Actinin, CapZ, Connectin and Titin: what's in a name? *Trends Biochem. Sci*. **27,** 264–266.

Nature's Robots: A History of Proteins
Tanford, C., Reynolds, J.; Oxford University Press, 2001, 304 pp., ISBN 019-850-4667, $27.50.

The authors justify their title, *Nature's Robots*, by noting that proteins and robots are both automatons that perform programmed functions. The objective of the authors is to inform contemporary protein scientists that their work rests on the shoulders of numerous predecessors; their book is designed to identify the pioneers (great and less great) and to define their achievements. The story begins in the mid-18th century when albumin, fibrin, and gelatin were recognized animal proteins, a century before the acceptance of the tetravalence of carbon championed by Kekulé. We learn that Jacob Berzelius (1779–1848), who was an organic chemist, and Gerrit Mulder (1802–1880), who practiced medicine and dabbled in chemistry, were responsible for the name protein, which means "standing in front."

The book consists of four parts, "Chemistry" Chapters 1–9, "Detailed structure" Chapters 10–13, "Physiological function" Chapters 14–19, and "How are proteins made?" Chapters 20–22. By 1900 the notion that proteins are built up mainly from amino acids was accepted; a table provides the dates of the discoveries of the amino acids found in proteins beginning with leucine in 1819 and culminating with threonine in 1936. It is a remarkable coincidence that the nature of the peptide bond was announced at the same meeting on the same day in 1902 by Franz Hofmeister (in the morning) and Emil Fischer (in the afternoon). The authors refer to the announcement of the peptide bond as a watershed; on a single day the development of the entire field was changed.

The authors describe the personalities and idiosyncrasies of many of the pioneers of protein science including Fischer. He obtained his Ph.D. under von Baeyer, "one of the most creative organic chemists of all time." von Baeyer, in turn, studied with Kekulé. Fischer received the Nobel Prize for his work on carbohydrates in 1902. However, his work on proteins, peptides, and the peptide bond also represent distinguished contributions. He coined the terms "peptide" and "polypeptide." Otto Warburg, one of the most influential biochemists of the 20th century, synthesized the first optically active peptides in Fischer's laboratory during the years 1903–1906.

During his prime, Fischer commanded an institute of 250 people in Berlin. Fischer's work on the enzymatic degradation of glycosides led to his famous "lock-and-key" hypothesis. Fischer emulated Baeyer's penchant for working at the bench but suffered for it. Fischer developed mercury poisoning after inhaling gaseous diethylmercury. He also suffered from long term poisoning from phenylhydrazine (a key reagent in carbohydrate chemistry). Moreover, Fischer grieved the losses of two sons (who were killed in battle); he committed suicide in 1919.

The nature of proteins as macromolecules or colloids was a debate that occupied scientists from 1920 to 1940. Colloid refers to an aggregate of lower molecular weight substances. Theodor Svedberg was an influential Swedish scientist who embraced initially the colloid hypothesis. Svedberg thought that the ultracentrifuge would reveal multiple boundaries from different components of "colloidal" hemoglobin. When the experiment was performed, however, a single moving boundary in a centrifugal field resulted; this outcome and Svedberg's conversion helped to turn the tide in favor of the macromolecule hypothesis. Other work showed that a single protein has multiple positive and negative charges; this result was a new and

unexpected finding at the time. Arne Tiselius, a pioneer protein scientist who trained with Svedberg, separated complex protein mixtures by electrophoresis.

The story of amino acid analyses begins with microbiological bioassays and progresses to the development of the ion-exchange column-based amino acid analyzer in the 1950s by William Stein and Stanford Moore at the Rockefeller Institute (now University; Moore's identification badge at scientific meetings read Rockefeller Institute long after its transition to University status). In the 1940s and 1950s, Fred Sanger worked out the amino acid sequence of bovine insulin. He performed this by partial acid hydrolysis (a procedure that was supplanted by Edman degradation). Sanger presented his preliminary results on the amino acid sequence at the 1st International Congress of Biochemistry in England (1949); he was told by those who attended his presentation that his experiment would never produce any positive results. After Sanger's watershed accomplishment, Stein and Moore determined the amino acid sequence of bovine ribonuclease, the first enzyme to be sequenced.

The authors describe the importance of hydrogen bonds, salt bridges, and hydrophobic interactions in determining the three-dimensional structure of a protein. The role of Linus Pauling in formulating the α-helix and β-sheet is described. Irving Langmuir formulated a theory of the hydrophobic bond. Langmuir studied the surface layers of organic chemicals at air-water interfaces; he received the Nobel prize for this work in 1932. For a while Langmuir supported Dorothy Wrinch's cyclol theory of protein structure, which was strongly opposed by J. D. Bernal, who favored the peptide bond hypothesis. A debate between Langmuir and Bernal (1938) prompted Langmuir to develop the notion of a hydrophobic interaction in determining the three-dimensional structure of proteins (conflict is the engine of progress). Langmuir soon withdrew his support of the cyclol theory, but Bernal became a champion of the hydrophobic effect. This is a case where Langmuir's correct idea (hydrophobic effect) came about by reasoning from an incorrect chemical structure (Wrinch's cyclol theory) claiming to explain the compact structure of proteins. Walter Kauzmann's role in describing the hydrophobic bond is chronicled, but the important role of Tanford in explaining the hydrophobic effect is not mentioned in the text or cited in the notes and references.

The authors describe the determination of the tertiary structures of hemoglobin by Max Perutz and myoglobin by John Kendrew using X-ray crystallography. They stood on the scientific shoulders of William and Laurence Bragg, William Astbury, J. D. Bernal, Dorothy Hodgkin, and others. Max Perutz emigrated from Austria to England in 1936 to work as a research student with Bernal. Perutz was considered an enemy alien in 1939 (as were all German and Austrian citizens). Perutz was interned on the Isle of Man and then in Canada. The British government, realizing the absurdity of this situation, released Perutz. He returned to Cambridge, England in 1941 where he took up defense work despite being an "enemy alien." At the end of the war, he returned to his x-ray studies and was joined by John Kendrew.

The authors indicate the great importance of the elucidation of the structure of myoglobin and hemoglobin. A surprising finding is that these molecules have irregular structures lacking symmetry. Furthermore, apolar groups occur in the interior, and charged groups occur on the surface of proteins. This points to the importance of bonds other than (Pauling's) hydrogen bonds in determining the three-dimensional structure of proteins. In 1962, Perutz and Kendrew received the Nobel prize for their work. Watson and Crick, from the same laboratory, and Maurice Wilkins received the Nobel prize the same year. The authors state that this "was an unprecedented triumph for a single laboratory" (a photo showing this group at the Nobel Prize ceremony in 1962 occurs on p. 225).

The subjects covered in the third part of the book ("Physiological function") include the role of antibodies in immunity, rhodopsin in vision, actin and myosin in muscle contraction, and the sodium pump in ion transport across cell membranes. The authors, who chose well studied proteins, provide clear and understandable explanations for these particular "robots."

In the third part, we learn that there was considerable resistance to the idea that enzymes were proteins; the influential Richard Willstater (who also trained with von Baeyer) argued against the idea of enzymes as proteins. The crystallization of jack bean urease by James B. Sumner and bovine pepsin by John H. Northrop led the way in providing such evidence. Sumner lost his left arm in an shooting accident as a young boy; such loss of a limb was a greater handicap for Sumner, because he was left-handed. He was discouraged from entering chemical research, but he persevered and proved himself at the laboratory bench. We learn that Sumner started his project at Cornell University with little equipment, sparse research funds, a single graduate assistant, and a heavy teaching load (lecture and laboratory courses in biochemistry for medical and home economics students, two advanced courses, and a seminar). His work, which started in 1917, culminated in a short paper in 1926. It was followed by 18 papers in the next six years. In contrast, Northrup, at the Rockefeller Institute, had no teaching duties and ample research support. Sumner accomplished his task with milligram amounts of scarce protein, but Northrup produced two kilograms of pepsin crystals during the course of his studies. These workers shared the Nobel Prize for their work in 1946.

The fourth part of the book considers the nature of the genetic material. It took many years for the scientific community to accept the notion that enzymes were proteins. Afterward, proteins were considered to be the workhorse of nature, a theme that recurs throughout this book. Later there was resistance to the idea that DNA was the genetic material because of the bias that proteins do all of the work. The elucidation of the structure of DNA by Watson and Crick initiated the new age of molecular biology. We are led through the discovery of messenger RNA and the elucidation of the genetic code.

Tanford and Reynolds, who made fundamental contributions to protein chemistry, are appropriate authors to produce this history. Their sources are cited in notes that accompany each chapter in this scholarly work. Although much research over the last 30 years focuses on nucleic

acids, with the elucidation of the primary structure of thousands of proteins inferred from the genetic code, we are a long way from understanding the function of a large fraction of these proteins. Many predict that the study of the levels and interactions of all proteins (proteomics) represent a important research objective. Moreover, pharmaceutical and biotechnology companies are developing proteins as medicines. Because of these trends, the authors contend that there will be an increasing need for protein chemists. Furthermore, they provide the relevant history and perspectives for current and future protein scientists. The book provides an understandable but penetrating account of the development of protein science. The text is at a level that can be understood readily by undergraduate students, as well as more experienced scholars.

Robert Roskoski, Jr.
Department of Biochemistry and Molecular Biology,
Louisiana State University Health Sciences Center,
New Orleans, Louisiana 70119