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978-0-521-88446-4 - Biological Thermodynamics, Second Edition
Donald T. Haynie
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Biological Thermodynamics

This inter-disciplinary guide to the thermodynamics of living organisms has been thoroughly revised and updated. Providing a uniquely integrated and notably current overview of the subject, the second edition retains the refreshingly readable style of the first edition and serves as an eminently useful introduction to the study of energy transformation in the life sciences. *Biological Thermodynamics* is a particularly accessible means for biology, biochemistry, and bioengineering undergraduate students to acquaint themselves with the physical dimension of their subject. Graduate students, too, will find the book useful. The emphasis throughout the text is on internalizing basic concepts and sharpening problem-solving skills. The mathematical difficulty increases gradually by chapter, but no calculus is required. Topics covered include energy and its transformation, the First and Second Laws of thermodynamics, the Gibbs free energy, statistical thermodynamics, binding equilibria, and reaction kinetics. Each chapter comprises numerous illustrative examples taken from different areas of biochemistry, as well as a broad range of exercises and references for further study.

Reviews of the first edition:

In my opinion, the author has covered a traditionally “boring field” with vivid description and interesting examples. My overall impression is that this book is comprehensive, illustrative and up-to-date ... and I would certainly recommend it to my students.

Professor Yigong Shi, Department of Molecular Biology,
Princeton University, USA

... an outstanding supplement to the treatment offered in most textbooks of biochemistry ... very rewarding for students majoring in biochemistry, biophysics, or biotechnology

Professor Frank Vella, Department of Biochemistry,
University of Saskatchewan, Canada

... a very readable and informed introduction to energy transformation at several levels of biological organization: molecules, cells, and multicellular organisms ... a good introduction to the new field of biological thermodynamics and represents an important contribution to the literature.

Dr. Lloyd Demetrius, Department of Organismic
and Evolutionary Biology, Harvard University, USA, and
Max Planck Institute for Molecular Genetics, Berlin, Germany

Don Haynie is the Co-Founder and Chief Scientist of Artificial Cell Technologies, Inc., Director of the Bionanosystems Engineering Laboratory and Research Professor of Biochemistry and Biophysics at Central Michigan University, and a Clinical Professor at the University of Connecticut School of Medicine. Former members of his research group are at Harvard Medical School, King's College London, Schering-Plough, and Pacific Nanotechnology. He has held academic appointments at The Johns Hopkins University, the University of Oxford, the University of Manchester Institute of Science and Technology, and Louisiana Tech University, in departments of biophysics, biomolecular sciences, biomedical engineering, chemistry, and physics. He has taught thermodynamics to biology, biochemistry, and engineering students world-wide.

Weblink to Don Haynie's site:
http: //www.biologicalthermodynamics.com.

Biological Thermodynamics

Second edition

Donald T. Haynie

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In memory of
BUD HERSCHEL

The trouble with simple things is that one must understand them very well

ANONYMOUS

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Preface to the second edition

Interest in the biological sciences has never been greater. Today, biology, biochemistry, biophysics, and bioengineering are engaging the minds of young people in the way that physics and chemistry did thirty, forty, and fifty years ago. There has been a massive shift in public opinion and in the allocation of resources for university-based research. Breakthroughs in genetics, cell biology, and medicine are transforming the way we live, from improving the quality of produce to eradicating disease; they are also stimulating pointed thinking about the origin and meaning of life. Growing awareness of the geometry of life, on length scales extending from an individual organism to a structural element of an individual macromolecule, has led to a reassessment of the principles of design in all the engineering disciplines, including computation. And a few decades after the first determination at atomic resolution of the structures of double-stranded DNA and proteins, it is becoming increasingly apparent that both thermodynamic and structural information are needed to gain a deep sense of the functional properties of biological macromolecules. Proteins, nature's own nanoscale machines, are providing inspiration for innovative and controlled manipulation of matter at the atomic scale.

This book is about the thermodynamics of living organisms. It was written primarily for undergraduate university students; mostly students of the biological sciences, but really for students of any area in science, engineering, or medicine. The book could serve as an introductory text for undergraduate students of chemistry or physics who are interested in biology, or for graduate students of biology or biochemistry who did their first degree in a different subject. The style and depth of presentation reflect my experience of learning thermodynamics as an undergraduate student, doing graduate-level research on protein thermodynamics at the Biocalorimetry Center at Johns Hopkins University, teaching thermodynamics to biochemistry undergraduates in the Department of Biomolecular Sciences at the University of Manchester Institute of Science and Technology and to pre-meds at Johns Hopkins, discussing thermodynamic properties of proteins with colleagues in the Oxford Centre for Molecular Sciences, and developing biomedical applications of nanofilms and nanowires in the Institute for Micromanufacturing and Center for Applied Physics Studies at Louisiana Tech University.

My sense is that an integrated approach to teaching this subject, where the principles of physical chemistry are presented not as a stand-alone course but as an aspect of biology, has both strengths and weaknesses. On the one hand, most biological science students prefer to encounter physical chemistry in the context of learning about living organisms, not in lectures designed for physical chemists. On the other hand, applications-only courses tend to obscure fundamental concepts. The treatment of thermodynamics one finds in general biochemistry textbooks compounds the difficulties, as the subject is usually treated separately, in a single chapter, with applications being touched on only here and there in the remainder of the text. Moreover, most general biochemistry texts are written by scientists who have little or no special training in thermodynamics, making a coherent and integrated presentation of the subject that much more difficult. A result is that many students of the biological sciences complete their undergraduate study with a shallow or fragmented knowledge of thermodynamics, arguably the most basic area of all the sciences and engineering. Indeed, many scientists would say that the Second Law of Thermodynamics is the most general idea in science and that energy is its most important concept.

It is hardly difficult to find compelling statements in support of this view. According to Albert Einstein, for example, "Classical thermodynamics . . . is the only physical theory of universal content concerning which I am convinced that, within the framework of applicability of its basic concepts, will never be overthrown." Einstein, a German–American physicist, lived 1879–1955. He was awarded the Nobel Prize in Physics in 1921 and described as "Man of the Century" by *Time* magazine in late 1999. Sir Arthur S. Eddington (1882–1944), the eminent British astronomer and physicist, has said, "If your theory is found to be against the Second Law of Thermodynamics I can give you no hope; there is nothing for it but to collapse in deepest humiliation." C. P. Snow, another British physicist, likened lack of knowledge of the Second Law to ignorance of Shakespeare, to underscore the importance of thermodynamics to basic awareness of the character of the physical world. And M. V. Volkenstein, member of the Institute of Molecular Biology and the Academy of Sciences of the USSR, has written, "A physical consideration of any kind of system, including a living one, starts with its phenomenological, thermodynamic description. Further study adds a molecular content to such a description."

The composition and style of this book reflect my own approach to teaching thermodynamics. Much of the presentation is informal and qualitative. This is because knowing high-powered mathematics is often quite different from knowing what one would like to use mathematics to describe. At the same time, however, a firm grasp of thermodynamics and how it can be used can really only be acquired through numerical problem solving. The text therefore does not avoid expressing ideas in the form of equations where it seems fitting. Each chapter is imbued with *l'esprit de géométrie* as well as *l'esprit de finesse*. In general, the mathematical difficulty of the material increases on the journey from alpha to omega. Worked examples are provided to illustrate how to use and appreciate the mathematics, and a long list of references and suggestions for further reading are given at the end of each chapter. In addition, each chapter is accompanied by a broad set of study questions. These fall into several categories: brief calculation, extended calculation, multiple choice, analysis of experimental data, short answer, and "essay." A few of the end-of-chapter questions are open-ended; it would be difficult to say that a "correct" answer could be given. This will, I hope, be seen as more of a strength of the text than a weakness. For the nature of the biological sciences is such that some very "important" aspects of research are only poorly defined or understood. Moreover, every path to a discovery of lasting significance has its fair share of woolly thinking to cut through.

Several themes run throughout the book, helping to link the various chapters into a unified whole. Among these are the central role of ATP in life processes, proteins, the relationship between energy and biological information, and the human dimension of science. The thermodynamics of protein folding/unfolding is used to illustrate a number of key points. Why emphasize proteins? About 50% of the dry mass of the human body is protein, no cell could function without protein, a logical next step to knowing the amino acid sequence encoded by a gene is predicting the three-dimensional structure of the corresponding functional protein, and a large portion of my research activity has involved peptides or proteins. I also try to give readers a sense of how thermodynamics has developed over the past several hundred years from contributions from researchers of many different countries and backgrounds.

My hope is that this text will help students of the biological sciences gain a clearer understanding of the basic principles of energy transformation as they apply to living organisms. Like a physiologically meaningful assembly of biological macromolecules, the organization of the book is hierarchical. For students with little or no preparation in thermodynamics, the first four chapters are essential and may in some cases suffice for undergraduate course content. Chapter 1 is introductory. Certain topics of considerable complexity are dealt with only in broad outline here; further details are provided at appropriate points in later chapters. The approach is intended to highlight both the independence of thermodynamics from biological systems and processes and applicability of thermodynamics to biology; not simply show the consistency of certain biological processes with the laws of thermodynamics. The second and third chapters discuss the First and

Second Laws of thermodynamics, respectively. This context provides a natural introduction to two thermodynamic state functions, enthalpy and entropy. Chapter 4 discusses how these functions are combined in the Gibbs free energy, a sort of hybrid of the First and Second Laws and the main thermodynamic potential function of interest in biology. Chapter 4 also elaborates several basic areas of physical chemistry relevant to biology. In Chapter 5, the concepts developed in Chapter 4 are applied to a wide range of topics in biology and biochemistry, the aim being to give students a good understanding of the physics behind the biochemical techniques they might use in an undergraduate laboratory. Chapters 4 and 5 are designed to allow maximum flexibility in course design, student ability, and instructor preferences. Chapters 6 and 7 concern molecular interpretations of thermodynamic quantities. Specifically, Chapter 6 introduces and discusses the statistical nature of thermodynamic quantities. In Chapter 7 these ideas are extended in a broad treatment of macromolecular binding, a common and extremely important class of biochemical phenomena. Chapter 8, on reaction kinetics, is included for two main reasons: the equilibrium state can be defined as the one in which the forward and reverse rates of reaction are equal, and the rate of reaction, be it of the folding of a protein or the catalysis of a biochemical reaction, is determined by the free energy of the transition state. In this way inclusion of a chapter on reaction kinetics gives a more complete understanding of biological thermodynamics. Finally, Chapter 9 touches on a number of topics at the forefront of biochemical research where thermodynamic concepts are of striking and relatively general interest.

A note on units. Both joules and calories are used throughout this book. Unlike monetary exchange rates and shares on the stock exchange, the values of which fluctuate constantly, the conversion factor between joules and calories is constant. Moreover, though joules are now more common than calories, one still finds both types of unit in the contemporary literature, and calories predominate in older but still useful and sometimes very interesting publications. Furthermore, the instrument one uses to make direct heat measurements is a called a calorimeter not a joulimeter! In view of this it seems fitting that today's student should be familiar with both types of unit.

Three books played a significant role in the preparation of the text: *Introduction to Biomolecular Energetics* by I. M. Klotz, *Foundations of Bioenergetics* by H. J. Morowitz, and *Energy and Life* by J. Wrigglesworth. My own interest in biophysics was sparked by the work of Ephraim Katchalsky (not least by his reflections on art and science!) and Max Delbrück,[1] which was brought to my attention by my good

[1] Delbrück played a key role in the development of molecular biology and biophysics. Raised in Berlin near the home of Max Planck, Nobel Laureate in Physics, Delbrück was, like Planck, son of a professor at Berlin University, and one of his great-

friend Bud Herschel. I can only hope that my predecessors will deem my approach to the subject a helpful contribution to thermodynamics education in the biological sciences.

The support of several other friends and colleagues proved invaluable to the project. Joe Marsh provided access to historical materials, lent me volumes from his personal library, and encouraged the work from an early stage. Paul C. W. Davies offered me useful tips on science writing. Helpful information was provided by a number of persons of goodwill: Rufus Lumry, Richard Cone, Alan Eddy, Klaus Bock, Mohan Chellani, Bob Ford, Andy Slade, and Ian Sherman. Van Bloch was a steady and invaluable source of encouragement and good suggestions on writing, presenting, and publishing this work. I thank Chris Dobson. Alan Cooper, Bertrand Garcia-Moreno Esteva, and Terry Brown, and several anonymous reviewers read parts of the text and provided valuable comments. I wish to thank my editors, Katrina Halliday and Ward Cooper, for the energy and enthusiasm they brought to this project, and Beverley Lawrence for expert copy-editing. I am pleased to acknowledge Tariq, Khalida, and Sarah Khan for hospitality and kindness during the late stages of manuscript preparation. I am especially grateful to Kathryn, Kathleen, and Bob Doran for constant encouragement and good-heartedness.

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grandfathers was Liebig, the renowned biochemist. Delbrück studied astronomy and physics. Having obtained relatively little background in experimental physics, he failed his Ph.D. oral exam in the first attempt. Nevertheless, he went on to study with Niels Bohr in Copenhagen and Wolfgang Pauli in Zürich, each of whom was recognized for contributions to quantum theory by a Nobel Prize in Physics. In 1937 Delbrück left Germany for the USA; his sister Emmi and brother-in-law Klaus Bonhoeffer (brother of the theologian Dietrich) stayed behind, working in the German Resistance against the Nazi regime. Delbrück became a research fellow at Caltech and devoted himself to the study of bacterial viruses, which he regarded as sufficiently simple in hereditary mechanism for description and understanding in terms of physics. There are reasons to believe that Delbrück was a significant source of inspiration for some of Richard Feynman's remarks in his 1959 talk, "Plenty of Room at the Bottom," which has come to play a seminal role in the development of nanotechnology (see Haynie *et al.*, 2006, *Nanomedicine: Nanotechnology, Biology, and Medicine*, **2**, 150–7 and references cited therein). Delbrück was awarded the Nobel Prize in Medicine or Physiology in 1969 for his work on bacteriophages.

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D. T. H.
15th September, 2007
New Haven, Connecticut

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