Biological Thermodynamics

Biological Thermodynamics provides an introduction to the study of energy transformation in the biological sciences. Don Haynie uses an informal writing style to discuss this core subject in a way which will appeal to the interests and needs of undergraduate students of biology and biochemistry. The emphasis throughout the text is on understanding basic concepts and developing problem-solving skills, but mathematical difficulty is kept to a minimum. Each chapter comprises numerous examples taken from different areas of biochemistry, as well as a broad range of exercises and list of references for further study. Topics covered include energy and its transformation, the First Law of Thermodynamics, the Second Law of Thermodynamics, Gibbs free energy, statistical thermodynamics, binding equilibria, reaction kinetics, and a survey of the most exciting areas of biological thermodynamics today, particularly the origin of life.

Don Haynie has a B.S. in physics (South Florida) and a Ph.D. in biophysics (Biocalorimetry Center, The Johns Hopkins University). Following postdoctoral research in physical biochemistry at the University of Oxford, he took up a lectureship in biochemistry in the Department of Biomolecular Sciences at the University of Manchester Institute of Science and Technology (UMIST), UK. He has taught thermodynamics, to biology, biochemistry, and engineering students at Johns Hopkins and UMIST, and at Louisiana Tech University, where he is now Associate Professor in the Institute for Micromanufacturing.

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Donald T. Haynie

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For my great-grandfather
JOSEPH RAFFEL

my grandmother
HELENE MINDER

and my friend
BUD HERSCHEL

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

ANONYMOUS

Contents

Chapter 7 | Binding equilibria

Chapter 8 | Reaction kinetics

Chapter 9 | The frontier of biological thermodynamics

Preface

Interest in the biological sciences has never been greater. At the dawn of twenty-first century, biology and biochemistry are captivating the minds of young people in the way that physics did 40–50 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.

This book is about the thermodynamics of living organisms. It was written primarily for undergraduate university students of the biological, biochemical and medical sciences. It could also serve as an introductory text for undergraduate students of chemistry or physics who are interested in biology, and 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 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, and discussing thermodynamic properties of proteins with colleagues in Oxford Centre for Molecular Sciences.

My sense is that an integrated approach to teaching this subject, where the principles of physical chemistry are presented not as a standalone 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 can compound 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 of this is that many students of the biological sciences complete their undergraduate study with either 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 not 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 from 1879 to 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.' Sir Charles P. Snow, another British physicist, likened lack of knowledge of the Second Law of Thermodynamics to ignorance of Shakespeare, to underscore the importance of thermodynamics to basic awareness of the character of the physical world. Finally, 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 quantitative 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 with *l'esprit de finesse*. In general, the mathematical difficulty of the material increases from beginning to end. 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, and it would be difficult to say that a 'correct' answer could be given to them. 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 had its fair share of woolly thinking to cut through. Password-protected access to solutions to problems is available on line at http://chem.nich.edu/homework

Several themes run throughout the book, helping to link the various chapters into a unified whole. Among these are the central role of ATP and glucose in life processes, the proteins lysozyme and hemoglobin, 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 points because it is well known to me and because it is of more general significance than some people might think. After all, about 50% of the dry mass of the human body is protein, no cell could function without it, and 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. We also draw attention to how thermodynamics has developed over the past several hundred years from contributions from researchers of many different countries and backgrounds.

The principal aim of this text is to 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 text 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. This follows the basic plan of the book, which highlights the unity and primacy of thermodynamic concepts in biological systems and processes and not simply the consistency of specific 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 important 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 to biological scientists. 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, an 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 intended to allow maximum flexibility in course design, student ability, and instructor preferences. Chapters 6 and 7 focus on the molecular interpretation of thermodynamic quantities. Specifically, Chapter 6 introduces and discusses the statistical nature of thermodynamic quantities. In the next chapter these ideas are extended in a broad treatment of macromolecular binding, a very common and extremely important class of biochemical phenomenon. Chapter 8, on reaction kinetics, is included in this book 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 considerable importance.

A note about 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 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 interest in biophysics was sparked by the work of Ephraim Katchalsky (not least by his reflections on art and science!) and Max Delbrück, which was brought to my attention by my good 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 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, Bertrand Garcia-Moreno Esteva, Alan Eddy, Klaus Bock, Mohan Chellani, Bob Ford, Andy Slade, and Ian Sherman. Van Bloch was an invaluable source of encouragement and good suggestions on writing, presenting, and publishing. I thank Chris Dobson. Norman Duffy, Mike Rao, Alan Cooper, Bertrand Garcia-Moreno Esteva, John Ladbury, Alison Roger, Terry Brown, and several

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Every attempt has been made to produce a spotless textbook. I alone am responsible for any infelicities that may have escaped the watchful eyes of our red pens.

D. T. H.
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Oxford, England

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