Equilibria and Kinetics of Biological Macromolecules

Jan Hermans
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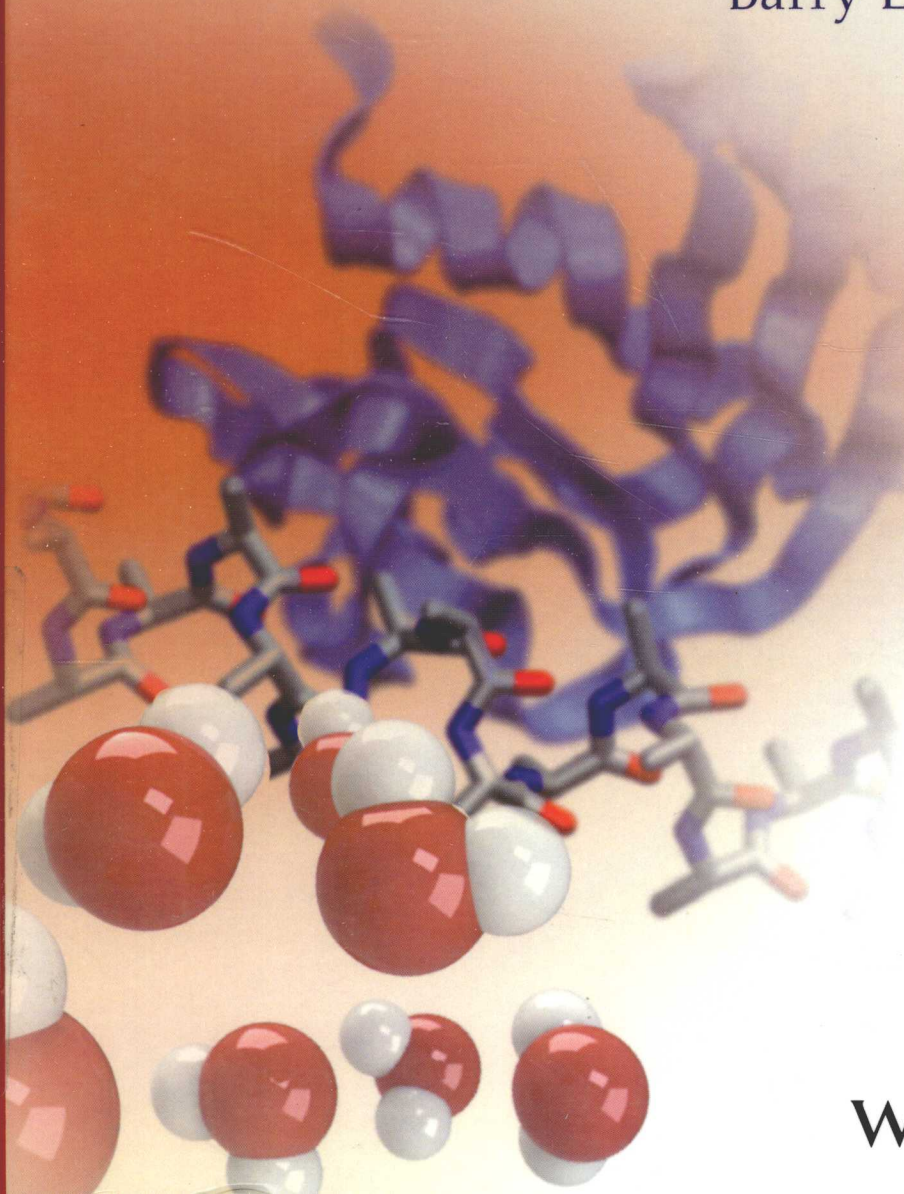

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For Harold Scheraga

Preface

It is only by attempting to explain our science to each other that we find out what we really know.
—J. M. Ziman, Nature 252: 318–324 (1969)

This book has grown out of circa 12 years of collaborative teaching of a 6-credit biophysics course that forms the core of the didactic teaching for the Molecular and Cellular Biophysics Program at UNC CH. Thus the book is directed at an audience of first year graduate students. However, the book has grown well beyond the content of those courses, also thanks to input and suggestions from colleagues who have shared our teaching the course (see Acknowledgments), and it is our hope that it will prove useful to working biochemists who seek a deeper understanding of modern biophysics.

The book is not meant to be a complete text in biophysics, as it focuses on the input of physics and physical chemistry to experimental studies and theoretical models of equilibria and kinetics of biological macromolecules (largely, proteins). A chapter is devoted to methods of molecular simulations; applications of molecular dynamics are included in several chapters. On the other hand, we limited the size of this book by devoting no space to spectroscopy and structure determination.

The book assumes some knowledge of physics and/or physical chemistry, but in Part 1, the chapters on thermodynamics, simple quantum mechanics and molecular structure and intra- and intermolecular forces shore up what may be shaky backgrounds of some students, and provide references for later chapters. Part 1 concludes with a chapter on water and the hydrophobic effect.

Two chapters in Part 2 introduce various ensembles of statistical mechanics, and these are followed by the aforementioned chapter on molecular simulations.

Next, in Part 3, we discuss equilibria of binding of "ligands" to macromolecules from different standpoints: chemical equilibrium theory, thermodynamics, and statistical mechanics. These are followed by a discussion of linked equilibria, and a chapter that focuses on hemoglobin as an example of allosteric control of function.

Part 3 concludes with a chapter on charge–charge interactions of macromolecules in solution.

In Part 4, we deal with folding equilibria. A brief overview of the physics of polymer solutions is followed by a chapter on the theory of helix-coil transitions of polypeptides and its many applications, and it ends with a section on helix-coil equilibria of double-stranded nucleic acids. This is followed by a long chapter on equilibria of protein folding. Part 4 concludes with a chapter on elasticity with elastin and tenascin as examples of two different mechanisms.

The final part of the book is devoted to kinetics. The first chapter describes kinetic measurement methods and a variety of kinetic models, ranging from simple rate equations to transition state theory. This is followed by a chapter on experiments and theory of kinetics of protein folding. Part 5 concludes with a chapter on stochastic processes and theories from the Langevin equation to Kramers' theory of reaction rates.

Finally, in a series of Appendices we have covered technical (mostly mathematical) details which we had skipped earlier to make the main content of this book easier to follow.

The authors will maintain a web page devoted to corrections and discussion of this book. Please consult the authors' personal web pages at the University of North Carolina.

Acknowledgments

This book's inception was in the form of lecture notes for the introductory class in molecular biophysics given at UNC each fall semester. An enormous help has been the feedback we received from students taking the class.

We have received help from many colleagues. We are grateful to professors Papoian (now at the University of Maryland) and Dokholyan, who have each taught part of the course, for letting us base important sections of the book on new presentations given by them in their lectures. Individual chapters have had input from Gary Ackers at Washington University, from Gary Pielak in the UNC Chemistry Department, from Gary Felsenfeld at the NIH, from Andy McCammon at UCSD, from Weitao Yang at Duke, from Austen Riggs at the University of Texas, from Robert Baldwin at Stanford and from Hao Hu at the University of Hong Kong.

We thank Dr. M. Hanrath, University of Cologne for the computer drawings of hydrogen atom wave functions shown in Chapter 2, and Dr. Chad Petit for microcalorimeter results discussed in Chapter 8. Some figures of molecular structures were prepared with the vmd graphics program.* We acknowledge many answers to questions involving basic Physics, found by consulting Wikipedia.

JH and BRL

September 2012

*Humphrey, W., Dalke, A., Schulten, K. VMD - visual molecular dynamics. *J. Mol. Graphics Modell.* **14**: 33–38 (1996).

CONSTANTS

Elementary charge	$e = 1.602189 \times 10^{-19}$ C
Atomic mass unit	amu $= 1.660566 \times 10^{-27}$ kg
Proton rest mass	$m_p = 1.672648 \times 10^{-27}$ kg $= 1.0073$ amu
Electron rest mass	$m_e = 9.109534 \times 10^{-31}$ kg
Boltzmann's constant	$k_B = 1.380662 \times 10^{-23}$ J K^{-1} $= 8.31441$ J K^{-1} mol^{-1} $= 1.987$ cal K^{-1} mol^{-1}
Planck's constant	$h = 6.626176 \times 10^{-34}$ J s
Avogadro's number	$N_A = 6.022 \times 10^{23}$ mol^{-1}
$k_B T$ at 300 K	$k_B T = 4.142$ zJ $= 2.494$ kJ mol^{-1} $= 0.596$ kcal mol^{-1}
Freezing point of water	273.15 K
Viscosity of water at 20 °C	1.003×10^{-3} Pa s
Gravity	$g = 9.8066$ m s^{-2}
Permittivity of vacuum	$\varepsilon_0 = 8.854 \times 10^{-12}$ C^2 N^{-1} m^{-2}

PREFIXES OF THE METRIC SYSTEM

Name	Prefix	Value	Name	Prefix	Value
yotta	Y	10^{24}	yocto	y	10^{-24}
zotta	Z	10^{21}	zepto	z	10^{-21}
exa	E	10^{18}	atto	a	10^{-18}
peta	P	10^{15}	femto	f	10^{-15}
tera	T	10^{12}	pico	p	10^{-12}
giga	G	10^{9}	nano	n	10^{-9}
mega	M	10^{6}	micro	μ	10^{-6}
kilo	k	10^{3}	milli	m	10^{-3}
- - -	- - -	10^{0}	- - -	- - -	10^{0}

Also deka (da, 10^1), hekto (h, 10^2), deci (d, 10^{-1}) and centi (c, 10^{-2}).

GREEK ALPHABET

α	A	alpha	η	H	eta	ν	N	nu	τ	T	tau
β	B	beta	θ, ϑ	Θ	theta	ξ	Ξ	xi	υ	Y,Υ	upsilon
γ	Γ	gamma	ι	I	iota	o	O	omicron	ϕ	Φ	phi
δ	Δ	delta	κ	K	kappa	π	Π	pi	χ	X	chi
ε	E	epsilon	λ	Λ	lambda	ρ	P	rho	ψ	Ψ	psi
ζ	Z	zeta	μ	M	mu	σ,ς	Σ	sigma	ω	Ω	omega

Suggested pronunciation:
like "pie": π (pie), χ (kie);
like "bee": ξ (ksee), ϕ (fee), ψ (psee)

Contents