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978-1-107-01447-3 - Thermodynamics and Statistical Mechanics of Macromolecular Systems

Michael Bachmann

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Thermodynamics and Statistical Mechanics of Macromolecular Systems

The structural mechanics of proteins that fold into functional shapes, polymers that aggregate and form clusters, and organic macromolecules that bind to inorganic matter can be understood only through statistical physics and thermodynamics.

This book reviews the statistical mechanics concepts and tools necessary for the study of structure formation processes in macromolecular systems that are essentially influenced by finite-size and surface effects. Readers are introduced to molecular modeling approaches, advanced Monte Carlo simulation techniques, and systematic statistical analyses of numerical data. Applications to folding, aggregation, and substrate adsorption processes of polymers and proteins are discussed in great detail. Particular emphasis is placed on the reduction of complexity by coarse-grained modeling, which allows for the efficient, systematic investigation of structural phases and transitions.

Providing insight into modern research at this interface between physics, chemistry, biology, and nanotechnology, this book is an excellent reference for graduate students and researchers.

Michael Bachmann is Associate Professor in the Department of Physics and Astronomy at the University of Georgia. His major fields of interest include theoretical physics, computational physics, statistical physics, biophysics, and chemical physics.

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MICHAEL BACHMANN

The University of Georgia



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Dedicated to my family

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Contents

<i>Preface and outline</i>	<i>page</i> xiii
1 Introduction	1
1.1 Relevance of biomolecular research	1
1.2 Proteins	3
1.2.1 The trinity of amino acid sequence, structure, and function	3
1.2.2 Ribosomal synthesis of proteins	6
1.2.3 From sequence to function: The protein folding process	7
1.3 Molecular modeling	9
1.3.1 Covalent bonds	9
1.3.2 Effective noncovalent interactions and nanoscopic modeling: Toward a semiclassical all-atom representation	11
1.4 All-atom peptide modeling	12
1.5 The mesoscopic perspective	14
1.5.1 Why coarse-graining...? The origin of the hydrophobic force	15
1.5.2 Coarse-grained hydrophobic–polar modeling	17
1.6 Polymers	20
1.6.1 DNA and RNA	20
1.6.2 Modeling free DNA	22
1.6.3 Flexible, attractively self-interacting polymers	23
1.6.4 Elastic polymers	27
2 Statistical mechanics: A modern review	31
2.1 The theory of everything	31
2.2 Thermodynamics and statistical mechanics	33
2.2.1 The thermodynamic limit	33
2.2.2 Thermodynamics of closed systems: The canonical ensemble	34
2.2.3 Thermodynamic equilibrium and the statistical nature of entropy	36
2.3 Thermal fluctuations and the statistical path integral	43
2.4 Phase and pseudophase transitions	46
2.5 Relevant degrees of freedom	48
2.5.1 Coarse-grained modeling on mesoscopic scales	48
2.5.2 Macroscopic relevant degrees of freedom: The free-energy landscape	49
2.6 Kinetic free-energy barrier and transition state	51

2.7	Microcanonical statistical analysis	53
2.7.1	Temperature as a derived quantity	54
2.7.2	Identification of first-order transitions by Maxwell construction	55
2.7.3	Systematic classification of transitions by inflection-point analysis	62
3	The complexity of minimalistic lattice models for protein folding	67
3.1	Evolutionary aspects	67
3.2	Self-avoiding walks and contact matrices	68
3.3	Exact statistical analysis of designing sequences	69
3.4	Exact density of states and thermodynamics	76
4	Monte Carlo and chain growth methods for molecular simulations	81
4.1	Introduction	81
4.2	Conventional Markov-chain Monte Carlo sampling	82
4.2.1	Ergodicity and finite time series	82
4.2.2	Statistical error and bias	84
4.2.3	Binning–jackknife error analysis	88
4.3	Systematic data smoothing by using Bézier curves	93
4.3.1	Construction of a Bézier curve	93
4.3.2	Smooth Bézier functions for discrete noisy data sets	96
4.4	Markov processes and stochastic sampling strategies	100
4.4.1	Master equation	100
4.4.2	Selection and acceptance probabilities	101
4.4.3	Simple sampling	102
4.4.4	Metropolis sampling	103
4.5	Reweighting methods	104
4.5.1	Single-histogram reweighting	104
4.5.2	Multiple-histogram reweighting	105
4.6	Generalized-ensemble Monte Carlo methods	108
4.6.1	Replica-exchange Monte Carlo method: Parallel tempering	108
4.6.2	Simulated tempering	109
4.6.3	Multicanonical sampling	109
4.6.4	Wang–Landau method	117
4.7	Elementary Monte Carlo updates	118
4.8	Lattice polymers: Monte Carlo sampling vs. Rosenbluth chain growth	123
4.9	Pruned-enriched Rosenbluth method: Go with the winners	126
4.10	Canonical chain growth with PERM	127
4.11	Multicanonical chain-growth algorithm	129
4.11.1	Multicanonical sampling of Rosenbluth-weighted chains	129
4.11.2	Iterative determination of the density of states	130
4.12	Random number generators	133
4.13	Molecular dynamics	134

5 First insights to freezing and collapse of flexible polymers	137
5.1 Conformational transitions of flexible homopolymers	137
5.2 Energetic fluctuations of finite-length polymers	138
5.2.1 Peak structure of the specific heat	138
5.2.2 Simple-cubic lattice polymers	139
5.2.3 Polymers on the face-centered cubic lattice	141
5.3 The Θ transition	144
5.4 Freezing and collapse in the thermodynamic limit	147
6 Crystallization of elastic polymers	149
6.1 Lennard-Jones clusters	149
6.2 Perfect icosahedra	150
6.3 Liquid–solid transitions of elastic flexible polymers	152
6.3.1 Finitely extensible nonlinear elastic Lennard-Jones polymers	152
6.3.2 Classification of geometries	153
6.3.3 Ground states	155
6.3.4 Thermodynamics of liquid–solid transitions toward complete icosahedra	156
6.3.5 Liquid–solid transitions of elastic polymers	158
6.3.6 Long-range effects	162
6.4 Systematic analysis of compact phases	164
6.5 Dependence of structural phases on the range of nonbonded interactions	165
7 Structural phases of semiflexible polymers	175
7.1 Structural hyperphase diagram	175
7.2 Variation of chain length	180
8 Generic tertiary folding properties of proteins on mesoscopic scales	181
8.1 A simple model for a parallel β helix lattice protein	181
8.2 Protein folding as a finite-size effect	184
8.3 Hydrophobic–polar off-lattice heteropolymers	185
9 Protein folding channels and kinetics of two-state folding	191
9.1 Similarity measure and order parameter	192
9.2 Identification of characteristic folding channels	195
9.3 Gō kinetics of folding transitions	198
9.3.1 Coarse-grained Gō modeling	199
9.3.2 Thermodynamics	201
9.3.3 Kinetics	204
9.3.4 Mesoscopic heteropolymers vs. real proteins	208
9.4 Microcanonical effects	209
9.5 Two-state cooperativity in helix–coil transitions	213

10	Inducing generic secondary structures by constraints	217
10.1	The intrinsic nature of secondary structures	217
10.2	Polymers with thickness constraint	218
10.2.1	Global radius of curvature	218
10.2.2	Modeling flexible polymers with constraints	219
10.2.3	Thickness-dependent ground-state properties	220
10.2.4	Structural phase diagram of tube-like polymers	222
10.3	Secondary-structure phases of a hydrophobic–polar heteropolymer model	223
11	Statistical analyses of aggregation processes	227
11.1	Pseudophase separation in nucleation processes of polymers	227
11.2	Mesoscopic hydrophobic–polar aggregation model	228
11.3	Order parameter of aggregation and fluctuations	229
11.4	Statistical analysis in various ensembles	230
11.4.1	Multicanonical results	230
11.4.2	Canonical perspective	233
11.4.3	Microcanonical interpretation: The backbending effect	235
11.5	Aggregation transition in larger heteropolymer systems	239
12	Hierarchical nature of phase transitions	243
12.1	Aggregation of semiflexible polymers	243
12.2	Structural transitions of semiflexible polymers with different bending rigidities	244
12.3	Hierarchies of subphase transitions	247
12.4	Hierarchical peptide aggregation processes	249
12.5	Hierarchical aggregation of GNNQQNY	252
13	Adsorption of polymers at solid substrates	255
13.1	Structure formation at hybrid interfaces of soft and solid matter	255
13.2	Minimalistic modeling and simulation of hybrid interfaces	256
13.3	Contact-density chain-growth algorithm	258
13.4	Pseudophase diagram of a flexible polymer near an attractive substrate	259
13.4.1	Solubility–temperature pseudophase diagram	260
13.4.2	Contact-number fluctuations	261
13.4.3	Anisotropic behavior of gyration tensor components	263
13.5	Alternative view: The free-energy landscape	264
13.6	Continuum model of adsorption	269
13.6.1	Off-lattice modeling	269
13.6.2	Energetic and structural quantities for phase characterization by canonical statistical analysis	270
13.6.3	Comparative discussion of structural fluctuations	271
13.6.4	Adsorption parameters	273
13.6.5	The pseudophase diagram of the hybrid system in continuum	274
13.7	Comparison with lattice results	277

Cambridge University Press

978-1-107-01447-3 - Thermodynamics and Statistical Mechanics of Macromolecular Systems

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Frontmatter

[More information](#)

13.8	Systematic microcanonical analysis of adsorption transitions	279
13.8.1	Dependence on the surface attraction strength	280
13.8.2	Chain-length dependence	282
13.8.3	Translational entropy	284
13.9	Polymer adsorption at a nanowire	286
13.9.1	Modeling the polymer–nanowire complex	287
13.9.2	Structural phase diagram	288
14	Hybrid protein–substrate interfaces	293
14.1	Steps toward bionanotechnology	293
14.2	Substrate-specific peptide adsorption	294
14.2.1	Hybrid lattice model	294
14.2.2	Influence of temperature and solubility on substrate-specific peptide adsorption	295
14.3	Semiconductor-binding synthetic peptides	301
14.4	Thermodynamics of semiconductor-binding peptides in solution	303
14.5	Modeling a hybrid peptide–silicon interface	307
14.5.1	Introduction	307
14.5.2	Si(100), oxidation, and the role of water	308
14.5.3	The hybrid model	309
14.6	Sequence-specific peptide adsorption at silicon (100) surface	312
14.6.1	Thermal fluctuations and deformations upon binding	312
14.6.2	Secondary-structure contents of the peptides	313
14.6.3	Order parameter of adsorption and nature of adsorption transition	315
15	Concluding remarks and outlook	319
	<i>References</i>	323
	<i>Index</i>	337

Cambridge University Press

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Frontmatter

[More information](#)

Preface and outline

The idea to write this book unfolded when I more and more realized how equally frustrating and fascinating it can be to design research projects in molecular biophysics and chemical physics – frustrating for the sheer amount of inconclusive and contradicting literature, but fascinating for the mechanical precision of the complex interplay of competing interactions on various length scales and constraints in conformational transition processes of biomolecules that lead to functional geometric structures. Proteins as the “workhorses” in any biological system are the most prominent examples of such biomolecules.

The ability of a “large” molecule consisting of hundreds to tens of thousands of atoms to form stable structures spontaneously is typically called “cooperativity.” This term is not well defined and could easily be replaced by “emergence” or “synergetics” – notions that have been coined in other research fields for the same mysterious feature of macroscopic ordering effects. There is no doubt that the origin of these net effects is of “microscopic” (or better nanoscopic) quantum nature. By noting this, however, we already encounter the first major problem and the reason why heterogeneous polymers such as proteins have been almost ignored by theoretical scientists for a long time. From a theoretical physicist’s point of view, proteins are virtually “no-no’s.” Composed of tens to thousands of amino acids (already inherently complex chemical groups) linearly lined up, proteins reside in a complex, aqueous environment under thermal conditions. They are too large for a quantum-chemical treatment, but too small and too specific for a classical, macroscopic description. They do not at all fulfill the prerequisites of the thermodynamic limit and do not scale. In consequence, the standard statistical theory of phase transitions is not directly applicable, although many aspects of molecular structure formation processes resemble those known from phase transitions. Since 20 types of amino acids occur frequently in bioproteins, the number of possible compositions is astronomically large, but only of the order of 100 000 highly specific types of bioproteins are functional in the human cell system. Beside this obviously elementary evolutionary aspect, the heterogeneous composition (which causes glass-like behavior) and their high specialization level raise the question, to what extent folding properties can be generic at all. This is actually one of the key questions. A negative answer is not very likely; nature has always proven that even the most complex structures possess symmetries (in a more general context), which explain their stability. Stability is necessary, because these molecular systems exist and function in a thermal environment. It is even appropriate to formulate the whole problem in the following way: it is the interplay and balance between system and environment that stabilizes the structure of the system. Having said that, there is no reasonable way to try to understand any structure formation process without including thermodynamics and, therefore, statistical mechanics.

Another apparent problem is that analytical approaches virtually fail to explain processes of heterogeneous systems, leaving computer simulations the only available tool for theoretical studies. Since protein folding is a relatively slow process (microseconds to seconds), it is almost impossible to use molecular dynamics simulations, operating on nanosecond timescales, for folding studies. Alternatively, Monte Carlo methods are inefficient, if the surrounding water molecules are explicitly simulated. The models are generally not well defined and computer simulations on atomic scales often require large-scale supercomputing resources. The abovementioned key question of generics affects the possibility and limitation of using much more efficient coarse-grained models. For these reasons, studies of biomolecular systems remain a true challenge to theoretical and computational biologists, chemists, and physicists. However, the fact that, among others, neurodegenerative diseases such as Alzheimer's and all virus infections are associated with structural properties of biomolecules makes it worth the efforts to research macromolecular systems of such scale.

This book is a "research book" for the interdisciplinary community. This means it offers many approaches to deal with molecular systems by means of statistical mechanics and computer simulation, yet it will give no precise answers to the above questions. It shall provide young scientists from all affected disciplines of natural and technological sciences with the background to get started, but it also addresses senior scientists by promoting alternative views. The book could also be of value as a compendium as it includes widely accepted research results, in particular for homopolymer systems.

More specifically, we are going to discuss thermodynamic properties of conformational transitions for single- and multiple-chain polymer and protein systems, with particular focus dedicated to molecular folding, aggregation, and adsorption processes to solid substrates. In most of the presented examples, we will investigate the structural transitions by statistical analyses of simplified models. This is based on the idea that in cooperative processes like structural transitions, the collective action of the mechanical degrees of freedom allows for a reduction of the phase space. In other words, the essential features of these transitions are expected to be described qualitatively correctly by models in which a strongly reduced number of effective degrees of freedom is considered only. This reduction of mechanical complexity is called coarse-graining and has proven to be extremely successful in the understanding of complex phenomena and phase transitions of macroscopic systems. If the analogy of structural transitions in rather small molecular systems and phase transitions of macroscopic systems holds true, then coarse-grained approaches can also be valuable tools for the description of molecular behavior. Coarse-grained modeling and simulation will, therefore, play a vital role in this book.

The finiteness of molecular systems, the geometric nature of the structural transitions, and the constraints (e.g., stiff bonds) that affect the mechanical motion render a theoretical treatment typically very difficult. For this reason, the design of efficient algorithms is inevitable for unraveling the properties of structural transitions of molecular systems. We will discuss various examples throughout this book, where sophisticated computer simulation methodologies were employed to obtain the statistical information needed for a thermodynamic analysis of such transitions. Therefore, a short review of modern

simulational methods is also included, as it is considered to be beneficial for readers who wish to get started or who would simply like to know where the results discussed in this book originated from.

In the first chapter of this book, we begin with an introduction of the molecular structure and the modeling of linear macromolecules. Fundamental aspects of thermodynamics and statistical mechanics, with emphasis on finite-size effects and their statistical analysis, are reviewed in Chapter 2. In Chapter 3, properties of the complete sequence and conformation space are systematically analyzed for short lattice proteins by exact enumeration of a minimalistic hydrophobic–polar heteropolymer model. Computer simulations of larger systems require efficient algorithms. Such algorithms are reviewed in Chapter 4 and important aspects of analyses of finitely long time series of data generated by these algorithms are discussed. As a first application, the study of homopolymer freezing and collapse transitions on regular lattices is the subject of Chapter 5. In this regard, the influence of surface and finite-size effects upon crystallization of elastic flexible and semiflexible polymers is addressed in detail in Chapters 6 and 7, respectively. Returning to proteins, characteristic folding properties of proteins and the classification of folding channels are investigated in Chapters 8 and 9. Generic local geometries like secondary structures induced by constraints that effectively reflect many-body effects are discussed in Chapter 10 by introducing tube-like polymers. The extension of coarse-grained modeling to multiple-chain systems is described in Chapter 11, where also analyses of aggregation transitions of short heteropolymers in different statistical ensembles are presented. In Chapter 12, we unravel the hierarchical nature of phase transitions by discussing the exemplified aggregation transition of homopolymers. Pseudophase diagrams of adsorption processes of lattice and off-lattice homopolymers to solid substrates are investigated in detail in Chapter 13. An introductory, simple example for substrate-specific binding of peptides to solid substrates is studied in detail in Chapter 14.

I am indebted to Wolfhard Janke for many years of successful cooperation, advice, and support. For constant support and extremely helpful discussions, I am also thankful to David P. Landau, Kurt Binder, Hagen Kleinert, and Gerhard Gompper. The collaboration with Thomas Neuhaus, Anders Irbäck, Joan Adler, Axel Pelster, and Qianqian Cao is also very much appreciated. It is a particular pleasure to thank my long-term collaborators Thomas Vogel, Stefan Schnabel, Karsten Goede, Monika Möddel, Christoph Junghans, Jonathan Groß, Daniel T. Seaton, and Tristan Bereau for the joint successful work, without which it would not have been possible to write this book. Many other people have also actively and passively helped streamline my thoughts in the exciting field of structural biophysics, which I am also quite thankful for. I would also like to thank Érica de Mello Silva and Paulo H. L. Martins at the Universidade Federal de Mato Grosso, Cuiabá, for their kind hospitality during my current visit to Brazil.



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