

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 G $\ddot{o}$ kinetics of folding transitions	198
9.3.1 Coarse-grained G $\ddot{o}$ 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

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