

---

## Contents

### 1 Mapping Protein Folding Landscapes by NMR Relaxation

<i>P.E. Wright, D.J. Felitsky, K. Sugase, and H.J. Dyson</i> .....	1
1.1 NMR Techniques for Studying Protein Folding .....	1
1.2 The Apomyoglobin Folding Landscape .....	2
1.3 Structure of the Kinetic Molten Globule State .....	2
1.4 The Upper Reaches of the Folding Landscape .....	2
1.5 Paramagnetic Relaxation Probes: Spin Labeling of Apomyoglobin	4
1.6 Model for Transient Interactions .....	4
1.7 Information from Relaxation Dispersion Measurements .....	8
1.8 Folding of an Intrinsically Disordered Protein Upon Binding to a Target .....	8
References .....	11

### 2 Experimental and Simulation Studies of the Folding/Unfolding of Goat $\alpha$ -Lactalbumin

<i>K. Kuwajima, T. Oroguchi, T. Nakamura, M. Ikeguchi, and A. Kidera</i> ..	13
2.1 Introduction .....	13
2.2 Goat $\alpha$ -Lactalbumin .....	14
2.3 Differences Between the Unfolding Behaviors of Authentic and Recombinant Goat $\alpha$ -Lactalbumin .....	15
2.3.1 Experimental Studies .....	15
2.3.2 Simulation Studies .....	18
2.3.3 Conclusions .....	22
2.4 Folding/Unfolding Pathways of Goat $\alpha$ -Lactalbumin .....	23
2.4.1 Experimental Studies .....	23
2.4.2 Simulation Studies .....	26
2.4.3 Conclusions .....	32
2.5 Summary and Perspectives .....	32
References .....	33

### 3 Transition in the Higher-order Structure of DNA in Aqueous Solution

<i>T. Sakaue and K. Yoshikawa</i> .....	37
3.1 Introduction .....	37
3.2 Long DNA Molecules in Aqueous Solution .....	38
3.2.1 Primary, Secondary, and Higher-order Structures .....	38
3.2.2 DNA Condensation .....	40
3.2.3 Looking at Single DNA Molecules .....	40
3.3 Statistical Physics of Folding of a Long Polymer .....	42
3.3.1 Some Basis .....	42
3.3.2 Continuous Transition in Flexible Polymers: Coil-Globule Transition .....	43
3.3.3 Discontinuous Transition in Semiflexible Polymers .....	45
3.3.4 Instability Due to the Remanent Charge .....	51
3.4 Summary and Perspectives .....	55
3.4.1 Higher-order Structure and Genetic Activity .....	56
3.4.2 Toward Chromatin Structure .....	56
References .....	58

### 4 Generalized-Ensemble Algorithms for Studying Protein Folding

<i>Y. Okamoto</i> .....	61
4.1 Introduction .....	61
4.2 Generalized-Ensemble Algorithms .....	63
4.2.1 Multicanonical Algorithm .....	63
4.3 Multidimensional Extensions of Multicanonical Algorithm .....	67
4.3.1 Replica-Exchange Method .....	69
4.3.2 Multidimensional Extensions of Replica-Exchange Method .....	73
4.4 Examples of Simulation Results .....	75
4.5 Conclusions .....	90
References .....	90

### 5 Protein Folding and Binding: Effective Potentials, Replica Exchange Simulations, and Network Models

<i>A.K. Felts, M. Andrec, E. Gallicchio, and R.M. Levy</i> .....	97
5.1 Introduction .....	97
5.2 Methods .....	100
5.2.1 The OPLS-AA/AGBNP Effective Potential .....	100
5.2.2 Replica Exchange Molecular Dynamics .....	102
5.2.3 The Network Model of Protein Folding .....	103
5.2.4 Loop Prediction with Torsion Angle Sampling .....	103
5.3 Folding of Peptides .....	104
5.3.1 G-Peptide Folding .....	104
5.3.2 Folding of Other Small Peptides .....	105
5.3.3 Loop Prediction .....	105

5.4	Kinetic Model of the G-Peptide .....	108
5.4.1	The G-Peptide has Apparent Two-State Kinetics After a Small Temperature Jump Perturbation .....	108
5.4.2	The G-Peptide has an $\alpha$ -Helical Intermediate during Folding from Coil Conformations .....	108
5.4.3	A Molecular View of Kinetic Pathways .....	109
5.5	Ligand Conformational Equilibrium in a Cytochrome P450 Complex .....	110
5.5.1	Methodology .....	111
5.5.2	The Population of the Proximal State as a Function of Temperature .....	112
5.6	Simple Continuous and Discrete Models for Simulating Replica Exchange .....	112
5.6.1	Discrete Network Replica Exchange (NRE) .....	114
5.6.2	RE Simulations using MC on a Continuous Potential ....	114
5.7	Conclusion .....	116
	References .....	116
 <b>6 Functional Unfolded Proteins: How, When, Where, and Why?</b>		
	<i>H.J. Dyson, S.-C. Sue, and P.E. Wright</i> .....	123
6.1	What is a Functional Unfolded Protein? .....	123
6.2	Where do Functional Unfolded Proteins Occur? .....	124
6.3	How Are Functional Unfolded Proteins Studied? .....	124
6.4	NMR Spectra: Practical Considerations .....	125
6.5	Dynamic Complexes in CBP .....	126
6.6	Role of Flexibility in the Function of I $\kappa$ B $\alpha$ .....	128
	References .....	134
 <b>7 Structure of the Photointermediate of Photoactive Yellow Protein and the Propagation Mechanism of Structural Change</b>		
	<i>M. Kataoka and H. Kamikubo</i> .....	137
7.1	Solution X-ray Scattering .....	137
7.2	Photoactive Yellow Protein .....	138
7.3	Solution Structure Analysis of Photointermediate of PYP .....	139
7.3.1	High-Angle X-ray Scattering of PYP in the Dark and in the Light .....	139
7.3.2	Analysis of High Angle Scattering .....	142
7.4	Propagation Mechanism of the Structural Change .....	144
7.5	Summary .....	145
	References .....	146

## 8 Time-Resolved Detection of Intermolecular Interaction of Photosensor Proteins

<i>M. Terazima</i> .....	149
8.1 Introduction .....	149
8.2 Principle .....	151
8.3 Diffusion Coefficient .....	154
8.4 Time-Resolved Detection of Interprotein Interactions.....	154
8.4.1 Protein-Protein Interaction of the Photoexcited Photoactive Yellow Protein .....	155
8.4.2 Photoinduced Dimerization of AppA .....	157
8.4.3 Photoinduced Dimerization and Dissociation of Phototropins .....	163
8.4.4 Diffusion Detection of Interprotein Interaction .....	168
References .....	170

## 9 Volumetric Properties of Proteins and the Role of Solvent in Conformational Dynamics

<i>C.A. Royer and R. Winter</i> .....	173
9.1 Introduction .....	173
9.2 Thermodynamics .....	174
9.3 Thermal Expansivity and $\Delta V$ .....	179
9.4 Conclusions .....	184
References .....	186

## 10 A Statistical Mechanics Theory of Molecular Recognition

<i>T. Imai, N. Yoshida, A. Kovalenko, and F. Hirata</i> .....	187
10.1 Introduction .....	187
10.2 Outline of the RISM and 3D-RISM Theories .....	190
10.3 Recognition of Water Molecules by Protein .....	196
10.4 Noble Gas Binding to Protein .....	199
10.5 Selective Ion-Binding by Protein .....	201
10.6 Pressure-Induced Structural Transition of Protein and Molecular Recognition .....	204
10.7 Perspective .....	207
References .....	208

## 11 Computational Studies of Protein Dynamics

<i>J.A. McCammon</i> .....	211
11.1 Introduction .....	211
11.2 Brief Survey of Protein Motions .....	211
11.3 Binding and Selectivity .....	213
11.4 Concerted Binding and Release .....	216
11.5 Molecular Clocks .....	216
References .....	217

**12 Biological Functions of Trehalose as a Substitute for Water**

<i>M. Sakurai</i> .....	219
12.1 Introduction .....	219
12.2 Hydration Property of Trehalose .....	221
12.2.1 Property of the Aqueous Solution of Trehalose .....	221
12.2.2 Atomic-Level Picture of Hydration of Trehalose .....	223
12.3 Solid-State Property of Trehalose .....	225
12.3.1 Polymorphism .....	225
12.3.2 Glassy State of Trehalose .....	227
12.4 Biological Roles of Trehalose .....	229
12.4.1 Possible Mechanisms of Anhydrobiosis .....	229
12.4.2 Strategy for Desiccation Tolerance in the Sleeping Chironomid .....	230
12.4.3 Other Biological Roles of Trehalose .....	234
12.5 Conclusion .....	236
References .....	238

**13 Protein Misfolding Diseases and the Key Role Played by the Interactions of Polypeptides with Water**

<i>C.M. Dobson</i> .....	241
13.1 Introduction .....	241
13.2 The Importance of Normal and Aberrant Protein Folding in Biology .....	242
13.3 Protein Aggregation and Amyloid Formation .....	247
13.4 Molecular Evolution and the Control of Protein Misfolding .....	253
13.5 Impaired Misfolding Control and the Onset of Disease .....	255
13.6 Probing Misfolding and Aggregation in Living Organisms .....	257
13.7 The Recent Proliferation of Misfolding Diseases and Prospects for Effective Therapies .....	260
13.8 Concluding Remarks .....	262
References .....	263

**14 Effect of UV Light on Amyloidogenic Proteins: Nucleation and Fibril Extension**

<i>A.K. Thakur and Ch. Mohan Rao</i> .....	267
14.1 Introduction .....	267
14.2 Amyloid .....	268
14.2.1 Structural Perturbation .....	268
14.2.2 Nucleation .....	272
14.2.3 Fibril Extension .....	272
14.3 UV Light as a Potent Structural Perturbant .....	272
14.3.1 UV-Induced Aggregation of Prion Protein .....	273
14.3.2 Prevention of UV-Induced Aggregation of Prion Protein ..	274
14.3.3 UV Exposure Alters Conformation of Prion Protein .....	274
14.3.4 UV-Exposed Proteins Failed to Form Amyloid <i>De Novo</i> ..	277

XIV Contents

14.3.5	Is Subcritical Concentration of UV-Exposed Protein Responsible for Failure to Form Amyloid Fibrils? . . . . .	279
14.3.6	UV-Exposed Amyloidogenic Proteins Form Amyloid Upon Seeding . . . . .	280
14.3.7	UV-Exposed Prion Protein Fibrils Show Altered Fibril Morphology . . . . .	282
14.4	Discussion . . . . .	283
	References . . . . .	286
 <b>15 Real-Time Observation of Amyloid Fibril Growth by Total Internal Reflection Fluorescence Microscopy</b>		
	<i>H. Yagi, T. Ban, and Y. Goto</i> . . . . .	289
15.1	Introduction . . . . .	289
15.2	Total Internal Reflection Fluorescence Microscopy . . . . .	290
15.3	Real-Time Observation of $\beta$ 2-m and A $\beta$ Fibrils . . . . .	291
15.4	Effects of Various Surfaces on the Growth of A $\beta$ Fibrils . . . . .	292
15.5	Spontaneous Formation of A $\beta$ (1–40) Fibrils and Classification of Morphologies . . . . .	295
15.6	Conclusion . . . . .	297
	References . . . . .	298
	<b>Index</b> . . . . .	301

Water and Biomolecules

Physical Chemistry of Life Phenomena

Kuwajima, K.; Goto, Y.; Hirata, F.; Terazima, M.; Kataoka,  
M. (Eds.)

2009, XVII, 307 p., Hardcover

ISBN: 978-3-540-88786-7