

---

---

# CONTENTS

<b>Preface</b>	<b>ix</b>
Outline of the work . . . . .	ix
Remarks about notations . . . . .	xiii
Acknowledgment . . . . .	xiv
<b>1 Biological, Chemical, and Physical Background</b>	<b>1</b>
1.1 Introduction . . . . .	1
1.2 Chemical structure of proteins . . . . .	3
1.3 Chirality of amino acids . . . . .	6
1.4 Ionization of amino acid residues . . . . .	8
1.5 Intramolecular interactions . . . . .	12
1.5.1 Principles of quantum mechanics and atomic orbitals . . . . .	13
1.5.2 Covalent bonding . . . . .	28
1.5.3 Electrostatic interactions . . . . .	30
1.5.4 Van der Waals forces . . . . .	32
1.5.5 Hydrogen bonding . . . . .	34
1.6 Three-dimensional structure of proteins . . . . .	36
1.6.1 Dihedral angles . . . . .	36
1.6.2 Elements of secondary structure . . . . .	47
1.6.3 Tertiary and quaternary structure of proteins . . . . .	50

---

1.7	Influence of environment . . . . .	51
1.7.1	The hydrophobic effect . . . . .	52
1.7.2	Interaction of charged groups with solvent . . . . .	54
1.7.3	Chaperones and assisted protein folding . . . . .	56
1.7.4	Prions . . . . .	57
1.8	Protein synthesis . . . . .	58
1.8.1	Ribosomes . . . . .	59
1.8.2	Mechanism of translation . . . . .	61
1.8.3	Cotranslational protein folding . . . . .	63
1.8.4	Posttranslational modifications . . . . .	67
1.9	Experimental protein structure determination . . . . .	68
1.9.1	X-ray crystallography . . . . .	68
1.9.2	Nuclear magnetic resonance (NMR) spectroscopy . . . . .	69
1.10	Structure databases . . . . .	71
<b>2</b>	<b>Approaches for Protein Structure Prediction</b>	<b>73</b>
2.1	From <i>ab initio</i> to knowledge-based approaches . . . . .	73
2.1.1	<i>Ab initio</i> protein folding . . . . .	73
2.1.2	Knowledge-based structure prediction . . . . .	76
2.2	Empirical force fields . . . . .	79
2.2.1	Harmonic approximation for bond lengths and angles . . . . .	80
2.2.2	Torsion angles and out-of-plane bending . . . . .	81
2.2.3	Non-bonded interactions and assignment of atom charges . . . . .	83
2.2.4	Models for hydrogen bonding . . . . .	87
2.3	Solvation models . . . . .	88
2.3.1	Estimation of solvent-exposed area . . . . .	88
2.3.2	Poisson-Boltzmann equation . . . . .	89

---

<b>3</b>	<b>Modeling Intracellular Protein Folding</b>	<b>91</b>
3.1	The general idea of the new approach . . . . .	91
3.2	Interatomic distances versus dihedral angles . . . . .	92
3.3	Energy as a function of torsion angles . . . . .	109
3.4	Modeling hydration . . . . .	112
3.4.1	Rationale . . . . .	113
3.4.2	Grid generation . . . . .	116
3.4.3	Accessibility check . . . . .	118
3.5	Modeling cotranslational folding . . . . .	120
3.5.1	Operations for coordinate transformations . . . . .	122
3.5.2	Appending a new amino acid residue . . . . .	126
3.6	Twisting forces . . . . .	130
3.7	Dynamics in dihedral angle space . . . . .	137
<b>4</b>	<b>SiViProF Software</b>	<b>141</b>
4.1	SiViProF – a new simulation software . . . . .	141
4.2	Implementation of the model . . . . .	145
4.2.1	Listing degrees of freedom . . . . .	145
4.2.2	Generation of initial coordinates . . . . .	148
4.2.3	Chirality correction . . . . .	153
4.2.4	Overall organization . . . . .	155
4.2.5	Enhancement of computational efficiency . . . . .	157
4.3	Simulations . . . . .	158
4.3.1	Contributions of different interaction types . . . . .	158
4.3.2	Minimization of energy . . . . .	163
4.4	Conclusions and outlook . . . . .	166

---

<b>A</b>	<b>Implementation Details</b>	<b>169</b>
A.1	Visual representation of molecular elements . . . . .	169
A.2	Atom numeration in amino acids . . . . .	170
A.3	SiViPROF input format . . . . .	173
<b>B</b>	<b>Physical Quantities, Constants and Units</b>	<b>175</b>
<b>C</b>	<b>Mathematical Notations</b>	<b>177</b>
C.1	General notations . . . . .	177
C.2	General expressions . . . . .	177
C.3	Problem-specific notations . . . . .	178
C.4	Introduced operations . . . . .	178
C.5	Conventional notations . . . . .	179
<b>D</b>	<b>Parameters</b>	<b>181</b>
	<b>References</b>	<b>185</b>