Chapter 1: Introduction

Molecular Dynamics as a Tool for Understanding Molecular Function
Importance of Molecular Dynamics for Macromolecular Recognition
Current Models for Macromolecular Recognition
Influence of the Dynamics on the Thermodynamics of Macromolecular Recognition
Mutational Investigation of Protein-Protein Recognition Sites
Different Choices for Amino Acid Substitution
Hot Spots
Structural Response to Mutations at Protein-Protein Interfaces
Linkage of Interactions in Macromolecular Recognition
Scope of the Present Thesis

Chapter 2: Role of Dynamics in Sickle Hemoglobin Fiber Formation

Introduction
The Structure and Higher Order Organization of Hemoglobin S
Rationale of This Study
Polymerization Behavior of the Designed Mutants

Methods
Molecular Dynamics Simulations
Starting Coordinates
Forcefield and Simulation Protocol
Electrostatic Potential Calculations

Results
Surface Electrostatic of the Mutants
Molecular Dynamics Simulations
Stability of the Simulations
Root Mean Squared Fluctuations of Cα Atoms
Effect of Mutations on the Conformational Dynamics of the AB Inter-Helical Region
Analysis of Fluctuations in Inter-Residue Distances
Analysis of Dynamic Cross-Correlation Maps
Chapter 3: An Alternative Approach for Interpreting MD Simulation Data: Identification of Residue Positions Mutating Which Could Affect Protein Dynamics

Introduction

Theory

Results and Discussion
- Reproducibility of the GA Optimizations
- Quality of Fit
- Analysis of the Dynamic Effect of Mutational Perturbations Using GNM
- Identification of Residues Critical for Protein Structure Function on the Basis of GNM
- *In Silico* Mutagenesis for the Identification of Dynamically Linked Residues

Chapter 4: Conclusions and Future Outlook

Bibliography

Appendix