

Abstract

Sequence-specific interactions between proteins and nucleic acids play an essential role in the cell biology. While several molecular mechanisms contributing to the binding specificity have been identified empirically, no general protein–DNA recognition code has been described to date. In this thesis, I explore selected characteristics of protein–DNA interactions using computational methods. First, the pairwise interactions between the basic biomolecular building blocks—amino acids and nucleotides—are investigated. It is shown that several statistically enriched, biologically relevant interaction motifs correspond to the most energetically favorable configurations of the respective binding partners. In addition, a relationship between the physico-chemical properties of the amino acid residues found at the protein–DNA interface and the local geometric features of the DNA helix is presented. Next, the applicability of molecular dynamics-based setups to the description of binding equilibria in protein–DNA systems is investigated. Discrepancies are observed between the description offered by the computer simulations and experimental results, as well as between the results obtained using two molecular mechanical force fields. Finally, the more general evolutionary aspects of protein organization are explored, and a tool for the study of evolutionary conservation is introduced.