Abstract

Structural and mechanical properties of nucleic acids play a key role in a wide range of biological processes, as well as in the field of nucleic acid nanotechnology. The thesis presents results of several studies focused on modelling these properties. Extensive unrestrained atomic-resolution molecular dynamics (MD) simulations are used to investigate structural dynamics of nucleic acids, and to parametrize their mechanical models. The deformation energy is assumed to be a general quadratic function of suitably chosen internal coordinates. Two types of models are employed which differ in the level of coarse-graining. The first one is based on the description of conformation at the level of individual bases and the second, coarser one is used to study global bending and twisting flexibility. The models are applied to explain mechanical properties of A-tracts in the context of DNA looping and nucleosome positioning, to characterize twist-stretch coupled deformations in DNA and RNA, and to predict changes in the properties of damaged DNA that are likely to be relevant for damage recognition and repair. Besides that, we propose a general model of DNA allostery, applied to study the effect of minor groove binding of small ligands and the allosteric coupling between proteins mediated by the DNA. A careful comparison of our results with available experimental data demonstrates the general reliability of contemporary nucleic acid force fields and the adopted modeling approach. Our results should help to better understand the role of mechanical properties of nucleic acids in their biological function with potential application in the development of new drugs. The work presented in the thesis resulted in 11 publications in impacted international journals.