Adaptive Resolution Simulation of Oligonucleotides

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INTRODUCTION

Because of the structural peculiarities, the computational study of DNA demands the use of multiscale simulation methods, in order to describe sequence or conformation-dependent interactions while keeping the global constraints of the whole molecule. The Adaptive Resolution Simulation Scheme (AdResS) [1] is one of the most promising multiscale methods. AdResS couples two systems with different resolution: an atomistic system and a coarse-grained one, using a hybrid region in between. In this work we describe the implementation of AdResS to the simulation of oligonucleotides,

METHODS

The oligonucleotide d(CGCGAATTCGCG)$_2$ [2] was built with X3DNA [3] and simulated using parameters of the AMBER force field [4]. This oligonucleotide and also TIP3P water molecules and ions (Na+ and Cl-) are simulated explicitly and surrounded by coarse-grained water and ions[5] in an elongated box setup (X-split AdResS, Figure 1). The interaction potentials were derived by the iterative Boltzmann inversion (IBI) method [6] using VOTCA [7]. The simulations were run using GROMACS [8]. In order to achieve a flat density profile for water and ions through the simulation box, thermodynamic force corrections for all species were applied [9]. The results, regarding density profiles and DNA structural parameters were compared with reference atomistic simulations.

RESULTS AND DISCUSSION

The interaction potentials and thermodynamic force corrections were optimized using simulations of aqueous salt solutions. With the derived parameters, in the simulations of the full system the DNA was kept in the center of the atomistic region and interacts only with the explicit molecules Water and ions, however, can migrate freely in the system and interact with the species in the hybrid and coarse grained regions. The root mean square deviation of the macromolecule's structure, the density profiles for the species and the geometrical parameters for the DNA are essentially the same as in the atomistic reference simulations. The AdResS simulations performed faster than the reference atomistic simulations, especially if the atomistic region is chosen to be sufficiently small.

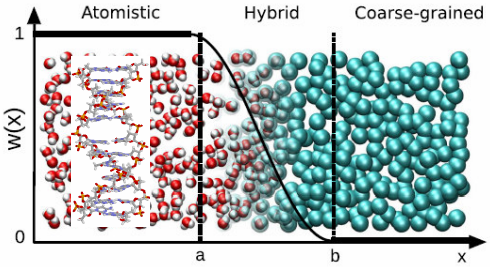

Figure 1. Geometrical setup of X-split AdResS (adapted from [10]).

CONCLUSIONS

The multiscale method AdResS was sucessfully applied to a complex system, composed by a oligonucleotide (dodecamer) in a salt solution. Despite of some simplifications the use of AdResS resulted in a improvement on the performance of the simulations, without affecting the structural stability of the nucleic acid.

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