Structural states of a RNA aptamer, molecular dynamics simulation study.

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Motivation

RNA, which adopts a wide range of secondary structures is involved in several kind of chemical interactions and shows a notable structural plasticity. Due to remarkable chemical properties and an important physiological role of RNAs, there is a growing interest in development of RNA-based drugs and ligands of clinical relevance. However, RNAs structural and dynamic features as well as the main RNA-protein recognition effects remain largely unaddressed.

We have studied the conformational behaviour and the dynamic of two different structural arrangements of an aptamer binding the bacillus anthracis ribosomal protein S8. This RNA aptamer has experimentally shown two different topologies in free state and in protein-bound state, although sequences differ for just few residues beyond the common internal loop. The role of the interacting protein on the RNA folding, stabilizing or inducing a particular conformation will be discussed.

Methods

Three molecular dynamic simulations of 300 ns each have been performed starting from three distinct aptamer structures: i) the aptamer free-state, using a representative model of a NMR ensemble of structures (pdb 2lun); ii) a similar aptamer bound to its target protein (4pdb) iii); an aptamer model built using the sequence of the RNA in the free state but with the structural arrangement of the bound-state to investigate a possible influence of the sequence on the RNA folding. All the systems under investigations were solvated in a truncated octahedral water box using explicit water models, with a least a 1.1 Å distance to the border, using Na+ counter-ions to neutralize. 6 steps of heating simulation from 50 K to 300K were carried out before to perform the final MD run of 300 ns in NPT conditions without restrains. The trajectories were analysed using the GROMACS utilities and X3DNA program.

Results

Our data show that both bound-state RNA arrangements are structurally stable, holding all the main interactions since the beginning of the simulations. The free-state RNA is the system with the largest flexibility, reaching an equilibrium after 40 ns of simulation. Although the NMR structure appears less rigid, during the total run it never matches the arrangement of the bound state. Definitely, within our time scale, a convergence of the free state with the bound-state trajectories has never been observed and the two different arrangements show differences in flexibility. Preliminary data suggest a significantly different behaviour of the free- and bound-state structures supporting a preeminent role of the interacting partner protein on the RNA overall folding to induce a particular stable structural arrangement.

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