A Thermodynamic Study of 3' Overhangs in the RNAi Mechanism

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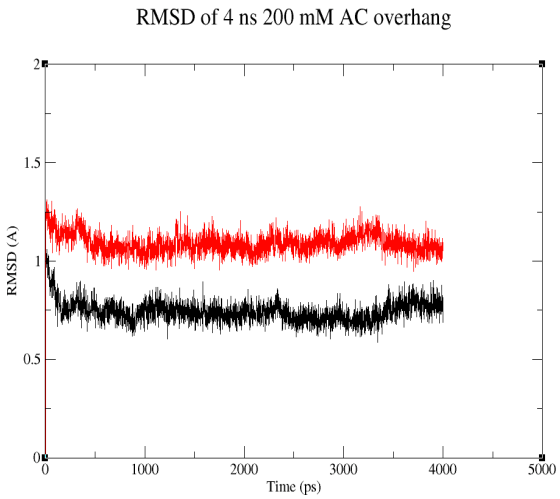
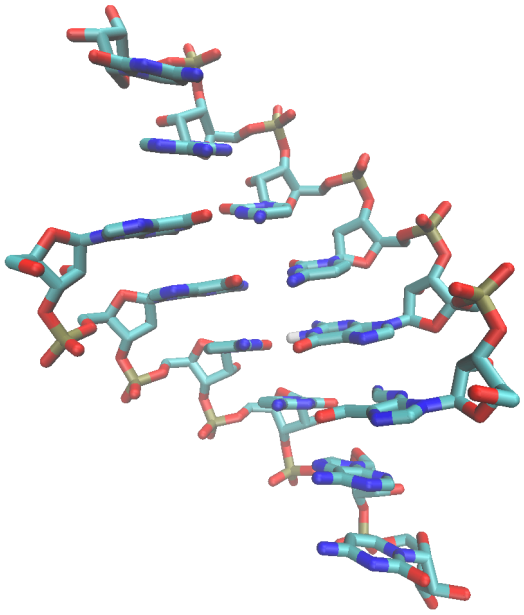
RNA interference (RNAi) is the mechanism of post-transcriptional gene repression conserved in eukaryotes. Because of the outstanding specificity of the RNAi mechanism and our ability to engineer double stranded RNA (dsRNA), RNAi can be used as a novel means of "turning off" malevolent genes. The objective of this study is to computationally characterize 10 sets of 3' overhangs previously studied in a wet bench environment.

100 nanosecond molecular dynamics simulations of 10 sets of 3' overhangs on a GGCC core were ran at 200 mM and 1 M NaCl ion concentrations. The force field utilized includes the ff99 force field, the Bsc0 and χ_{OL3} backbone modifications, the OPC water model, the TIP4PEW ion model, additionally, backbone oxygens O3', O5', O1P and O2P utilized Case's phosphate parameters for phosphate oxygens. Preliminary RMSD calculations indicate low deviations from both starting and average structures. RDF calculations of the 200 mM system reveal non-aggregating sodium and chloride ions, which was expected at the lower ion concentration. The future direction of this work includes RDF calculations of the 1 M systems, constructing base stacking plots to map out the interactions between the overhanging bases and the terminal base pair and RMSD's for the full 100 ns simulations.

The conclusions drawn from this work will give insight into the RNAi mechanism, specifically the way in which Dicer cleaves long dsRNA into the 21-25 base pair segments characteristic of the RNAi pathway.



Indicates a well equilibrated system (Black from Avg., Red from Starting).



PDB image taken on VMD highlighting the overhanging bases.