Studying Synthetic DNA using Molecular Dynamics Simulations

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Recently, the creation and stable growth of a semisynthetic organism (SSO) originating from *E. Coli* was reported [1]. Besides the natural guanine-cytosine (G-C) and adenine-thymine (A-T) base pairs, its DNA also contains an unnatural base pair (UBP), X-Y. The bases used in the UBP are named NaM (X) and 5SICS/TPT3 (Y) respectively [1], [2], [3]. The X-Y base pair is hydrophobic, and the two bases are stabilized via packing interactions instead of hydrogen bonds. In the present work, the conformational dynamics of a large DNA fragment (39 base pairs) containing a X-Y base pair is investigated using classical molecular dynamics simulations. Both NaM-5SICS (moderate SSO growth, only under restricted conditions [1]) and NaM-TPT3 (robust SSO growth [1]) UBPs have been considered. Two different simulations were ran for each UBP, placing it in an A-T rich and a G-C rich region of the DNA fragment, respectively. Preliminary analysis (UBP in the A-T rich region) indicates that both UBPs adopt a configuration that resembles the natural Watson-Crick base pairing, and each base is stabilized via packing interactions with its neighboring bases. This finding is in agreement with a recent computational study of a DNA 11mer containing a NaM-5SICS pair [4].

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