Sequence-dependent effects on the stability of PNA•DNA duplexes

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Peptide nucleic acid (PNA) is a DNA analogue in which the phosphodiester backbone has been replaced by a 2-aminoethyl-glycine backbone that is neutral and achiral (Figure 1). PNA is able to hybridize with high affinity and specificity to Watson-Crick complementary sequences of DNA, RNA, or other PNA strands. Since its discovery, PNA has shown great promise for use in the detection of gene mutations as well as gene-targeted drugs. Recent experiments have suggested that PNA·DNA duplexes are significantly stabilized when purine bases are present in the PNA strand rather than the DNA strand. These studies, however, could not elicit the origin of the different stabilities between purine-rich PNA versus pyrimidine-rich PNA heteroduplexes with DNA. In this study, we use molecular dynamics simulations to investigate the sequence dependence effects on the structure and dynamics of both purine-rich PNA and pyrimidine-rich PNA heteroduplexes with DNA. Analysis of the time evolution of the root-mean-squared-deviation (RMSD) values shows a noticeable difference in the dynamics for purine rich PNA strands that form antiparallel duplexes with DNA (N terminus of the PNA strand is oriented toward the 3' end of the DNA strand) in contrast to the parallel formation. Energy analysis of base content was performed by systematically changing the PNA strand content from containing only purine bases to only pyrimidine bases. Analysis of the duplex energy shows that as the purine content of the PNA strand increases, the duplex becomes more stable.

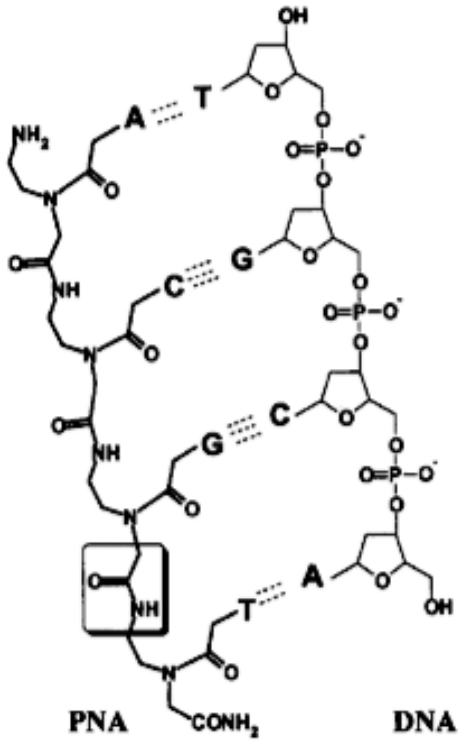

Figure 1