Sequence-dependent changes in PNA•DNA duplex conformations

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Peptide nucleic acid (PNA), a DNA analogue, can form heteroduplexes with DNA and RNA single strands, creating more stable structures than homoduplex structures. Its neutral backbone, flexibility, and increased stability in comparison to pure DNA duplexes make PNA a potential candidate for use in antisense and antigene therapies. Previous studies have shown that PNA·DNA duplexes are significantly stabilized when pyrimidine bases are present in the DNA strand. Using molecular dynamics simulations, we have investigated the structural properties of a series of PNA·DNA duplexes systems for which the pyrimidine base content of the DNA strand was systematically decreased from containing only pyrimidine to only purine bases. Backbone dihedral angles and sugar puckering of the DNA strand in the hybrid indicate that the purine rich DNA strand samples both A-/B- like conformations, while the more stable pyrimidine rich DNA hybrid exhibits more A-like conformations. This suggests less stable PNA·DNA duplexes form when the DNA strand retains some of its homoduplex B-type structural characteristics.

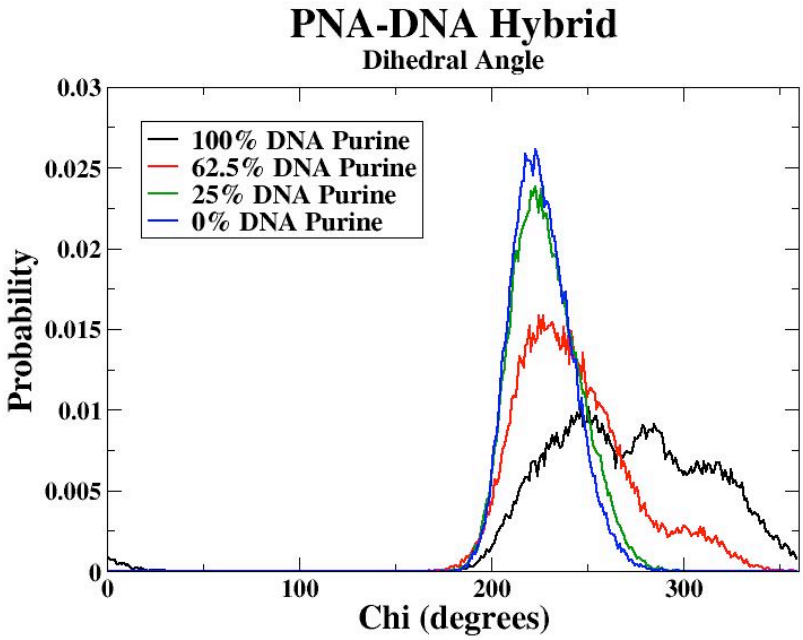

Figure 1: Probability distributions of the backbone dihedral angle χ (C1′ - N9 for purines and C1′ - N1 for pyrimidines) for the DNA strand in four different PNA•DNA hybrid duplexes. While the number (and identity) of the purine bases was the same for each 8-mer duplex, the number of purines attached to the DNA strand varied from 0 to 8 bases.