MESOSCOPIC MODELING OF DNA

Researchers are working to develop a mesoscopic theoretical model that captures the physico-chemistry of DNA hybridization.

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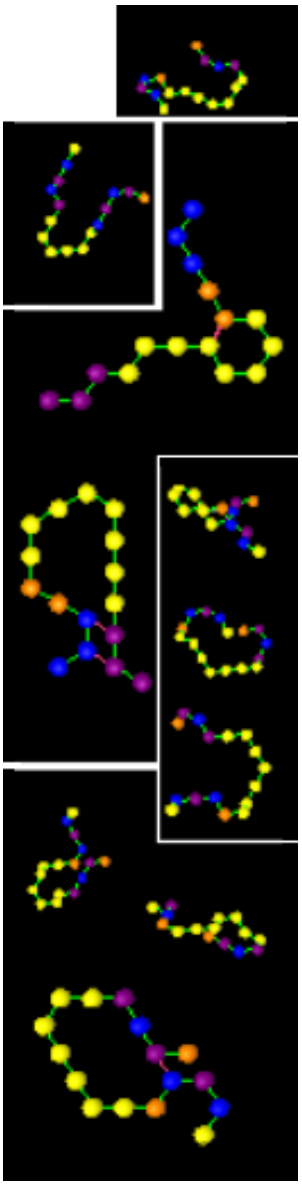
Objective: Recent advances in experimental techniques have made possible single DNA molecule manipulations and provided detailed information on the mechanical properties of both ssDNA and dsDNA. In contrast, there is presently a lack of theoretical quantification of various nucleotide-nucleotide molecular interactions that determine DNA mechanical properties, which in turn affect any hybridization reaction between complimentary DNA strands as well as DNA/RNA hairpin and ring formation. Hence, a success in theoretical simulation of DNA interactions such as stacking and hydrogen bonding may provide means to control the hybridization process and help to design more efficient and reliable hybridization microarrays (gene chips) used in medical diagnosis.

Approach: Meso-scale models that capture the features necessary for predicting physical processes at a molecular level would be more useful than either *ab initio* calculations, which are restricted to very small entities (nucleotides or their dimers), or force-field models, which treat energy as the function of atom positions only. Several groups have recently developed meso-scale models to study long-time dynamics of DNA molecules and correctly predicted dsDNA melting temperatures. These models, however, lack base-specificity and thus are not useful for studies of sequence-dependent properties. In the model proposed by the Amaral team, DNA is depicted as a chain of beads lying on a 3D lattice; each bead represents only the pentose nucleotide sugar and has a base (AGCTU) attached to it rigidly to form the complete nucleotide. Each different base has a different set of interactions, of which two types are considered: complementary and stacking interactions. Eventually, simulations will include interactions of DNA with the solvent that fills the unoccupied nodes of the lattice. The nature of these interactions will be attractive, repulsive, or neutral depending on the modeled experimental conditions.

Results: The research team led by Dr. Amaral has developed a theoretical model that simulates the elastic properties of ssDNA of different base sequence as well as the kinetics of the DNA hairpin formation. This model can be used for detailed studies of cross-hybridization and the mismatch formation in DNA hybridization microarrays to improve their performance.



Examples of various hairpins configurations. Each bead represents a nucleotide (**A** is shown in orange, **T** – in yellow, **G** – in purple, and **C** – in blue). Lines between complementary bases represent hydrogen bonds.