

Project 3: Factors influencing H-bonding in DNA base pairs.

The structure of DNA was brilliantly deduced by Watson and Crick from X-ray photographs to be the double helix we are familiar with, with the hydrophilic phosphate backbone on the exterior, and the two strands held together by hydrogen-bonding interactions between complementary bases [1]. This is the form of DNA found in virtually all living creatures, and is now known as the *B* form.

While the *B* form is that which occurs under physiological conditions (pH 7, ~300 K, 0.2 M Na⁺), the complex DNA molecule has the capacity to take several other forms: among these are *B'*-DNA (non-coplanar bases), *A*-DNA (empty center channel, formed under dehydrated conditions), *Z*-DNA (left-handed helices), and *ps*-DNA (parallel-stranded, formed in all-AT DNA under some conditions) [2]. Also, in addition to the usual duplex form of DNA, triplexes and quadruplexes are known.

Transformations between DNA structures can occur under conditions of changed temperature, solvent character (pH, polarity, or ionic strength), or base sequence. DNA undergoes a helix-coil transition (melting to single strands) on heating, and under conditions of high ionic strength the equilibrium between *B* and *Z* forms tilts towards *Z*. At the level of base pair interactions, ionization, electron attachment, or chemical modification (any of which can occur through radiation damage) can alter the preferred H-bonding conformation from the usual Watson-Crick structure to one of several other possibilities (Hoogsteen, wobble, ...).

Our goal in this project is to apply computational chemistry and experimental spectroscopy to the study of DNA base pair interactions and DNA conformational changes. We will calculate structures using a mixture of density functional and molecular mechanics methods as appropriate for the size of the molecular fragment considered, and apply UV-Vis absorption and fluorescence methods to pH-dependence, ionic strength dependence, and temperature-dependence of DNA properties.

Initial references:

1. Watson, J. D., Crick, F. H. C., *Nature* **171** (1953) 737.
2. Frank-Kamenetskii, M. D., *Phys. Rep.* **288** (1997) 13.