Atomistic simulation of the DNA helix-coil transition.

Stefano Piana

Nanochemistry Research Institute, Curtin University of Technology, GPO Box U1987, 6845 Perth, WA. Australia. piana@ivec.org

SUPPLEMENTARY MATERIAL

Definition of the collective variables used in the Bias Exchange simulation.

In order to perform an enhanced sampling simulation a set of variables that describe the reaction must be selected. The helix to coil transition is a complex process that involves changes in the base-base pairing and changes in the DNA strand structure. In this work, the space of conformations was defined by 6 collective variables. These six collective variables were of two types: one describing the process of formation and rupture of DNA base pairs, and one describing the conformation of the DNA phosphate backbone.

The first type is a coordination variable that is related to the distance between two atoms or two groups of atoms:

$$N_{AB} = \sum_{i=1}^{N_A}\sum_{j=1}^{N_B}\frac{1-\frac{r_{ij}^8}{r_0^8}}{1-\frac{r_{ij}^{10}}{r_0^{10}}}$$

where r_{ij} is the distance between atoms i and j and r_0 is a cutoff distance. The variable can assume any value between 0 (no pairs within the cutoff distance) and the total number of all possible pairs. Two variables of this type were used: one to describe the formation of A-T pairs and one to describe the formation of C-G pairs. The distance used to define the formation of a pair is the distance between the central nitrogens of the A-T and of the C-G base pairs and the cutoff distance was $r_0 = 4.0$ Å. The width of the Gaussians for this collective variable was 0.5. The height of the Gaussians was 0.1 kj mol^{-1} for all the collective variables.

The second type of collective variables describes the conformation of the phosphate backbone. This type is defined as:

$$\Phi = \sum_{i=1}^{N}\sqrt{1+\cos^2\left(\frac{\varphi_i-\varphi_{i-1}}{2}\right)}$$

where Φ can range from $N\sqrt{2}$, if all consecutive dihedrals have the same value (as for the phosphate backbone angles in B-DNA), to N if all consecutive dihedrals have different values. 4 variables of this type have been used, two for each DNA strand. The first runs over the ∠O3'-P-O5'-C5' phosphate backbone dihedral angles (α) and the second between the ∠C3'-O3'-P-O5' phosphate backbone dihedral angles (ζ). The width of the Gaussians for these collective variables was 0.05.

Calculations performed with the Amber99 force field indicated that the collective variables acting on α and ζ dihedrals are highly correlated. For this reason, in the subsequent set of calculations performed with the modified Amber99 force field the ζ variable was not used. The reduction in the total number of collective variables improves the convergence properties of the BE-META simulations.