Supporting Methods

The solvent-accessible surface area around the major groove was evaluated by considering the atoms, N6 of adenine, O6 of guanine, O4 of thymine, and N4 of cytosine, and around the minor groove by selecting the N2 of guanine, N3 of purine, and O2 of pyrimidine bases.

For the evaluation of DCC of each protein–DNA complex, all configurations were translated and rotated by means of a least-squares-fitting procedure using all of the backbone $C^\alpha$ atoms of the protein and the phosphorous atoms of the DNA to align on the minimized structure. The crosscorrelation coefficient for the displacement of any two atoms $i$ and $j$ was computed as:

$$C_{ij} = \langle \Delta r_i \Delta r_j \rangle / [\langle \sqrt{\Delta r_i^2} \sqrt{\Delta r_j^2} \rangle]$$

$\Delta r_i = (\langle r_i \rangle - r_i)$ is the displacement from the mean position of the $i$th atom during an MD step and the $\langle \rangle$ represents the configurational average over the MD trajectory. Positive and negative values of $C_{ij}$ represent a correlated (in the same direction) and anticorrelated (in opposite direction) motions between residues (or atoms) $i$ and $j$, respectively. The baseline values for correlated motions are greater than 0.31, and, for anticorrelated motions, they are lower than $-0.14$.

The order parameter $S^2$ for $\phi/\psi$ torsion angles of the protein backbone of ETS–GGAA and ETS–GGAG structures was calculated according to the equation:

$$C_i(t) = \langle P_2(h_i(\tau + t)\cdot h_i(\tau)) \rangle$$

$$S^2 = \lim_{t \to \infty} C_i(t)$$

$P_2$ is the second-order Legendre polynomial, and $h$ is a unit vector that describes the orientation of the interaction bond vector for residue $i$ in the macromolecular frame. The normalized autocorrelation function related to the protein backbone N–C$^\alpha$ and C–C$^\alpha$ bond vectors were evaluated for the averaged MD trajectory (starting from 900 ps of dynamics). The estimate of $S^2$ for each residue was based on the plateau value of the autocorrelation curve. Before initiating the calculations, the overall motion of the instantaneous protein structure was removed by best-fit rms positions of the respective atoms onto the minimized coordinates. The $S^2$ gives a measure of the structural flexibility, with a value 1 for complete rigidity, and a value of 0 for total flexibility (where all of the possible conformations are sampled).