A Generalized Theory of DNA Looping and Cyclization

DAVID WILSON, TODD LILLIAN, NOEL PERKINS, University of Michigan, ALEXEI TKACHENKO, Brookhaven National Laboratory, JENS-CHRISTIAN MEINERS, University of Michigan — We have developed a semi-analytic method for calculating the Stockmayer Jacobson J-factor for protein mediated DNA loops. The formation of DNA loops on the order of a few persistence lengths is a key component in many biological regulatory functions. The binding of LacI protein within the Lac Operon of E.coli serves as the canonical example for loop regulated transcription.

We use a non-linear rod model to determine the equilibrium shape of the inter-operator DNA loop under prescribed binding constraints while taking sequence-dependent curvature and elasticity into account. Then we construct a Hamiltonian that describes thermal fluctuations about the open and looped equilibrium states, yielding the entropic and enthalpic costs of loop formation. Our work demonstrates that even for short sequences of the order one persistence length, entropic terms contribute substantially to the J factor. We also show that entropic considerations are able to determine the most favorable binding topology. The J factor can be used to compare the relative loop lifetimes of various DNA sequences, making it a useful tool in sequence design. A corollary of this work is the computation of an effective torsional persistence length, which demonstrates how torsion bending coupling in a constrained geometry affects the conversion of writhe to twist.