Computer Simulations of DNA Supercoiling at the Atomic Level

Sarah Harris, School of Physics and Astronomy, University of Leeds

Co-authors: Jon Mitchell (Leeds); Charlie Laughton (Nottingham) and Tannie Liverpool (Bristol).

The discovery of the structure of duplex DNA revealed how cells store genetic information. However, we are far from understanding the more complex biological question of how this information is regulated and processed by the cell. DNA topology and supercoiling is known to affect DNA transcription and other DNA-associated processes. Changes in topology affect DNA conformation, and can thereby modify the interaction between regulatory DNA-binding proteins and their target sites. However, there is still little understanding of how cells use supercoiling to regulate gene expression at the molecular level. Genetic regulation involves many complex factors that are difficult to isolate *in vivo*, and it is difficult to obtain experimental information as to the supercoiling dependent structures of DNA and its complexes with other molecules.

Small DNA circles offer a controllable model system for the systematic exploration of the dependence of DNA structure on supercoiling. We use computational methods to explore the supercoiling-dependent conformation of small DNA circles, and how this is affected by supercoiling, salt concentration, DNA sequence and the size of the circles. The calculations use atomistic molecular dynamics simulation, and employ both implicit and explicit solvent models.