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**Seeing Supercoiled DNA with Atomistic Simulations: A New Twist on a Familiar Structure**

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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 supercoiling is generated whenever a gene is transcribed, and complex cellular machinery, such as toposisomerases, are required to modulate the effect of this induced torsional stress. Supercoiling has been implicated in the packaging and 3D arrangement of both prokaryotic and eukaryotic DNA, which in turn has fundamental consequences for transcription regulation and genome stability.

In spite of the ubiquity of supercoiled DNA in cells, no experimental tool has been able to capture atomically detailed structural information. Small DNA circles containing between 100 and 400 base pairs, however, offer a controllable model system for the systematic exploration of the dependence of DNA structure on supercoiling through cryo-electron microscopy, atomic force microscopy, and computer modelling. We use atomistic molecular dynamics simulations to explore the supercoiling-dependent conformation of small DNA circles. We show that kinks and denaturation bubbles are generated in the DNA by high torsional stress, that the compaction of the DNA is highly dependent on salt, and that the DNA adopts writhed structures that are highly dynamic and which offer additional opportunities for DNA/protein interactions in 3D space. We then offer an atomistic interpretation for the growing experimental data that shows the regulatory role proposed for supercoiling in the genome.