

NewsBytes

DNA Shows Surprising Flexibility

For decades, scientists have believed that DNA of short lengths (150 base pairs or fewer) behaves as a relatively stiff rod—able to quiver a bit, but rarely forming a circle or tight angle without help from outside forces. But a new simulation, reported in the December issue of *Biophysical Journal*, puts a kink in this theory.

“We observed fairly sharp bends that are inconsistent with classical theory. We see DNA bending quite a bit,” says **Alexey Onufriev, PhD**, assistant professor of computer science and physics at Virginia Tech. “If this idea holds up, it may be a paradigm shift in how we think about protein-DNA complexes.”

DNA’s flexibility on this length scale has implications for DNA packaging, gene transcription, and gene regulation.

For example, in the nucleosome (the fundamental unit of DNA packaging), 147 base-pair segments of DNA wrap 1.65 times around a core of proteins. DNA also twists in and out of loops to turn certain genes off and on. Under the old theory, scientists had to reach for *ad hoc* explanations, such as helper proteins, to explain how unbendable DNA could manage these feats.

Onufriev and doctoral student **Jory Z. Ruscio** modeled a nucleosome worth of DNA (147 base pairs) at the atomic level. The key to their simulation was use of the “implicit solvent” method; rather than modeling every molecule of water, they modeled water as a continuous mass. This method saves enormous computing power and speeds up the simulation by about 100-fold by removing water’s viscosity—the property that makes it so hard to move quickly in

swimming pools, Onufriev says. “Whatever happens conformationally happens fast,” he says.

At the same time, water’s thermodynamic properties are perfectly preserved. “We cannot ask any questions like what are the diffusion coefficients, because those would be skewed. But we can ask thermodynamic questions—is this conformation more preferable than the other one?” Onufriev says.

This innovation plus use of Virginia Tech’s super computer, System X, allowed Onufriev and Ruscio to explore DNA’s range of motion on a longer length and time scale than any atomic-level simulation before them.

Their simulation showed that DNA of 147 base pairs wiggles and bends much more than traditional theory predicts—and at a much lower energy cost than expected. The bonds of the double helix remained intact in all simulations, so their results are not an artifact of the DNA simply unraveling to create soft spots.

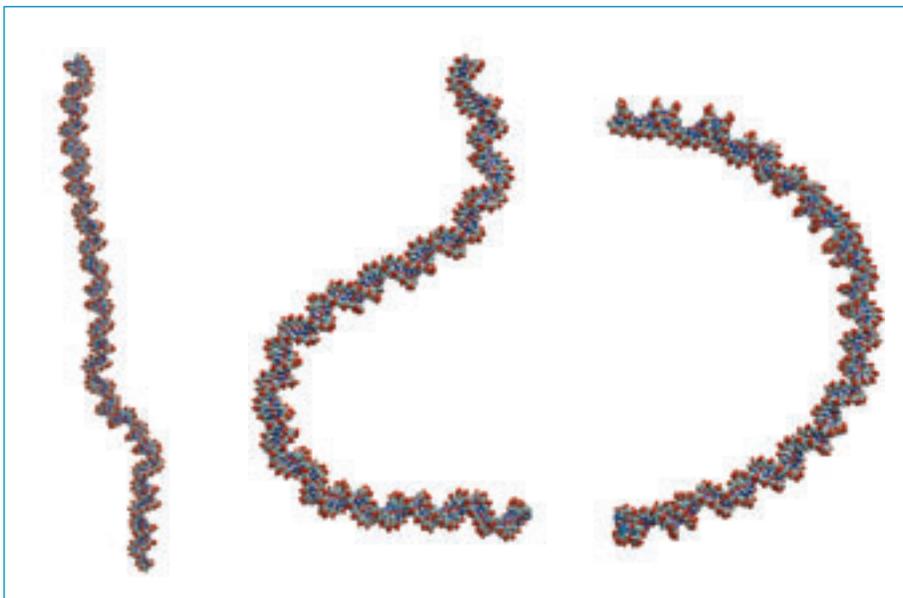
Onufriev’s results agree nicely with two independent threads of experimental evidence that have recently emerged, says **Philip Nelson, PhD**, professor of physics at the University of Pennsylvania. A 2004 paper showed that DNA of 100 base pairs spontaneously forms circles in physiological conditions; and, using atomic force microscopy, Nelson’s team recently showed that DNA of this length kinks more frequently than the old theory predicts.

The emerging picture finally makes it clear how nucleosomes, DNA regulatory loops, and viral packaging are possible, Nelson says. “No *ad hoc* mechanisms for promoting tight bending are needed.”

“This is one of those beautiful moments where simulation and theory and experiment all converge,” he says.

—By **Kristin Cobb, PhD**

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Three different images showing the simulation of DNA’s flexibility over a length of 147 base pairs. Courtesy of Alexey Onufriev.

The Geometry of Adhesion

A single cell caught up in the flow of blood, air, or water often depends on its ability to latch onto passing surfaces—in short, its ability to stick. That’s why researchers in Germany created a model