Unraveling the physics of DNA's double helix

July 12 2007

Researchers at Duke University's Pratt School of Engineering have uncovered a missing link in scientists' understanding of the physical forces that give DNA its famous double helix shape.

"The stability of DNA is so fundamental to life that it's important to understand all factors," said Piotr Marszalek, a professor of mechanical engineering and materials sciences at Duke. "If you want to create accurate models of DNA to study its interaction with proteins or drugs, for example, you need to understand the basic physics of the molecule. For that, you need solid measurements of the forces that stabilize DNA."

In a study published online by *Physical Review Letters* on July 5, Marszalek's team reports the first direct measurements of the forces within single strands of DNA that wind around each other in pairs to form the complete, double-stranded molecules. The work was supported by the National Science Foundation and the National Institutes of Health.

Each DNA strand includes a sugar and phosphate "backbone" attached to one of four bases, which encode genetic sequences. The strength of the interactions within individual strands comes largely from the chemical attraction between the stacked bases. But the integrity of double-stranded DNA depends on both the stacking forces between base units along the length of the double helix and on the pairing forces between complementary bases, which form the rungs of the twisted ladder.

Earlier studies have focused more attention on the chemical bonds between opposing bases, measuring their strength by "unzipping" the molecules' two strands, Marszalek said. Studies of intact DNA make it difficult for researchers to separate the stacking from the pairing forces.

To get around that problem in the new study, the Duke team used an atomic force microscope (AFM) to capture the "mechanical fingerprint" of the attraction between bases within DNA strands. The bonds within the molecules' sugar and phosphate backbones remained intact and therefore had only a minor influence on the force measurements, Marszalek said.

They tugged on individual strands that were tethered at one end to gold and measured the changes in force as they pulled. The AFM technique allows precise measurements of forces within individual molecules down to one pico-Newton--a trillionth of a Newton. For a sense of scale, the force of gravity on a two-liter bottle of soda is about 20 Newtons, Marszalek noted.

They captured the range of stacking forces by measuring two types of synthetic DNA strands: some made up only of the base thymine, which is known to have the weakest attraction between stacked units, and some made up only of the base adenine, known to have the strongest stacking forces. Because of those differences in chemical forces, the two types of single-stranded DNA take on different structures, Marszalek said. Single strands of adenine coil in a fairly regular fashion to form a helix of their own, while thymine chains take on a more random shape.

The pure adenine strands exhibited an even more complex form of elasticity than had been anticipated, the researchers reported. As they stretched the adenine chains with increasing force, the researchers noted two places—at 23 and 113 pico-Newtons--where their measurements leveled off.

"Those plateaus reflect the breaking and unfolding of the helix," Marszalek explained. With no bonds between bases to break, the thymine chains' showed little resistance to extension and no plateau.

Based on the known structure of the single stranded DNA molecules, they had expected to see only one such plateau as the stacking forces severed. Exactly what happens at the molecular level at each of the two plateaus will be the subject of continued investigation, he said.

Source: Duke University