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Charged graphene gives DNA a stage to perform molecular gymnastics

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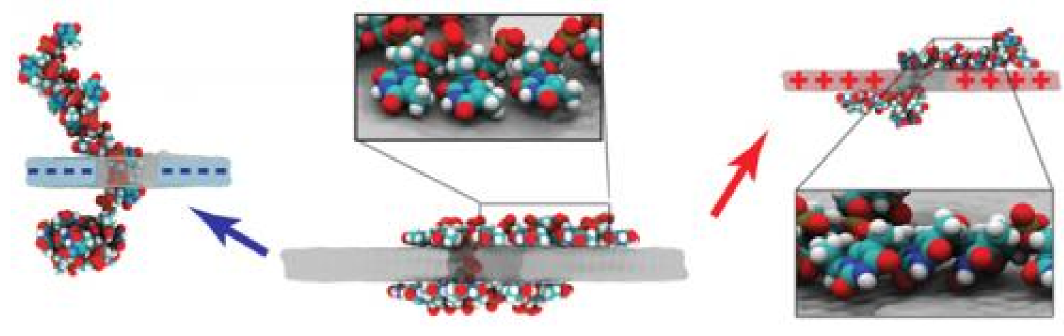

DNA interacts with charged graphene and contorts into sequence-specific shapes when the charge is changed. | Photo courtesy Alek Aksimentiev

(Phys.org) —When Illinois researchers set out to investigate a method to control how DNA moves through a tiny sequencing device, they did not know they were about to witness a display of molecular gymnastics.

Fast, accurate and affordable DNA sequencing is the first step toward personalized medicine. Threading a DNA molecule through a tiny hole, called a nanopore, in a sheet of graphene allows researchers to read the DNA sequence; however, they have limited control over how fast the DNA moves through the pore. In a new study published in the journal *Nature Communications*, University of Illinois physics professor Aleksei Aksimentiev and graduate student Manish Shankla applied an electric charge to the graphene sheet, hoping that the DNA would react to the charge in a way that would let them control its movement down to each individual link, or nucleotide, in the DNA chain.

"Ideally, you would want to step the DNA through the nanopore one nucleotide at a time," said Aksimentiev. "Take a measurement and then have another nucleotide in the sensing hole. That's the goal, and it hasn't been realized yet. We show that, to some degree, we can control the process by charging the graphene."

The researchers found that a positive charge in the graphene speeds up DNA movement through the nanopore, while a negative charge stops the DNA in its tracks. However, as they watched, the DNA seemed to dance across the graphene surface, pirouetting into shapes they had never seen, specific to the sequence of the DNA nucleotides.

"It reminds me of Swan Lake," Aksimentiev said. "It's very acrobatic. We were very surprised by the variety of DNA conformations that we can observe at the surface of graphene when we charge it. There is one sequence that starts out laying down on the surface, and when we change the charge, they all tilt on the side like they are doing a one-armed push-up. Then we also have nucleotides that would lay back, or go up like a ballerina en pointe."

See a video animation of DNA dancing as the graphene charge changes:

Aksimentiev hypothesizes that the conformations are so different and so specific to the sequence because each nucleotide has a slightly different distribution of electrons, the negatively charged parts of the atoms. There is even a visible difference when a nucleotide is methylated, a tiny chemical change that can turn a gene on or off.

By switching the charge in the graphene, the researchers can control not only the DNA's motion through the pore, but also the shape the DNA contorts into.

"Because it's reversible, we can force it to adopt one conformation and then force it to go back. That's why we call it gymnastics," Aksimentiev said.

The researchers extensively used the Blue Waters supercomputer at the National Center for Supercomputing Applications, housed at the University of Illinois. They mapped each individual atom in the complex DNA molecule and ran numerous simulations of many different DNA sequences. Supercomputing power was essential to carrying out the work, Aksimentiev said.

"This is a really computationally intensive project," he said. "Having access to Blue Waters was essential because with the sheer number of simulations, we would not have been able to finish them. It would have taken too long."

The next step is to combine a charged nanopore setup with a sensor to build a DNA sequencing device that would incorporate both motion control and nucleotide recognition. The researchers also hope to explore the unexpected conformational changes for insights into epigenetics, the field that studies how genes are expressed and moderated.

"DNA is much more complicated than just a double helix. It's a complex molecule that has many properties, and we are still uncovering them," Aksimentiev said.

More information: "Conformational transitions and stop-and-go nanopore transport of single-stranded DNA on charged graphene." *Nature Communications* 5, Article number: 5171 DOI: 10.1038/ncomms6171

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