



News and opinions

## Graphene takes steps toward precise DNA delivery

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Tiny step-like defects in single-layer sheets of graphene could offer a new way of transporting DNA and other biomolecules to specific locations, according to researchers from the University of Illinois [Shankla and Aksimentiev, *Nature Nanotechnology* (2019), <https://doi.org/10.1038/s41565-019-0514-y>].

“We were interested in finding a way to bring single biomolecules towards a nanopore in a graphene membrane for sensing and sequencing applications,” explains Aleksei Aksimentiev of the Beckman Institute for Advanced Science and Technology.

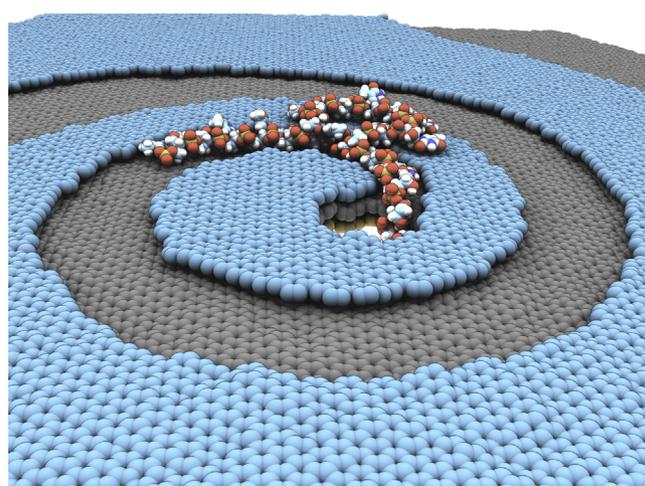
The precise delivery and placement of biomolecules such as DNA is key to a range of detection and manipulation methods in which single molecules are sorted, separated, and identified from mixed sources. The use of nanopore-based sensors to attract and identify charged biomolecules is now emerging as an attractive prospect. However, nanopore sequencing is highly dependent on how molecules are delivered to pores, which can also become clogged.

Aksimentiev and his colleague Manish Shankla base their approach on nanopores in graphene layers, which offer a very precise means of containing biomolecules because of the material's single-atom thickness. Until now, however, the strong physisorption of DNA to graphene has seemed to rule out its use in practical terms.

Using molecular dynamics simulations, Aksimentiev and Shankla have found, however, that DNA can move easily along step-like defects on the surface of a form of graphene known as highly oriented pyrolytic graphene (HOPG) when propelled by the tip of an atomic force microscope (AFM). DNA also appears to prefer going down step defects rather than up.

“In simple terms, we pulled a molecule of DNA adhered to a single sheet of carbon atoms across a single-step defect,” explains Aksimentiev. “We found the force required to pull the molecule up the step to be substantially higher than moving the molecule down the step, which we found surprising as gravity is negligible at the nanoscale.”

Computational study of the effect led the researchers to design a spiral-like pattern in two overlaid graphene layers that delivers a DNA or protein molecule into a nanopore (Fig. 1). By applying a force to the biological molecule, either directly with an AFM tip or from



**Fig. 1.** Schematic of a DNA molecule directed towards nanopore at the center of a step-defect spiral in graphene. (Credit: Manish Shankla, University of Illinois.)

a flowing solution, it can be directed towards the nanopore along a pathway of step defects. The effect could be quite general, points out Aksimentiev, as long as the biomolecule and two-dimensional material have a hydrophobic attraction.

“For nanopore sensing of DNA, RNA, and other proteins, the spiral delivery system potentially enables both very high throughput analysis and detection of scarce analytes,” he says. “On a broader note, our work describes a general approach for deterministic motion of single molecules, which can be used for molecular sorting, analysis and chemical synthesis.”

It remains to be seen whether nanoscale step defects can transport and deliver biomolecules in practical systems but, although challenging, Aksimentiev and Shankla are confident that fabrication difficulties will be resolved in the near future.

“Shankla and Aksimentiev [provide] a very nice molecular dynamics demonstration that graphene step-defects could, in theory, be used to guide and deliver DNA to a nanopore,” comments Daniel Branton of BioLabs at Harvard University.

However, he cautions that because current electrophoretic methods used to deliver DNA to nanopores are easily implemented,

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the new approach should ideally offer practical advantages such as concentrating specific DNA molecules or delivering DNA to nanopores in a deterministically controlled way.

“Experimental evidence showing that Shankla and Aksimentiev’s proposed graphene steps-nanopore setup can achieve such delivery would be highly desirable,” he adds.

Cees Dekker of Delft University of Technology (TU Delft) in the Netherlands agrees that it may be challenging to realize the guided delivery of ssDNA to a graphene nanopore experimentally.

“But as always, this is very original and inspiring work by Aksimentiev who is a world leader in molecular dynamics simulations of nanopores,” he says.