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Nanopores sequence DNA

Oct 12, 2009

Adam Hall

Researchers at the Delft University of Technology have developed a new technique that can measure both the charge and diameter of a single molecule for the first time. The method, which employs solid-state nanopores, can clearly distinguish between molecules of DNA that have a protein coating and those that do not – something that could be useful for DNA sequencing and detecting markers for genetically inherited diseases.

"Our technique will eventually allow us to rapidly differentiate spots along an individual molecule, for example, on multiple DNA-bound proteins," team member Adam Hall said.

The scientists, led by Cees Dekker, began by attaching DNA molecules coated with RecA proteins on a microbead. Next, they placed the molecules near the opening of a solid-state nanopore in ionic solution. By then applying an appropriate voltage across the pore, a single molecule was pulled into the pore where it was statically held by the bead tether.

Changes in current

The presence of the molecule changes the current measured through the pore, which allows its size to be determined, explains Hall. And, varying the applied force across the pore produces a 1D force curve on the molecule that then provides information about the overall charge on it.

The net force measured is mainly the electrostatic force acting on the charged molecule due to the applied voltage. Since DNA filaments coated with protein have a greater net charge, they feel a larger force than bare DNA molecules for the same applied voltage.

By using the trapped bead as a "handle", the researchers can also control the position of the molecule inside the nanopore. They can thus choose the position at which to perform force measurements and locate a region of interest.

Faster protein mapping

"Our study provides a possible route towards fast, direct mapping of

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Nano Lett. DOI: 10.1021/nl9027318

the entire library of proteins that bind to genomic DNA," said Hall. "This could have important implications for sequencing, as well as detecting markers for genetically inheritable diseases."

The team will now look at sequence-dependent proteins rather than co-operatively binding proteins that coat the DNA entirely. "Such an approach will allow us to push the limits of our resolution and rapidly detect structures that are important in a wide range of disease, such as cancer."

The work was published in *Nano Letters*.

About the author

Belle Dumé is a contributing editor to *nanotechweb*.

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