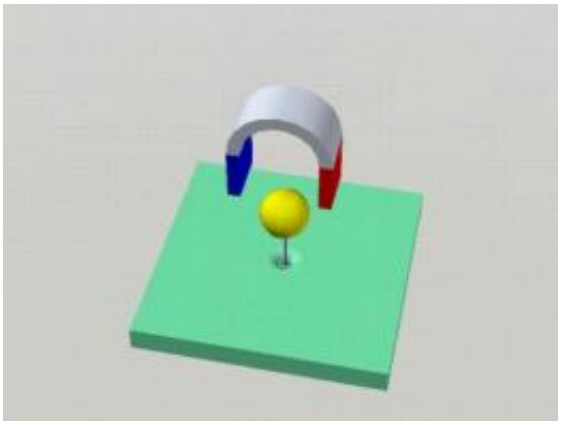
Researchers create novel nanotechnique to sequence human genome

April 15 2009



In this illustration, a DNA strand is leashed to a magnetized, iron-oxide bead, with a magnet hovering over it. As the bead moves toward the magnet, the DNA strand passes through nano-sized opening slowly enough that its base pairs can be read. Credit: Hongbo Peng/IBM Research

Since the human genome was sequenced six years ago, the cost of producing a high-quality genome sequence has dropped precipitously. More recently, the National Institutes of Health called for cutting the cost to $1,000 or less, which may enable sequencing as part of routine medical care.

The obstacles to reaching that goal have been primarily technological: Scientists have struggled to figure out how to accurately read the 3 billion base pairs - the amount of DNA found in humans and other

mammals - without time-consuming, inefficient methods.

Physicists at Brown University may have an answer. They introduce a novel procedure to vastly slow the DNA's movement through openings that are used to read the code. In the journal *Nanotechnology,* the physicists report the first experiment to move DNA through a solid-state nanopore using magnets. The approach is promising because it allows multiple segments of a DNA strand to be threaded simultaneously through numerous tiny pores and for each fragment to move slowly enough through the opening so that the base pairs can be accurately read.

"When it comes to sequencing anyone's genome, you need to do it cheaply, and you need to do it quickly," explained Xinsheng Sean Ling, professor of physics, who joined the Brown faculty in 1996. "This is a step in that direction."

The idea of reading DNA by threading strands through tiny openings is not new. Scientists have shown that an applied electric field can drive the DNA molecules through a nanopore, a tiny hole in a membrane. But in those experiments, the base pairs moved too quickly through the openings for the code to be read accurately. So, while a large electric field is needed to draw the DNA molecules into the pore, Ling explained, the same field moves the DNA too quickly, a classic scientific Catch-22.

The trick is to figure out how to slow the strands' movement through the opening so the base pairs (A, T, C, and G) can be read. To solve that, Ling and Hongbo Peng, the lead author who performed the work as a graduate student at Brown and who now works at IBM, attached the DNA strand to a bead using a streptavidin-biotin bond. Like previous researchers, they used an electric field to drive the DNA strand toward the pore. But while the strand could pass through the pore, the bead, with a 2.8-micron diameter, was too large for the pore, which has a diameter

of only 10 nanometers. So the bead was stuck in the hole with the attached DNA strand suspended on the other side of the membrane.

The Brown researchers then used magnets — they call them "magnetic tweezers" — to draw the iron-oxide bead away from the pore. As the bead moves toward the magnets, the attached DNA strand moves through the pore — slowly enough so that the base pairs can be read.

The scientists named their process "reverse DNA translocation" because, as Ling explained, "the DNA is essentially caught in a tug-of-war. And the speed of translocation will be controlled not solely by the electric field but by striking some balance between the magnetic and the electric fields. From there, we can tune it to dictate the speed."

The scientists report their technique reduces the average speed of the DNA strand's passage by more than 2,000-fold. "It can be slower even. There is no limit," Ling said.

A similar experiment has been done using optical tweezers, Ling said, but it involves only one DNA strand at a time. The Brown method sends multiple strands through the nanopores simultaneously. "It is scalable," Ling said.

The researchers expect to test their technique in experiments using bacterial DNA.

Source: Brown University (news : web)

Citation: Researchers create novel nanotechnique to sequence human genome (2009, April 15) retrieved 28 April 2024 from https://phys.org/news/2009-04-nanotechnique-sequence-human-genome.html

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