Nanotechnology meets biology and DNA finds its groove

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Pity the molecular biologist.The object of fascination for most is the DNA molecule. But in solution, DNA, the genetic material that hold the detailed instructions for virtually all life, is a twisted knot, looking more like a battered ball of yarn than the famous double helix. To study it, scientists generally are forced to work with collections of molecules floating in solution, and there is no easy way to precisely single out individual molecules for study.

Now, however, scientists have developed a quick, inexpensive and efficient method to extract single DNA molecules and position them in nanoscale troughs or "slits," where they can be easily analyzed and sequenced.

The technique, which according to its developers is simple and scalable, could lead to faster and vastly more efficient sequencing technology in the lab, and may one day help underpin the ability of clinicians to obtain customized DNA profiles of patients.

The new work is reported this week (Feb. 8, 2007) in the *Proceedings of the National Academies of Science* by a team of scientists and engineers from the University of Wisconsin-Madison.

"DNA is messy," says David C. Schwartz, a UW-Madison genomics researcher and chemist and the senior author of the PNAS paper. "And in order to read the molecule, you have to present the molecule."

To attack the problem, Schwartz and his colleagues turned to nanotechnology, the branch of engineering that deals with the design and manufacture of electrical and mechanical devices at the scale of atoms and molecules. Using techniques typically reserved for the manufacture of computer chips, the Wisconsin team fabricated a mold for making a rubber template with slits narrow enough to confine single strands of elongated DNA.

The new technique is akin to threading a microscopic needle with a thread of DNA, explains Juan de Pablo, a UW-Madison professor of biomedical engineering and a co-author of the study. The team has a way, he says, of "positioning the DNA molecule right where we want it to be. It is important that we can manipulate it with such fidelity."

The system, says Schwartz, promises bench scientists a convenient and easy way to make large numbers of individual DNA molecules accessible for study. The ability to quickly get lots of molecules lined up for sequencing and analysis, says Schwartz, means entire genomes - for species or individuals - could soon become more accessible to science.

Scientists, Schwartz explains, already know how to take DNA and stiffen it by removing salts from its chemical makeup. But confining the molecule and presenting it for analysis is laborious, engaging armies of lab techs worldwide to prepare DNA samples for their moment in the lab.

"To get DNA molecules to do this on surfaces is really hard," says Schwartz.
The system developed by Schwartz, de Pablo and their colleagues could change all of that. By figuring out a way to take individual DNA molecules and present them in a confined, linear fashion, the genetic information encoded in the arrangement of the base pairs that make up the molecule can be scanned and read like a bar code.

The key to the new technology, argues Schwartz, is that the system is comprehensive, inexpensive and simple enough to lend itself to large-scale efforts to analyze DNA.

"It's a simple technology that works, and that's demonstrated to work for genome analysis," says de Pablo. "It's a very robust method that can be used in a variety of settings."

In addition to Schwartz and de Pablo, authors of the PNAS study include Kyubong Jo, Dalia M. Dhingra, Michael D. Grahm, Rod Runnheim and Dan Forrest, all of UW-Madison, and Theo Odijk of the Delft University of Technology.

Source: University of Wisconsin-Madison