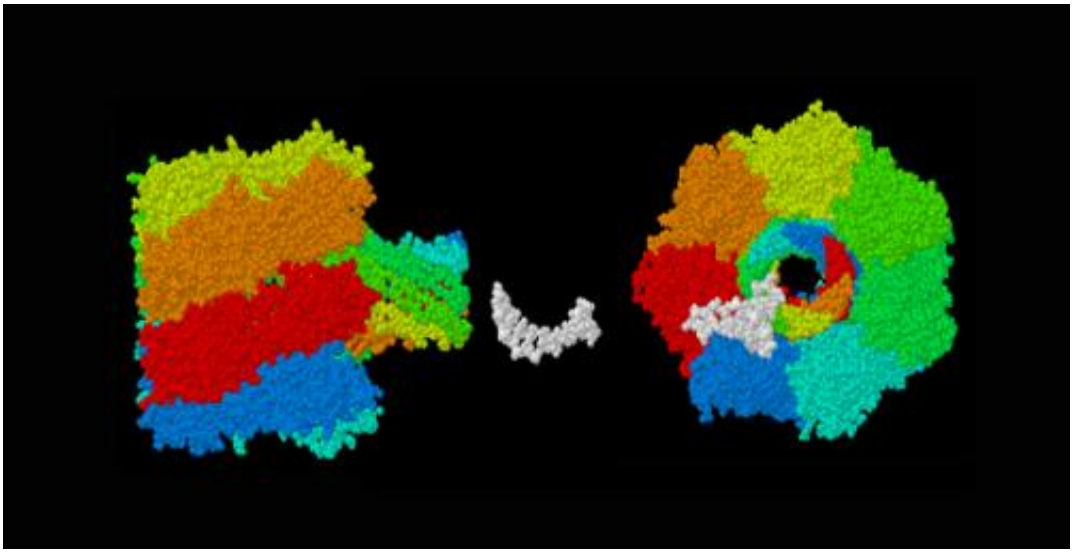
Pull with caution: A DNA strand should be driven gently through a nanopore

November 8 2012



This is an image of alpha-hemolysin pore (made up of 7 identical subunits in 7 colors) and 12-mer single-stranded DNA (in white) on the same scale to illustrate DNA effects on conductance when moving through a nanopore. Below is an orthogonal view of the same molecules. Image created 5-Oct-2008 by George Church using Rasmol_2.6 and coordinates from 7AHL.pdb and 1BNA.pdb
Credit: George Church

It's not easy to drive long molecule chains - such as DNA - through a "nanopore" (a pore which is just few millionths of a millimeter wide) because they tend to tangle up. A simulation carried out by an international group of scientists - among whom are SISSA researchers - has suggested a solution: it's better to "pull" gently without applying too

much force, otherwise the molecule could be stopped due to excessive friction. That is an important observation to create innovative DNA sequencing methods.

As nanotechnology progresses, it becomes increasingly important to know in detail the dynamics of the nanoworld (the world at the scale of a millionth of a millimeter). What happens, for example, when we try to drive a polyelectrolyte (a long chain of electrically charged molecules, such as DNA) through a nanopore if knots cause the translocation process to jam? It's not a pointless question, because now a new DNA sequencing method to electrochemically analyze every single strand by driving it through a nanopore, is being developed. Since those strands tend to tangle up if they are very long, Angelo Rosa of the International School for Advanced Studies and his colleagues set out to study the dynamics of this translocation theoretically, by carrying out a simulation.

The model chosen by the scientists has shown that jamming is not caused by the mere presence of the knot, but by the relationship between friction and the force applied to drive the molecule into the gap."The result is not so obvious if compared to what happens at a macro level," explained Cristian Micheletti, researcher at SISSA and one of the authors of the paper published in Physical Review Letters. "Knots introduce an effective friction that increases with the applied force and pulls the polymer to the other side of the nanopore. Translocation is only halted above a threshold force".

"According to what we observed in the simulation, to avoid obstruction of the pore and halt of the translocation, the force applied should be controlled, without pulling too much" explained Rosa.

This study is just a first step. For quantitative details on this process (what this threshold is and how the force should be measured out to maximize the effectiveness of this sequencing method) more in-depth

examinations will be needed both at the theoretical (the model developed by Rosa, Di Ventra and Micheletti is mesoscopic, not atomistic) and at the experimental level.

More in detail…

Nanoporesequencing is an innovative technique, an alternative to more traditional methods such as PCA. This method involves separating the two nucleobase strands which make up the double helix of the DNA and analyzing them one by one. Each strand is driven through a nanopore as the electric variations in the translocation are recorded. That is an electrochemical method: alterations in the electric field give information on the chemical composition of the molecule driven through the pore and the composition is thus reconstructed. Up to now this method has yielded good results with short DNA fragments, while difficulties have been encountered for longer ones, because of the knots. That's why studies such as Rosa, Di Ventra and Micheletti's are an important step to increase its efficiency.

Provided by International School of Advanced Studies (SISSA)

Citation: Pull with caution: A DNA strand should be driven gently through a nanopore (2012, November 8) retrieved 27 June 2024 from https://phys.org/news/2012-11-caution-dna-strand-driven-gently.html