DNA Interactions in Crowded Nanopores

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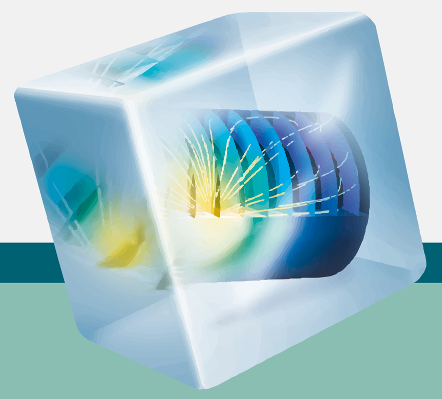
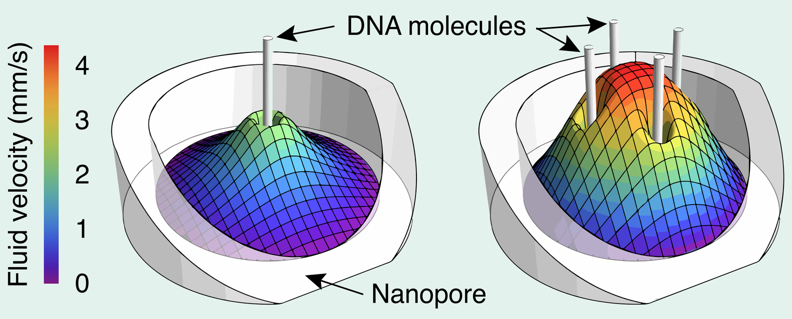


Abstract

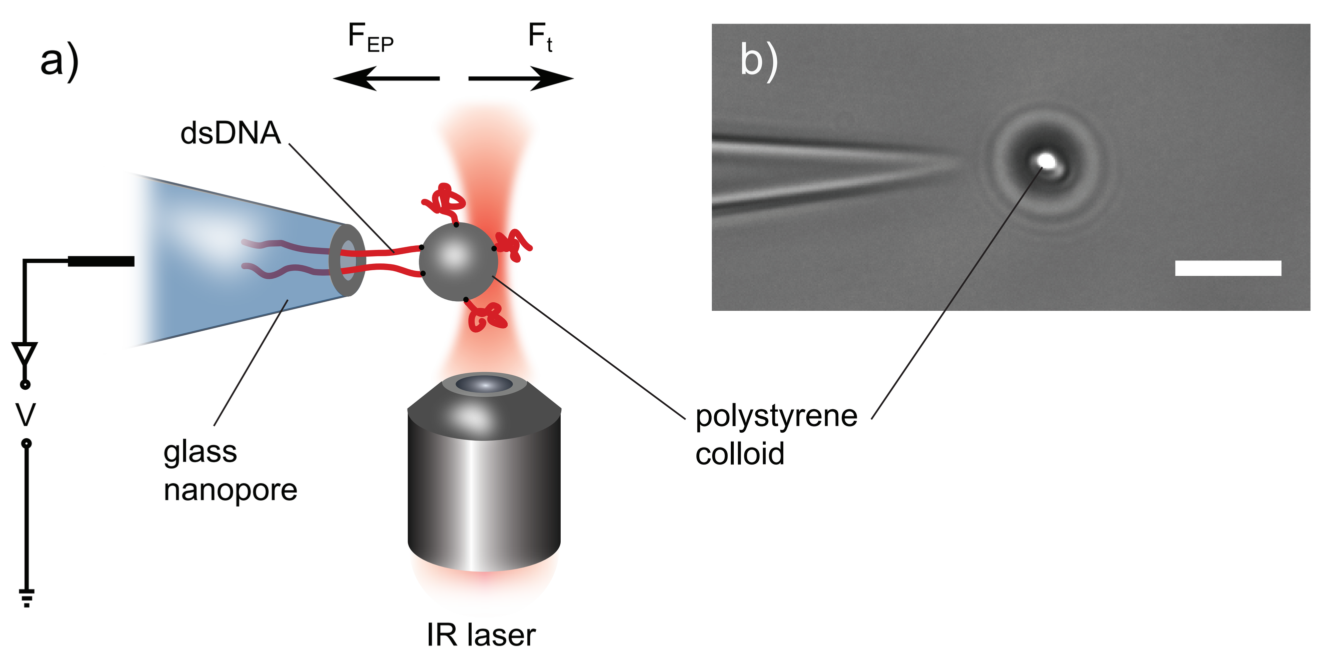


The motion of DNA in crowded environments is a common theme in physics and biology. Examples include gel electrophoresis and the self-interaction of DNA within cells and viral capsids. Here we study the interaction of multiple DNA molecules within a nanopore by tethering the DNA to a bead held in a laser optical trap to produce a "molecular tug-of-war". We measure this tether force as a function of the number of DNA molecules in the pore and show that the force per molecule decreases with the number of molecules. A simple scaling argument based on a mean field theory of the hydrodynamic interactions between multiple DNA strands explains our observations. At high salt concentrations, when the Debye length approaches the size of the counter-ions, the force per molecule becomes essentially independent of the number of molecules. We attribute this to a sharp decrease in electro-osmotic flow which makes the hydrodynamic interactions ineffective.

Take Home Message:

- Force on DNA molecules in an electric field is competition between electrostatics and flow drag
- In nanopores multiple DNA molecules interact via electro-osmotic flow

1. Experiment

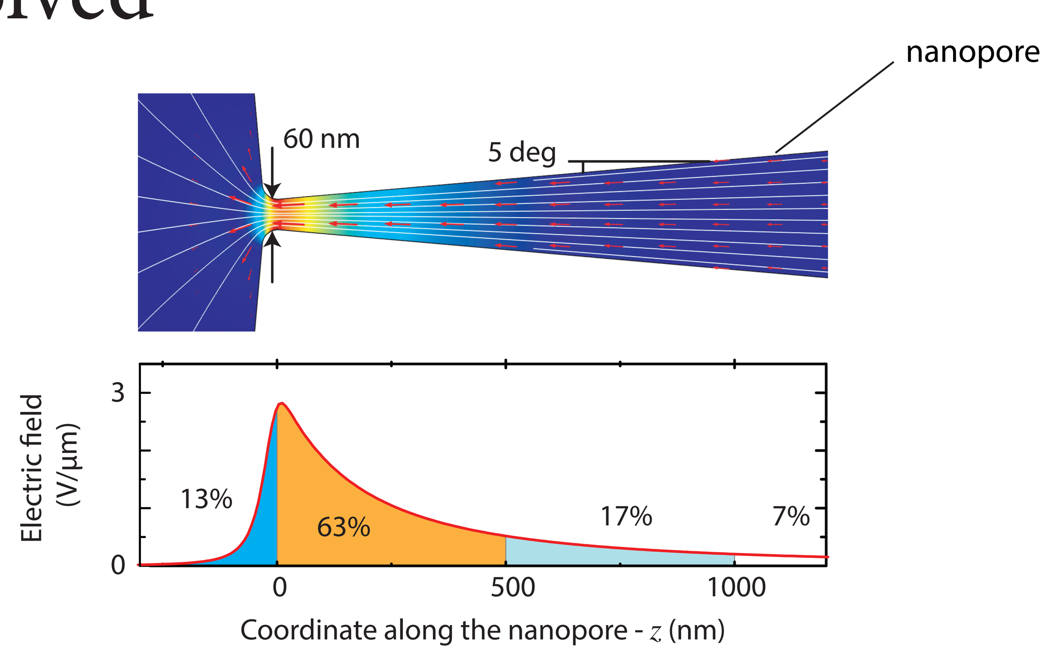


Measure force on DNA molecules that are tethered inside a nanopore

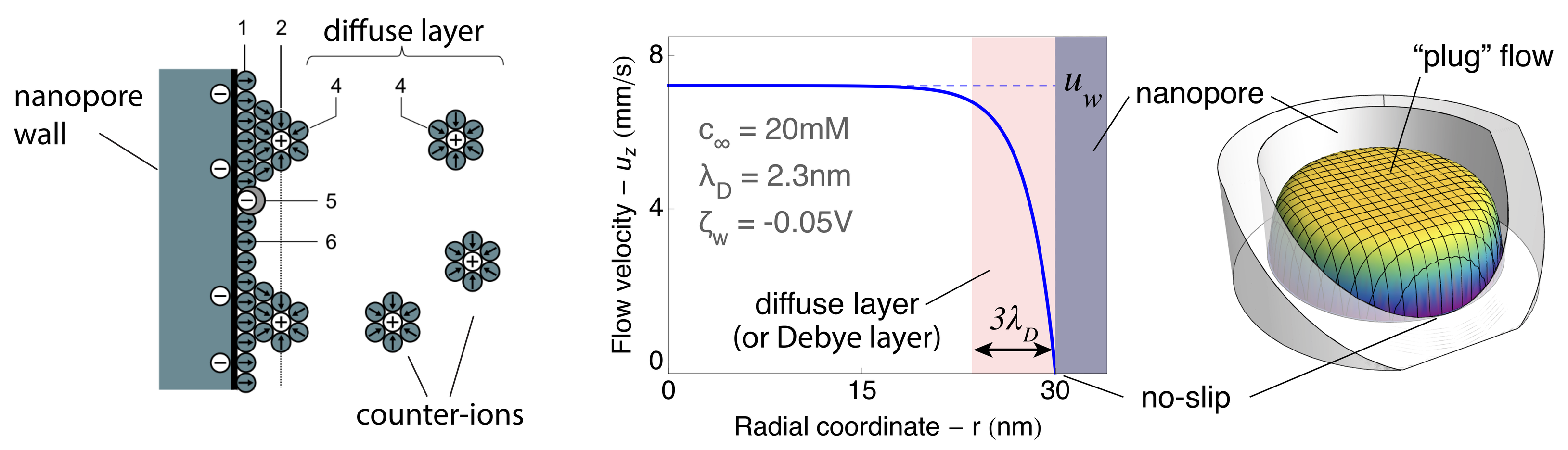
- Experiment is in water
- DNA molecules are attached to colloid that is optically trapped
- Apply electric potential across nanopore to drive the DNA molecules inside

2. Physics involved

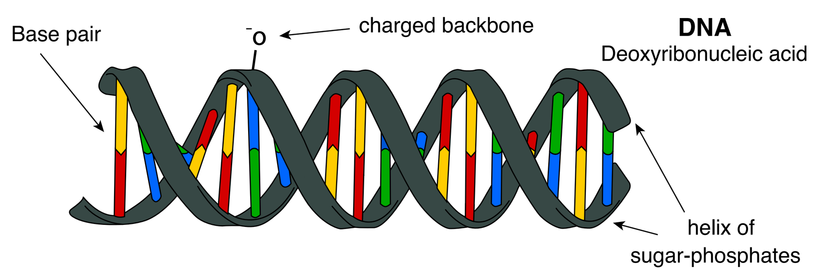
Electric field is focused inside a nanopore. It can reach ~10^6 V/m.



Nanopores surface is charged and thus it attracts counter-ions. In an external electric field excess ions propel the liquid that creates characteristic plug flow. This is **electro-osmosis.**



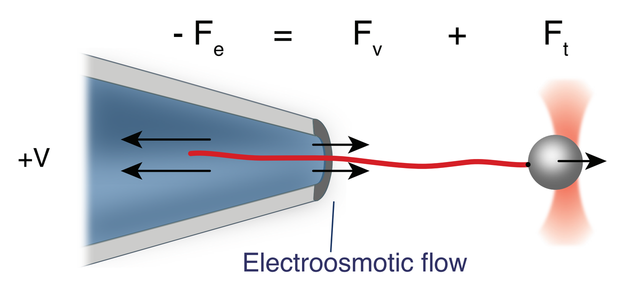
DNA molecule is also charged because of phosphate groups in its backbone. The bare charge density is 2 e / 0.34 nm. This moves in electric field and also induced electro-osmosis.

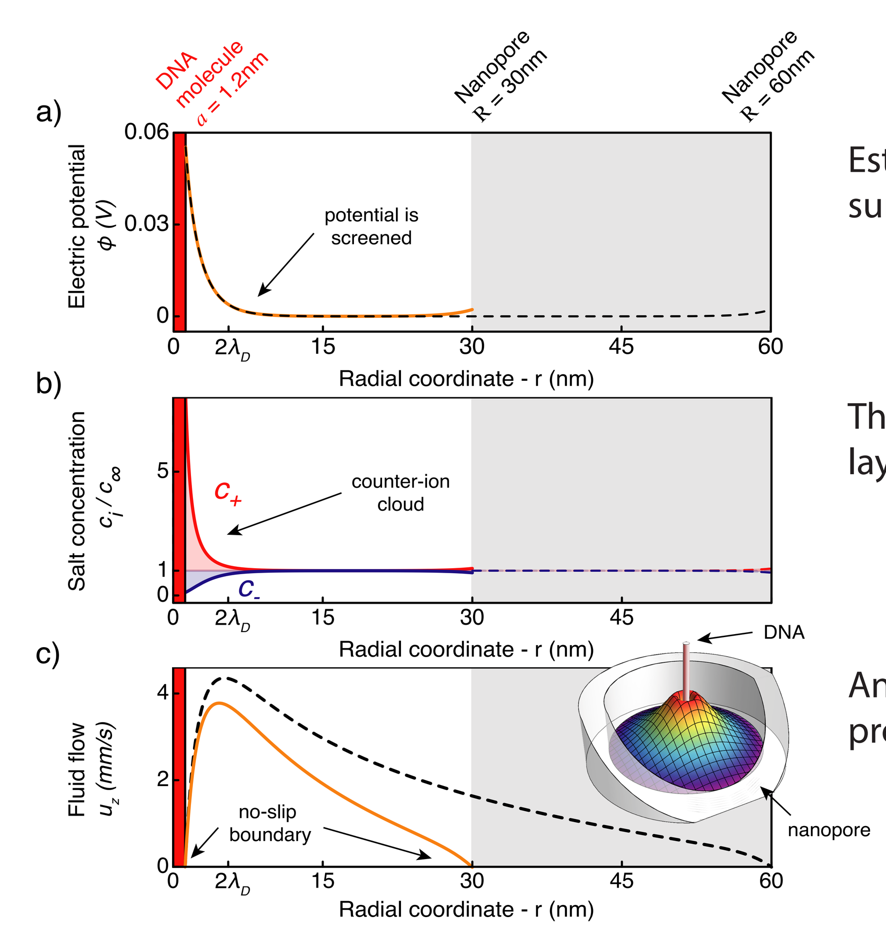


3. Single DNA molecule inside a nanopore

Force on tethered DNA molecule is given by the difference between:

- Electrostatic pull inwards on the charged DNA
- Fluid drag outward





Estimate electric potential next to a charged surfaces using Poisson-Boltzmann equation

$$\nabla^2 \phi = \frac{2\,e\,c_\infty}{\varepsilon}\,\sinh\left(\frac{e\phi}{k_B T}\right)$$

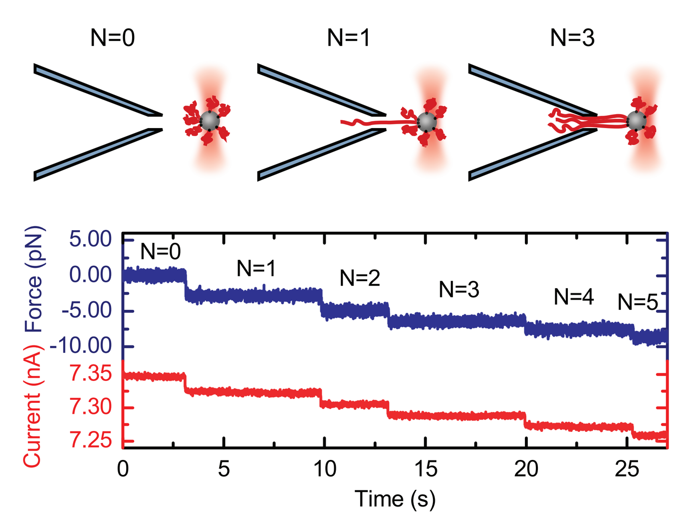
Then count the excess free ions in the Debye layer

$$c_\pm = c_\infty\,\exp\left[\mp\frac{e\phi}{k_B T}\right]$$

And thus calculate the electro-osmotic flow profile using the Stokes equation

$$\eta\nabla^2\vec{u} = \vec{\nabla}p - \vec{E}\,e\,(c_+ - c_-)$$

4. Multiple DNA molecules

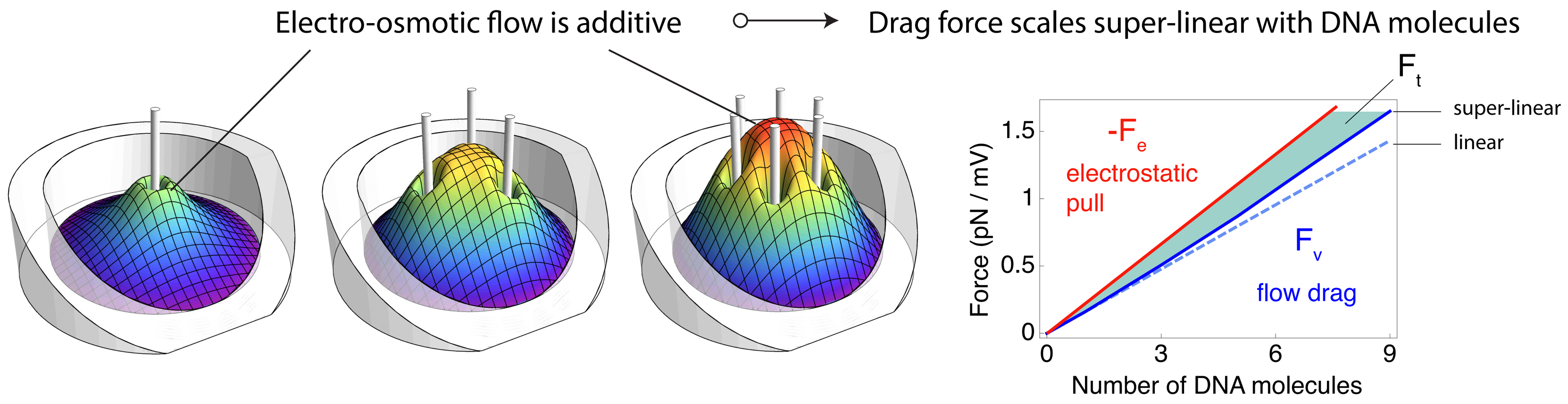


Experiment measured multiple DNA insertions

- Each insertion produced a current step
- Each insertion produced a force step
- Both confirm there was an insertion

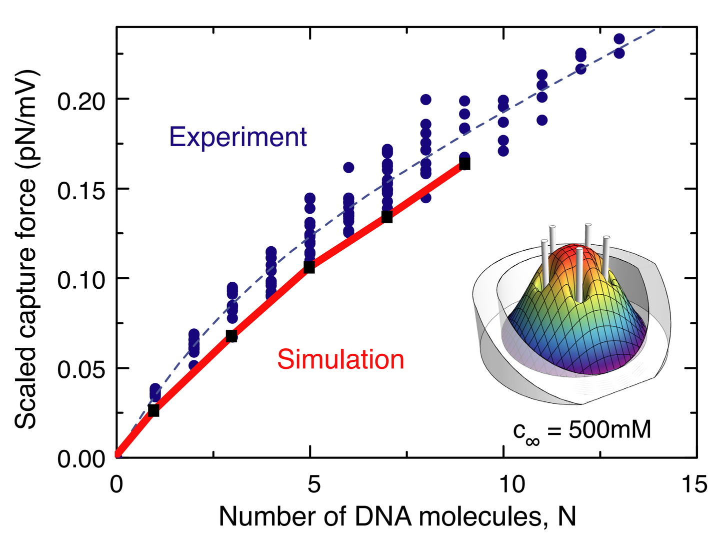
- Each force step is slightly smaller
- Not expected from a linear model

Electro-osmotic flow is additive → Drag force scales super-linear with DNA molecules



Force on multiple DNA molecules scales in sub-linear way because electrostatics is the pull into nanopore is the same for all molecules, but the outward flow drag increases with DNA molecule number.

Numerical model agrees well with experiment.



Institutions and Funding

EPSRC
Pioneering research and skills

[1] N. Laohakunakorn, S. Ghosal, O. Otto, K. Misiunas, and U. F. Keyser, "DNA Interactions in Crowded Nanopores," Nano Lett., vol.

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