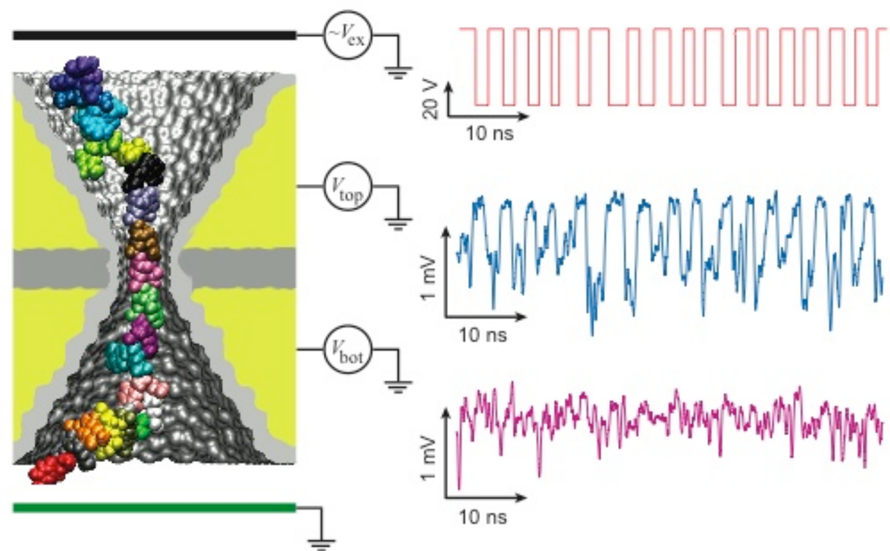
Effective force, electro-osmotic flow and charge inversion in a solid-state nanopore

Aleksei Aksimentiev

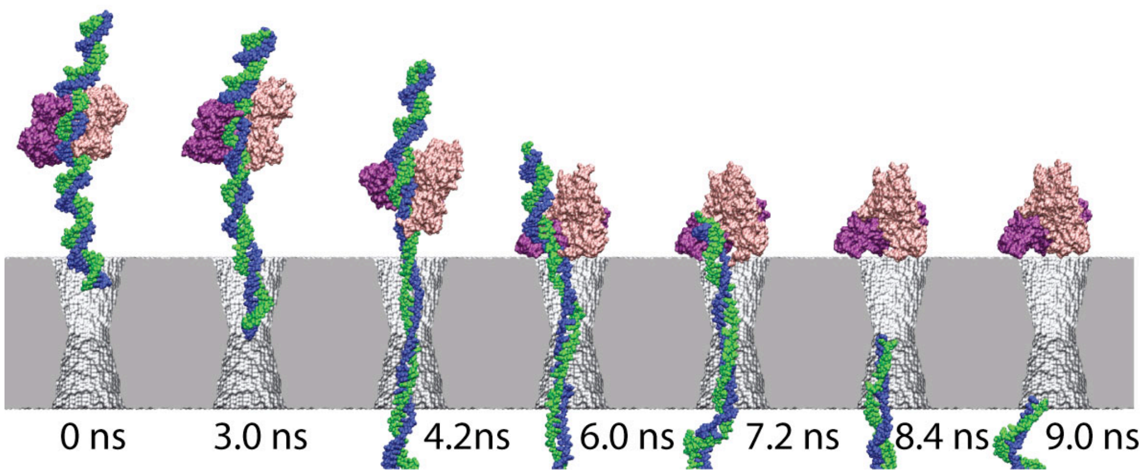
University of Illinois at Urbana-Champaign

Motivation: Force is the key factor

DNA sequencing

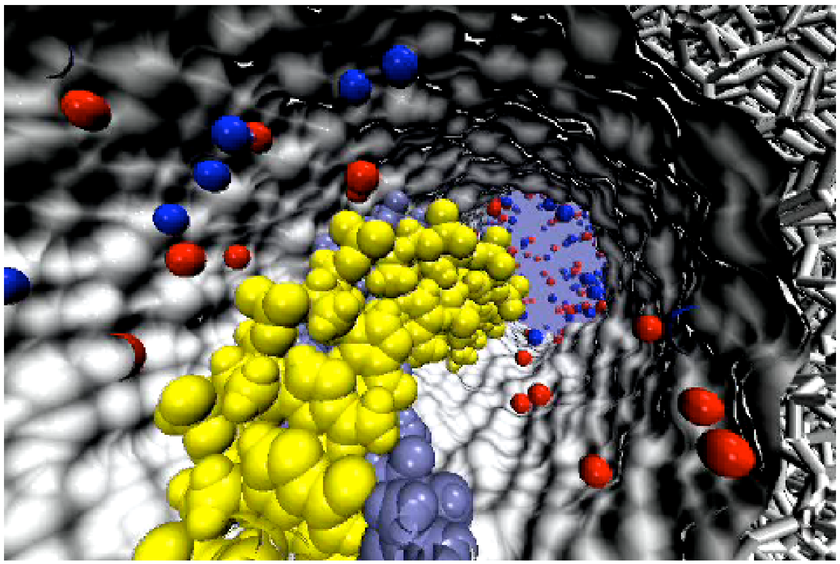


Force spectroscopy



Computational microscope

Atoms move according to classical mechanics (F= ma)



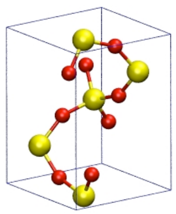
Interaction between atoms is defined by molecular force field (AMBER95, CHARMM27)

Massive parallel computer (PSC, Lemieux)

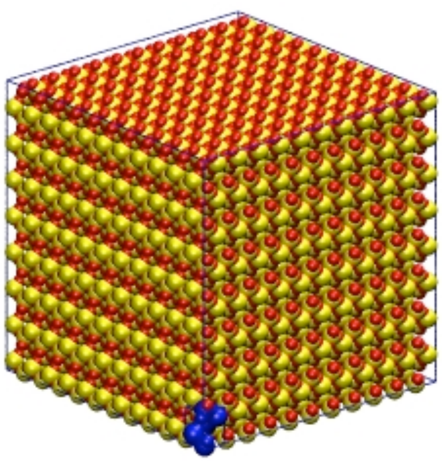
<u>Time scale</u>: < 10 μs

<u>Length scale</u>: up to 10^8 atoms or $(< 100\ \text{nm})^3$

Building Amorphous SiO_2

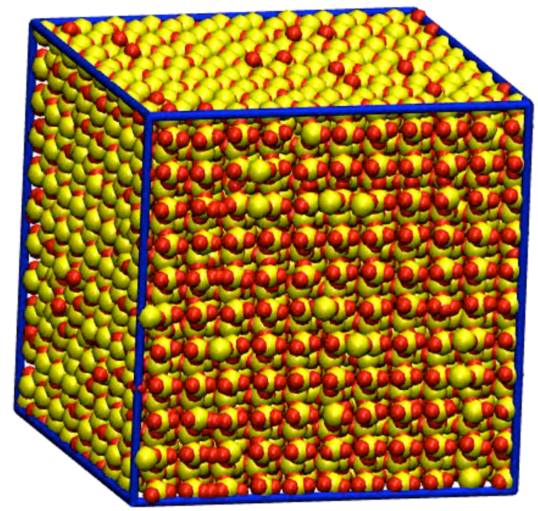


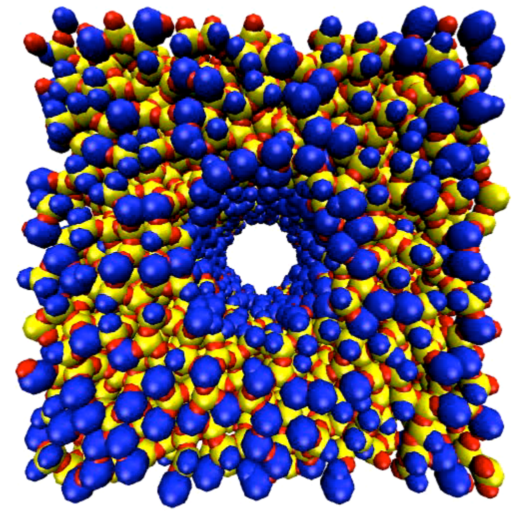
Replicated
11x11x8
~ 55 A cube

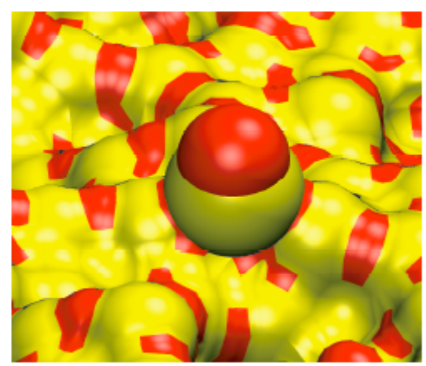


f

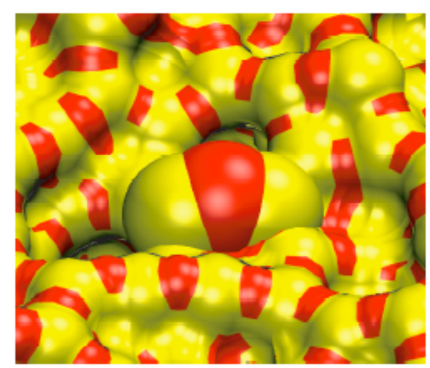
Eduardo Cruz-Chu
(J. Phys. Chem. B, 2006)





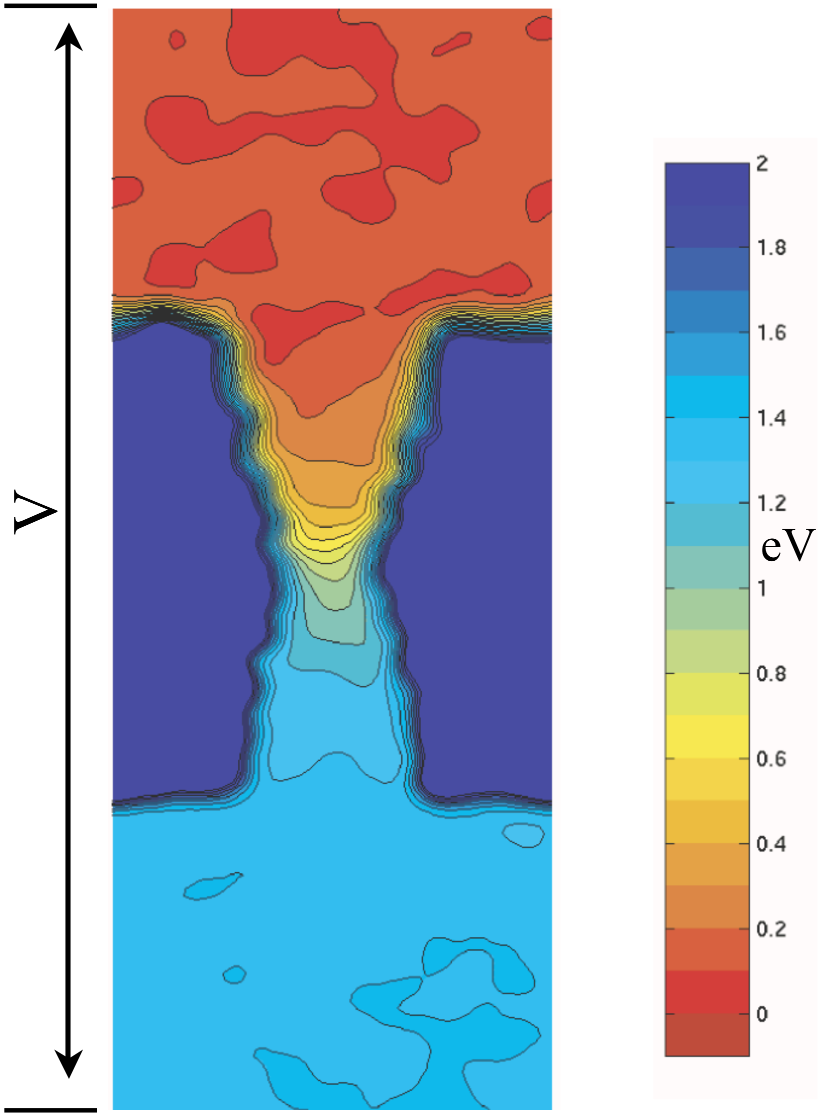


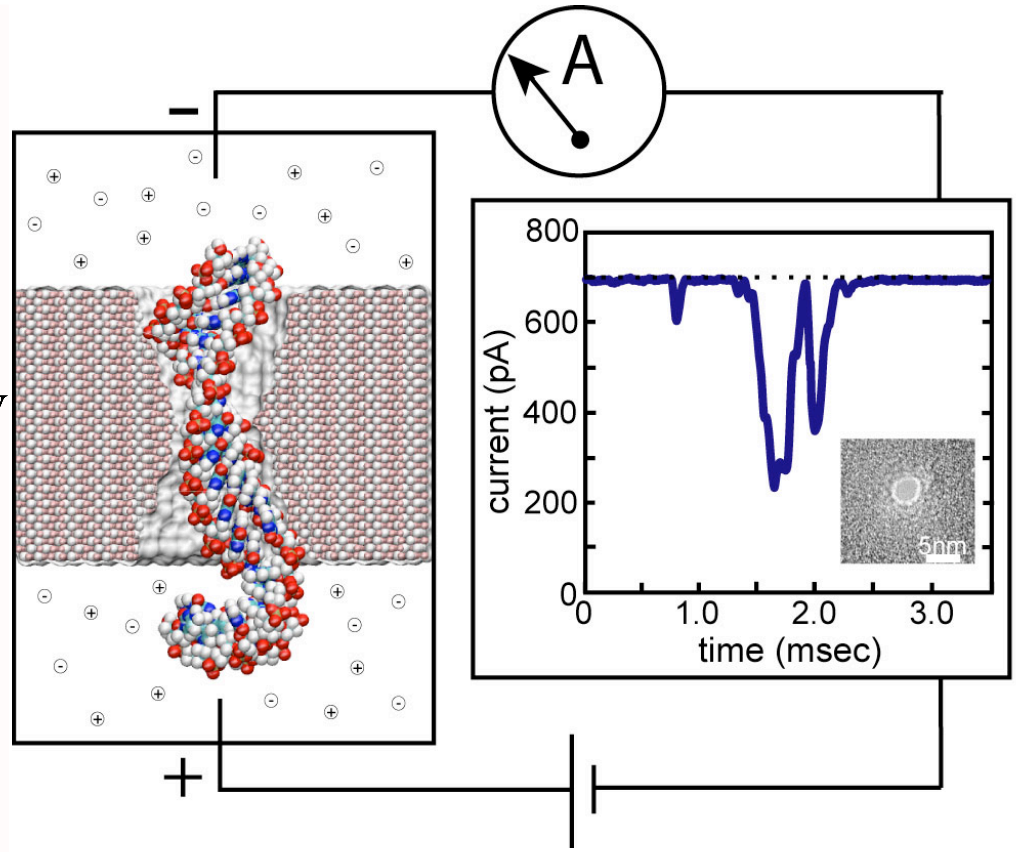
Dangling Oxygen



Non-Dangling Oxygen

Microscopic model of a nanopore

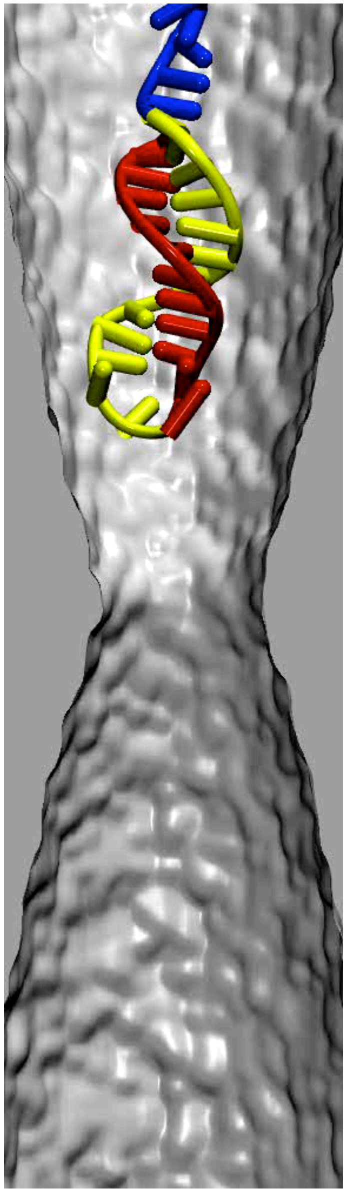


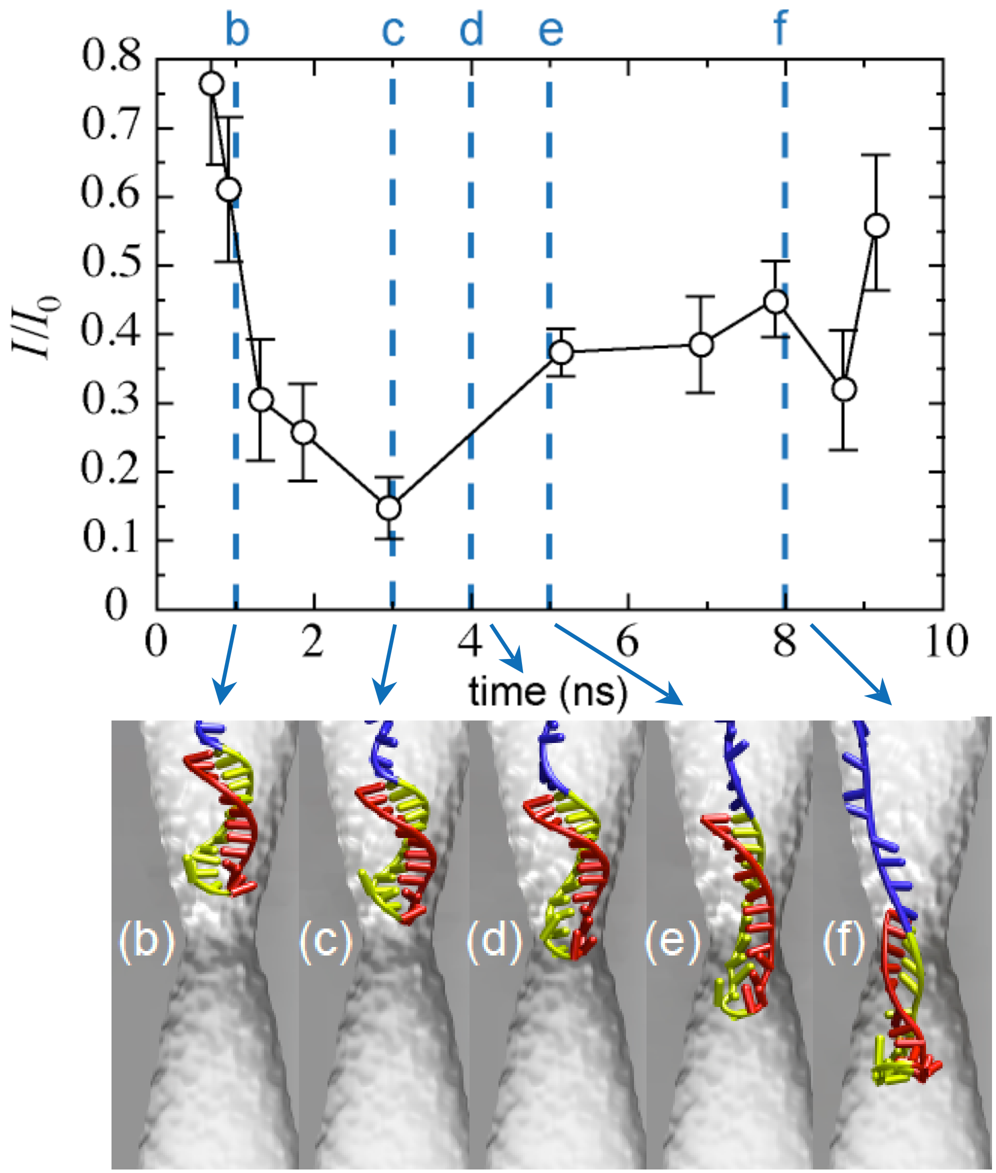


Resulting voltage bias:

$V=-EL_z$

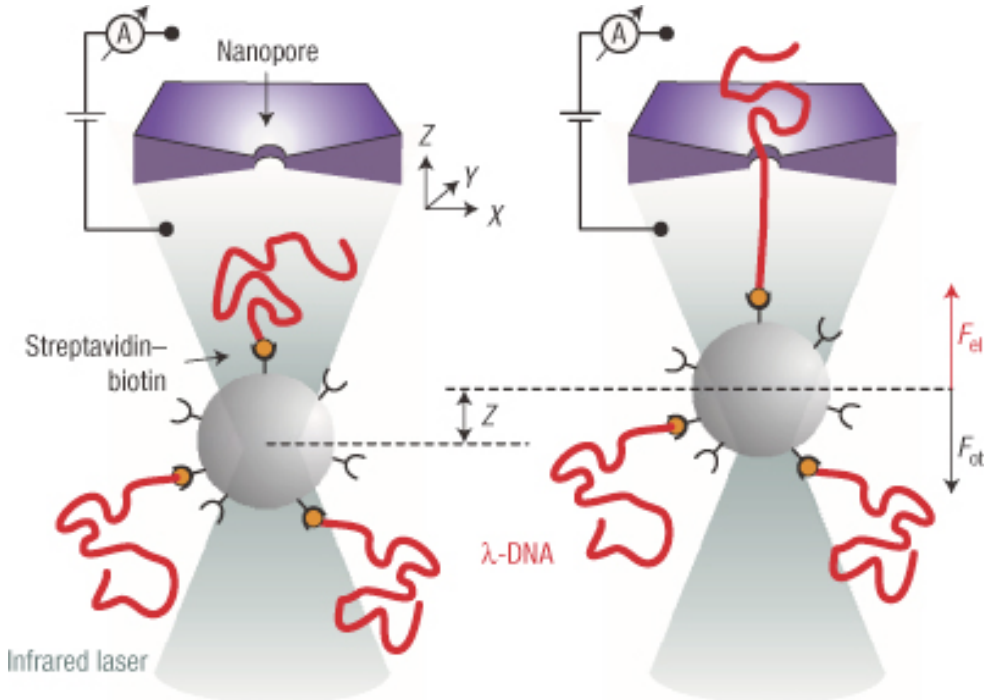
Illustrative example: hpDNA permeation

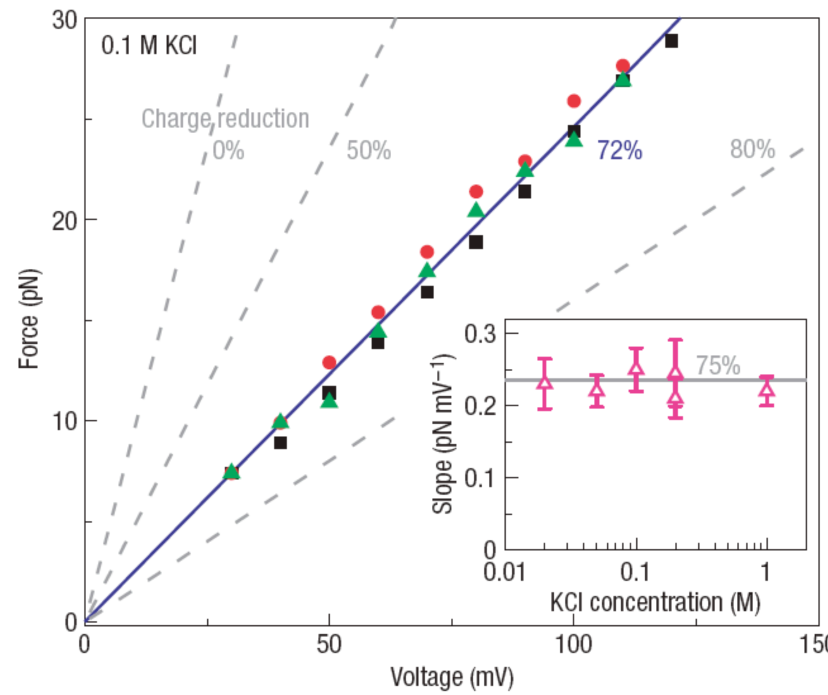




(Comer et al.,2008)

Direct force measurement using a nanopore



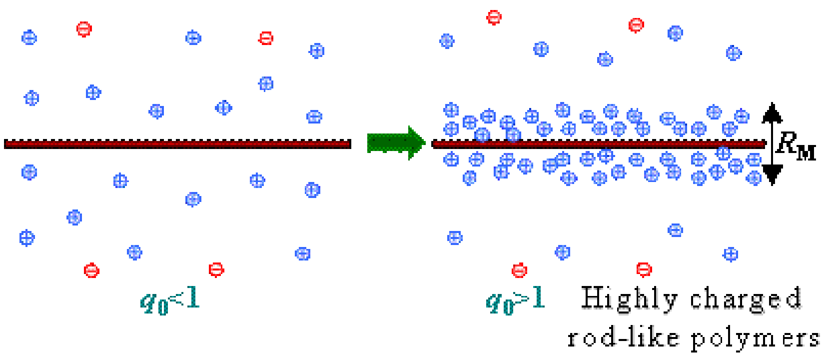


Keyser et al. Nature Physics, ***2*** *473, (2006).*

Results: $F=q_{eff}E$, where q_{eff}~1/4 of the DNA's bare charge

Effective charge

Manning condensation



$q_0 = l_B / l_{charge}$ $\qquad$ $l_B = e^2/(\varepsilon k_B T)$

$q_{man} = f^* Q$

$f^{(1)}_{man} = 0.25$ for z=1

$f^{(2)}_{man} = 0.05$ for z=2

Stall force F relates to the electric field E via effective charge:

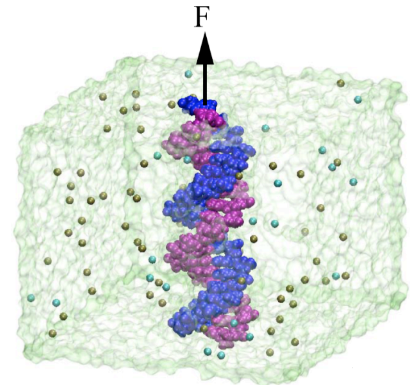
$$F = q_{eff} E$$

Long et al., PRL **76** 3858 (1996)

$$\boxed{q_{eff} = \xi\ \mu}$$

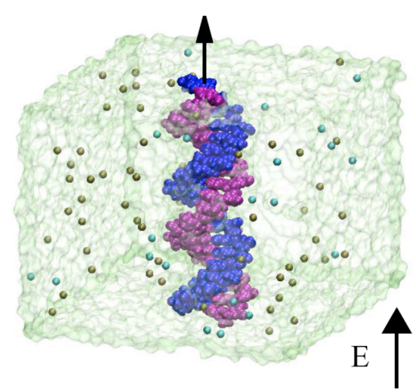
Only mechanical force:

$F = \xi V$



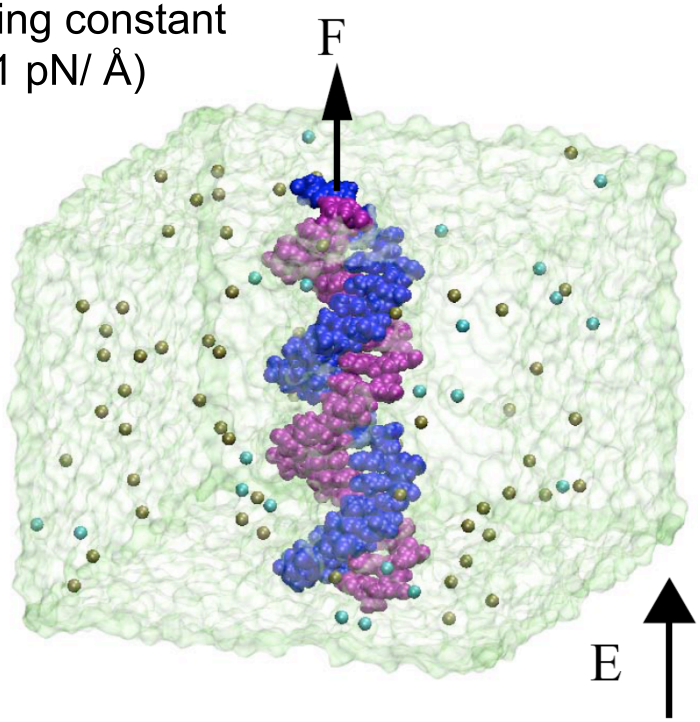
Only electrostatic force:

$V = \mu E$



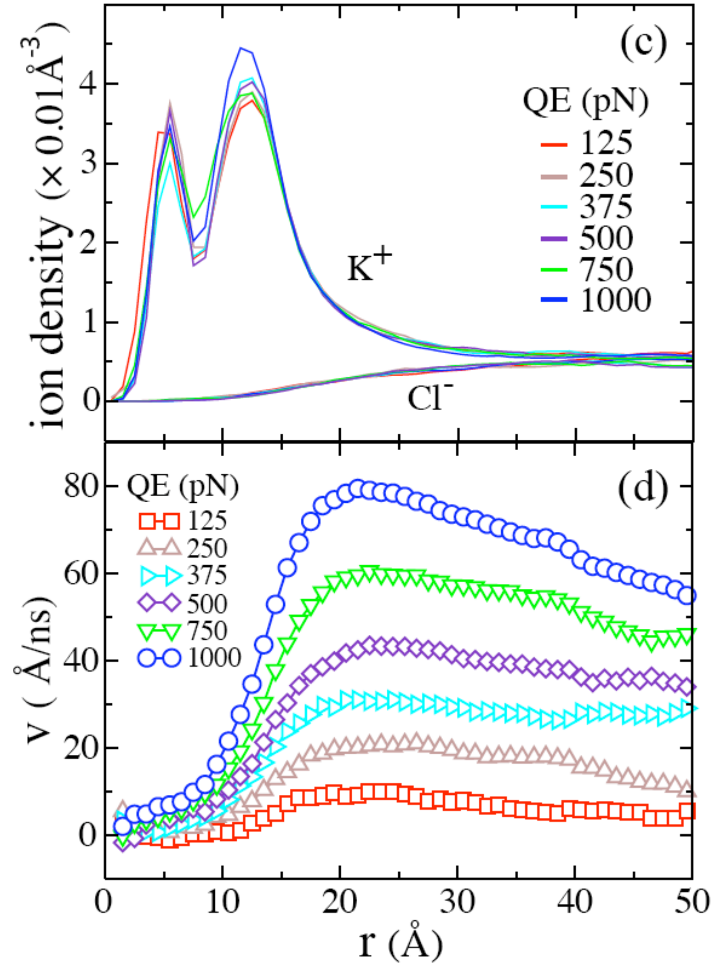
DNA in bulk electrolyte

Spring constant
(k=1 pN/ Å)



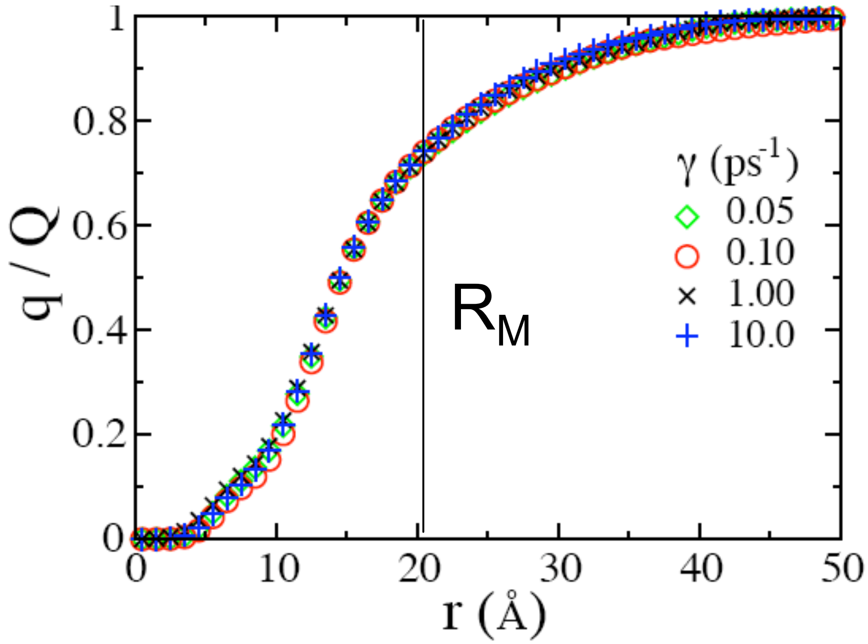
QE: 125~1000pN

T=310K, 0.1 M KCl
dsDNA is periodic along the field
(Q: charge of bare DNA)



Hydrodynamic friction!

Force in solvents of different viscosity

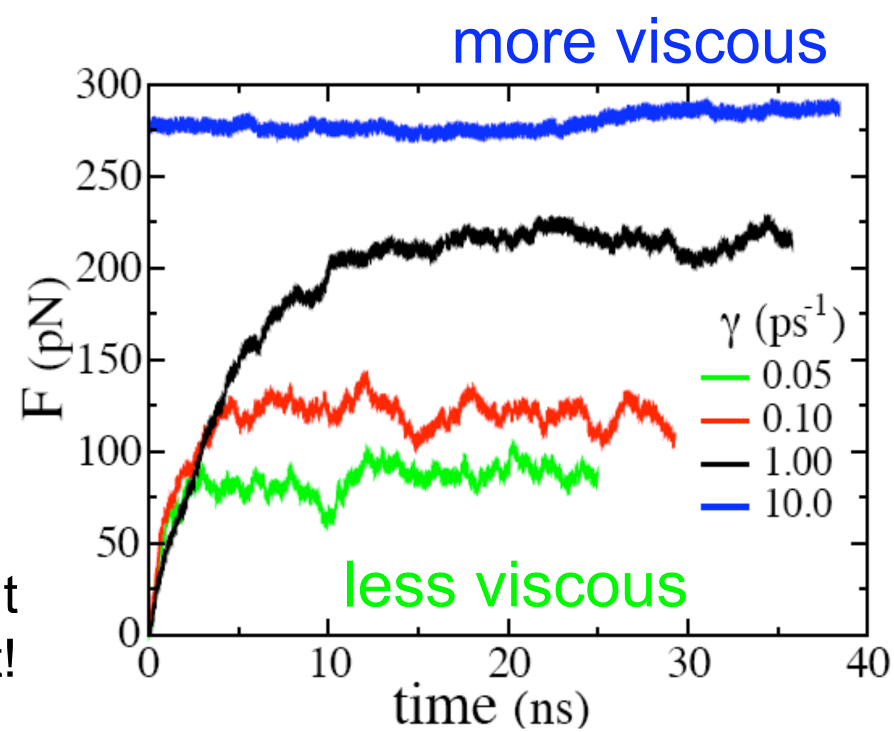


The cumulative distribution of ions around DNA is consistent with the Manning theory.

$q=\Sigma q_{ion}(r_{ion}<r)$
Q is the bare DNA charge

In MD simulations, effective viscosity of the thermostat is controlled by a bulk friction coefficient γ, (the damping rate of the Langevin thermostat).

The stall force depends on the solvent viscosity, but the distribution does not!



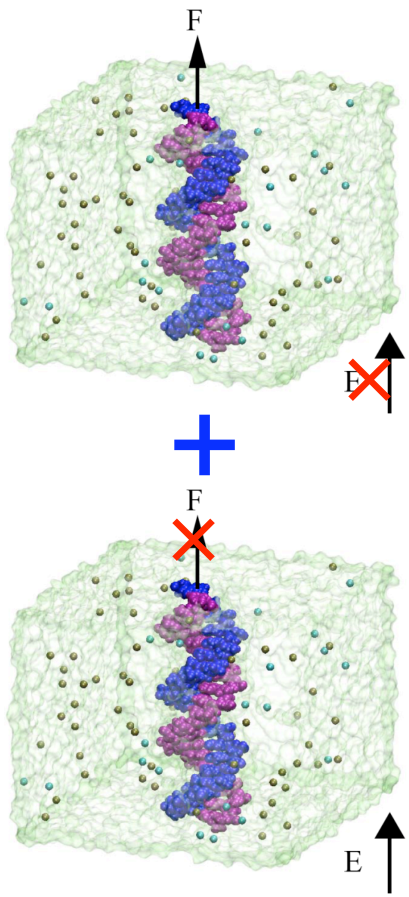
Simultaneous actions of non-electric and electric forces on DNA

can be decomposed into two independent motions

*Long et.al PRL **76** 3858 (1996)*

$\xi = F/v_1$

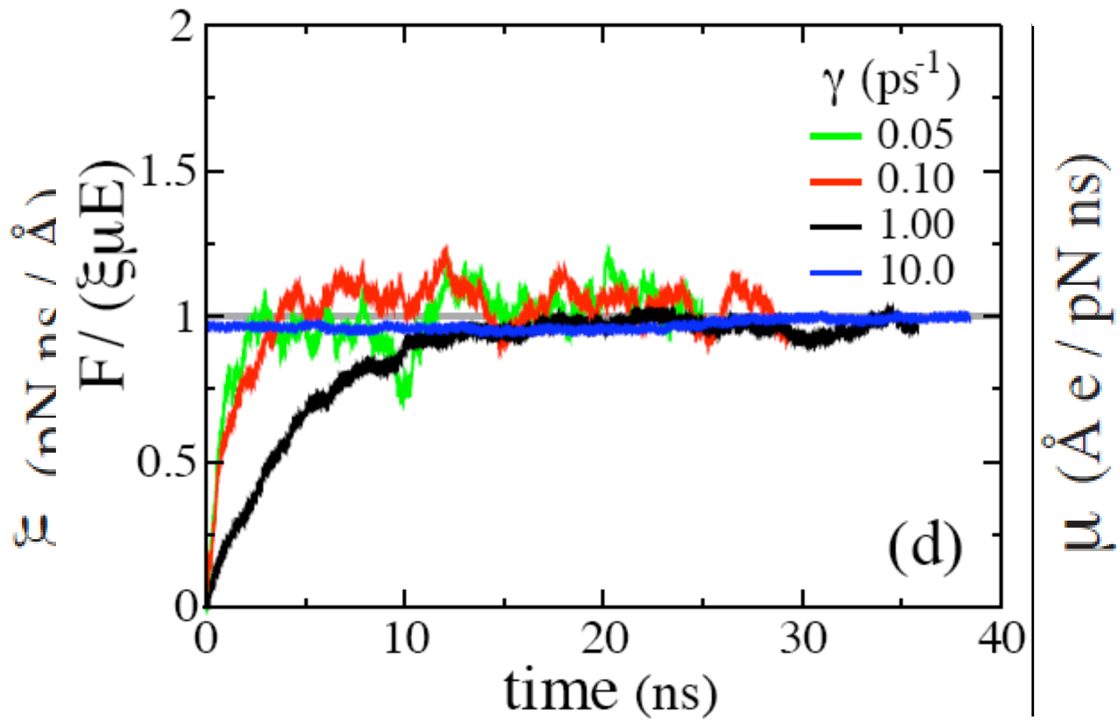
$v_1 \uparrow$



$\mu = v_2/E$

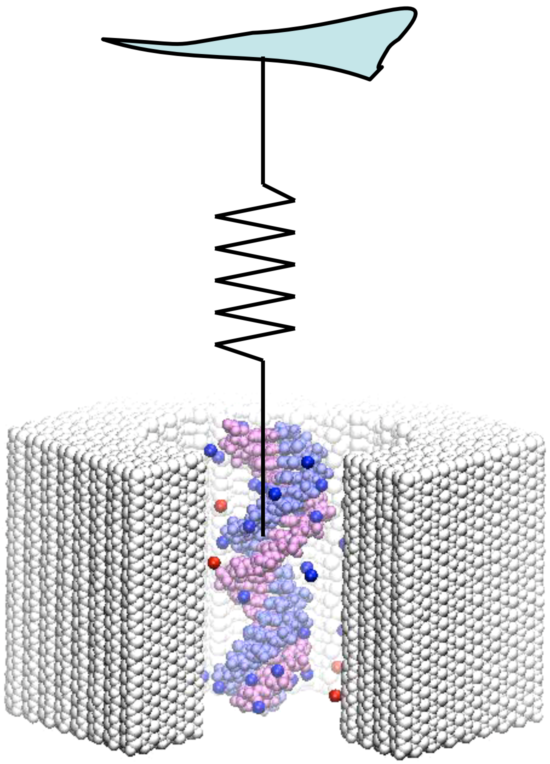
$v_2 \downarrow$

When DNA stalls, v1+v2=0 and <u>F= ξμE</u>

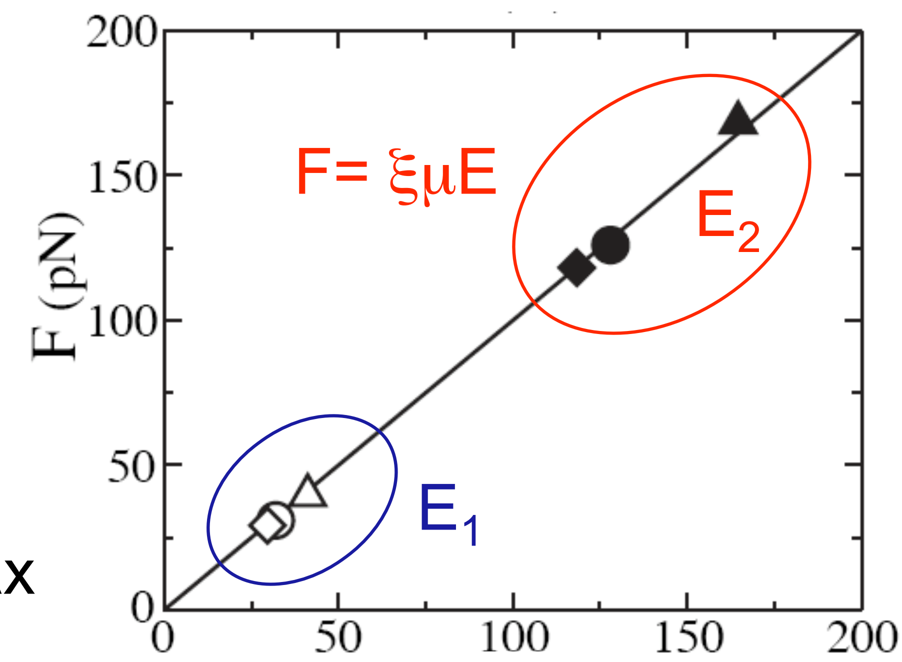


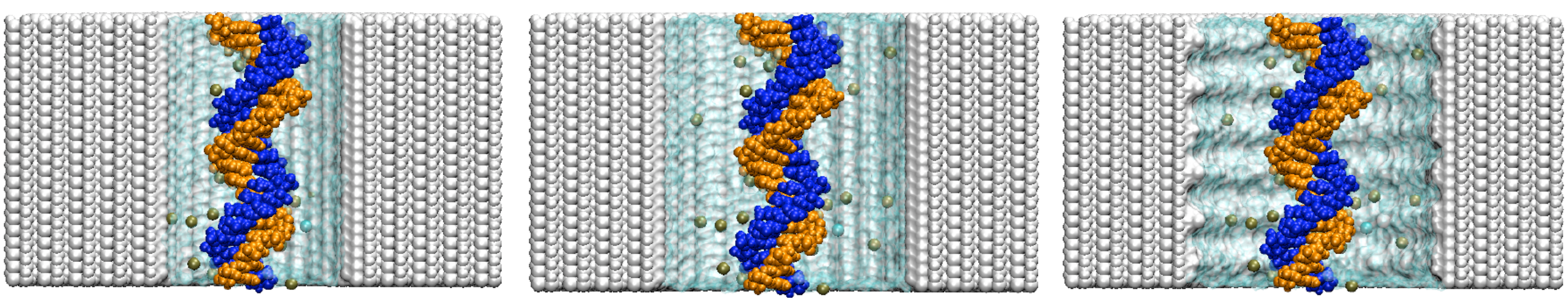
After scaling with ξμ, all curves collapse on a master curve

Stall force in a nanopore



$F=-k\Delta x$



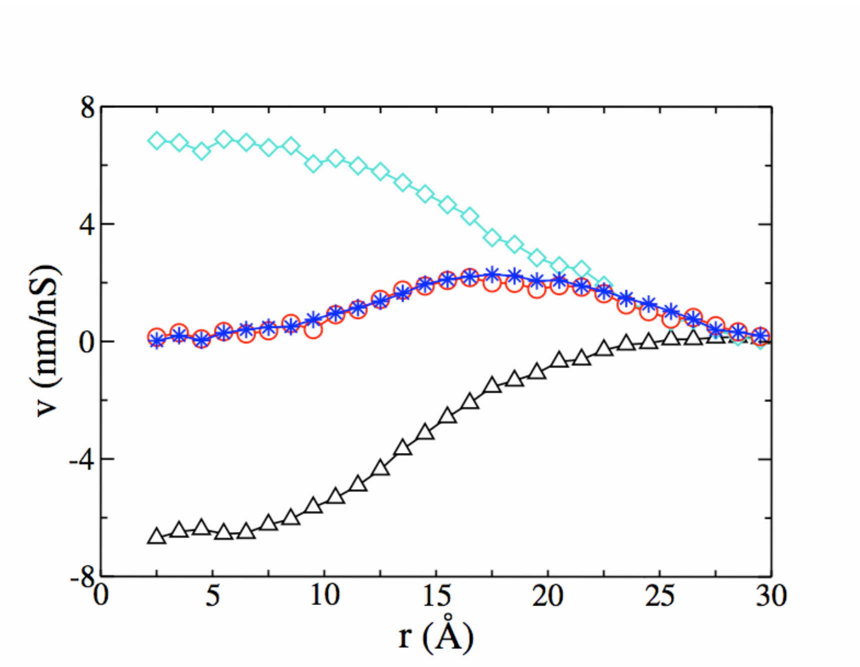


22.5-Å pore ○ ●

30.0-Å pore ◇ ◆

wavy 30.0-Å pore △ ▲

Why does F=ξμE work?



Under action of both forces:

v_{DNA}=0, QE=500pN , F=118pN

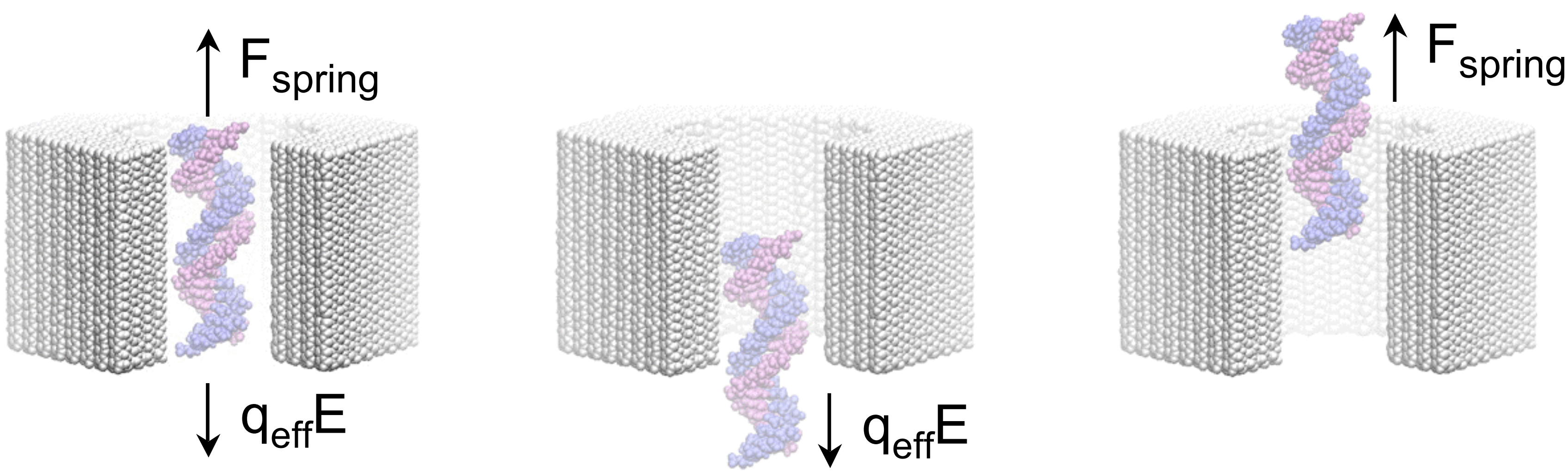
Electric force only:

QE=500pN; V_{DNA}=-7nm/ns

Spring force only:

V_{DNA}=7nm/ns; F=118pN

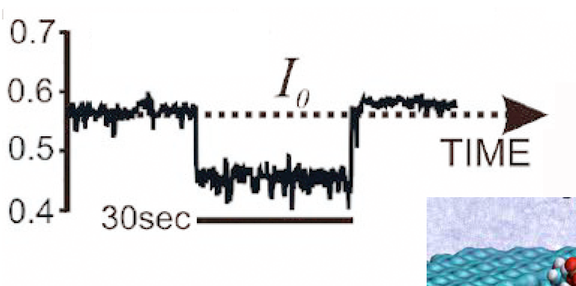
○ Sum of r and ◇

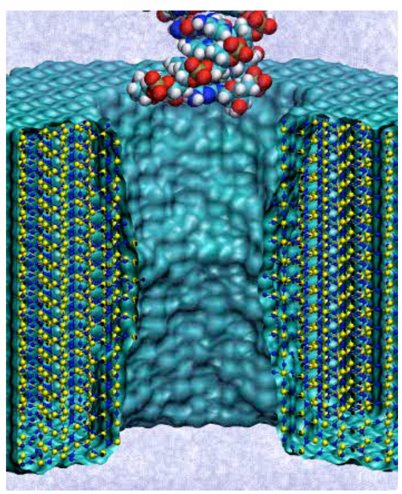


Method to measure the effective force

To use $F=\xi\mu E$, one needs to measure independently ξ and μ

μ: DNA translocation experiments

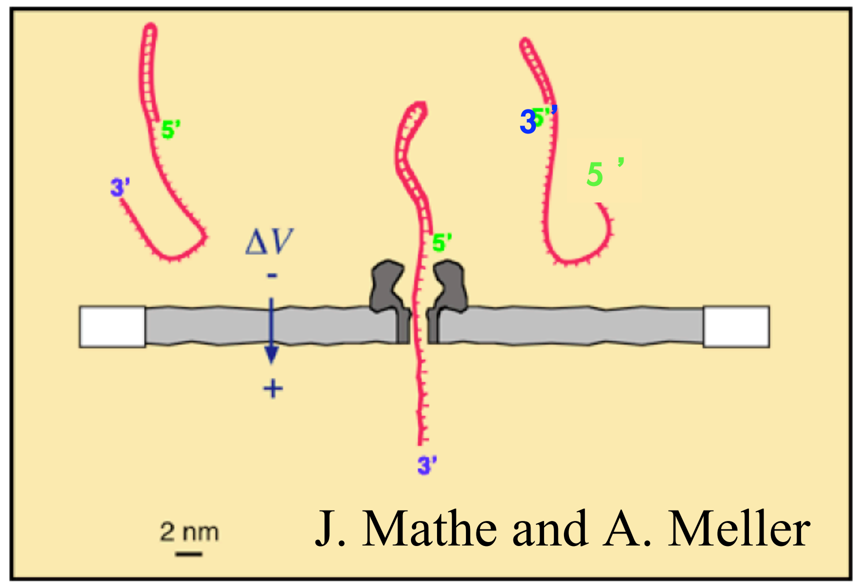




$v=\mu E$

$L_{DNA}/t=\mu\, U/L_{mem}$

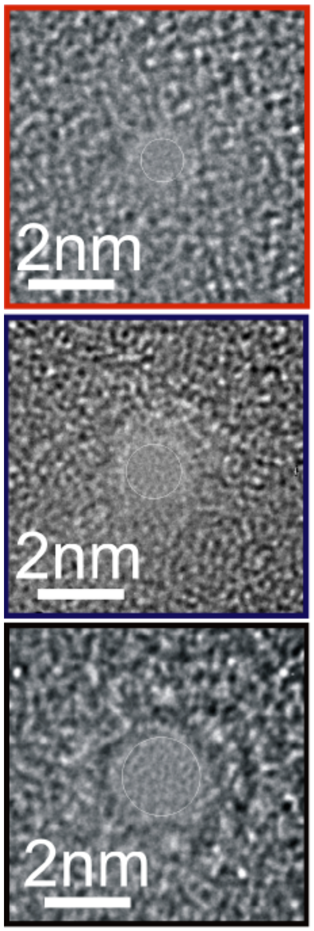
ξ: diffusive escape rate

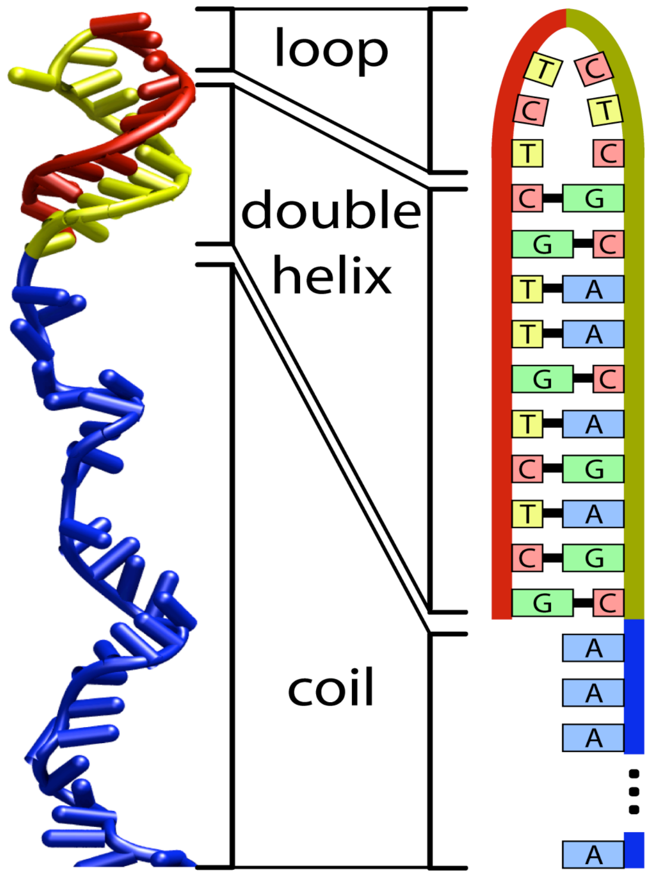


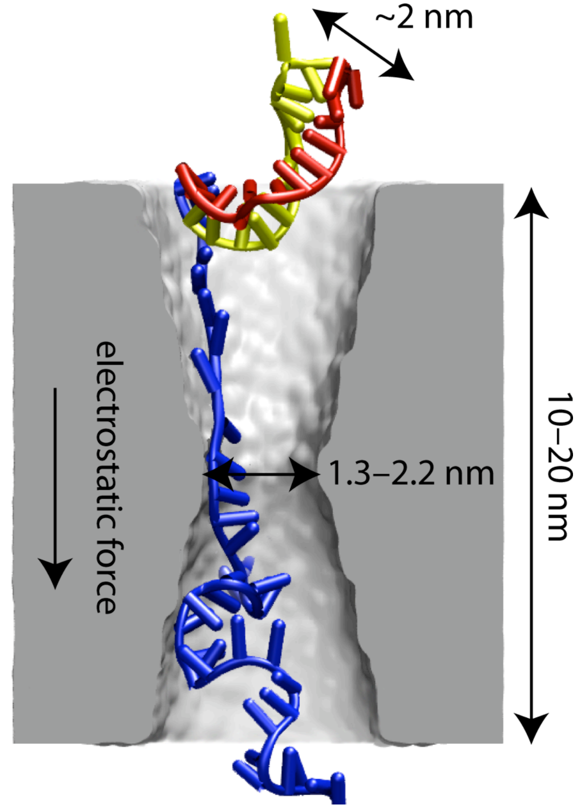
$D=k_B T/\xi$

Luan and Aksimentiev, PRE 78:021912 (2008)

hpDNA in Synthetic Pores





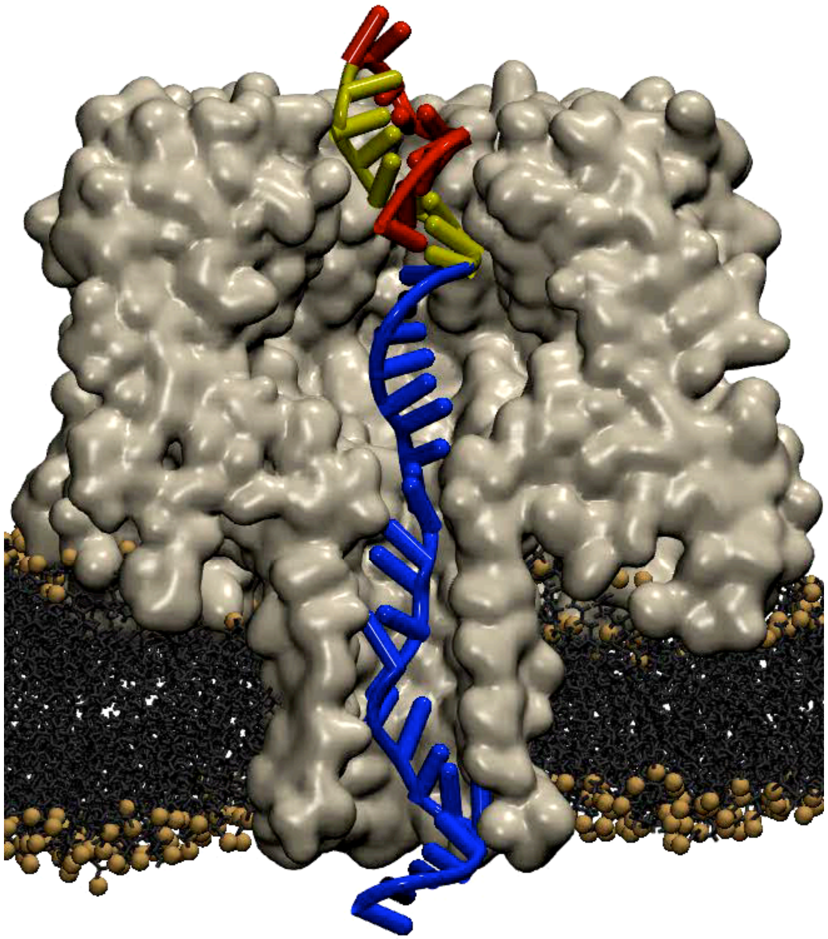


G. Timp (ECE, UIUC)

Persistence length: dsDNA: ~50 nm

ssDNA: ~2 nm

Modes of hpDNA Translocation

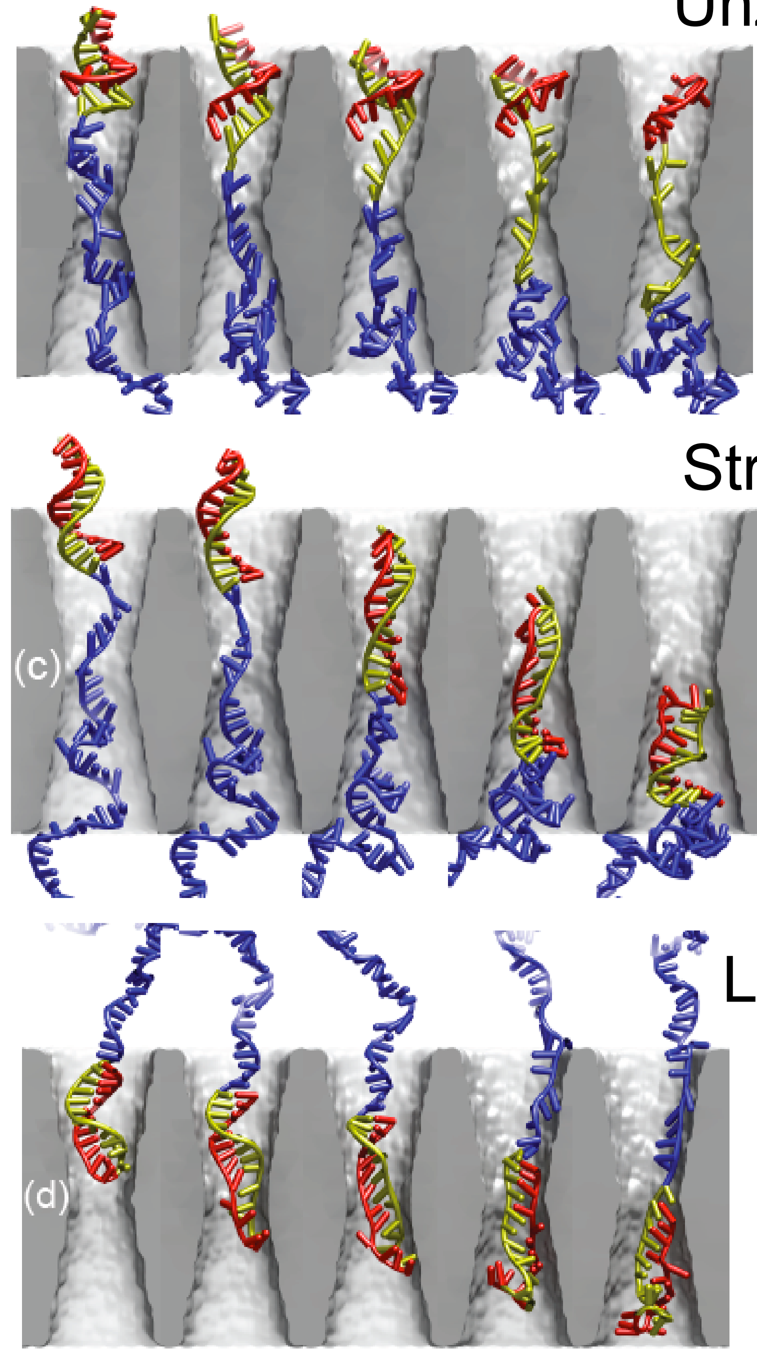


a-hemolysin

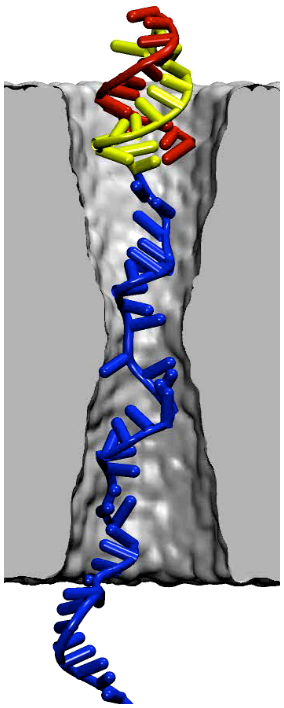
Unzipping

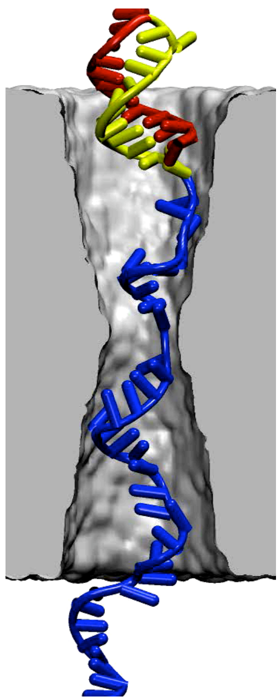
Stretching

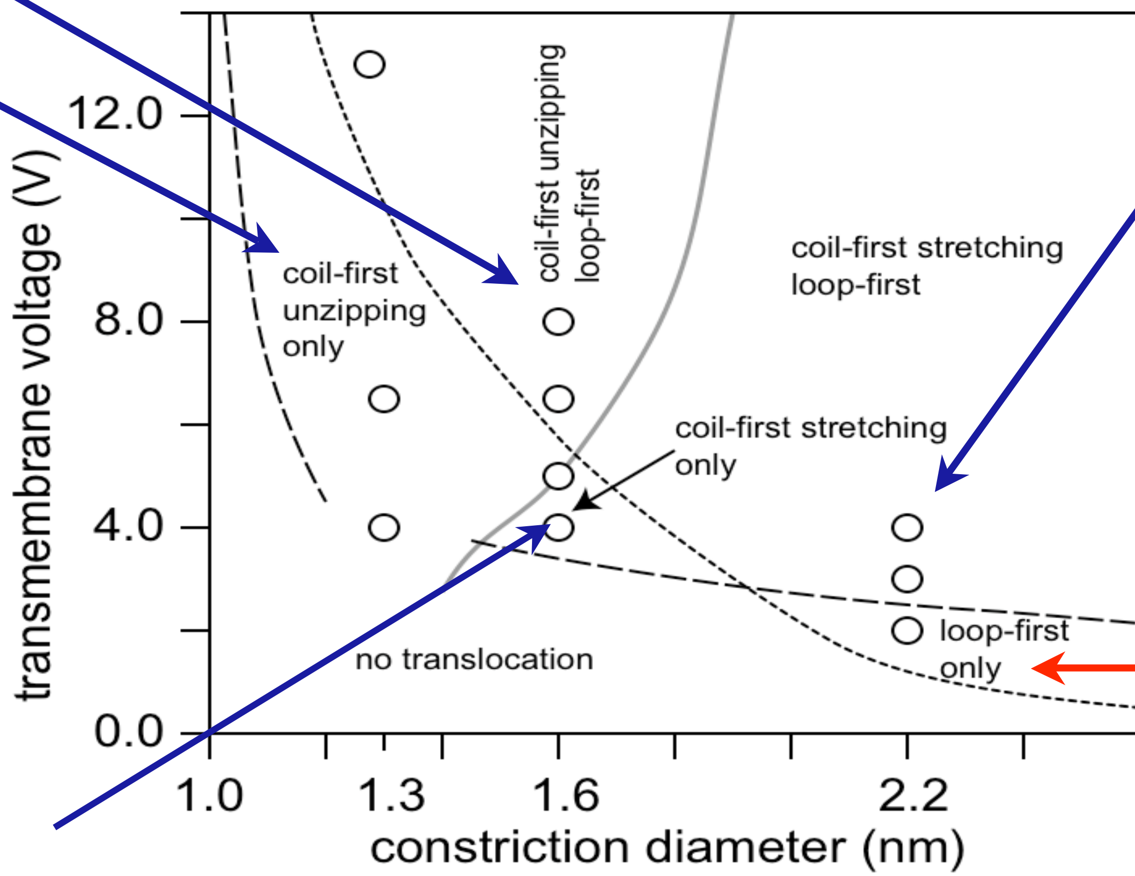
Loop first

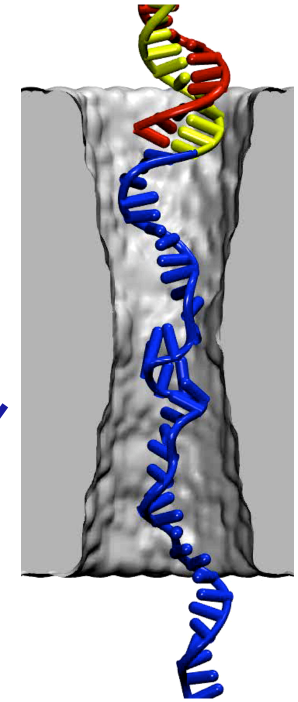


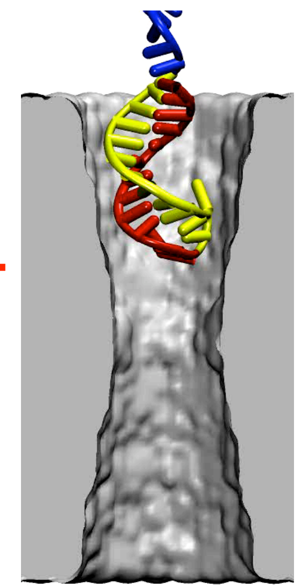
“Phase Diagram”









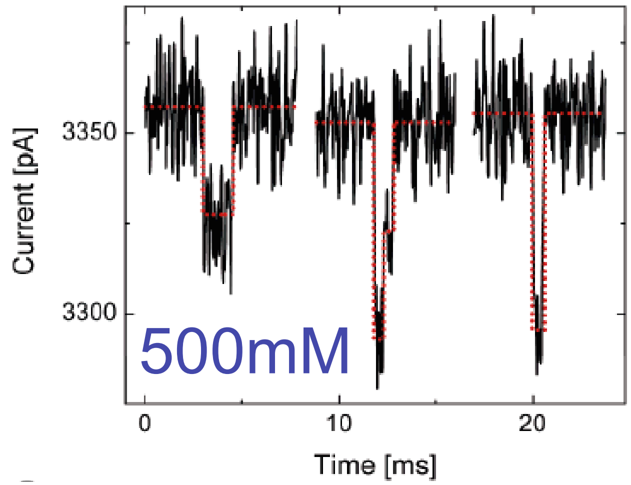


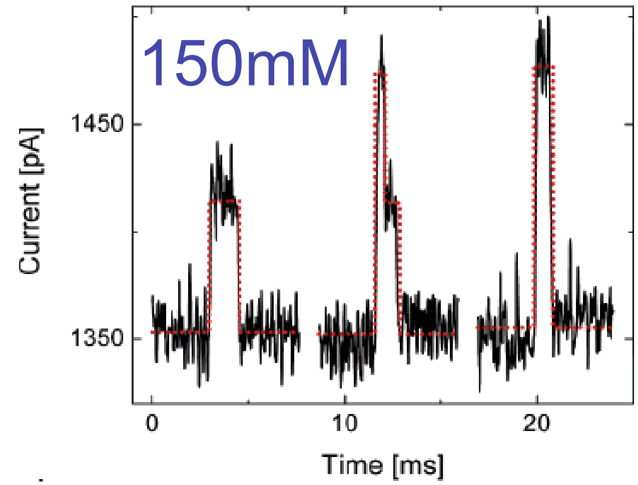
Comer et al.(2008)

Not always blockades

dsDNA in 10nm diameter pore

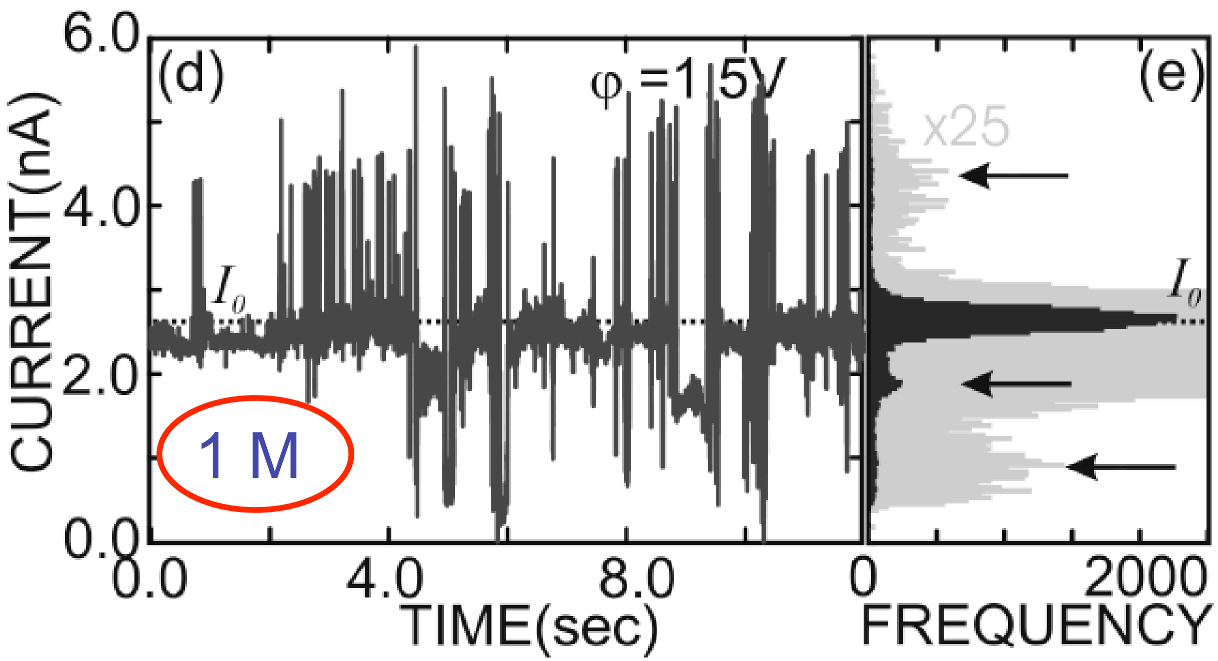
Smeets et al.,
Nano Let. 6:89-95



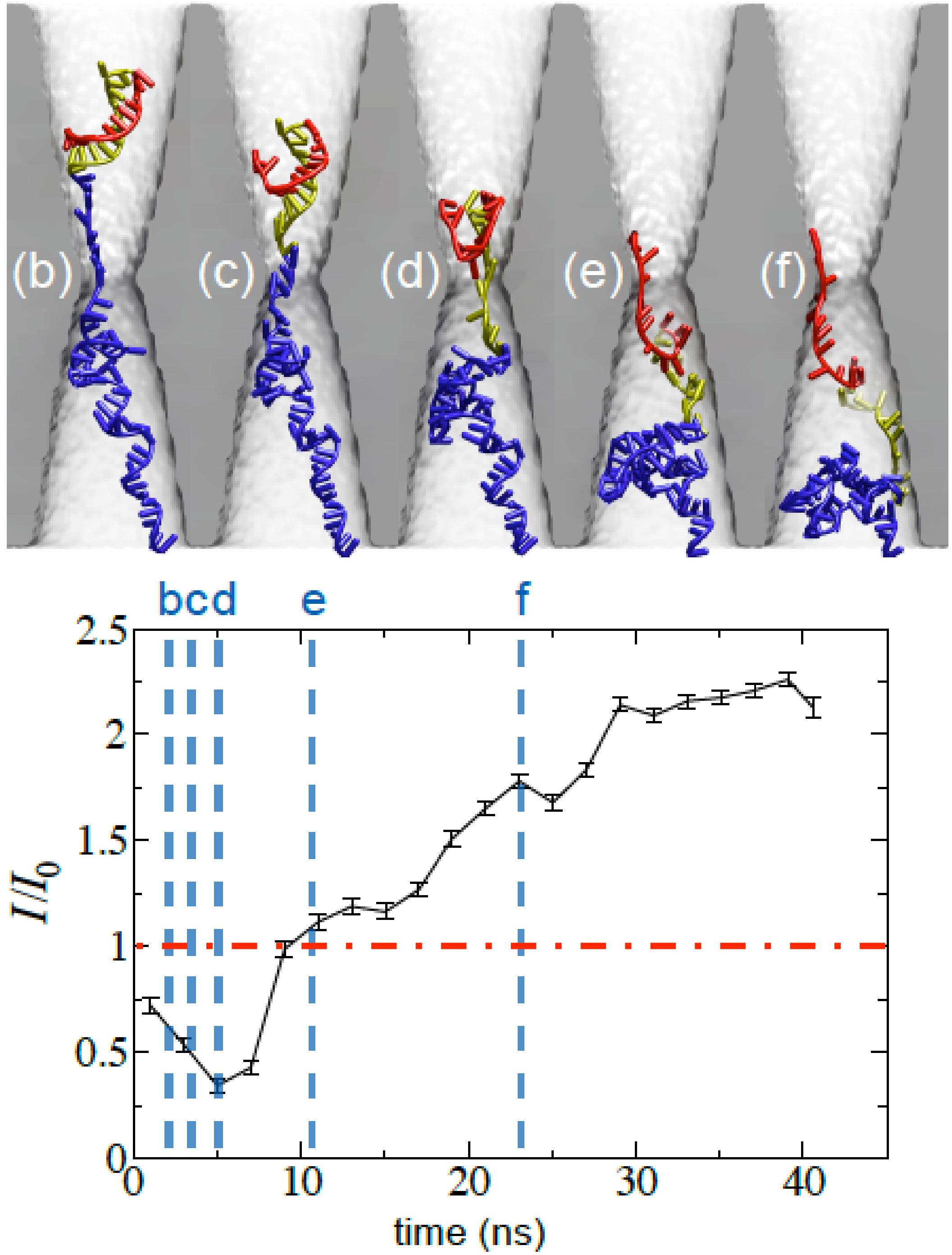


hpDNA in 2nm diameter pore

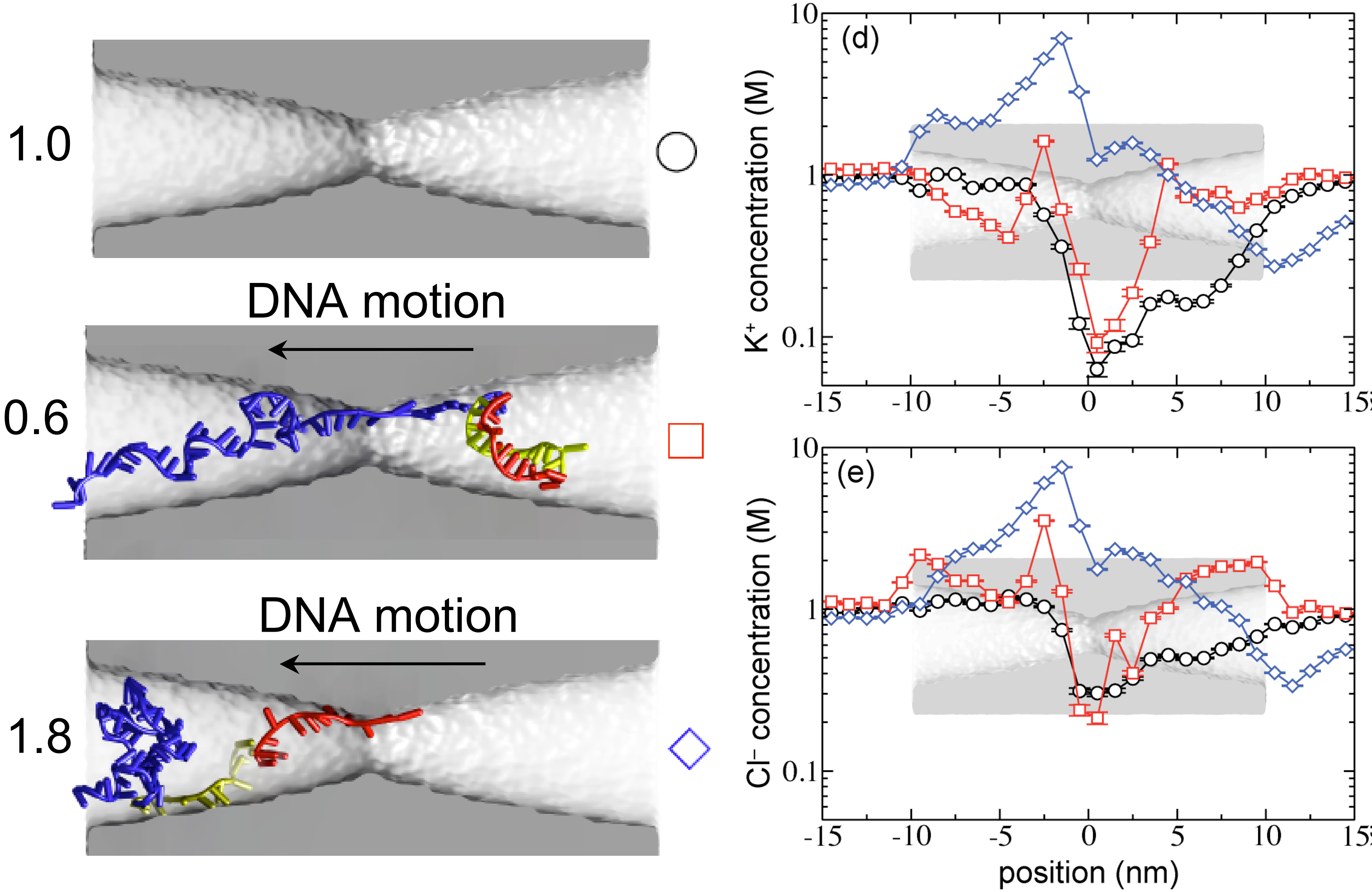
Zhao et al.,
Nucleic Acid Res.
36:1532-1541



Blockades and enhancements can be observed in the same simulation



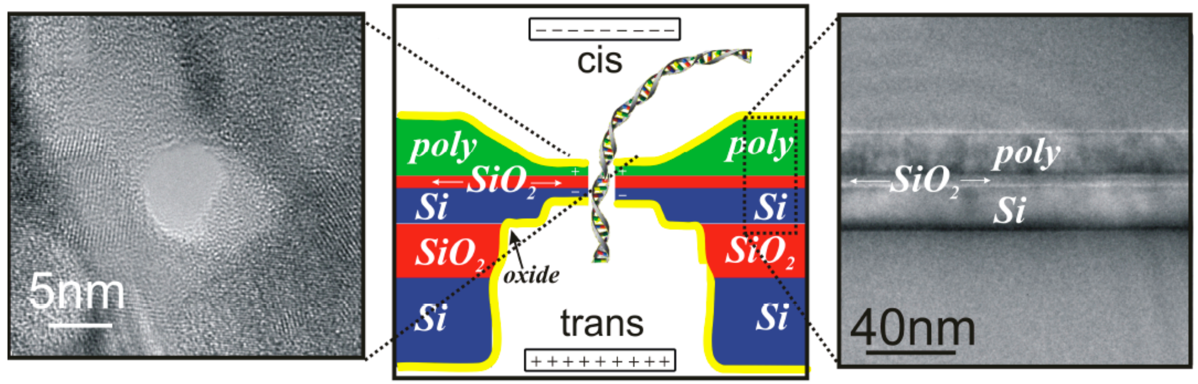
Microscopic origin of the current enhancement



Sequencing DNA using a synthetic nanopore

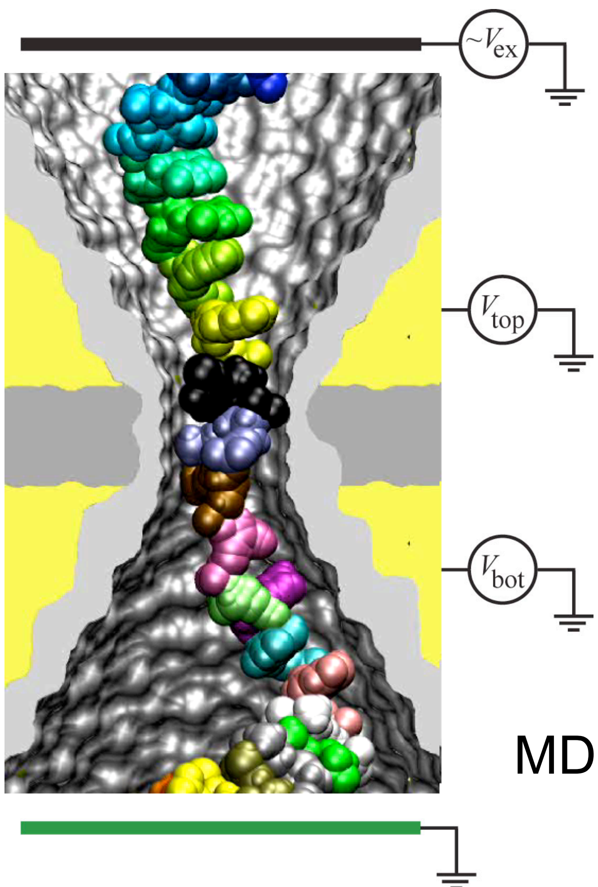
Goal: Electrical recording of DNA sequence using a nanopore capacitor.

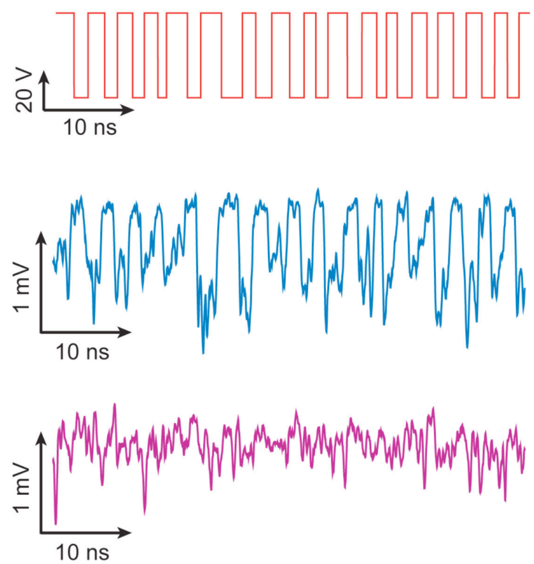
Experiment: G. Timp

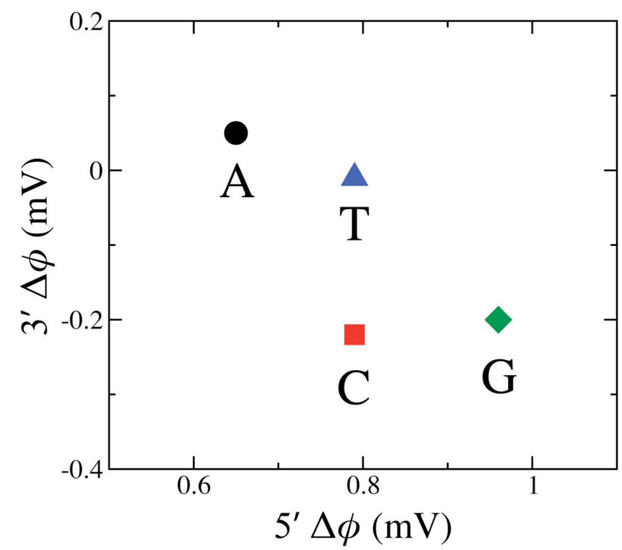


Nanopore

MOS membrane

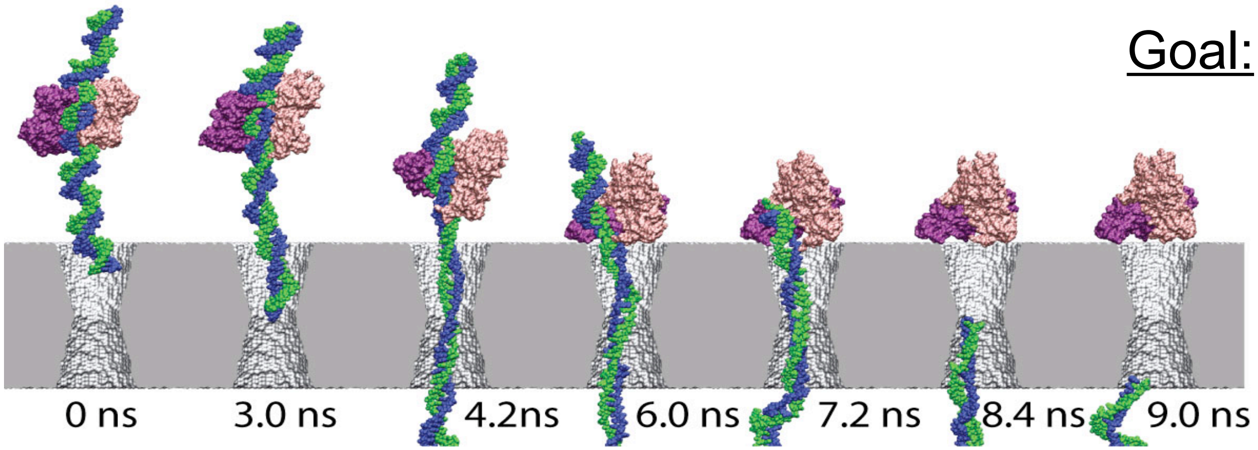






MD simulation of DNA translocation experiments
Sigalov et al., Nano Letters 8:56-63 (2008)

Genotyping using a synthetic nanopore



MD simulation of protein-DNA rupture

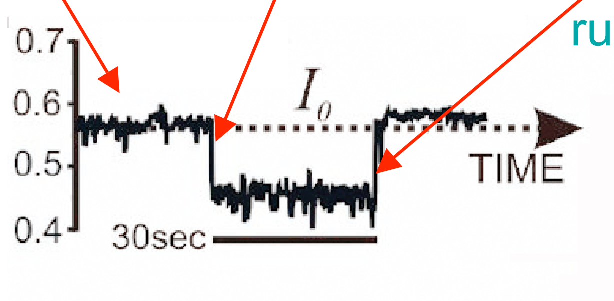
Goal: Detect single-nucleotide mutation in human DNA by measuring the affinity of a DNA-binding protein

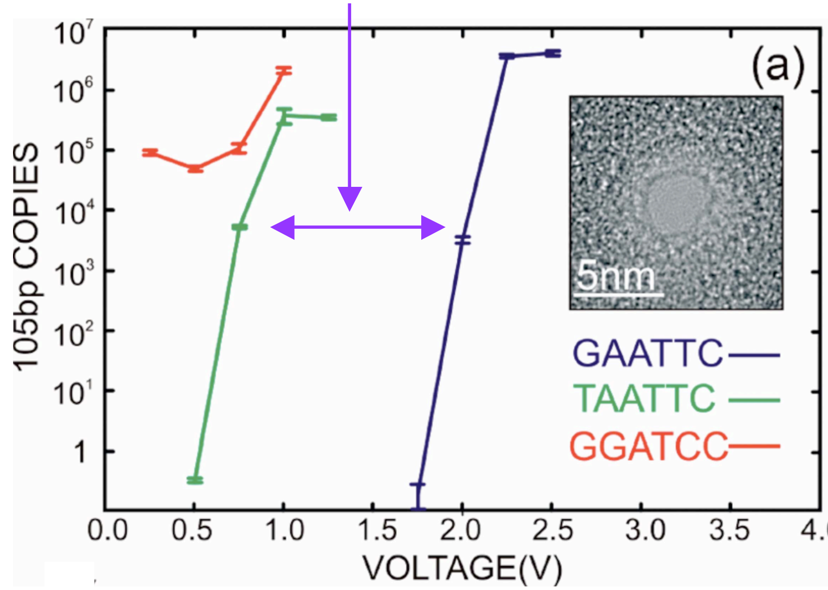
Mutation alters rupture bias (force)

open pore

capture of DNA-protein complex

DNA-protein rupture





Simulations relate measurements to underlying microscopic events

Nano Letters 7:1680-1685 (2007)

Acknowledgements

Grigori Sigalov
Jeff Comer
David Wells
Binquan Luan

Gregory Timp
Zhao Qian
Val Dimitrov
Ben Heng

Klaus Schulten
Eduardo Cruz-Chu

Jean-Pierre Leburton
Maria Gracheva

Steve Sligar
Elena Grinkova

Software: VMD, NAMD

Funding: NIH, UIUC

Supercomputer time at NCSA, PCS.