Dynamics of Biopolymers in Nanopores and Nanochannels

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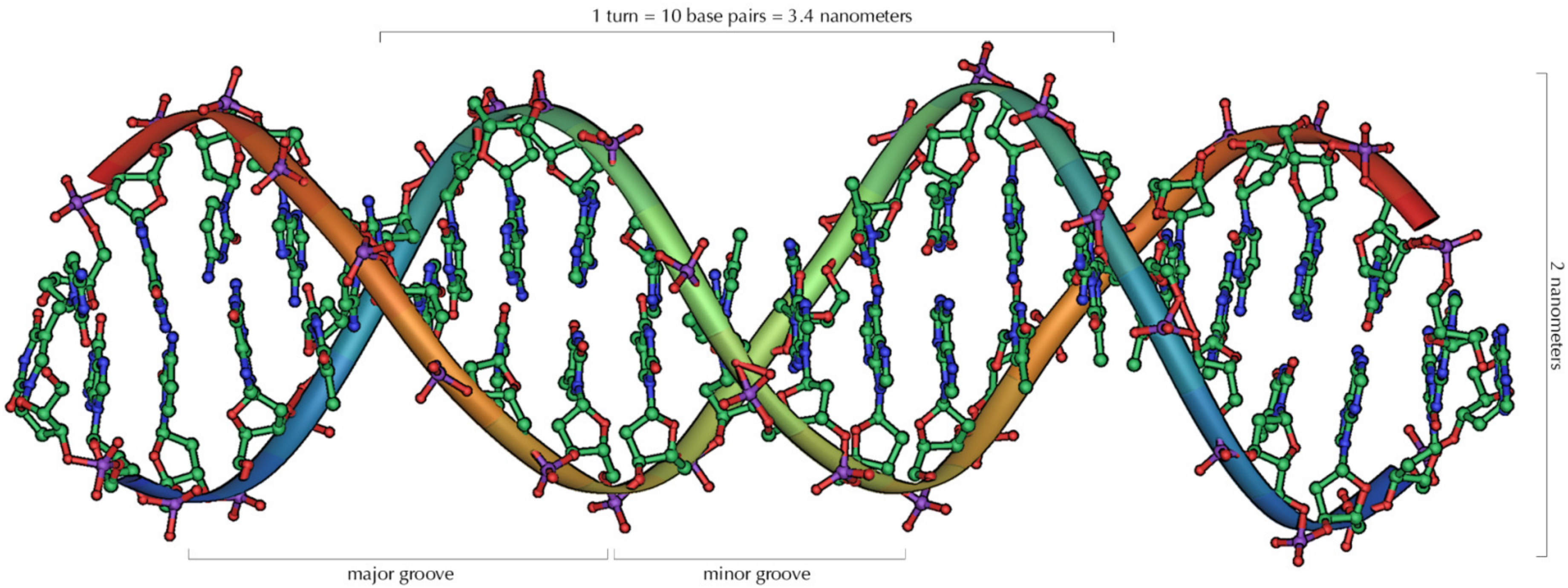
Ralf Metzler : :Technical University, München

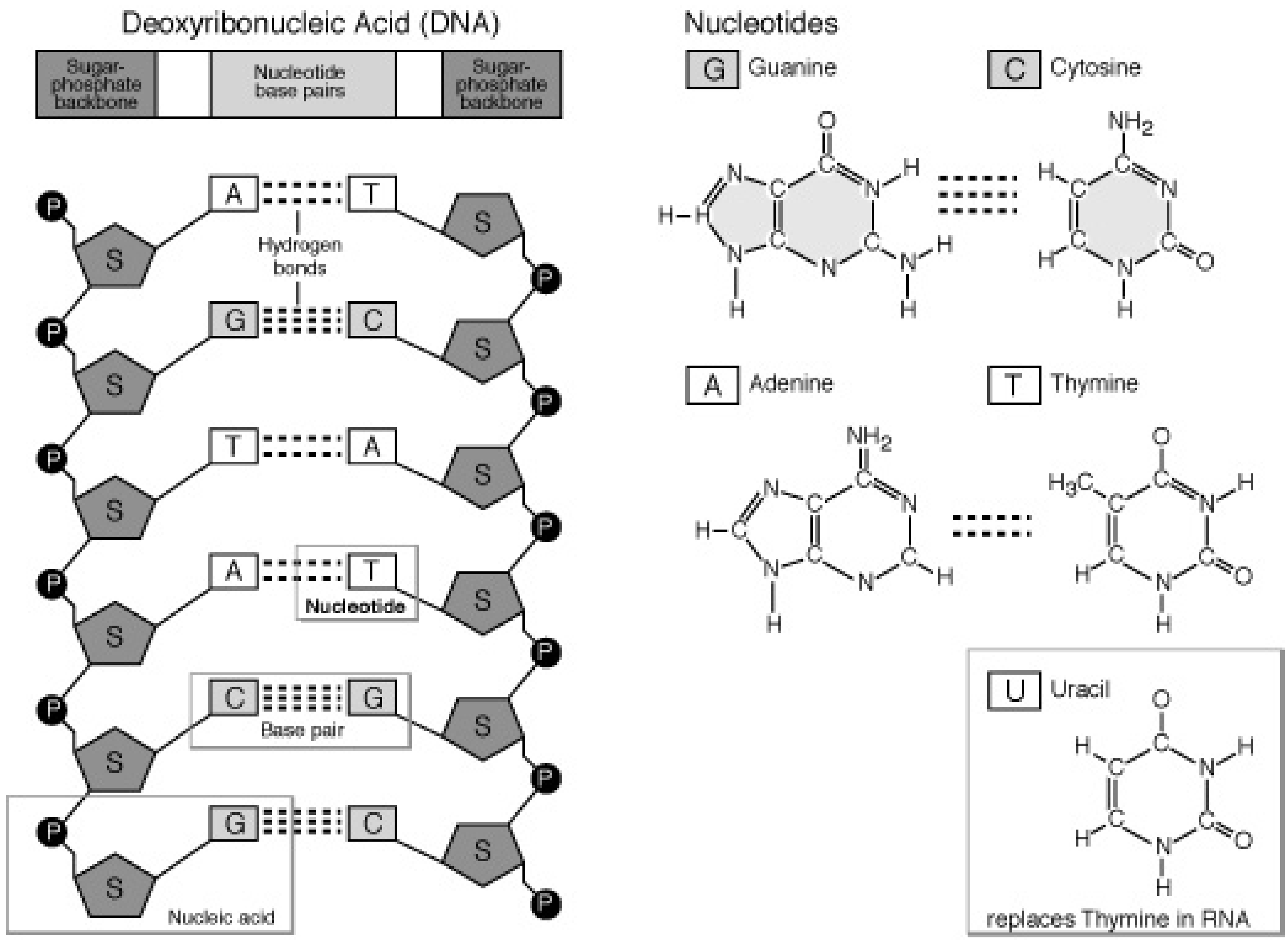
Aniket Bhattachyra :Central Florida University

Experimental:

Sean Ling : Brown University

Derek Stein


1 turn = 10 base pairs = 3.4 nanometers
2 nanometers
major groove
minor groove



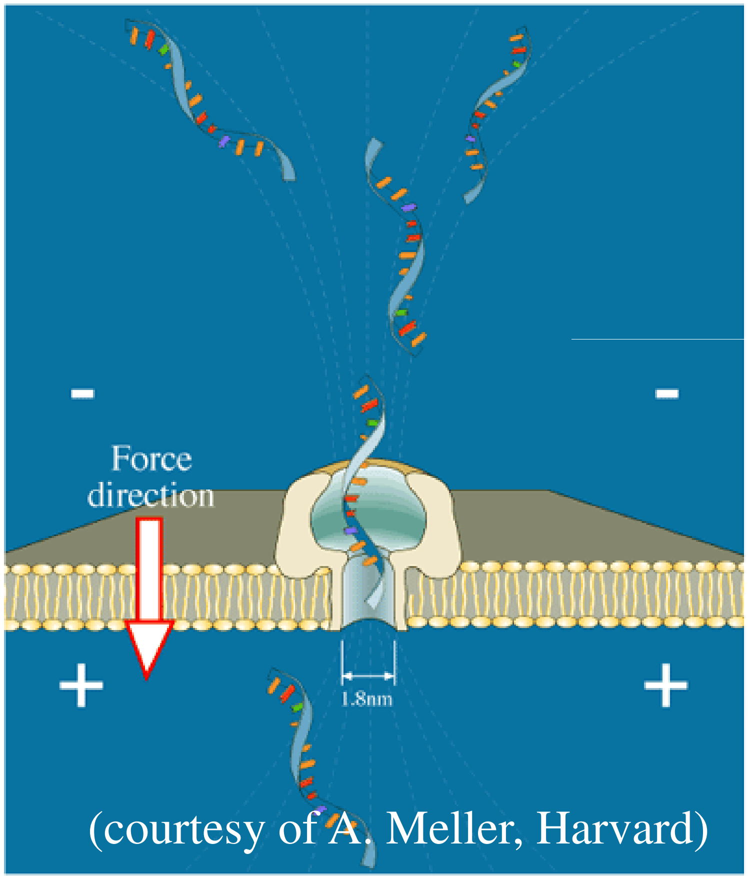
Deoxyribonucleic Acid (DNA)
Sugar-phosphate backbone
Nucleotide base pairs
Sugar-phosphate backbone
Hydrogen bonds
Nucleotide
Base pair
Nucleic acid
Nucleotides
Guanine
Cytosine
Adenine
Thymine
Uracil
replaces Thymine in RNA

- Kuhn Length r_K
- Over this length scale , the polymer behaves approximately as a rigid rod.

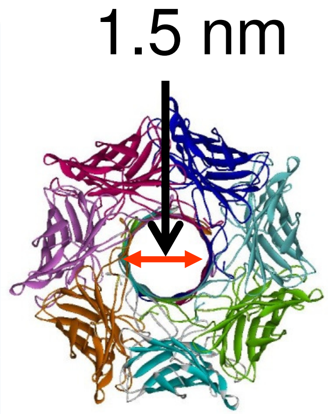
- r_K ranges from the separation for a few bases(nucleotides) for SSDNA to few hundred base pairs for DDSNA
- (1 to 10^2 nanometer)

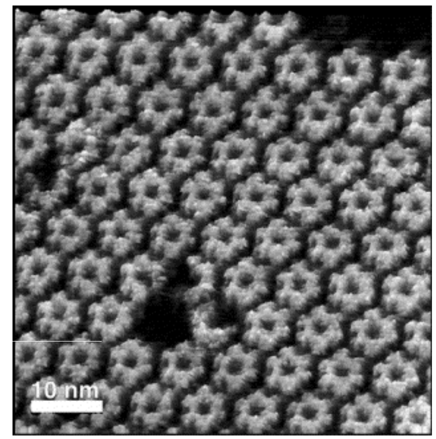
Biological nanopore: α-hemolysin

(a useful tool from a big bug: *Staphylococcus aureus)*



(courtesy of A. Meller, Harvard)





(D.M. Czajkowsky, 1998)

Fabrication of solid-state nanopores with single-nanometre precision

A. J. STORM[1], J. H. CHEN[1,2], X. S. LING[1,3], H. W. ZANDBERGEN[1] AND C. DEKKER*[1]
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[3]Permanent address: Department of Physics, Brown University, Providence, Rhode Island 02912, USA
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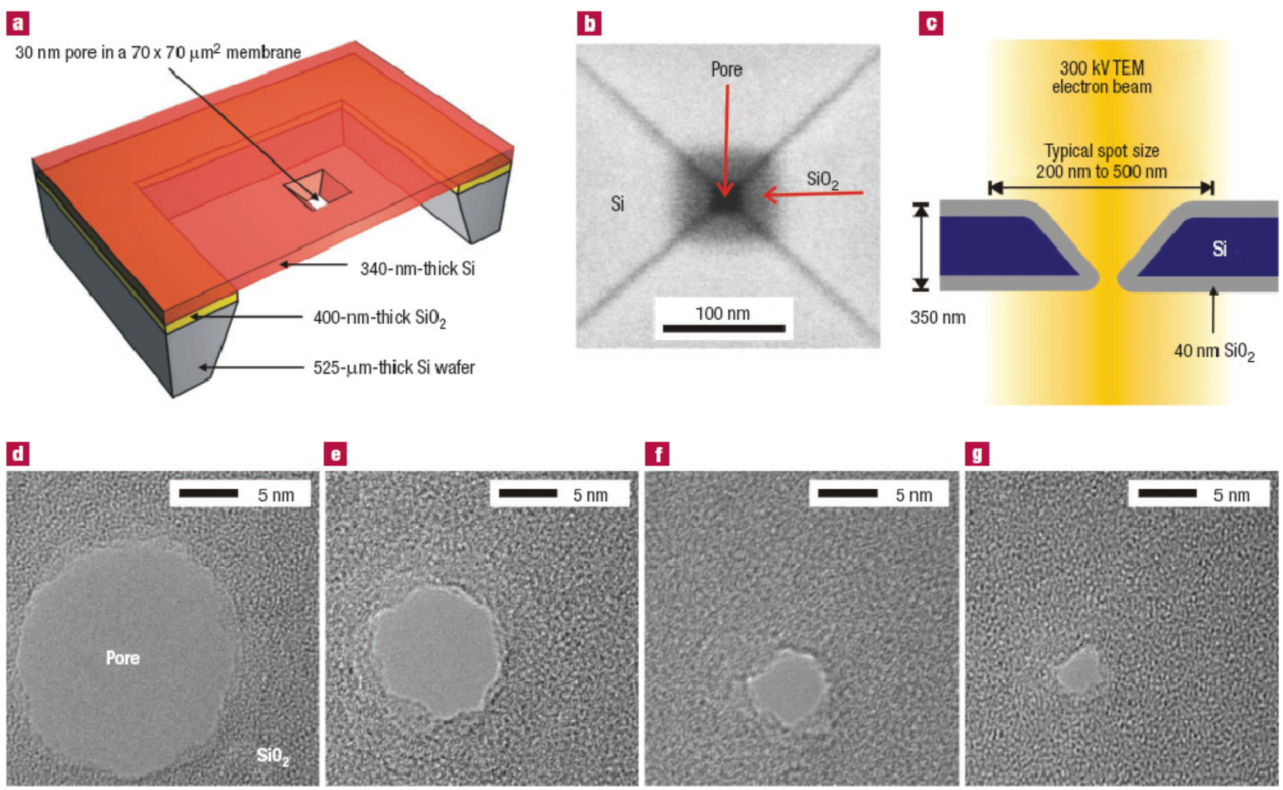
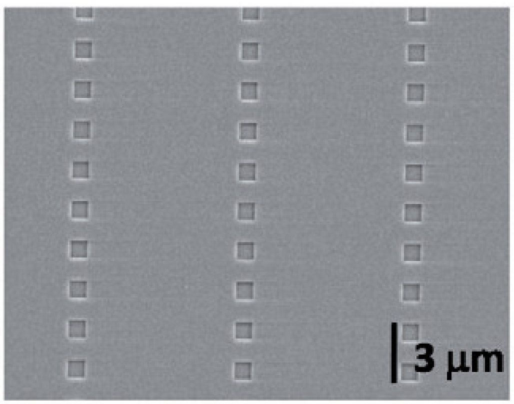
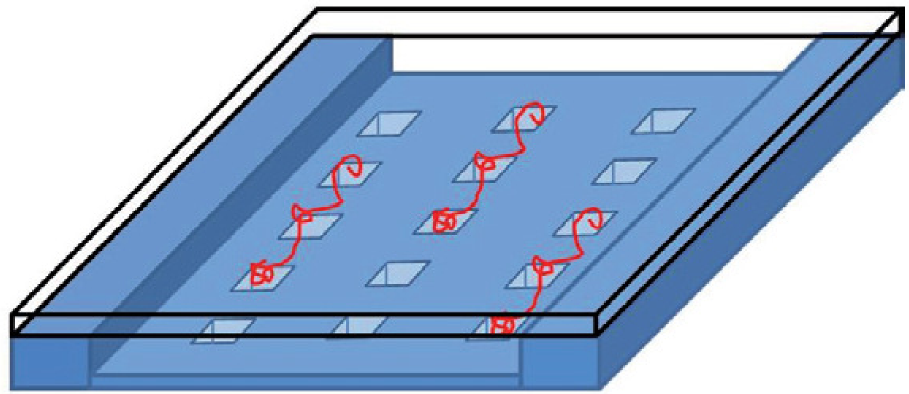


Free-Energy Landscaping:
Tailoring DNA Transport Across a Fluidic Nanotopography

(a)



(b)

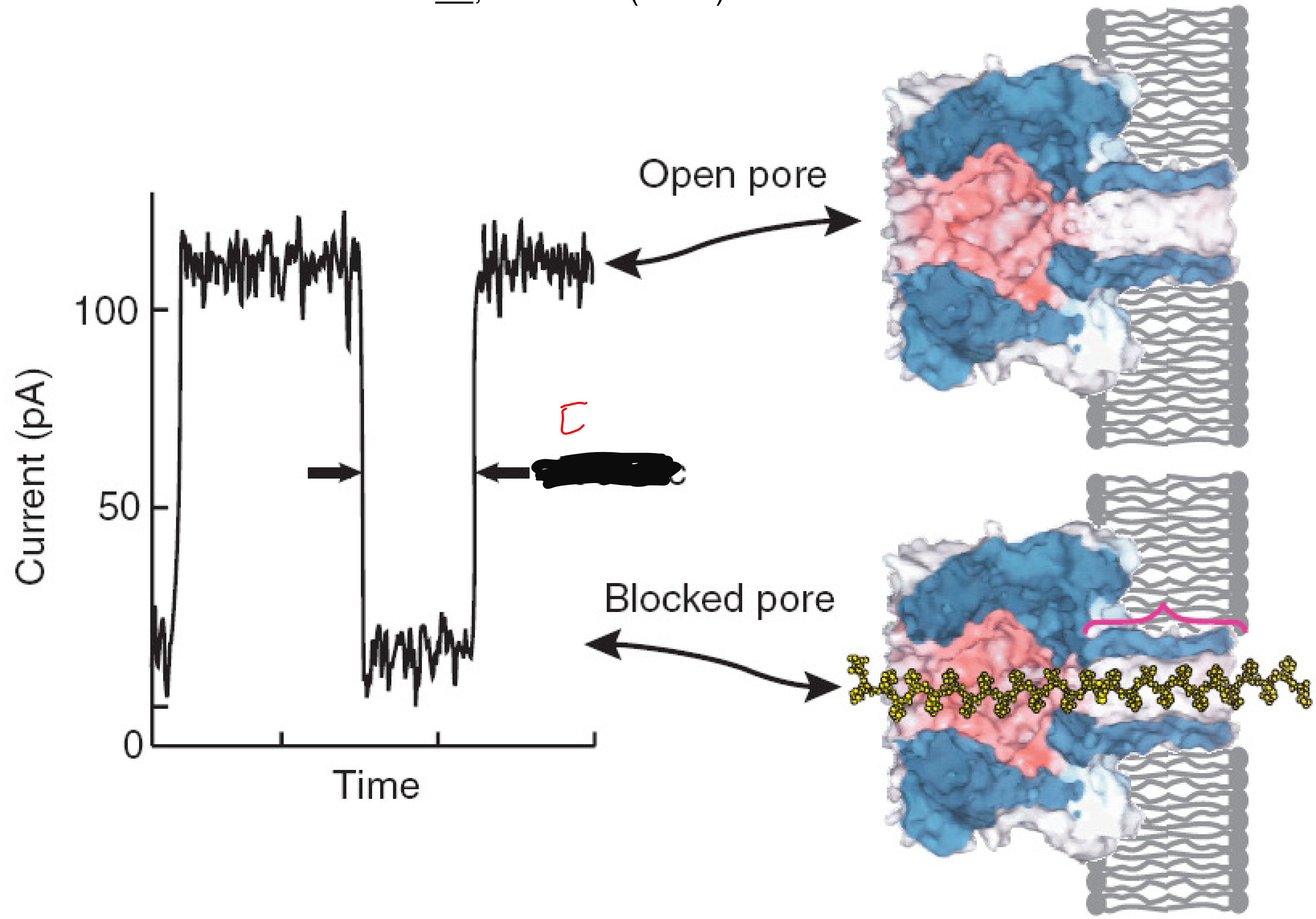


Pit spacing:0.5-20 μm channel and pit depth:100 nm pit dimension: 300 nm to 1 μm

Derek Stein, Jackson (Travis) Del Bonis-O'Donnell,
Walter Reisner Department of Physics
Brown University

Translocation of DNA molecule through Nanopores

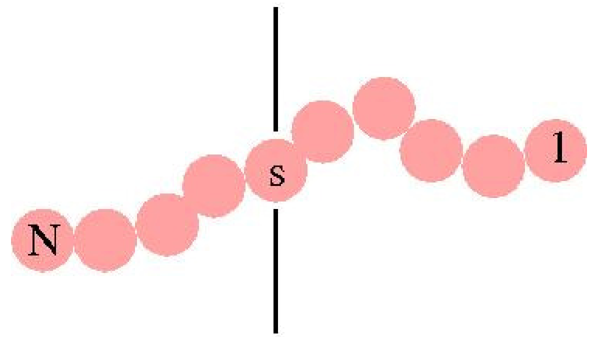
J.J. Kasianowicz, E. Brandin, D. Branton, and D. W. Deamer,
Proc. Natl. Acad. Sci. U.S.A. 93, 13770-3 (1996).



Contradicting results of scaling behavior of translocation time vs N from different studies both experimentally and theoretically over the last few years

Non-Universal Behavior due to strong non-equilibrium conditions!!

Translocation through a thin Pore :Effective Particle Apparaoach



One looks at the dynamics of a single monomer number (translocation coordinate s) at the pore which has similarities to the reaction coordinate for chemical processes. (Muthukumar, Sung and Park)

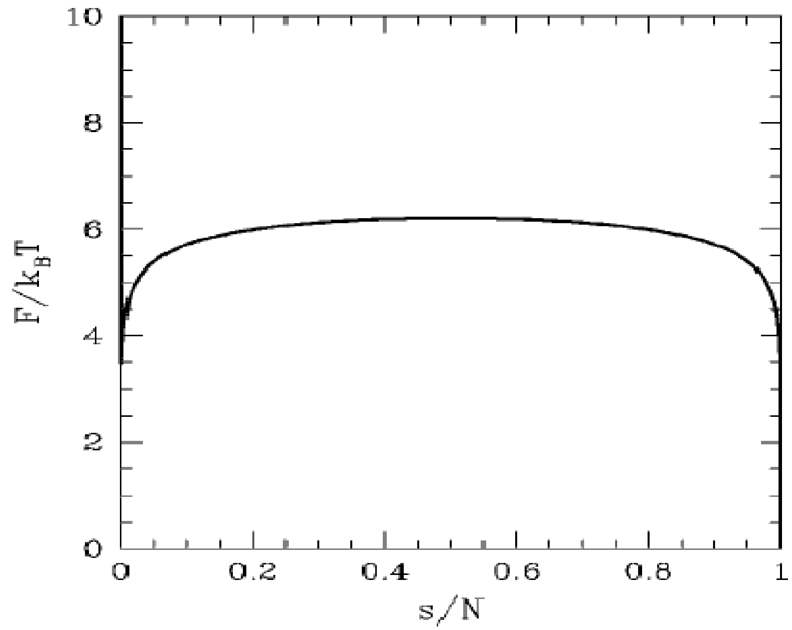


FIG. 2. The entropic potential barrier found in the single variable equivalent to the polymer translocation problem.

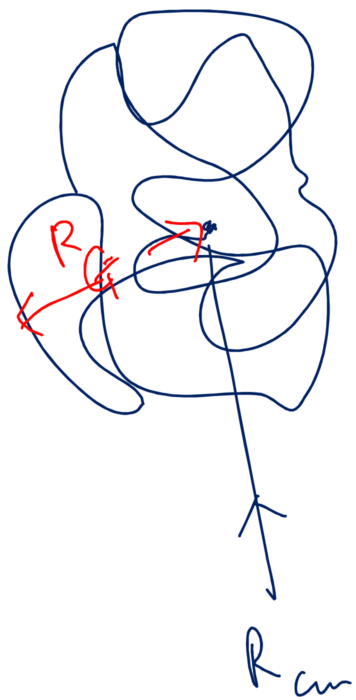
$$F = \gamma k_B T \ln[(N-s)s].$$

Assumption: the translocation problem is then reduced to escape of a particle (reaction coordinate"s") across the potential barrier caused by a thin idealized pore membrane. In this effective particle approach, it can be shown that $\tau \sim N^2$

Unfortunately, this result is not consistent with the single effective particle assumption !

Size of a Polymer: (Without Restrictions)

Radius of Gyration: $$\boldsymbol{R}_g^2 = \frac{1}{N}\sum_{n=1}^{N}\left\langle (\boldsymbol{R}_n - \boldsymbol{R}_{cm})^2 \right\rangle$$



Minimization of free energy

$$\Rightarrow R_g \sim N^{\nu}$$

Flory exponent: $$\nu = \frac{3}{d+2}$$

(=1/2 for phantom chains)

Effective particle picture not self consistent!

(Kardar)

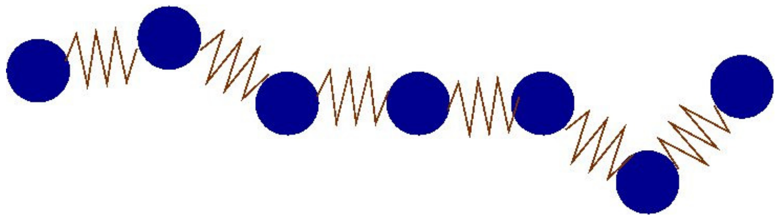
$$t_{eq} \sim \frac{1}{D}\langle R_g^2 \rangle \sim \frac{N^{1+2\nu}}{D_0}$$

$t_{eq} \sim N^{2.5}$ 2D

$t_{eq} \sim N^{2.2}$ 3D

Translocation time $\tau \sim N^2$ is smaller than t_{eq} for long polymers! Situation gets worse for Driven Translocation!!

Bead-spring model



Lennard-Jones Repulsion(all pairs)

$$U_{LJ}(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] + \varepsilon \qquad r \le 2^{1/6}\sigma;$$

$$= 0 \qquad r \ge 2^{1/6}\sigma$$

Anharmonic spring (FENE)(next neighbor)

$$U_{chain}(r) = -\frac{1}{2}kR^2 \ln\left[1 - \left(\frac{r}{R}\right)^2\right]$$

Langevin Dynamics Simulation

$$m\ddot{\boldsymbol{r}}_i = -\nabla_i U(\{r_{kl}\}) - \boldsymbol{F}(\boldsymbol{r}_i) - \nabla_i V_{pore}(\boldsymbol{r}_i) - \xi \mathbf{v}_\mathbf{i} - \boldsymbol{f}_i$$

$$< f_i(t) f_j(t') >= 2k_B T \xi \delta(t - t')$$

U Lennard-Jones interaction among beads

F External Force

V_{pore} Interaction with the Pore

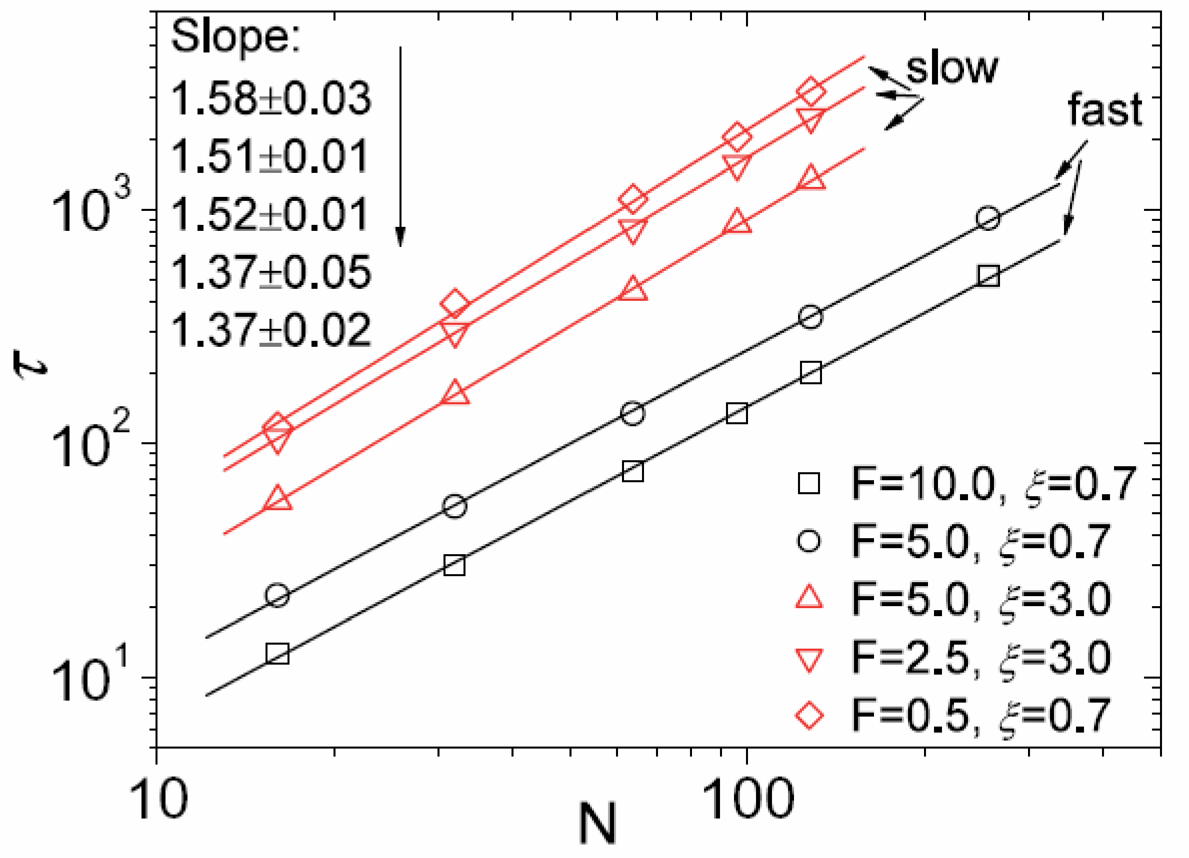
K.F.Luo, T. Ala-Nissila, SCY, A. Battachyra, PRL,100, 058101 (2008)

K.Luo, S. Ollila, I. Huopaniemi, T. Ala-Nissila,., P. Pomorski, M. Karttunen, A. Bhattachary, SCY, Phys. Rev. E **78**, Rapid Communications 050901(R):1-4 (2008).

A.Battachyra, W.H. Morrison, K.F. Luo, T. Ala-Nissila , A. Milchev , K. Binder, SCY European Physical Journal E **29**, pp. 423-429 (2009)

K.F. Luo, R. Metzler, T. Ala-Nissila,SCY, Phys. Rev. E **80**, 021907 ,(2009).

Numerical Study of Driven Translocation



K.F. Luo, T. Ala-Nissila, SCY, R. Meltzer: EPL, **88,** 68006 (2009)

Lower bound scaling estimate for Driven translocation time

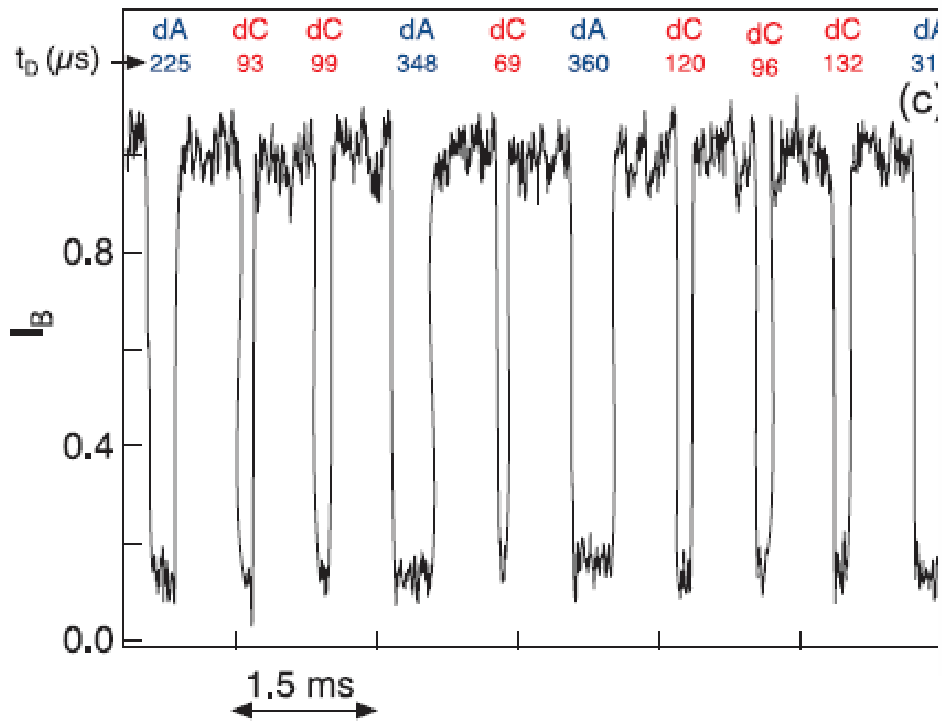
[Y. Kantor and M. Kardar, *PRE* **69**,021806 (2004)]

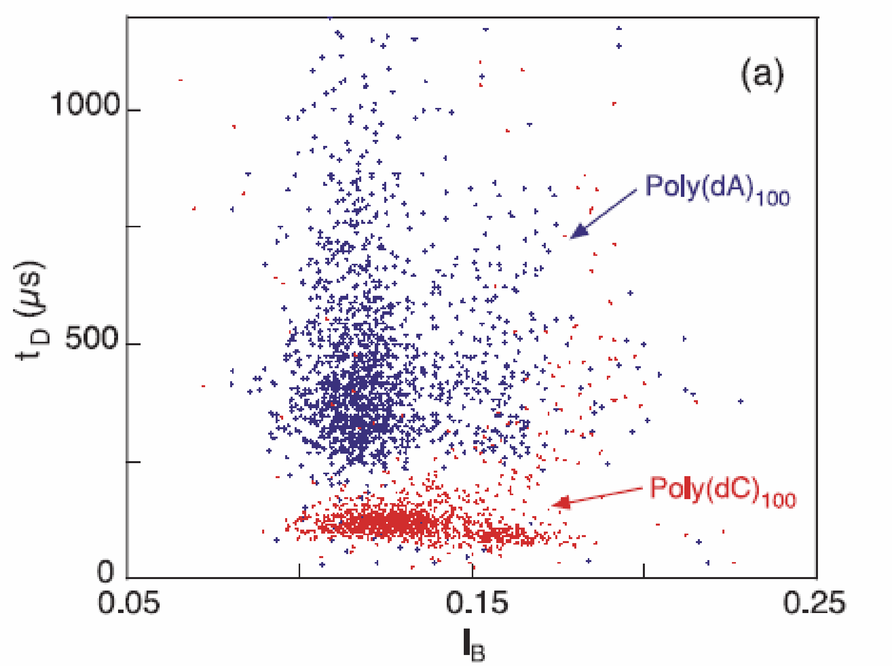
$$\tau(F) \sim \frac{R_g}{\mathrm{v}} \sim \frac{N^{\nu}}{F/N} \sim N^{1+\nu} F^{-1}$$

This assumes $R_g \sim N^{\nu}$ during translocation even when the system is not at full equilibrium at any time

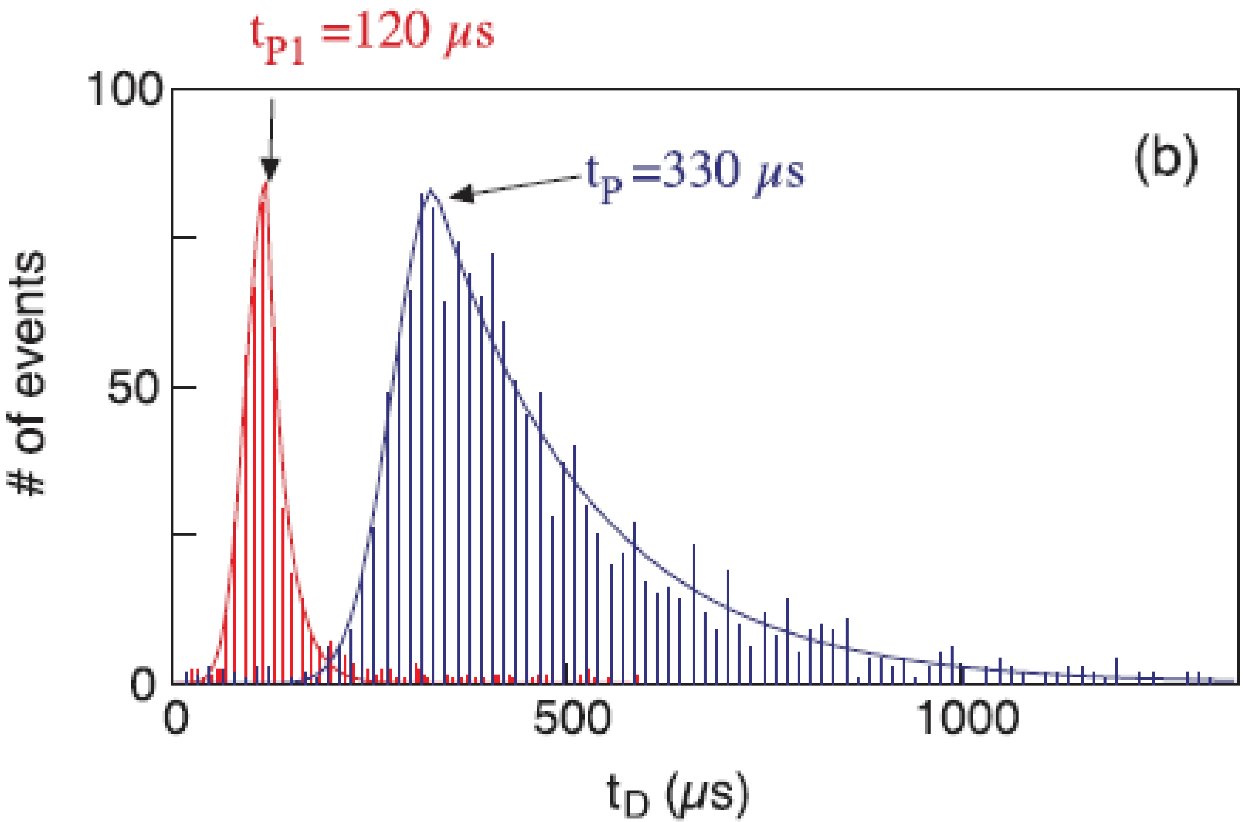
$$\tau \sim N^{1.6}$$ 3D

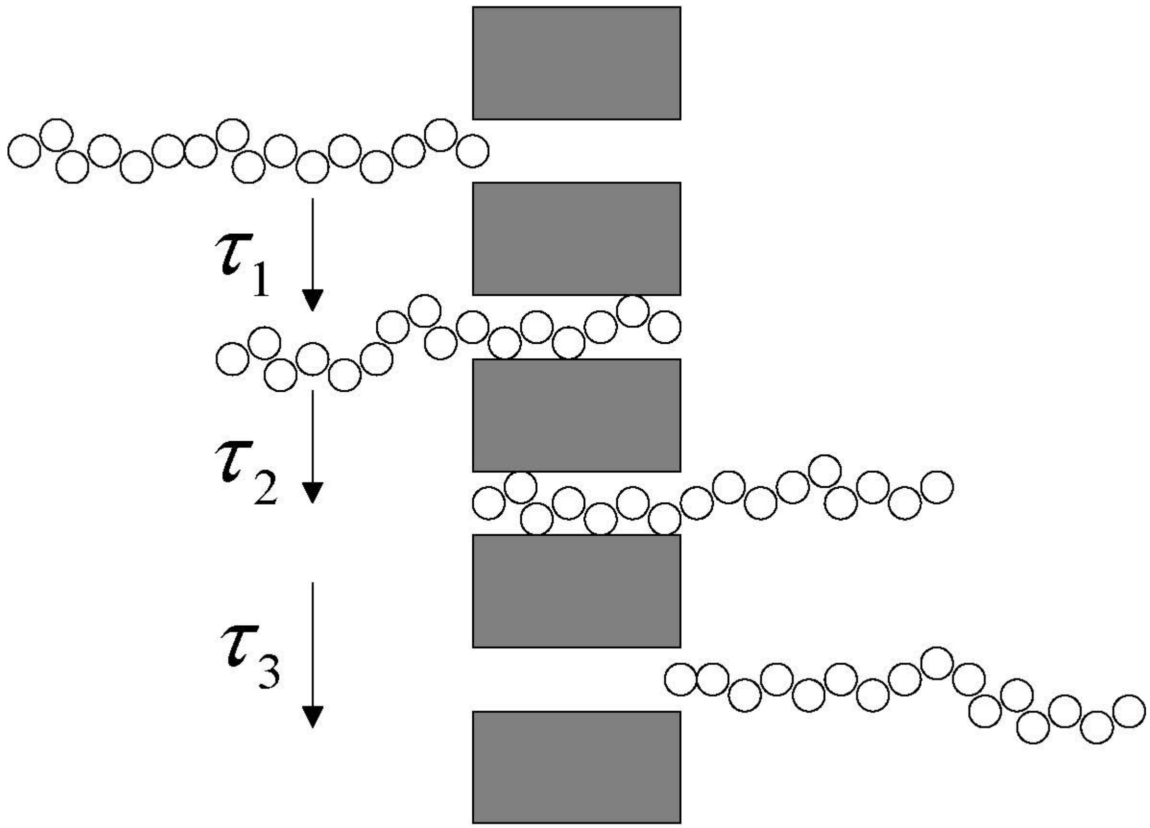
Effect of Interaction with the pore wall on Translocation





The event diagram of poly*(dA)100 (black/blue markers) and poly(dC)100 (grey/red*markers).Meller et al, PNAS 97,p.1079 (2000)

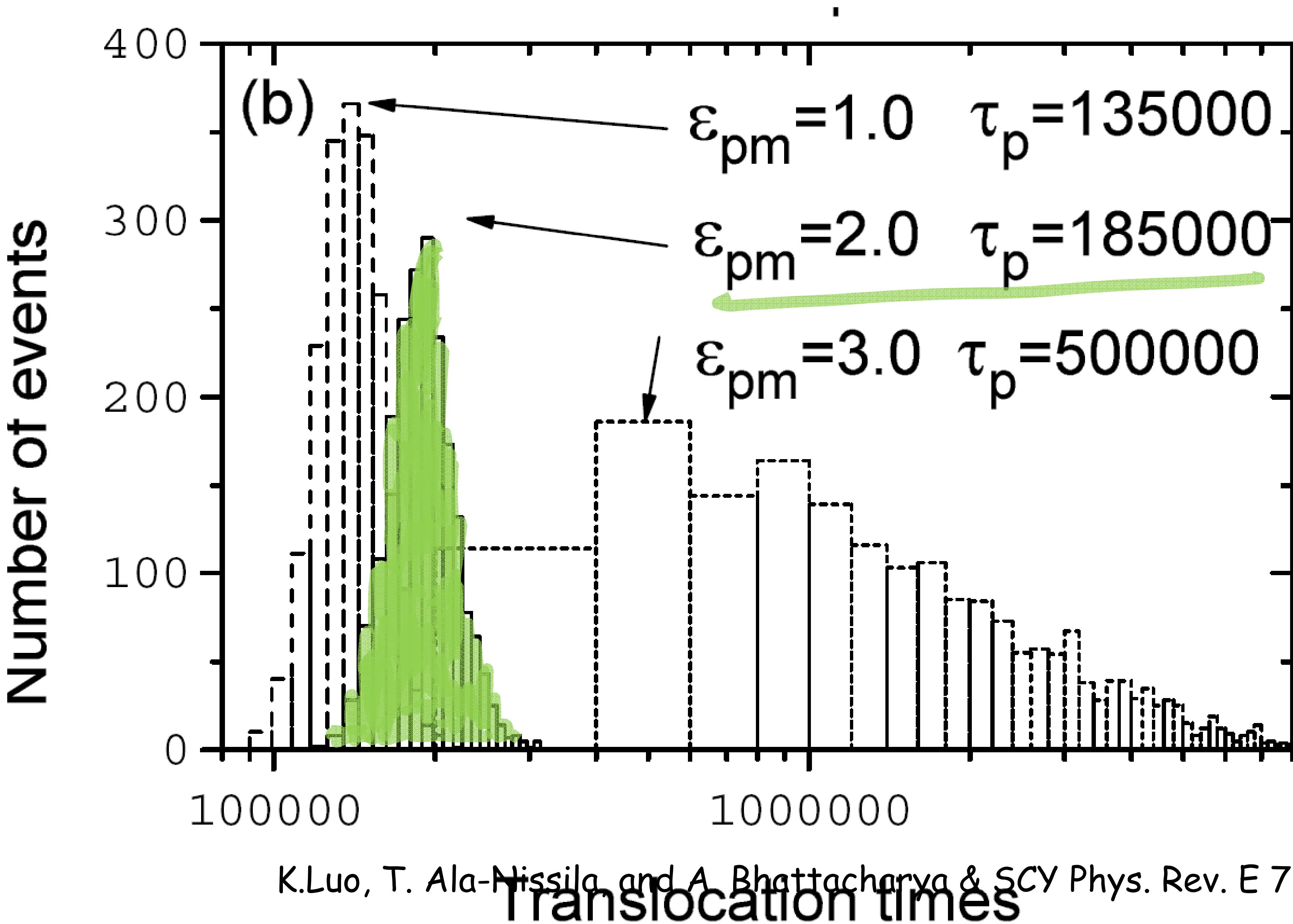

t_{P1} =120 μs
t_P =330 μs
(b)
100
50
0
0
500
1000
# of events
t_D (μs)



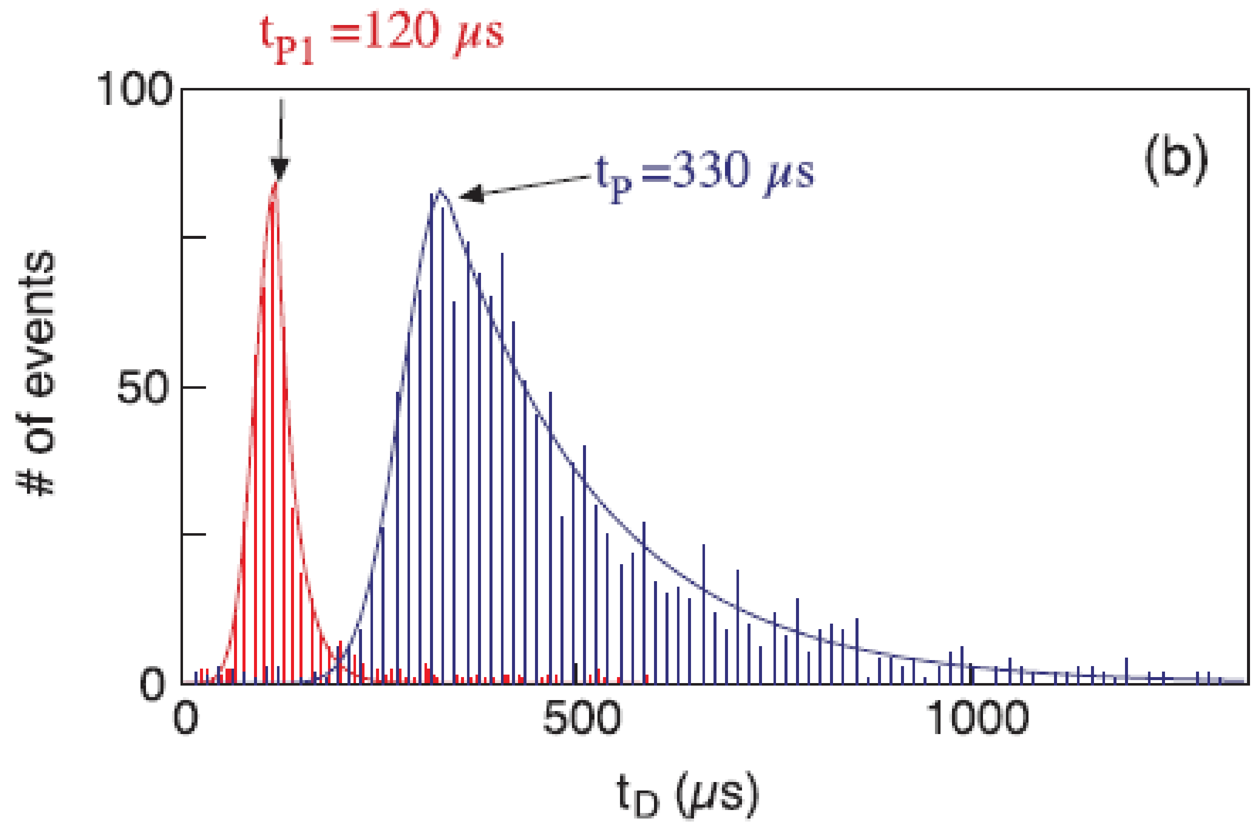
$$\tau \sim \tau_1 + \tau_2 + \tau_3$$

$$\tau_2 \sim F^{-1} N^{1+\nu}$$

$$\tau_3 \sim F^{-1} \exp + \beta L[\varepsilon_{pm} - F/2 + f(N)]$$



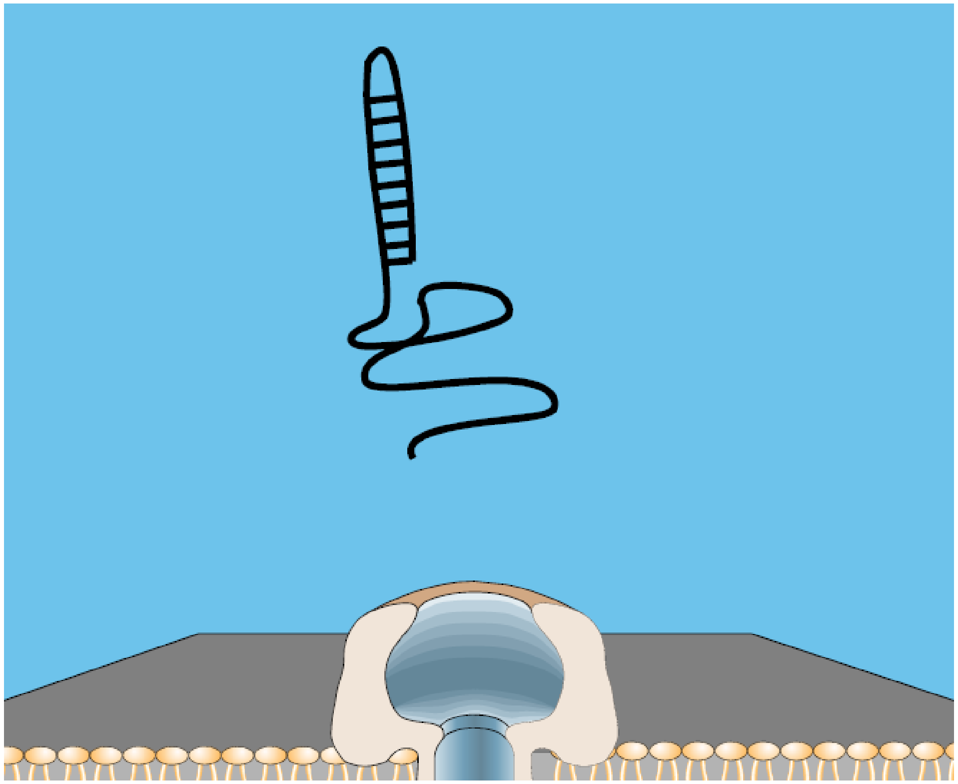
K.Luo, T. Ala-Nissila, and A. Bhattacharya & SCY Phys. Rev. E 78, 061

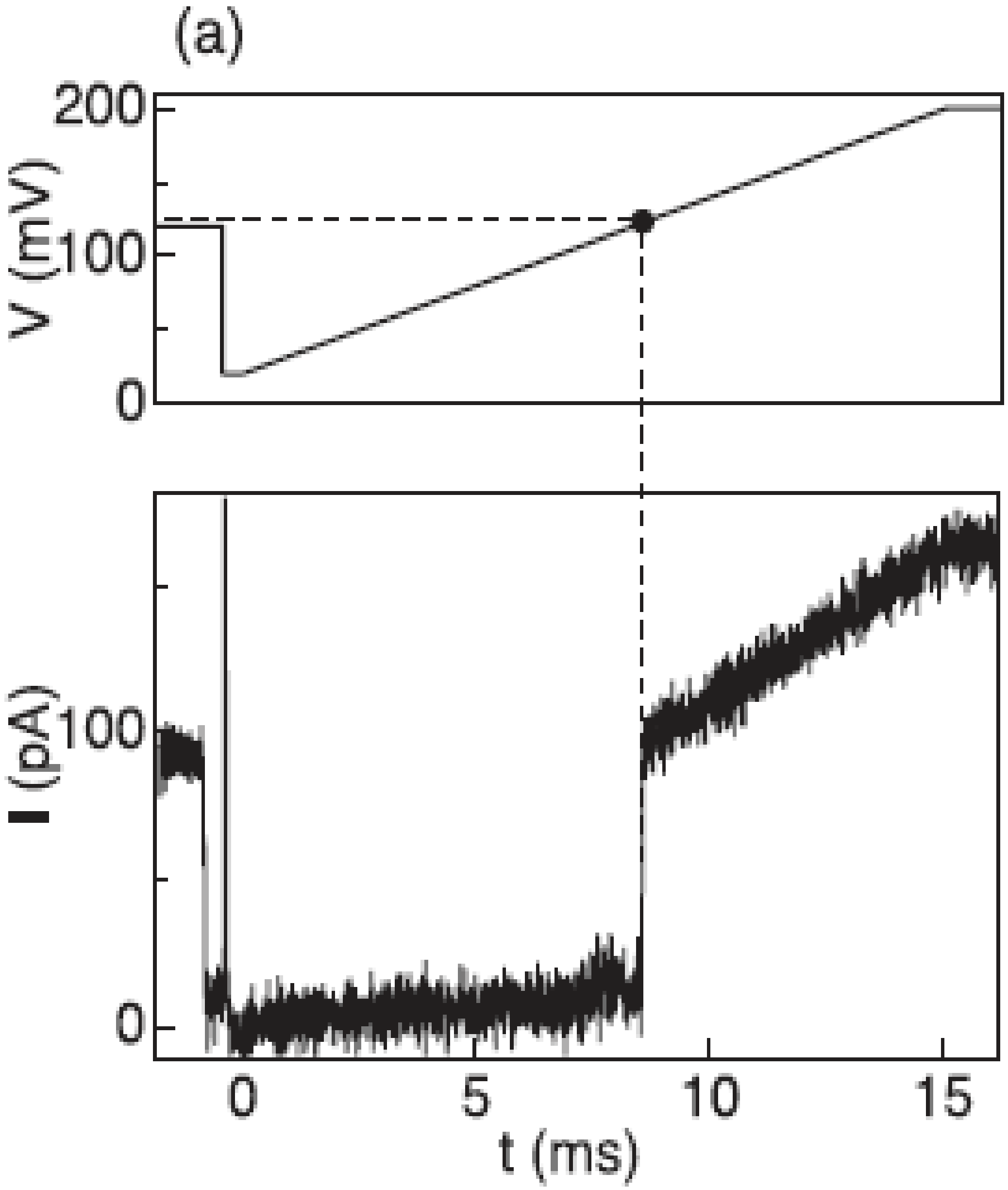


t_{P1} =120 μs
t_P =330 μs
(b)
100
50
0
0
500
1000
# of events
t_D (μs)

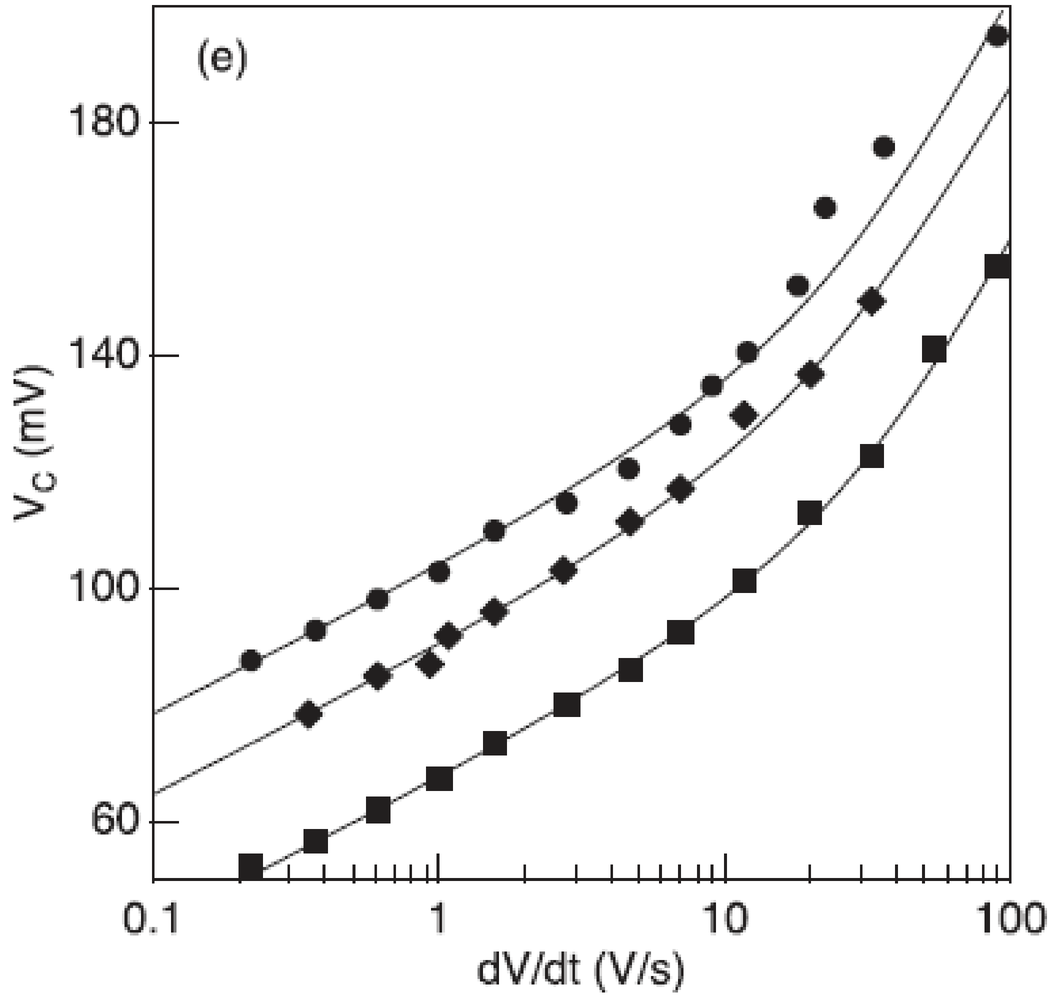
Unzipping of hairpin via Transport through Nanopore

The hairpins consist of a single stranded overhang of 50 adenines and a 7, 9 or 10 bp double stranded part separated by a loop of 6 bases (4 bases in the case of hairpin 3sequences)





Meller et al, Eur.Phys.Lett.
73, p.128 (2006)

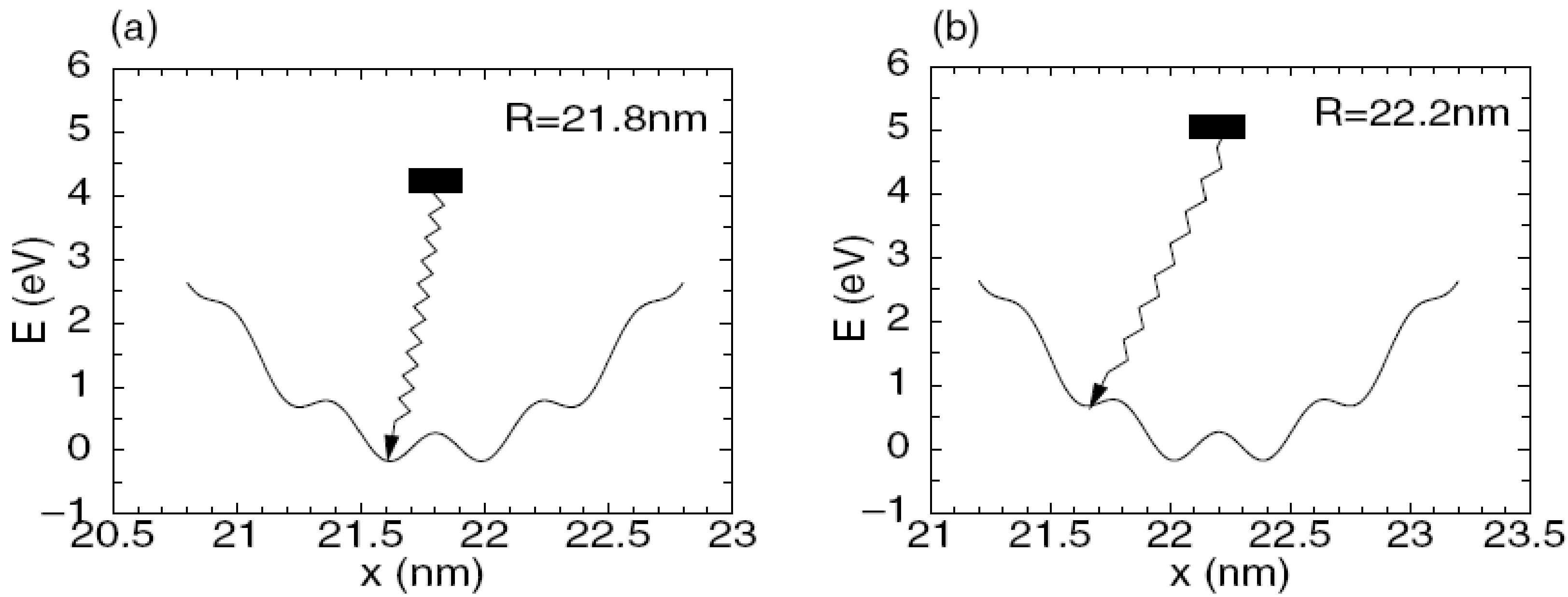


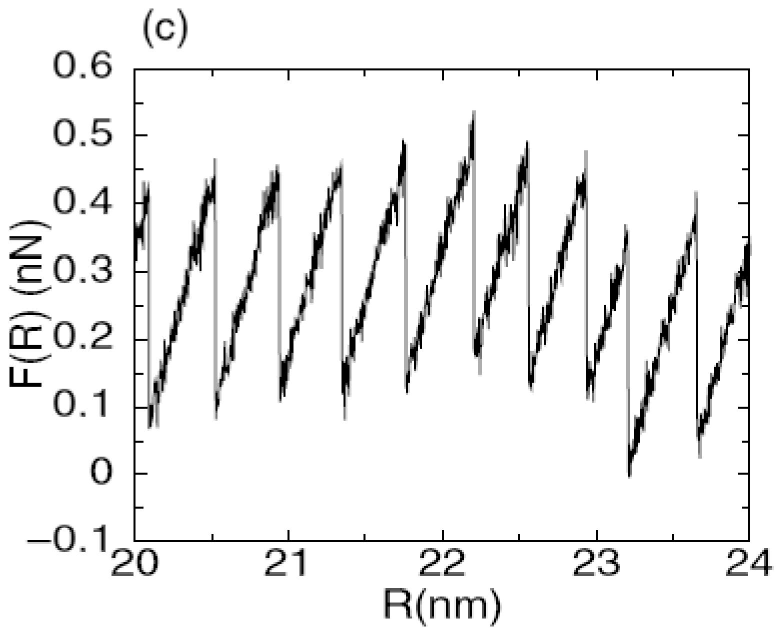
(e): the critical unzipping voltage as a function of the ramp for three different hairpins: HP1 (10 bp, circles), HP2 (9 bp, diamonds) and HP3 (7 bp, squares) as a function of the ramp level.

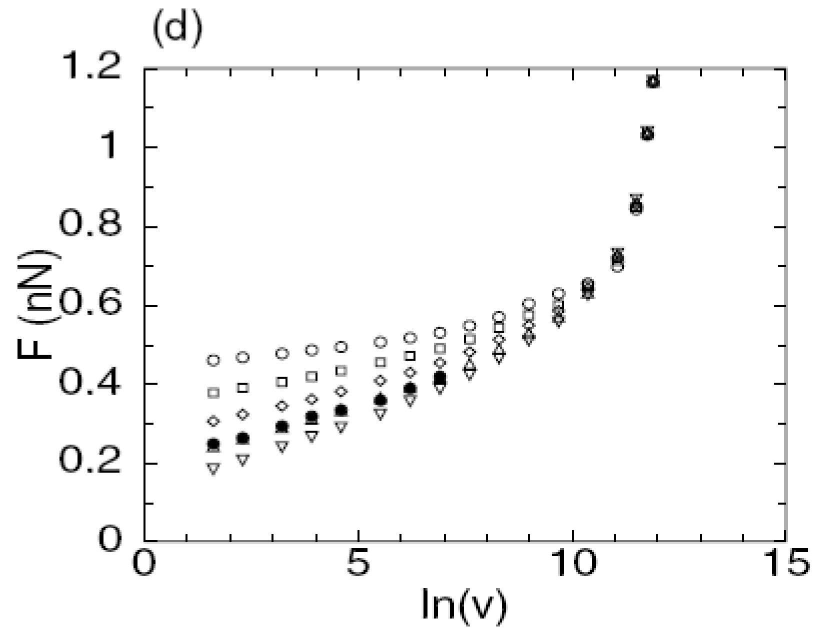
Grant et al, Phys.Rev. Lett. 87, 174301 (2001)

$$E(R,x) = \frac{k}{2}\left(R(t) - x\right)^2 - U\cos(2\pi x / a)$$

$$M\frac{d^2 x}{dt^2} + M\gamma\frac{dx}{dt} + \frac{\partial E(R,x)}{\partial x} = \xi(t)$$





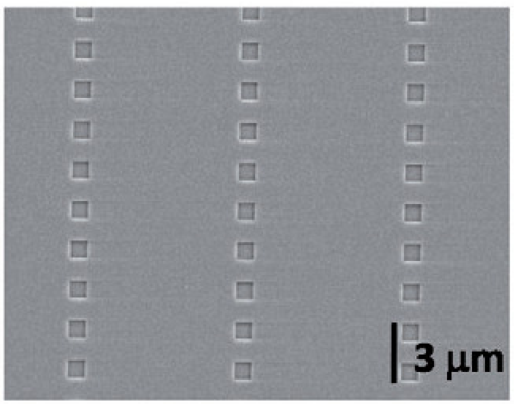


$$< F >= F_c - \Delta F \left| \ln \frac{v}{v_0} \right|^{2/3}$$

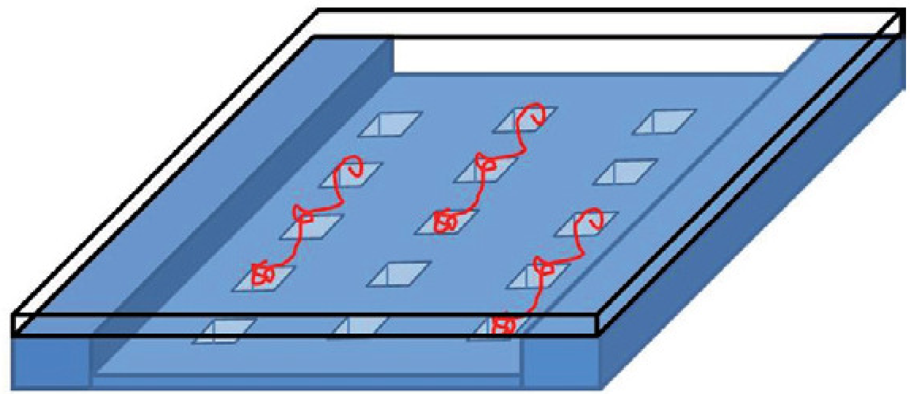
Free-Energy Landscaping:

Tailoring DNA Transport Across a Fluidic Nanotopography

(a)



(b)



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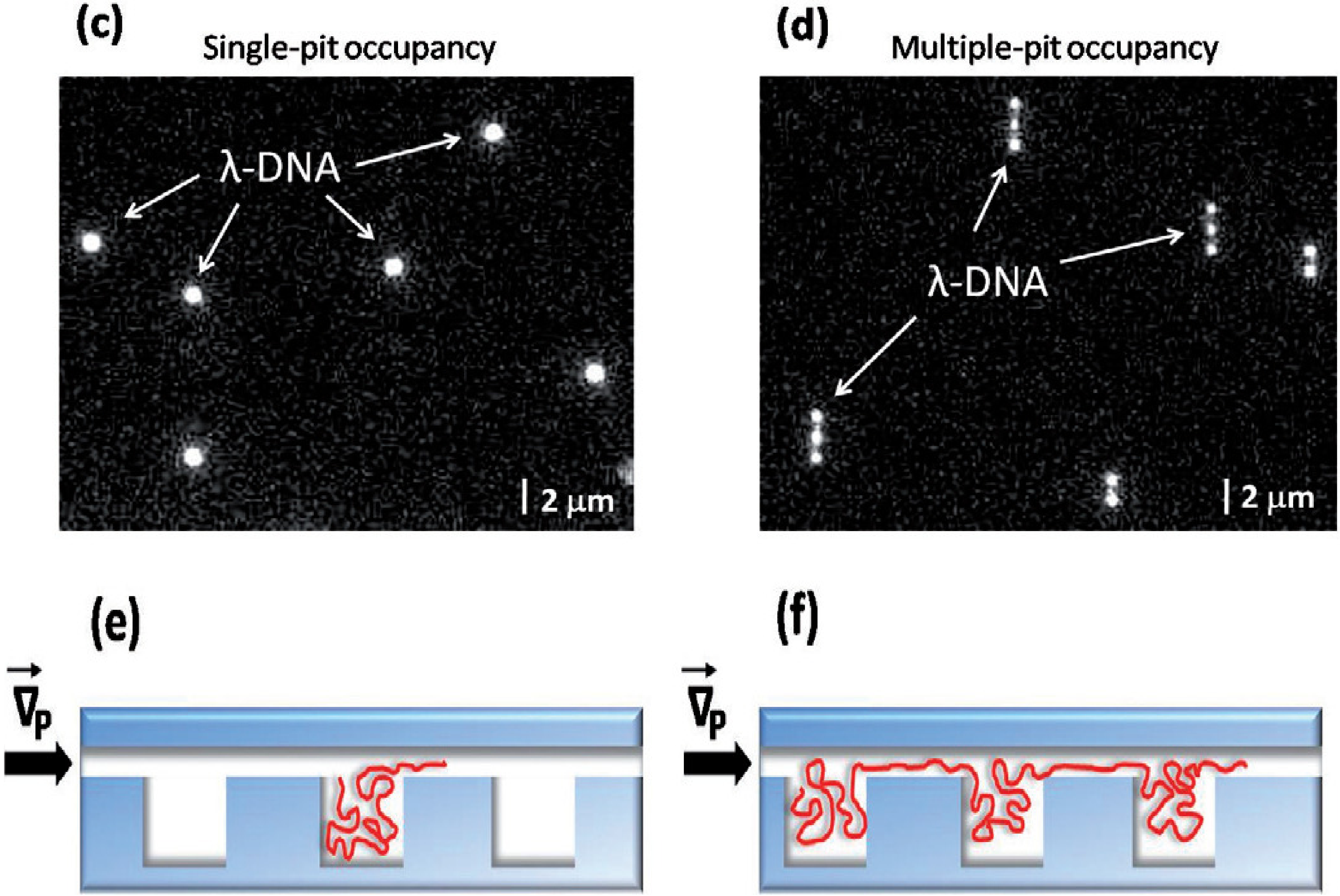
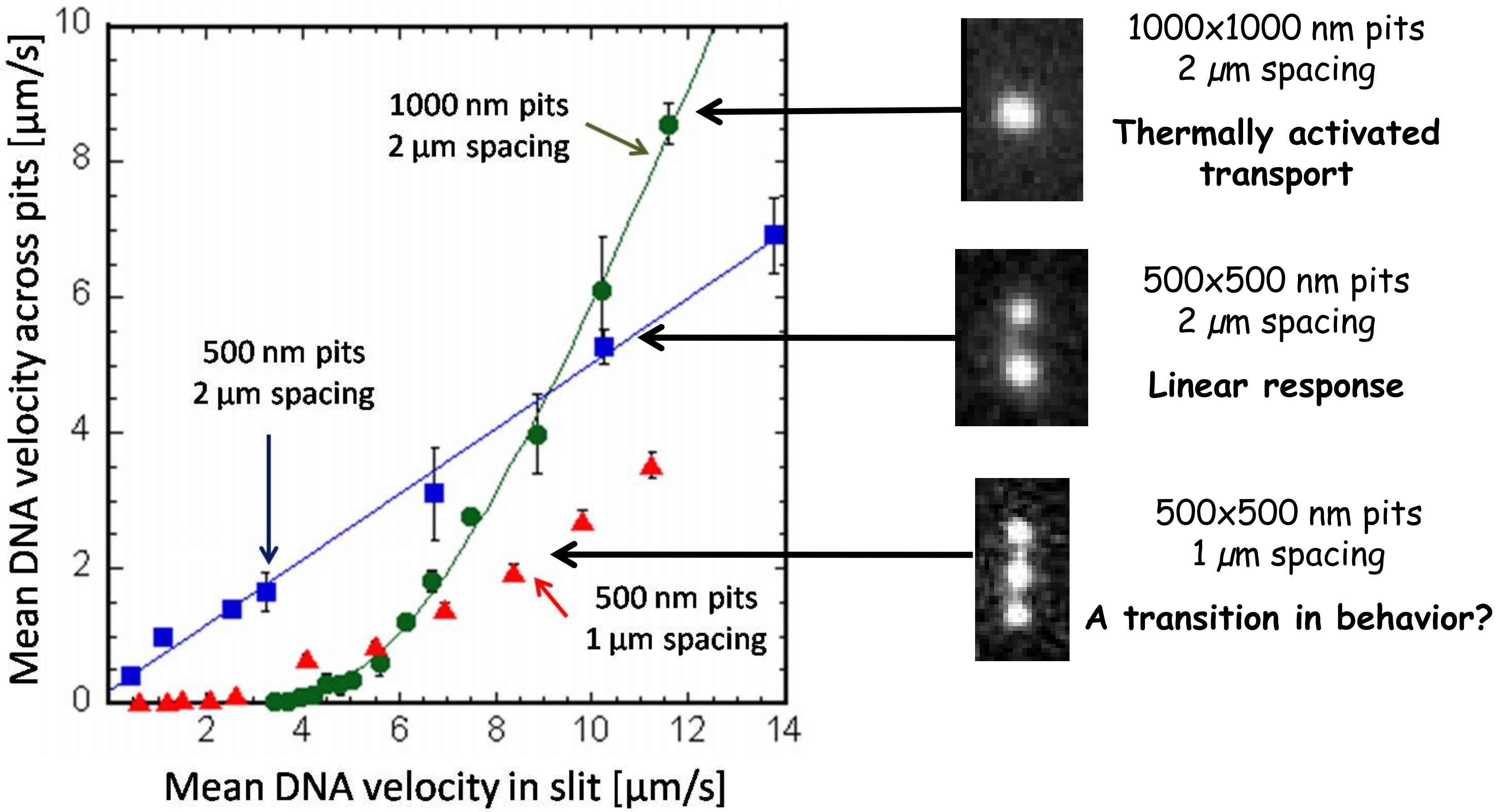
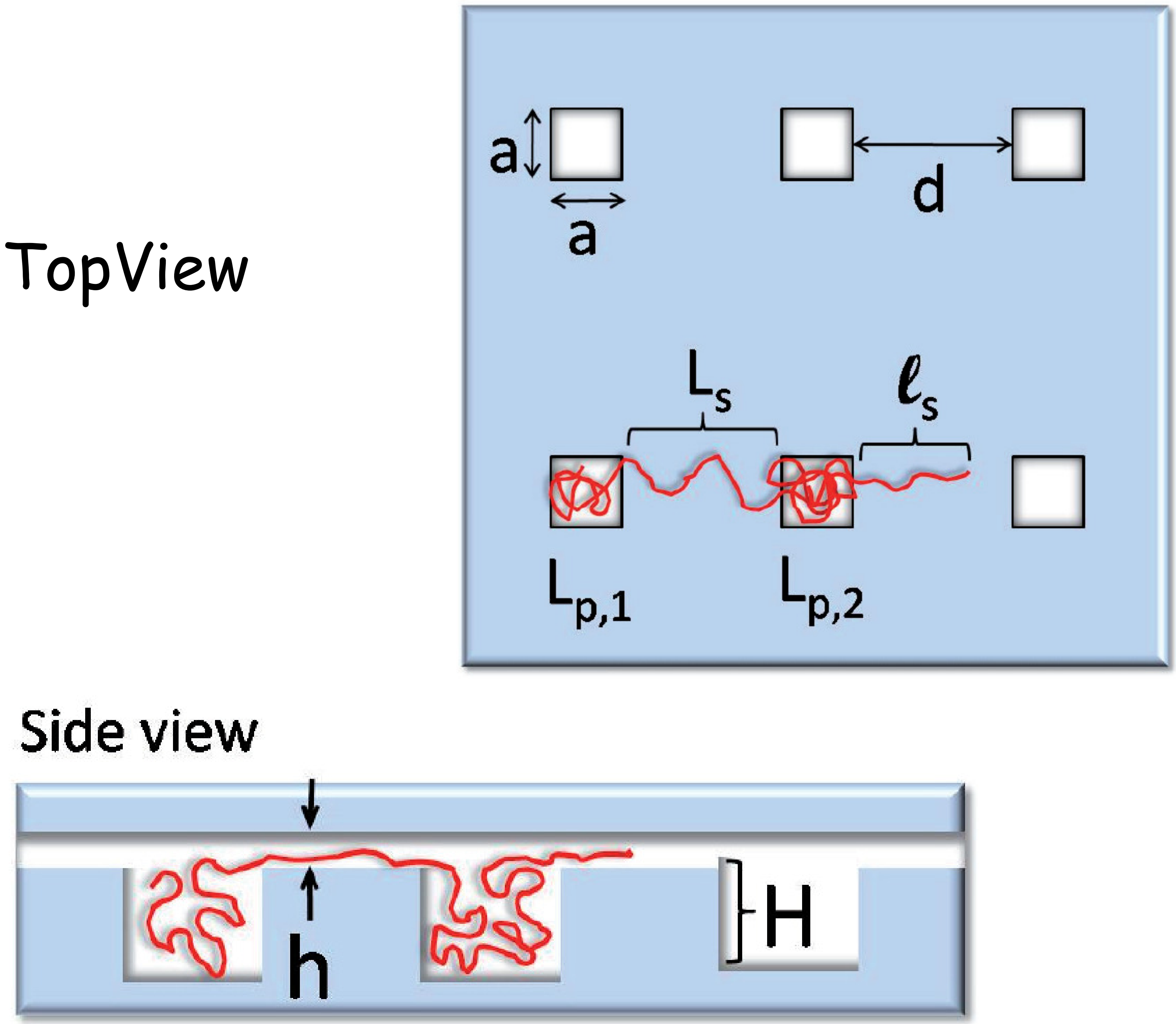
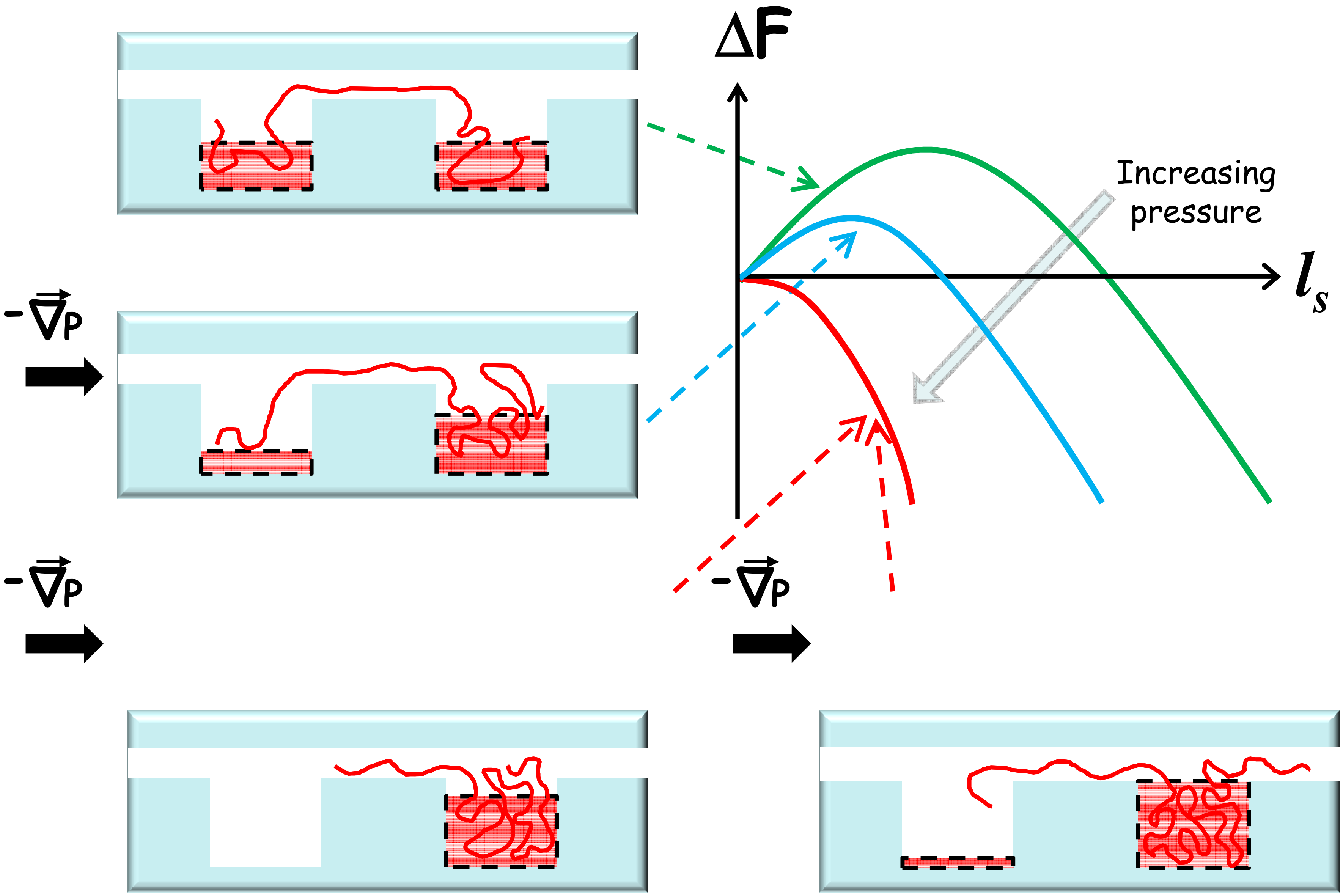

(c)
Single-pit occupancy
λ-DNA
2 μm
(d)
Multiple-pit occupancy
λ-DNA
2 μm
(e)
∇p
(f)
∇p

DNA mobility across nanotopographies




TopView
a
a
d
L_s
ℓ_s
$L_{p,1}$
$L_{p,2}$
Side view
h
H

DNA transport: double-pit occupancy



Summary

- Introduction and overview
- Coarse Grained Model and scaling arguments for Translocation through nanopore
- Effect of attractive pore interaction
- Breaking of base pairs in Hairpin Transport
- Equlibrium and Dynamics in Nanochannels with periodic array of Nanopits