Electrophoresis of DNA on a disordered two-dimensional substrate

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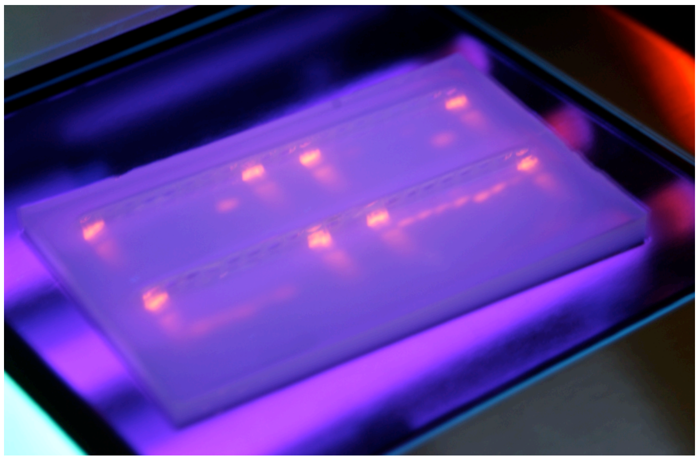
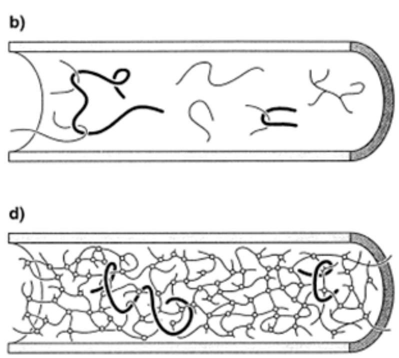
Outline

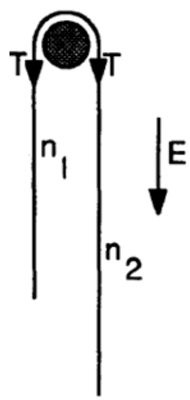
- Introduction: Electrophoretic separation techniques involving surfaces
- Micron-scale Brownian dynamics model for long polymers on a rough 2D surface
- Sorting polymers by length: short polymers move more slowly than long polymers
- Summary

Sorting polymers by length



LANL





(a)

G.W. Slater et al, Electroph. 21, 3873 (2000)

Charge-based sorting is not possible.

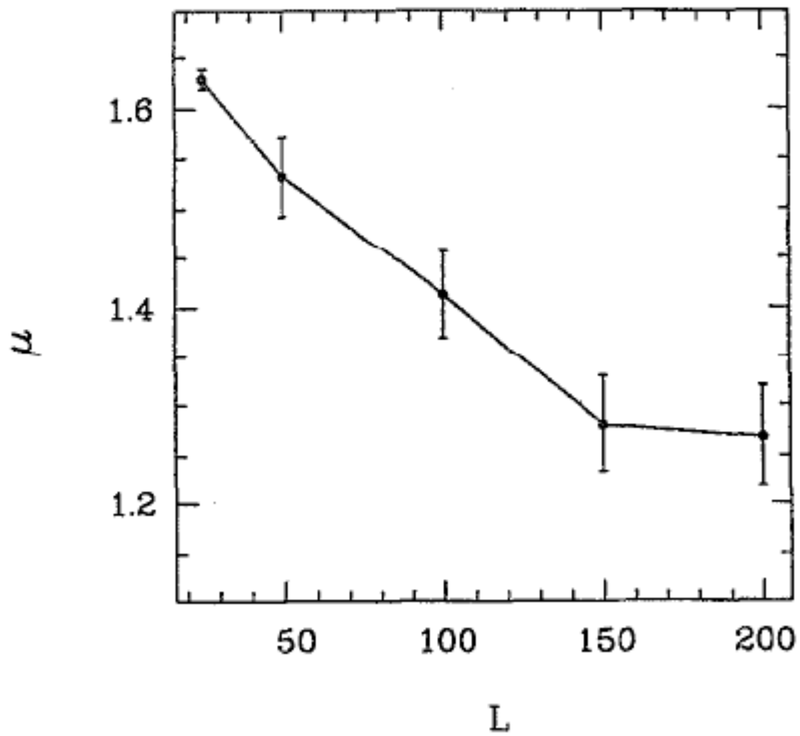
Polymers such as DNA are sorted by means of obstacles.

Gel electrophoresis: cross-links

Longer molecules move more slowly

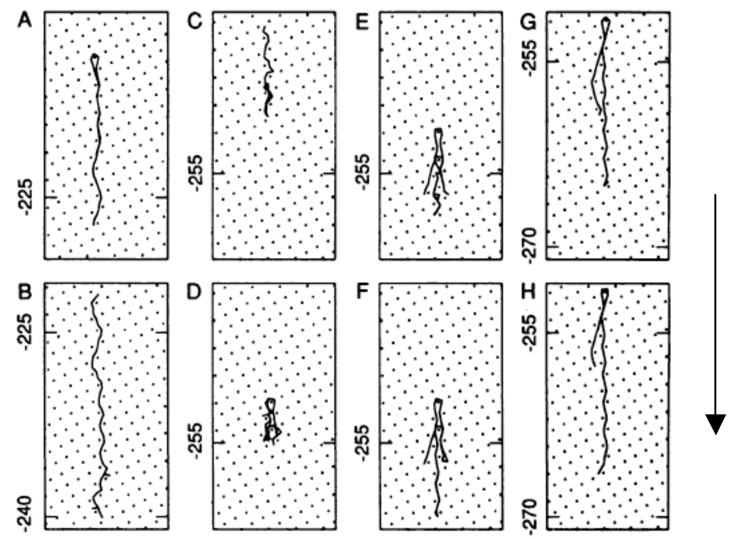
Very long molecules (such as DNA over 4 x 10^4 base pairs in length) cannot pass through the gel at all.

Simulation of gel electrophoresis



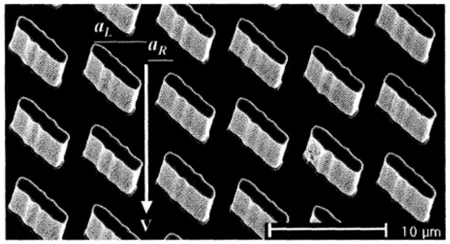
T.L. Madden, J.M. Deutsch, JCP 94, 1584 (1991)

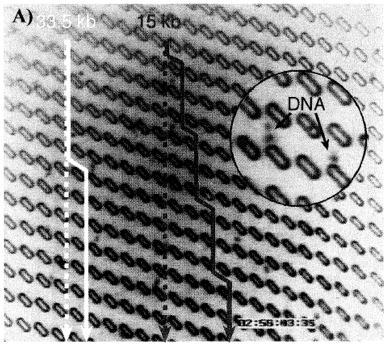
Hairpin formation

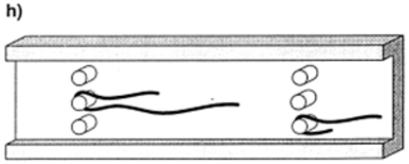


J.M. Deutsch, Science 240, 922 (1988)

Electrophoresis with artificial nanostructures

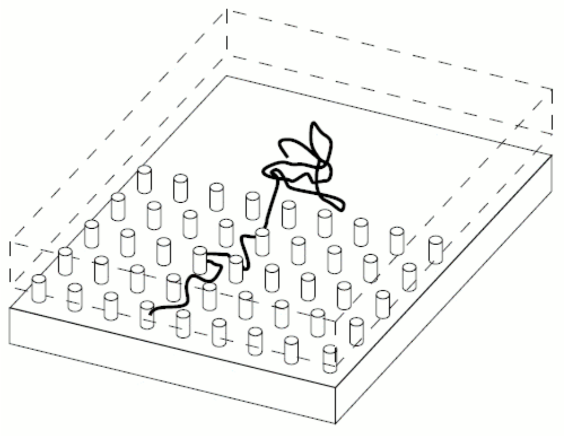






C.F. Chou et al
PNAS 96, 13762 (1999)

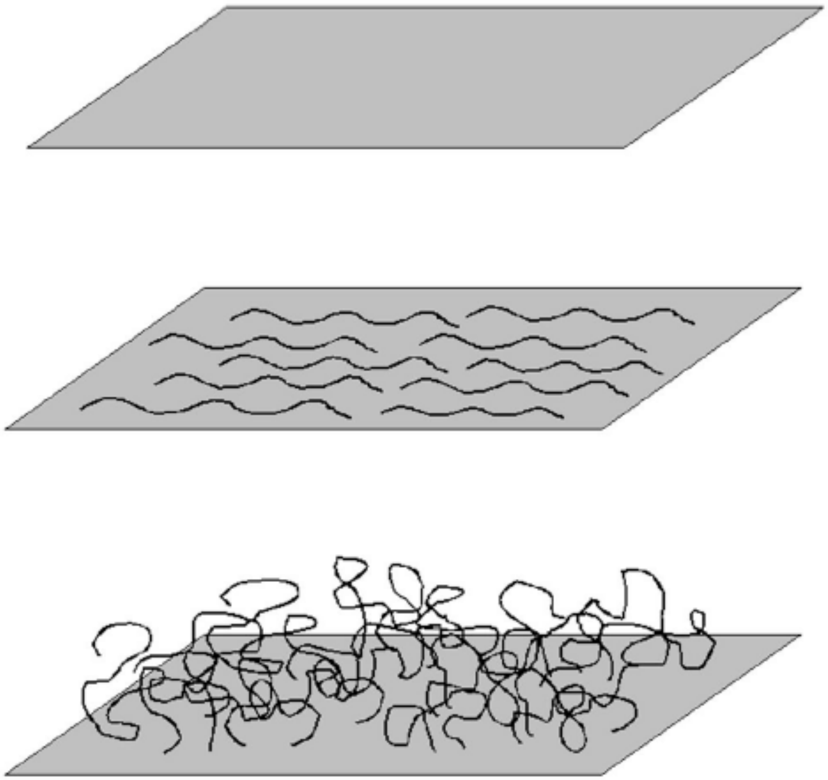
Structures must be tailored to size range of interest



S.W.P. Turner et al, PRL 88, 128103 (2002)

- W. Volkmuth, R.H. Austin, Nature 358, 600 (1992)
- T.A.J. Duke, R.H. Austin, PRL 80, 1552 (1998)
- J. Han, H.G. Craighead, Science 288, 1026 (2000)

DNA at a surface



S.C. Bae, F. Xie, S. Jeon, S. Granick, Curr Opin Solid State Mater Sci 5, 327 (2001)

Adsorption-based sorting

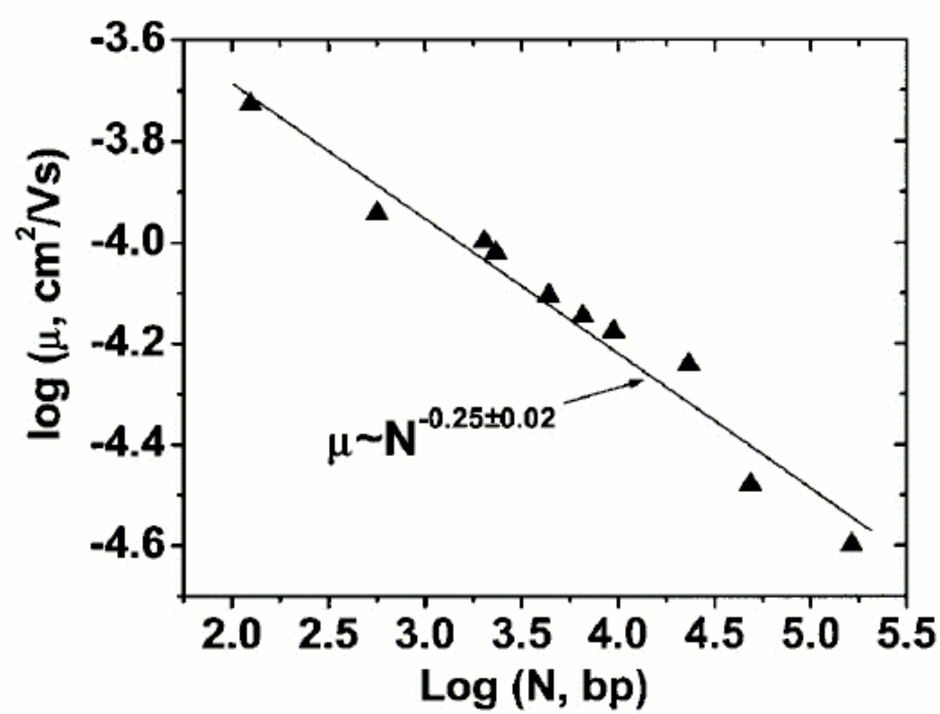
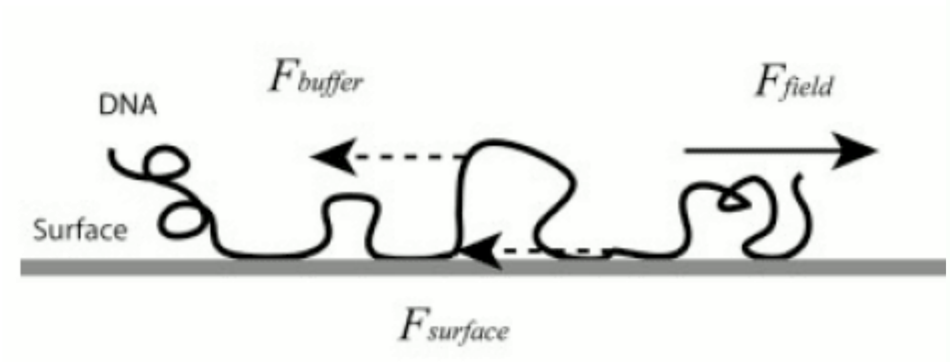


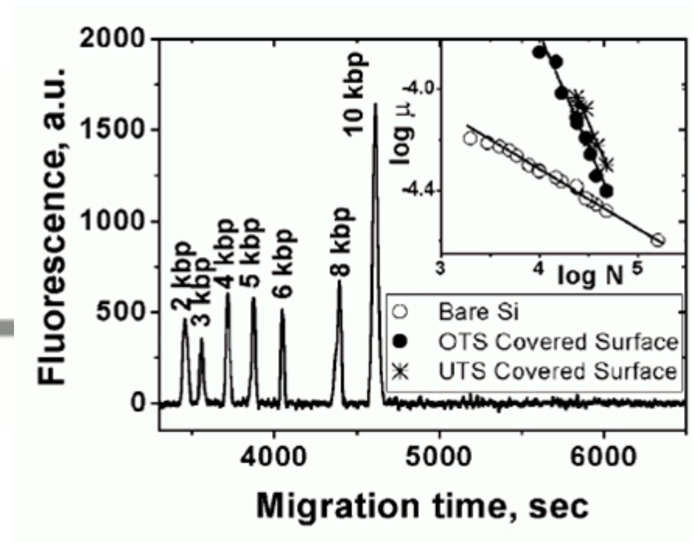
Figure 4. Log-log plot of mobility *versus* the number of dsDNA base pairs on flat native oxide covered Si wafer using λ-*Hind*III digest (Fig. 3), λ- and T2 DNA. The electrophoresis was done in 0.1 M TBE.

Y.-S. Seo, V.A. Samuilov, J. Sokolov, M. Rafailovich, B. Tinland, J. Kim, and B. Chu, Electrophoresis 23, 2618 (2002)

Electrophoresis at a surface



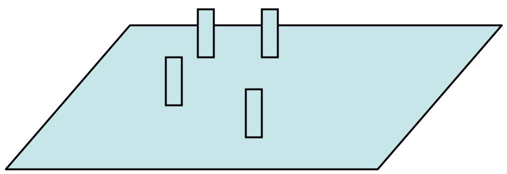
B. Li et al, Electrophoresis 27, 1312 (2006).



N. Pernodet et al, PRL 85, 5651 (2000)

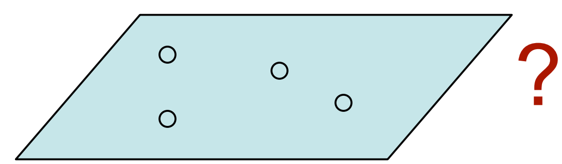
Claim: Separation is achieved due to loop-and-train configuration of DNA.
Advantage over posts: Lack of intrinsic length scale.
Separation is lost if polymer completely adsorbs or desorbs.

Alternative sorting geometries



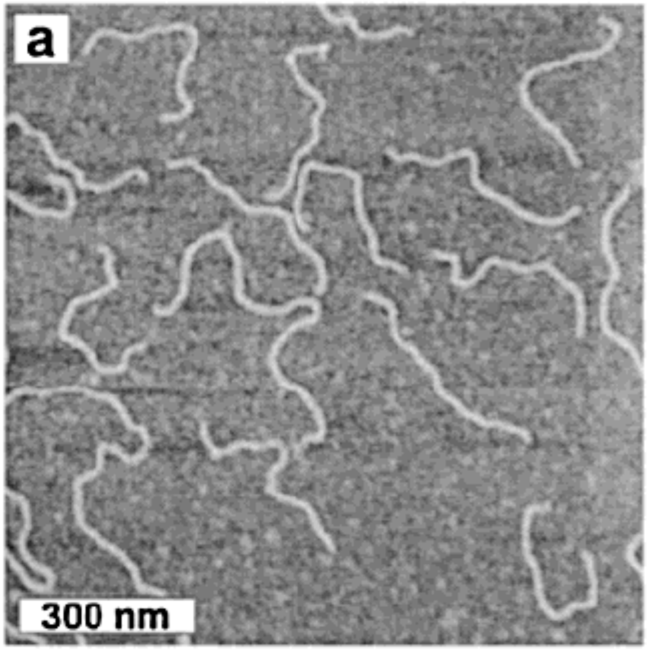
Posts
(Impenetrable obstacles)

Plain surface
(Partial adsorption sorting)



Sticky spots
(Penetrable obstacles)

Fully adsorbed DNA



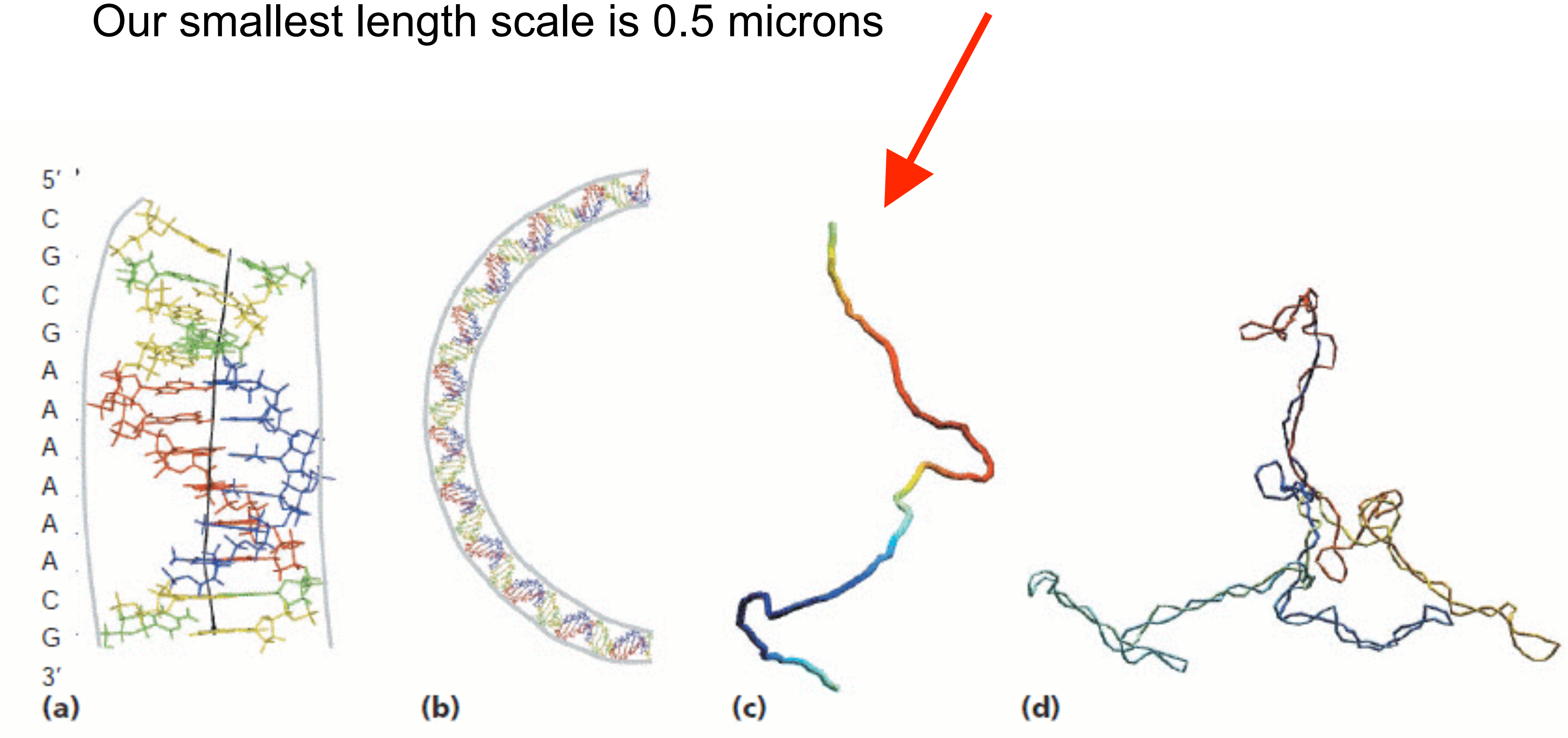
- Mica is negatively charged in water; repels DNA
- Surface charge is inverted in the presence of divalent cations such as Mn^{2+}, Mg^{2+}, Co^{2+}, Ca^{2+}
- DNA adhesion is promoted

DNA adsorbed on mica under physiological conditions

S.S. Sheiko, M. Moller, Chem. Rev. 101, 4099 (2001)

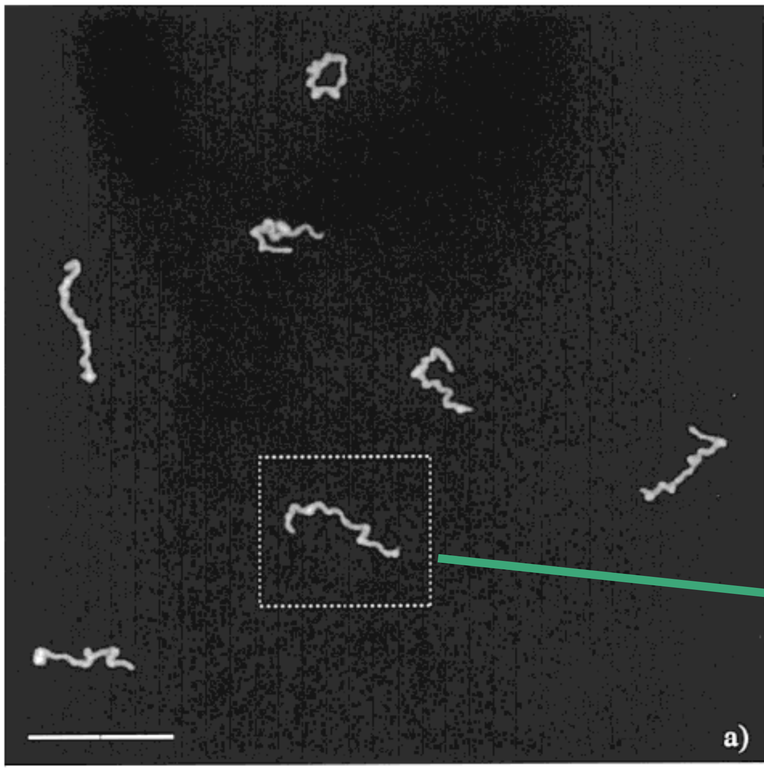
Length scale for DNA modeling

Consider long polymers up to 300 microns in length
Our smallest length scale is 0.5 microns



T. Schlick et al., Comput. Sci. Eng. 2, 38 (2000)

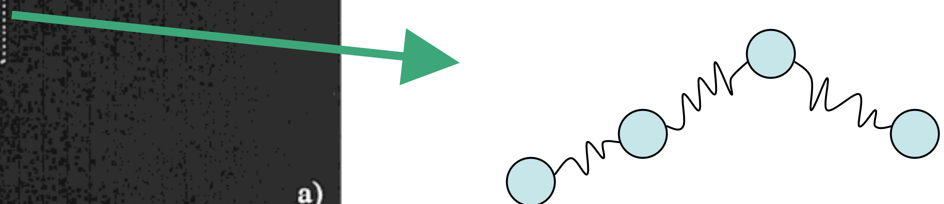
Model for DNA adsorbed to surface



10 microns

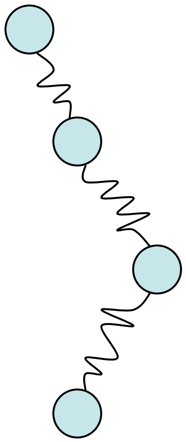
λ-DNA bound to a fluid glass-supported lipid membrane

Represent polymers by bead-spring model: beads are spaced many persistence lengths apart



B. Maier, J.O. Radler, Macromolecules 34, 5723 (2001)

Simulation model



Brownian dynamics – time steps of 0.1 ns

$$\mathbf{F}_i = \sum_{NN} \mathbf{F}_i^{FENE} + \sum_{j=1}^{N} \mathbf{F}_{ij}^{EV} + \sum_{k=i}^{N_p} \mathbf{F}_{ik}^{S} + \mathbf{F}^{E} + \mathbf{F}^{T},$$

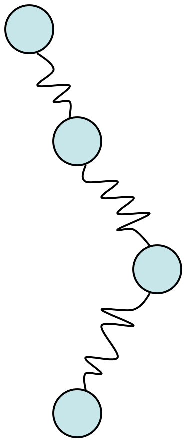
Finitely extensible spring between beads

$$F_i^{FENE} = \frac{-HQ}{1-(Q/Q_0)^2}\hat{\mathbf{Q}} \qquad H = 3/\sigma_s^3$$

$$\text{Kuhn length } b_k = 2l_p\text{; persistence length } l_p \approx 50 \text{ nm}$$
$$Q_0 = nb_k = 1.6\mu\text{m}; \; n = 16$$
$$\sigma_s = \sqrt{n}b_k = 0.4\mu\text{m}$$

Ionic strength of solution assumed strong enough to screen electrostatic interactions between chain elements

Simulation model (cont.)



$$\mathbf{F}_i = \sum_{\mathrm{NN}} \mathbf{F}_i^{FENE} + \sum_{j=1}^{N} \mathbf{F}_{ij}^{EV} + \sum_{k=i}^{N_p} \mathbf{F}_{ik}^{S} + \mathbf{F}^{E} + \mathbf{F}^{T},$$

Excluded volume between segments

$$\mathbf{F}_{ij}^{EV} = -A r_{bb} e^{-B r_{bb}^2} \hat{\mathbf{r}}_{bb}$$

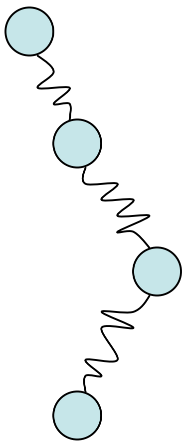
Overlap of two Gaussian coils

$$A = \left(\frac{3}{4S_s^2}\right)^{5/2} \sigma_s v n^2 \pi^{-3/2}, \quad B = \frac{3\sigma_s^2}{4S_s^2}.$$

$$S_s^2 = n b_k^2/6; \; v = b_k^3$$

$$A = \frac{243\sqrt{2n}}{4\pi^{3/2}}, \quad B = \frac{9}{2}.$$

Simulation model (concl.)



$$\mathbf{F}_i = \sum_{NN} \mathbf{F}_i^{FENE} + \sum_{j=1}^{N} \mathbf{F}_{ij}^{EV} + \sum_{k=i}^{N_p} \mathbf{F}_{ik}^{S} + \mathbf{F}^{E} + \mathbf{F}^{T},$$

Substrate: Randomly placed parabolic traps

$$\mathbf{F}_{ik}^{S} = f_p \frac{r_{bp}}{\sigma_p} \Theta(\sigma_p - r_{bp}) \hat{\mathbf{r}}_{bp}$$

Electrophoretic force

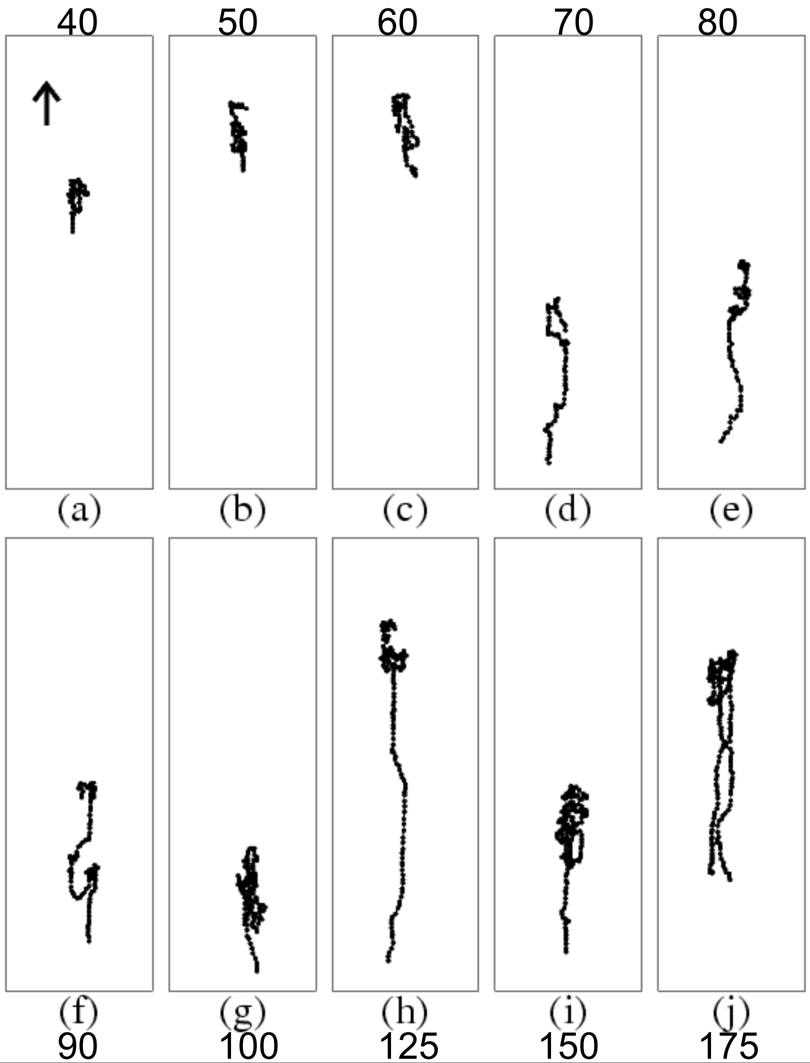
$$\mathbf{F}^{E} = qE\hat{\mathbf{y}}\,.$$

Temperature: Langevin kicks

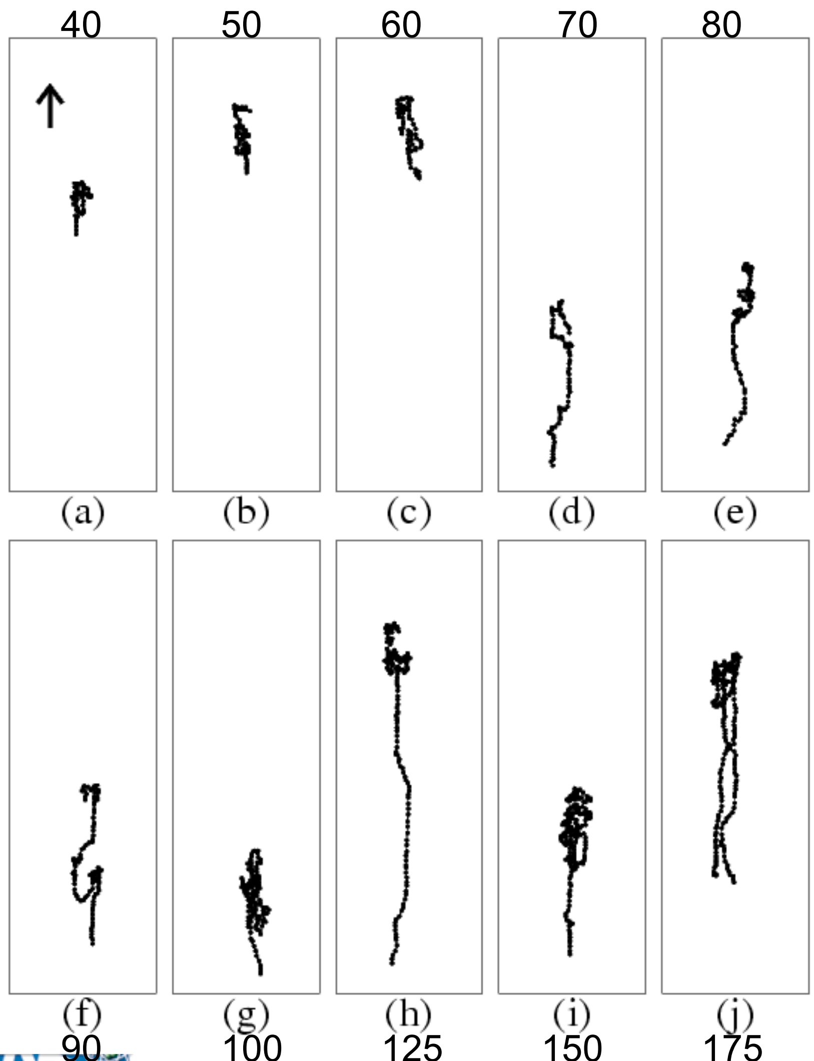
$$\langle F^T \rangle = 0;\ \langle F_i^T(t) F_i^T(t+\delta\tau) \rangle = 2k_B T \zeta^{-1} \delta\tau.$$

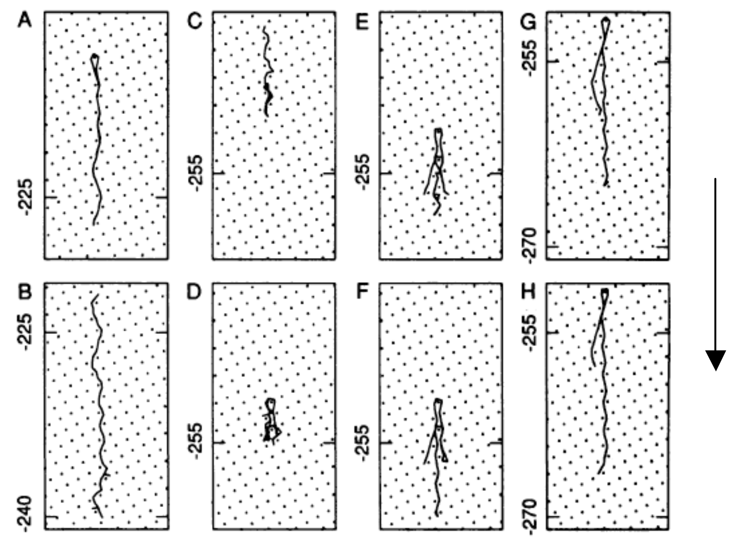
$$q = \lambda n b_k;\ \lambda = 0.3e^- / \text{Å}$$
$$\zeta = 6\pi\eta_s\sigma = 2.97 \times 10^{-7}\ \mathrm{Ns/m}$$

Polymer configurations



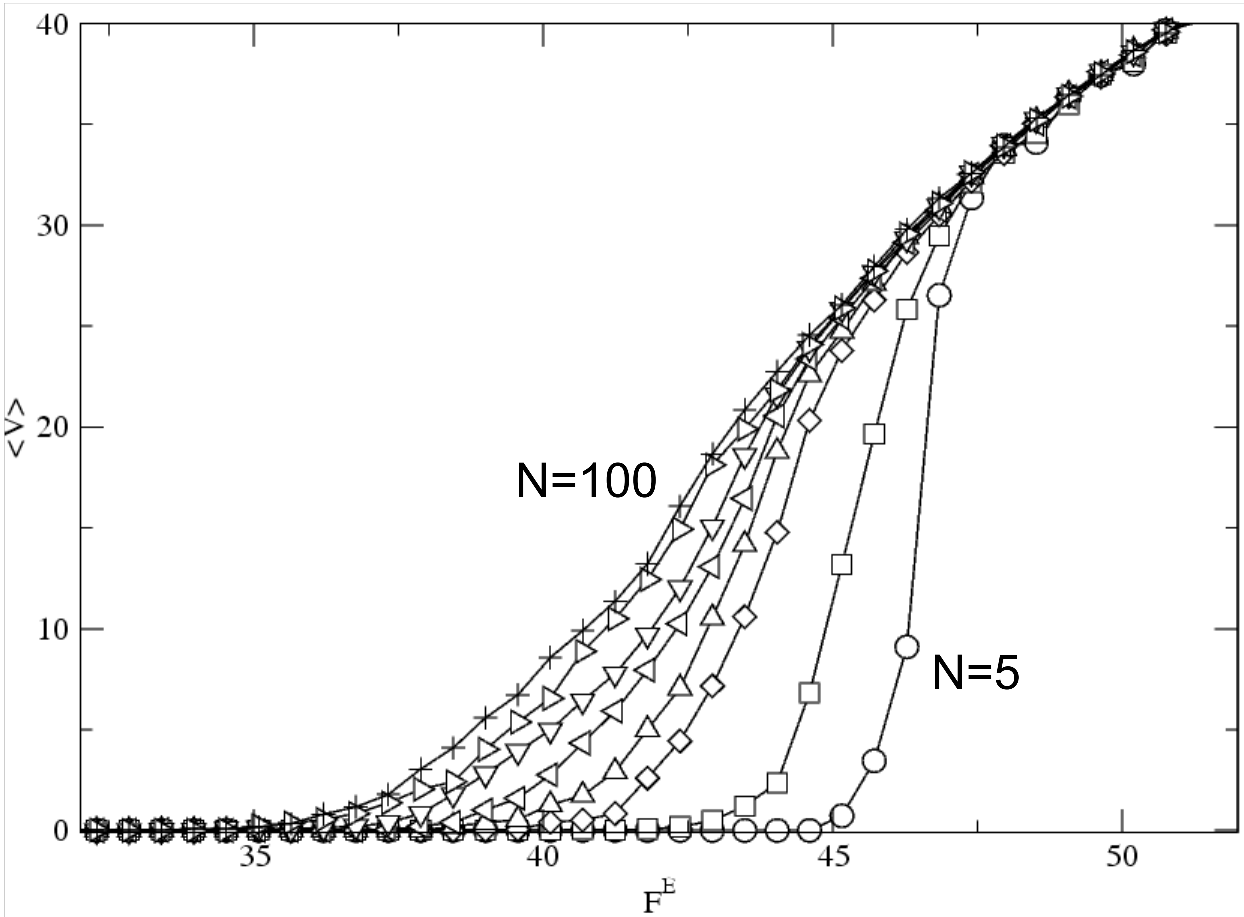
Polymer configurations





J.M. Deutsch, Science 240, 922 (1988)

Velocity-force response



ρ_p=0.8

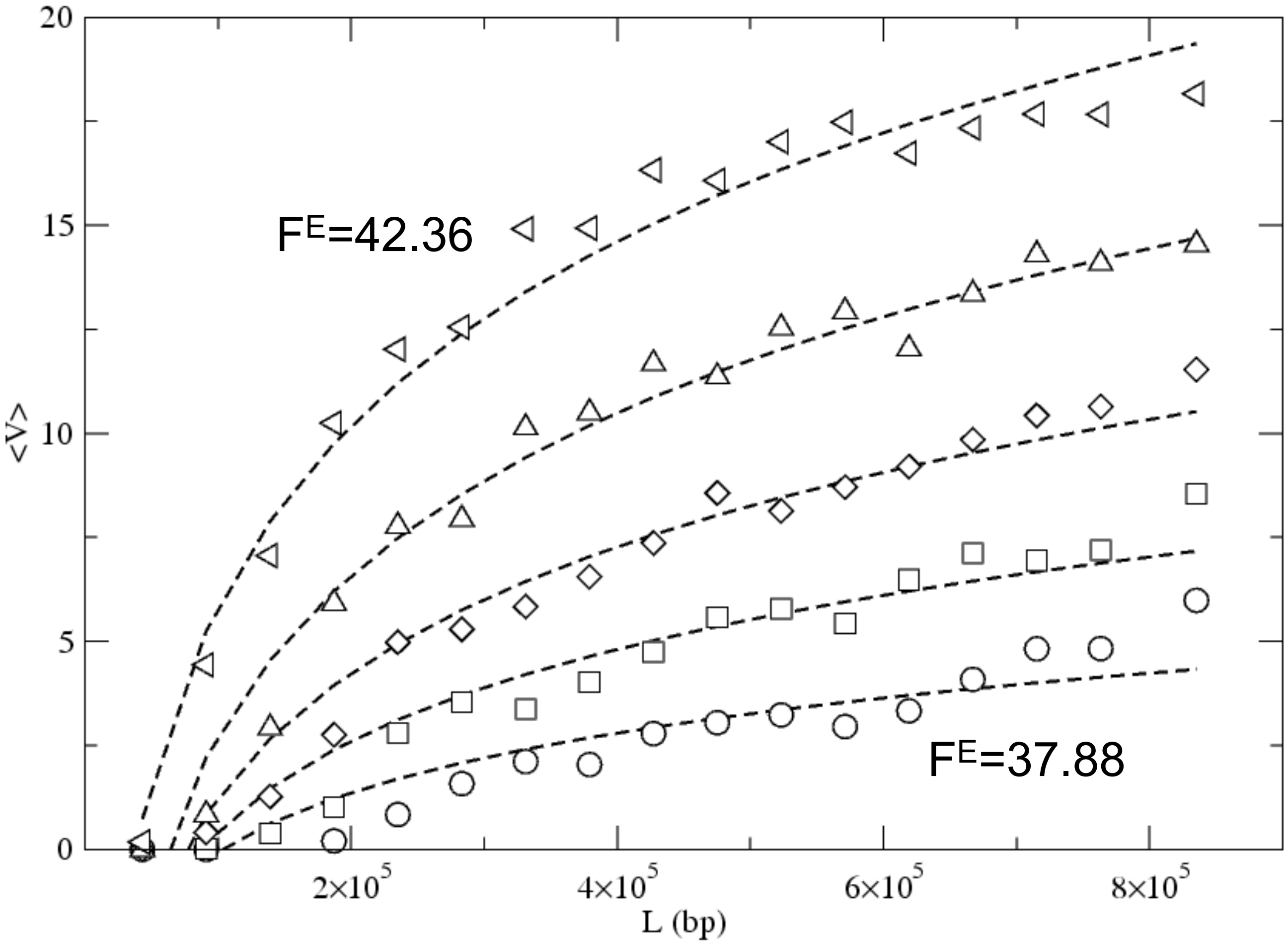
f_p=60

N=5, 10, 20, 30, 40, 50, 80, 100 (8 to 160 microns)

NNSA

Los Alamos

Average velocity vs length

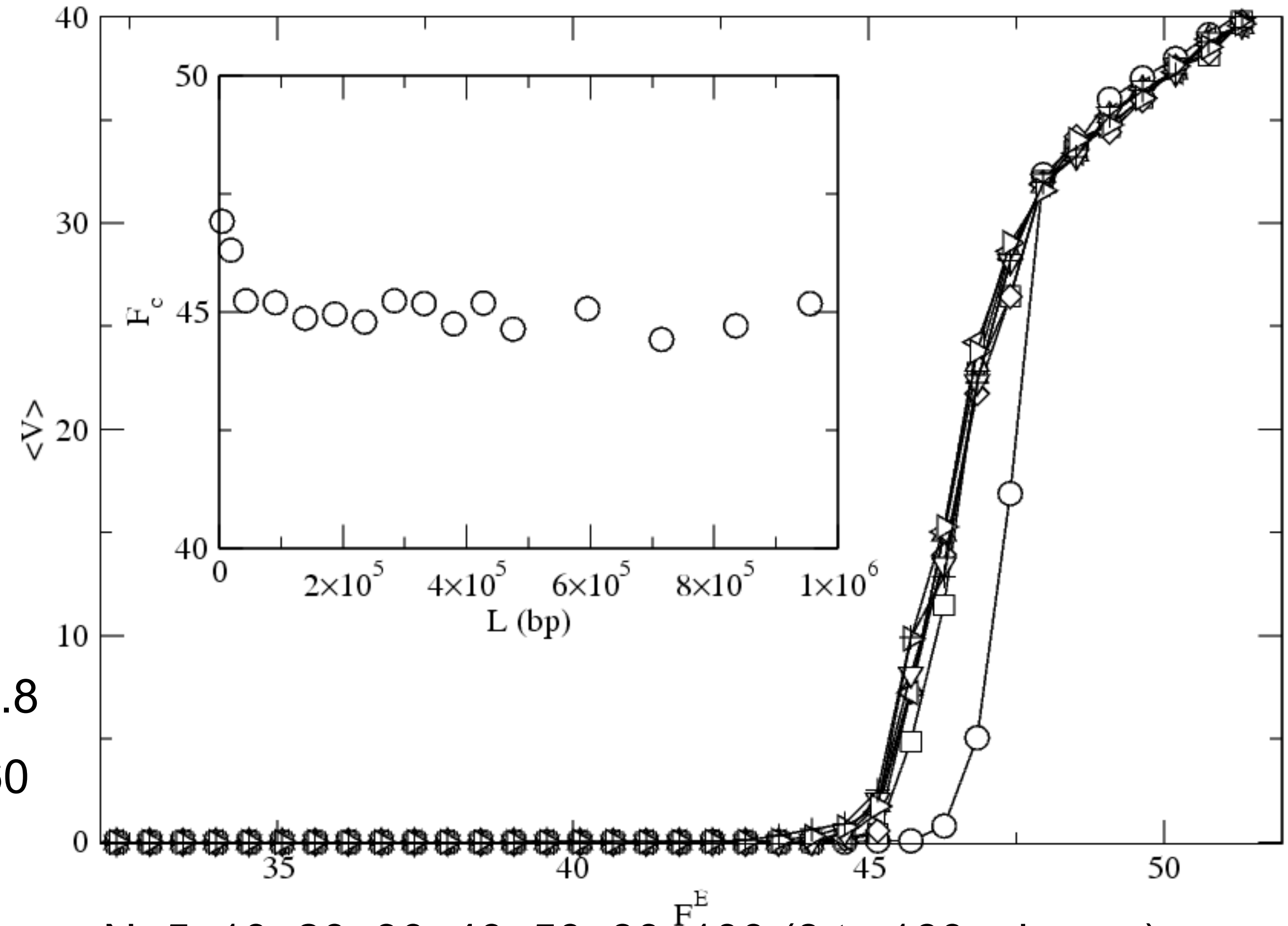


ρ_p=0.8

f_p=60

F^E=37.88, 39.0, 40.12, 41.24, 42.36

Effect of removing excluded volume

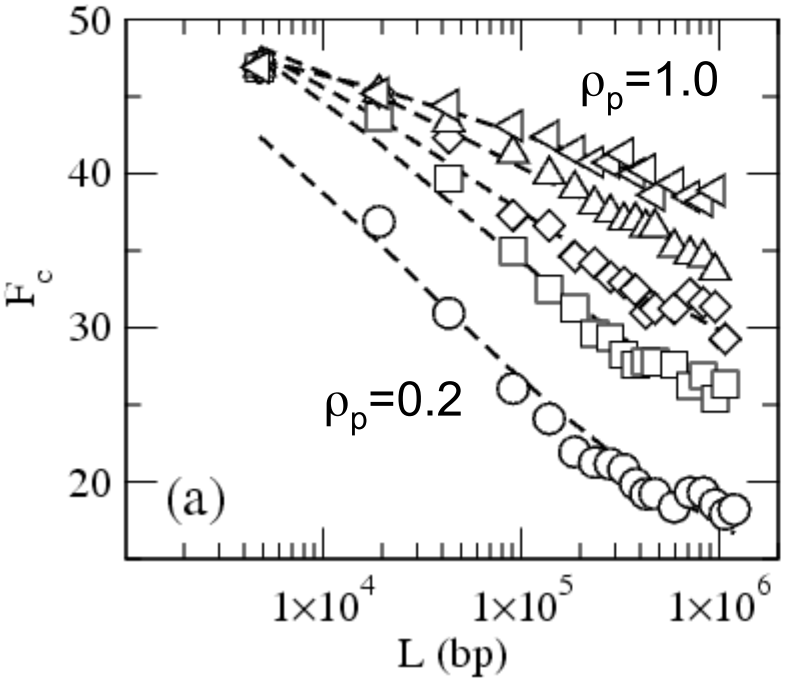


ρ_p=0.8

f_p=60

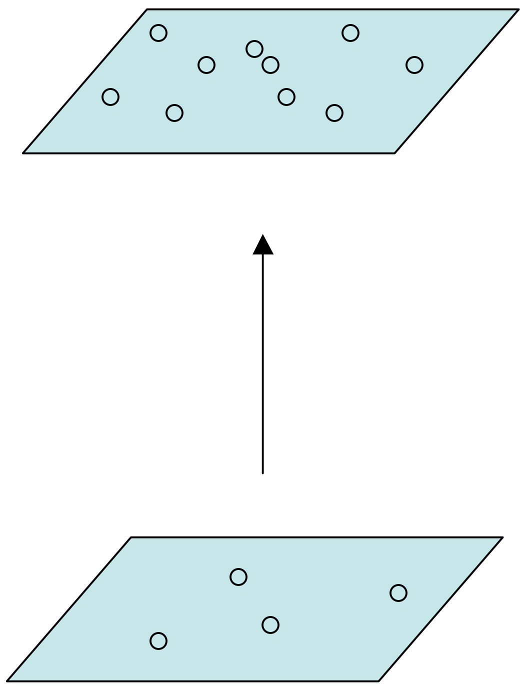
N=5, 10, 20, 30, 40, 50, 80, 100 (8 to 160 microns)

Critical depinning force for different pin densities

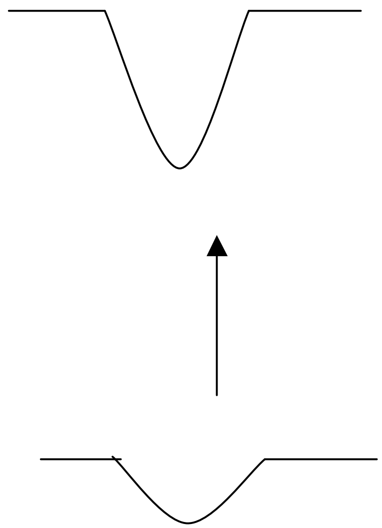


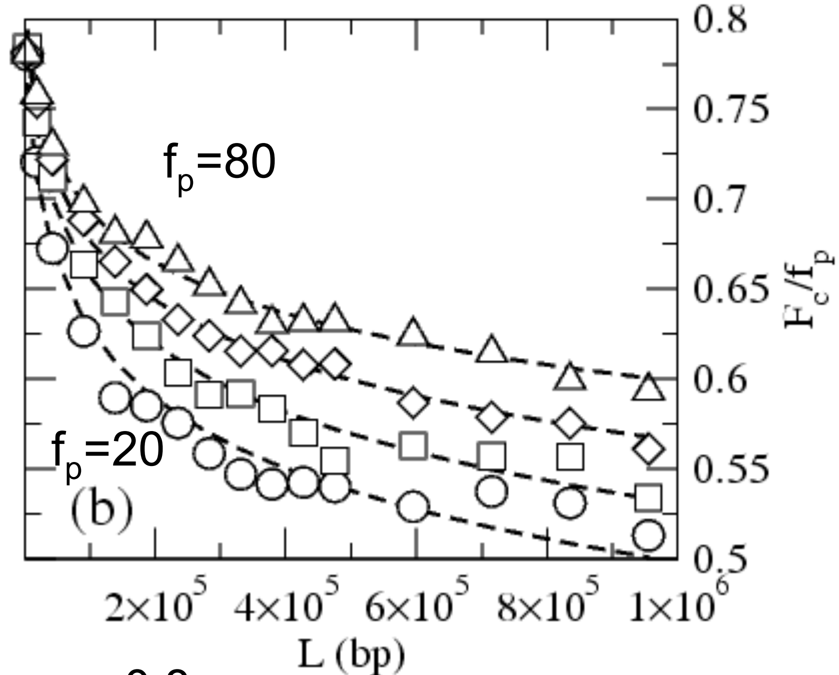
f_p=60

ρ_p=0.2, 0.4, 0.6, 0.8, 1.0



Critical depinning force for different pin strengths





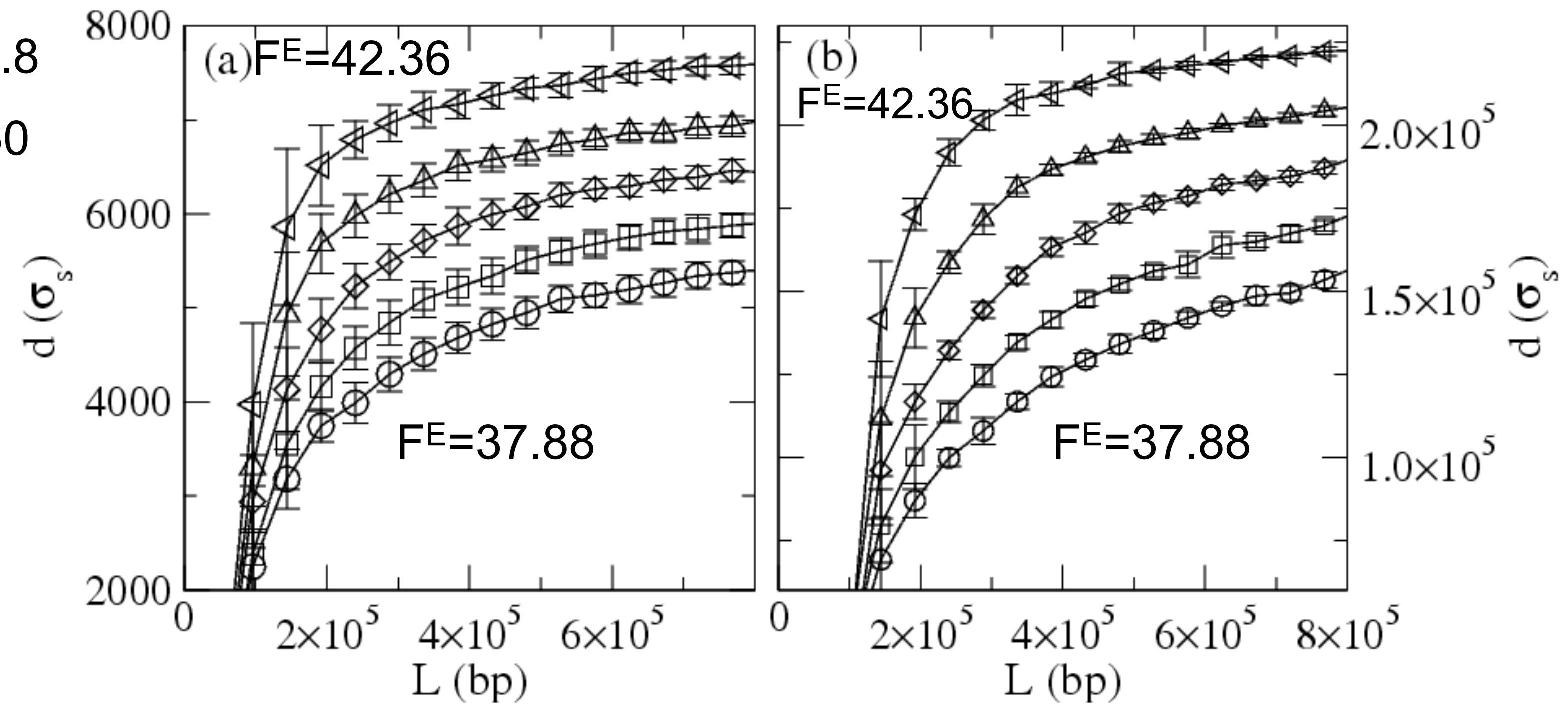
ρ_p=0.8

f_p=20, 40, 60, 80

Distance traveled vs length

ρ_p=0.8

f_p=60



Shorter time
100 realizations

Longer time
20 realizations

F^E=37.88, 39.0, 40.12, 41.24, 42.36

Resolution versus length

Selectivity:

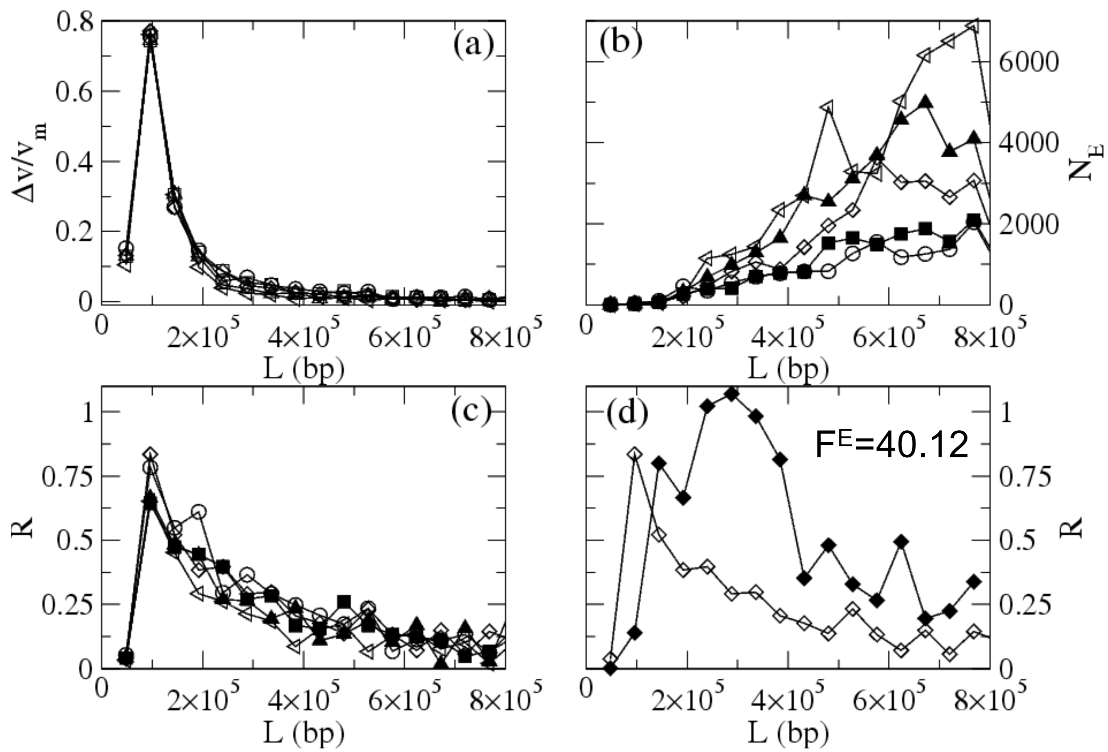
$$\frac{\Delta V_i}{V_m} = \frac{2(\langle V_{i+1}\rangle - \langle V_i\rangle)}{\langle V_{i+1}\rangle + \langle V_i\rangle}$$

Efficiency:

$$N_E = \frac{x^2}{\sigma_x^2}.$$

Resolution:

$$R = \frac{\sqrt{\bar{N}_E}}{4}\frac{\Delta V}{V_m}$$



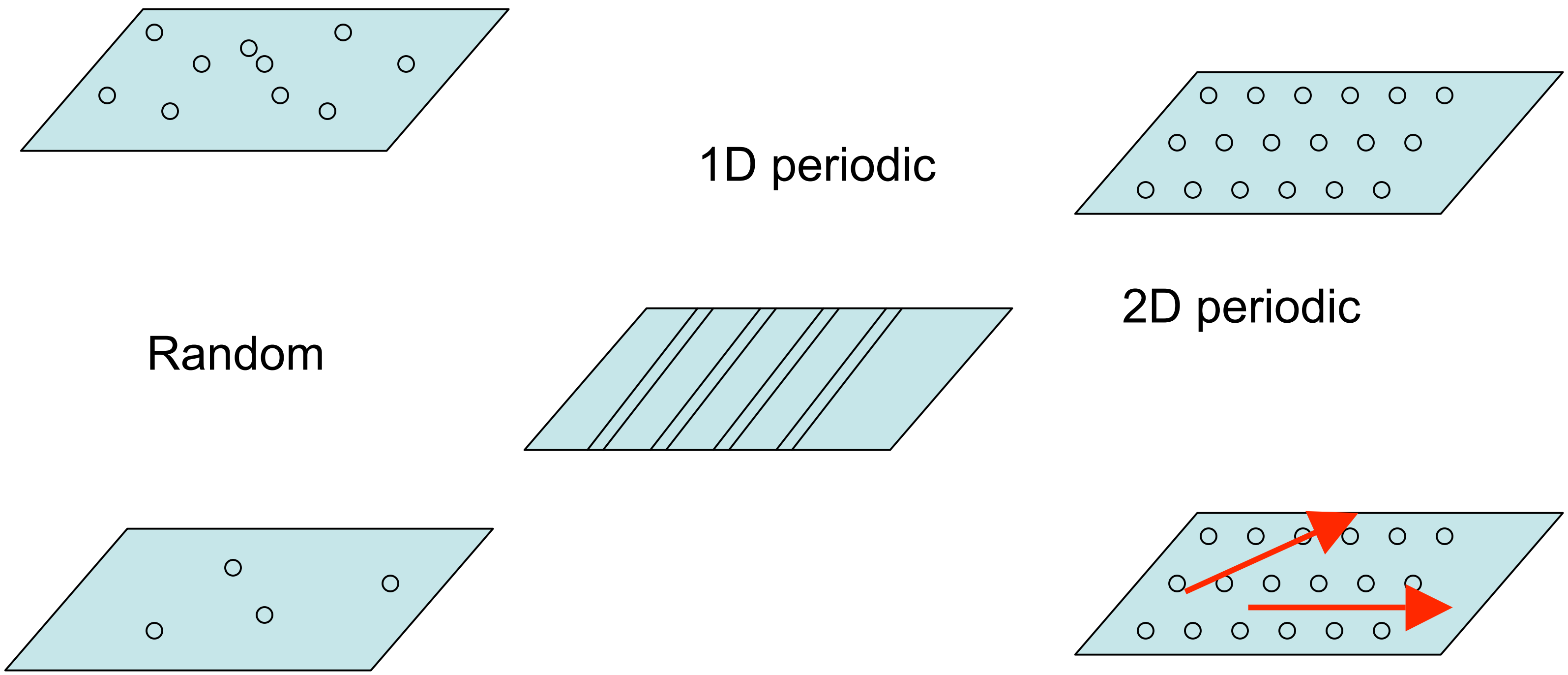
Short time

Short and long time

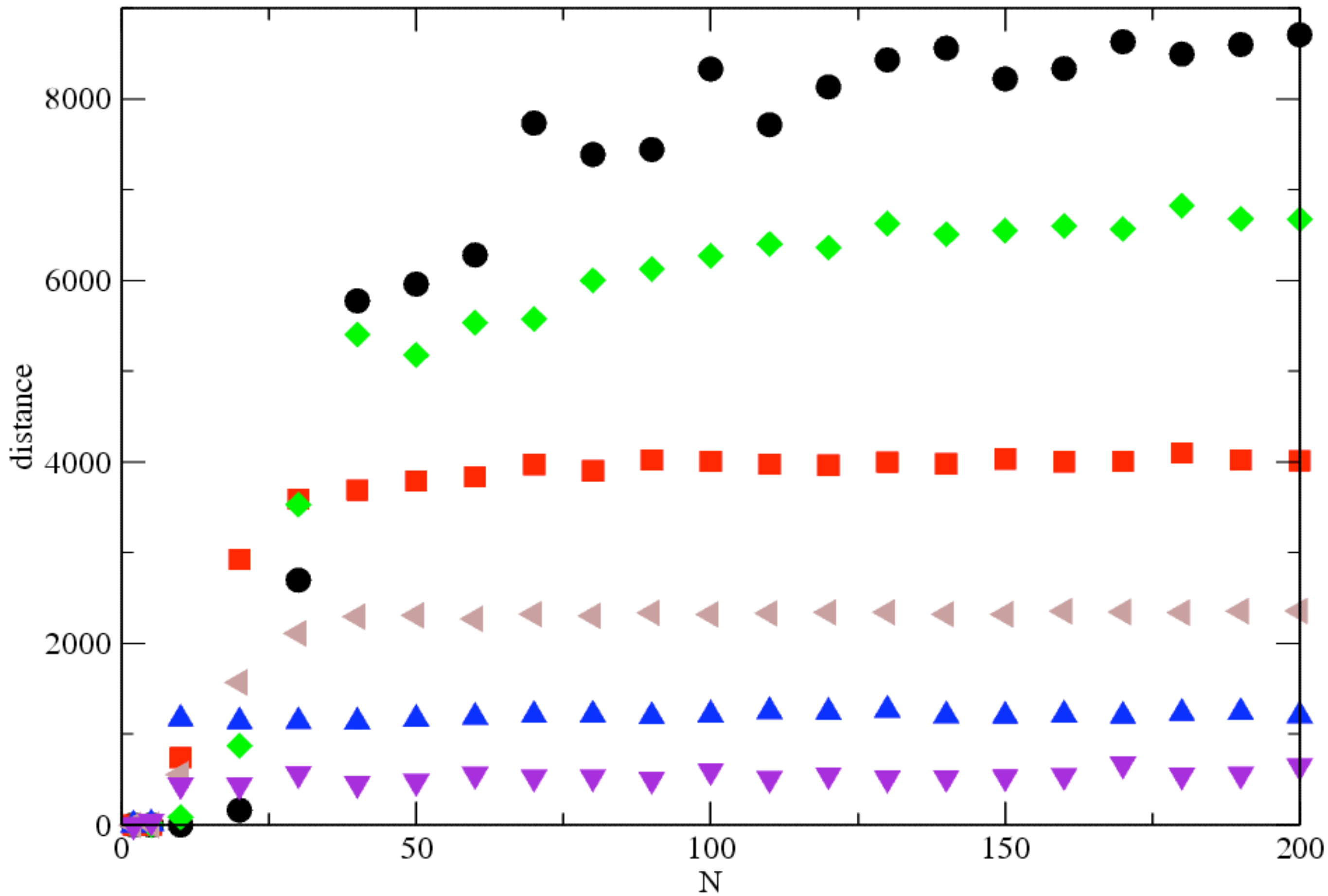
$\rho_p=0.8$ $f_p=60$

$F^E=37.88, 39.0, 40.12, 41.24, 42.36$

Different pinning geometries



One dimensional pinning



Summary

- We use a simulation of long DNA segments to study a new length separation mechanism for polymers adsorbed to a disordered two-dimensional substrate.
- Longer polymers are more mobile than short polymers, and the depinning force decreases logarithmically with polymer length.
- The separation mechanism relies on the excluded volume interaction between chain segments, which reduces the effectiveness of the pinning for longer polymers.
- The technique does not rely on thermal diffusion, so thermal broadening of the bands can be prevented.
- The resolution is highest for shorter polymers. By allowing the polymers to travel a longer distance, resolution is improved and the peak resolution also shifts to longer polymer lengths.

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