Simulation of polymer translocation

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- • Polymer scaling

- • Polymer dynamics

- • Translocation

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Polymer size

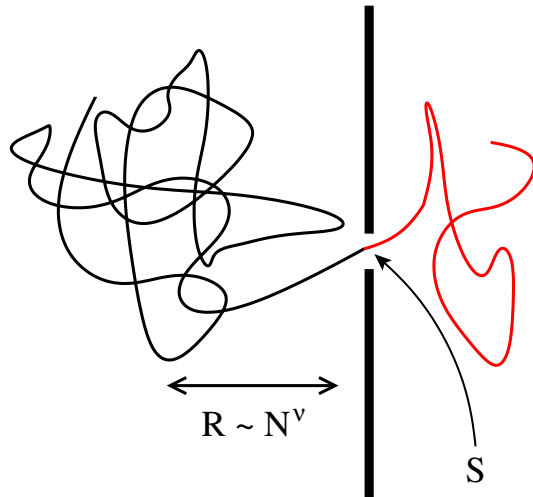Typical size of a single polymer of molecular mass (length) N:

$$R \sim N^{\nu}$$

$\nu = 1$ (one dimension)
$\nu = 3/4$ (two dimensions)
$\nu \approx 0.588$ (three dimensions)
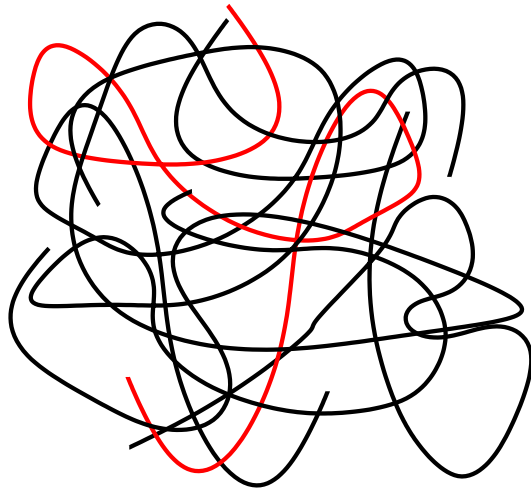$\nu = 1/2$ (four or more dimensions)

Same scaling for a tethered polymer
    (=polymer fixed to a surface)

Polymer in a melt: $\nu = 1/2$

$R \sim N^{\nu}$

S

Polymer dynamics

Melts are highly viscous, entangled systems.

Sideways movement is blocked;
polymer is trapped in a 'tube'-like space

Dominant mechanism for polymer
dynamics is REPTATION:
movement by diffusion
of stored length
Diffusion coefficient scales as $D \sim L^{-2}$
Relaxation time scales as $\tau \sim L^3$

Strong dilution avoids entanglement.
New diffusion mechanism opening up : Rouse dynamics (sideways polymer displacement).
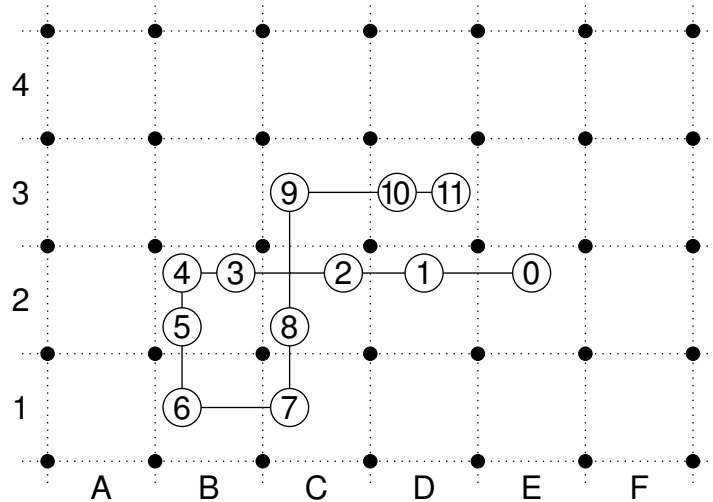Diffusion coefficient scales as $D \sim L^{-1}$
Relaxation time scales as $\tau \sim L^{1+2\nu}$

Modeling reptation: repton model

[M. Rubinstein, PRL 59, 1946 (1987)]

polymer $\leftrightarrow$ chain of monomers (black dots)

gel pores $\leftrightarrow$ faces on square (cubic) lattice

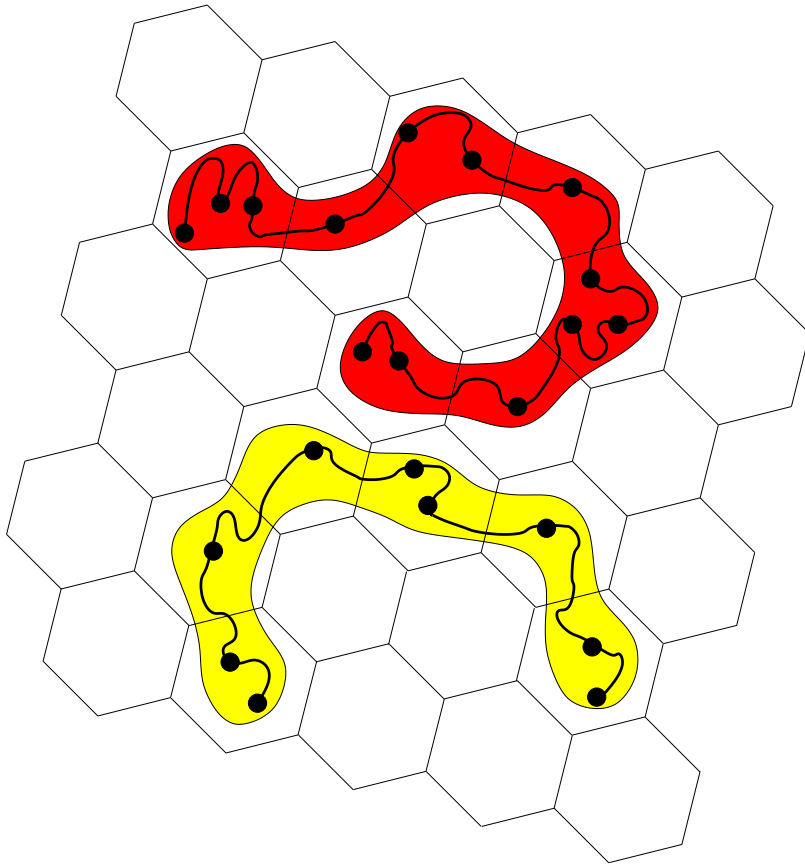<u>Static constraint</u>: neighbors along the chain are in same or neighboring faces

<u>Dynamical rules:</u>

- interior monomers join their neighbors along the chain

- end monomers retract or extrude in a random direction

Our extensions

- static constraints and dynamics as in the repton model

- additional dynamics: sideways single-monomer moves (works best on FCC lattice)

- additional static constraint: hard-core repulsion on same site, except for consecutive monomers

- (energetic) interactions between nearest-neighbour sites can be added

Why this model as a starting point?

Strong points of this model for our purposes:

- Dominant transport mechanism (reptation) occurs naturally and efficient

- no bond crossing

- multiple site occupation lifts ergodicity problems

- Model lends itself for highly efficient computer simulations

Polymer configuration: $\vec{x}_i$ for $i \in [1, .., N]$
Alternatively: $\vec{x}_1$ and $\vec{s}_i \equiv \vec{x}_{i+1} - \vec{x}_i$ for $i \in [1, .., N-1]$
$\vec{s}_i$ takes one of 13 values $\Rightarrow$ can be stored in 4 bits $\{t, u, v, w\}_i$

On 64-bit computers, store 16 polymers in parallel:
bits $k, k+16, k+32$ and $k+48$ of long int S_i describes step s_i of the kth polymer

- saves memory (fewer cache-misses)

- Clever programming allows to make moves in 16 polymers in one go!

- Reptation moves never violate excluded-volume constraints

Comparison to Bond-Fluctuation Model

[E. Reister, M. Müller and K. Binder, Phys. Rev. E 64, 041804 (2001)]
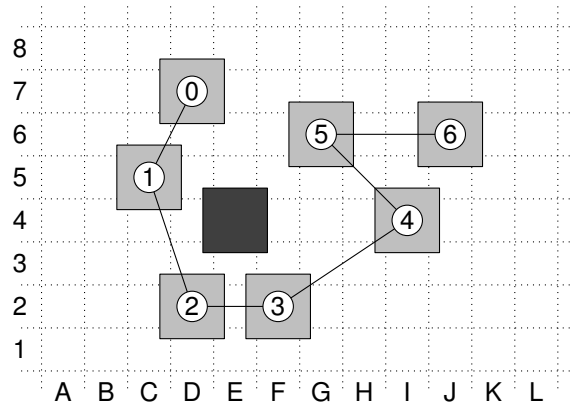
One update in the Bond Fluctuation Model takes $\approx 3\mu$s CPU-time

In our model:

- each reptation move takes **1.25 ns CPU-time**
  (over three orders of magnitude faster)

- sideways moves, end-point moves take **82 ns CPU-time**
  (almost two orders of magnitude faster)
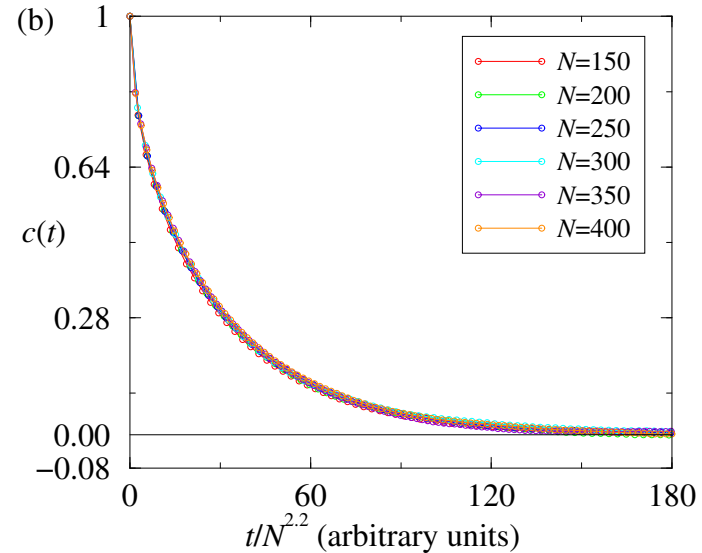
Polymer relaxation

Observable: time autocorrelation of the end-to-end vector:

$$c(t) = (\vec{x}_N(t) - \vec{x}_0(t)) \cdot (\vec{x}_N(0) - \vec{x}_0(0))$$

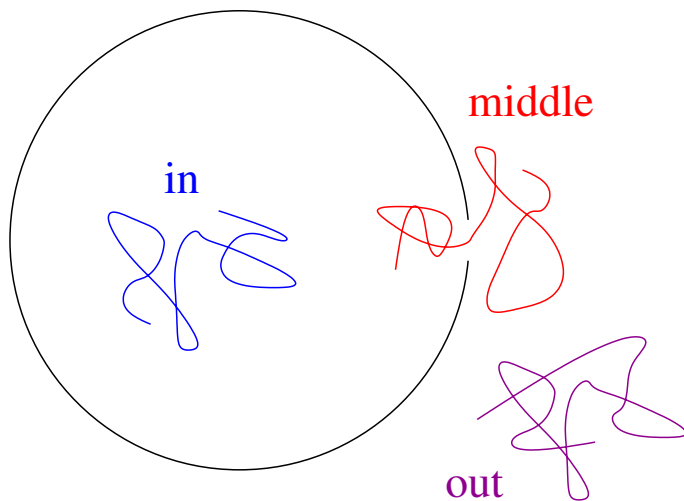**For phantom chains
(random walk statistics):**
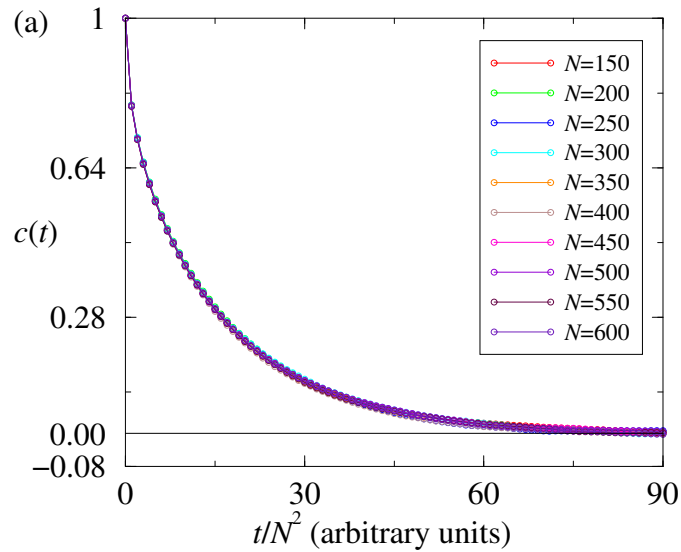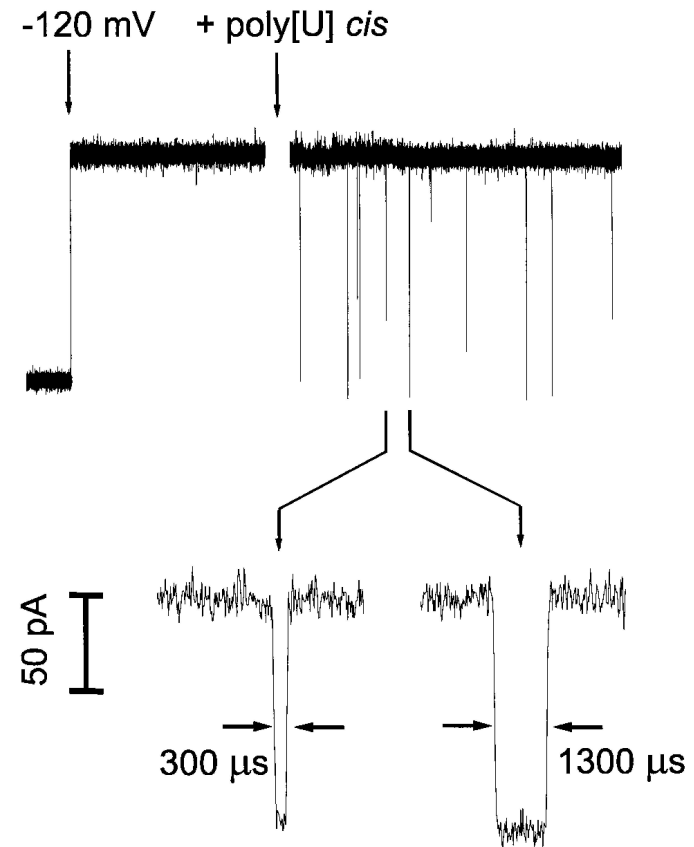
**For Rouse chains
(self-avoiding statistics):**

Polymer translocation, experiment

- How does the rate of escape of a polymer through a small hole depend on polymer length N?

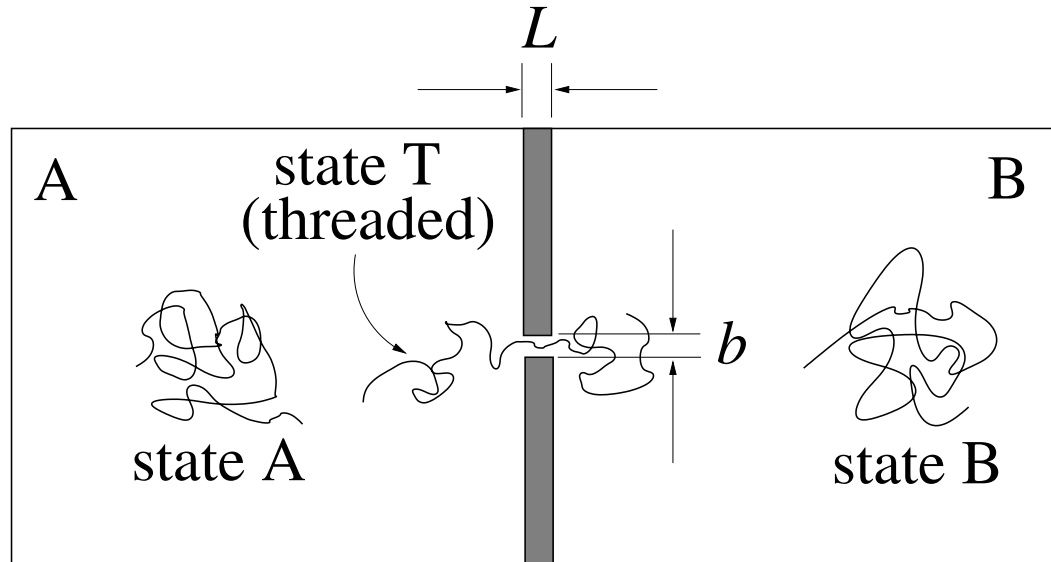- How long does such a translocating polymer dwell in the pore?

Experimental measurements:

-120 mV   + poly[U] *cis*

50 pA

300 μs   1300 μs

middle

in

out

Polymer translocation, simulation

Related system which we simulate:

- simulations in equilibrium

- equal boxes A and B

- observables are dynamic quantities:

average time between hops A $\leftrightarrow$ B
duration of these hops

Case I: unbiased translocation

Standard approach:

- consider which monomer $s(t)$ is located in the (middle of) the pore at time t.

- unless s is close to either end ($s = 0$ or N), negligable drift

- $\Rightarrow$ diffusion dominates: $\langle (s(t) - s(0))^2 \rangle \sim t$

- average dwell time $\tau_d \sim$ average unthreading time τ_u

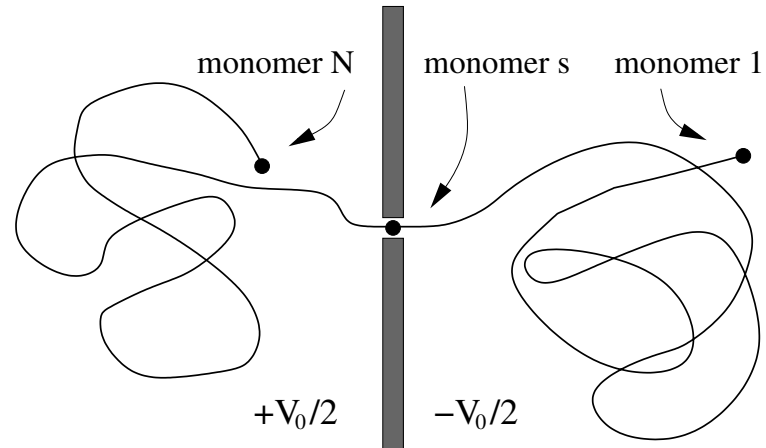- unthreading: $s^2(\tau_u) = N^2 \Rightarrow \tau_u \sim N^2$.

As shown by Kantor and Kardar (2004), this cannot be correct:

- wall does not make polymer more mobile $\Rightarrow$ lower limit: $\tau_u \geq N^{1+2\nu}$

  $\Rightarrow$ dynamics has to be anomalous: $\langle (s(t) - s(0))^2 \rangle \sim t^\alpha$ with $\alpha \leq \frac{2}{1+2\nu}$

  $\Rightarrow$ memory effects!

Unbiased translocation: cause of memory

Translocation velocity $v(t) \equiv \dot{s}(t)$ **induces restoring chain tension** $\phi(t)$

monomer N   monomer s   monomer 1

$+V_0/2$ $-V_0/2$

Assuming a linear response, $\phi(t)$ **and** $v(t)$ **are related:**

$$\phi(t) = \int_0^t dt' \mu(t - t')v(t') \quad \textbf{and} \quad v(t) = \int_0^t dt' a(t - t')\phi(t')$$

Laplace transform in inverse time $k \equiv t^{-1}$**:**

$$\phi(k) = \tilde{\mu}(k)v(k) \quad \textbf{and} \quad v(k) = \tilde{a}(k)\phi(k).$$

Consistency demands $\tilde{\mu}(k) = \tilde{a}^{-1}(k)$**.**

Unbiased translocation: memory kernel

Reminder: $\phi(t) = \int_0^t dt' \mu(t - t') v(t')$

$\mu(t)$, is response in $\phi(t)$ to a delta-function in $v(t)$, i.e., a step-function in $s(t)$.

Analytic argument:

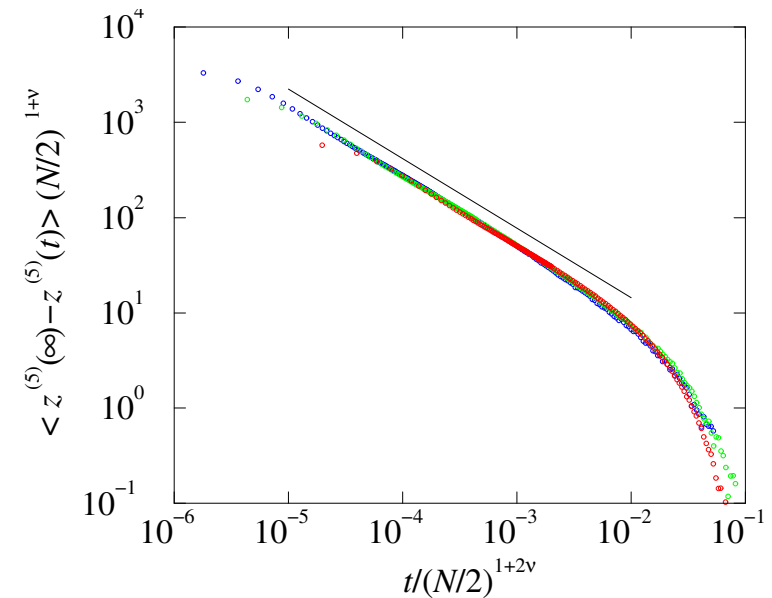At time $t \sim n(t)^{1+2\nu}$, monomers up to $n(t)$ are readjusted

Restoring force due to rest of polymer:
$F = \Delta r \cdot \frac{\partial F}{\partial r} \sim \left(\Delta n \cdot \frac{\partial r}{\partial n}\right) \cdot \frac{1}{r^2}$

Using $r(t) \sim n(t)^\nu$**:**

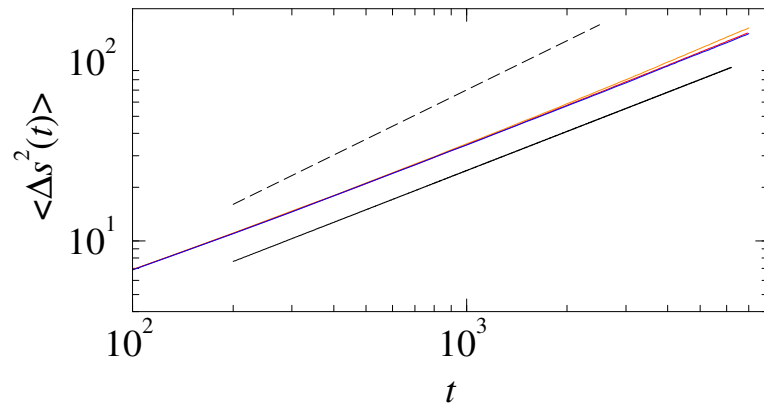$F \sim \Delta n \cdot n(t)^{-(1+\nu)} \sim t^{-(1+\nu)/(1+2\nu)} \equiv t^{-\alpha}$

Simulation results:

Unbiased translocation: consequences of memory kernel

$\mu(t) \sim t^{-\alpha} \exp(-t/\tau_R) \Rightarrow \langle s^2(t) \rangle \sim t^\alpha$ **for** $t < \tau_R$

Numerical checks:

$\Rightarrow \langle s^2(\tau_R) \rangle \sim N^{1+\nu}$.

No memory effects at $t > \tau_R$

$\Rightarrow$ **normal diffusion:**

$\Rightarrow \langle s^2(t) \rangle = \frac{t}{\tau_R} \langle s^2(\tau_R) \rangle$

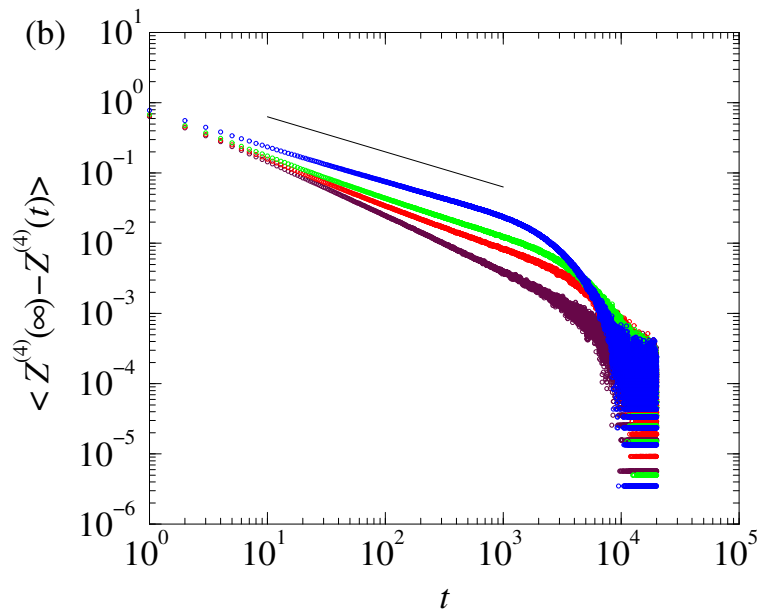$\Rightarrow s^2(t) = N^2$ **at** $\langle t \rangle \sim N^{2+\nu}$

N	τ_u	$\tau_u/N^{2+\nu}$
100	65136	0.434
150	183423	0.428
200	393245	0.436
250	714619	0.445
300	1133948	0.440
400	2369379	0.437
500	4160669	0.431

Case II: pulled translocation

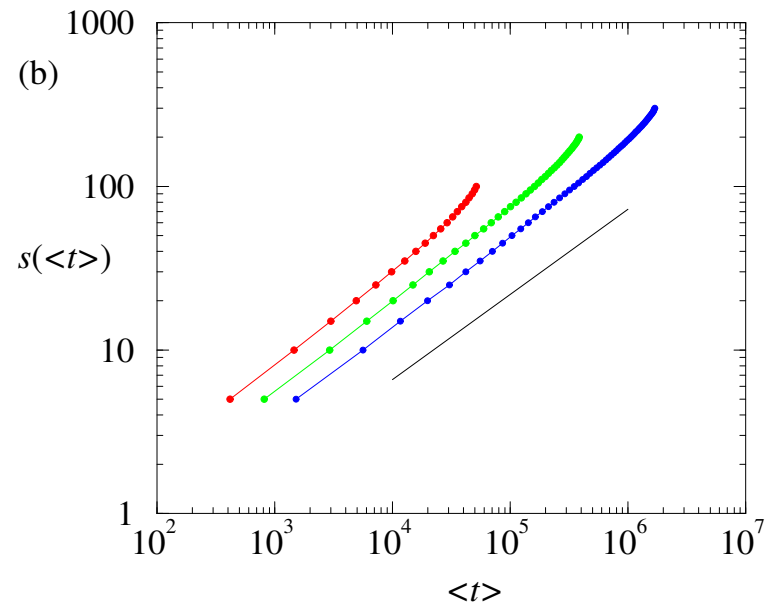Pulling one end of the polymer speeds up the unthreading time
Theoretical framework:
memory kernel (downstream side) becomes $\mu(t) \sim t^{-1/2} \exp(-t/N^2) \Rightarrow s(t) \sim t^{1/2}$

$N = 100$, $F = 0, 0.3, 0.5$ **and** 1.0;
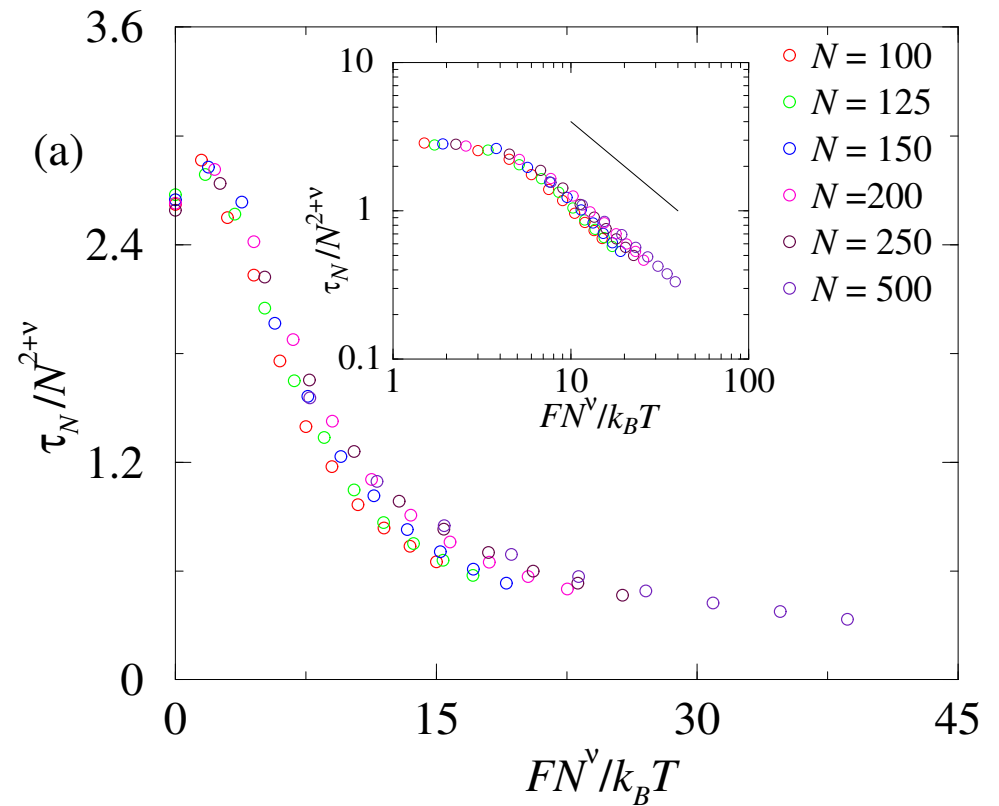[**1,280,000 measurements**]

$N = 100, 200$ **and** **300**; $F = 1.0$

Unthreading $s(t) = N \Leftrightarrow \tau_u \sim N^2$
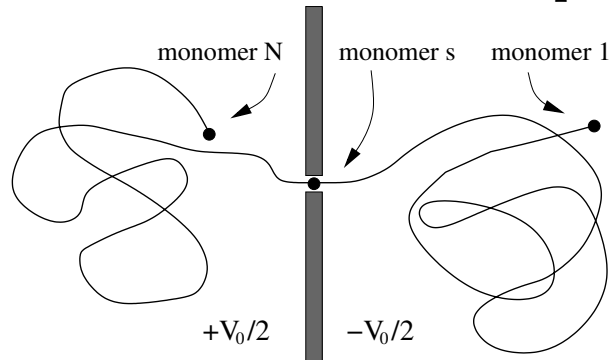
Case II: pulled translocation

A data collapse can be obtained
if $\tau_u/N^{2+\nu}$ is plotted
as a function of FN^ν:

Case III: driven translocation

Electric field drives the polymer

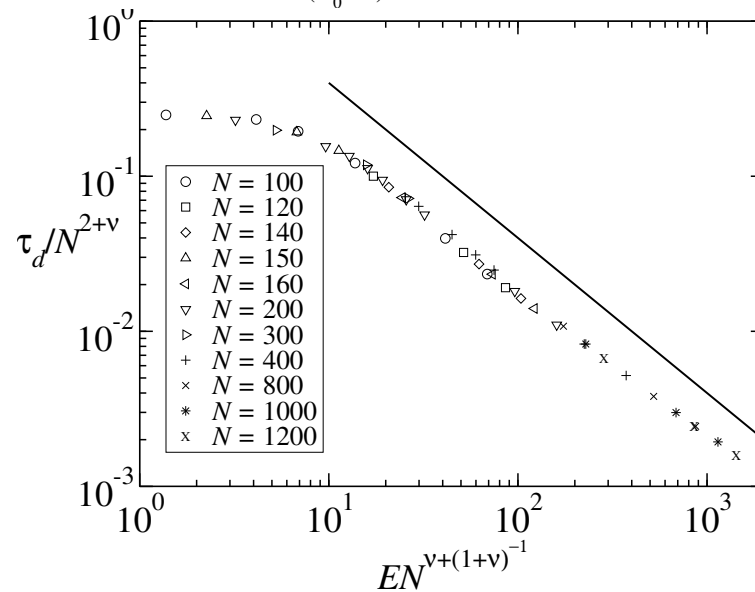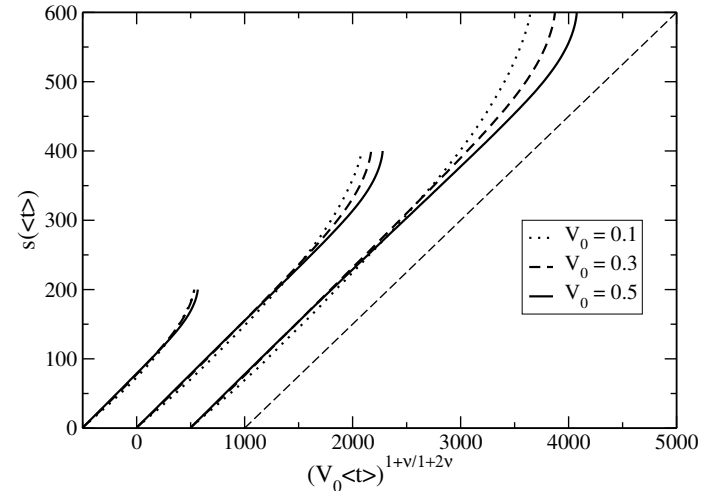**Theoretical framework:**

memory kernel is as before,
$$\mu(t) \sim t^{-(1+\nu)/(1+2\nu)} \exp(-t/\tau_R)$$

$$\Rightarrow \langle s(t) \rangle \sim t^{(1+\nu)/(1+2\nu)}$$
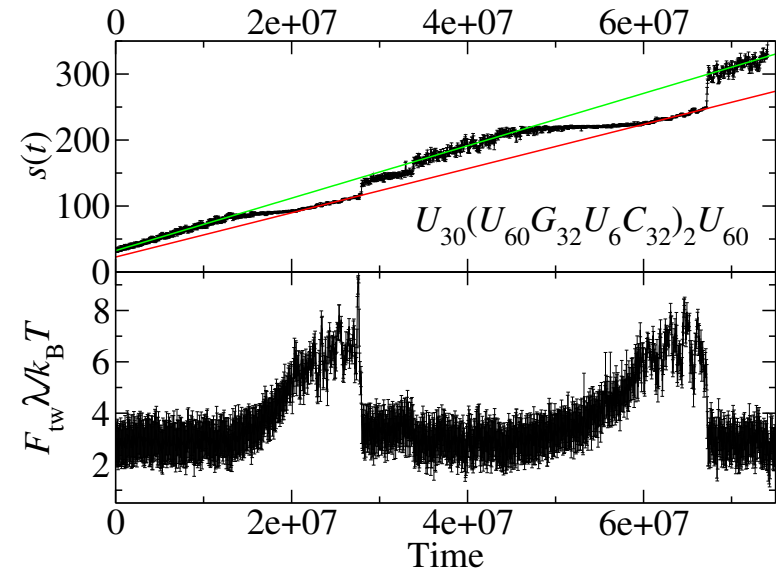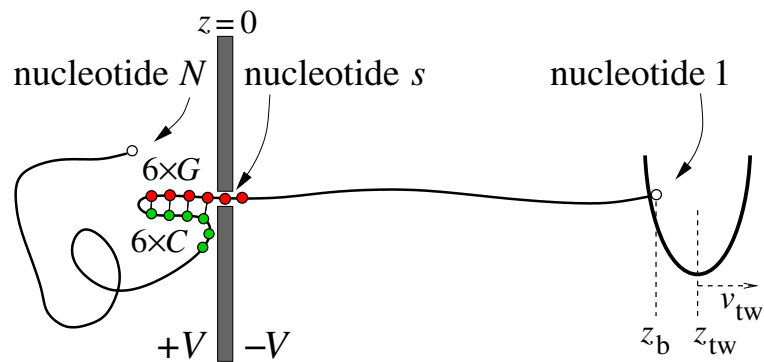
Unthreading:
$$s(t) = N \Leftrightarrow \tau_u \sim N^{(1+2\nu)/(1+\nu)}$$

Collapse if $\tau_u/N^{2+\nu}$ is plotted as a function of $EN^{\nu+(1+\nu)^{-1}}$
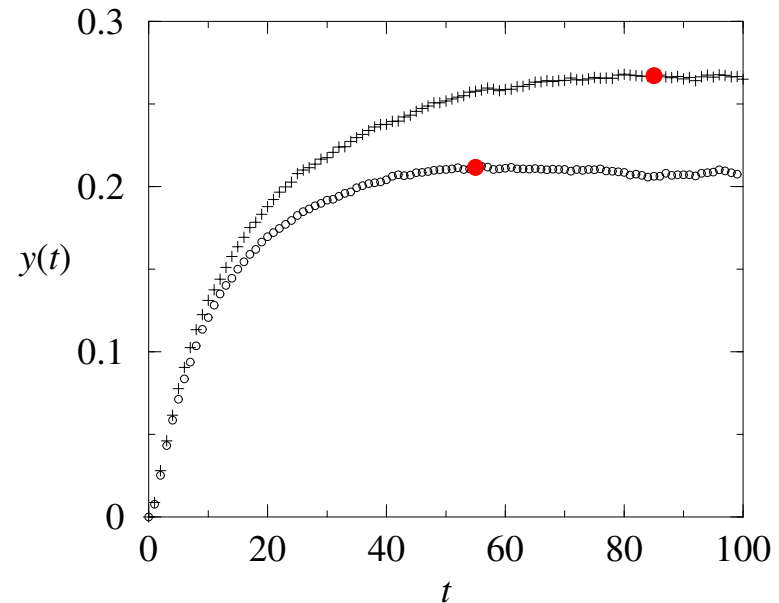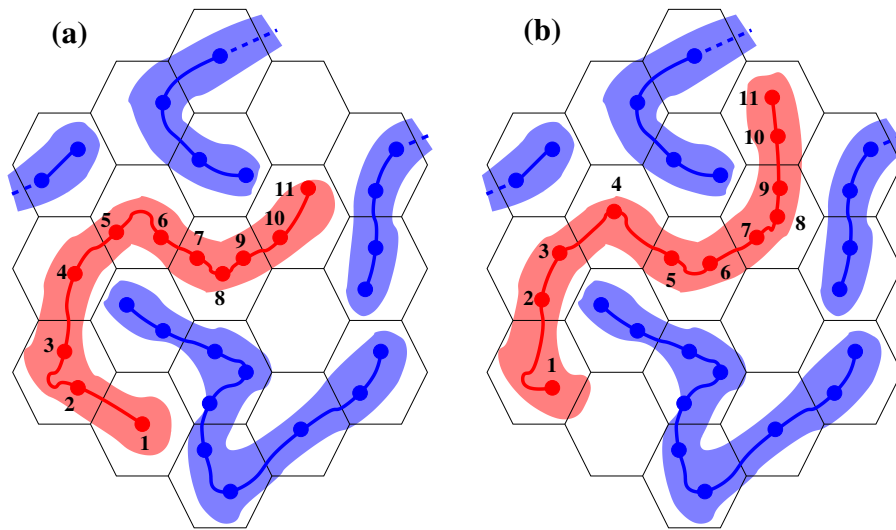
Secundary structure of RNA

- Pull RNA with an optical tweezer through a nanopore

- Record the pulling force vs. time

- Secondary structures give rise to peaks

Our analysis: thermal noise limits resolution to 5 to 10 nucleotides

Memory effects in polymer melts

- At time $t = 0$, slide a randomly tagged polymer along its contour
- According to standard reptation theory, no restoring tendency
- $y(t) \equiv \Sigma_i \left(\vec{x}_i(t) - \vec{x}_i(0) \right) \cdot \left(\vec{x}_{i+1}(0) - \vec{x}_{i-1}(0) \right)$ is however clearly non-zero
- $\Rightarrow$ longitudinal motion experiences a restoring force: memory effects

Memory effects in polymer melts
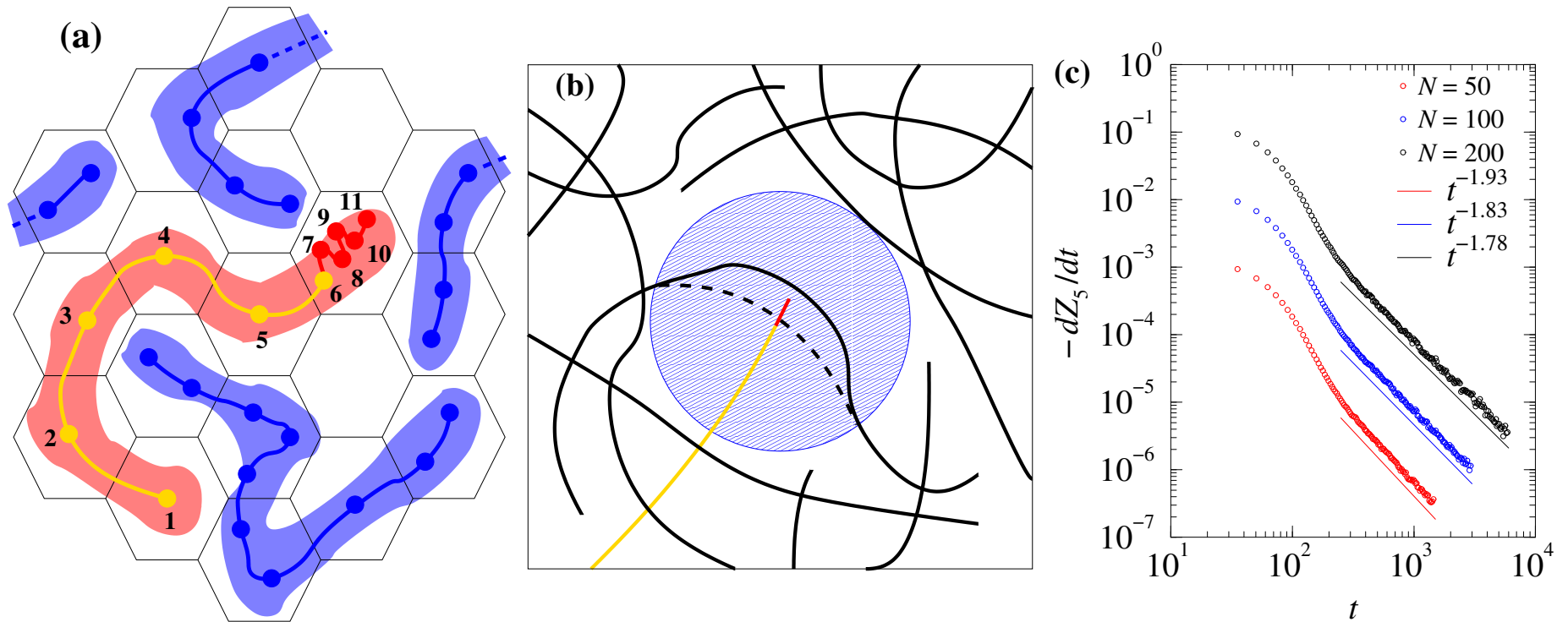
- **Probing memory kernel: response to a forced extrusion from one end**

- **Stored length density:** $Z_5(t) - Z_5(\infty) \sim t^{-\alpha} \Leftrightarrow -dZ_5/dt \sim t^{-(1+\alpha)}$
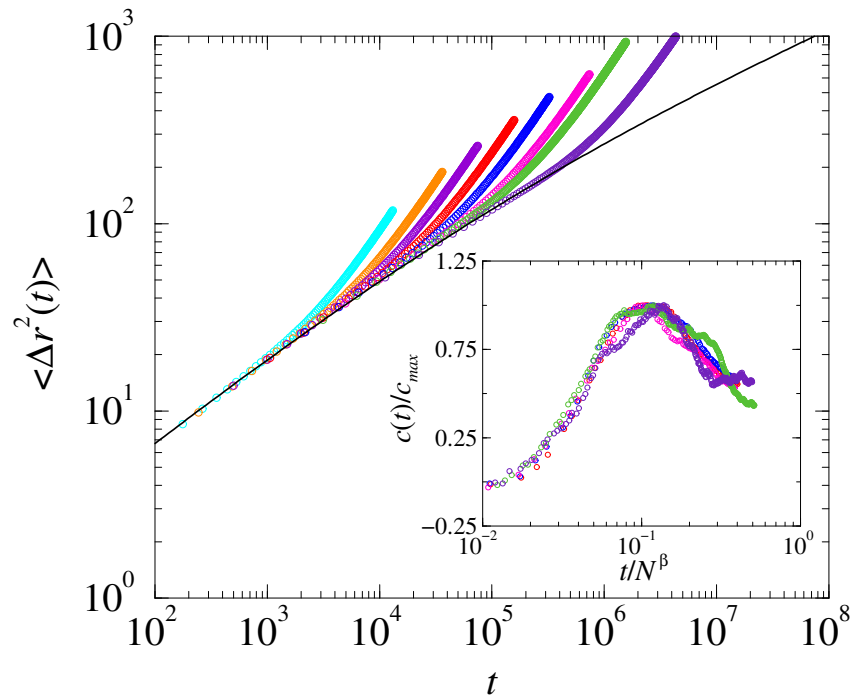
- **Result: power-law decay with exponent** $\alpha \approx 0.78 \pm 0.03$

- $\Rightarrow$ **longitudinal diffusion is** <u>anomalous</u> **till** $t \sim N^{\beta}$ **with** $\beta = 2/\alpha = 2.56 \pm 0.10$

Consequences of melt memory

- **Standard reptation theory:**
  Curvilinear diffusion crosses over from $\langle x^2 \rangle \sim t^{1/4}$ to $\sim t^{1/2}$ around $t \sim N^2$

- **We find this crossover at** $t \sim N^\beta$ **with** $\beta = 2/\alpha = 2.56 \pm 0.10$

- **Hence longest relaxation time (and viscosity) scaling as** N^{η_m} **with** $\eta_m = 3.28 \pm 0.05$

Summary and conclusions

- We have a very efficient lattice polymer program

- this allowed us to be investigate polymer translocation properly

- in unbiased translocation: $\tau_d \sim N^{2+\nu}$

- pulled translocation: $\tau_d \sim N^2$

- field-driven translocation: $\tau_d \sim N^{(1+2\nu)/(1+\nu)}$

- translocation velocity not constant; macroscopic ideas (friction e.d.) fail

- reptation theory is incomplete; many-polymer memory effects are missing

Outlook:

- further work on polymer melts

- understanding gelation

References

Polymer model:

- "Reaching large lengths and long times in polymer dynamics simulations",
  A. van Heukelum and G. T. Barkema, J. Chem. Phys. 119, 8197-8202 (2003).

Translocation:

- "Passage times for unbiased polymer translocation through a narrow pore",
  J. Klein Wolterink, G.T. Barkema and Debabrata Panja, Phys. Rev. Lett. 96, 208301 (2006).

- "Passage Times for Polymer Translocation Pulled through a Narrow Pore",
  D. Panja and G.T. Barkema, Biophys. J. 94, 1630-1637 (2008).

- "Anomalous dynamics of unbiased polymer translocation through a narrow pore",
  D. Panja, G.T. Barkema and R.C. Ball, J. Phys.: Condens. Matter 19, 432202 (2007).

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  D. Panja, G.T. Barkema and R.C. Ball, J. Phys.: Condens. Matter 20, 075101 (2008).

- "Pore-blockade Times for Field-Driven Polymer Translocation",
  H. Vocks, D. Panja, G.T. Barkema and R.C. Ball, J. Phys.: Condens. Matter 20, 095224 (2008).

- "Can Translocation Be Used to Determine RNA Secondary Structures?",
  H. Vocks, D. Panja and G.T. Barkema, submitted (2008).

Polymer melts:

- "Local strain relaxation dictates polymer melt viscosity",
  G.T. Barkema and D. Panja, submitted (2008).