Coarse-grained simulations of highly driven DNA translocation from a confining nanotube

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DNA Translocation

Nanopore

ions

Electric Field

cis-side

trans-side

membrane

$\frac{t}{\text{length}}$

Coarse-graining

atomistic
\( N = (a \text{ lot!}) \)

coarse-grained
\( N = 100 \text{ beads} \)

Coarse-graining

Finitely Extensible Nonlinear Elastic

\[ U_{\text{FENE}}(r) = -\frac{1}{2} k_{\text{FENE}} r_0^2 \ln \left[ 1 - \frac{r^2}{r_0^2} \right] \]

truncated Lennard-Jones

\[ U_{\text{LJ}}(r) = \begin{cases} 
4\epsilon \left[ (\frac{\sigma}{r})^{12} - (\frac{\sigma}{r})^6 \right] + \epsilon & \text{for } r < r_c \\
0 & \text{for } r \geq r_c 
\end{cases} \]

\[ \langle F_B^2 \rangle = \frac{2\zeta k_B T}{\Delta t} \quad \text{random Brownian force} \]

\[ m\ddot{\mathbf{r}} = \mathbf{F}^C - \zeta \dot{\mathbf{r}} + \mathbf{F}^B \]

Putting it all Together

short-ranged repulsive membrane:

\[ U_{\text{LJ}}(r) = \begin{cases} 
4\varepsilon \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^{6} \right] + \varepsilon & \text{for } r < r_c \\
0 & \text{for } r \geq r_c 
\end{cases} \]

field in the pore:

\[ F_{\text{drive}} = 50 \left[ \frac{k_BT}{\sigma} \right] \]

Highly-Driven limit!

N=100 beads

Problems with Driven Translocation

High variance amongst events.
Two main sources for this variation:

i) thermal noise

ii) initial conformations

![Graph showing translocation time distribution with counts for typical and fancy tricks]
Initial conformations matter!
Geometric Restrictions

Use a confining tube to reduce the variance

**Case 1**

**Case 2**

semi-infinite

finite

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Translocation Dynamics

semi-infinite tube

Percent Translocated

Time: \( t \) (arb. units)

\[ \xi_T = 3 \quad \xi_T = 4 \quad \xi_T = 5 \quad \xi_T = 6 \]

Reducing tube size

Tension Propagation

Net friction is determined by moving monomers

\[ F_{\text{drive}} = (k - s) \zeta \nu \]

Tension Propagation
first few simulation frames
Tension Propagation
First few simulation frames
Decreasing the Variance

\[ \xi_T = 2.5 \]

Recap: semi-infinite case

Use a confining tube to reduce the variance

Case 1

Results

- Reduces variance: $\sigma_{\tau}$
- Increases time: $\tau$
- Reduces coef. var: $\sigma_{\tau}/\tau$

- Require high confinement (free energy cost)
Confinement in a Finite-tube

Here, we have additional parameters.

Can we do better than before?

Cast into volume and aspect-ratio

\[ \frac{\xi_T}{L_T} \]

\[ V_T \]

\[ a = \frac{L_T}{\xi_T} \]
Iso-volume, vary $a = \frac{L_T}{\xi_T}$

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Tension Propagation

\[
\tau = \frac{\zeta}{F} \sum_{k=1}^{N} R_k
\]

\[
\langle \tau \rangle = \frac{\zeta}{F} N \langle R \rangle
\]

reducing \( \sigma_R \) should reduce \( \sigma_\tau \)

Why $a^* \approx 0.5$ ?

Since the pore (monomer sink) is centred, $a \approx 0.5$ corresponds to an isotropic span.

$$a = \frac{L_T}{\xi_T}$$

lower variance in these $R$ vectors
Hemisphere is the Optimal Shape

variation in distances: $\sigma_R/\langle R \rangle$

cylinder

$\alpha^* = 0.414$

$\sigma_R/\langle R \rangle = 0.277$

prism

$\alpha^* = 1/2$

$\sigma_R/\langle R \rangle = 0.289$

hemisphere

$\sigma_R/\langle R \rangle = 0.258$

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Recap: finite case

Use a confining tube to reduce the variance

Case 2

Results

✓ Reduces variance: $\sigma_\tau$

✗ Reduces time: $\tau$

✓ Reduces coef. var: $\sigma_\tau/\tau$

✓ Less confining
Conclusion

- We used a geometric constraint (tube) to limit initial conformations prior to translocation.
- Reduces the variance, and the coefficient of variation.
- Semi-infinite: small radius increases the mean time.
- Finite tube: ideal aspect ratio \( a \approx 0.5 \) (hemisphere).
Thanks!

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Average Distance in a Cavity
(if the polymer homogeneously fills the cavity)

\[ \langle R \rangle = \frac{1}{v_T} \int_{\phi=0}^{2\pi} \int_{\rho=0}^{\xi_T/2} \int_{z=0}^{L_T} R \rho d\phi d\rho dz \]

\[ \sigma_R^2 = \langle R^2 \rangle - \langle R \rangle^2 \]
Average Distance in a Cavity

$$a^* = 0.414$$

Theory: circular channel

Theory: square channel

Coefficient of variation: $\sigma_R/\langle R \rangle$

Aspect Ratio: $a = L_T/\xi_T$
Moderate Tube size
Reducing Volume

\[ R_{g0}^3 \]

Coefficient of variation: \( \sigma_T / \langle \sigma \rangle \)

Volume: \( \pi L_T (\xi_T/2)^2 (\sigma^3) \)

\( \xi_T = 9.0 \sigma \)
\( \xi_T = 11.0 \sigma \)
\( \xi_T = 5.0 \sigma \)

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Knots
Non-monotonic Fluctuations

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Net friction is determined by moving monomers.
Slowest state?

Blob-like
occurs later
(near the end)

Hairpin
occurs earlier
(about halfway)