Migration of DNA Due to a Combination of Parallel Pressure Gradient and External Electric Field

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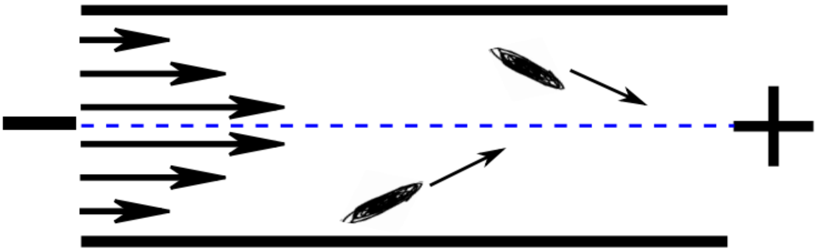
Motivation

- Experimental work provides evidence of DNA migration under a combination of pressure and electric field.
- The ability to spatially concentrate DNA can lead to many applications such as bio-sensing and genomic mapping
- We hypothesize that it is due to an electrically induced velocity disturbance, and use simulations to better understand the dynamics

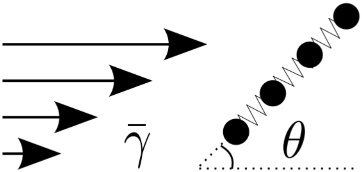


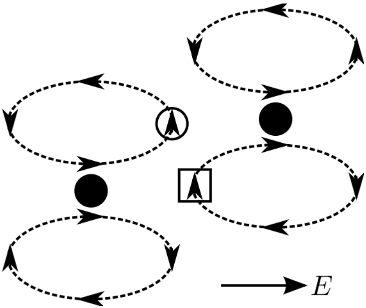
Video

Show video experiment.

How DNA Migrates: Our Theory

- The shearing flow extends and aligns the DNA molecules as shown
- A velocity disturbance induced by the electric field acting on the disturbed DNA molecule generates a net transverse migration



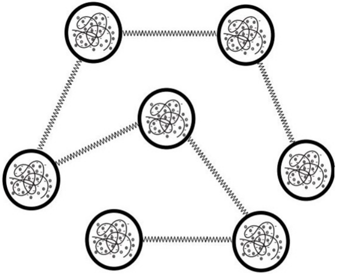


Force Balance

- A force balance is used to model a polymer chain with a given number of beads (molecules)

$$\mathbf{F}_i^D + \mathbf{F}_i^S + \mathbf{F}_i^R + \mathbf{F}_i^B + \mathbf{F}_i^W = 0$$

- FENE springs and excluded volume effects are incorporated
- Additionally, an electric field and a 2-D/3-D parabolic flow are included to study migration



FENE Springs

- FENE stands for Finitely Extensible Nonlinear Elastic

$$\Phi_{FENE} = \sum_{i>j}^{N} \phi_{FENE}(|\boldsymbol{r}_i - \boldsymbol{r}_j|)$$

  and

$$\phi_{FENE} = -\frac{1}{2}\kappa r_0^2 ln(1 - \frac{r^2}{r_0^2})$$

  where $\boldsymbol{r}_i$ and $\boldsymbol{r}_j$ are the vectorized positions of bead i and j, κ is the spring constant, and r_0 the maximum bond extension.

- It is easy to see the similarities between FENE and Hookeon springs, the former of which has a upper bound

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)

Excluded Volume Effects

- EV effects mainly apply when the center distance between two polymer molecules is below their diameter

$$\Phi_{EV} = \sum_{i>j} \phi_{EV}(|\boldsymbol{r}_i - \boldsymbol{r}_j|)$$

where

$$\phi_{EV} = A\exp(-\beta r^2)$$

- EV effects make it difficult for polymer molecules to be too close
- Wall repulsive force is similar to the EV effects between beads, but twice as large in magnitude

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R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)

2-D/3-D Parabolic Flow

- Parabolic flow (pressure gradient) is described by

$$u_x^\infty = 2\bar{\gamma}(r_y - r_y^2/h)$$

  where h is the width of the channel
- Additionally, the 3-D parabolic flows for the square and rectangular channel grids are obtained numerically and the flow field velocity for each bead is interpolated using the 4 adjacent grid points

Hydrodynamic Interactions with the RP Tensor

We use the Rotne-Proger (RP) tensor, $\boldsymbol{\mu}^{RP}$, to describe the hydrodynamic interactions between individual beads

$$\boldsymbol{\mu}_{ij}^{RP} = \frac{1}{6\pi\eta a}\begin{cases} C_1\mathbf{I} + C_2\dfrac{\boldsymbol{r}_{ij}\boldsymbol{r}_{ij}}{r_{ij}^2}, & r_{ij} \geq 2a, \\ C_1'\mathbf{I} + C_2'\dfrac{\boldsymbol{r}_{ij}\boldsymbol{r}_{ij}}{r_{ij}^2}, & r_{ij} < 2a, \\ \mathbf{I}, & i = j, \end{cases}$$

where

$$C_1 = \frac{3}{4}\frac{a}{r_{ij}} + \frac{1}{2}\frac{a^3}{r_{ij}^3}, \quad C_2 = \frac{3}{4}\frac{a}{r_{ij}} - \frac{3}{2}\frac{a^3}{r_{ij}^3},$$
$$C_1' = 1 - \frac{9}{32}\frac{r_{ij}}{a}, \qquad C_2' = \frac{3}{32}\frac{r_{ij}}{a}.$$

Note that a is the bead radius and η is the viscosity of the fluid.

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)

Electrically Induced Hydrodynamic Interactions

- Electric field with electro-HI and shear flow are included to study DNA migration. The electrophoretic mobility is

$$\boldsymbol{\mu}_{ij}^{E} = \begin{cases} \frac{\lambda_D^2}{4\pi\eta a^3 {r_{ij}}^3}\left[\frac{3\boldsymbol{r}_{ij}\boldsymbol{r}_{ij}}{{r_{ij}}^2} - \mathbf{I}\right], & r_{ij} \geq 2a, \\ 0 & r_{ij} < 2a, \\ \mu_0^E \mathbf{I}, & i = j, \end{cases}$$

  where λ_D is the Debye length, and μ_0^E the unsheared electrophoretic mobility
- The electric force is

$$\mathbf{F}^E = Q\boldsymbol{E}$$

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 011802 (2010)

Euler's Method with Differential Equation

- Combining all the contributions stated above, the differential equation to be used with Euler's method is

$$\frac{d\boldsymbol{r}}{dt} = [\mathbf{u}^{\infty} + \boldsymbol{\mu}^{RP} \cdot (\mathbf{F} + \mathbf{F}^{B}) + \boldsymbol{\mu}^{E} \cdot \mathbf{F}^{E}], \tag{1}$$

where $\boldsymbol{r}$ is the vectorized positions of all beads, $\mathbf{F}$, $\mathbf{F}^B$, and $\mathbf{F}^E$ are the vectorized forces, and $\boldsymbol{\mu}^{RP}$ and $\boldsymbol{\mu}^{E}$ are the grand mobility tensors for the hydrodynamic interactions and electrically induced fluid disturbances

Video

Show video shear.

Non-dimensionalization and Parameters

- Our simulation results are compared with Ladd and Kekre; their non-dimensionalization factors are as follows

Author	Energy	Length	Time
Ladd	$k_b T$	b	$\lambda * b^2 / k_b T$
Kekre	$k_b T$	b	$\lambda * b^2 / k_b T$

  where $b = \sqrt{k_b T / \kappa}$, and λ is the drag coefficient

- Below are specific (non-dimensional) values for the parameters

Author	κ	a	r_0	A	β
Ladd	1	0.36	5.48	2.71	1.5
Kekre	1	0.362	5	2.7	1.8

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)
A. J. Ladd, R. Kekre, and J. E. Butler, Phys. Rev. E. 80, 036704 (2009)

Static Properties

- Static properties using authors' parameters match quite well; end to end distance R_e results can be seen below with difference of less than 1%

Author	Our $< R_e^2 > /b^2$	Author's $< R_e^2 > /b^2$
Ladd	44.1	44.2
Kekre	40.11	40.25

- Radius of gyration results also show little deviation from literature

Author	Our $< R_g^2 > /b^2$	Author's $< R_e^2 > /b^2$
Ladd	7.49	7.5
Kekre	6.86	6.89

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)
A. J. Ladd, R. Kekre, and J. E. Butler, Phys. Rev. E. 80, 036704 (2009)

Rouse Relaxation Time

- The Rouse relaxation time is found from fitting the correlation function

$$P(t) = < \boldsymbol{Z}(t) \cdot \boldsymbol{Z}(0) >$$

where $\boldsymbol{Z}$ is the end to end vector, to a single exponential

$$A \exp(-t/\tau_r)$$

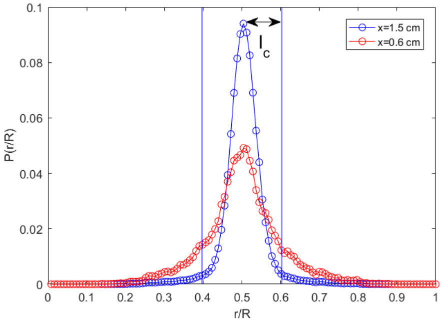
- By averaging over a large amount of time (about $8 * 10^8 t_0$), we obtained results that are in agreement with Ladd & Kekre; our fits in Matlab show R-values of 1

Author	Our τ_r/t_0	Author's τ_r/t_0
Ladd	16.4	16.4
Kekre	15.2	15.2

R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 050803(R) (2010)
A. J. Ladd, R. Kekre, and J. E. Butler, Phys. Rev. E. 80, 036704 (2009)

95% Concentration Layer Thickness

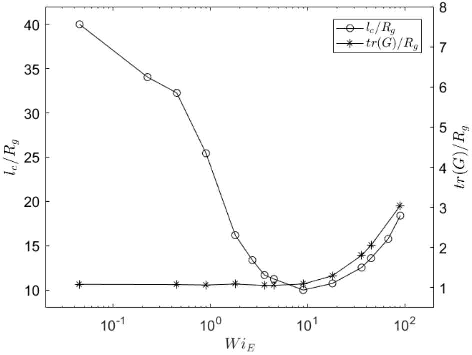
- We use 95% concentration layer to define the extent of migration
- 95% concentration layer is defined as the half width of the region encompassing 95% of the polymer concentration



R. Kekre, J. E. Butler, and A. J. C. Ladd, Phys. Rev. E 82, 011802 (2010)

Concentration Layer Thickness and Electric Field Strengths

- There is an optimal electric field where the 95% concentration layer reaches a minimum
- Our results match those in literature quantitatively



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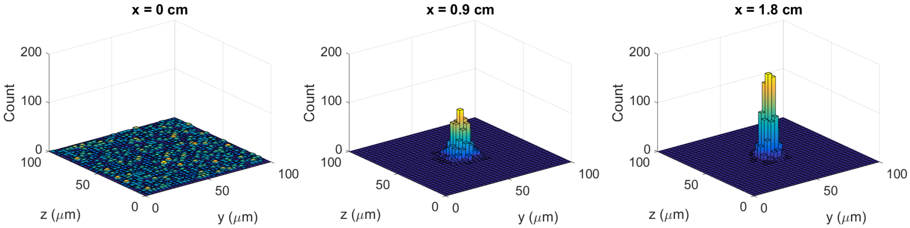
Positional Evolution of the Concentration Profile (Square Channel)



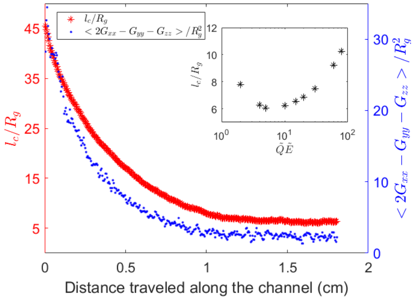
- DNA becomes highly concentrated as it travels through the channel
- By the exit of the channel, the profile is fully developed

Video

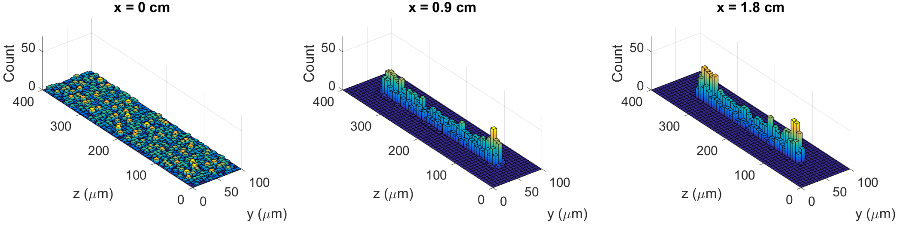
Show video square.

Positional Dependence of Concentration Layer Thickness (Square Channel)

- The channel length is 1.8 cm
- Steady state occurs at around 3/4 through the channel, consistent with experimental observations
- Similar to the simple parabolic flow, there exists an optimal electric field for maximum migration



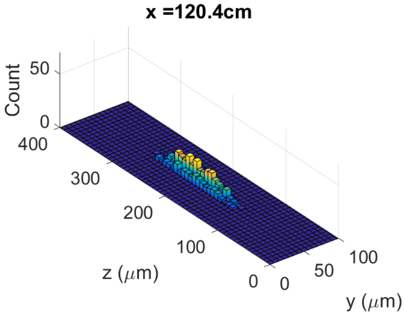
Positional Evolution of the Concentration Profile (Rectangular Channel)



- In the *y* direction, the concentration profile is fully developed by the end of the channel
- Far from fully developed in the *z* direction

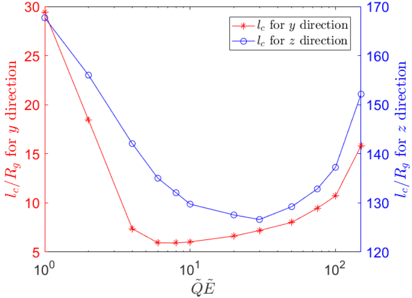
Fully Developed Concentration Profile (Rectangular Channel)

- Using optimal conditions to our knowledge, we obtained the fully developed concentration profile at x=1.2 m
- Concentration becomes much higher



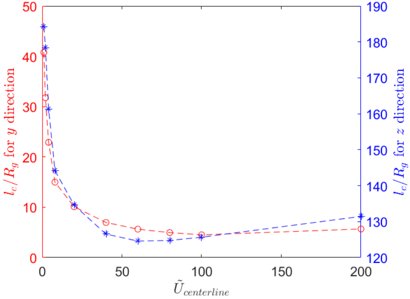
Concentration Layer Dependence on Electric Field Strength (Rectangular Channel)

- DNA concentration profile is far from fully developed at the exit using any conditions so far
- Different electric fields lead to different extents and rates of migration
- The optimal electric field differs depends on in which direction (*y* or *z*)



Concentration Layer Dependence on Pressure-Driven Flow (Rectangular Channel)

- There is an optimal pressure-driven flow velocity that leads to maximum migration
- Again, in different directions, the optimal is different
- Under optimal conditions, the entry length is 1.2 m



Conclusion and Future Work

- Preliminary results match our expectations qualitatively
- Migration rates and extents depend on flow, electric field, and channel dimensions in a complex way
- Simulation results will be compared with experimental data quantitatively in the future
- After both experiments and simulations are done, we will publish a paper with our results in the next few months

Thank you for your attention!
Any questions?