Microfabricated arrays

2-dimensional obstacle course for DNA

Advantages:
- well-defined & regular
- can observe DNA dynamics
- can choose design

Collisions with posts

Episodic motion in a regular lattice

- typical engagement time ~ L,
  but typical collision frequency ~ 1/L

Separation by collisions with posts

Rows of posts

- collision hinders molecule
- delay depends on length L

\[ t_{\text{disengagement}} \sim \frac{L}{2\mu_0 E} \log \left( \frac{L}{R_d (0)} \right) \]

Require DNA to relax in the time taken to travel own length
- works best for small DNA molecules
- could sequence 500 nucleotides in 10 mins, using 20 nm posts, separated by 400 nm

Collisions between DNA and a point obstacle

Strong-stretching regime

Impact parameter \( \frac{\varphi}{R_d} \)

Collisions between DNA and a point obstacle

Electrophoretic stretching

Electrophoresis:
- hydrodynamic interaction screened
  \( \mu \) independent of size
- DNA tethered in a field:
  \( v = \mu E \), equivalent to DNA tethered in a flow
Owing to extensional flow, collision probability depends also on a dynamical parameter

\[
D_C = \frac{2 \mu E}{R_e a} \tau_{e, a, 3}
\]

DNA confined in a thin slit, depth \( h \)
- driven by electric field
- transient stretching & relaxation

Hydrodynamic interactions screened on scale > \( h \)

Prediction: drag increases as depth decreases

Polymer appears as a stretched stem, capped by a flower of Pincus blobs, opaque to the flow

Generalize model to include:
- worm-like chain elasticity
- hydrodynamic interactions between blobs

\[
D_\alpha = \sqrt{\frac{n_{\alpha}}{S}} b
\]

\[
\zeta_e = \frac{\zeta}{\sqrt{n_{\alpha} \log(z/D_1)}}
\]

\[
\zeta_e = A \eta b \quad A \approx 6
\]
**Model equilibrium extension**

Perkins et al. ’95

Extension of a DNA molecule tethered in a uniform flow

- Flow velocity vs. extension

**Thin slit relaxation dynamics**

Perkins et al., ’94

Relaxation of tethered DNA

- Extension vs. time

**Zero-parameter model**

Bakajin et al. ’98

Free-draining scaling function ($z \sim L$)

- Zeta potential vs. velocity

**Thin slit relaxation dynamics**

- After disengaging from a post, the DNA relaxes

**Pulsed-field electrophoresis in regular arrays**

- Switch field alternately along two different directions

**Linear migration**

- Regular array of large posts with well-aligned field

- DNA migrates straight along channels
Pulsed-field arrays
molecular motion
Duke et al. '96; Bakajin et al. '01

Advantages of arrays:
- regular motion • good resolution
- high fields • fast separation
- linear fractionation
  \[ U = \kappa_0 \Omega^2 \left( \frac{\Theta}{2} \right) \left( 1 - \frac{L}{L_{\text{MAX}}} \right) \]
- straightforward recipe for choosing pulse parameters
  \[ L_{\text{MAX}} = \left( \frac{1}{T_0} \right) \left( \frac{E'}{E_b} \right)^b \]

Pulsed-field hex arrays
ultra-fast separation
Bakajin et al. '01

Separation of 100 kb DNA in 10 seconds!

Entropic trapping
Han, Turner & Craighead '99

Entropic trapping
Han, Turner & Craighead '99

\[
\begin{align*}
U &= \kappa_0 \Omega^2 \left( \frac{\Theta}{2} \right)
\end{align*}
\]
Entropic trapping mobility

\[ \frac{\mu}{\mu_0} = \frac{I_{\text{travel}}}{I_{\text{travel}} + I_{\text{trap}}} \]

\[ \tau_{\text{travel}} = \frac{L}{2} \left( \frac{1}{\mu_0 E_D} + \frac{1}{\mu_0 E_S} \right) \]

\[ t_{\text{trap}} \sim \frac{1}{d_S N^{1/5}} \exp \left( \frac{\alpha}{E_S kT} \right) \]

\[ \Delta F \approx \frac{\alpha}{E_S kT} \]

Entropic trapping separation

\[ E = E_D \]

\[ E = E_S \]

\[ \Delta F_{\text{max}} \approx 1/E_S \]

Dense array of posts

Cabodi, Turner & Craighead '02

'e-beam lithography'

'Start Emulsion Plate'

'Start Pattern'

'End Pattern'

'Cure Emulsion Plate'

'Cure Pattern'

'Photodevelop Emulsion Plate'

'Photodevelop Pattern'

'Etch Posts'

'Turner, Cabodi & Craighead '02

DNA is entropically inhibited from entering forest of posts...

... but can be driven in by a high field

Entropic recoil

Turner, Cabodi & Craighead '02

\[ \begin{align*}
L_1 & = 6 s \\
L_2 & = 1 s \\
L_3 & = 4 s \\
L_4 & = 6.5 s
\end{align*} \]

\[ \begin{align*}
L_5 & = 6.5 s \\
L_6 & = 27.5 s \\
L_7 & = 42.5 s \\
L_8 & = 76.5 s
\end{align*} \]
Entropic recoil retraction time
Tuner, Cabodi & Craighead '02
- Constant retraction force
- Friction proportional to unretracted length

$t_{\text{retract}} \sim L^2$

Entropic recoil: pulse time ramp
Cabodi, Turner & Craighead '02

Nanobottles
Tegenfeldt et al. '04
Nanoimprinting on fused silica wafers
DNA stretches due to self-avoidance
$\xi_{2} \sim L \left( \frac{h \eta}{D} \right)^{1/3}$

Nanobottles
10 nm channels created by sputtering deposition
Optical sizer
Foquet et al. '02; Chou et al. '99
Detect fluorescence from single DNA molecules flowing in a nanochannel
Optical sizer

Foquet et al. '02

Near-field scanner for moving molecules

Tegenfeldt et al. '00

100 nm slits illuminated from behind