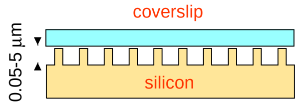
Microfabricated arrays

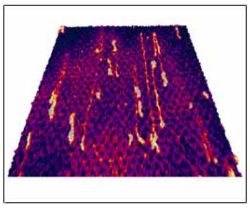
Volkmuth & Austin '92

2-dimensional obstacle course for DNA



Advantages:

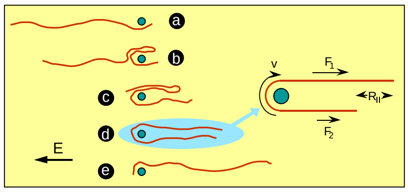
- well-defined & regular
- can observe DNA dynamics
- can choose design



Collisions with posts

Volkmuth et al. '94

Episodic motion in a regular lattice



- typical engagement time ~ L,

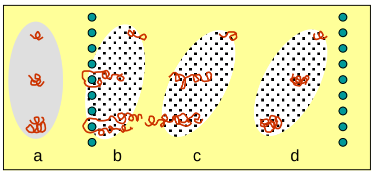
  … but typical collision frequency ~ $1/L$

→ fails to provide effective separation

Separation by collisions with posts

Duke et al. '97

Rows of posts



- collision hinders molecule
- delay depends on length L

$$t_{disengage} \sim \frac{L}{2\mu_0 E}\log\left(\frac{L}{R_{\parallel}(0)}\right)$$

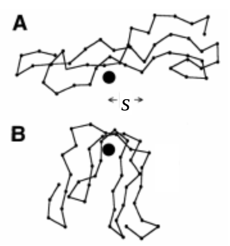
Require DNA to relax in the time taken to travel own length

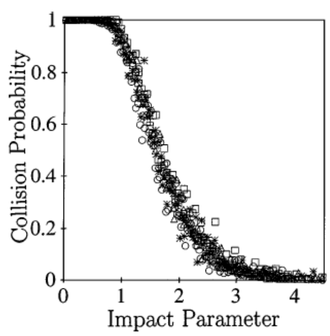
- works best for small DNA molecules
- could sequence 500 nucleotides in 10 mins, using 20 nm posts, separated by 400 nm

Collisions between DNA and a point obstacle

Sevick & Williams '96

Strong-stretching regime

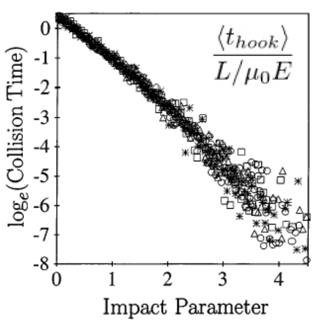


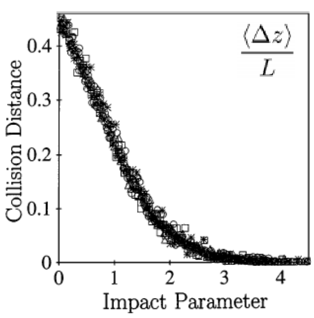


Impact parameter $\dfrac{s}{\langle R_x \rangle}$

Collisions between DNA and a point obstacle

Sevick & Williams '96





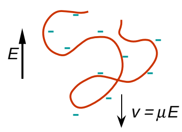
Electrophoretic stretching

Long, Viovy & Ajdari '96

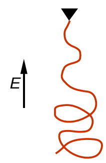
Electrophoresis:

- hydrodynamic interaction screened

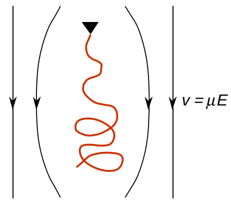
  → μ independent of size



DNA tethered in a field:



→

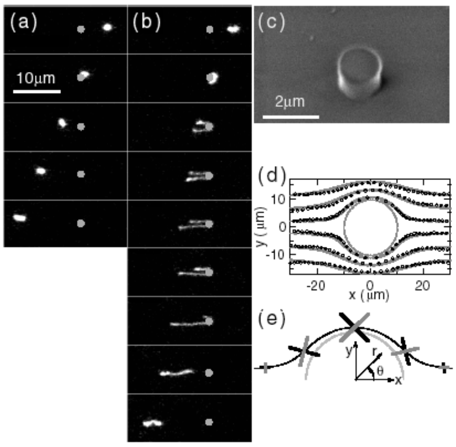


- hydrodynamics *not* screened

… equivalent to DNA tethered in a flow

DNA-post collisions

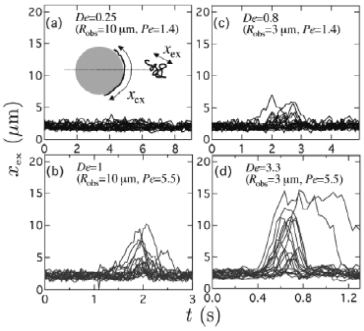
Randall & Doyle '04

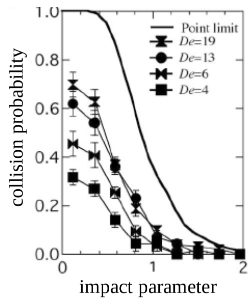


DNA-post collisions

Randall & Doyle '04

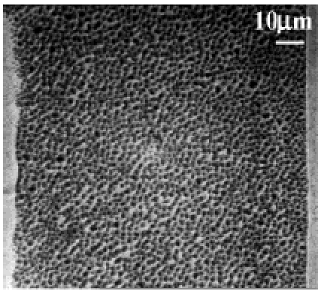
Owing to extensional flow,
collision probability depends also on a dynamical parameter $\mathrm{De} = \frac{2\mu E}{R_{obs}} \tau_{relax}$

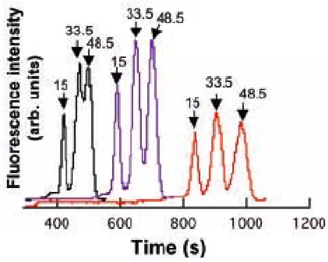




Separation in self-assembled magnetic matrices

Doyle et al. '02



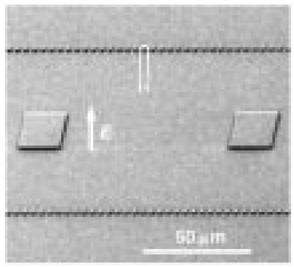


Electrophoretic stretching of DNA in a confined space

Bakajin et al. '98

DNA confined in a thin slit, depth h

- driven by electric field
- transient stretching & relaxation

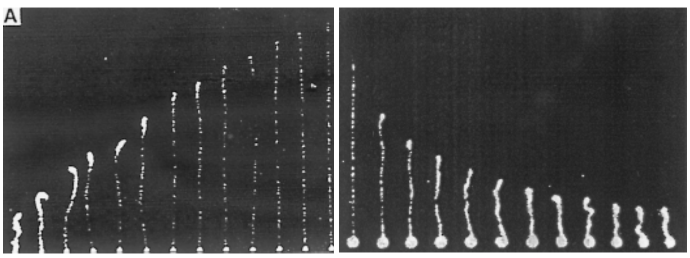


Hydrodynamic interactions screened on scale > h

Prediction: drag increases as depth decreases

Extension of tethered DNA in a flow

Perkins et al. '95



Stem & flower model

Brochard-Wyart '95

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

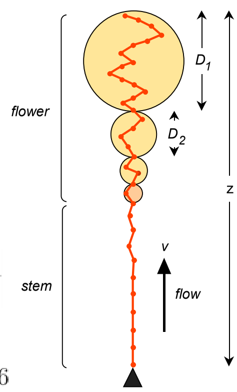
Generalize model to include:

- worm-like chain elasticity
- hydrodynamic interactions between blobs

blob α contains n_α beads $D_\alpha = \sqrt{\frac{n_\alpha}{3}}\, b$

effective friction of a bead $\zeta = \frac{\zeta_b}{\sqrt{n_\alpha}\log(z/D_1)}$

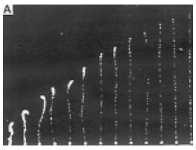
$\zeta_b = A\eta b \qquad A \approx 6$

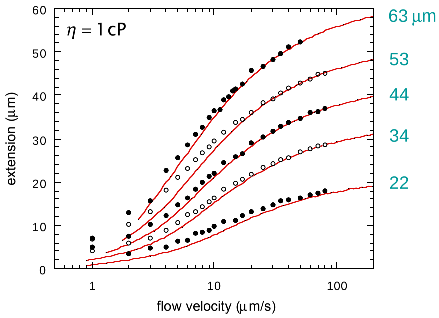


Model
equilibrium extension

Perkins et al. '95

Extension of a DNA molecule tethered in a uniform flow

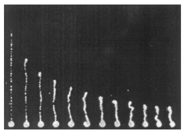


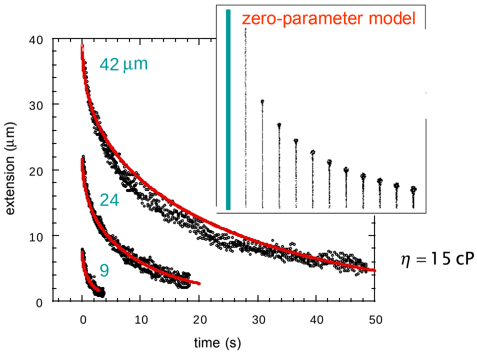


Model
relaxation

Perkins et al., '94

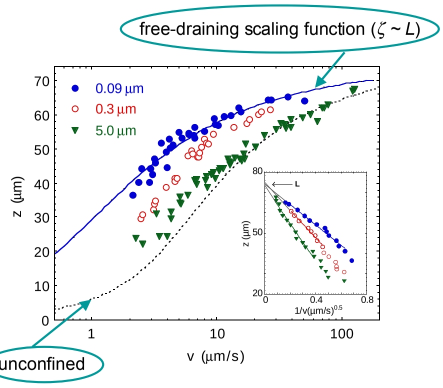
Relaxation of tethered DNA





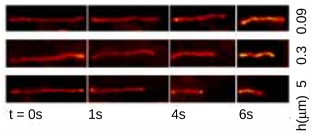
Thin slit
extension *vs* electrophoretic drift velocity

Bakajin et al. '98

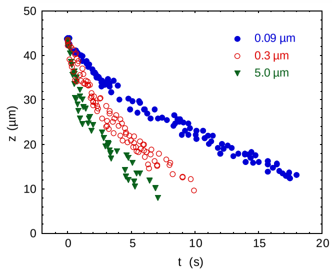


Thin slit
relaxation dynamics

After disengaging from a post, the DNA relaxes



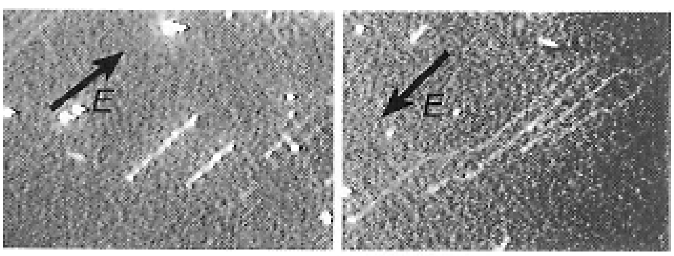
- slower dynamics in thin arrays



Linear migration

Regular array of large posts with well-aligned field

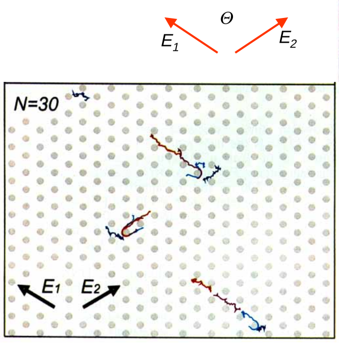
→ DNA migrates straight along channels

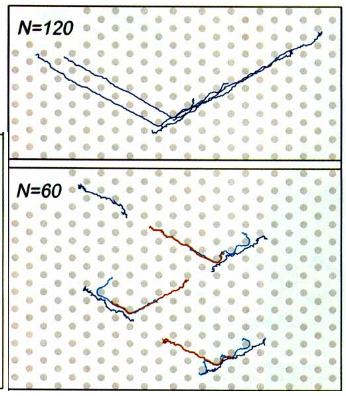


Pulsed-field electrophoresis in regular arrays

Duke et al. '96

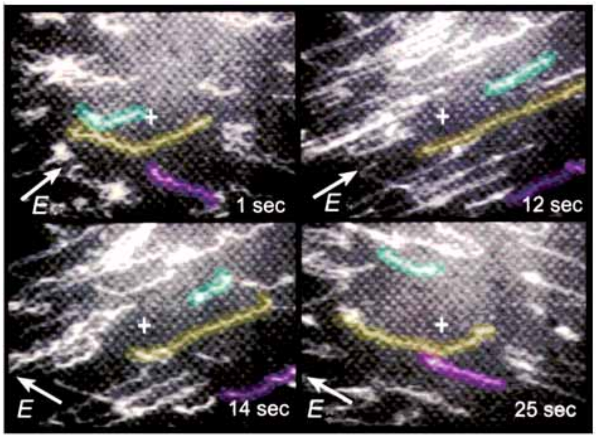
Switch field alternately along two different directions





Pulsed-field arrays
molecular motion

Duke et al. '96; Bakajin et al. '01



Pulsed-field arrays
separation

Duke et al. '96

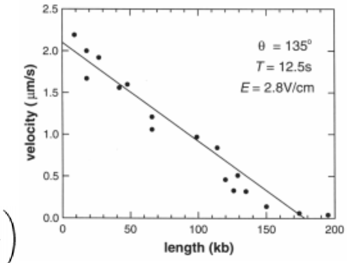
Advantages of arrays:

- regular motion → good resolution
- high fields → fast separation
- linear fractionation

$$v = v_0 \cos(\Theta/2)\left(1 - \frac{L}{L_{max}}\right)$$

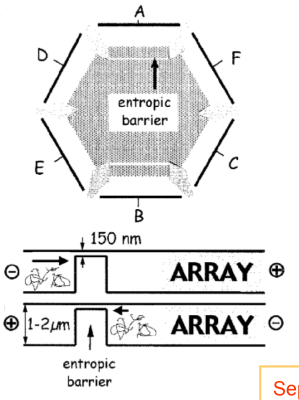
- straightforward recipe for choosing pulse parameters

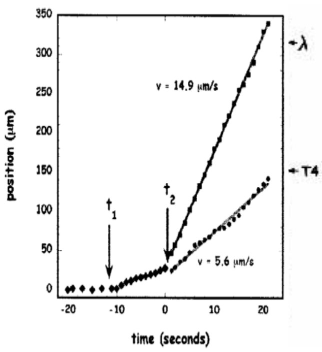
$$L_{max} = \left(\frac{T}{\tau_b}\right)\left(\frac{E}{E_b}\right) b$$



Pulsed-field hex arrays
ultra-fast separation

Bakajin et al. '01

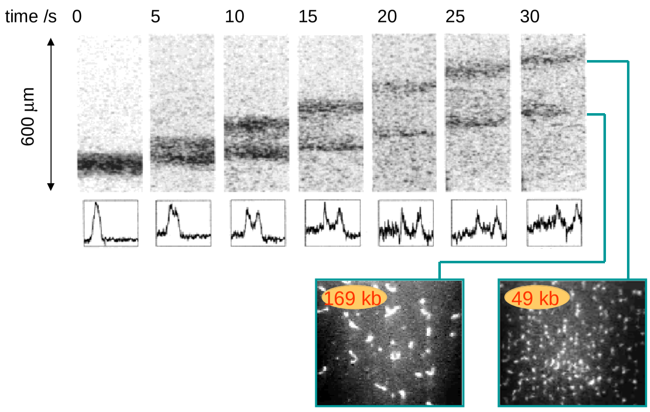




Separation of 100 kb DNA in 10 seconds!

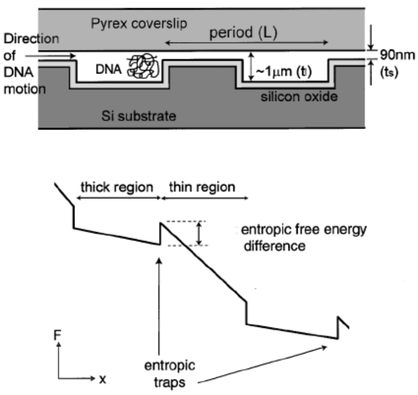
Pulsed-field hex arrays
ultra-fast separation

Bakajin et al. '01



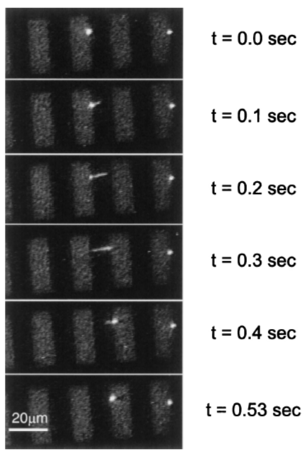
Entropic trapping

Han, Turner & Craighead '99



Entropic trapping

Han, Turner & Craighead '99

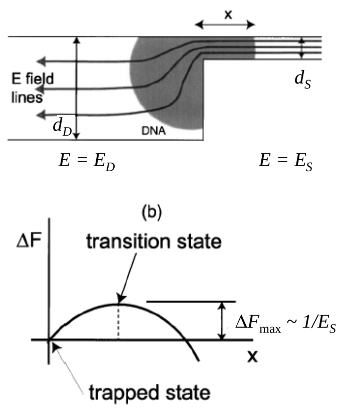


Entropic trapping
mobility

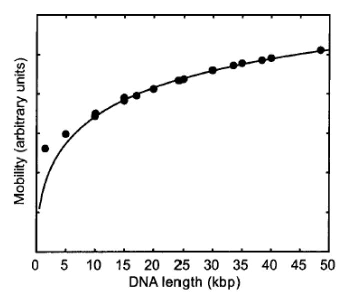
$$\frac{\mu}{\mu_0} = \frac{t_{travel}}{t_{travel} + t_{trap}}$$

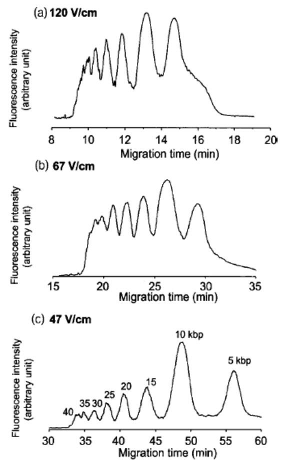
$$t_{travel} = \frac{L}{2}\left(\frac{1}{\mu_0 E_S} + \frac{1}{\mu_0 E_D}\right)$$

$$t_{trap} \sim \frac{1}{d_S N^{1/2}} \exp\left(\frac{\alpha}{E_S kT}\right)$$



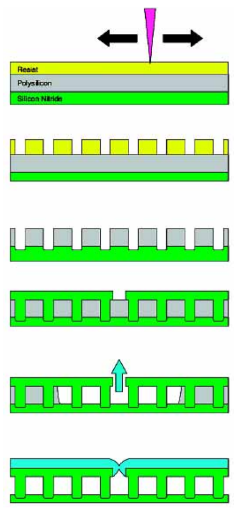
Entropic trapping
separation



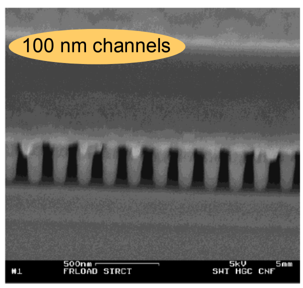


e-beam lithography

Cabodi, Turner & Craighead '02



'lost wax' process

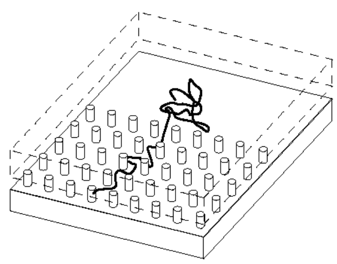


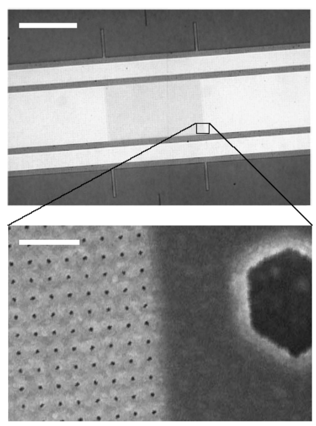
Dense array of posts

Turner, Cabodi & Craighead '02

DNA is entropically inhibited from entering forrest of posts…

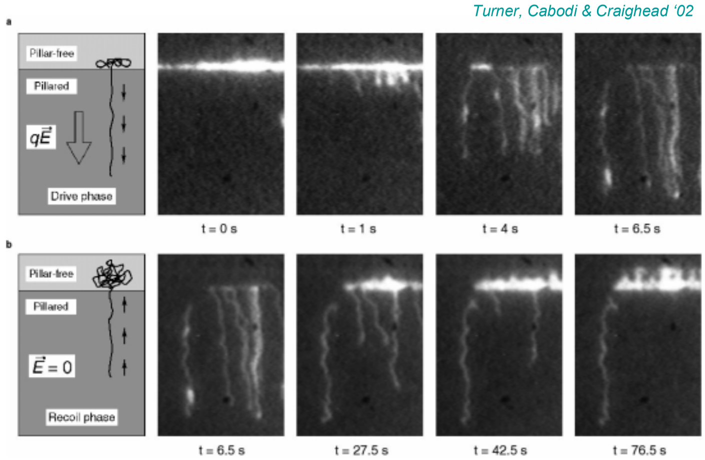
… but can be driven in by a high field





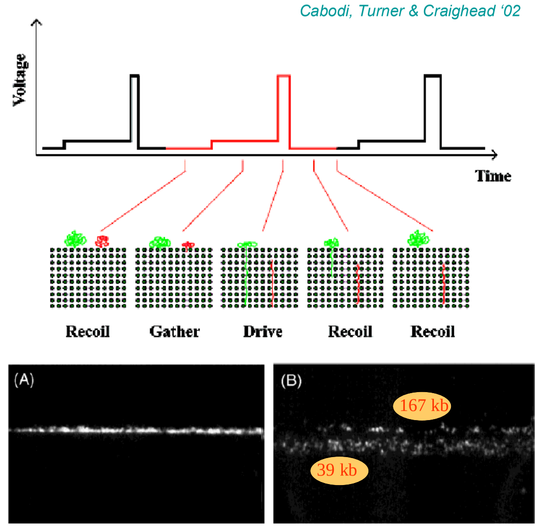
Entropic recoil

Turner, Cabodi & Craighead '02



Entropic recoil
separation

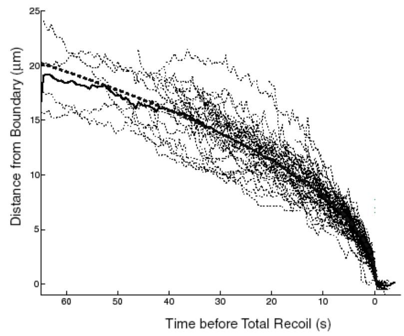
Cabodi, Turner & Craighead '02

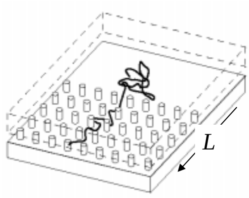


Entropic recoil
retraction time

Turner, Cabodi & Craighead '02

- constant retraction force
- friction proportional to unretracted length

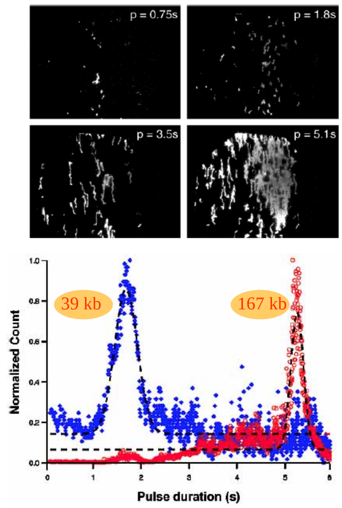




$$t_{retract} \sim L^2$$

Entropic recoil: pulse time ramp

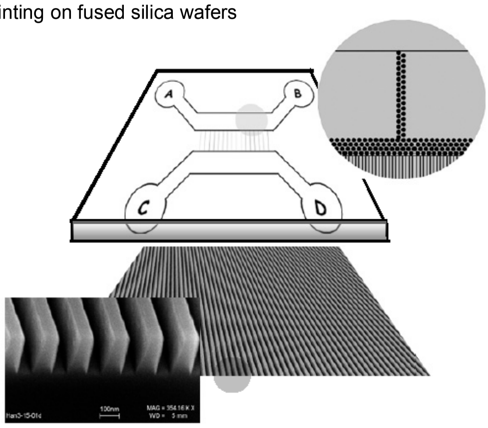
Cabodi, Turner & Craighead '02



Nanobottles

Tegenfeld et al. '04

Nanoimprinting on fused silica wafers

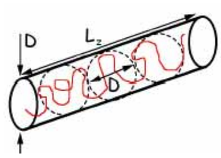


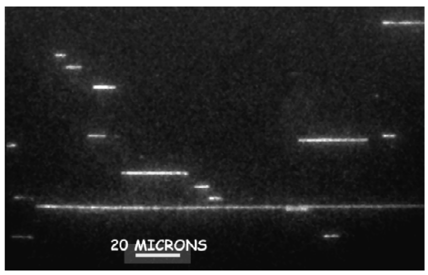
Nanobottles

Tegenfeldt et al. '04

DNA stretches due to self-avoidance

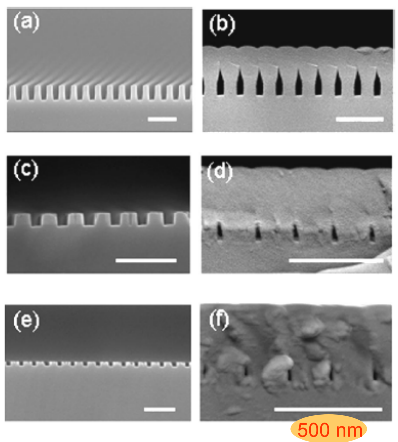
$$L_z \sim L\left(\frac{bd}{D^2}\right)^{1/3}$$





Nanobottles

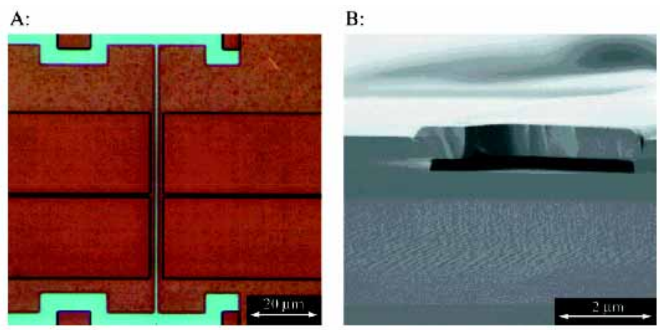
10 nm channels created by sputteting deposition



Optical sizer

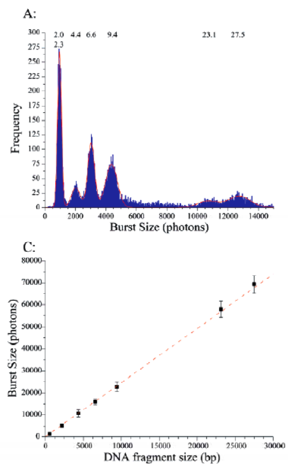
Foquet et al. '02; Chou et al. '99

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