



Introduction to Micro/Nanofluidics

- Reynold's number
- Diffusion
- Laminar flow
- Micromixer
- Microvalve
- Micropump
- Fluidic interfacing



Osborne Reynolds

1842 – 1912

Reynolds number:

$$\text{Re} = \frac{\textit{inertial forces}}{\textit{viscous forces}}$$



Osborne Reynolds in 1903



Claude-Louis Navier
French, 1785 – 1836



Sir George Gabriel Stokes
British, 1819-1903

Navier-Stokes Equation for Newtonian fluid:

$$\rho \left[\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} \right] = \eta \nabla^2 \mathbf{v} - \nabla p.$$

$$Re = \frac{\rho v_s^2 / L}{\eta v_s / L^2} = \frac{\rho v_s L}{\eta} = \frac{v_s L}{\nu} = \frac{\text{Inertial forces}}{\text{Viscous forces}}$$

v_s : the mean fluid velocity (SI units: m/s)

L : a length of the object that the flow is going through or around (m)

η : the dynamic viscosity of the fluid (Pa·s or N·s/m² or kg/m/s)

ν : the kinematic viscosity ($\nu = \eta / \rho$) (m²/s)

ρ : the density of the fluid (kg/m³)



D_H : *hydraulic diameter*

$$D_H = \frac{4A}{P}$$

For pipe flow:

For water, $\eta = 0.01 \text{ g/cm/s}$

$D_H \text{ (}\mu\text{m)}$	$v_s \text{ (cm/s)}$	$\text{Re } (D_H v_s / \nu)$
100	0.1	0.1
	100	100
200	0.1	0.2
	100	200
500	0.1	0.5
	100	500



Typical values of Reynolds number:

- * Spermatozoa $\sim 1 \times 10^{-2}$
- * Blood flow in brain $\sim 1 \times 10^2$
- * Blood flow in aorta (vein) $\sim 1 \times 10^3$

Onset of turbulent flow $\sim 2.3 \times 10^3$ for pipe flow to 10^6 for boundary layers:

- * Typical pitch in Major League Baseball $\sim 2 \times 10^5$
- * Person swimming $\sim 4 \times 10^6$
- * Blue whale $\sim 3 \times 10^8$
- * A large ship (RMS Queen Elizabeth 2) $\sim 5 \times 10^9$

Poiseuille flow

We'll start with the flow of a viscous fluid in a channel. The channel has a width in the y -direction of a , a length in the z -direction of l_z , and a length in the x -direction, the direction of flow, of l_x . There is a pressure drop along the length of the channel, so that the constant pressure gradient is $-\Delta p/l_x$ (such a pressure gradient could be supplied by gravity, for instance). Assuming the flow to be steady, $\partial \mathbf{v} / \partial t = 0$. Also, we'll assume that the flow is of the form $\mathbf{v} = v_x(y) \hat{x}$; then $\nabla \cdot \mathbf{v} = 0$. The no-slip boundary condition at the top and bottom edges of the channel reads $v_x(y = \pm a/2) = 0$. The Navier-Stokes equation then becomes

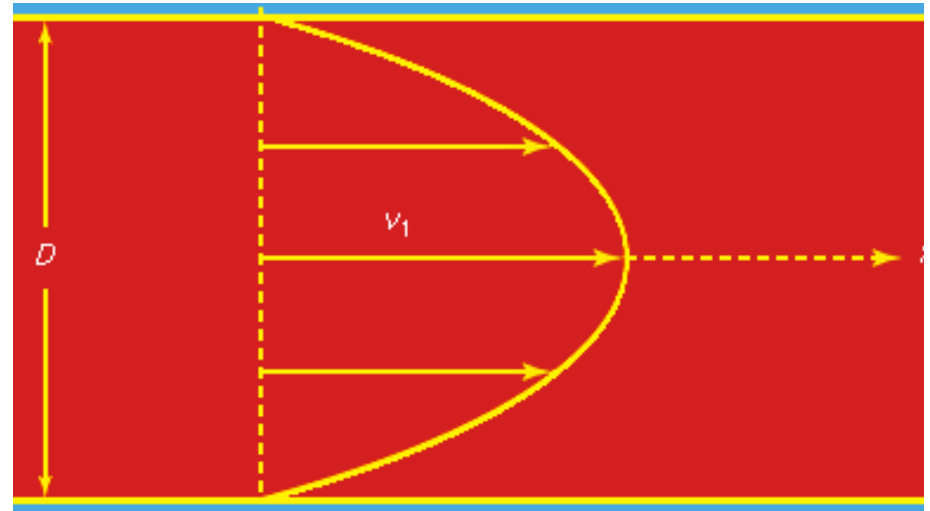
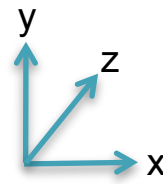
$$\eta \frac{\partial^2 v_x}{\partial y^2} + \frac{\Delta p}{l_x} = 0. \quad (3.14)$$

Integrating twice, we obtain

$$v_x(y) = -\frac{1}{2\eta} \frac{\Delta p}{l_x} y^2 + C_1 y + C_2, \quad (3.15)$$

where C_1 and C_2 are integration constants. To determine these, we impose the boundary conditions to obtain

$$v_x(y) = \frac{1}{2\eta} \frac{\Delta p}{l_x} \left[\left(\frac{a}{2} \right)^2 - y^2 \right]. \quad (3.16)$$



We see that the velocity profile is a parabola, with the fluid in the center of the channel having the greatest speed. Once we know the velocity profile we can determine the flow rate Q , defined as the volume of fluid which passes a cross section of the channel per unit time. This is obtained by integrating the velocity profile over the cross sectional area of the channel:

$$\begin{aligned} Q &= \int_0^{l_x} dz \int_{-a/2}^{a/2} dy v_x(y) \\ &= \frac{l_x a^3 \Delta p}{12\eta l_x}. \end{aligned} \quad (3.17)$$

The analogous result for flow through a pipe of radius a and length l in the presence of a uniform pressure gradient $\Delta p/l$ is

$$Q = \frac{\pi a^4 \Delta p}{8\eta l}. \quad (3.18)$$

Hydrodynamic resistance:

$$Z = p/Q = 8 \eta l / \pi a^4$$

Recall Ohm's law: $R = V/I$

The important feature of both of these results is the sensitive dependence upon either the channel width a or the pipe radius a . For instance, for a pipe with a fixed pressure gradient, a 20% reduction in the pipe radius leads to a 60% reduction of the flow rate! This clearly has important physiological implications -- small amounts of plaque accumulation in arteries can lead to very large reductions in the rate of blood flow.



Life at Low Reynolds Number

E.M. Purcell

Lyman Laboratory, Harvard University, Cambridge, Mass 02138

June 1976

American Journal of Physics vol 45, pages 3-11, 1977.



$$\eta = 1 \text{ centipoise} \quad \nu = 10^{-2} \text{ cm}^2/\text{sec}$$

$$R = 3 \times 10^{-5}$$

$$\left\{ \begin{array}{l} \text{coasting distance} \approx 0.1 \text{ \AA} \\ \text{coasting time} \approx 0.3 \text{ microsec.} \end{array} \right\}$$

Figure 4

Laminar Flow-movies



Laminar Flow-3 colors



ASU
ANBC



Diffusion

Diffusion is of fundamental importance in many disciplines of physics, chemistry, and biology.

Diffusion is of fundamental importance in many disciplines of physics, chemistry, and biology. Some example applications of diffusion:

- Sintering to produce solid materials (powder metallurgy, production of ceramics)
- Chemical reactor design
- Catalyst design in chemical industry
- Steel can be diffused (e.g., with carbon or nitrogen) to modify its properties
- Doping during production of semiconductors.

In cell biology, **diffusion** is a main form of transport for necessary materials such as amino acids within cells. Diffusion (eg. of water) through a semipermeable membrane is classified as **osmosis**.



Diffusion

$$\langle x^2 \rangle = 2Dt \quad \text{in 1-D}$$

$$\langle x^2 \rangle = 4Dt \quad \text{in 2-D}$$

$$\langle x^2 \rangle = 6Dt \quad \text{in 3-D}$$

Anomalous diffusion

$$\langle x^2 \rangle = 2Dt^\alpha \quad \text{in 1-D:}$$

$\alpha > 1$, super diffusion

$\alpha < 1$, sub-diffusion



Stokes formula:

Frictional force: $f = \xi v = 6\pi\eta a v$

$\xi = 6\pi\eta a$: frictional coefficient of a particle

η : fluid's viscosity (in $[\text{kg m}^{-1} \text{s}^{-1}]$)

a : the radius of the spherical object (in m)

v : the particle's velocity (in m/s)

Einstein relation: $\xi D = k_B T$



Fick's equation for diffusion

$$\text{Flux: } J(x,t) = -D \text{ grad } C(x,t)$$

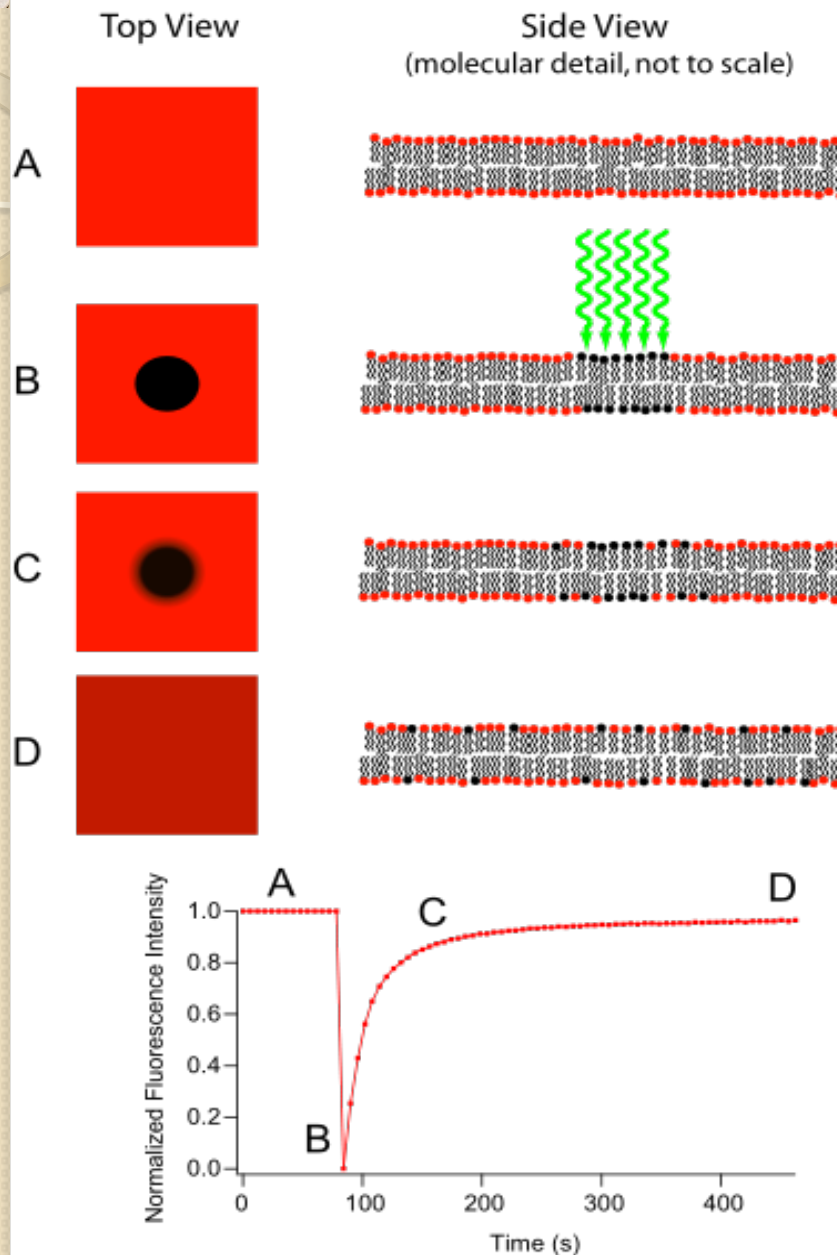
Fick's equation for diffusion with drift

$$\text{Flux: } J(x,t) = v C(x,t) - D \text{ grad } C(x,t)$$

Diffusion Equation:

$$dC(x,t)/dt = D \text{ grad}^2 C(x,t)$$

Principle of FRAP (Fluorescence Recovery After Photobleaching)



- A. The bilayer is uniformly labeled with a fluorescent tag.
- B. This label is selectively photobleached by a small (~30 micrometre) fast light pulse.
- C. The intensity within this bleached area is monitored as the bleached dye diffuses out and new dye diffuses in
- D. Uniform intensity is restored

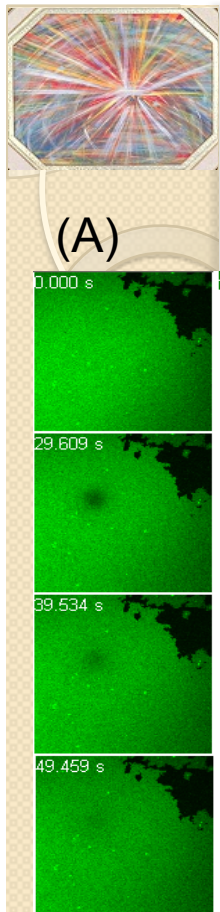
Assuming a Gaussian profile for the bleaching beam, the diffusion constant D can be simply calculated from:

$$D = \frac{w^2}{4t_{1/2}}$$

where w is the width of the beam and $t_{1/2}$ is the time required for the bleach spot to recover half of its initial intensity.

FRAP analysis

(Fluorescence Recovery After Photobleaching)

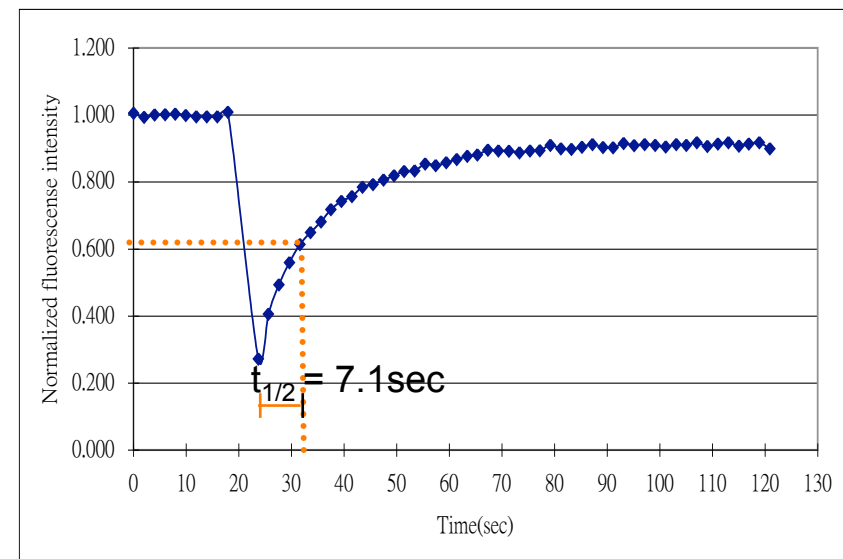


FRAP analysis on formation of a supported lipid bilayer. We used *E. coli* polar lipids to form a supported lipid bilayer on a clean glass surface. A region of interest (ROI; red arrow) was selected for photobleaching. Averaged fluorescence intensity was measured for ROI, total fluorescent area, and background area for estimating mobility of phospholipids in the supported bilayer. (A) A time series of an FRAP analysis, (B) Graph of fluorescence changes plotted using normalized fluorescence intensity from the time series shown in (A).

Purpose:

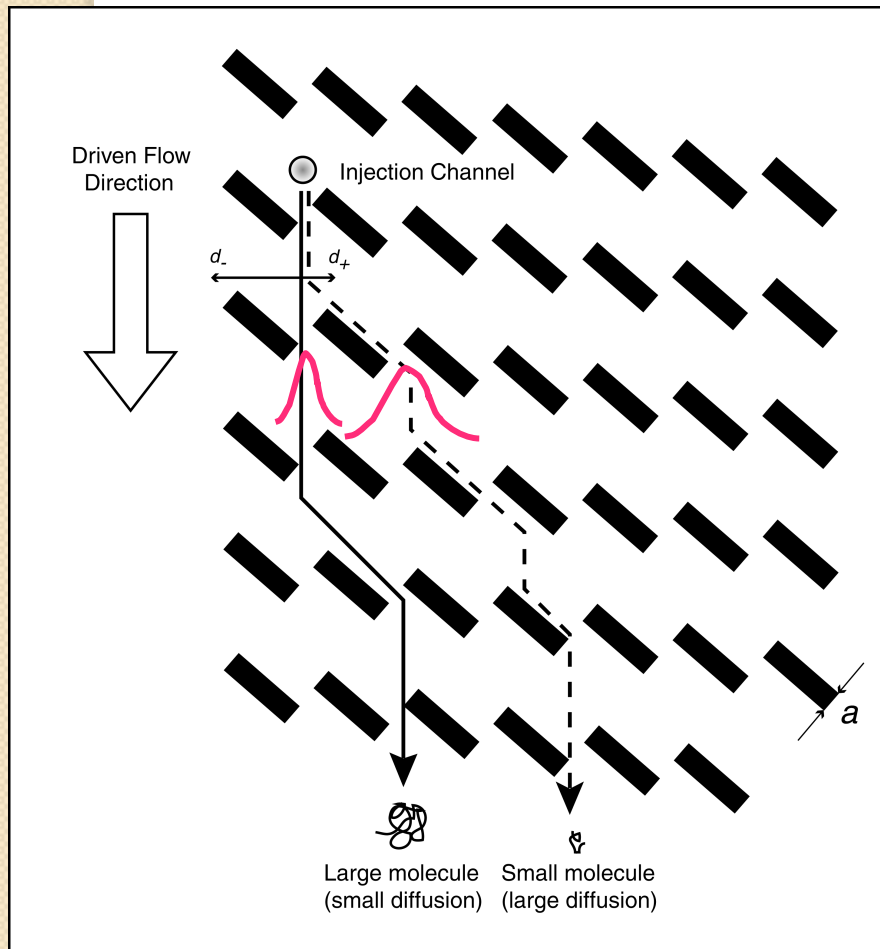
1. Validate the integrity of lipid bilayer
2. Calculate the diffusion constant

(B)



Courtesy Dr. YL Shih

Separation based on Rectified Brownian Motion

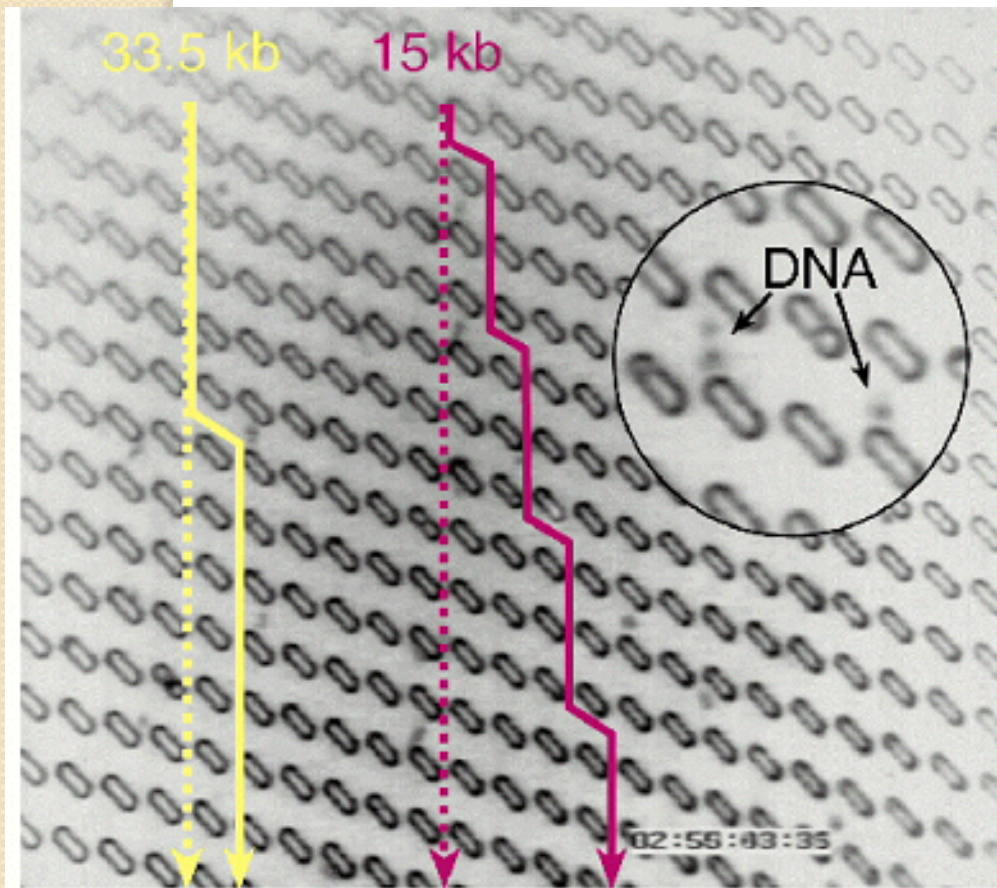


A simple idea: let the altered probabilities effectively move molecules to one side
— Rectified Brownian motion

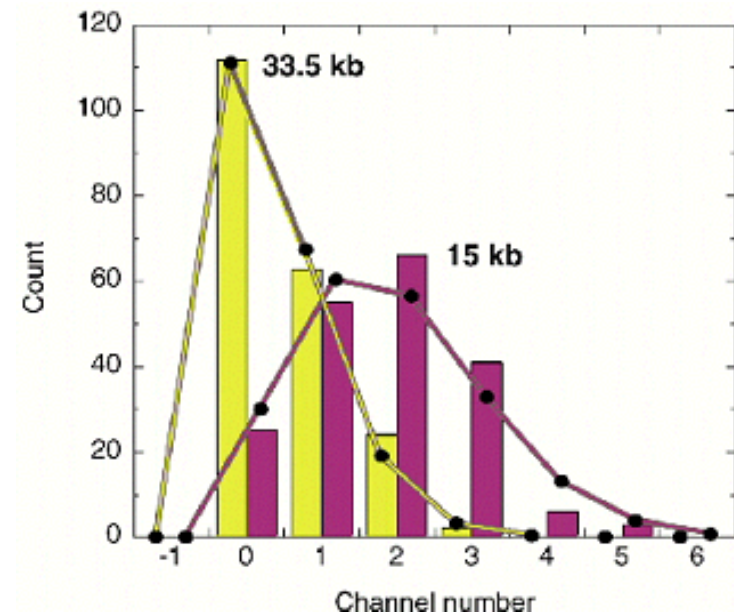
Duke and Austin, *PRL* (1998)
Ertas, *PRL* (1998)

Continuous molecular sorting by rectified Brownian motion

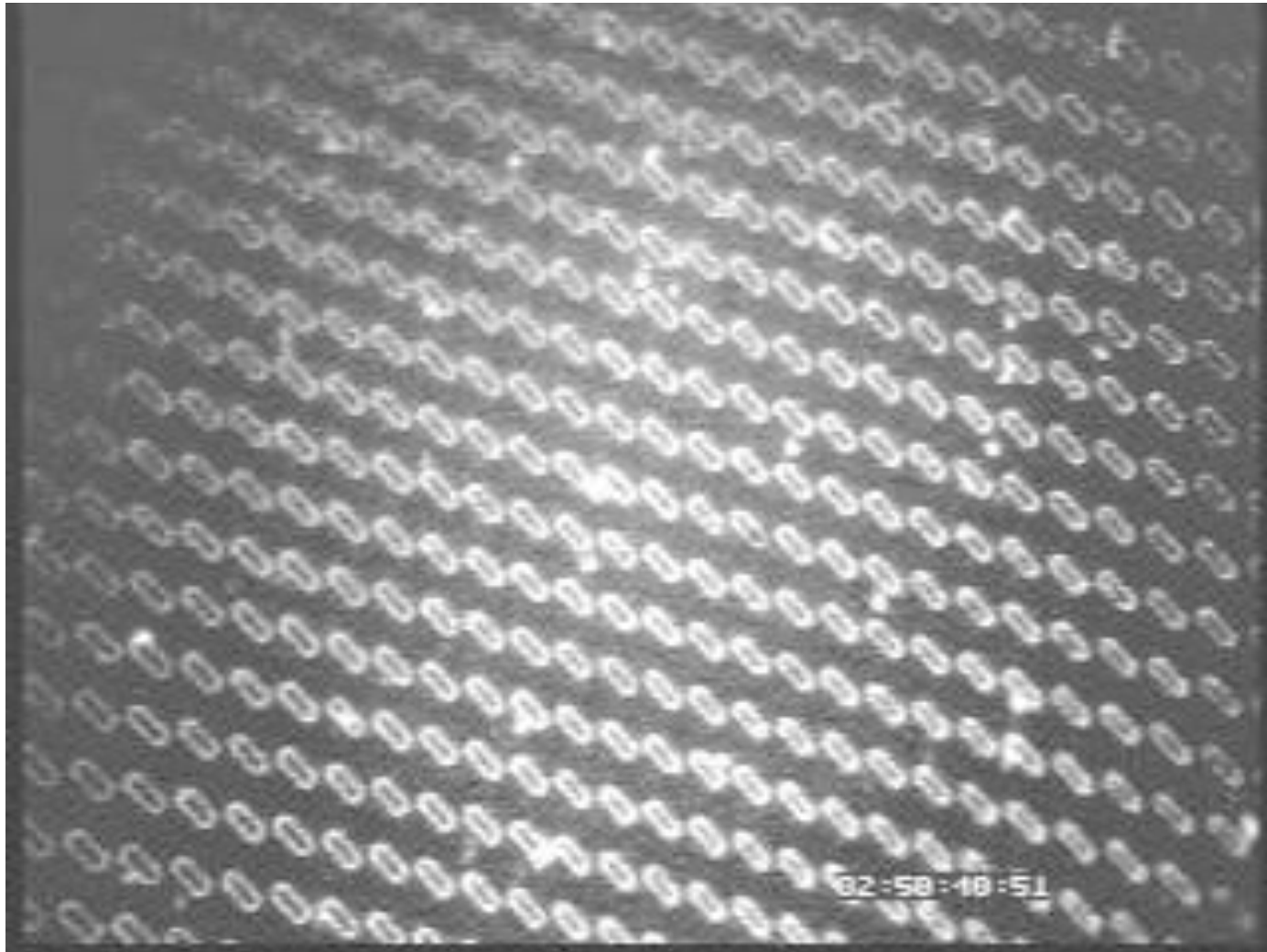
Continuous Lateral Separation



Chou et al, *PNAS* (1999)

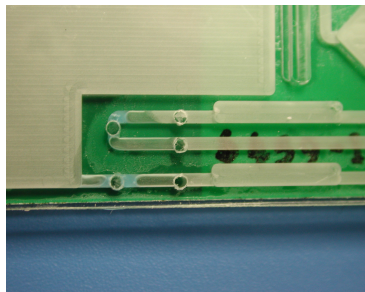
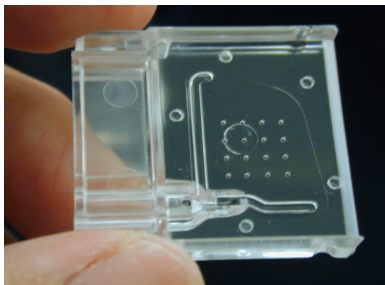
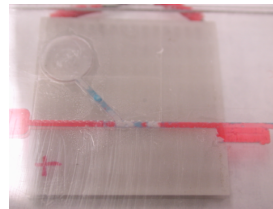
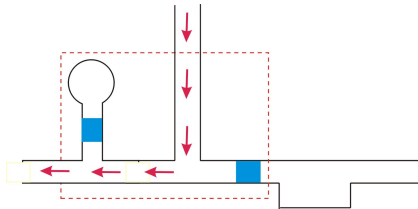


Continuous DNA sorting by rectified Brownian motion

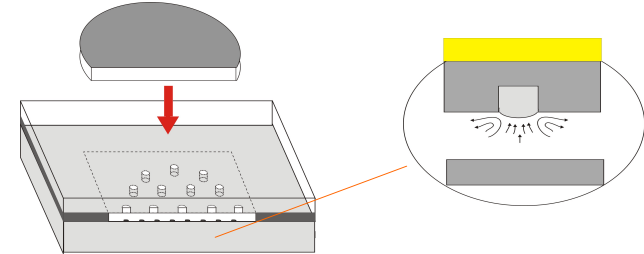


Microfluidic Components

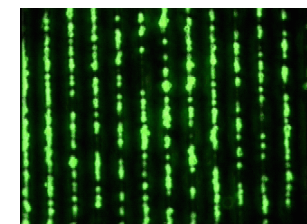
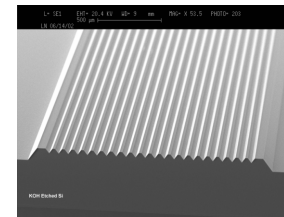
Microvalves (paraffin, pluronics)



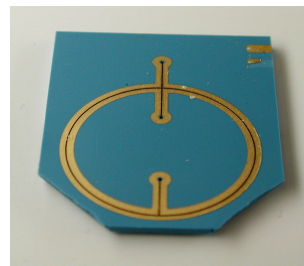
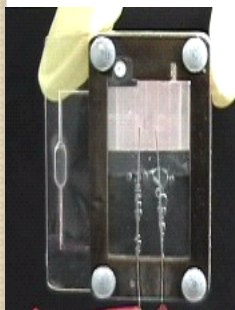
Piezoelectric mixing



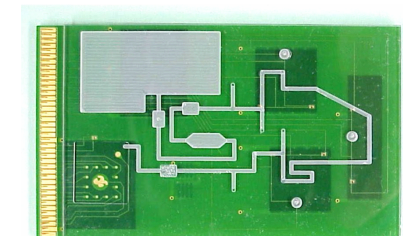
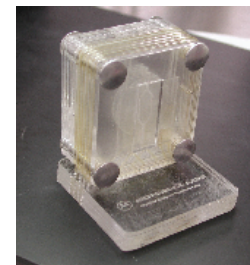
Rare target capture Localization of magnetic gradient



Electrochemical & MHD pumps

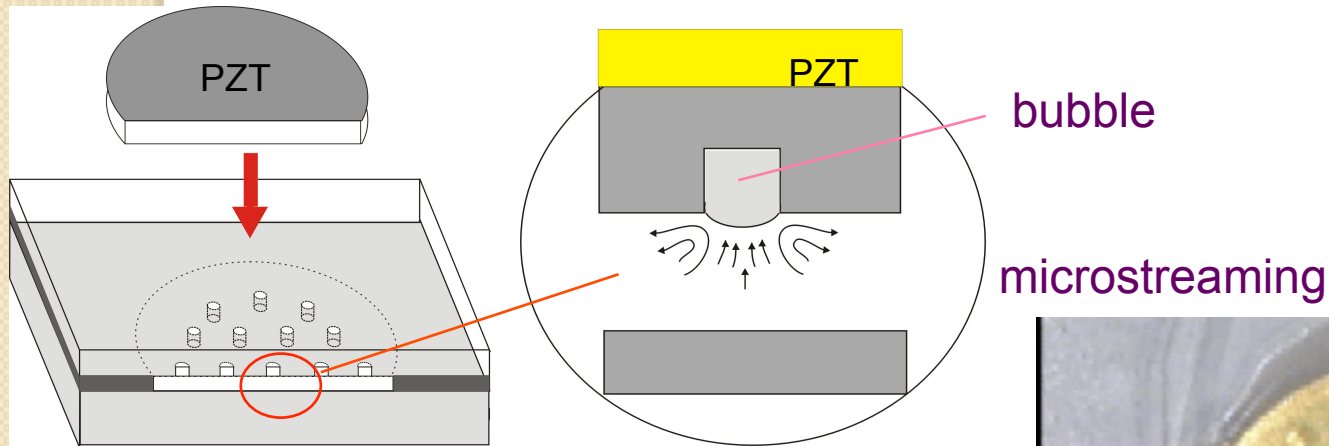


Stacked sample prep module



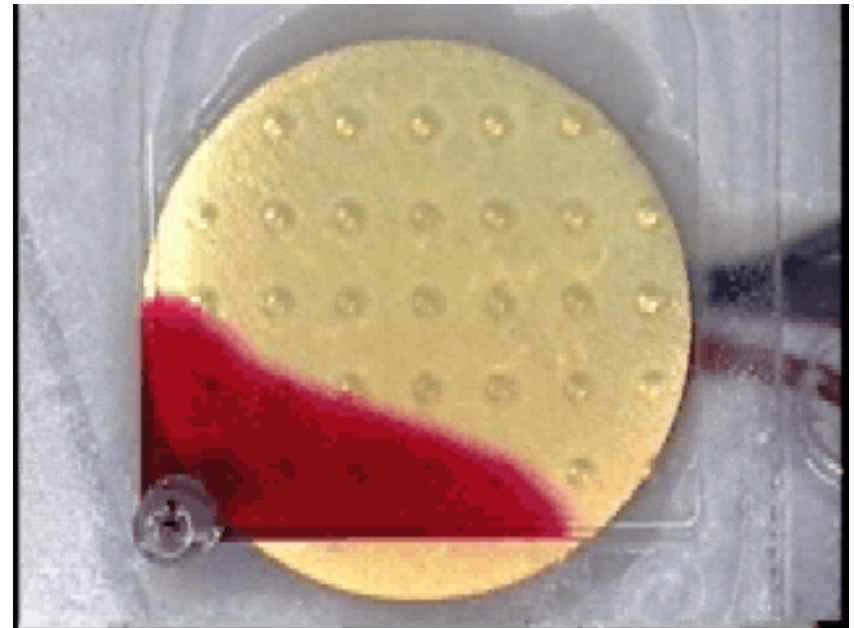
Micromixer: Cavitation Microstreaming

- Flow streaming around bubbles in an acoustic field
- Optimized mixing conditions (waveform, amplitude, etc.)

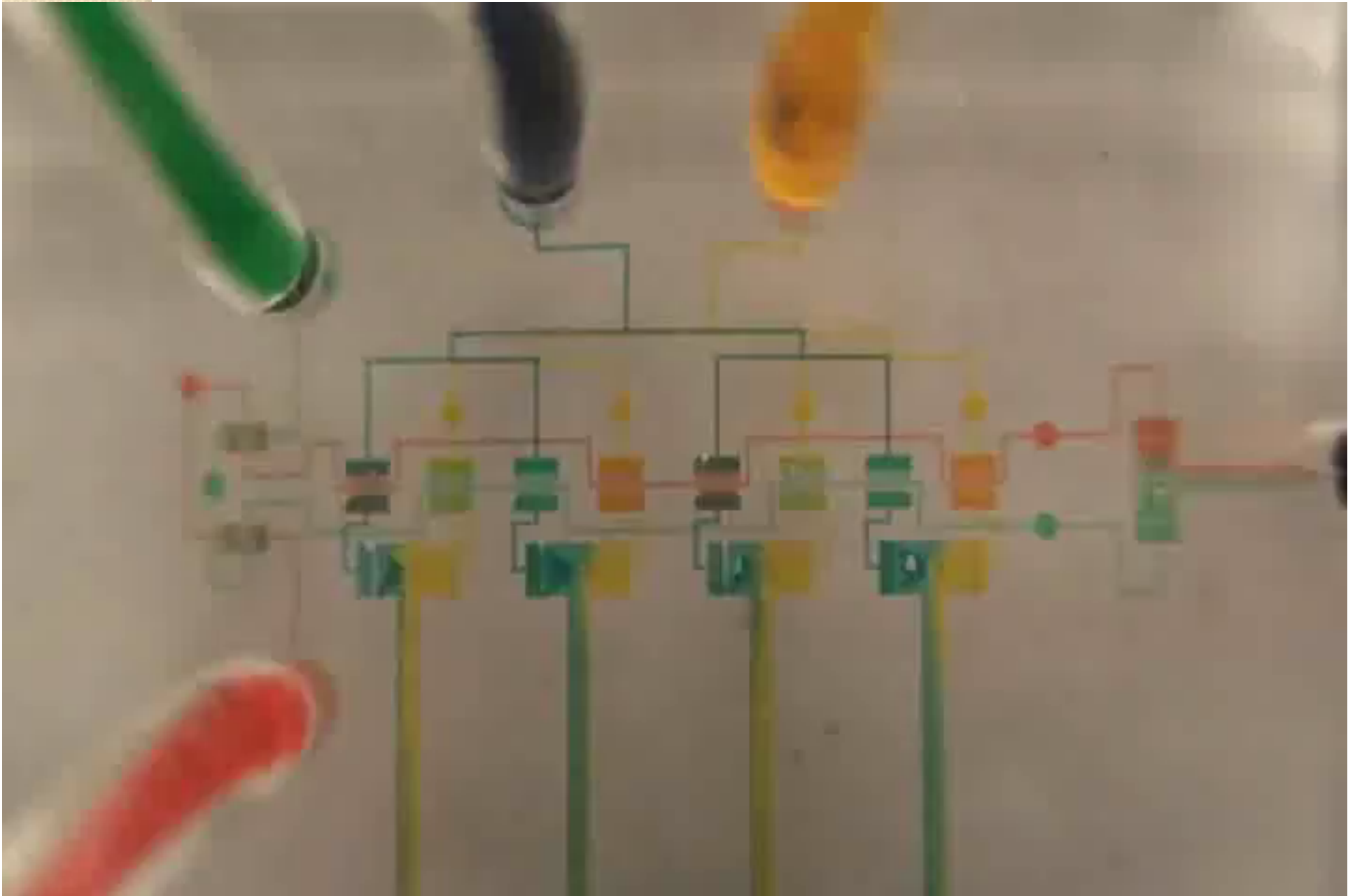


$$f = \frac{\sqrt{3\gamma P_o / \rho}}{2\pi a}$$

R. Liu *et al.*, Anal. Chem. 2003

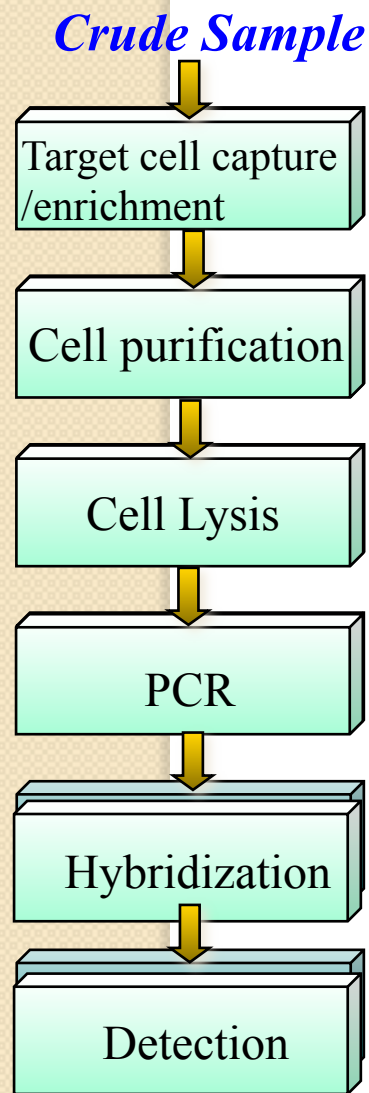


Now (10 sec for 100 uL)
5 kHz, 40 Vpp, square wave

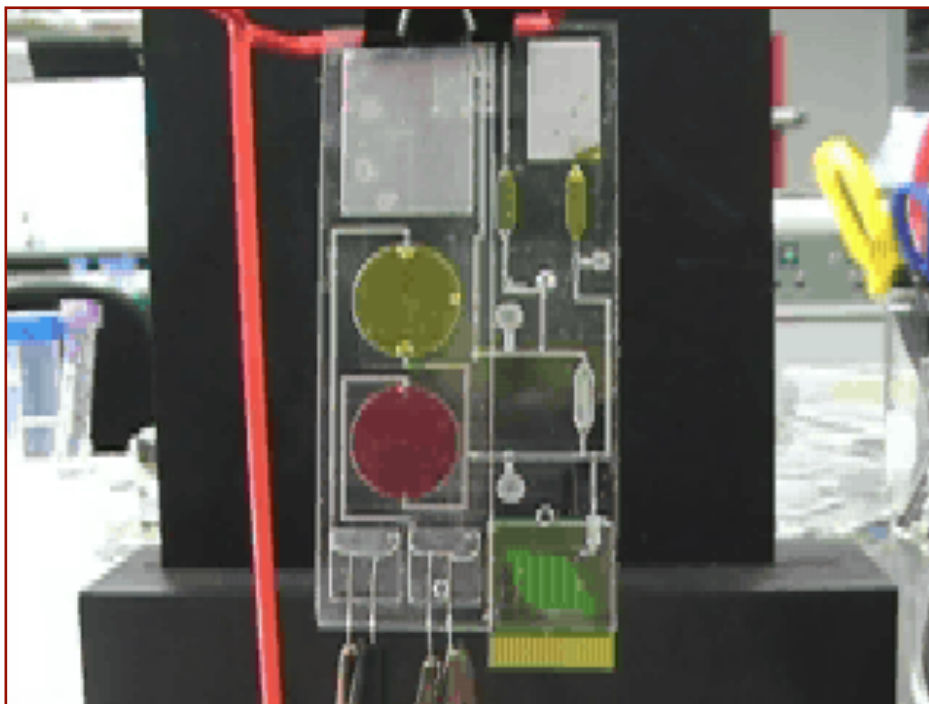


Integrated cartridge for low abundance bacteria detection

Objective: Integrate whole sample prep with microarray for low abundance bacteria detection from blood (1 mL)



Answer



Successfully demonstrated cell capture + purification + lysis + PCR + detection of 1000 *E. coli* K12 cells / 1mL sheep blood

Liu RH, Yang JN, et al. ANAL. CHEM. 76, 1824 (2004)

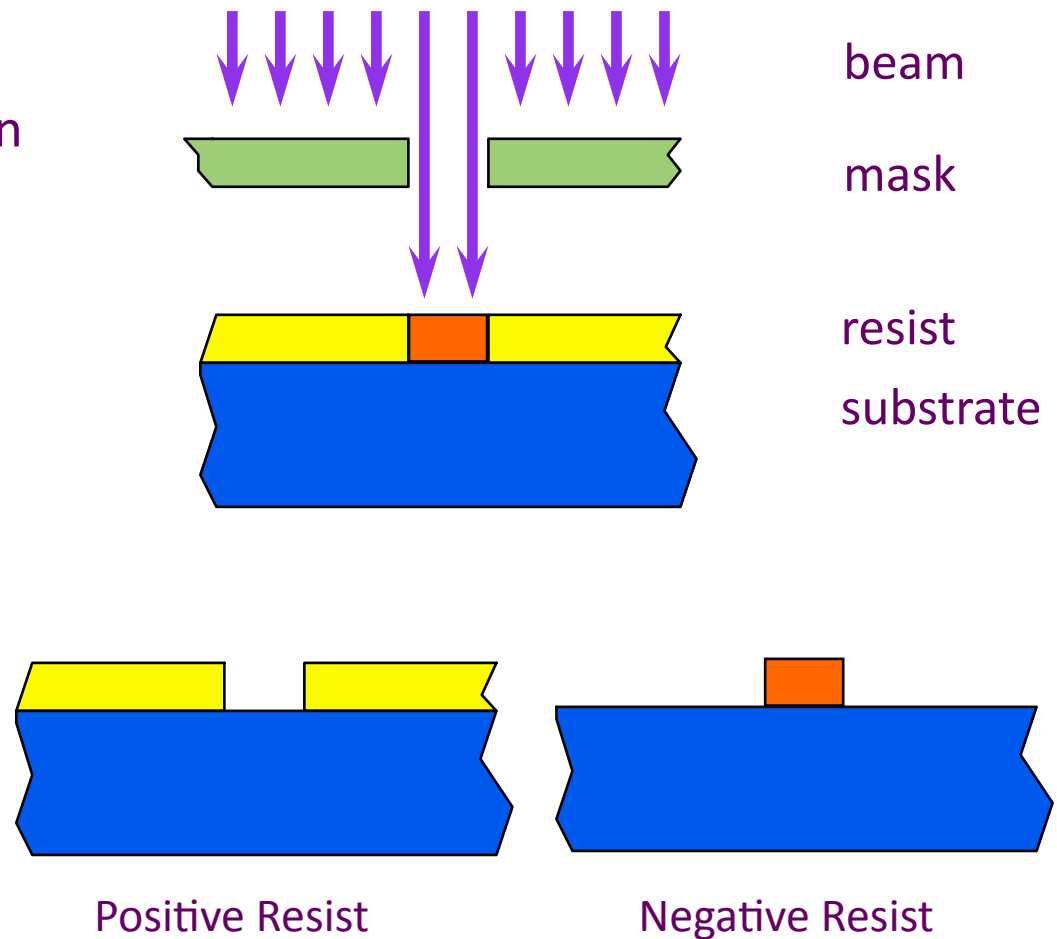
Principles of Traditional Lithography

Principle:

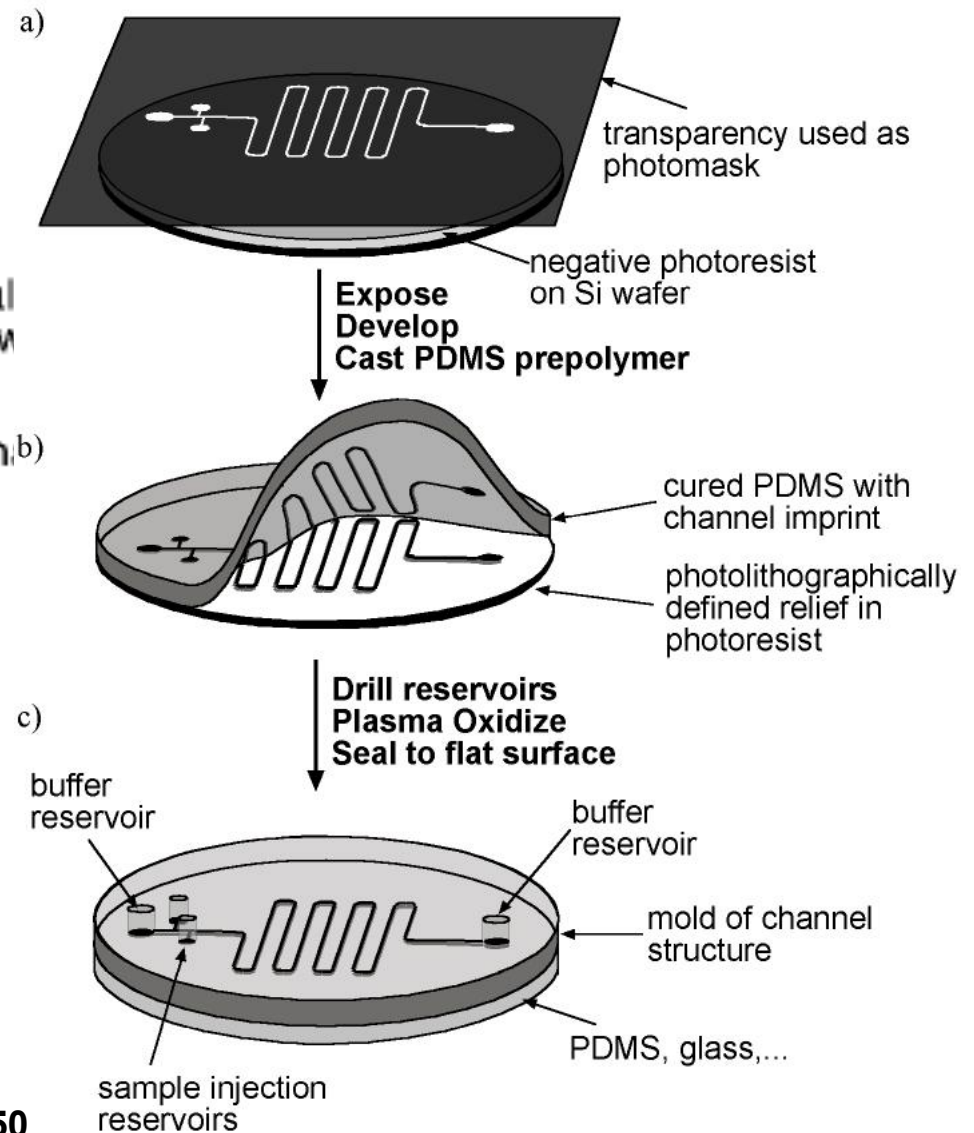
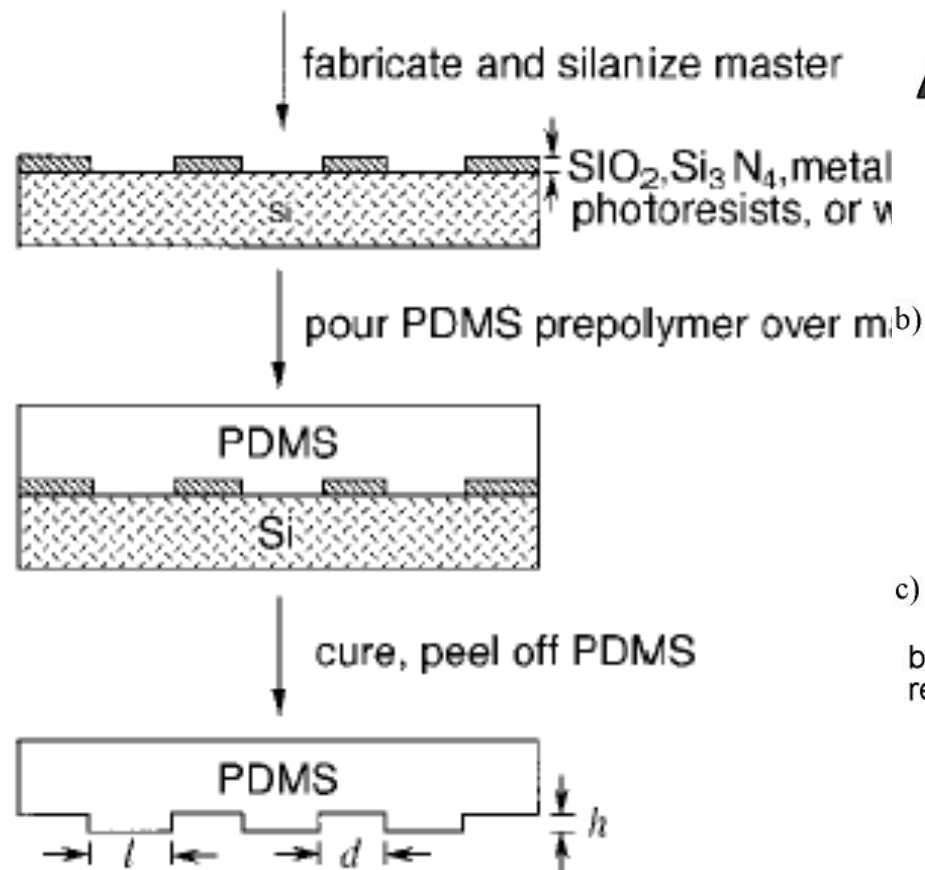
Change solubility using radiation

Factors limiting resolution:

- Diffraction limit
 $\lambda / 2NA \approx 0.5 \text{ wavelength}$
- Beam spot size
(for scanning tools)
- Scattering in resists
- Backscattering
- Resist properties
- Developer chemistry

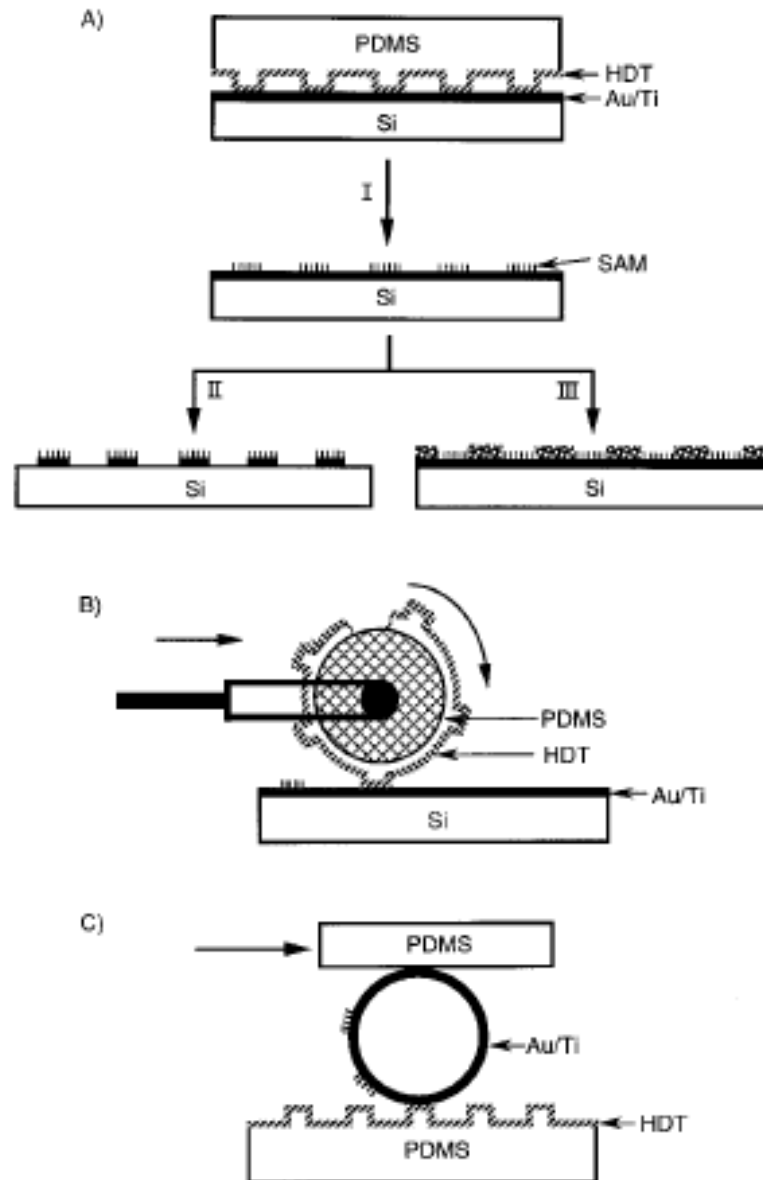


Soft Lithography



Xie, Whitesides, Angew. Chem. Int. Ed. 1998, 37, 550

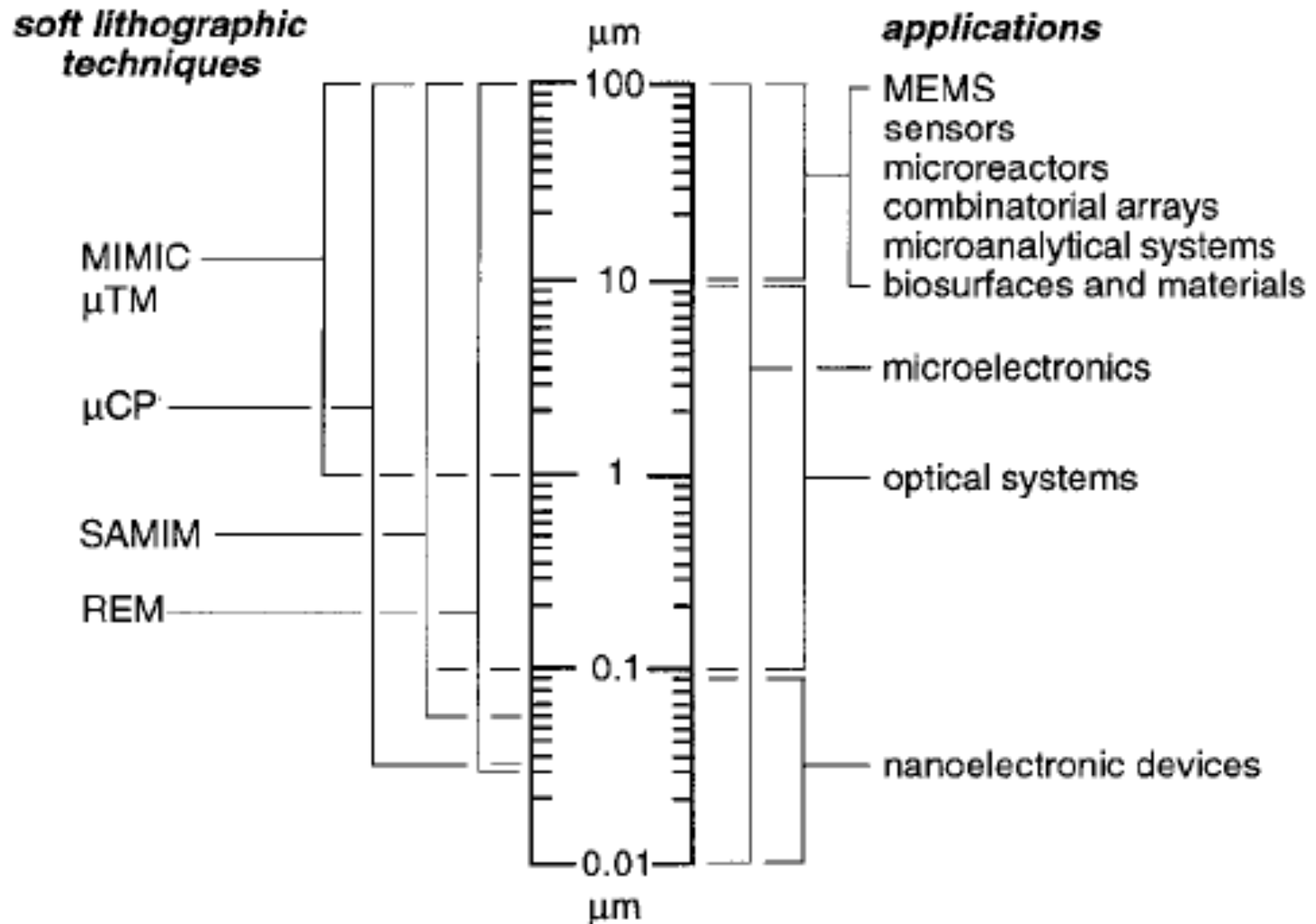
Micro-contact printing



Procedures for μ CP of hexadecanethiol (HDT) on a gold surface:

- A) printing on a planar surface with a planar stamp (I: printing of the SAM, II: etching, III: deposition)
- B) large-area printing on a planar surface with a rolling stamp
- C) printing on a nonplanar surface with a planar stamp

Applications of Soft Lithography

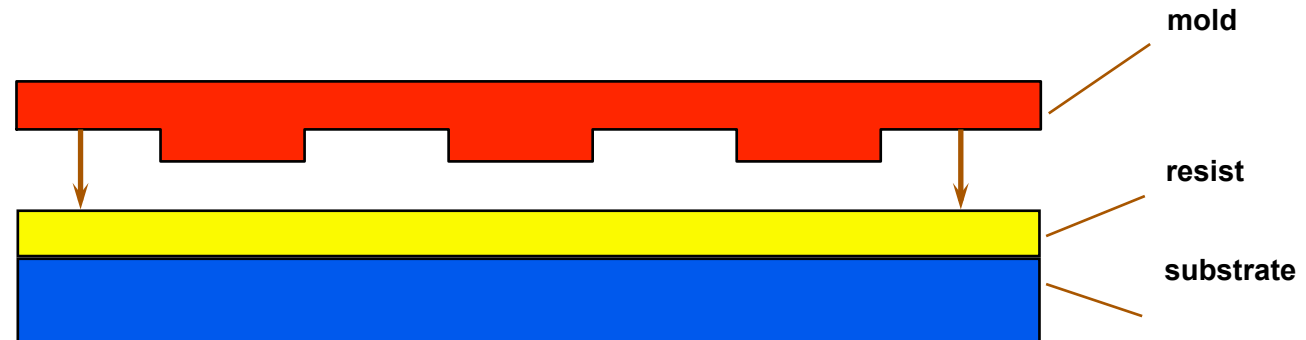




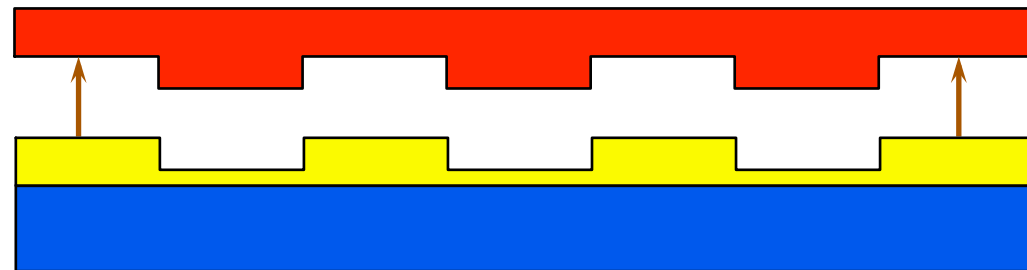
Nanoimprint Lithography

1. Imprint

- Press Mold



- Remove Mold



2. Pattern Transfer

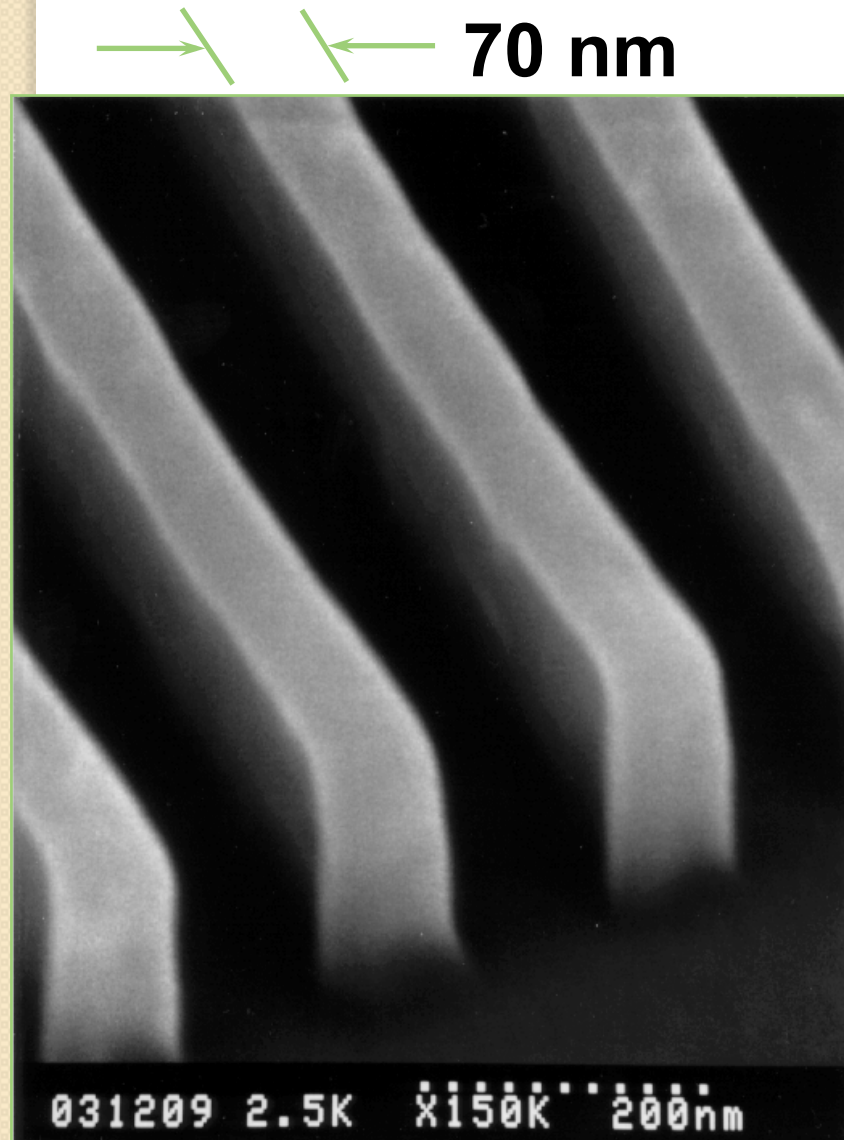
- RIE



Chou, Krauss, and Renstrom, APL, Vol. 67, 3114 (1995); Science, Vol. 272, 85 (1996)

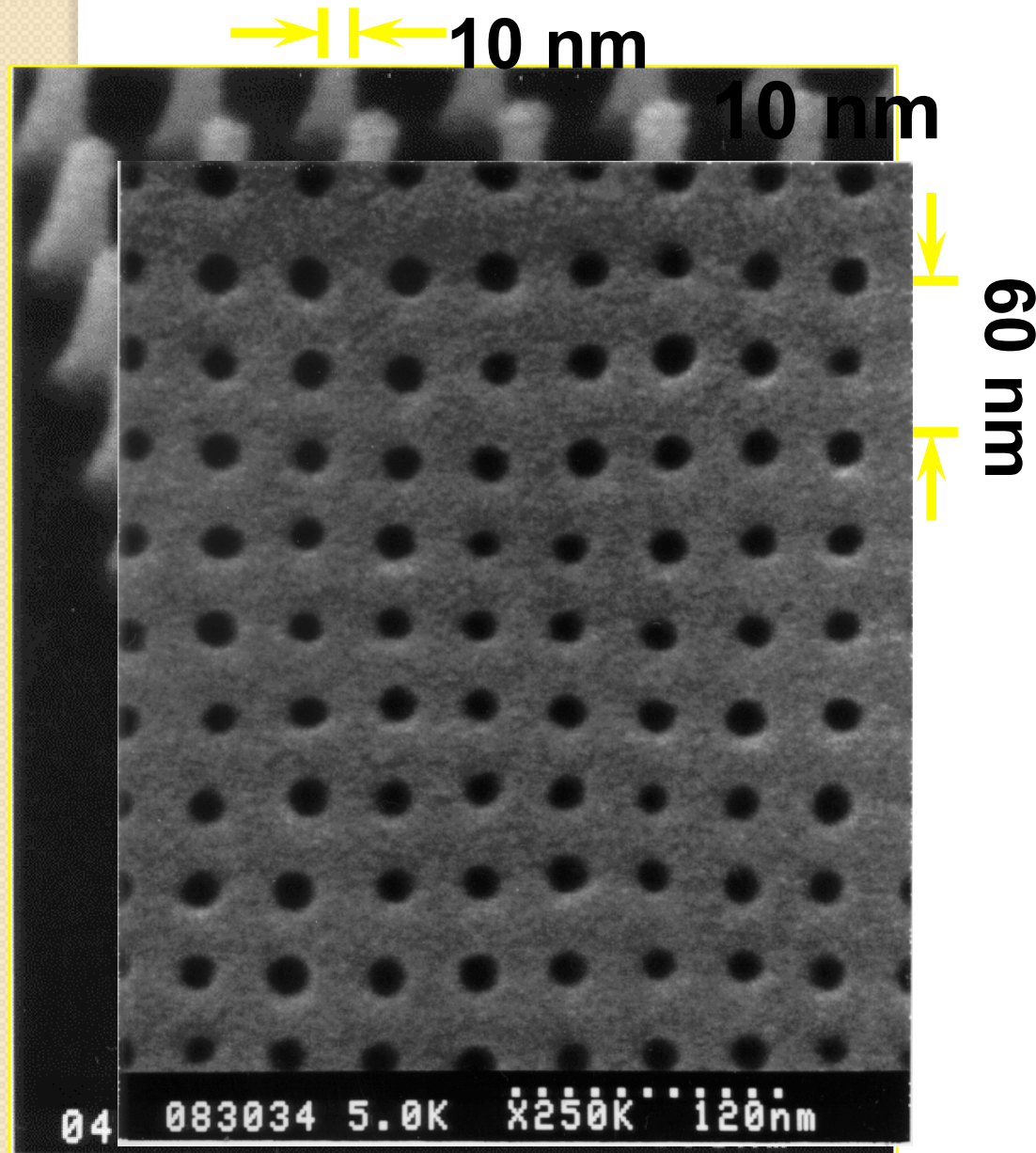
Imprinting–Footprint on the moon





- Nanoimprinted 70 nm wide PMMA lines
- Smooth sidewalls and 90° corners
- Pattern conformal to mold, mold surface variation reproduced in PMMA

S. Y. Chou, et al. "Sub-10 nm imprint lithography and applications," *J. Vac. Sci. Technol. B*, Vol. 15, 2897, 1997.

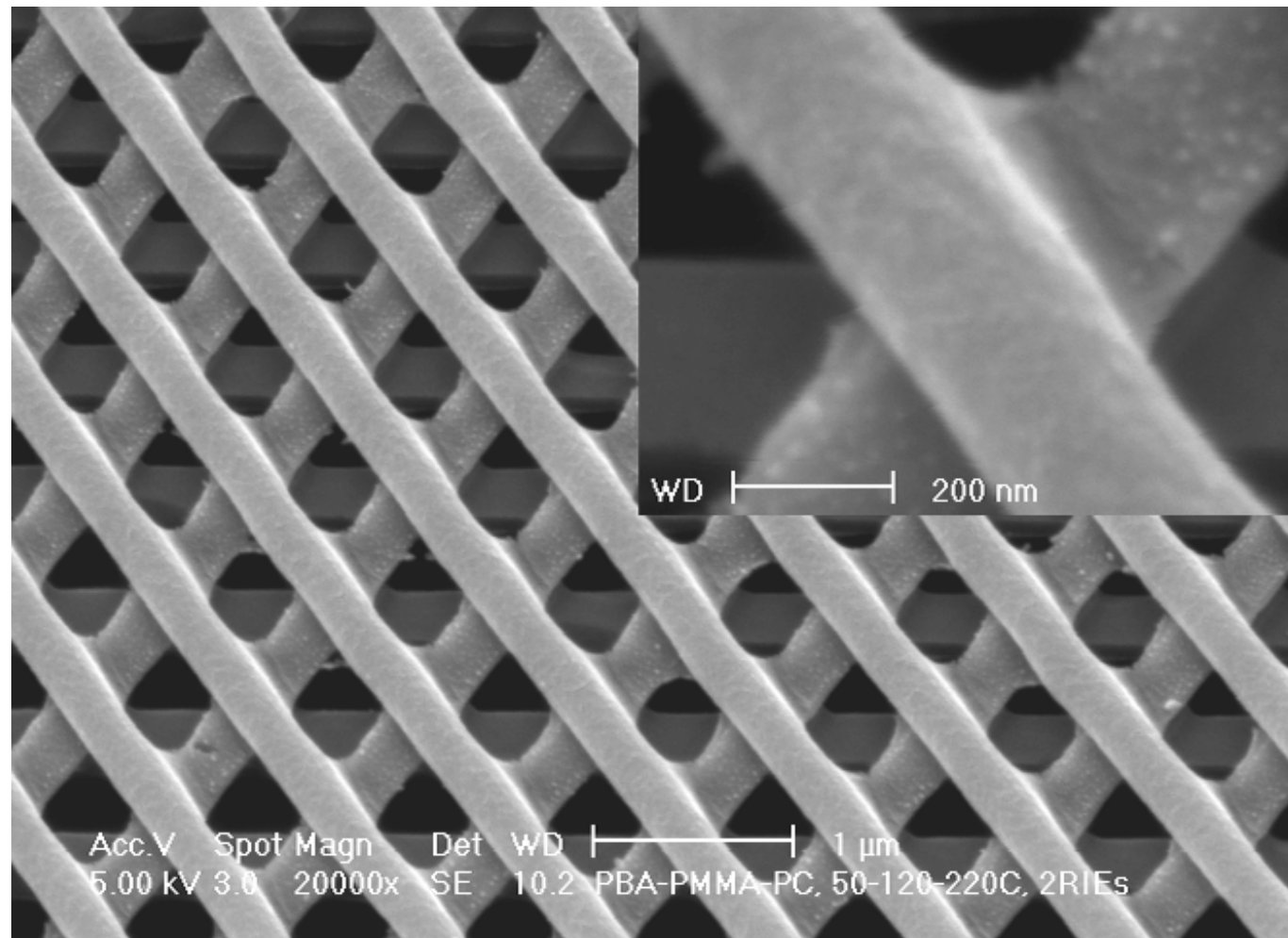


- Nanoimprinted hole arrays in PMMA
- 10 nm diameter, 40 nm period, and 60 nm deep

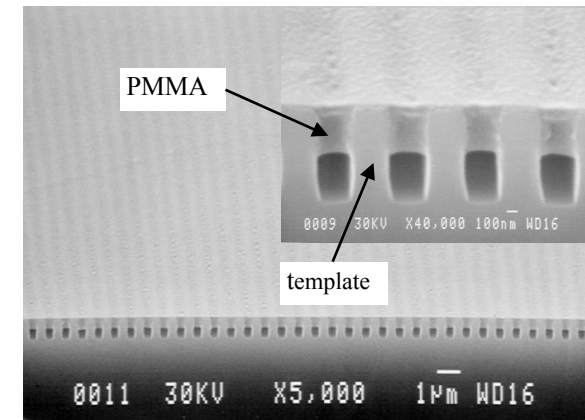
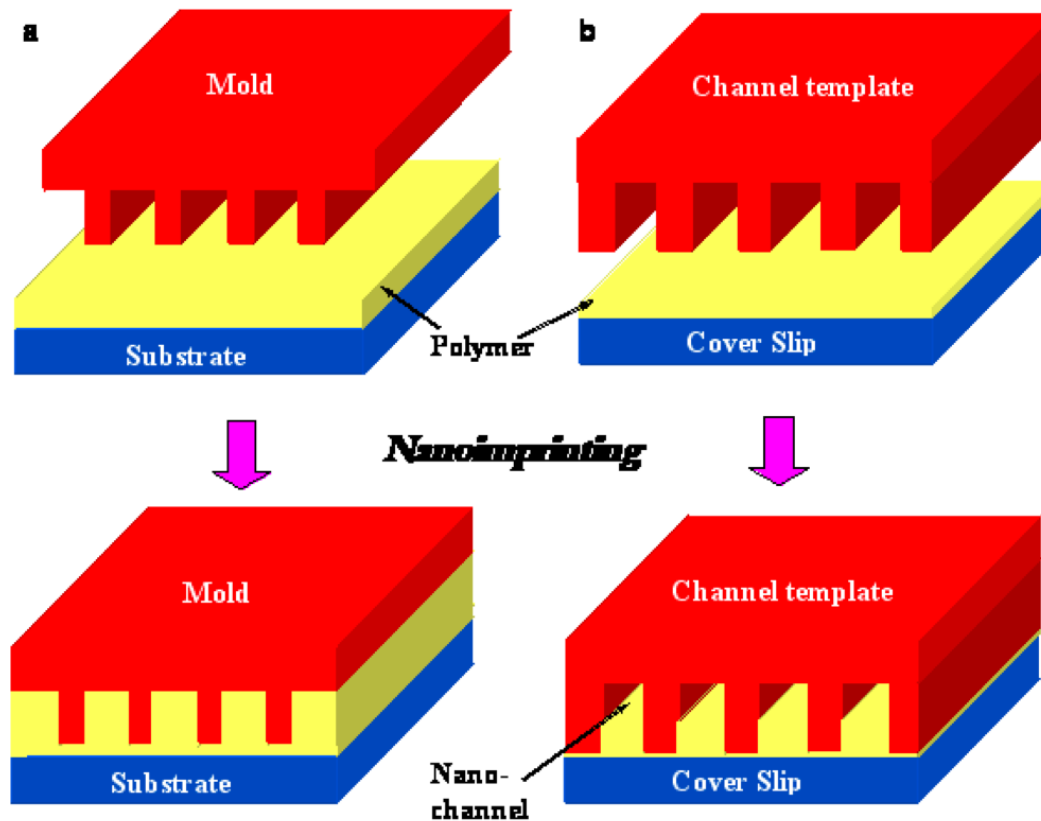
S. Y. Chou, et al.
J. Vac. Sci. Technol. B,
Vol. 15, 2897, 1997.



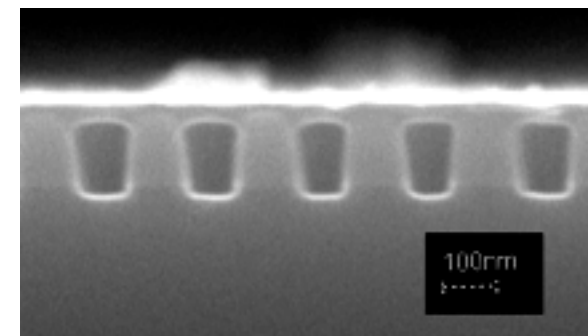
Imprinted 3-layer Polymer Structure



World-micro-nano Interfacing I: Reverse nanoimprinting



300(w)x500(h) nm

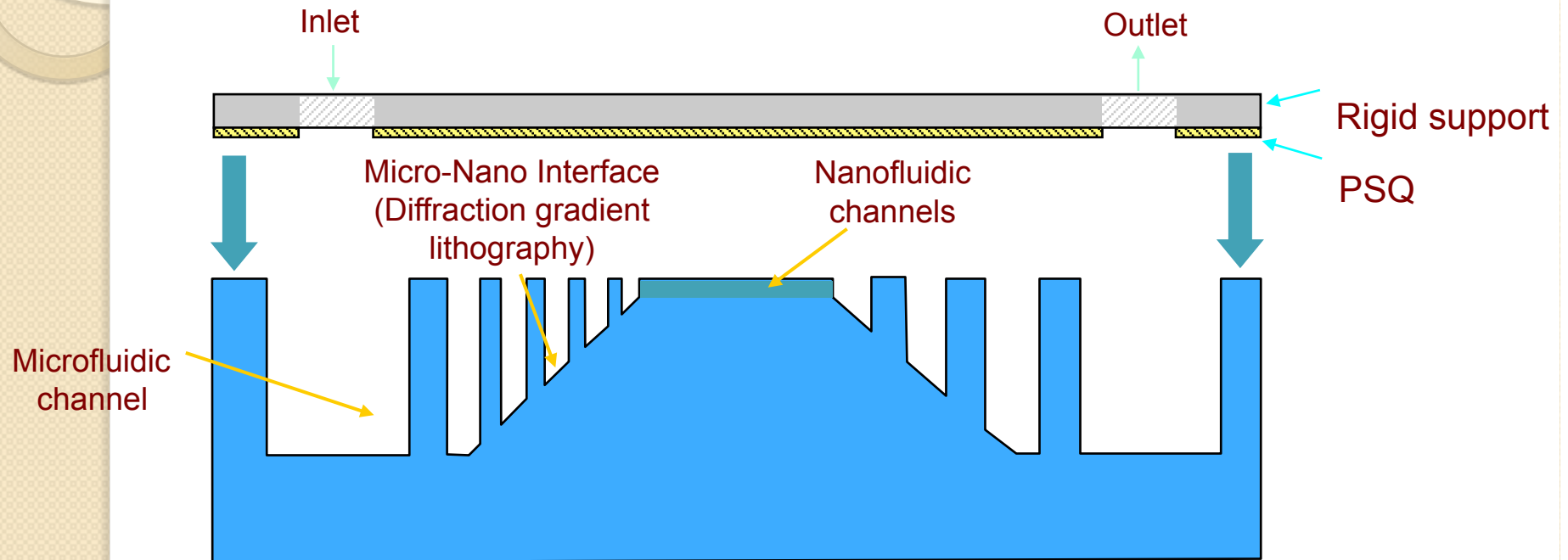


75(w)x120(h) nm

L.J. Guo, X. Cheng, CFC, Nano Lett. 4, 69 (2004)

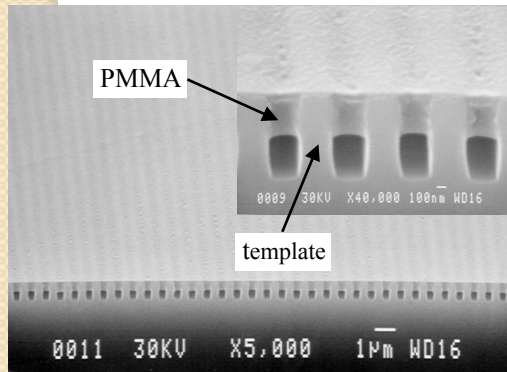
World-micro-nano Interfacing II

Simultaneous Packaging of Micro- and Nanofluidics

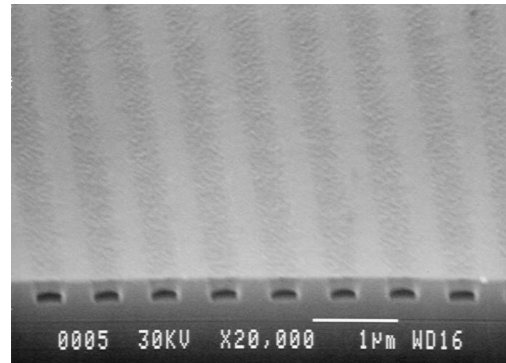


- *Permanent bonding at room temperature*
- *Conformal contact for low pressure operation*
- *Precise dimension control*
 - Sealing of 1D, 2D nano/microchannels below 10 nm
- *High throughput and low cost*

Nanofluidic Channels for DNA Stretching

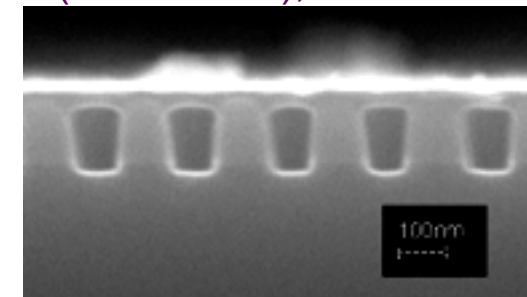


300(w)x500(h) nm

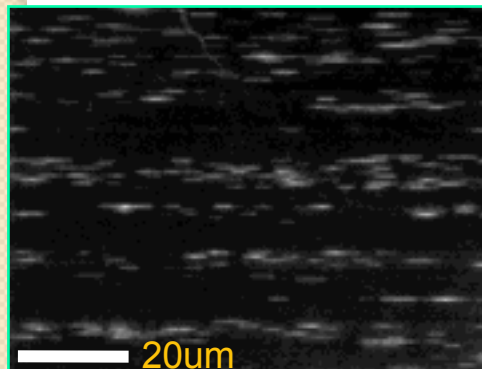


300(w)x130(h) nm

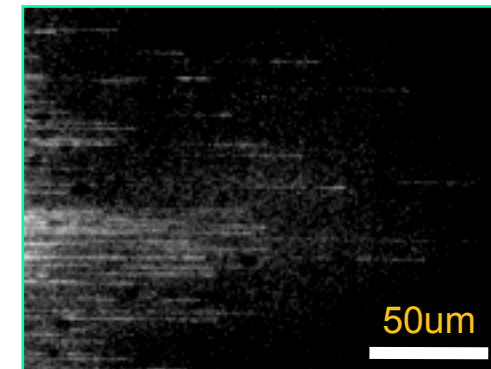
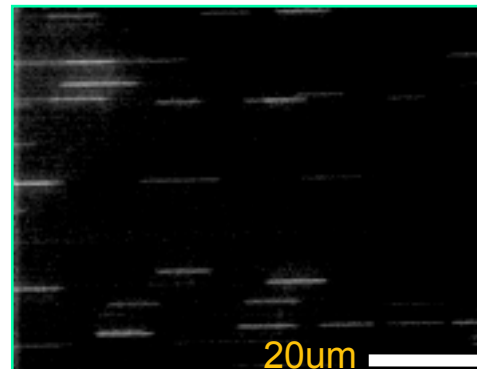
175°C and 50 kg/cm²
(4.9×10⁶ Pa), 5 min



75(w)x120(h) nm



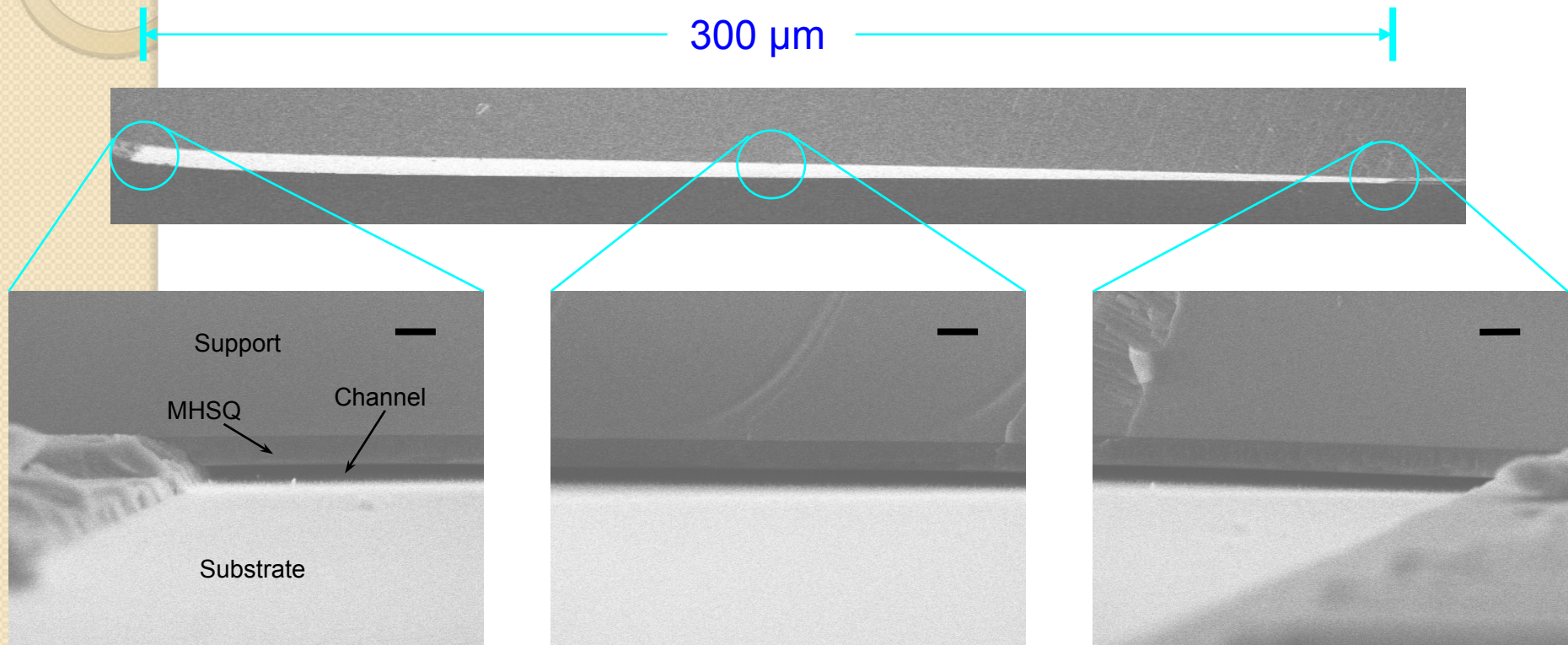
T5 phage DNA
103 kb (35 µm)



Channel dimension	Stretched DNA length	Percentage of stretching
300nm x 700nm	6.2 ± 1.3 µm	15%
300nm x 500nm	12.7 ± 4.5 µm	30%
75nm x 120nm	39.8 ± 7.7 µm	95%

L.J. Guo, X. Cheng, C.F. Chou, Nano Lett. 4, 69 (2004)

Composite Cap Sealed Low Aspect Ratio (~ 1:2000) 1D Nanochannel

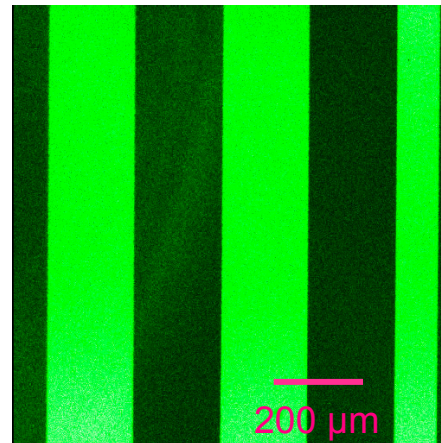
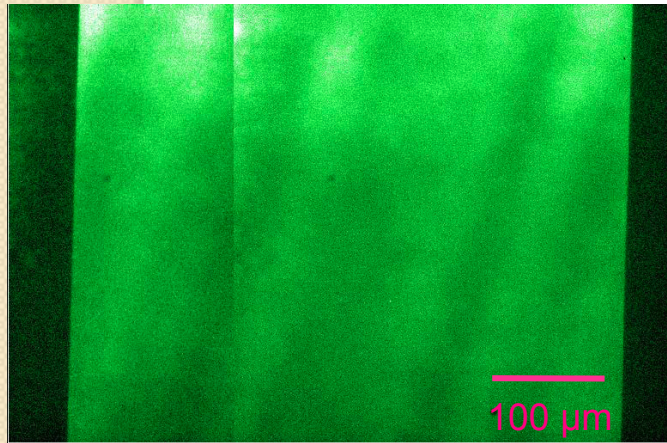


300 um x 150 nm, Scale bar is 400 nm

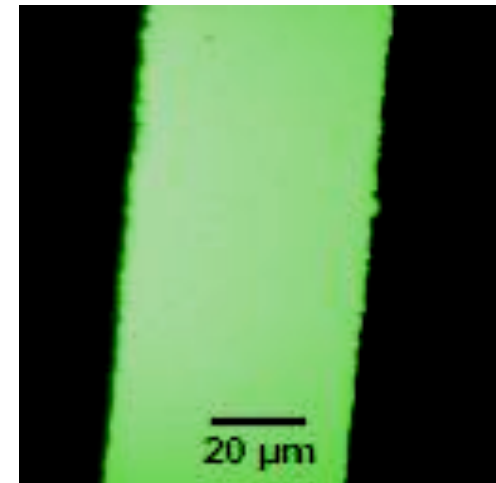
Gu, Gupta, Chou, Wei, *Lab Chip*, 7, 1198 (2007)

Ultralow Aspect Ratio ($< 4 \times 10^{-5}$) 1D Nanochannel

18 nm deep

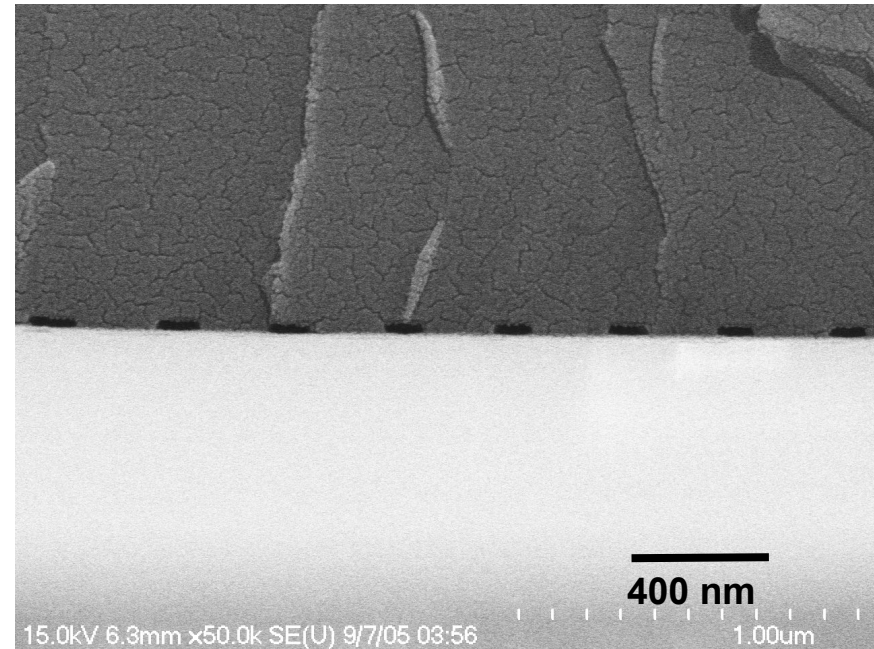
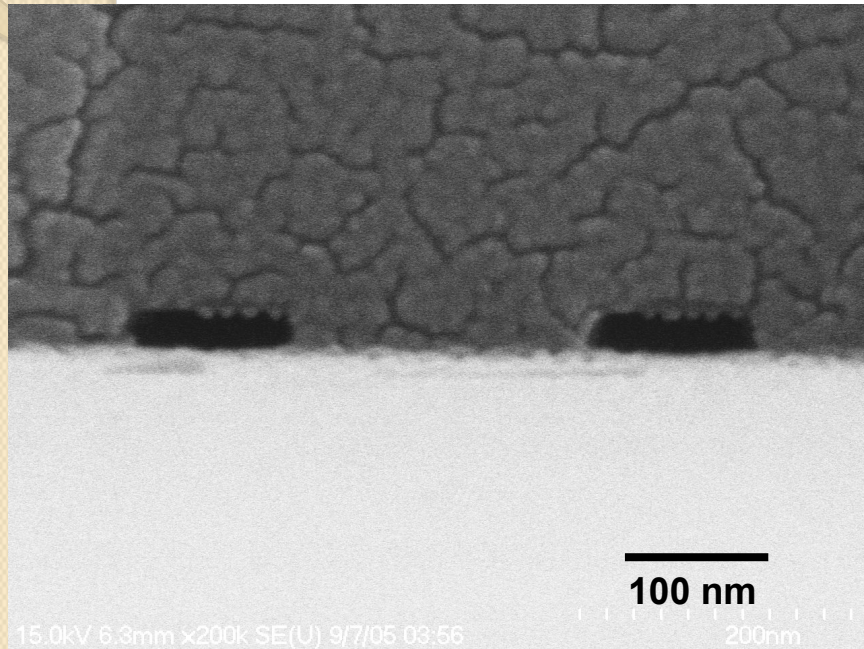


8 nm deep



Gu, Gupta, Chou, Wei, Zenhausern, *Lab Chip*, 7, 1198 (2007)

Composite Cap Sealed 2D Nanochannel Array



$30 \times 120 \text{ nm}^2$

Gu, Gupta, Chou, Wei, *Lab Chip*, 7, 1198 (2007)

Recent experiments

VOLUME 93, NUMBER 3

PHYSICAL REVIEW LETTERS

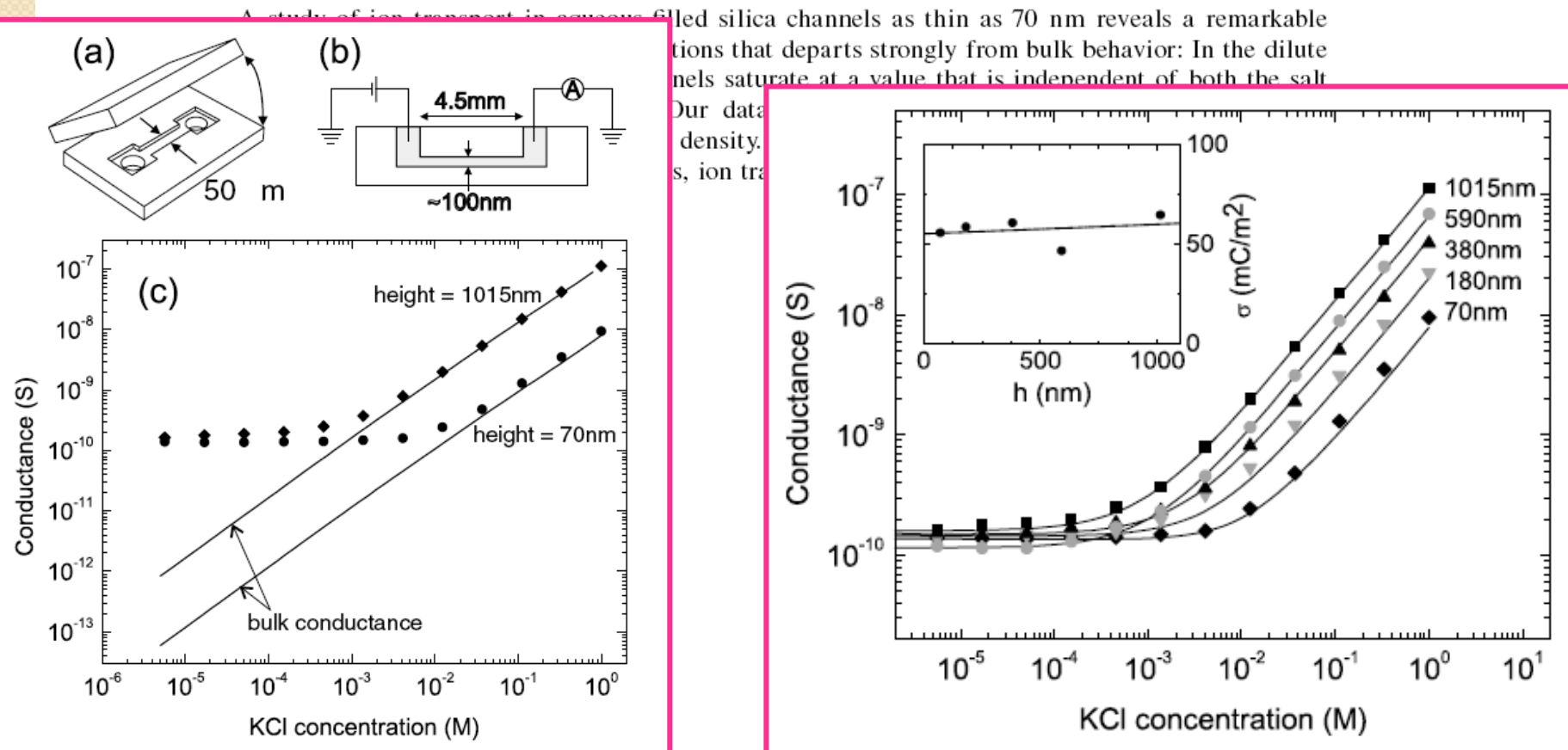
week ending
16 JULY 2004

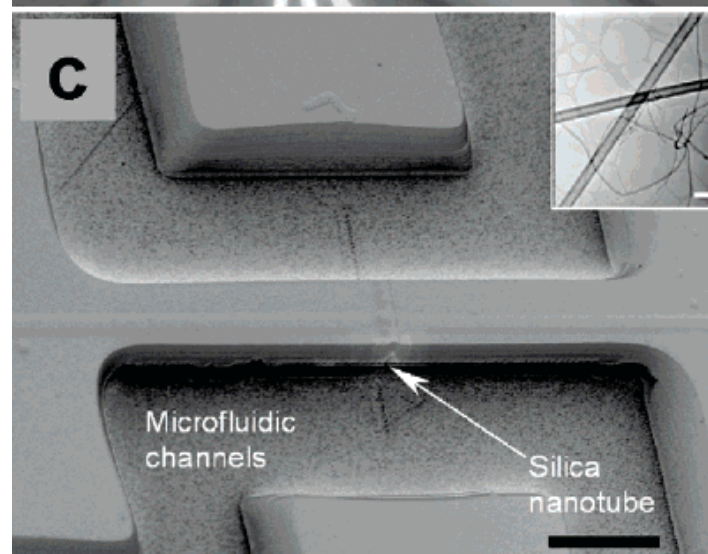
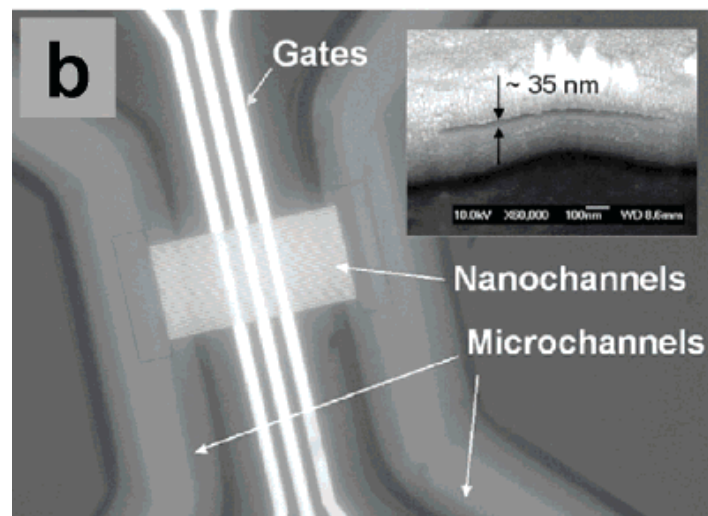
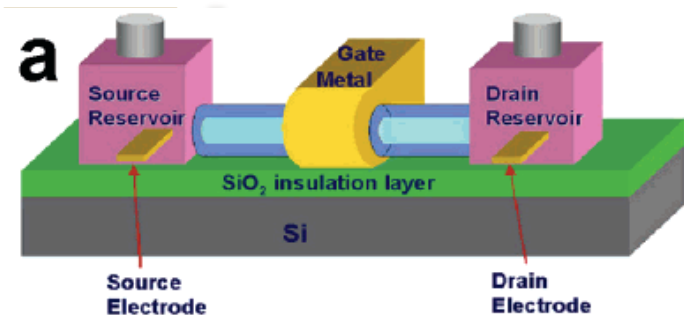
Surface-Charge-Governed Ion Transport in Nanofluidic Channels

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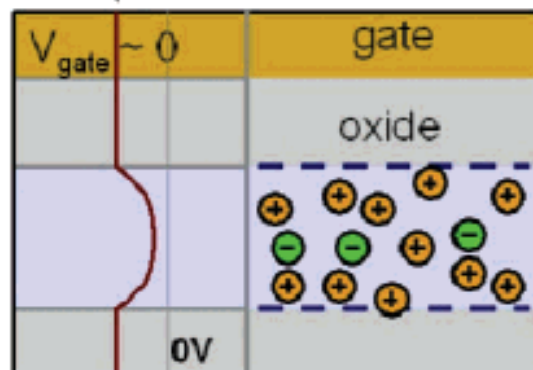




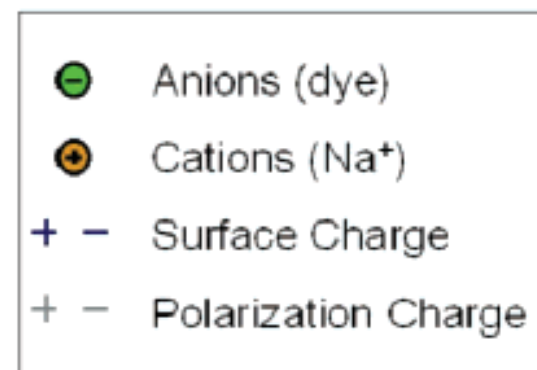
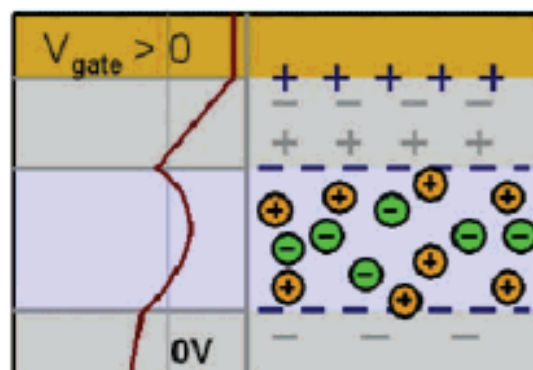
of Ions and dic Transistors

Li† Peidong Yan*,†,§ and

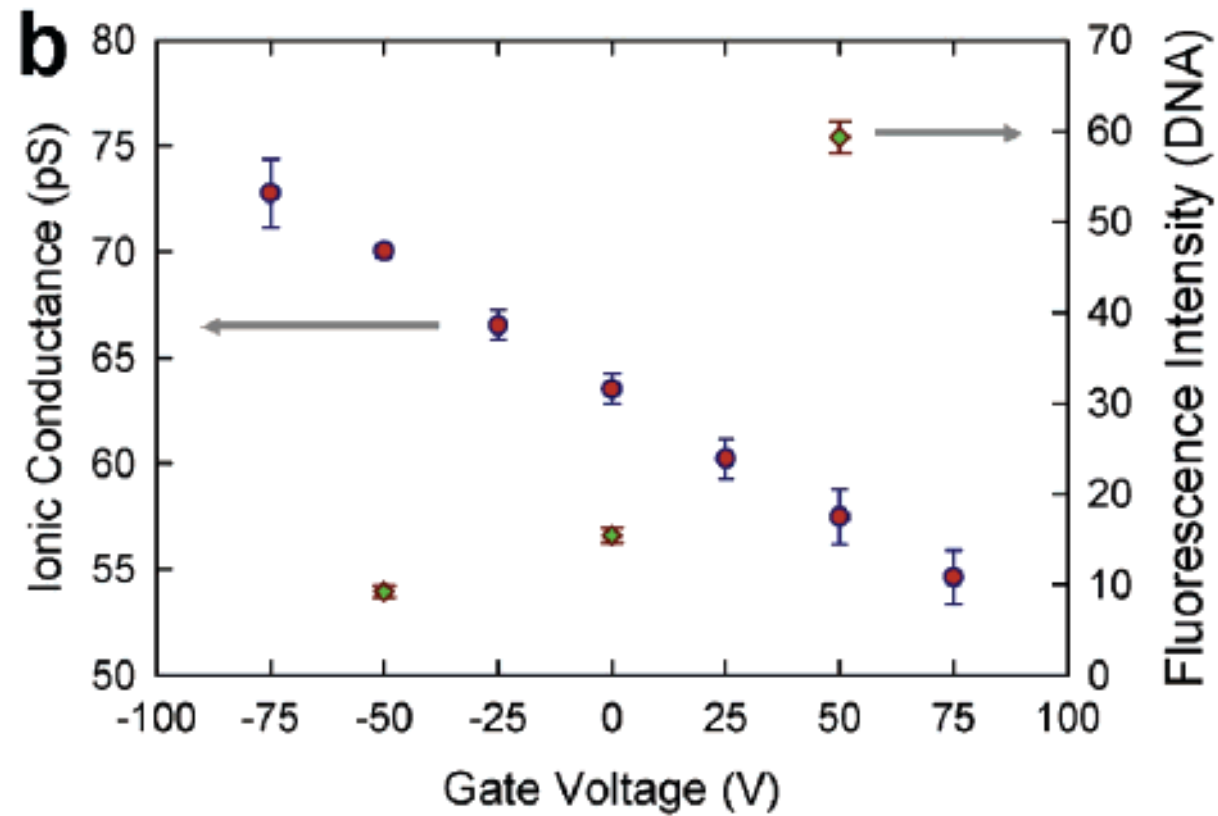
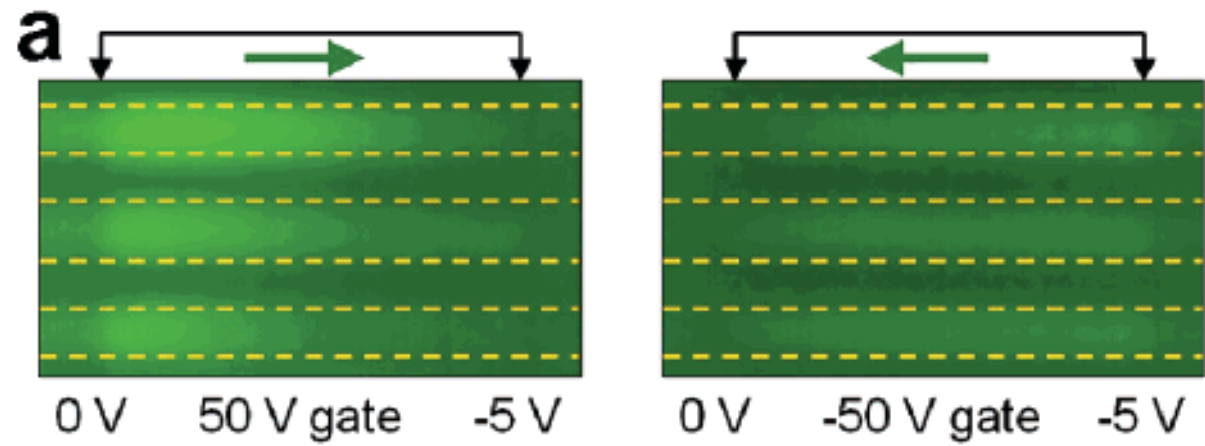
a Surface potential



potential →



- Anions (dye)
- Cations (Na⁺)
- + - Surface Charge
- + - Polarization Charge





Exercise

- E. coli coasting time and distance? Assume radius is 1 micrometer, velocity 30 $\mu\text{m/s}$.
- Diffusion (random walk) which is not Gaussian? Give examples (Steve Granick).