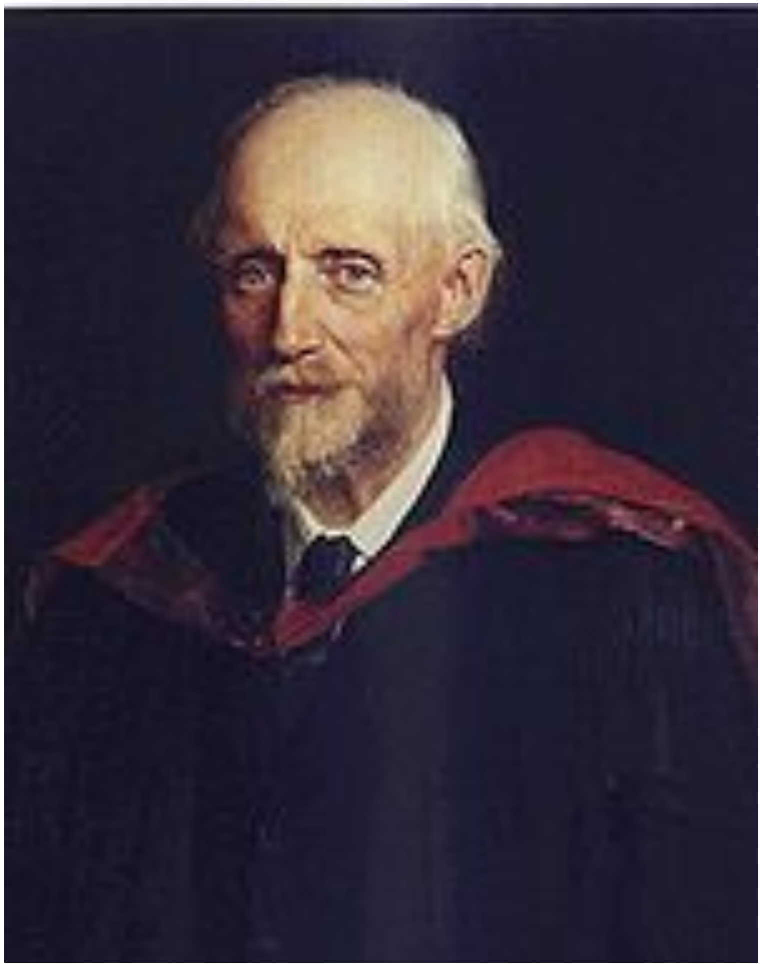
Introduction to Micro/Nanofluidics

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

Osborne Reynolds

1842 – 1912



Osborne Reynolds in 1903

Reynolds number:

$$\mathrm{Re} = \frac{inertial \quad forces}{viscous \quad forces}$$

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 (ν = η / ρ) (m²/s)
ρ : the density of the fluid (kg/m³)

D_H : hydraulic diameter

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

For pipe flow:

For water, η = 0.01 g/cm/s

D_H (μm)	v_s (cm/s)	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:

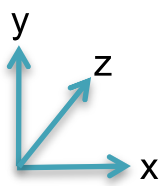
* Spermatozoa ~ 1×10^{-2}
* Blood flow in brain ~ 1×10^{2}
* Blood flow in aorta (vein) ~ 1×10^{3}

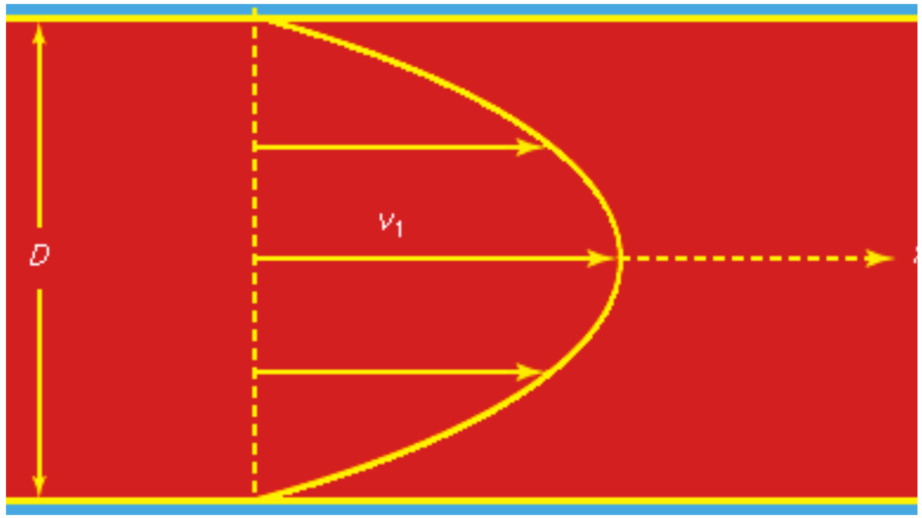
Onset of turbulent flow ~ 2.3×10^{3} for pipe flow to 10^{6} for boundary layers:

* Typical pitch in Major League Baseball ~ 2×10^{5}
* Person swimming ~ 4×10^{6}
* Blue whale ~ 3×10^{8}
* A large ship (RMS Queen Elizabeth 2) ~ 5×10^{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 . There is a pressure drop along the length of the channel, so that the constant pressure gradient is (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 ; then . 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

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

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:

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

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.

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

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

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

Figure 4

Laminar Flow-movies

Laminar Flow-3 colors

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

$<x^2> = 2Dt$ in 1-D

$<x^2> = 4Dt$ in 2-D

$<x^2> = 6Dt$ in 3-D

Anomalous diffusion

$<x^2> = 2Dt^{\alpha}$ in 1-D:

$\alpha > 1$, super diffusion

$\alpha < 1$, sub-diffusion

Stokes formula: $\xi = 6\pi\eta a = f/v$

Einstein relation: $\xi D = k_B T$

Fick's equation for diffusion

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

Fick's equation for diffusion with drift

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

Diffusion Equation:

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

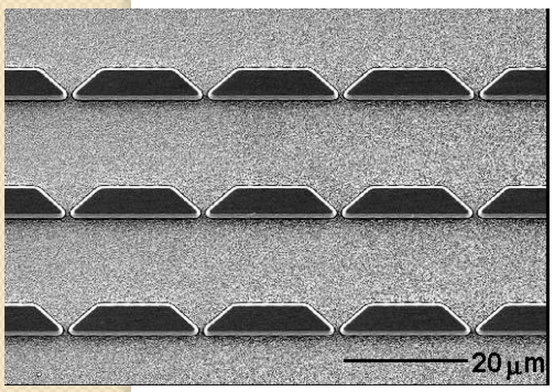
Diffusion of polymers

See "Polymer Dynamics" session

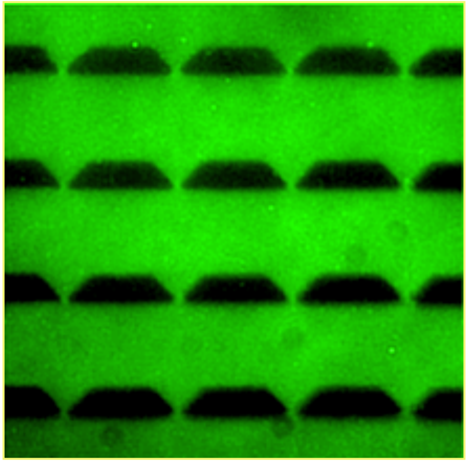
EDEP for DNA trapping

368 bp DNA

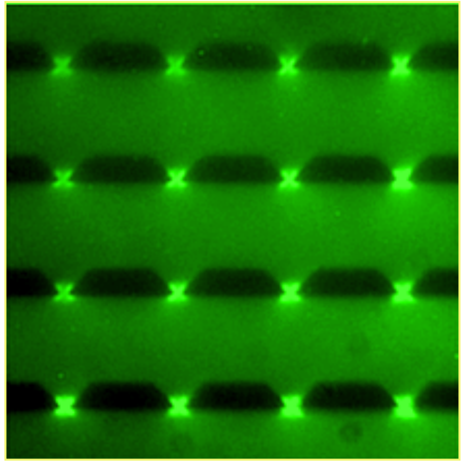
EDEP devicce



AC field off



AC field on



C.F. Chou et al., Biophys. J. 83: 2170 (2002);

US Patent # 6,824,664 (2004)

Fick's equation for diffusion with drift

Flux: $J(x,t) = v\, n(x,t) - D\, \mathrm{grad}[n(x,t)]$

Einstein relation

$= [DF(x,t)/kT]\, n(x,t) - D\, \mathrm{grad}[n(x,t)]$

At equilibrium: $J(x,t) = 0$

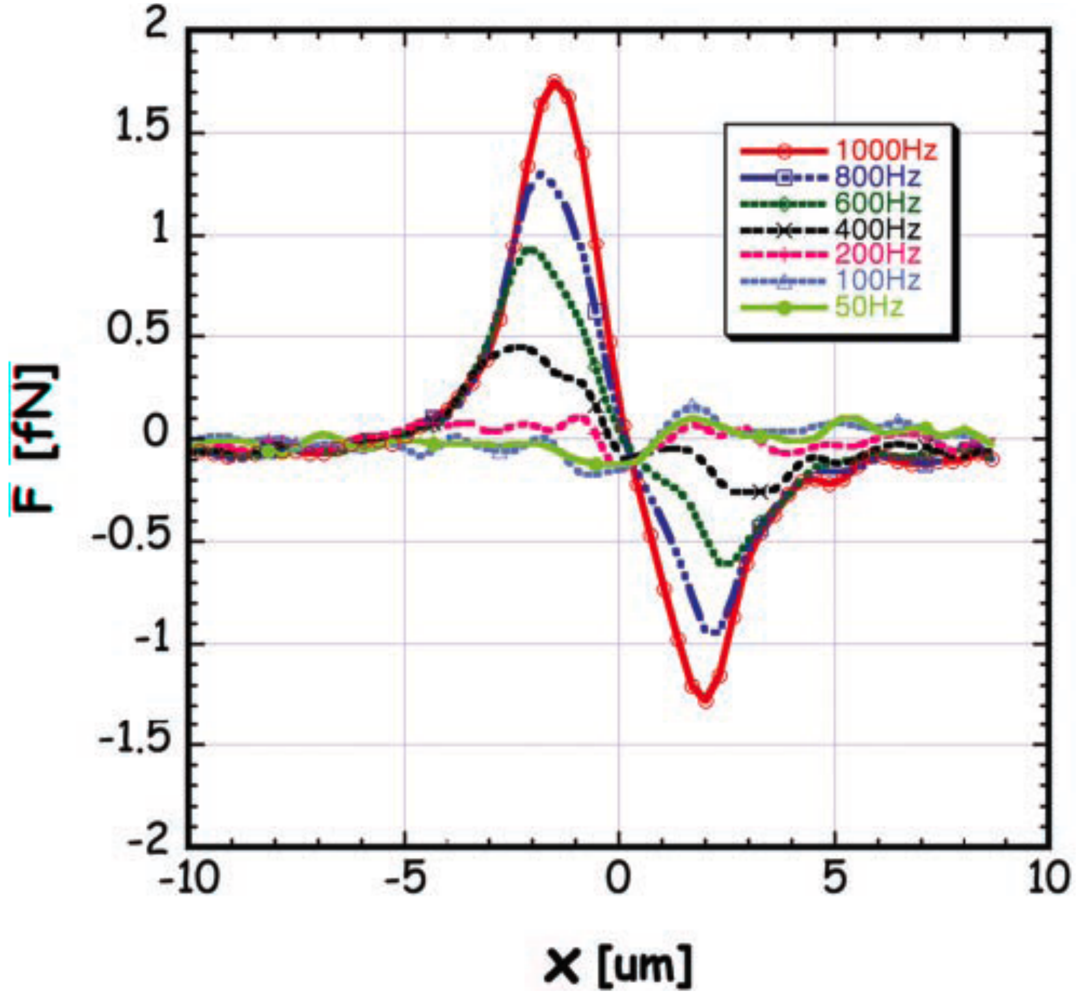
$$F(x) = kT\, \mathrm{grad}[n(x)]/n(x)$$

$kT = 4$ pN·nm
$= 4$ fN·μm

Force field:

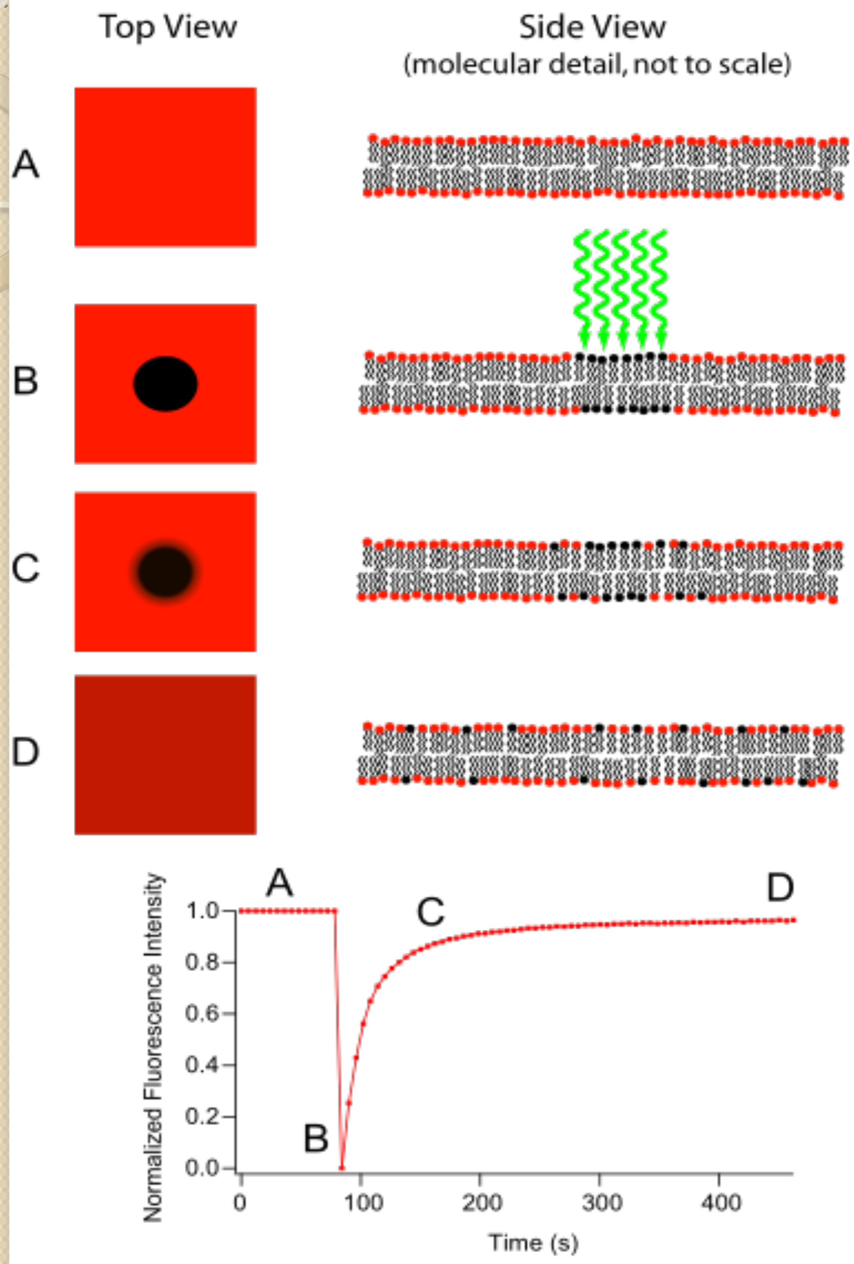
Frequency response at a fixed field

368 bp@1000Vpp/cm (5Vpp/#cell)



C.F. Chou et al., Biophys. J. 83: 2170 (2002)

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:

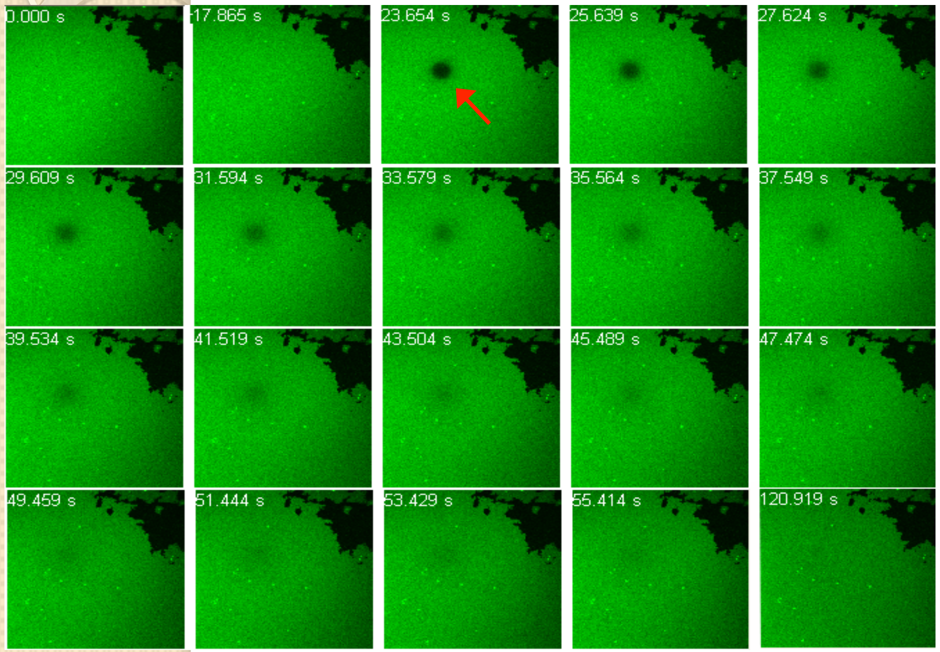
$$D = \frac{w^2}{4t_{1/2}}$$

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

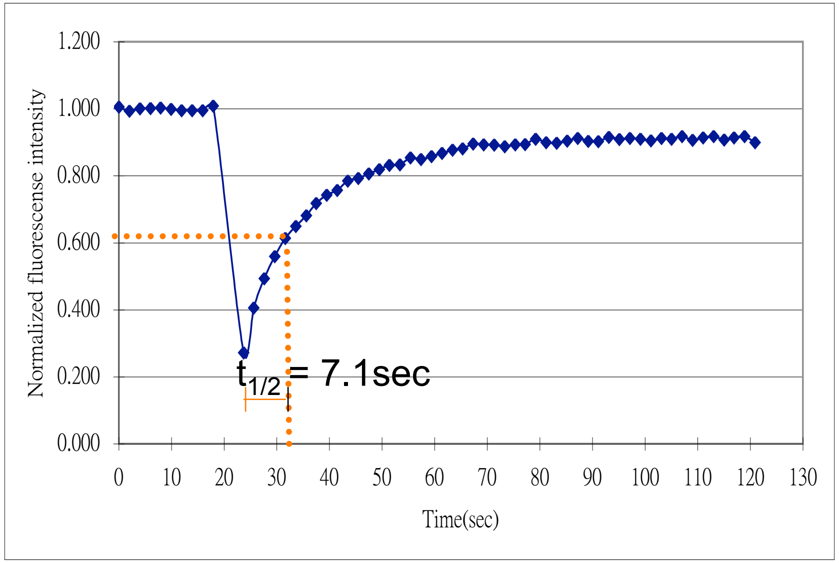
(Fluorescence Recovery After Photobleaching)

(A)



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).

(B)

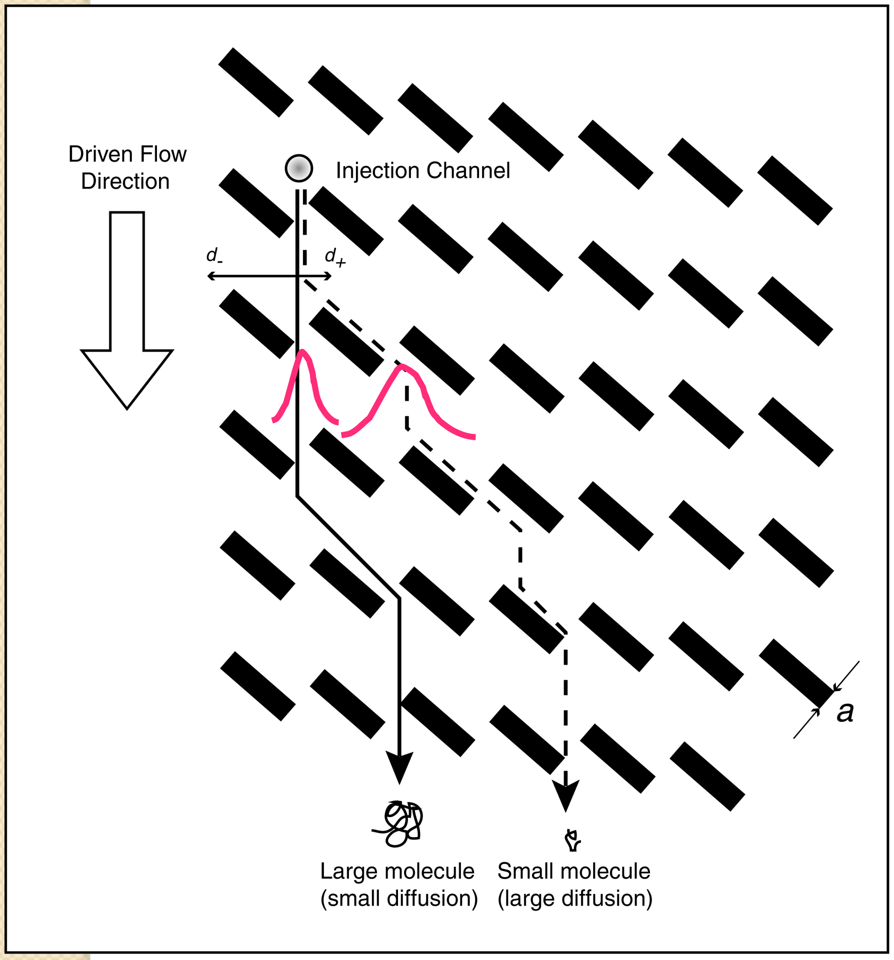


Purpose:

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

Courtesy Dr. YL Shih

Separation based on Rectified Brownian Motion



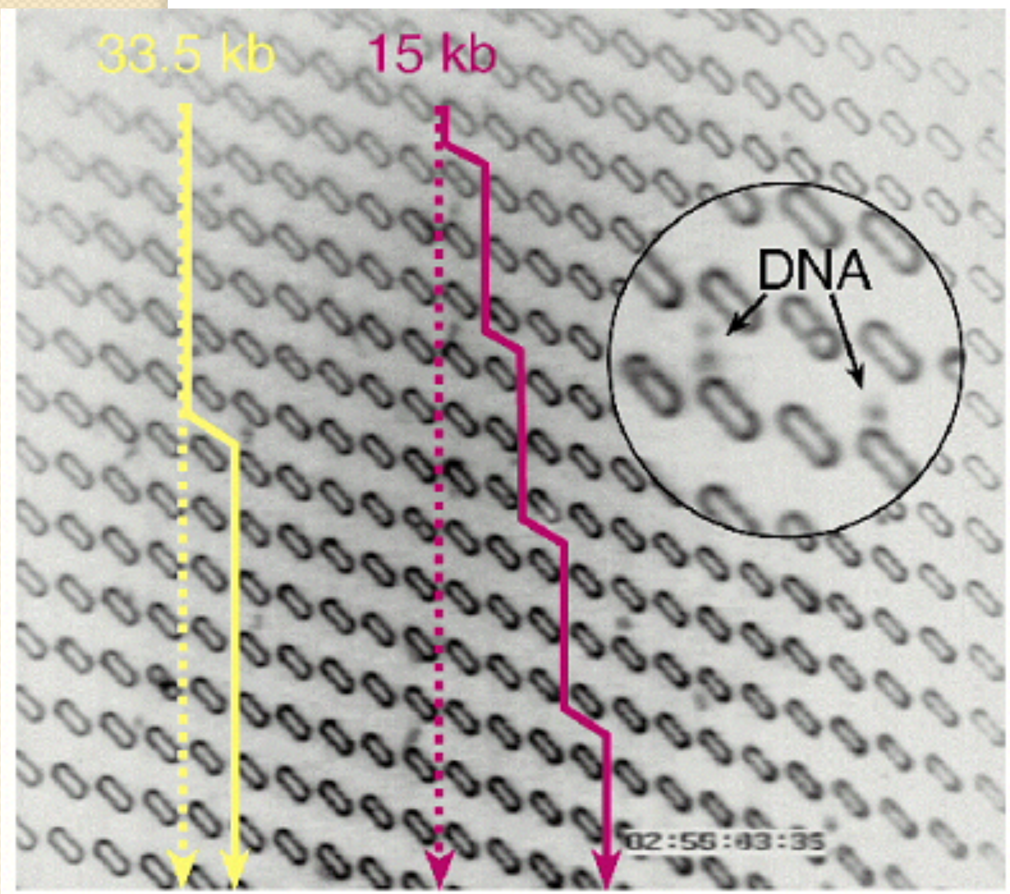
A simple idea: let the altered probabilities effectively move molecules to one side

— Rectified Brownian motion

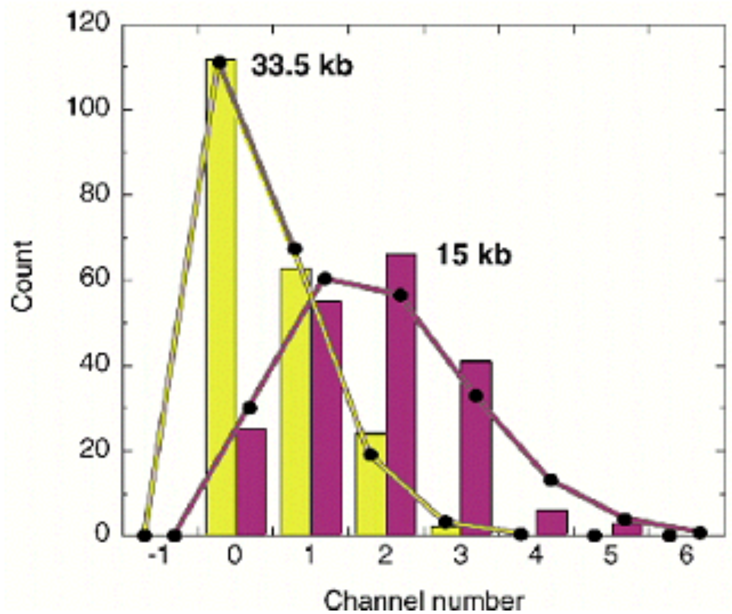
Duke and Austin, *PRL (*1998)
Ertas, *PRL (*1998)

Continuous molecular sorting by rectified Brownian motion

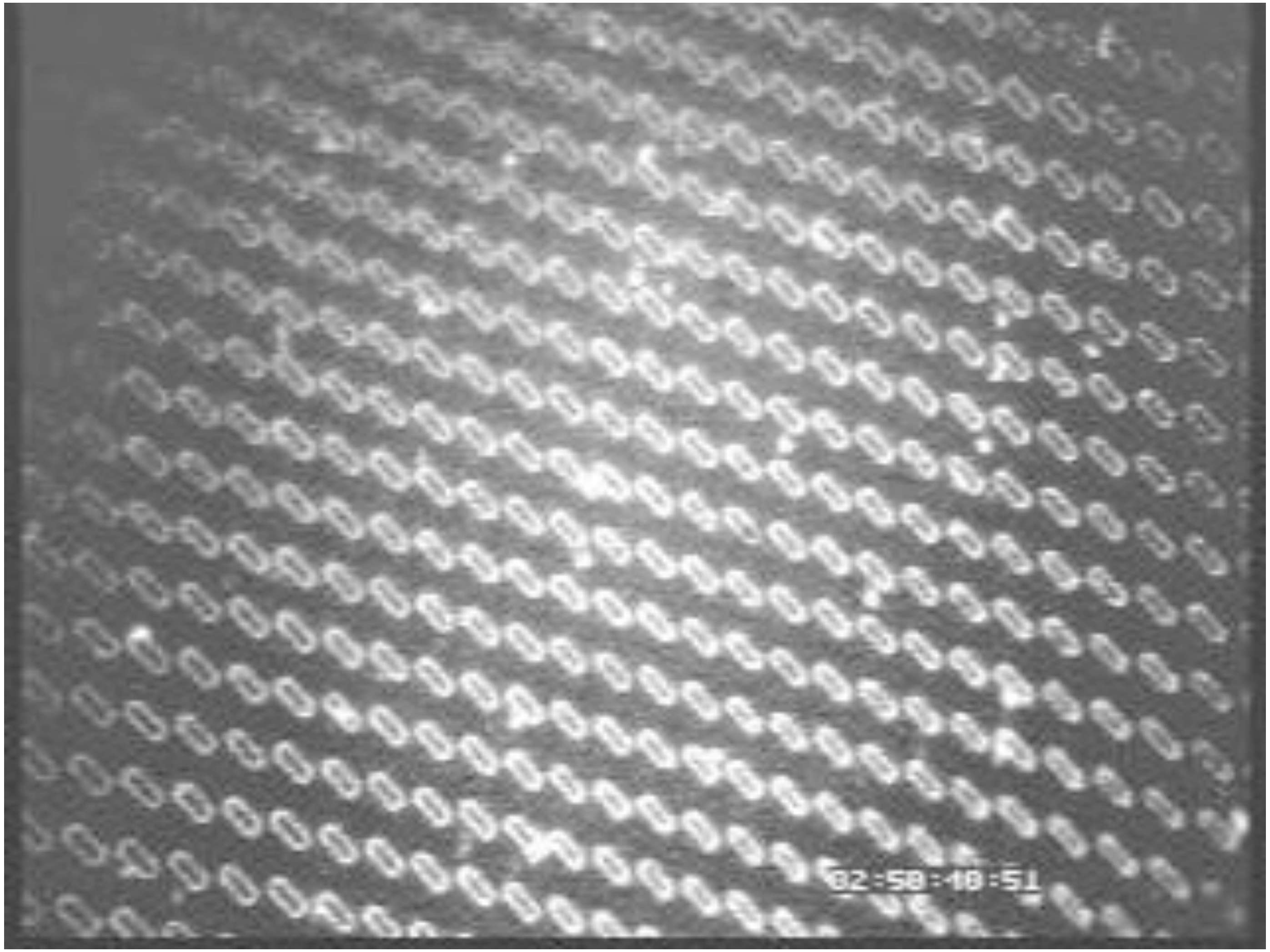
Continuous Lateral Separation



Chou et al, *PNAS* (1999)

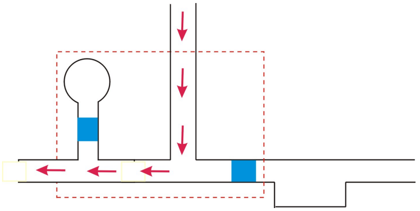


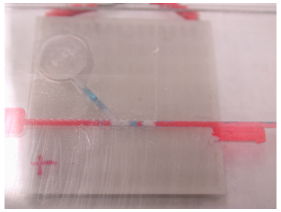
Continuous DNA sorting by rectified Brownian motion

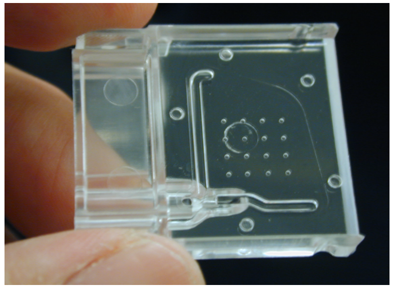


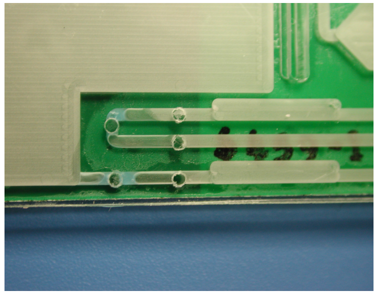
Microfluidic Components

Microvalves (paraffin, pluronics)

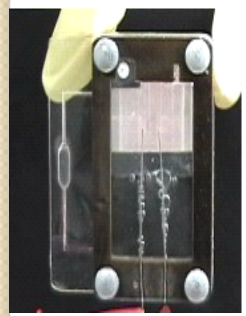


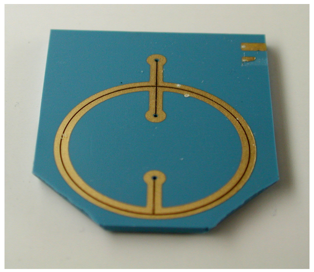




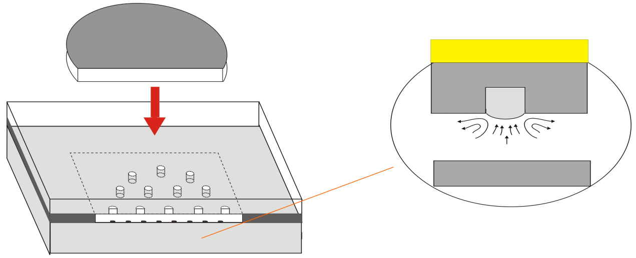


Electrochemical & MHD pumps



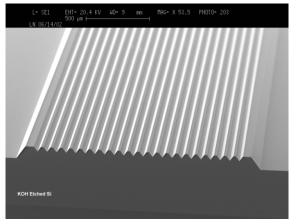


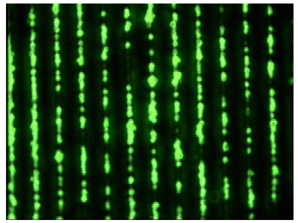
Piezoelectric mixing



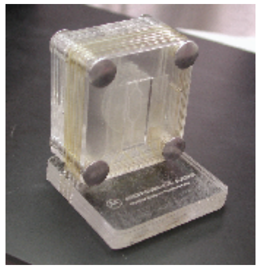
Rare target capture

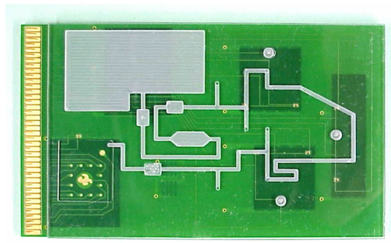
Localization of magnetic gradient





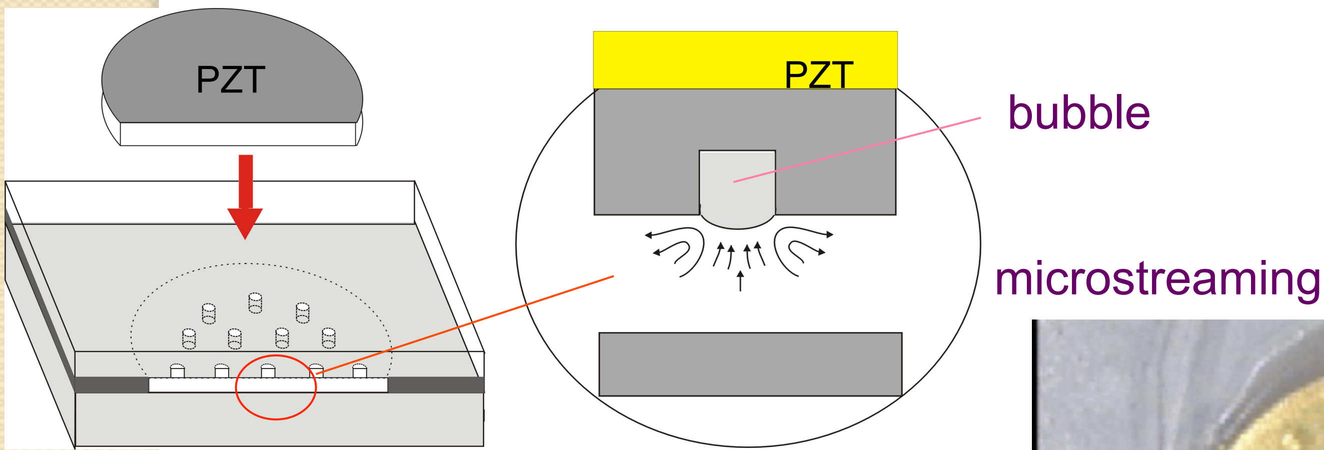
Stacked sample prep module



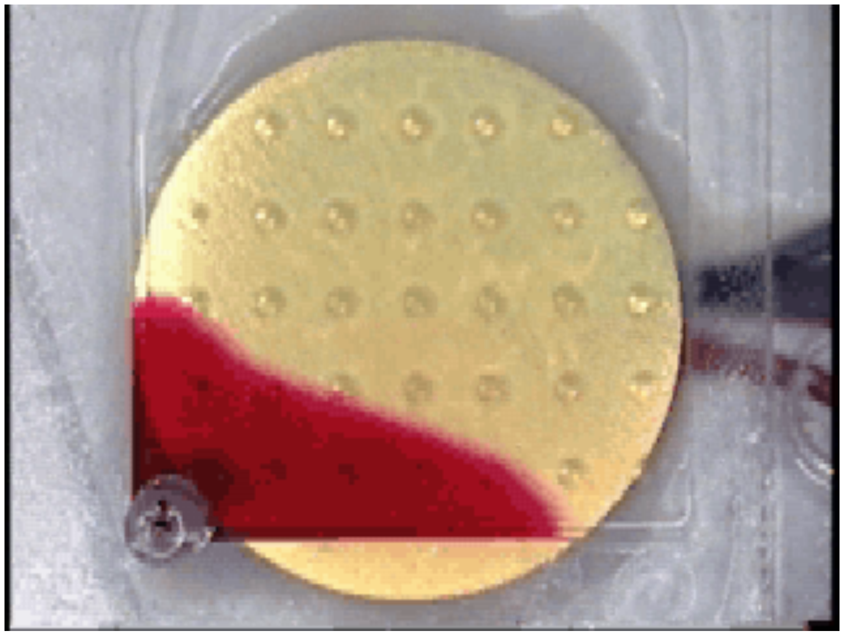


Micromixer: Cavitation Microstreaming

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



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



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

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

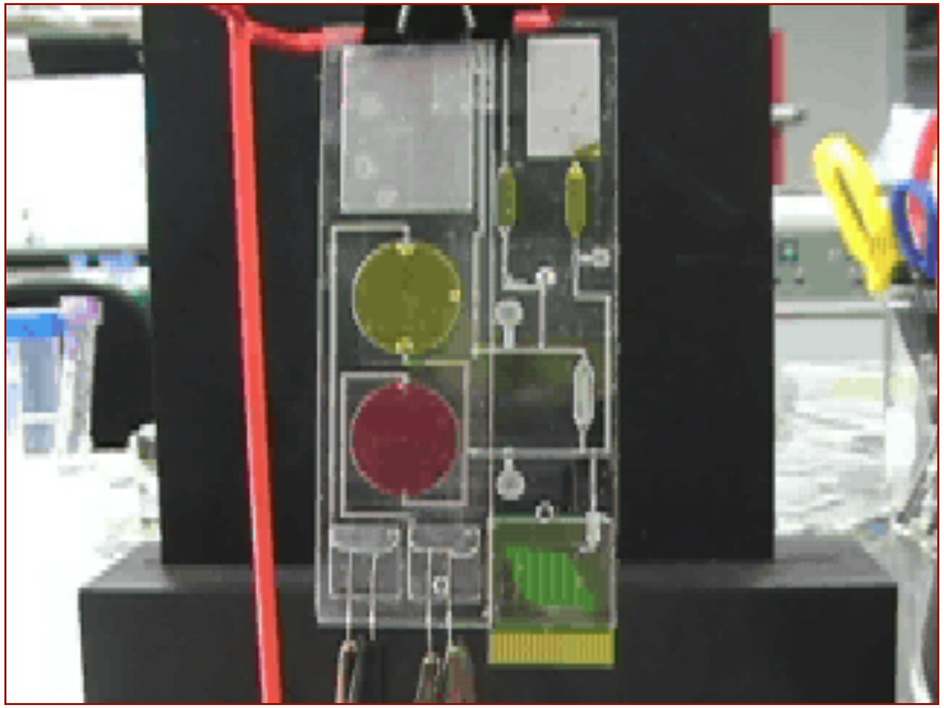
Integrated cartridge for low abundance bacteria detection

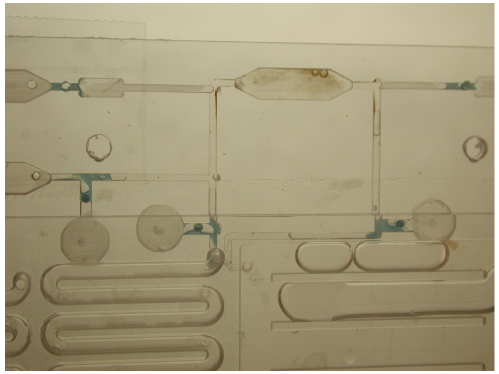
Crude Sample

- Target cell capture /enrichment
- Cell purification
- Cell Lysis
- PCR
- Hybridization
- Detection

Answer

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





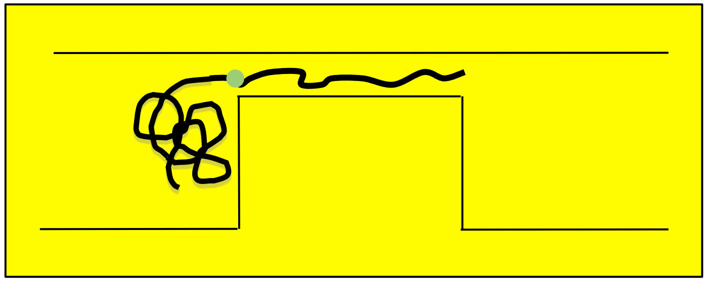
Successfully demonstrated cell capture + purification + lysis + PCR + detection of 1000 *E. coli* K12 cells / 1mL sheep blood

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

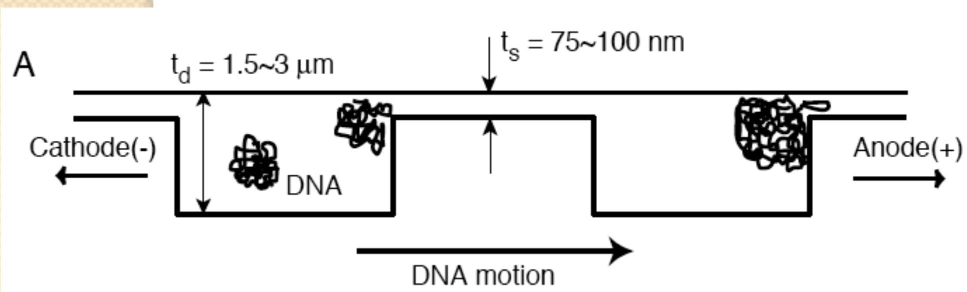
Micro- to Nanofluidic Interface

…A wonderland…

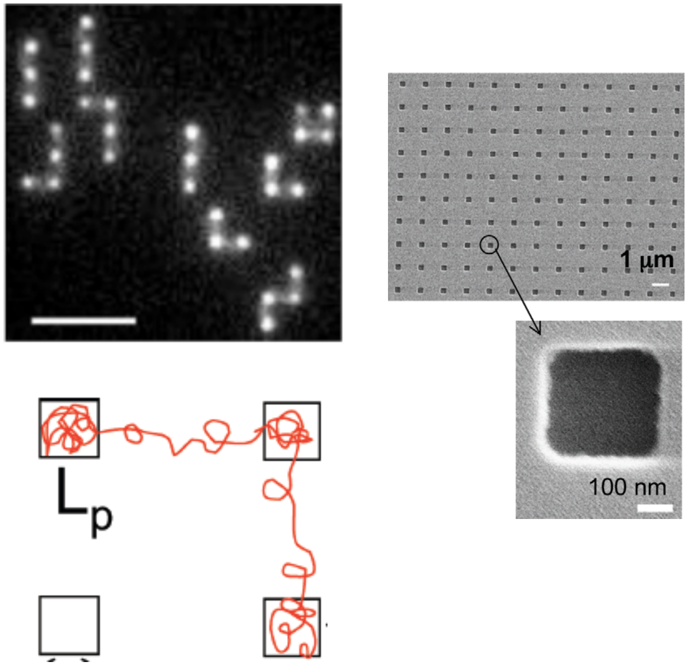
(1) Entropic barrier



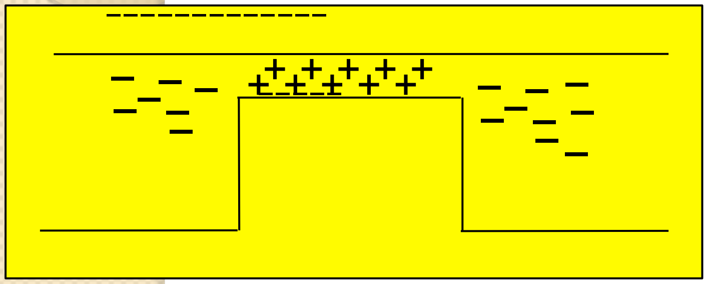
Nanoseparators
J. Han et al., Science 2000

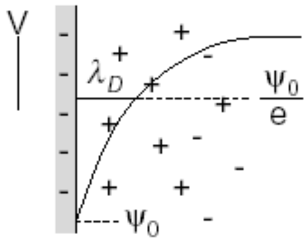


Digital DNA
Reisner et al., PNAS 2009



(2) Debye layer overlapping



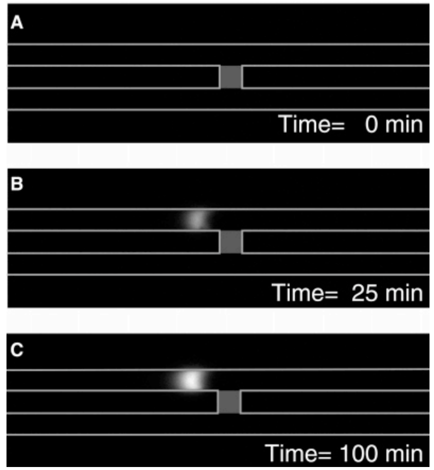


$$\lambda_D = \sqrt{\frac{\varepsilon RT}{2F^2 c}}$$

Conc / M	λ_D / nm
10^{-5}	100
10^{-4}	30
10^{-3}	10
10^{-2}	3
10^{-1}	1

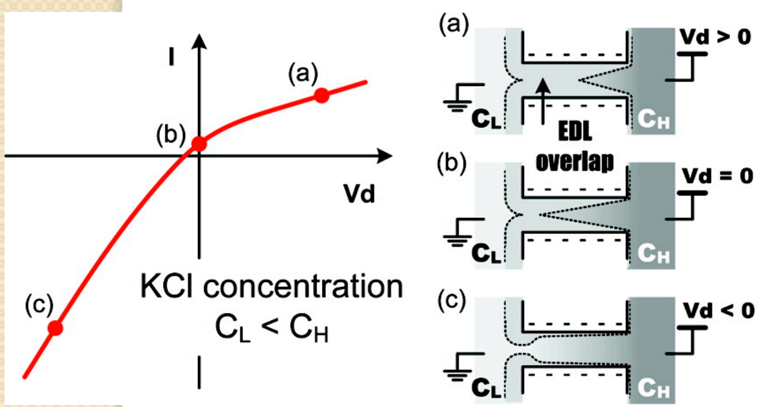
Nanoconcentrators

Wang et al., Anal. Chem. 2005



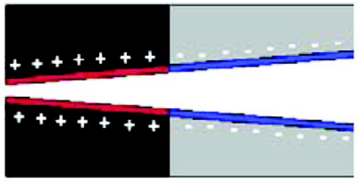
Rectified Ion Transport

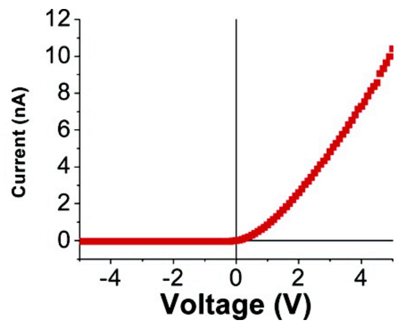
Cheng & Guo, Nano Lett. 2007



Nanofluidic diode

Vlassiouk and Siwy, Nano Lett. 2007





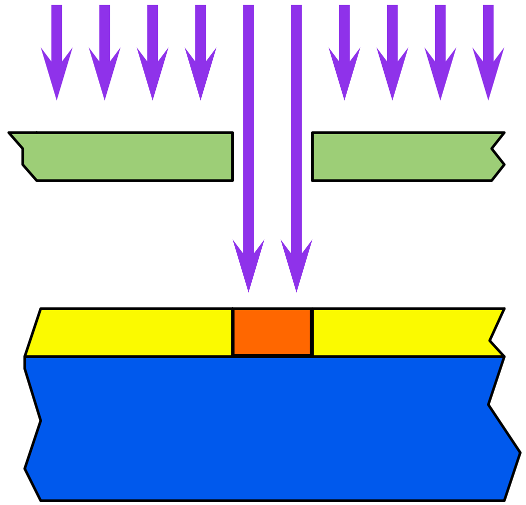
Principles of Traditional Lithography

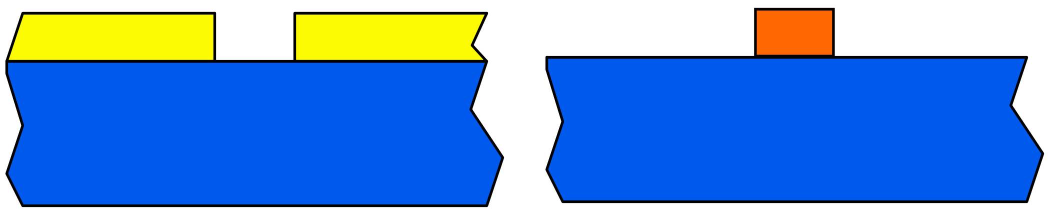
<u>Principle:</u>

Change solubility using radiation

<u>Factors limiting resolution:</u>

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

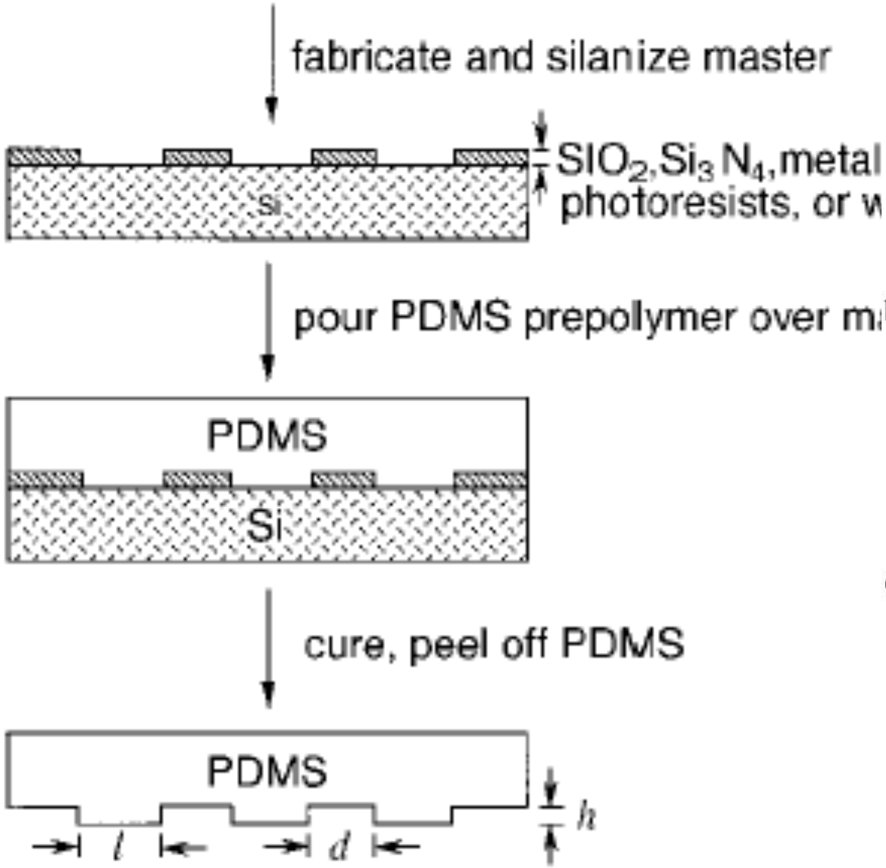


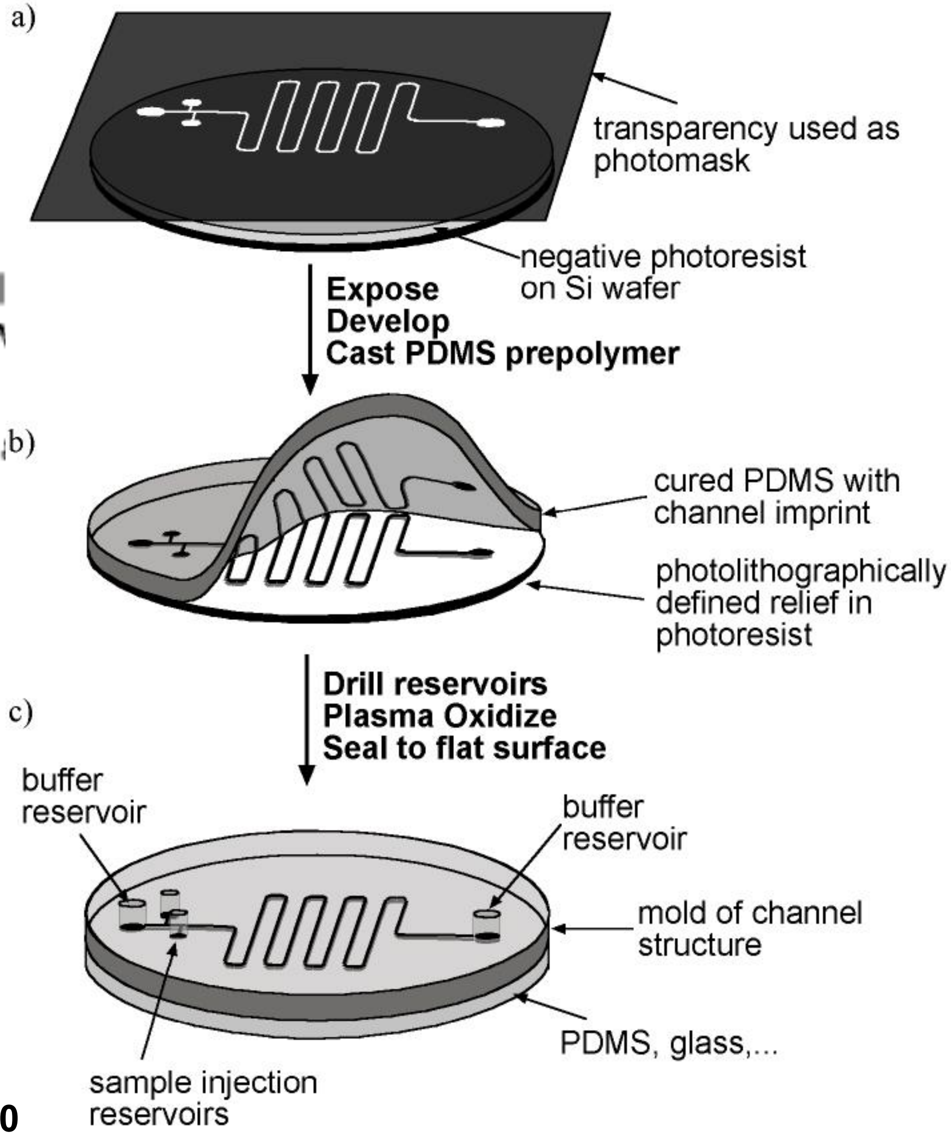


Positive Resist

Negative Resist

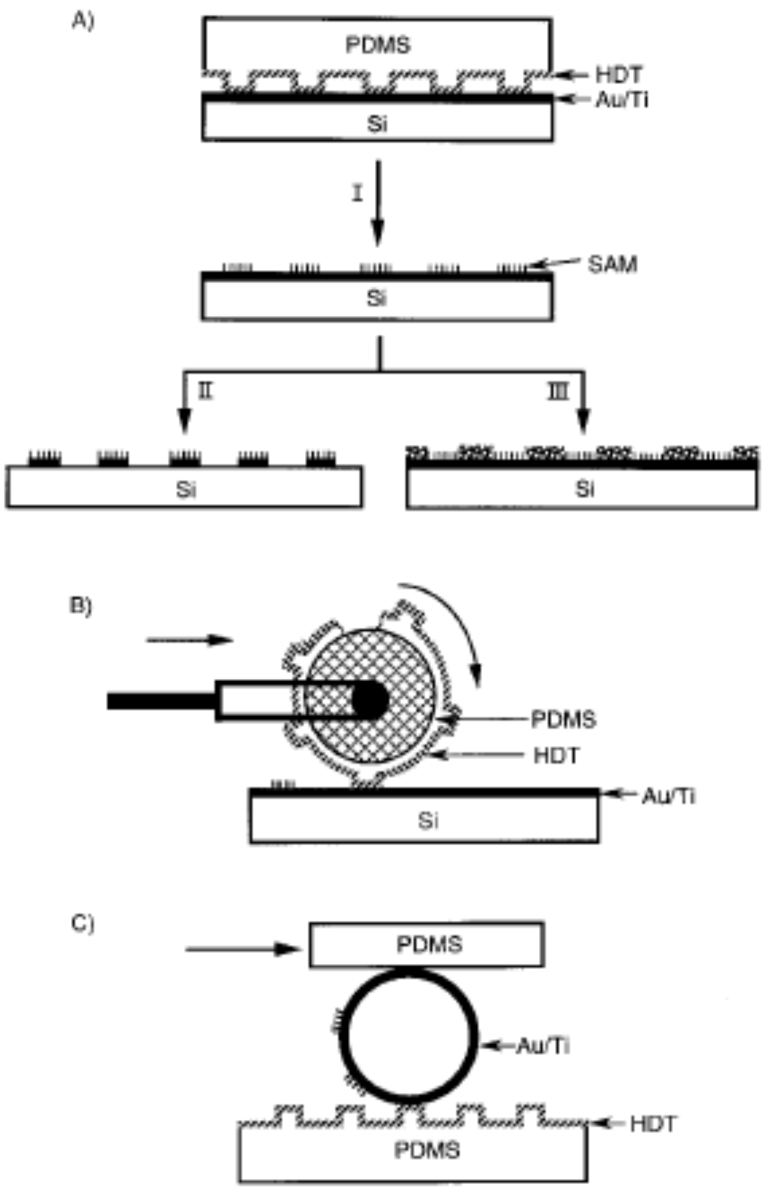
Soft Lithography





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

Micro-contact printing

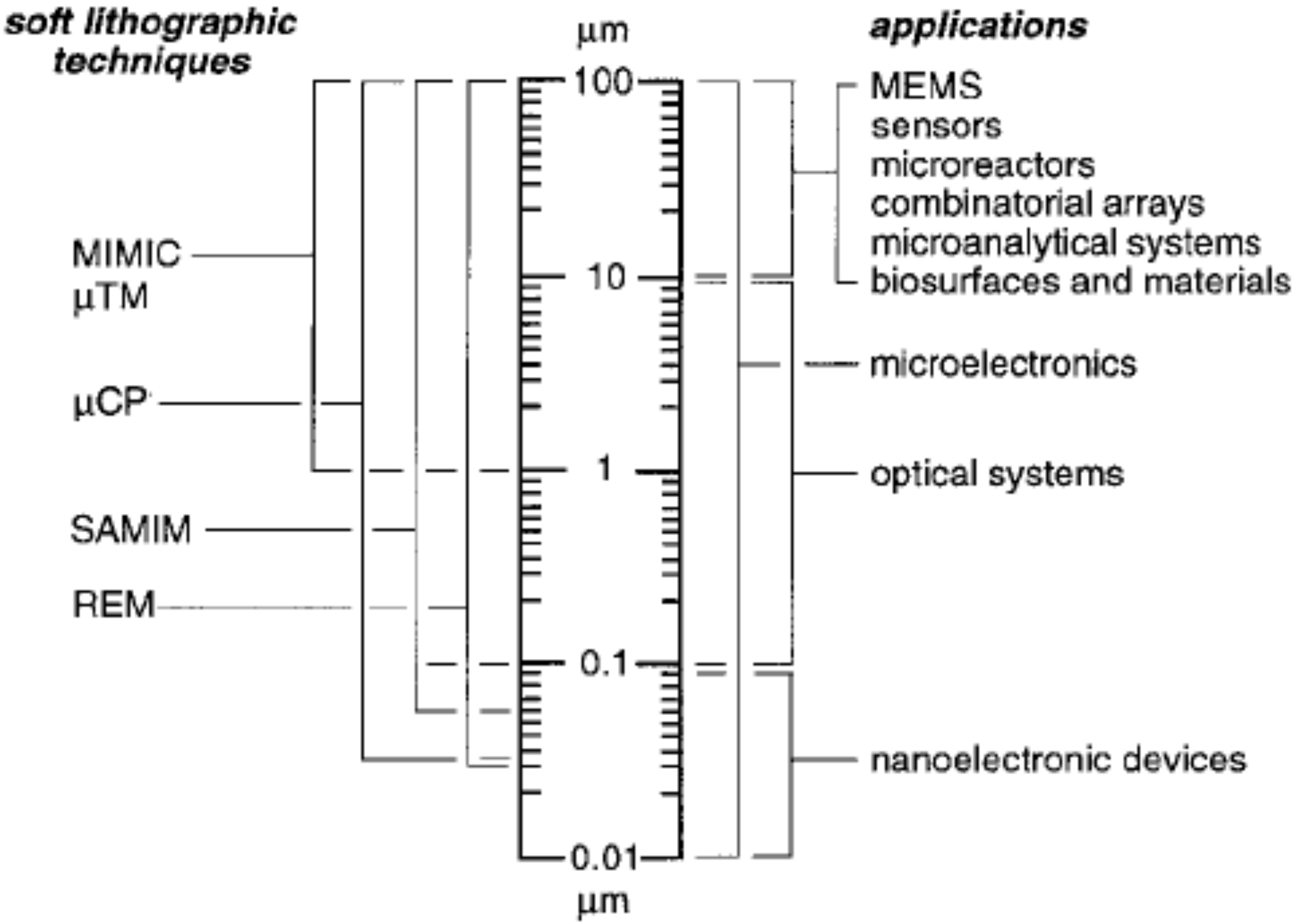


Procedures for µCP of hexadecanethiol (HDT) on a gold surface:

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

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

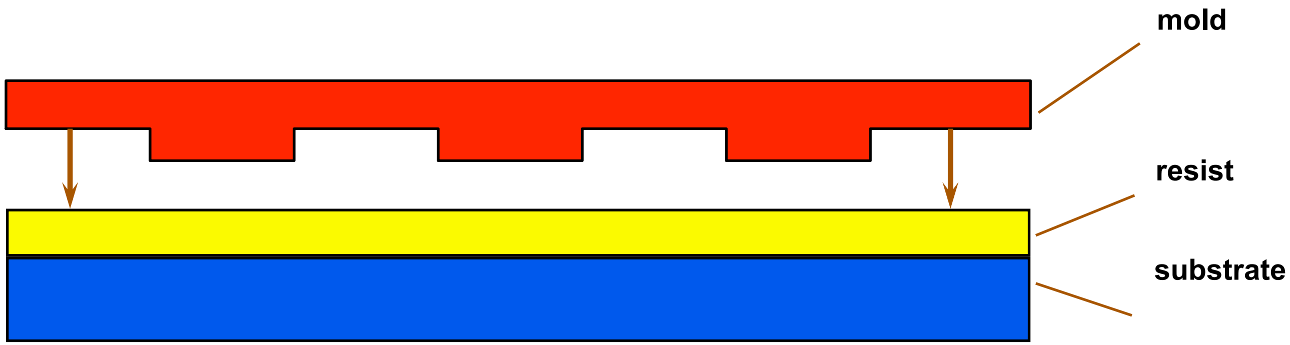
Applications of Soft Lithography



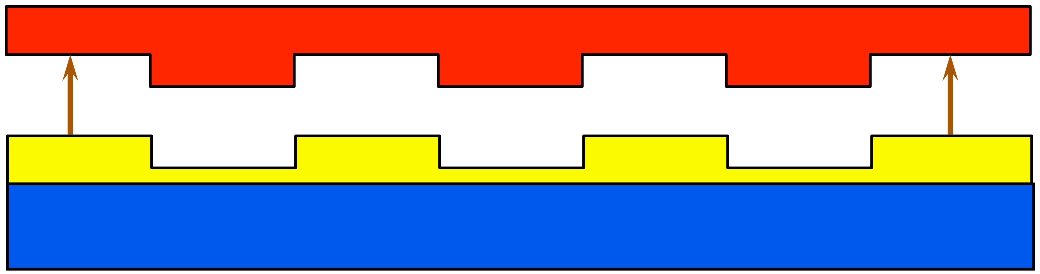
Nanoimprint Lithography

1. Imprint

- **Press Mold**



- **Remove Mold**

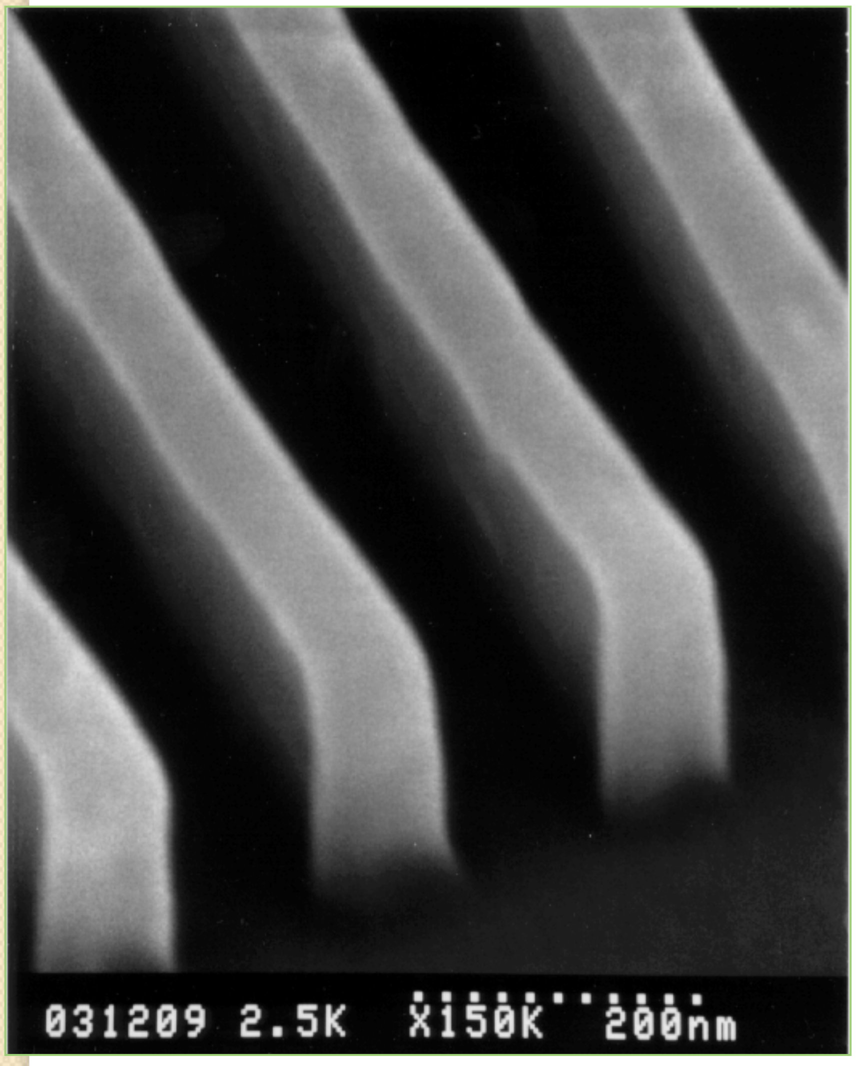


2. Pattern Transfer

- **RIE**

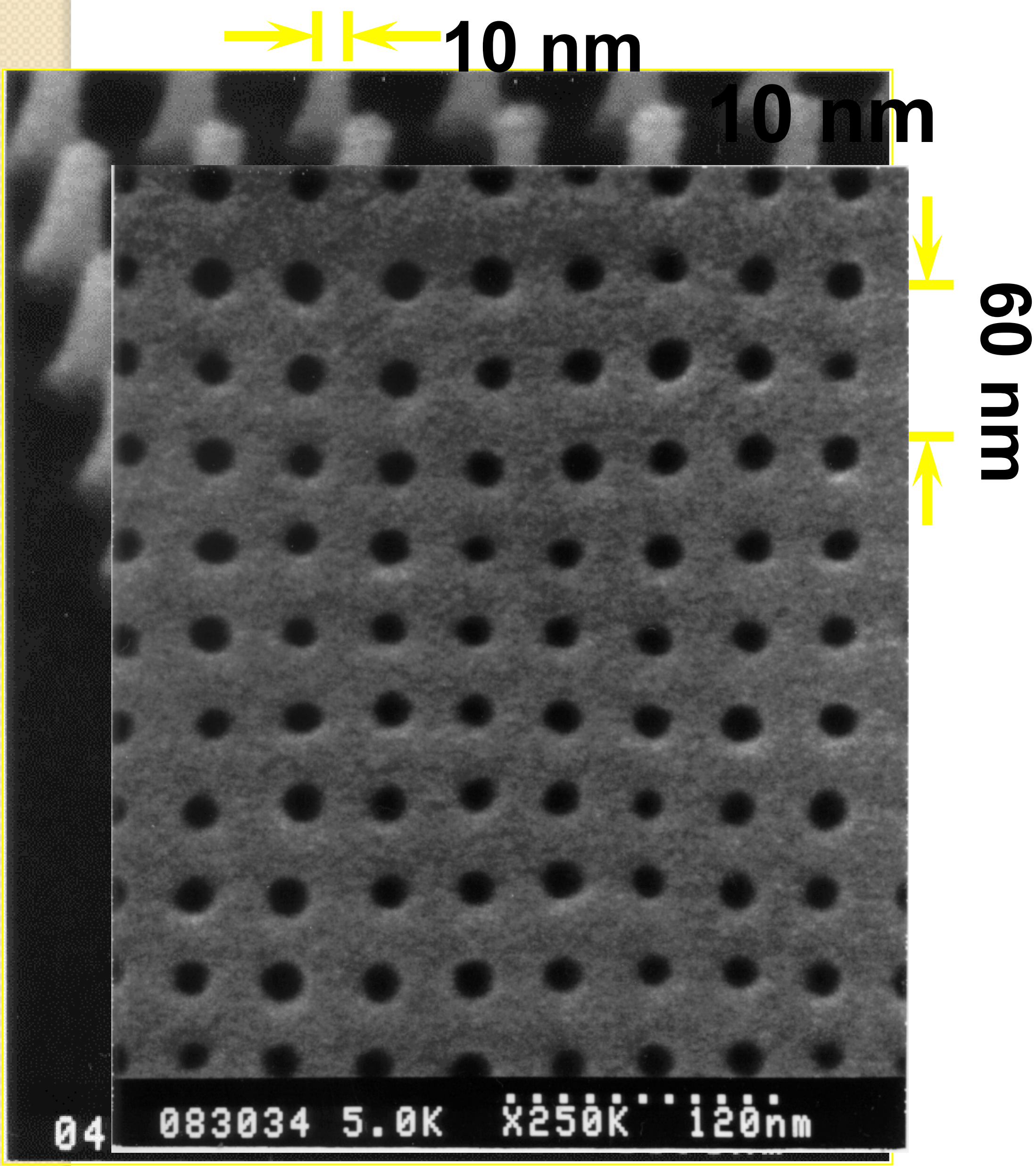
Chou, Krauss, and Renstrom, APL, Vol. 67, 3114 (1995); Science, Vol. 272, 85 (1996)

Imprinting–Footprint on the moon



- **Nanoimprinted 70 nm wide PMMA lines**
- **Smooth sidewalls and 90^{O} corners**
- **Pattern conformal to mold, mold surface variation reproduced in PMMA**

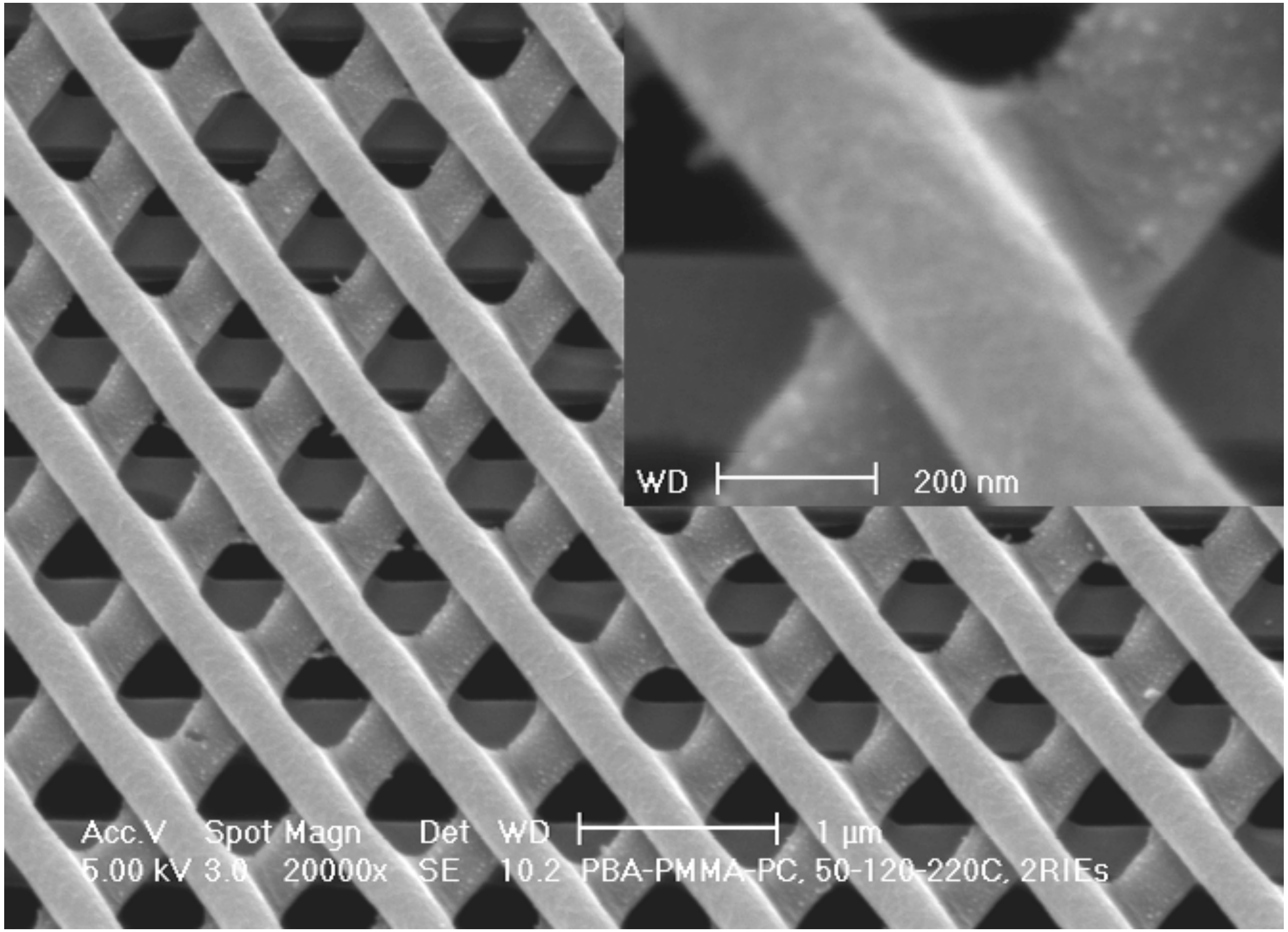
S. Y. Chou, et al. "Sub-10 nm imprint lithography and applications," ***J. Vac. Sci. Technol*****. B, Vol. 15, 2897, 1997.**



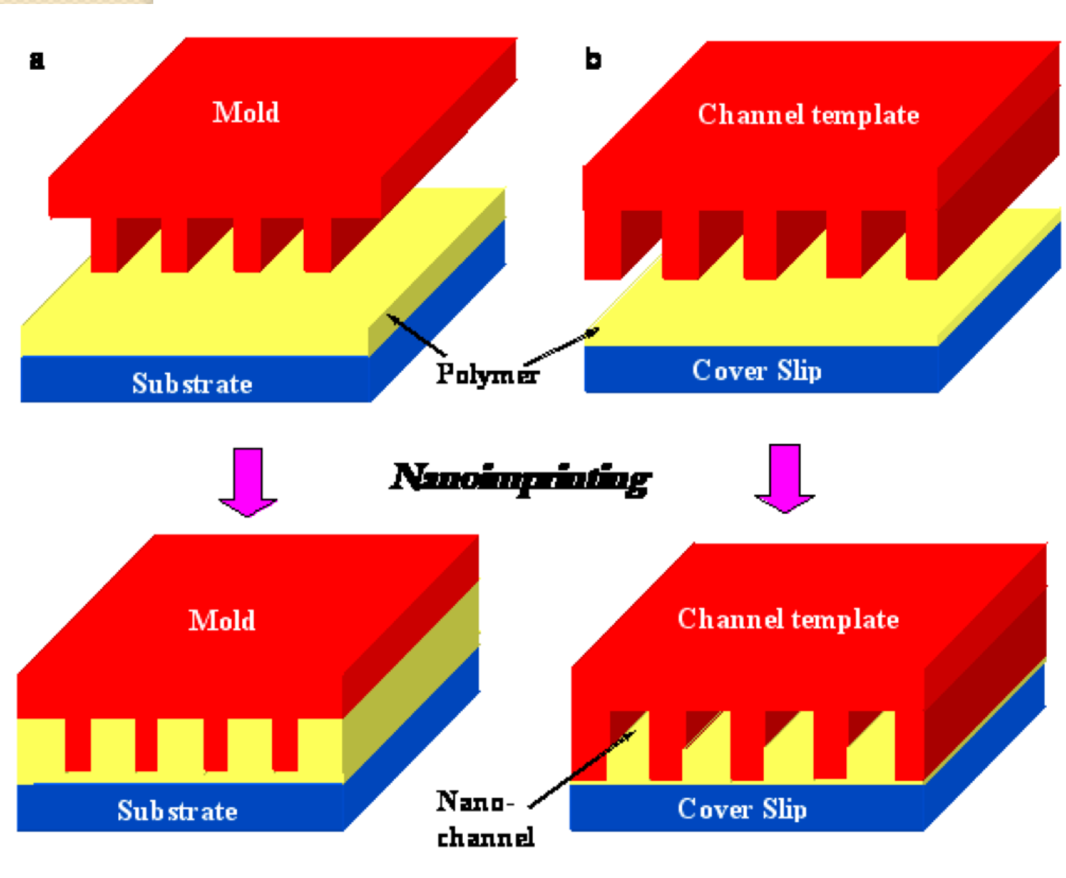
- **Nanoimprinted hole arrays in PMMA**
- **10 nm diameter, 40 nm period, and 60 nm deep**

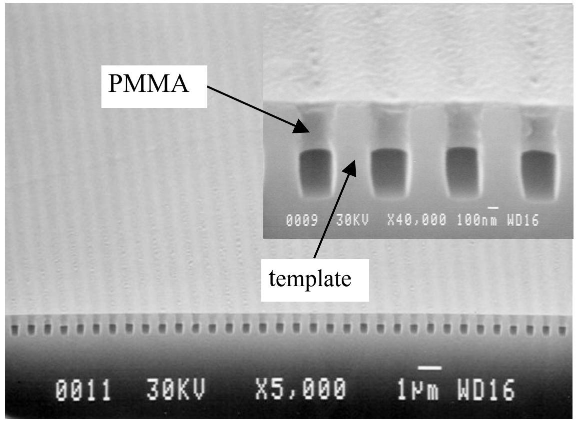
S. Y. Chou, et al.
***J. Vac. Sci. Technol*. B, Vol. 15, 2897, 1997.**

Imprinted 3-layer Polymer Structure

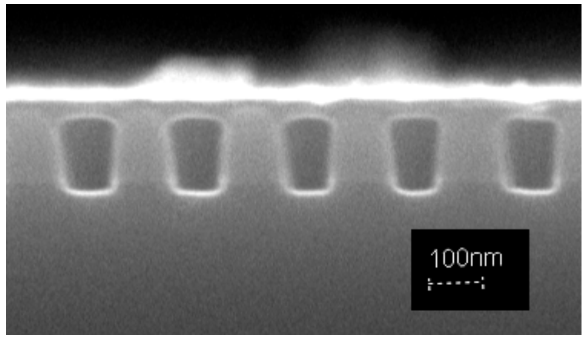


World-micro-nano Interfacing I: Reverse nanoimprinting





300(w)x500(h) nm

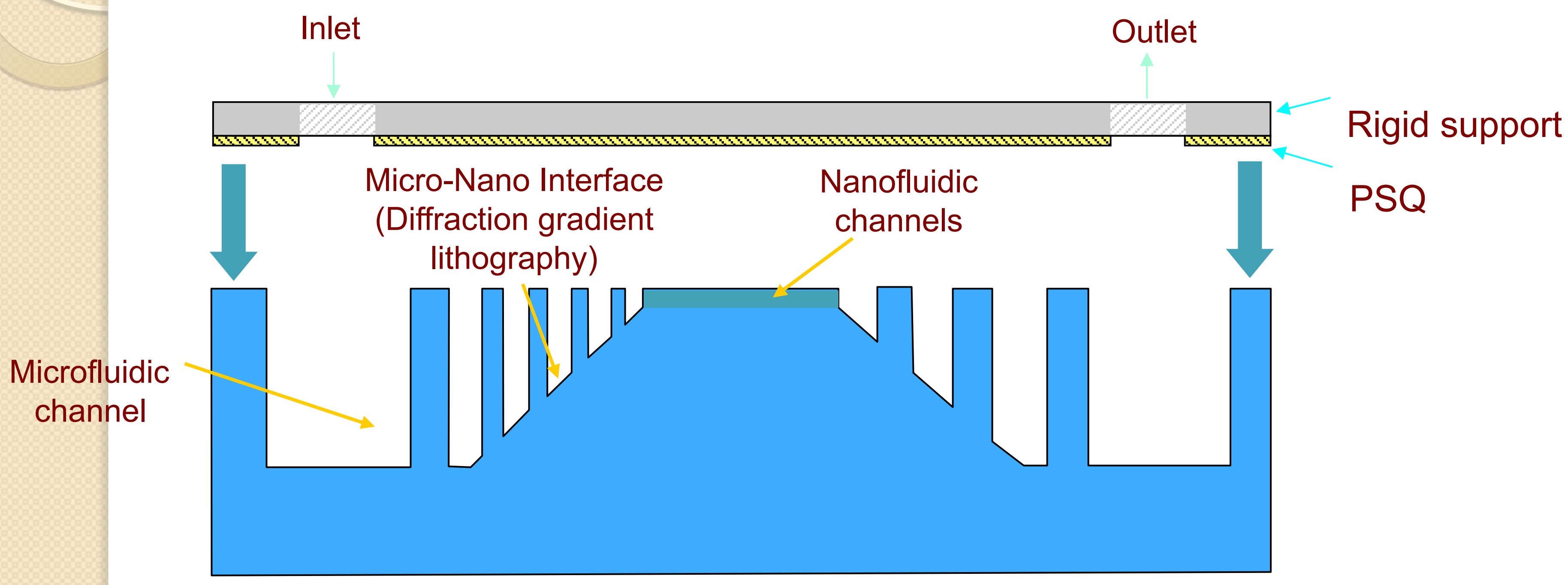


75(w)x120(h) nm

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

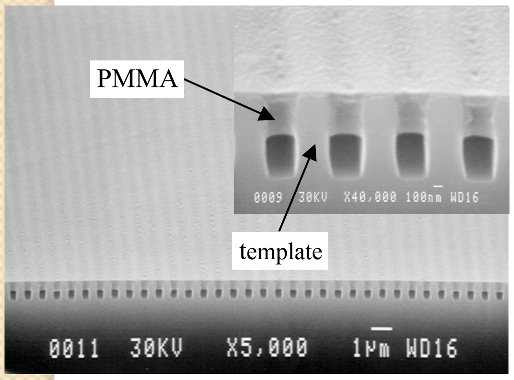
World-micro-nano Interfacing II

Simultaneous Packaging of Micro- and Nanofluidics

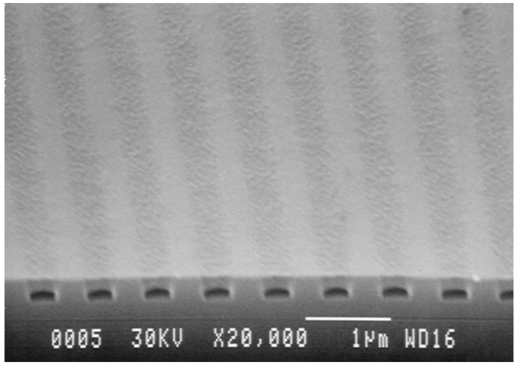


- *Permanent bonding at room temperature*
- *Conformal contact for low pressure operation*
- *Precise dimension control*
  - Sealing of 1D, 2D nano/microchannels below 10 nm
- *High throughput and low cost*

Nanofluidic Channels for DNA Stretching

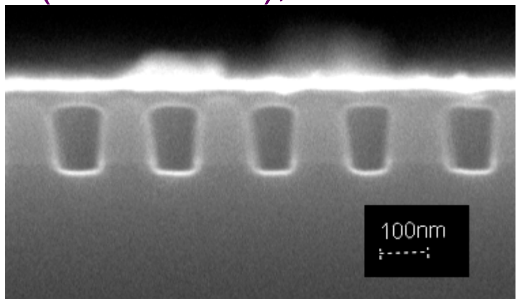


300(w)x500(h) nm

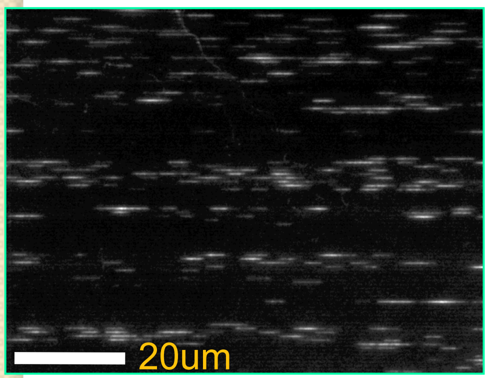


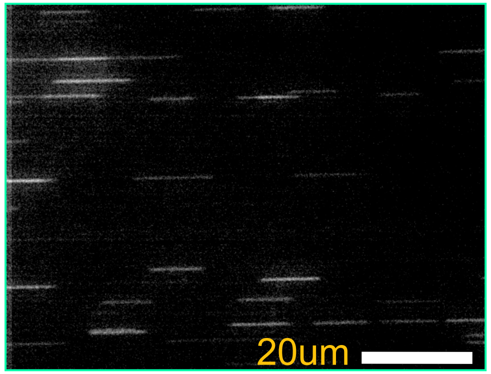
300(w)x130(h) nm

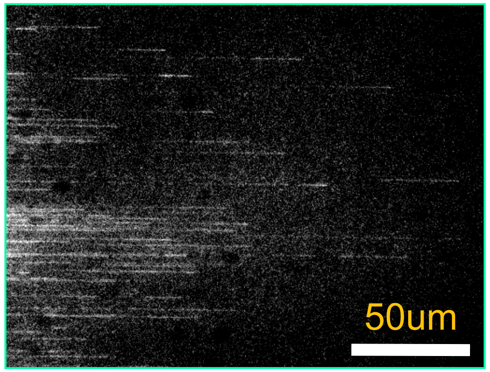
175^{o}C and 50 kg/cm^2 (4.9×10^6 Pa), 5 min



75(w)x120(h) nm





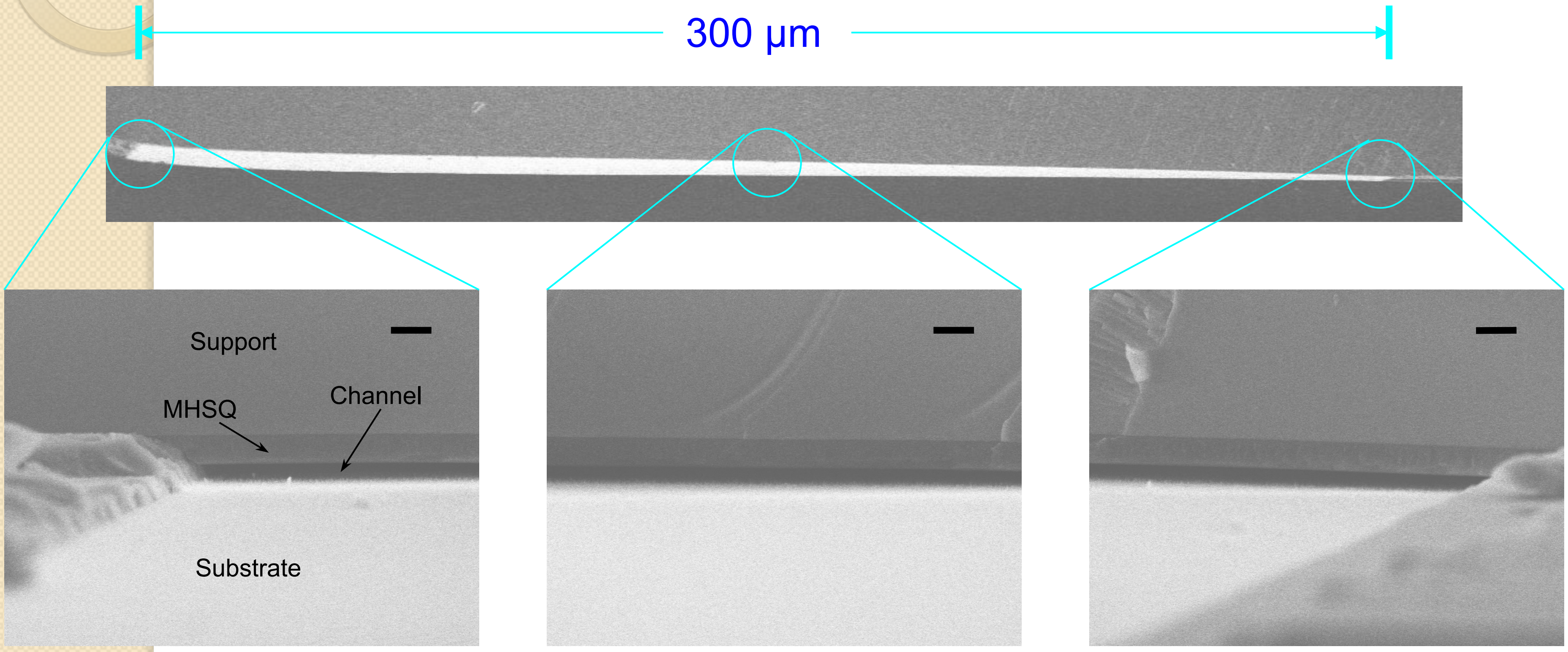


T5 phage DNA
103 kb (35 μm)

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

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

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

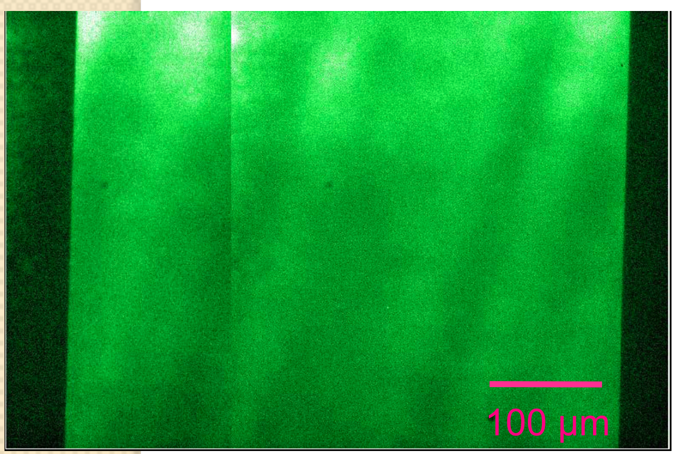


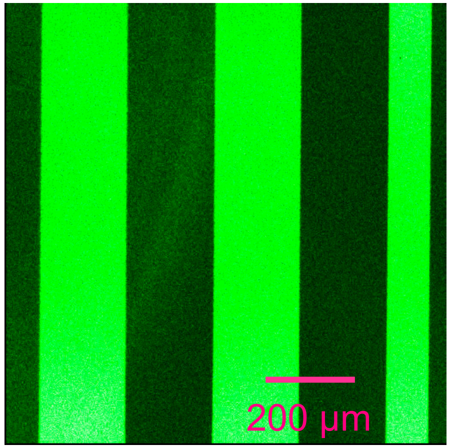
300 um x 150 nm, Scale bar is 400 nm

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

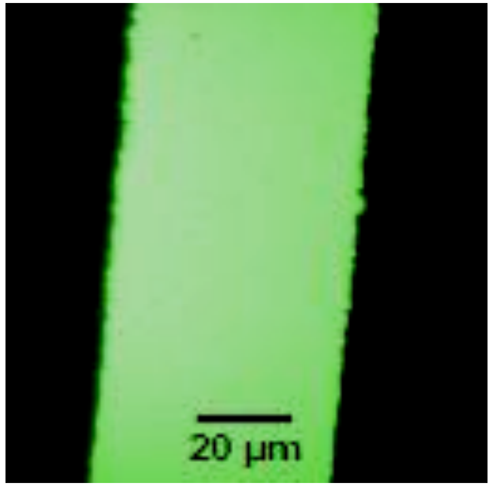
Ultralow Aspect Ratio (< 4×10^{-5}) 1D Nanochannel

18 nm deep



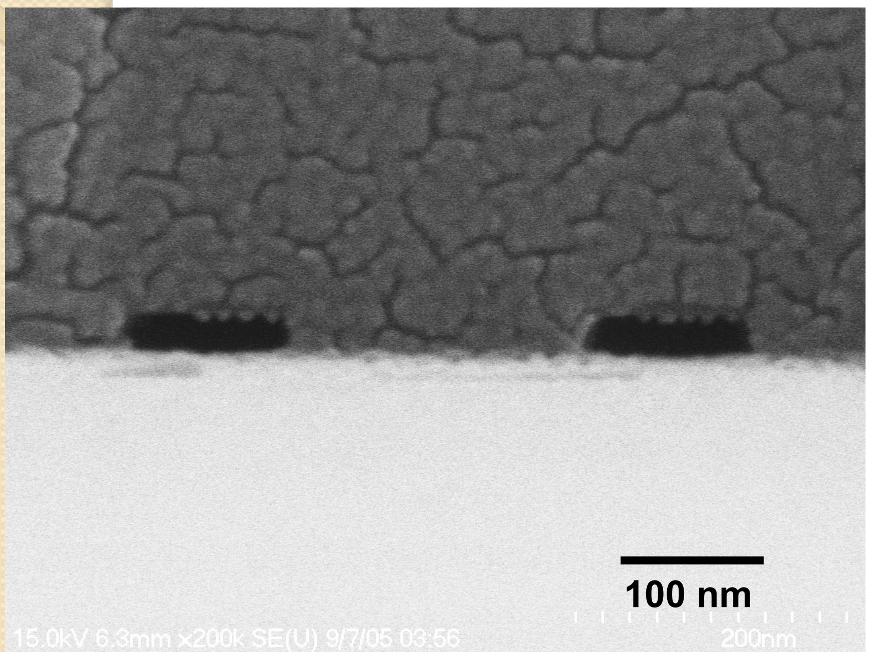


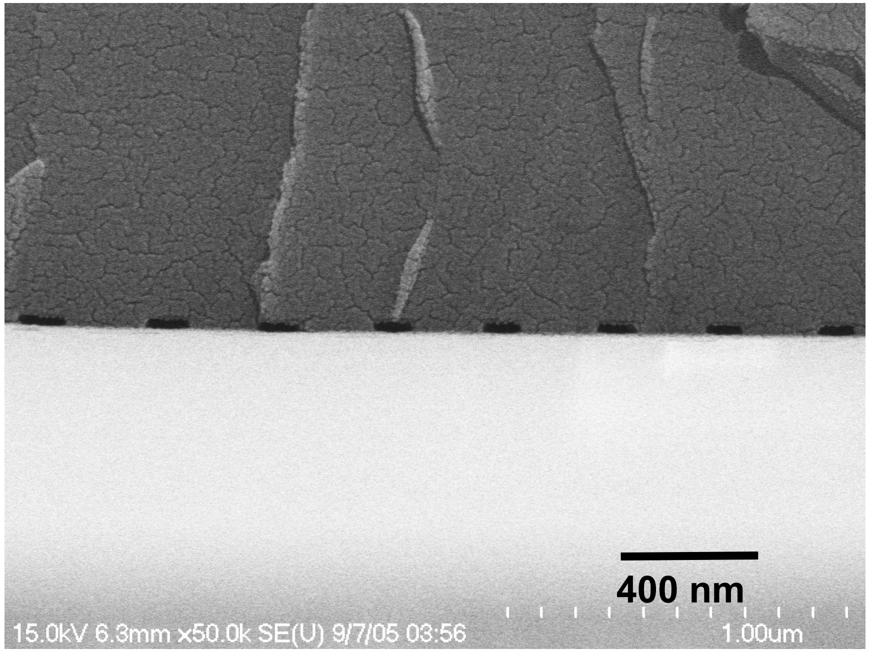
8 nm deep



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

Composite Cap Sealed 2D Nanochannel Array

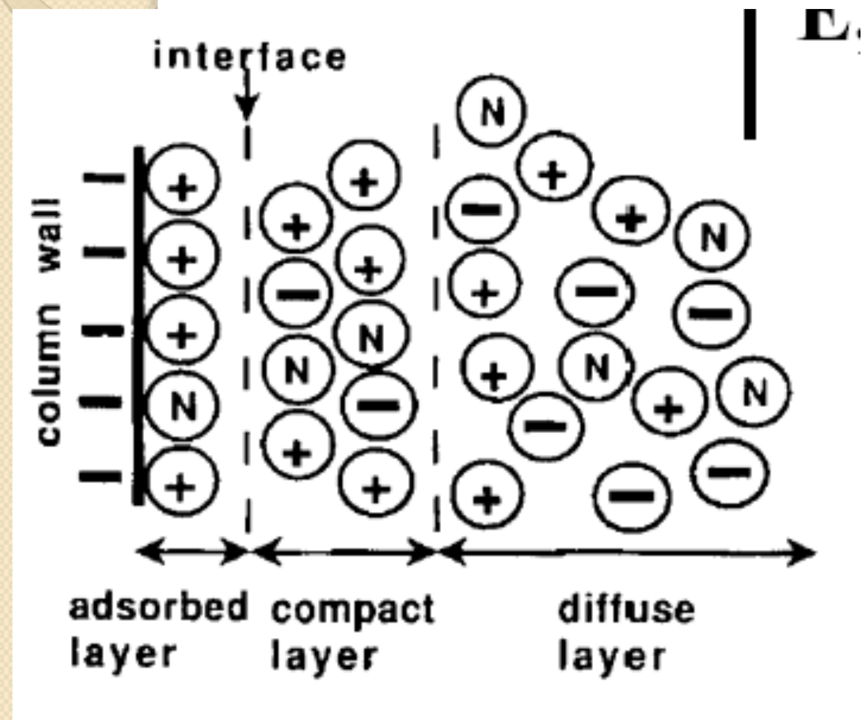




30x120 nm^2

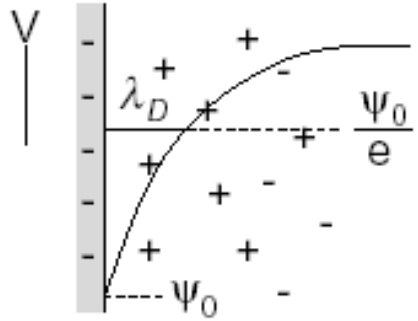
Gu, Gupta, Chou, Wei, *Lab Chip*, 7, 1198 (2007)

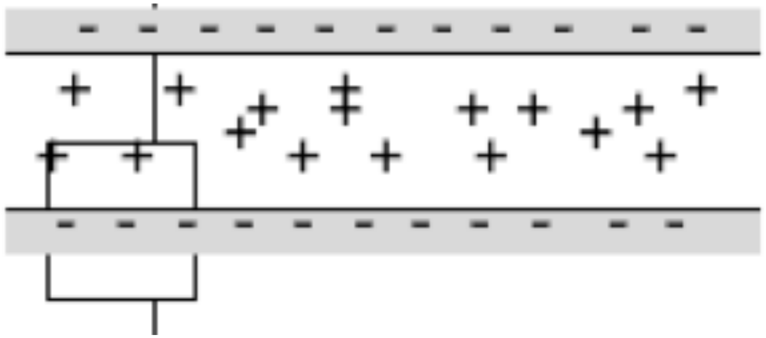
Double Layer Model



- Maxwell-Poisson Equation
- Debye-Hükel length
- Interaction form
- Constant charge assumption
- Constant potential assumption

Electrostatic force





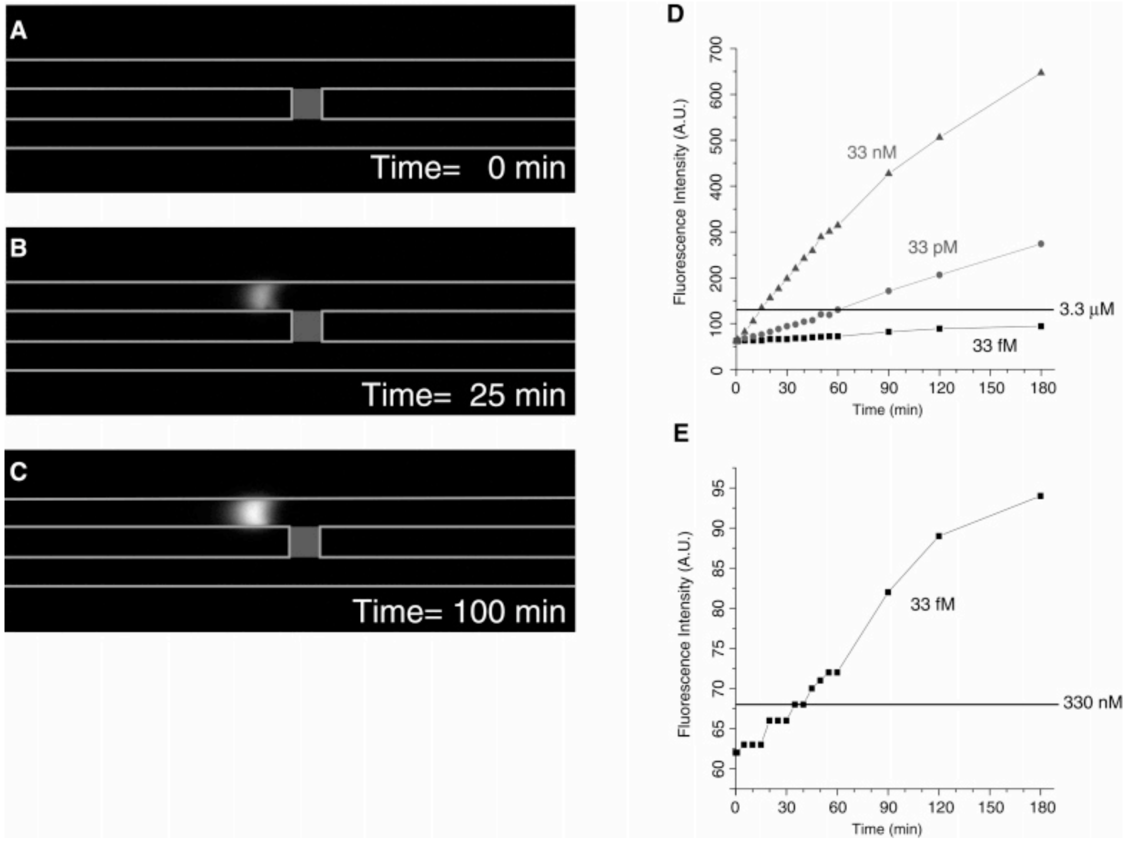
Thickness of double layer is characterized by Debye screening length λ_D; for a 1:1 electrolyte of *c* M, λ_D in nm is:

$$\lambda_D = \sqrt{\frac{\varepsilon RT}{2F^2 c}}$$

Conc / M	λ_D / nm
10^{-5}	100
10^{-4}	30
10^{-3}	10
10^{-2}	3
10^{-1}	1

Protein preconcentration

Debye layer overlapping



YC Wang, AL Stevens, JY Han,
Anal. Chem. 2005, 77, 4293

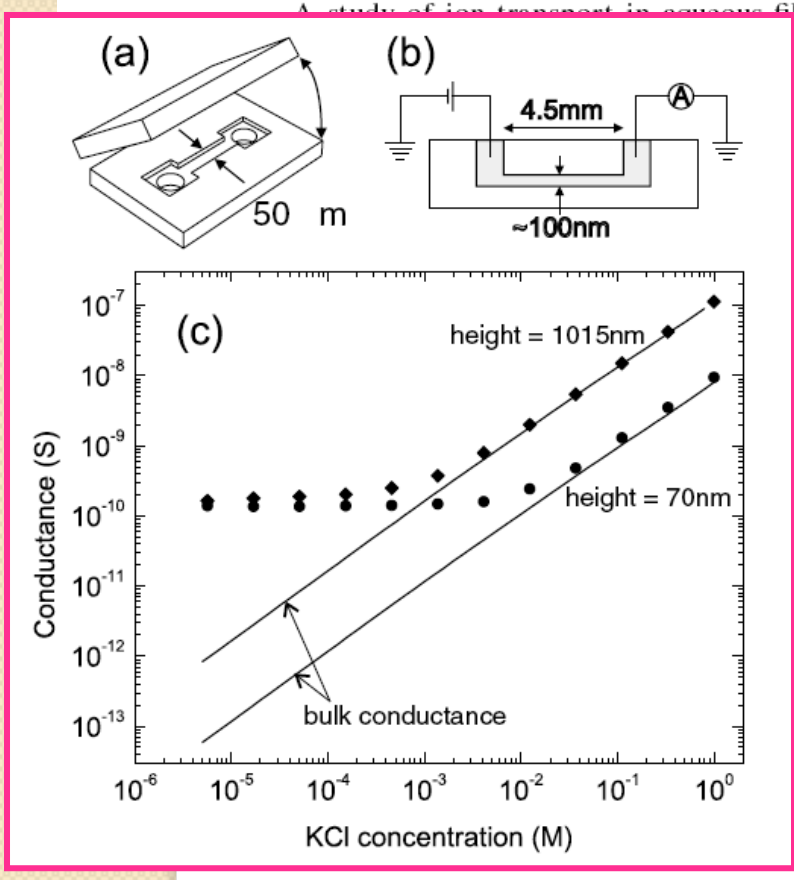
Recent experiments

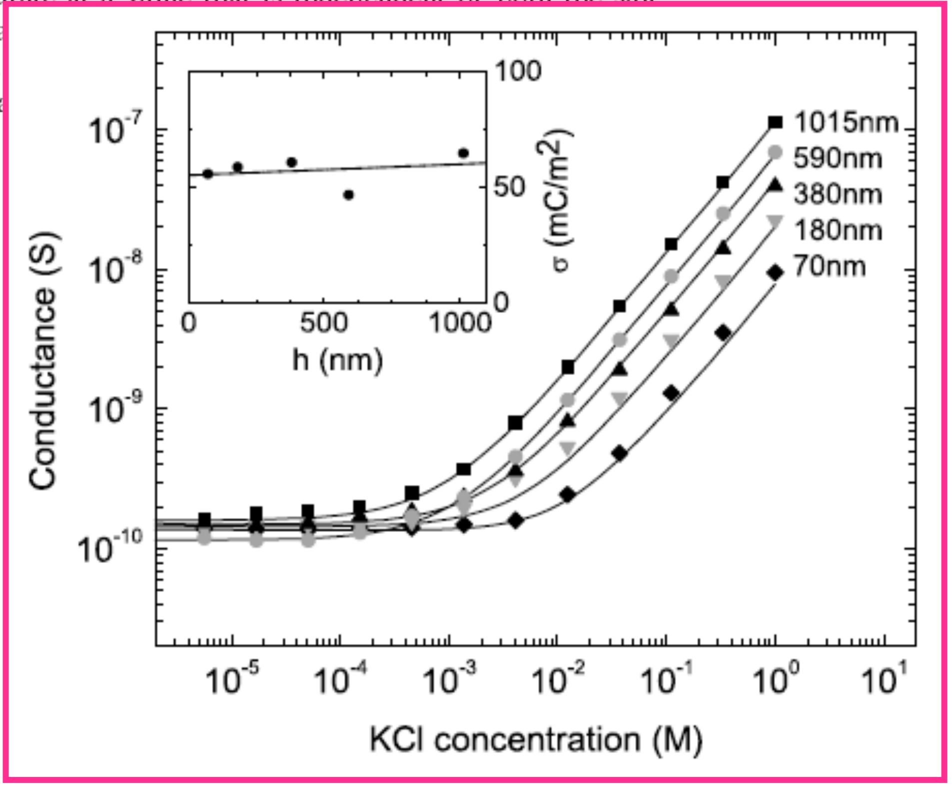
VOLUME 93, NUMBER 3 PHYSICAL REVIEW LETTERS week ending 16 JULY 2004

Surface-Charge-Governed Ion Transport in Nanofluidic Channels

Derek Stein, Maarten Kruithof, and Cees Dekker
Kavli Institute of Nanoscience, Delft University of Technology, Lorentzweg 1, 2628 CJ Delft, The Netherlands
(Received 15 April 2004; published 15 July 2004)

A study of ion transport in aqueous filled silica channels as thin as 70 nm reveals a remarkable
...tions that departs strongly from bulk behavior: In the dilute
...nels saturate at a value that is independent of both the salt
...Our data
...density.
...s, ion tra





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2005
Vol. 5, No. 5
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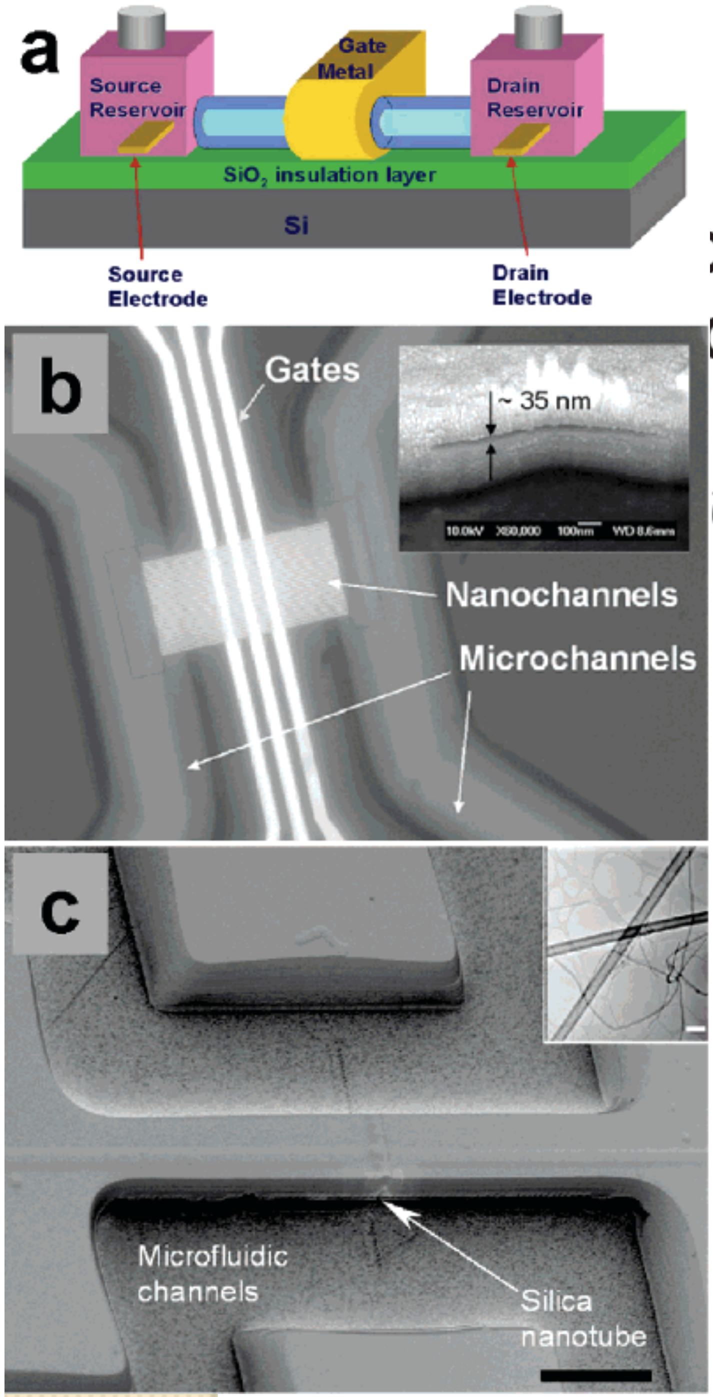
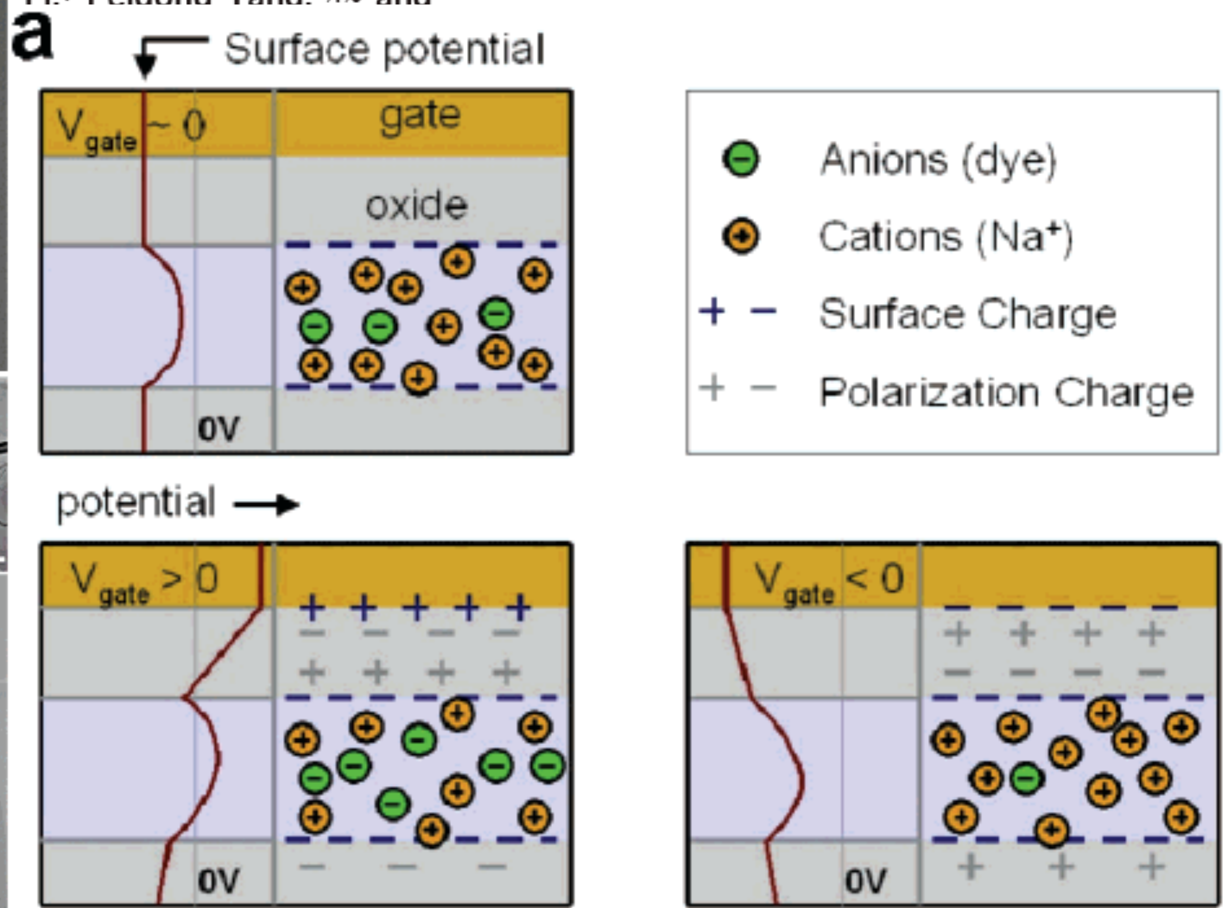
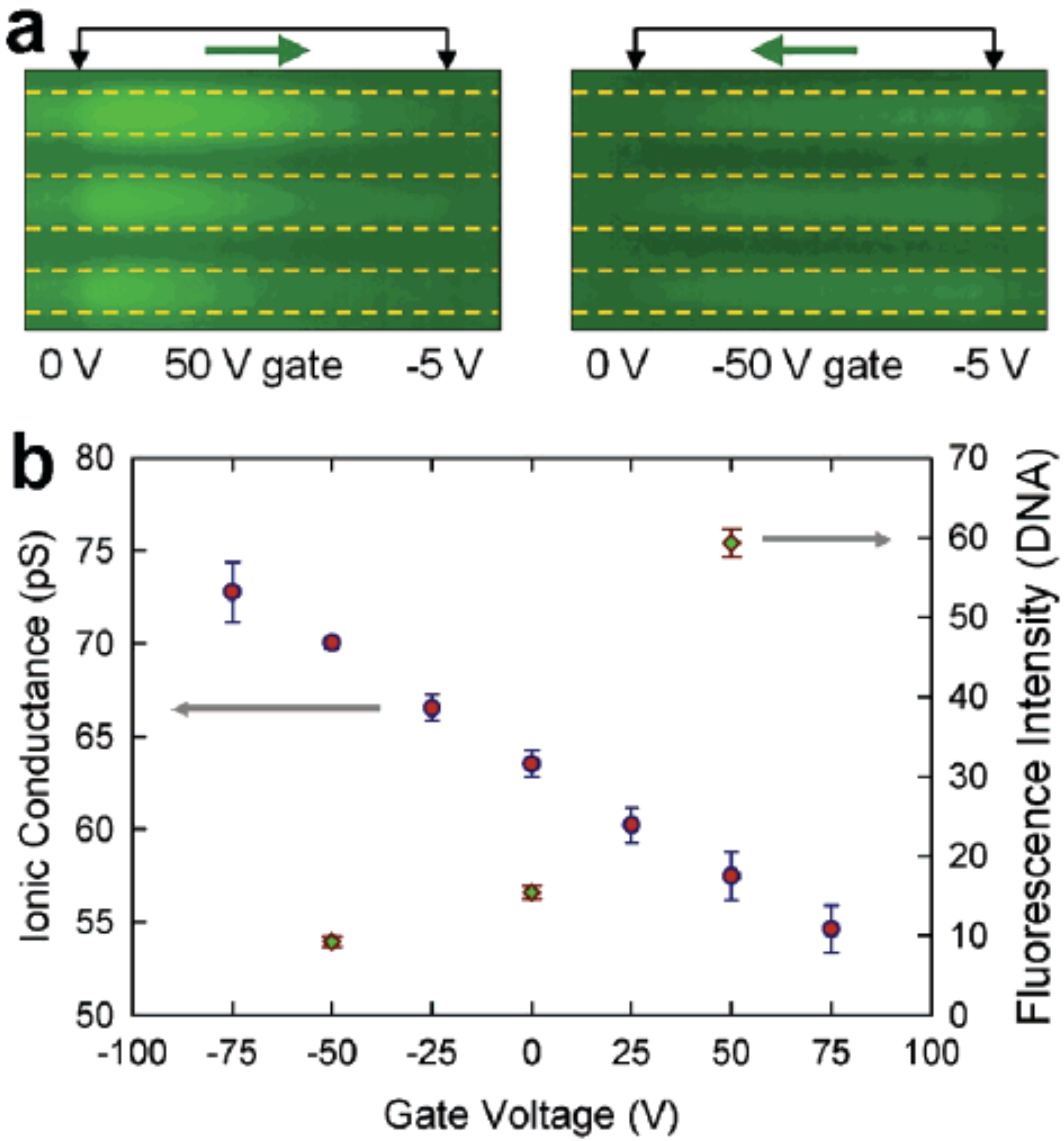


f Ions and
dic Transistors

Li,† Peidong Yang,*,‡,§ and




a
0 V
50 V gate
-5 V
0 V
-50 V gate
-5 V
b
Ionic Conductance (pS)
Fluorescence Intensity (DNA)
Gate Voltage (V)
80
75
70
65
60
55
50
70
60
50
40
30
20
10
0
-100
-75
-50
-25
0
25
50
75
100

Exercise

- E. coli coasting time and distance? Assume radius is 1 micrometer, velocity 30 um/s.
- Diffusion (random walk) which is not Gaussian? Give examples (Steve Granick).
- How to use FCS (fluorescence correlation spectroscopy) to determine diffusion coefficient "D"?

Fluorescence correlation spectroscopy

Point spread function: $PSF(r,z) = I_0 e^{-2r^2/\omega_{xy}^2} e^{-2z^2/\omega_z^2}$

Autocorrelation Function: $G(\tau) = \frac{\langle \delta I(t) \delta I(t+\tau) \rangle}{\langle I(t) \rangle^2} = \frac{\langle I(t) I(t+\tau) \rangle}{\langle I(t) \rangle^2} - 1$

$\delta I(t) = I(t) - \langle I(t) \rangle$ **the deviation from the mean intensity**

Autocorrelation for Normal Diffusion:

$$G(\tau) = G(0) \frac{1}{(1+(\tau/\tau_D))(1+a^{-2}(\tau/\tau_D))^{1/2}} + G(\infty)$$

Fitting parameters

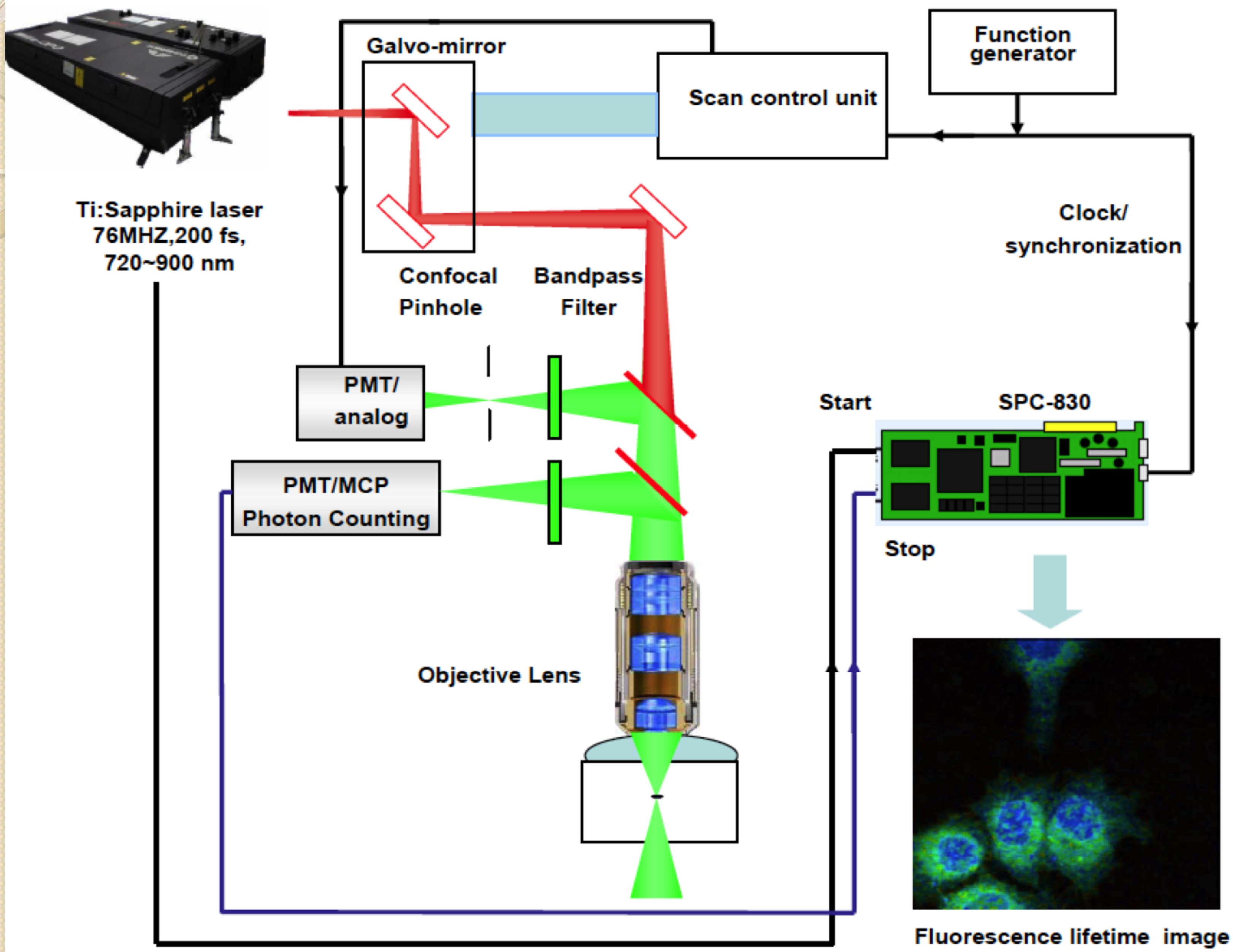
where $a = \omega_z / \omega_{xy}$ is the ratio of axial to radial e^{-2} radii of the measurement volume, and τ_D is the characteristic residence time.

$$G(0) = \frac{1}{<N>} = \frac{1}{V_{eff} <C>}$$

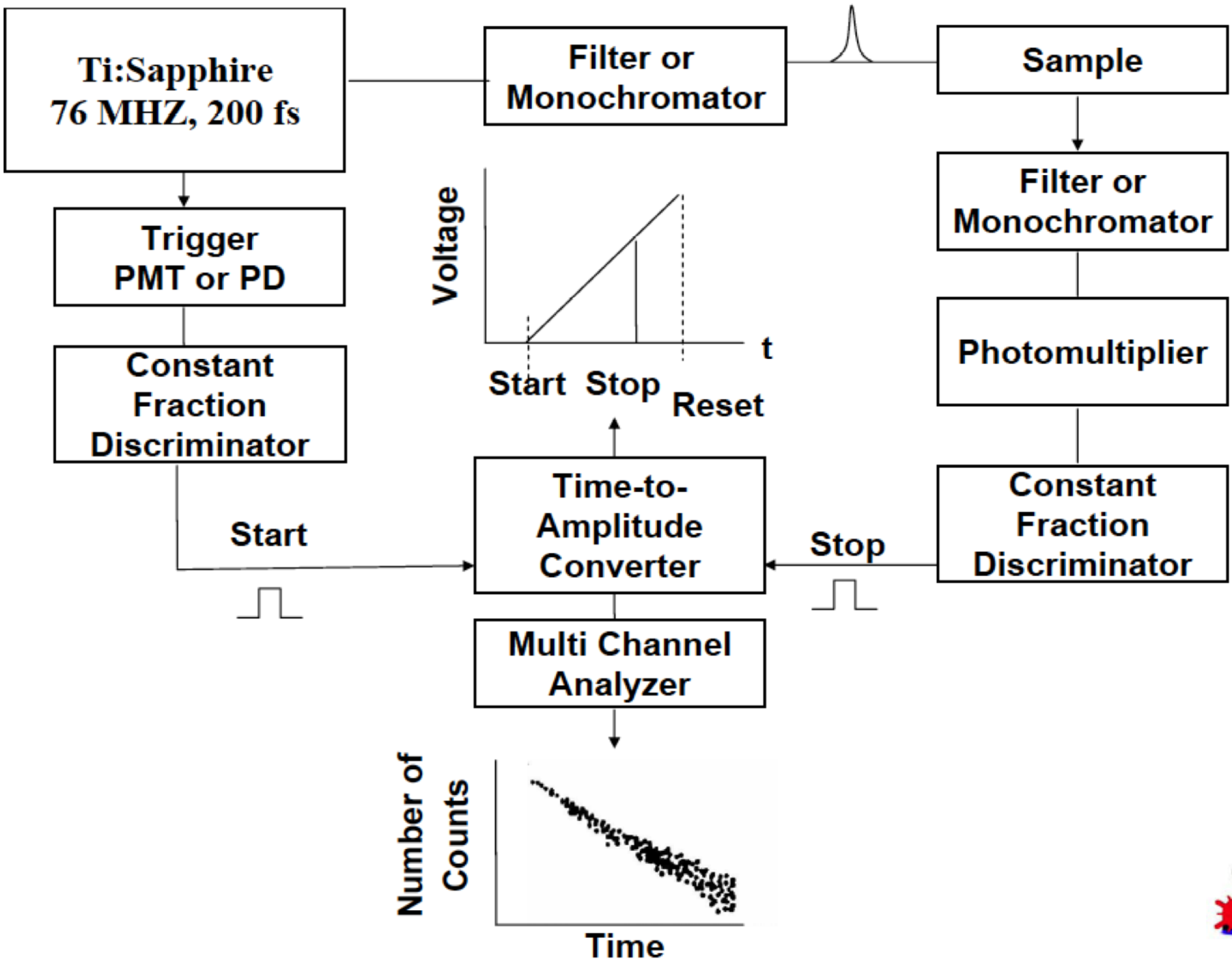
$V_{eff} = \pi^{3/2} \omega_{xy}^2 \omega_z$ **effective volume**

$$D = \omega_{xy}^2 / 4\tau_D.$$

Optical setup of the TCSPC FLIM/FRET system



Courtesy Prof. FJ Kao



Courtesy Prof. FJ Kao