

Flow sensors

Must be able to quantify flow rates on the fly.

This is challenging because of the small amounts of fluid being pumped.

Consider a moderately extreme example:

Flow channel 10 μm by 10 μm , with an averaged flow speed of 100 $\mu\text{m}/\text{sec}$.

Volume flow rate: 0.6 nL/min (!).

Things only get more challenging as devices shrink.

Main approaches:

- Differential pressure
- Drag force
- Thermal flow

Differential pressure flow measurement

Many microfluidic flows are laminar and pressure driven.

This means that it's possible to measure the differential pressure across a channel and directly infer the flow rate.

For laminar flow,

$$\frac{\Delta P}{L} = u \frac{\mu}{2D^2} \text{Re } f$$

D = "hydraulic diameter"

= 4 x Area / perimeter

f = friction coefficient

$\text{Re } f$ = 64 for circular channels,
50-60 for rectangular.

For the example on the previous slide, $D = 10 \mu\text{m}$; for water, $\mu = 1 \times 10^{-3} \text{ kg/m-s}$, $\text{Re } f \sim 50$.

So, $\Delta P/L = 500 \text{ Pa/m}$, and a 100 μm long channel would mean a pressure difference of 0.05 Pa = $5 \times 10^{-7} \text{ atm}$.

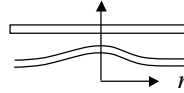
This is pretty tough to do, but it can be done.

Differential pressure flow measurement

One approach (with some useful formula) is a **capacitive** measurement.

Thin disk-shaped transducer of radius R . For Young's modulus E and Poisson ratio ν , deflection vs. r given by

$$y(r) \approx \frac{3(1-\nu^2)}{16Et^3} (R^2 - r^2)^2 p$$

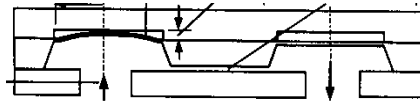


Integrating up to get change in capacitance for initial spacing d ,

$$\frac{\Delta C}{C} \approx \frac{(1-\nu^2)}{16Edt^3} R^4 p$$

So, for $d = 100 \text{ nm}$, $t = 100 \text{ nm}$, $R = 100 \text{ }\mu\text{m}$, $\nu \sim 0.25$, $E = 170 \text{ GPa}$, $p = 0.05 \text{ Pa}$, we get around a 1.7 % change in C .
Certainly measurable, though not trivially.

Alternative: **piezoresistive** measurement.



Nguyen and Wereley

Drag force

Because of viscosity, laminar flow around an object (cantilever) (through a gap of area A_g) exerts a drag force on the object that has two components:

$$F_d = F_1 + F_2 = \frac{C_1 L \mu}{A_g} \dot{Q} + \frac{C_2 \rho}{A_0 A_g} \dot{Q}^2$$

pure viscous effect

pressure drop effect

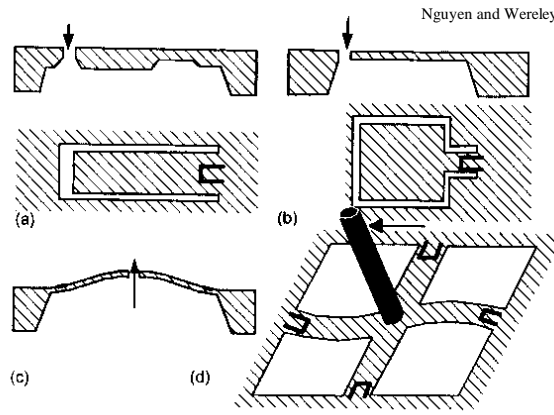
Low flow rates: deflection \sim linear in volume flow rate.

High flow rates: deflection \sim quadratic in volume flow rate.

Basic idea is to construct a flexible obstacle, and use some means (*e.g.* piezoresistive) to measure its deflection.

Clearly, low flow rates require a very flexible transducer (nanoscale thicknesses).

Drag force



Several examples of drag sensor geometries.

Thermal approaches

Idea here is to use thermal transport to sense mass transport.

Common approaches:

- Time-of-flight (heater + remote thermometers)
- Heater temperature at constant heater power
- Heater power at constant heater temperature

Latter two give electrical signals, since heater temperature is sensed by looking at the resistance.

h = heat transfer coefficient (Power per unit area per temperature difference = W/m^2-K)

Thermal approaches

Relevant dimensionless quantities:

Prandtl number: $Pr \equiv \frac{c_p \mu}{\kappa_T}$ momentum diffusion / thermal diff.

Nusselt number: $Nu \equiv \frac{hd}{\kappa_T}$ total heat transfer / conductive part

So, for heaters, if a heater power W is being applied, then the temperature offset of the heater from the nearby fluid is given by

$$W = \frac{Nu \kappa_T A \Delta T}{L}$$

Can back out flow speed because, for laminar flow over flat plates and wires,

$$Nu \approx 0.664 \sqrt{Re^3} \sqrt{Pr}$$

Mixers

We've said before that one major issue for using microfluidic systems to do useful reactions, assays, etc. is the slowness of fluid mixing when flows are laminar.

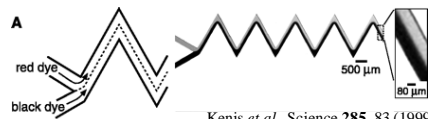
In strict laminar flow, mixing at the molecular scale is governed by diffusion.

Diffusion constant for most liquids $\sim 10^{-9} \text{ m}^2/\text{s}$.

So, typical distance over which mixing is accomplished in a time τ goes like

$$d \sim \sqrt{2D\tau}$$

How good is diffusive mixing if we have two parallel streams 5 microns wide in our original 100 micron long, 100 micron/sec flow channel? Pretty good - d for 1 sec is ~ 50 microns, many times the width of the flow channel. Often, though, we're not so lucky.



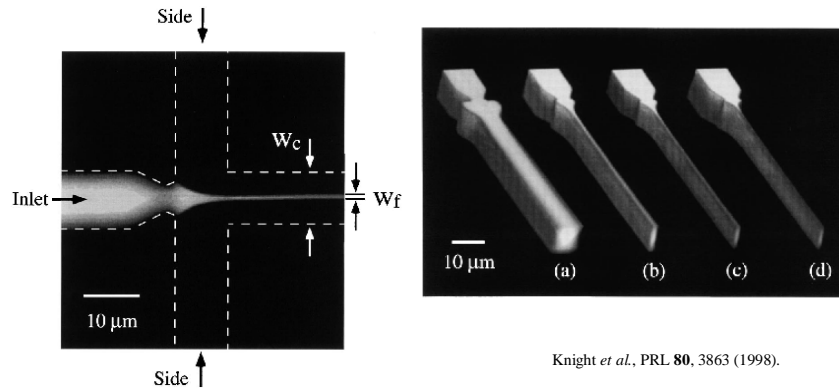
Kenis *et al.*, Science 285, 83 (1999)

Mixers

So, one sensible approach is to divide the flow stream into as many narrow parallel streams as possible!

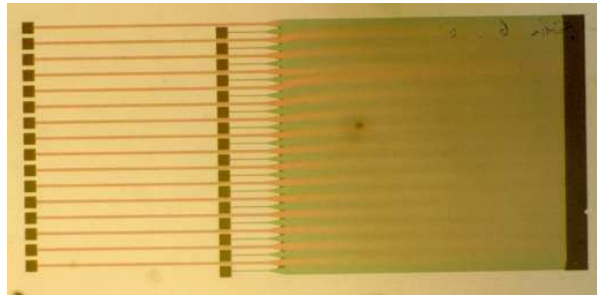
Then one only needs diffusion over \sim the width of one stream.

Ordered way to do this: hydrodynamic focusing.

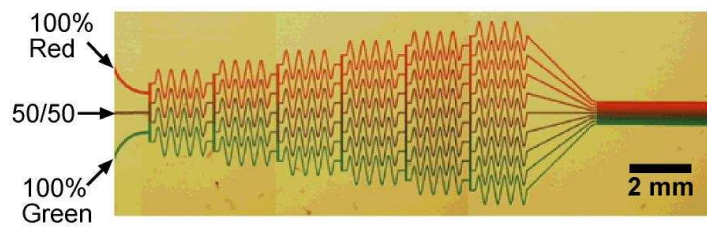


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Mixers



Whitesides, Harvard



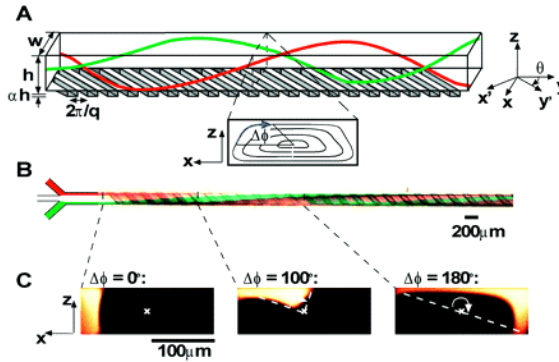
Mixers

Another way to do this is by chaotic mixing.

Turbulence is effective at mixing because streams break up into eddies on length scales going down to the very small, for which the diffusion process we've been discussing is rapid.

Need to mimic this in a laminar system.

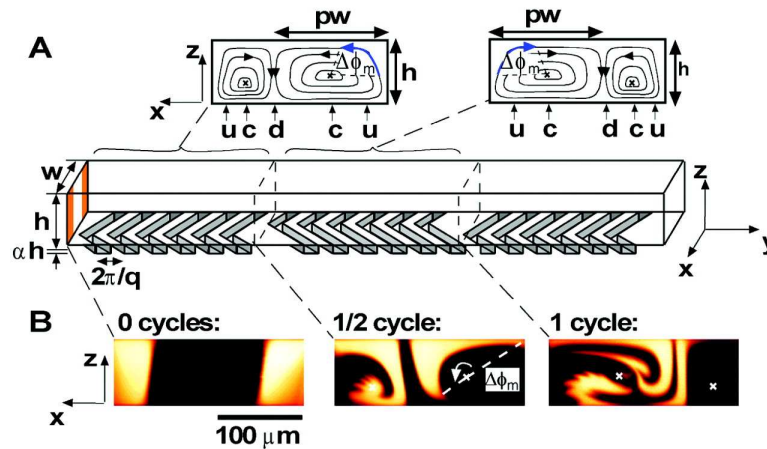
Ridges on bottom of flow channel can cause chaotic motion in cross-section.



Stroock *et al.*, Science 295, 647 (2002)

Mixers

Stroock *et al.*, Science 295, 647 (2002)



By making less regular patterns of ridges, can produce chaotic flow patterns laterally.

These sorts of techniques can lead to much more rapid mixing.

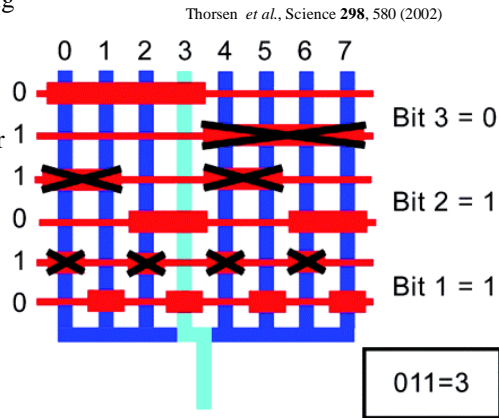
Integration capabilities

While it's early yet for the field of microfluidics (first use of the term: c. 1983), rapid progress has already been made in terms of large scale integration of microfluidic devices.

Key idea: multiplexing

Instead of trying to individually control every valve, use a clever binary scheme to direct fluid.

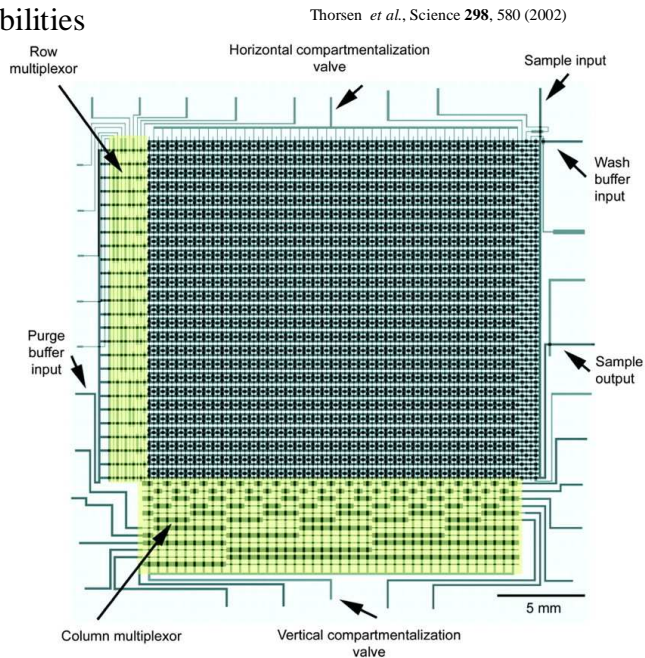
Valves here work by pneumatically pressing down a thin membrane of PDMS.



Integration capabilities

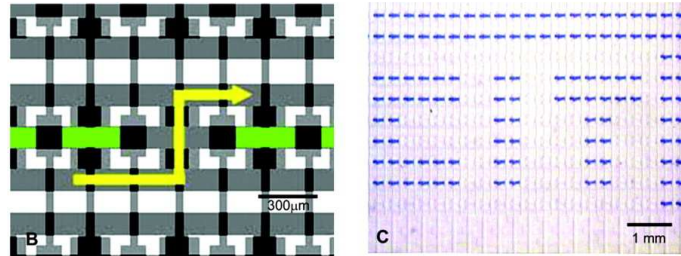
Here's an example of a fluidic "memory", with 1000 chambers (each ~ 250 pL) that are individually addressable.

Think about combinatorial surveys for analytical chemistry or biology.



Integration capabilities

Thorsen *et al.*, Science **298**, 580 (2002)

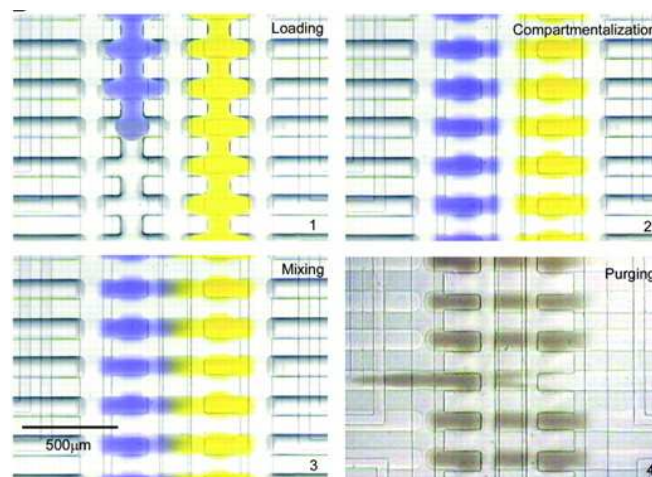


With this approach, can purge individual chambers one at a time with a buffer solution.

An example of this control is at the right....

Integration capabilities

Thorsen *et al.*, Science **298**, 580 (2002)



These capabilities can permit assay strategies that would otherwise be extremely difficult....

Integration capabilities

Thorsen *et al.*, Science **298**, 580 (2002)

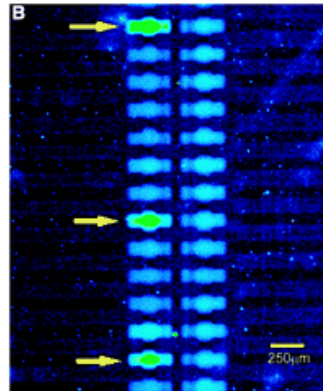
An example of this:

Left-hand chambers filled with a dilute solution of *E. coli* containing a particular enzyme.

Typical occupancy of left chambers is ~ 20% with single cells, rest empty.

Right hand chambers filled with indicator that reacts with enzyme to form fluorescent product.

Can check individual cells, but in parallel this way.



Applications of microfluidics

We've already touched on a number of applications for microfluidic technology (*e.g.* inkjet printers).

Far and away, the fields with the most interest right now in these techniques are analytical chemistry and (molecular and cellular) biology.

Analytical chemists foresee means of automating massive combinatorial surveys.

The real advantages over bulk techniques:

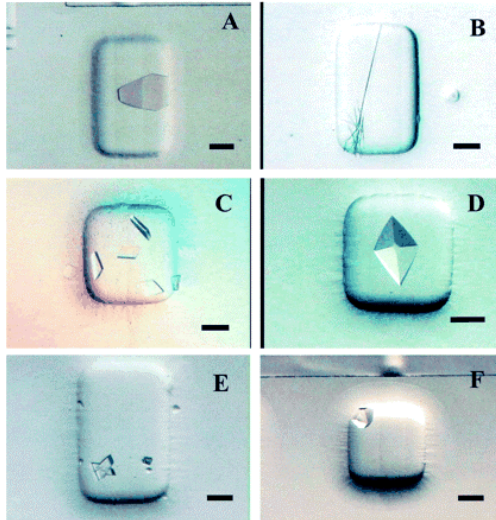
- Can get away with using much less analyte (tiny reaction volumes)
- May be integrated and automated into a small, stand-alone package much more readily.

Applications of microfluidics

Another possibility is performing chemical reactions under precisely controlled conditions in a very quiescent environment.

Example: protein crystal growth

Can use integrated microfluidics to explore a huge parameter space of crystallization conditions while using a miniscule amount of protein (which can be very hard to isolate and purify).



Hansen *et al.*, PNAS **99**, 16531 (2002)

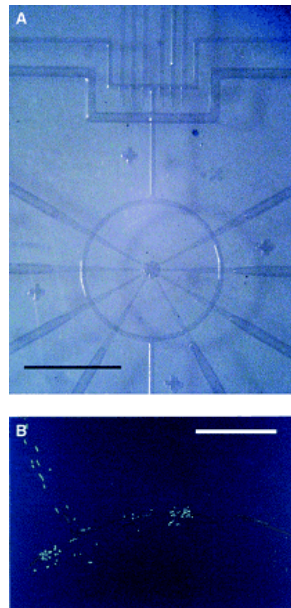
Applications of microfluidics

As for biology, a couple of examples.

Using the rotary (peristaltic) pump at right, a solution containing beads tagged with a fluorescent analyte were pumped past binding sites patterned in the large channels.

Result: could get binding 60x faster with active pumping than without.

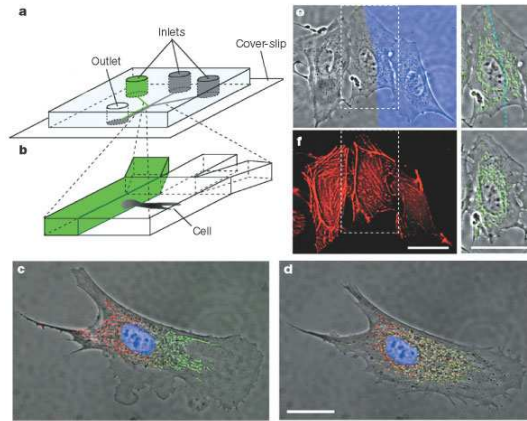
Again, speeds up surveys and assays.



Quake and Scherer, Science **290**, 1536 (2000)

Applications of microfluidics

Takayama *et al.*, Nature **411**, 1016 (2001)



Can control fluid flows on length scales smaller than cellular sizes.

Great for tagging certain organelles and watching intracellular transport.

Limits and applications of fluids at the nanoscale

Two particular areas of concern:

- Do hydrodynamic assumptions fail at the nanoscale?
What are the consequences?
- Does the continuum approximation underlying our treatment of fluid mechanics fail? What are the consequences?

Also, how do we prepare and study nanoconfined fluids?

Of what use is “nanofluidics”?

Do hydrodynamic assumptions break down at the nanoscale?

Yes - we've already discussed the no-slip boundary condition for fluids at liquid-solid interfaces.

The no-slip condition is an idealization assuming moderately strong attractive interactions between the fluid particles and the walls.

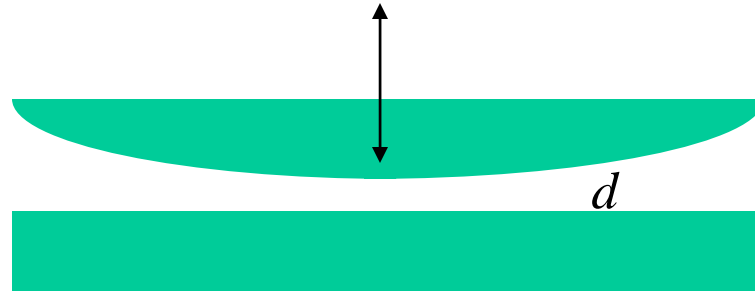
Clearly, if we can tune the surface chemistry or otherwise (*e.g.* electrowetting) alter the interfacial energy, one has to wonder about the no-slip situation.

Important because sometimes we care about the details of hydrodynamic flow on the nanometer scale!

The demise of the no-slip condition

You have two papers on your problem set that deal with experiments claiming to measure deviations from the no-slip condition on nanometer scales.

Here's another approach:



Take two atomically smooth (mica-coated) crossed cylinders immersed in fluid, and oscillate their spacing (d) vertically.

A hydrodynamic viscous force will act to damp this motion.

Solving the N-S equations with no-slip condition,

$$F_H = f^* 6\pi R^2 \mu \frac{\dot{d}}{d}$$

Demise of the no-slip condition

$$F_H = f^* 6\pi R^2 \mu \frac{\dot{d}}{d}$$

So, if one works with an apparatus that vibrates at a particular frequency ν and measures the peak force, one can define a parameter

$$G \equiv \frac{6\pi R^2 \nu}{F_{H,peak}} = \frac{d}{\mu}$$

The experiment: measure the force as a function of cylinder separation d for a variety of fluid combinations (different wetting conditions as determined by contact angle measurements).

No-slip: a plot of G vs. d should extrapolate to 0 as d goes to 0.

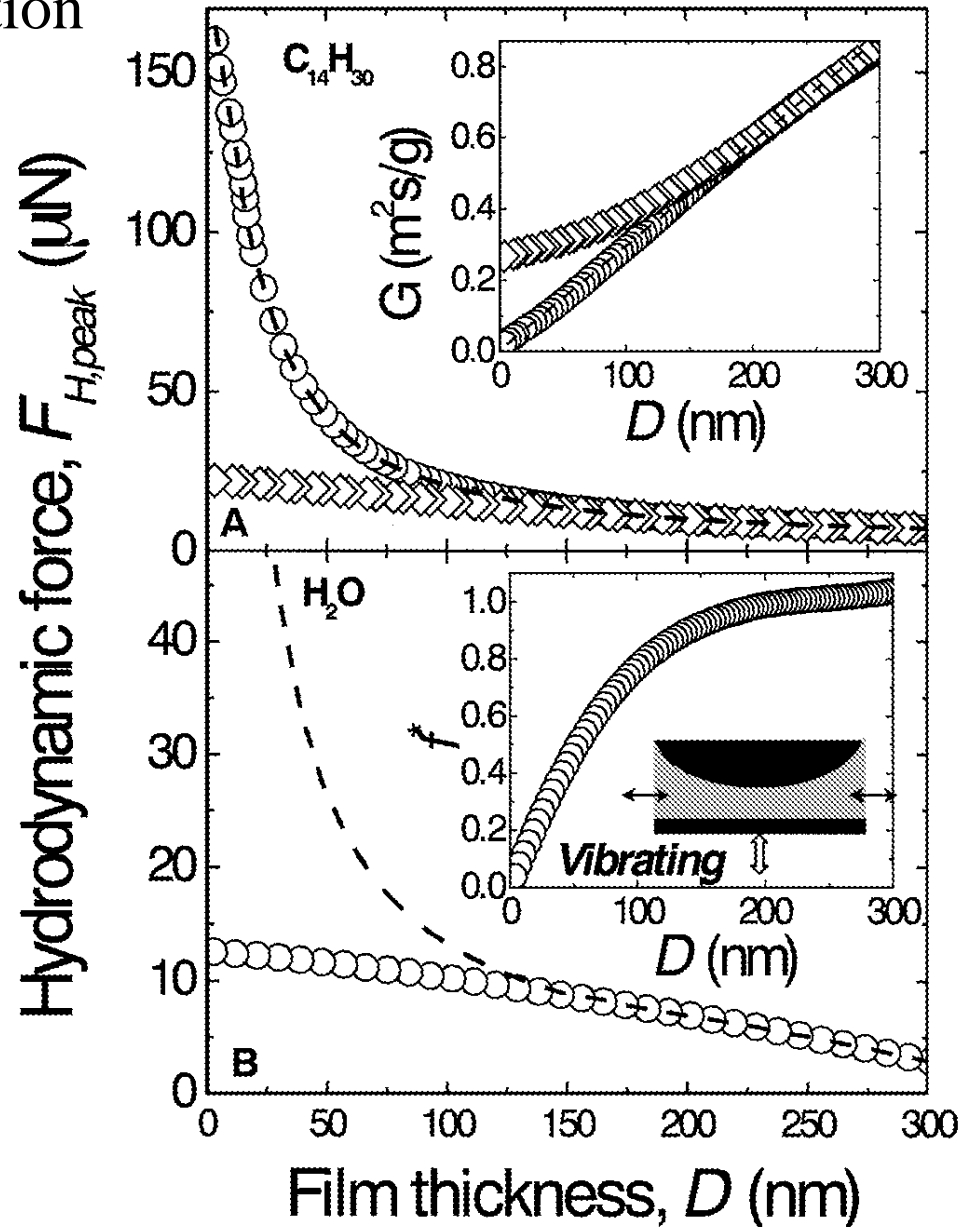
Demise of the no-slip condition

Upper case: tetradecane on mica (wetting = circles) and on a methyl-terminated SAM (contact angle = 44 degrees = diamonds).

Lower case: water on SAM-coated mica.

Dashed lines = no-slip predictions.

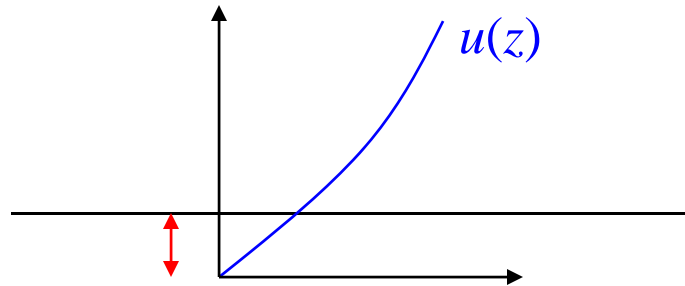
Insets: curves supposed to extrapolate to zero....



Demise of the no-slip condition

So, for poorly wetting interfaces, there appears to be slippage.

Can quantify this by a **slip length**:



Slip length = fictitious distance inside the solid where liquid velocity extrapolates to zero.

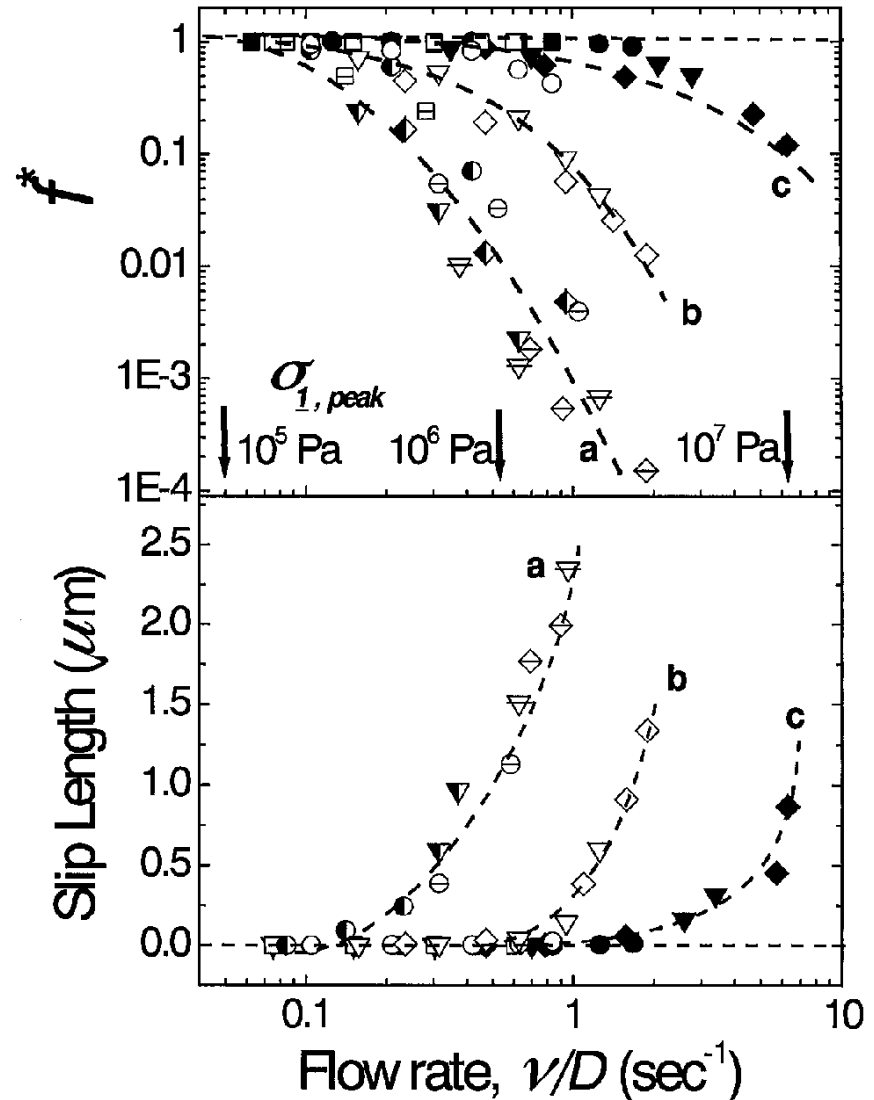
With this simple assumption, can then analyze data to get slip length and see how it depends on, *e.g.*, flow rate.

Demise of the no-slip condition

Two trends are observed in the data:

- The higher the would-be induced shear stress, the more slip.
- Deviation from no-slip happens at lower effective shear stresses in poorly wetting surfaces than in well-wetting surfaces.

Still an active topic of investigation!



When should the continuum approximation break down?

One can define the Knudsen number for a fluid:

$$\text{Kn} \equiv \frac{\ell}{L}$$

←———— mean free path for particle
←———— characteristic dimension of interest

In a gas, a high Knudsen number means that flow is in the “molecular regime” - particles are vastly more likely to scatter off the walls of the container, for example, than each other.

This means that using continuum hydrodynamics to describe many of the gas’ properties is not appropriate.

In a liquid, Kn approaching 1 implies that the **fluid is confined on scales comparable to the interparticle separation** (since the mean free path is that short).

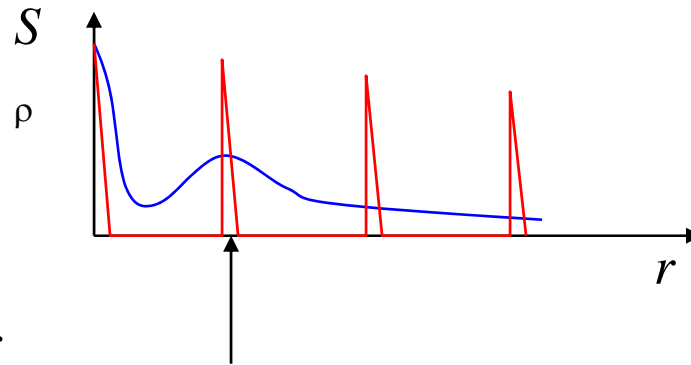
How should the continuum approximation break down?

This gets to the heart of our definitions of a homogeneous liquid.

One typical aspect of this definition is the idea that the density-density correlation function of a liquid has a particularly simple form:

$$S_{\rho}(r) \equiv \frac{\langle \rho(0)\rho(r) \rangle}{\langle \rho(0)\rho(0) \rangle}$$

In a **liquid**, average relative positions of other particles can be quite variable - no long range order.



typical interparticle separation

In a crystalline **solid**, relative positions take on very specific values.



Under confinement (or within molecular scales of interfaces), expect to see signs of ordering....

Example: nontrivial changes in viscosity

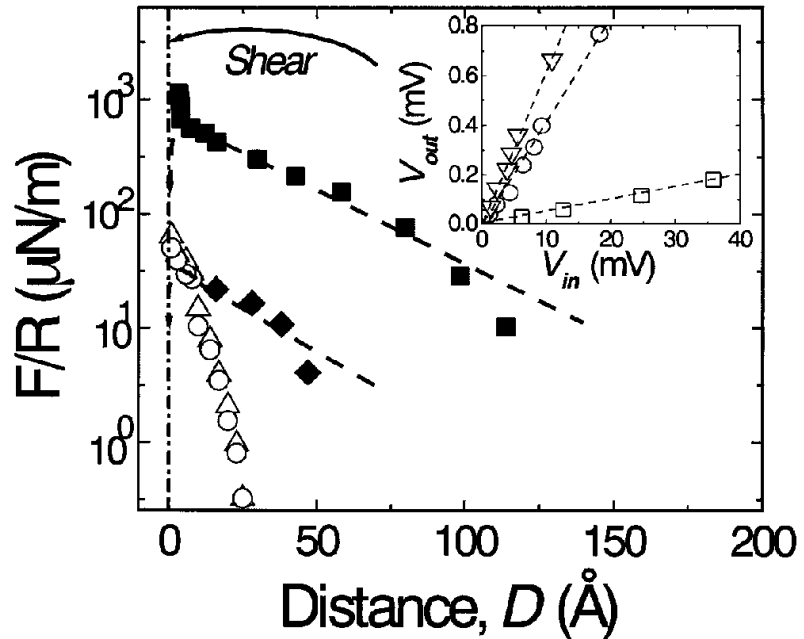
- Same basic geometry as no-slip experiment described above, but reduce spacing between cylinders toward the molecular scale.
- NOTE: requirement of charge neutrality + surface charge effects at interfaces mean that ionic concentration in fluid when spacing gets small becomes *much* larger than in bulk (*e.g.* 15 M even when starting with ~ deionized water).
- At low frequencies, try to oscillate sliding of one cylinder past the other
- Can measure amplitude and phase of resulting oscillations, and convert into some effective viscoelastic modulus (real part like shear modulus; imaginary part like viscosity).

Nontrivial changes in viscosity:

Zhu *et al.*, PRL **87** 096104 (2001)

Nothing too odd happens when spacing is larger than ~ 1 nm.

Data at right show expected drag forces for given experimental conditions; dashed lines are in line with expectations of bulk fluid behavior.



Note that something happens at very small distances.

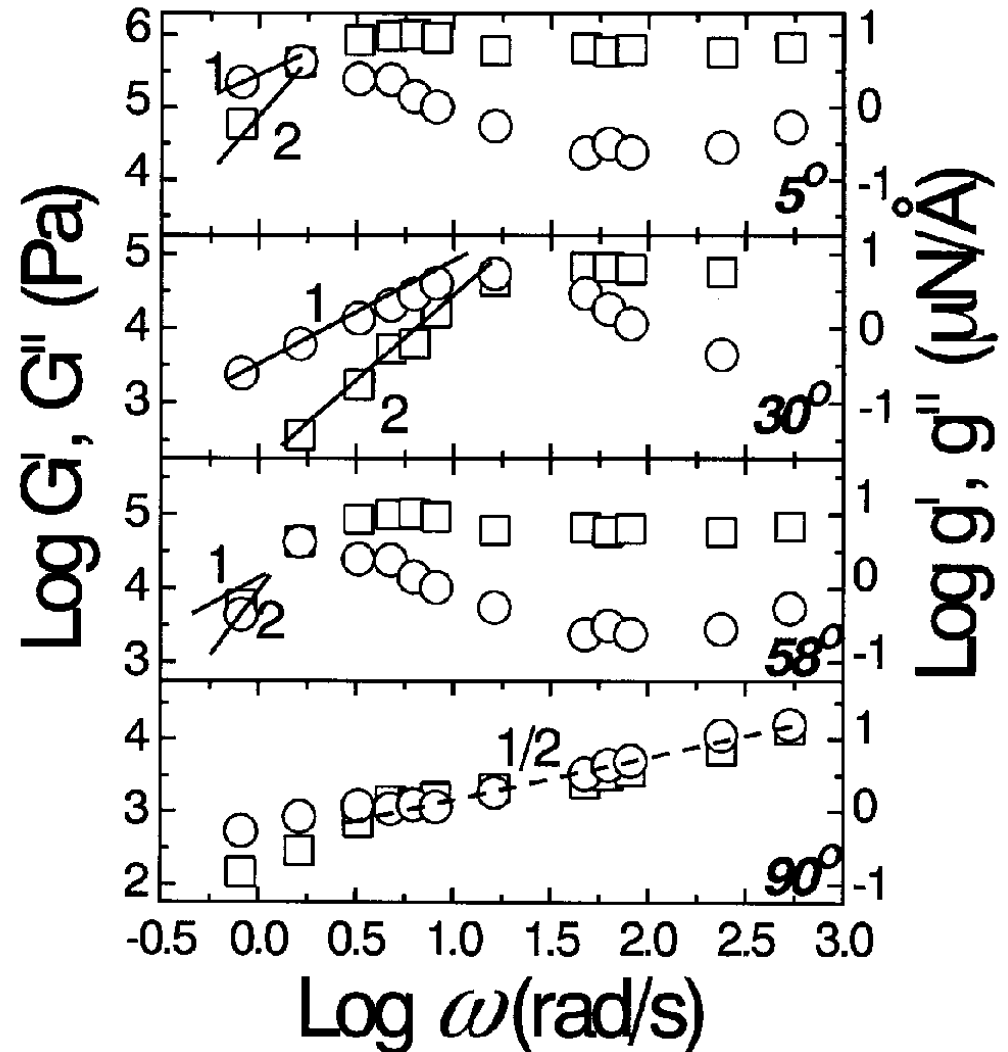
A number to recall: typical thickness of a water molecule is 0.25 nm.

Nontrivial changes in viscosity:

Zhu *et al.*, PRL **87** 096104 (2001)

First indications of weirdness: at small (< 2 nm) separations, *relative orientations of mica crystals* lead to impressively varied, frequency-dependent response!

Water apparently orders between the two crystals, and whether the surfaces are commensurate or not significantly modifies the water ordering and its elastic response.

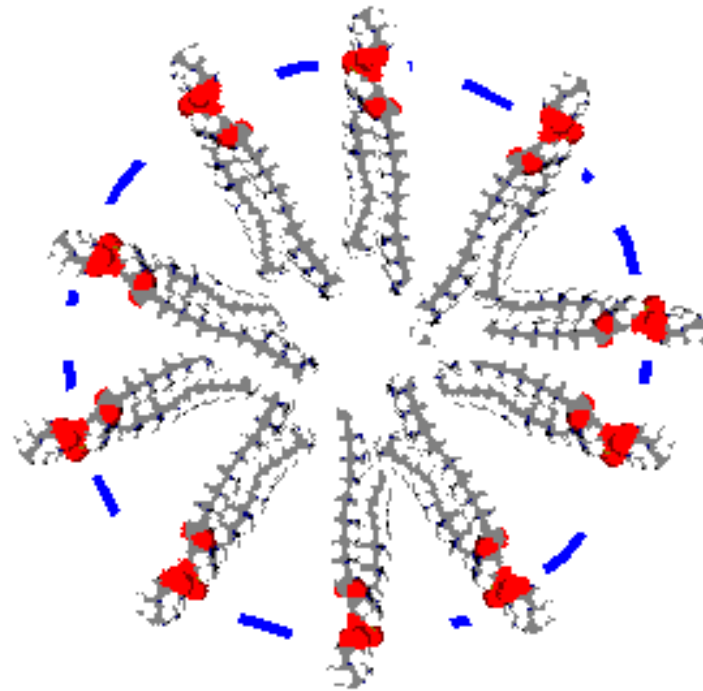


Example: nontrivial changes in vibrational properties

Can confine water into nanometer-sized regions using micelles (ordered membrane of surfactant molecules that closes on itself)

As water is increasingly confined and begins (?) to order, one might expect a change in its vibrational properties.

Also, since water is polar and has a reasonable dielectric response, this could be probed with some kind of EM scattering technique.

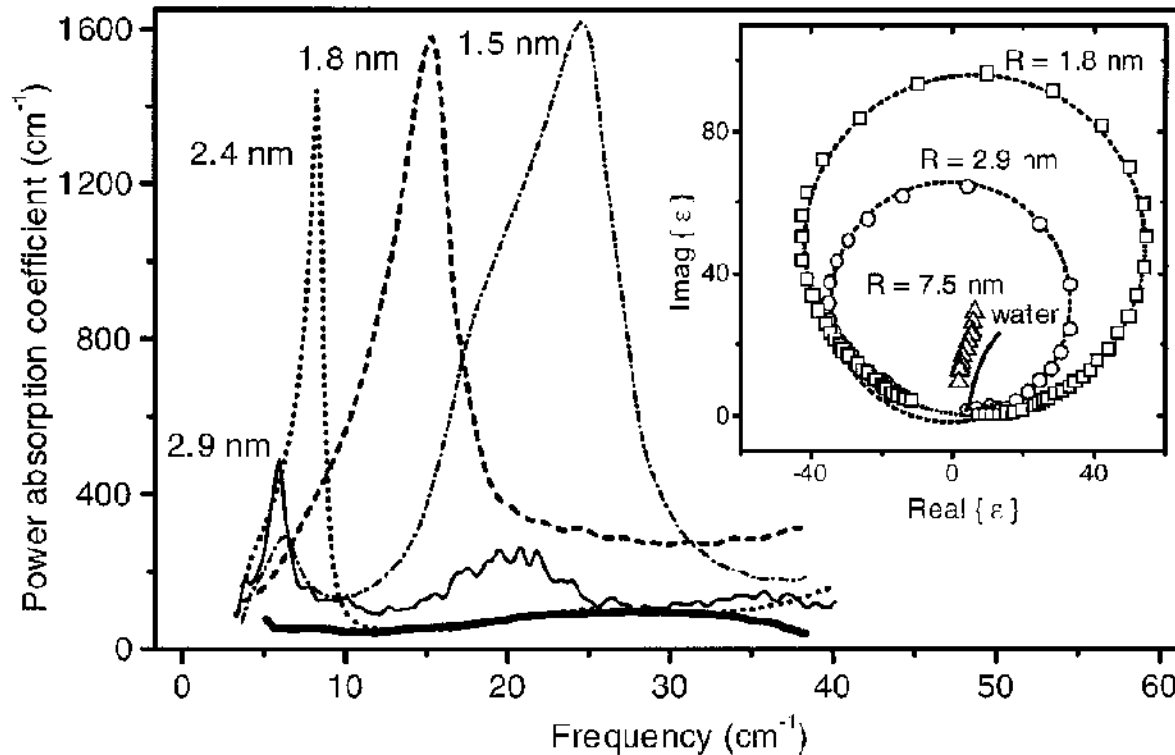


Univ. of Twente, Netherlands

Note: the vibrational frequencies we're talking about end up being in the terahertz regime.

Nontrivial changes in vibrational properties

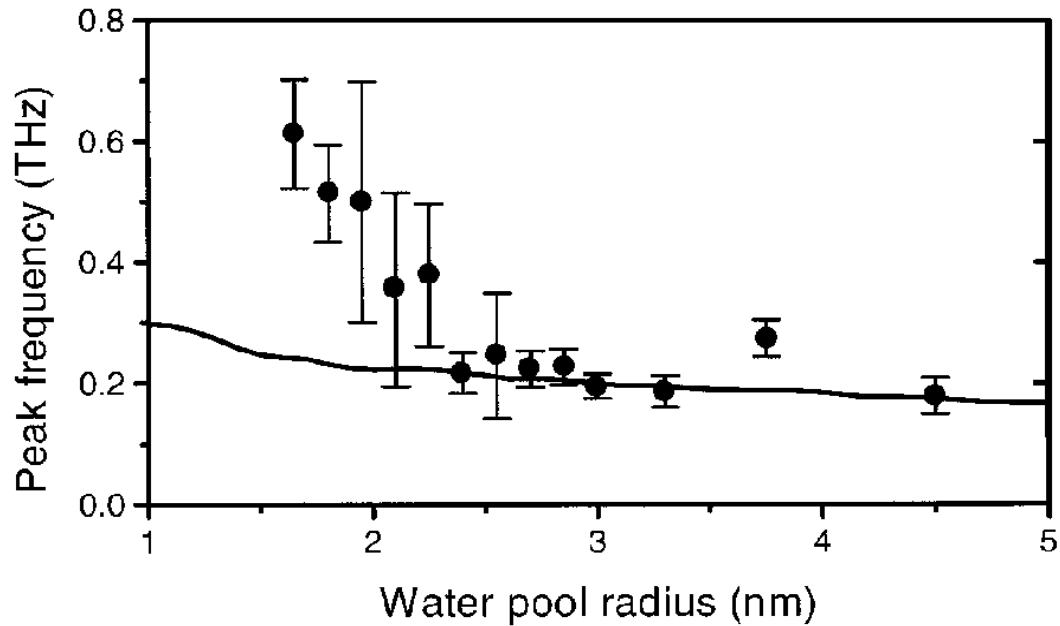
Boyd *et al.*, PRL **87**, 147401 (2001)



Note that absorption coefficient varies dramatically, and absorption peak pushes toward higher frequencies with increasing confinement.

Nontrivial changes in vibrational properties

Boyd *et al.*, PRL **87**, 147401 (2001)



The water nanopools become *vibrationally stiffer* with increasing confinement!

Evolution of elastic properties is due to molecule-molecule ordering and interactions.

Example: nontrivial changes in density

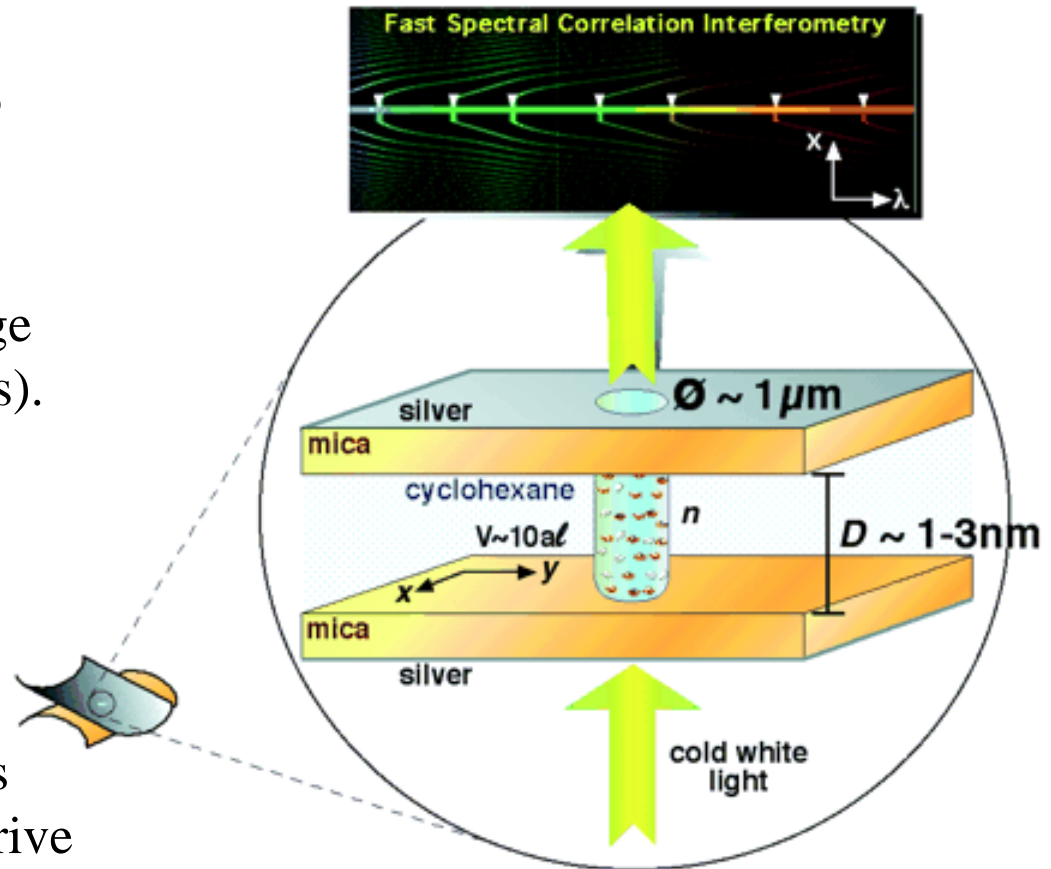
Hueberger *et al.*, Science **292**, 905 (2001)

Use fact that thin mica is optically transparent to do another optical study of nanoconfined fluid.

Cyclohexane: weak charge effects (nonpolar, few ions).

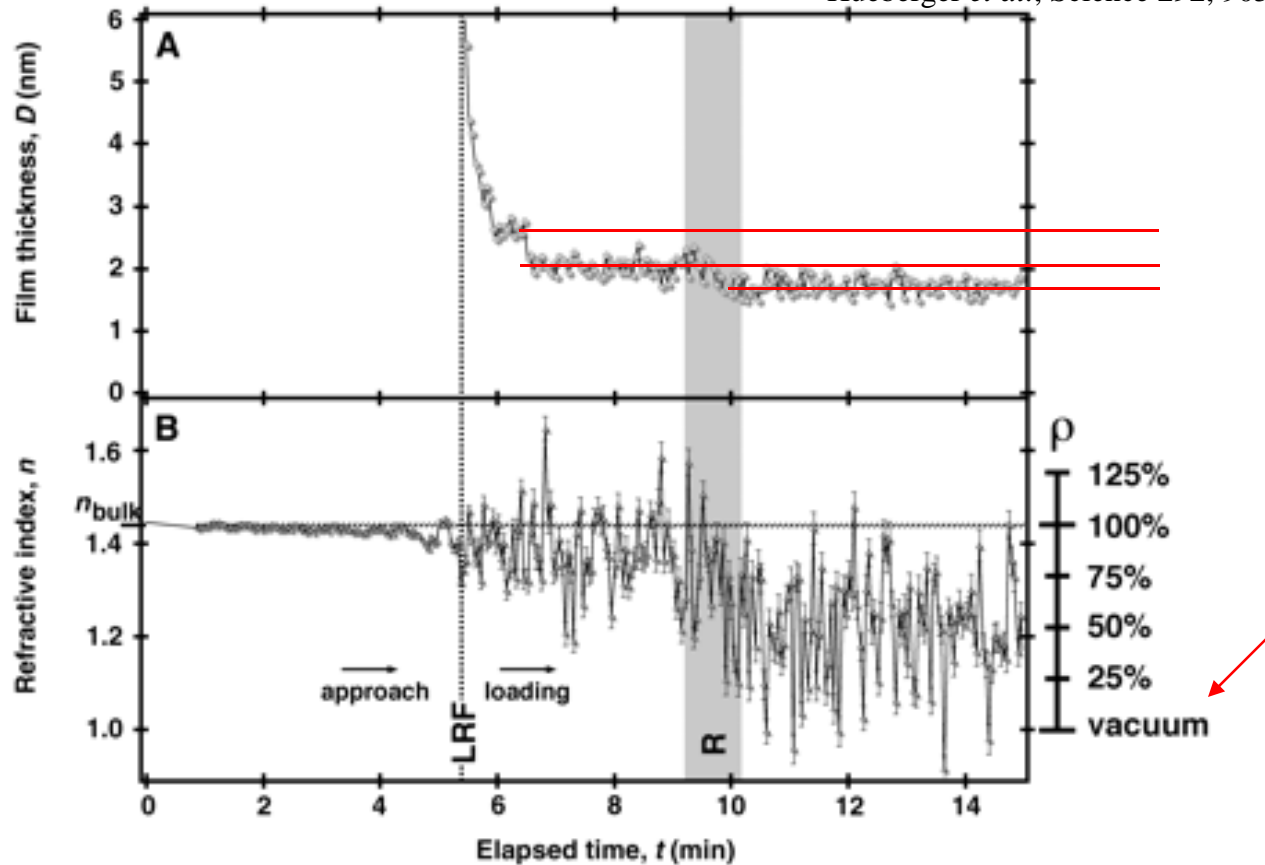
With this approach, the optical spectroscopy is sensitive to \sim *attoliter* volumes (!).

Can do correlations across multiple frequencies to arrive at fluctuations in density and mica spacing as load is varied.



Nontrivial changes in density

Hueberger *et al.*, Science **292**, 905 (2001)

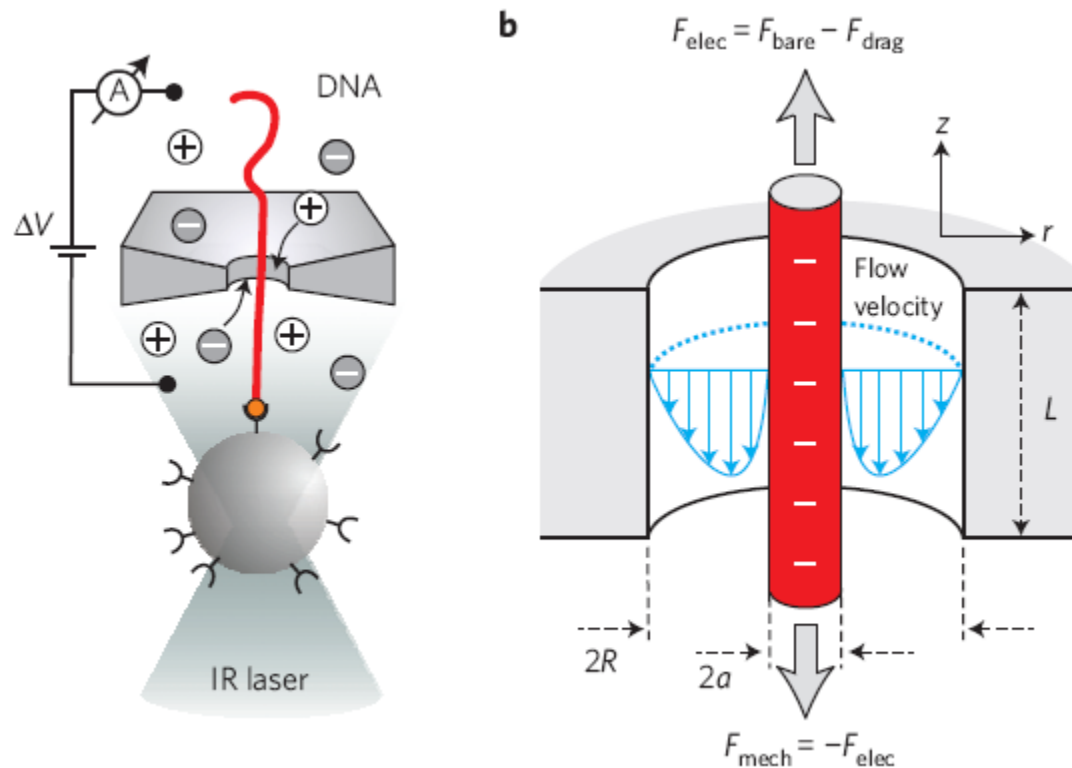


- When greatly confined, thickness of film fluctuates with time.
- Thickness has certain preferred values for given loading.
- Index of refraction (and therefore density) also **really fluctuates!**

Challenges: nanoscale effects on ion concentration

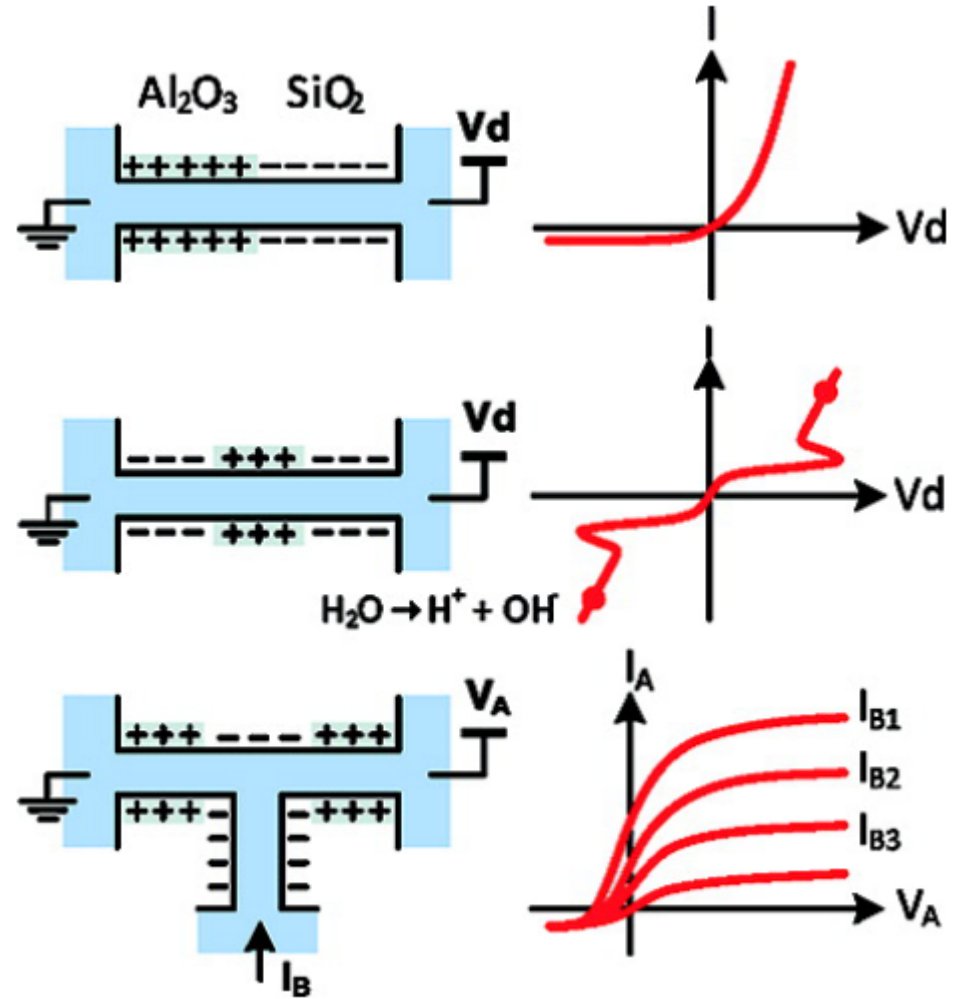
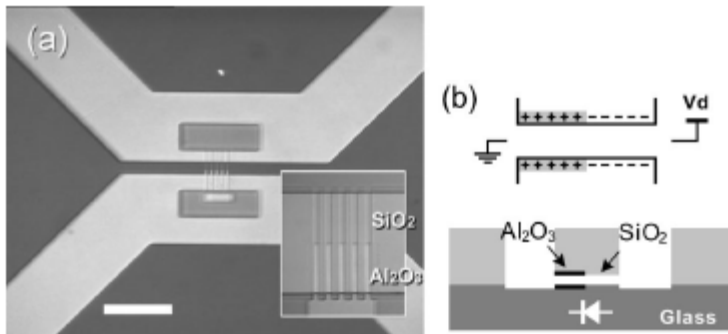
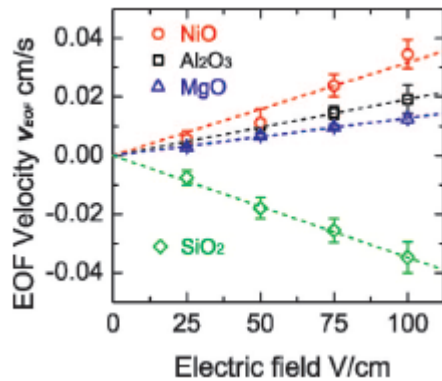
Origin of the electrophoretic force on DNA in solid-state nanopores

Stijn van Dorp¹, Ulrich F. Keyser^{2,3}, Nynke H. Dekker¹, Cees Dekker¹ and Serge G. Lemay^{1*}



Challenges: nanoscale effects on ion concentration

Can use interplay between walls and ionic concentrations to control ionic conduction in solutions!

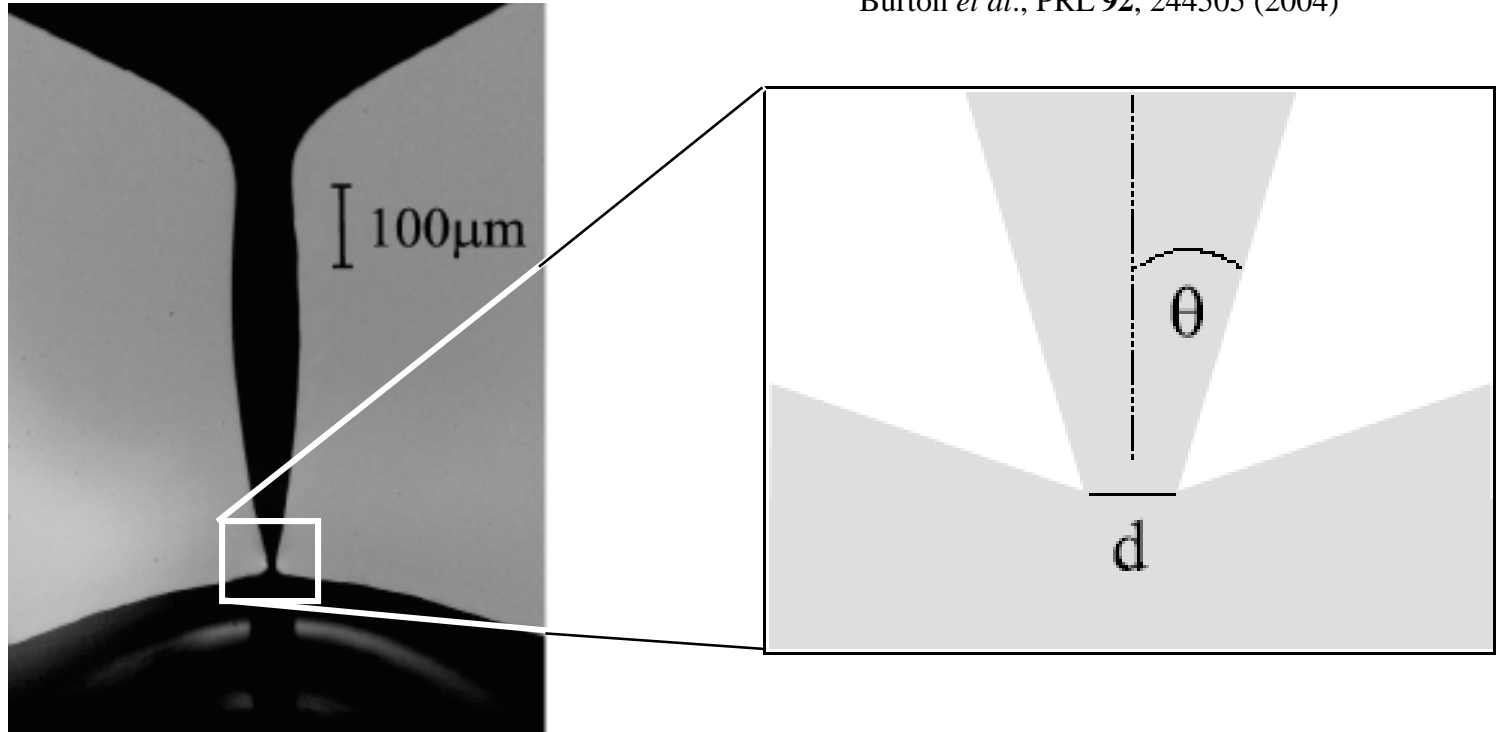


Ionic Current Rectification, Breakdown, and Switching in Heterogeneous Oxide Nanofluidic Devices

Li-Jing Cheng, and L. Jay Guo

Sometimes hydrodynamics works *better* than expected!

Burton *et al.*, PRL **92**, 244505 (2004)



Use electrical resistance to monitor diameter of constriction as mercury drops pinch off from each other.

Sometimes hydrodynamics works *better* than expected!

Burton *et al.*, PRL **92**, 244505 (2004)

Scaling analysis in limit of surface tension and inertia dominating:

$$d \propto \left(\frac{\sigma \tau^2}{\rho} \right)^{1/3}$$

Here, τ is the time remaining until pinch-off.

$$R = \frac{2\rho_r \cot(\theta)}{\pi d}$$

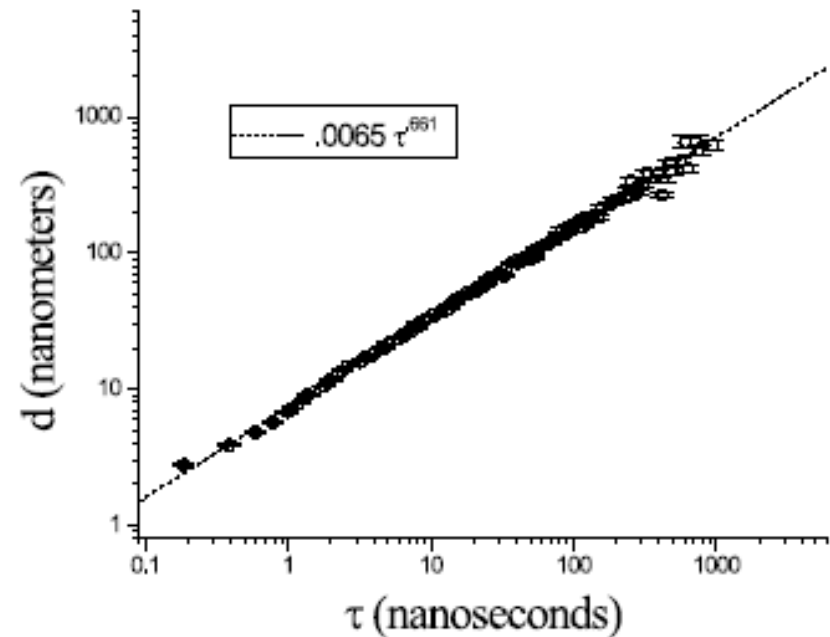
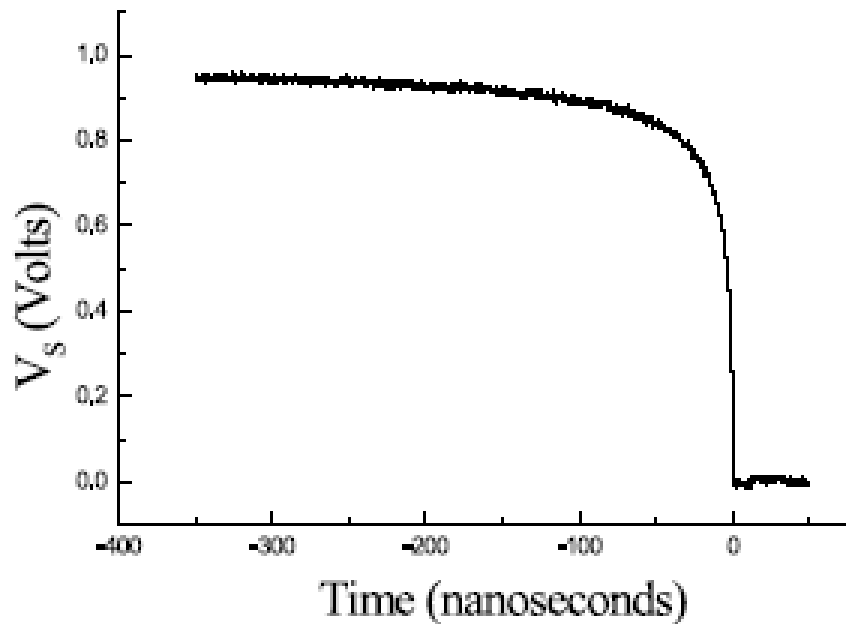
Here, ρ_r is the electrical resistivity, and it turns out that θ approaches 18 degrees universally in this limit (!).

Can pass current through the neck, and use voltage across a series resistor as an effective ammeter, and can trigger scope accordingly.

Sometimes hydrodynamics works *better* than expected!

Burton *et al.*, PRL **92**, 244505 (2004)

Result of all this:



Simple hydrodynamic picture works all the way down to neck diameters ~ 5 nm.

Applications of nanoscale fluid flow

We see that under true nanoscale confinement, liquids may no longer act much like liquids! Can develop properties that look much more like those of solids, and exhibit significant dynamic effects.

Why are people interested in fluid flows at these scales?

Two quick applications:

- Sorting of macromolecules (electrophoresis)
- Sorting of micro/nanoparticles

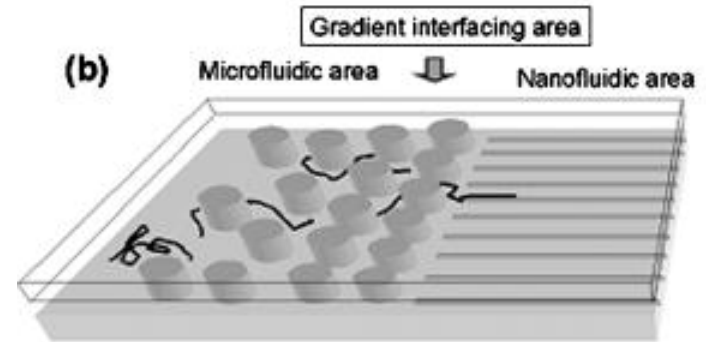
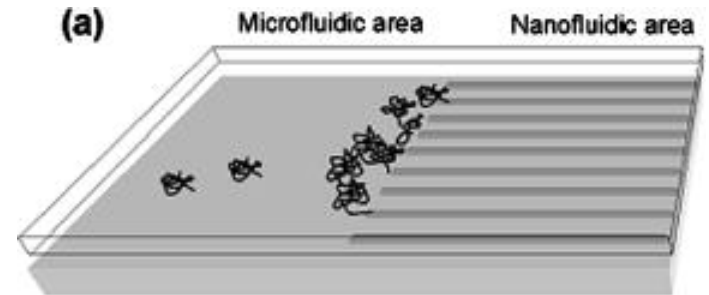
Sorting of macromolecules

Sorting macromolecules by length can be a painful process - is there any way we can let nanoscale fluid dynamics make our lives easier?

Yes - viscous flow through long channels tends to stretch out these molecules.

Tricky bit: want channels narrow enough that only one molecule fits per channel, but also need to find way for coiled molecule to get itself straight and in there....

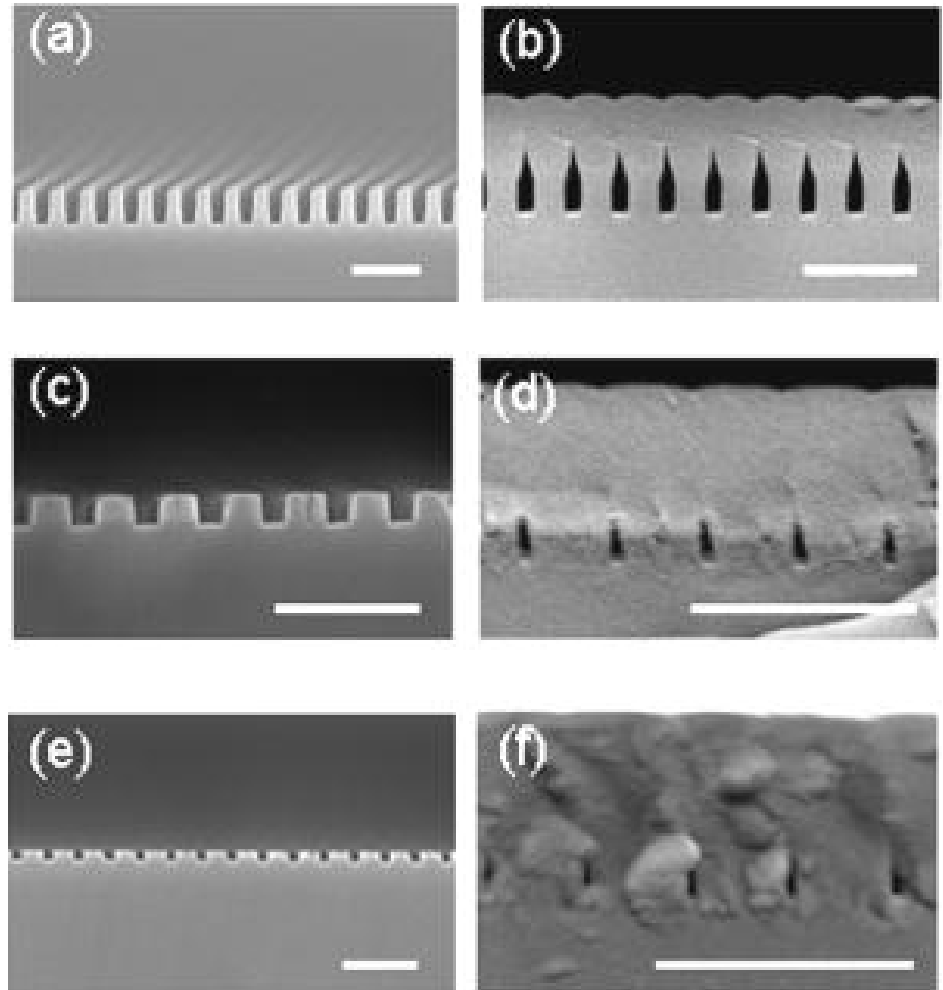
Answer: “entropic sieve”.



Sorting of macromolecules

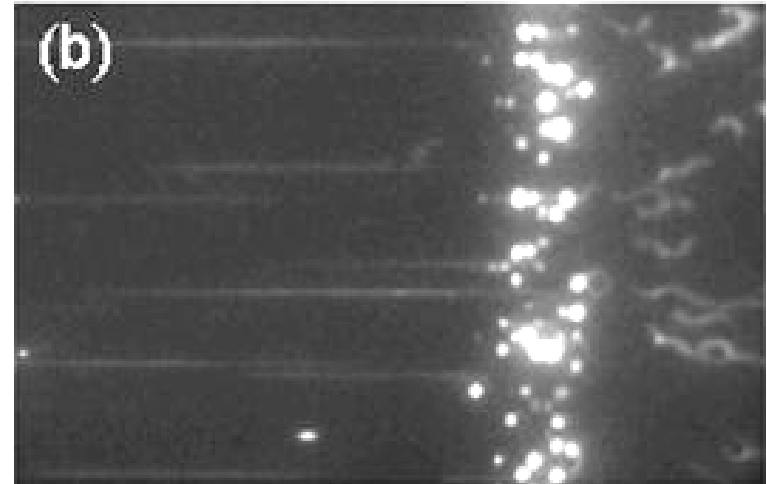
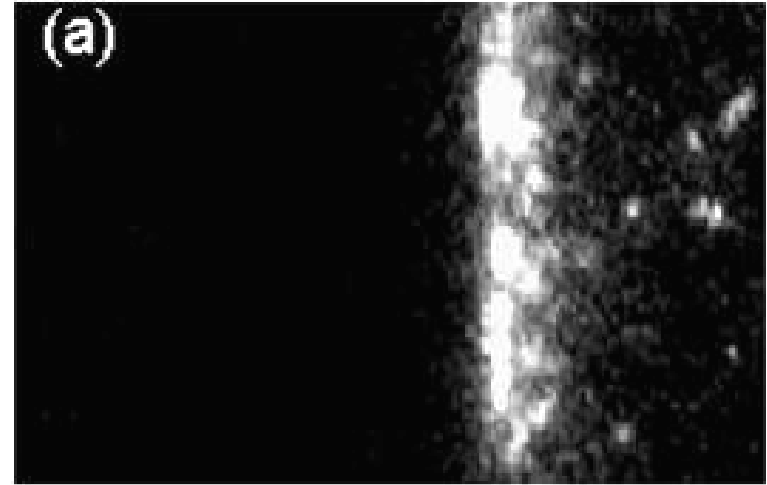
Can make nanoscale enclosed channels by clever combination of large area patterning and kinetics of sputtering.

Scale bars = 500 nm.



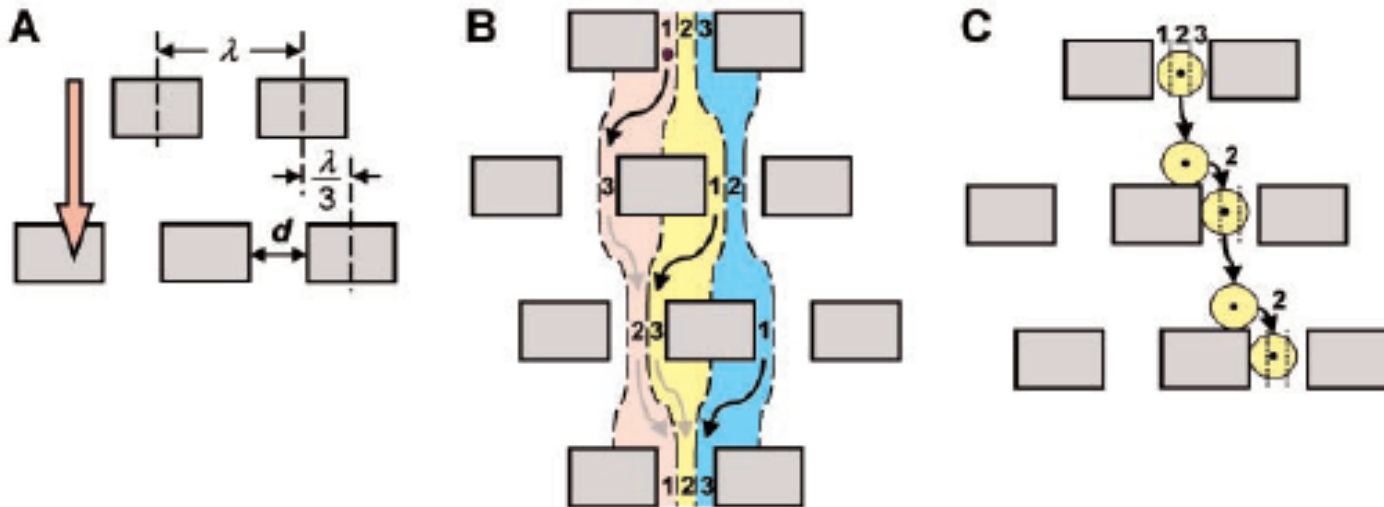
Sorting of macromolecules

By having a gradient of mesoscale obstacles, molecules explore more microstates - more likely to end up in a configuration that allows them to enter the nanoscale channels.



Sorting of micro/nanoparticles

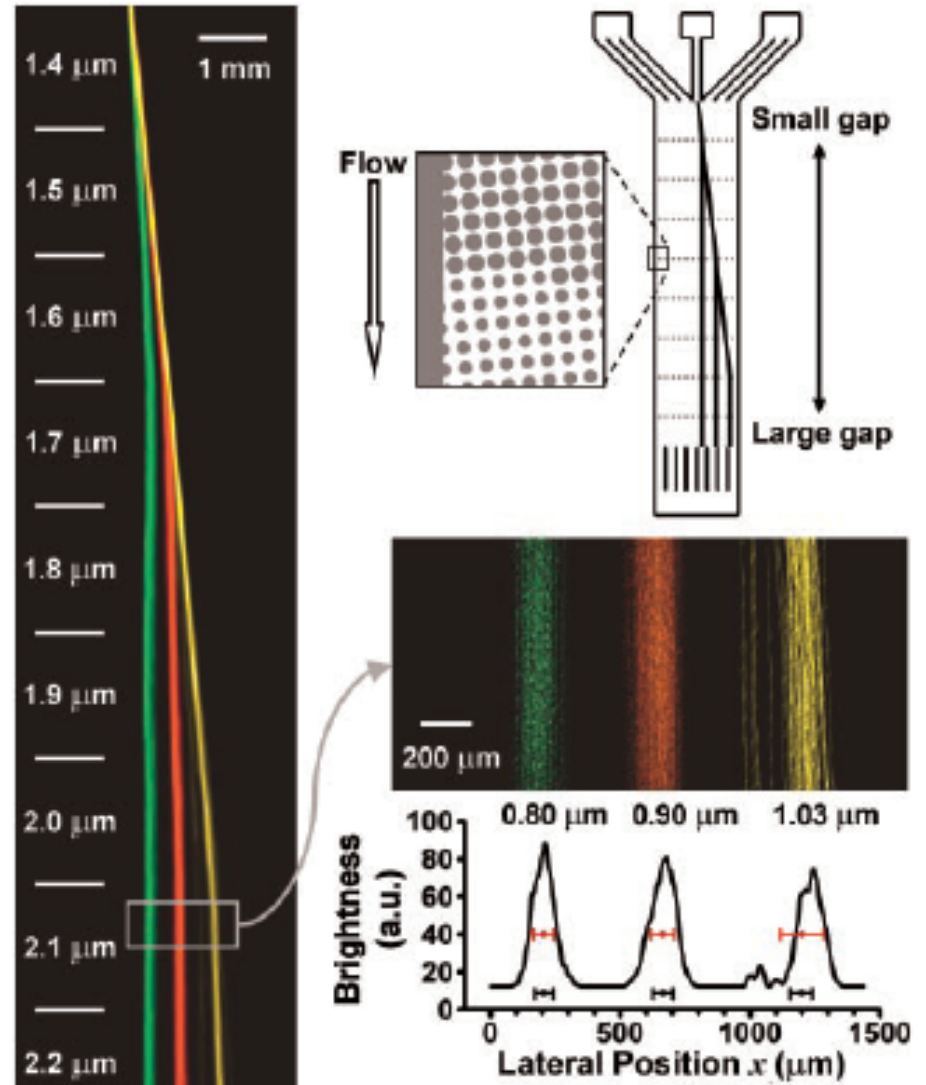
- Laminar flow around asymmetrically positioned obstacles divides asymmetrically.
- Can take advantage of this to separate particles by size.



- Particle too big for “lane 1” ends up getting shunted laterally....

Sorting of micro/nanoparticles

- Can keep lattice spacing and registry of obstacles constant and vary the spacing.
- Use fluorescently tagged microspheres of different diameters to watch the sorting.



Summary

- Microfluidics is a rich and exciting area of research, and is just really getting going.
- Potential chemical and biological applications are huge.
- Fundamental physics, physical chemistry and surface science questions arise when considering fluid really confined on the nanoscale.