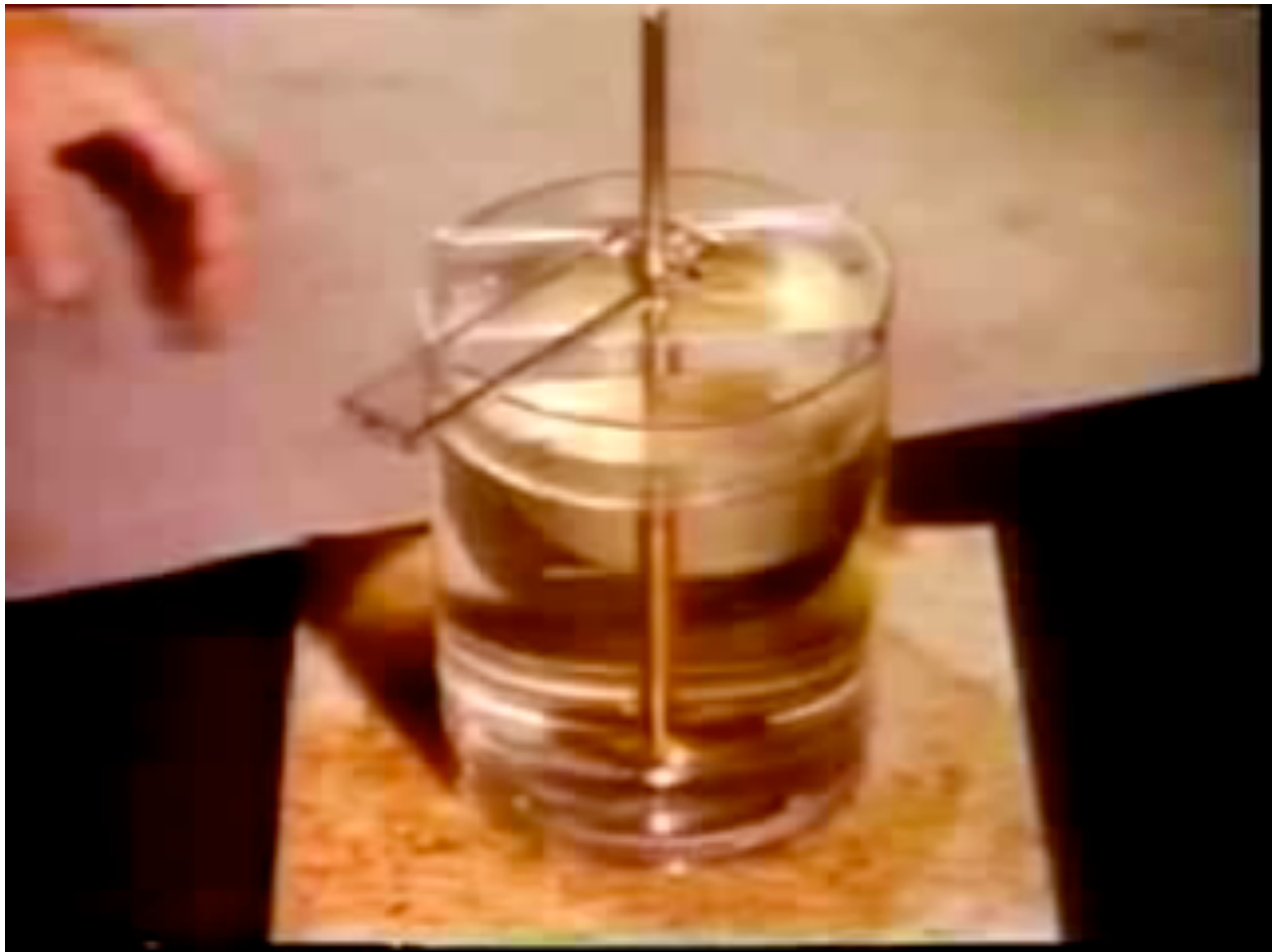


Lecture 2. Arrays of obstacles and how particles move in them

This is actually out of historical order, in the sense that I got into nanofluidics through trying to fractionate DNA as a function of length, and only moved into transport of particles as I learned more about the capabilities of micro and nanofabrication technologies.

However, this couples most closely with Lecture 1 were I TRIED to explain the foundations of the flow of viscous fluids, so it seems appropriate.

I only do micro and nanofluidics because there are interesting biological physics problems that I want to solve, and this technology is one way to get at the problem. I'd do something else if that was a quicker way.

As I'll discuss tomorrow, I got involved first in this area because I was trying to rapidly sequence large DNA molecules.

Along the way, I realized that I could also mix and sort biological molecules rapidly using ideas we had developed. Perhaps pedagogically it is best to start with mixing and sorting molecules first.

I did mention diffusion and how it is through diffusion that mixing occurs, usually through the diffusion of vorticity that I discussed briefly yesterday.

However, I also discussed that it is difficult to introduce vorticity into a fluid at low Re because the advective term, which makes things tumble over one another as they surge forward becuase viscosity can't suck the the kinetic energy out fast enough.

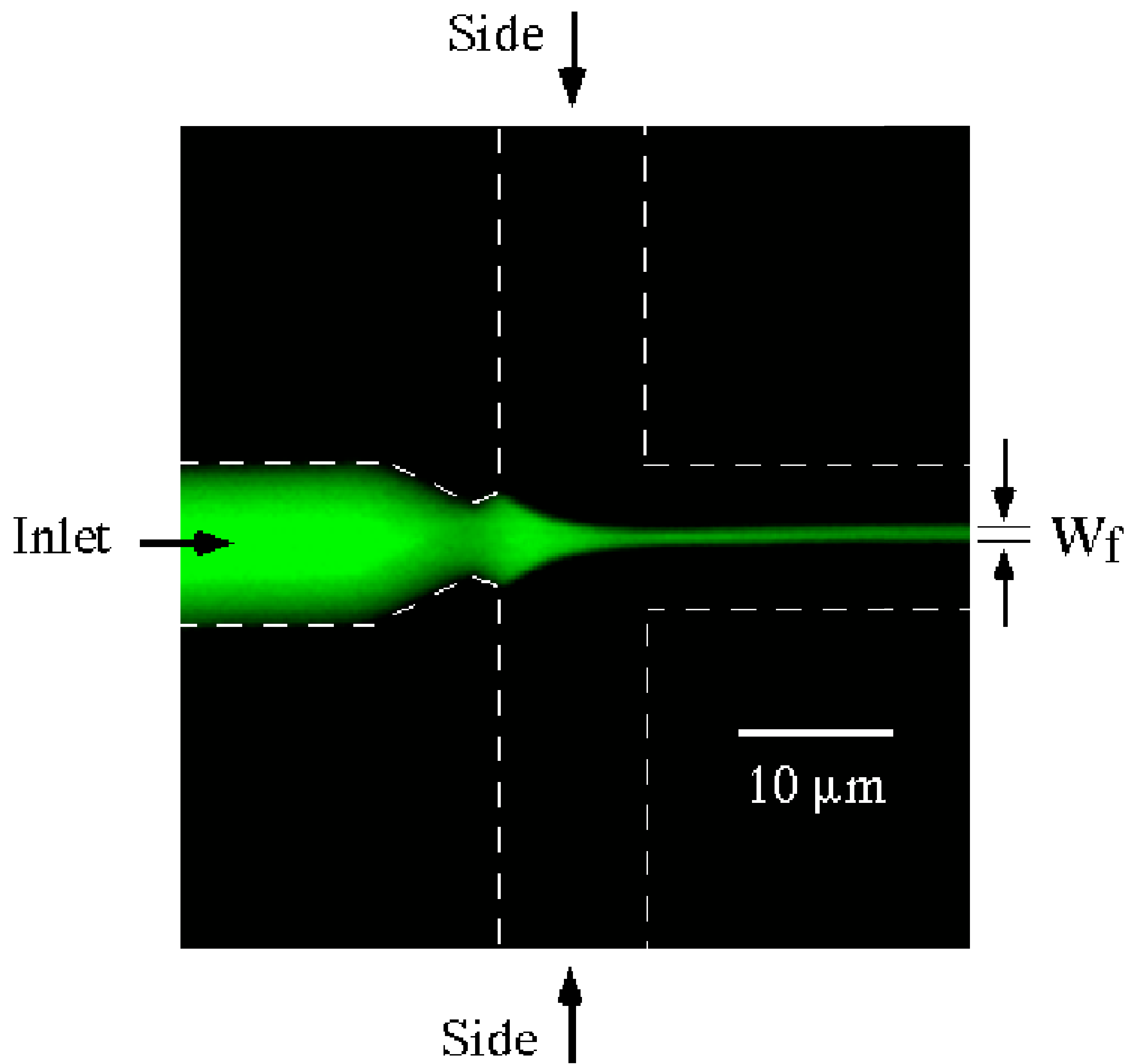
At low Re the viscous drag just sucks the bejesus out of the kinetic energy, no chaos, no vorticity, no mixing! That is more than naive, but somewhat true.

So, simple mindedly, mixing on the micro/nanoscale is all pure diffusion.

The rapid mixing of fluids is interesting to me as a biological physicist because I am interested in the protein folding problem:

How do proteins rapidly find their correct conformation so quickly?

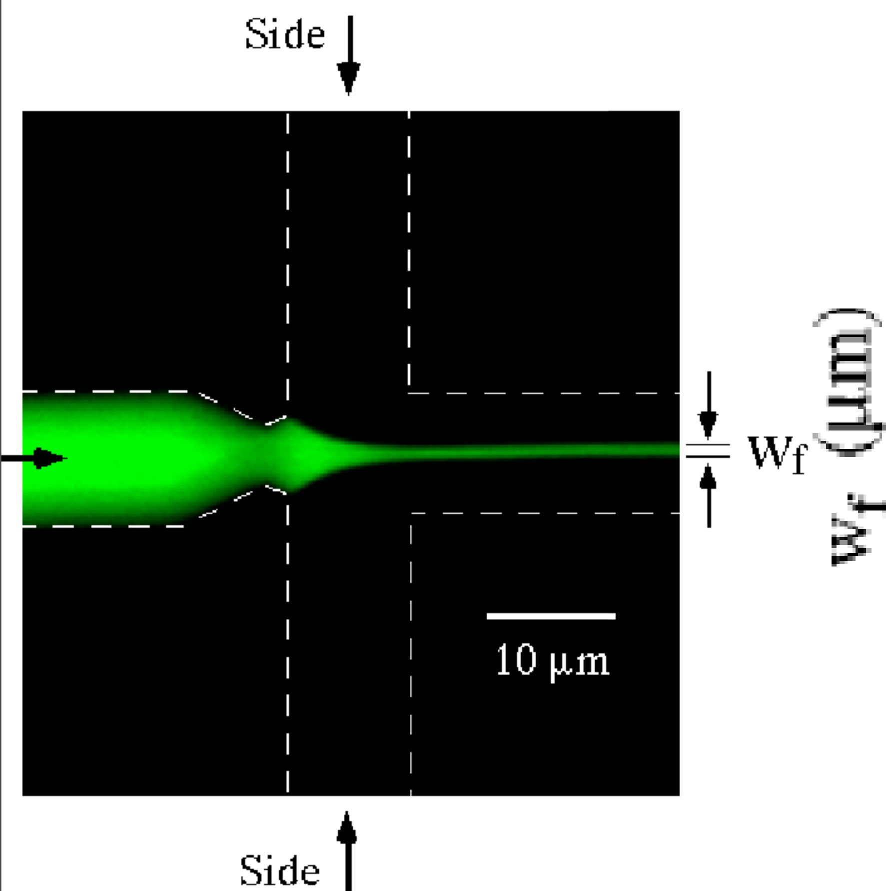
I realized that using low Re techniques I actually could mix fluids more rapidly than by the normal high Re turbulent mixers, paradoxically, through pure diffusion and getting the length scale small enough (sub-micron).


Side
Inlet
W_f
10 µm
Side

You CANNOT simply inject a fast moving thin stream of fluid into a larger area at low Re!!! That's so high Re thinking! There is no inertial plowing ahead at low Re.

Due to the massive dominance of shear forces, the incoming fluid has to come to an abrupt halt, and by conservation of mass has to spread out in a huge area. The key is to realize that low Re flow is much like electrons in a wire at room temperature: diffusive.

That means that you simply add the currents coming in as if the pressure head was a voltage source, and of course you have to conserve atoms like you have to add charge. The piping coming in acts like a resistor, so the problem really becomes very freshman physics.



w_f (μm)

1
0.1
0.01

1 1.1 1.2 1.3

α

αV_i
I_s R
I_i I_o
V_i γR σR
R
I_s
αV_i

For laminar flow, flow is exactly like current in a resistor (Ohm's law!). Amazingly, jet widths can get to 20 nm in width.

Of course, “mixing” times go roughly as:

$$t = w^2/2D$$

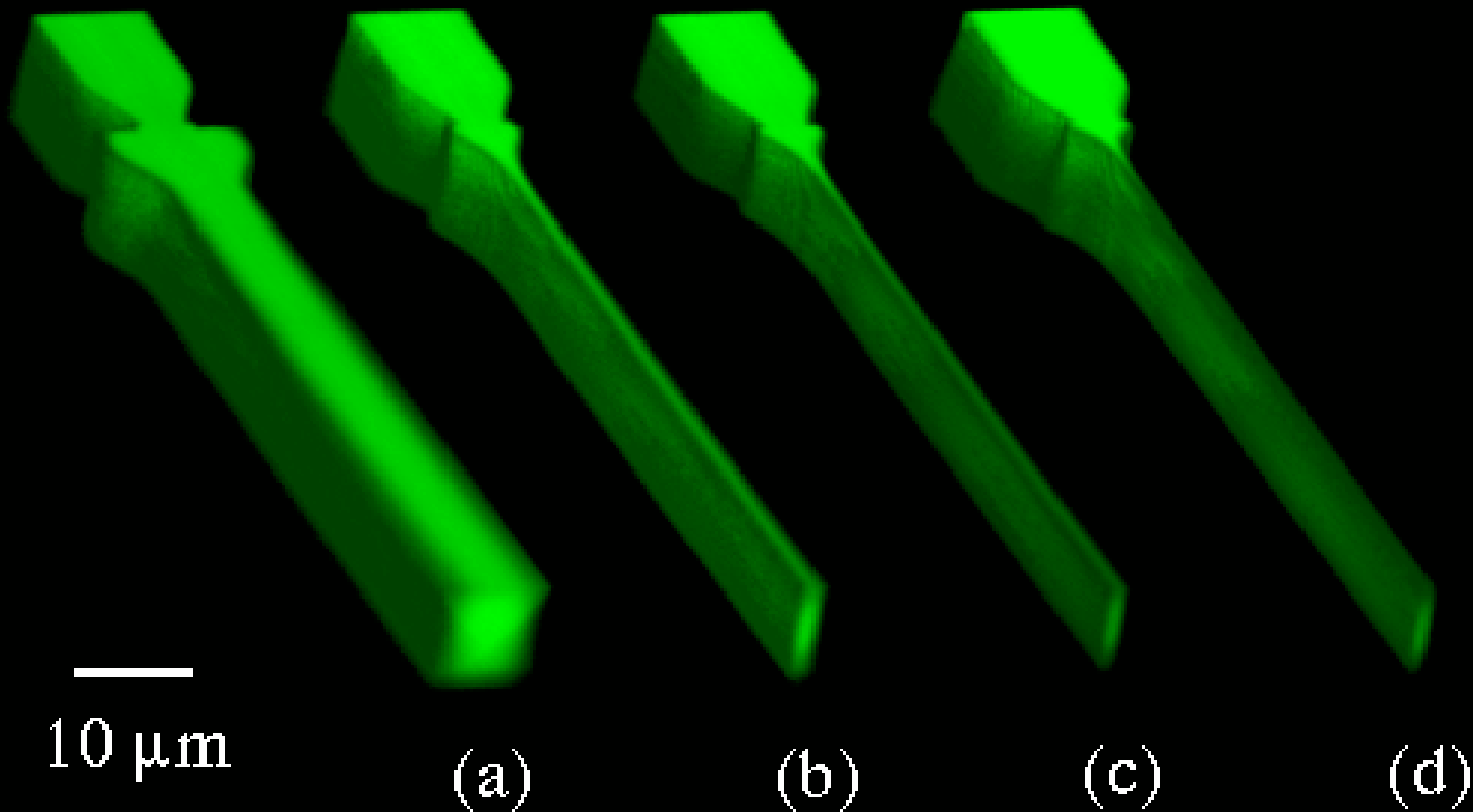
So for w = 1 micron and $D=10^{-4}\ cm^2 sec^{-1}$

you get t= 50 microseconds, smaller even faster.

HOWEVER, the real power of this technique is the ability to exactly model the flow and know the convolution of the profile with the time.

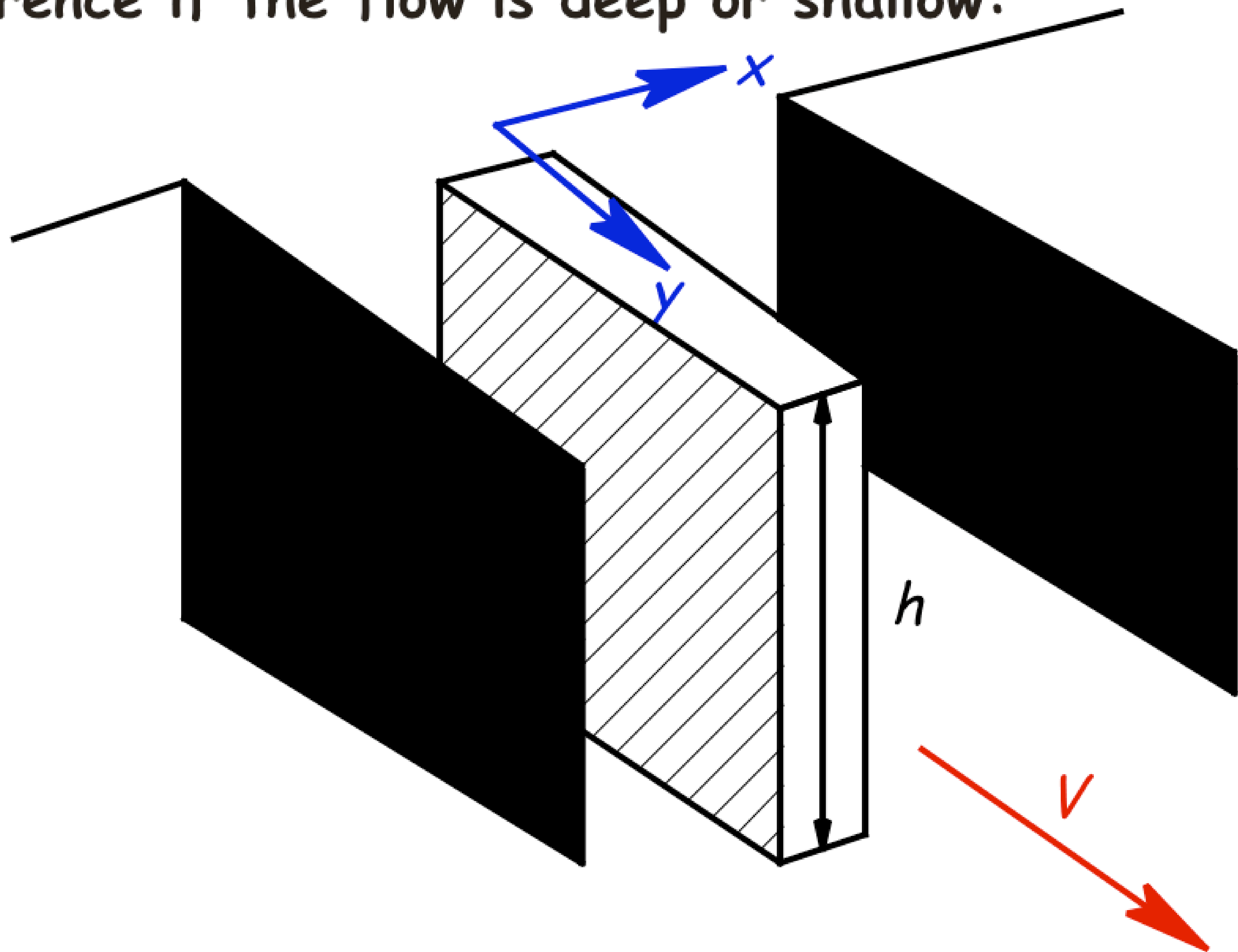
There has been some remarkable advances in reactive ion etching over the past 10 years. the Bosch deep-etch process makes it possible to make vertical wells a couple of microns wide and and 400 microns (for example) deep, so it is possible to make moving curtains of fluid.

This means that the technique can be used for rather insensitive techniques such as X-ray scattering in addition to fluoresence.

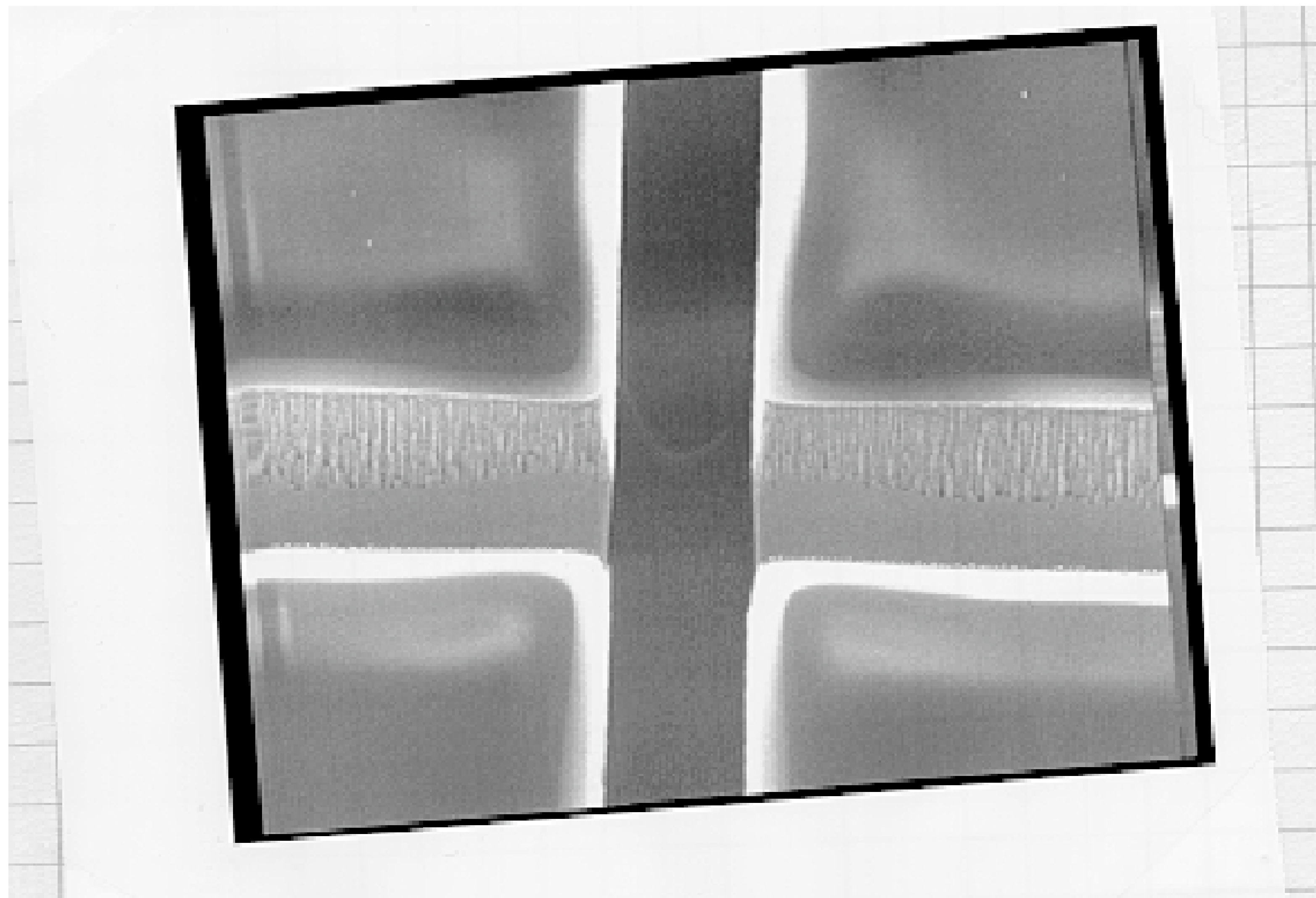


velocities can exceed 1 m/sec (1 um/usec) at 100 psi

One of the biggest problems, which I have slowly grown to understand, is that even at low R it makes a difference if the flow is deep or shallow:

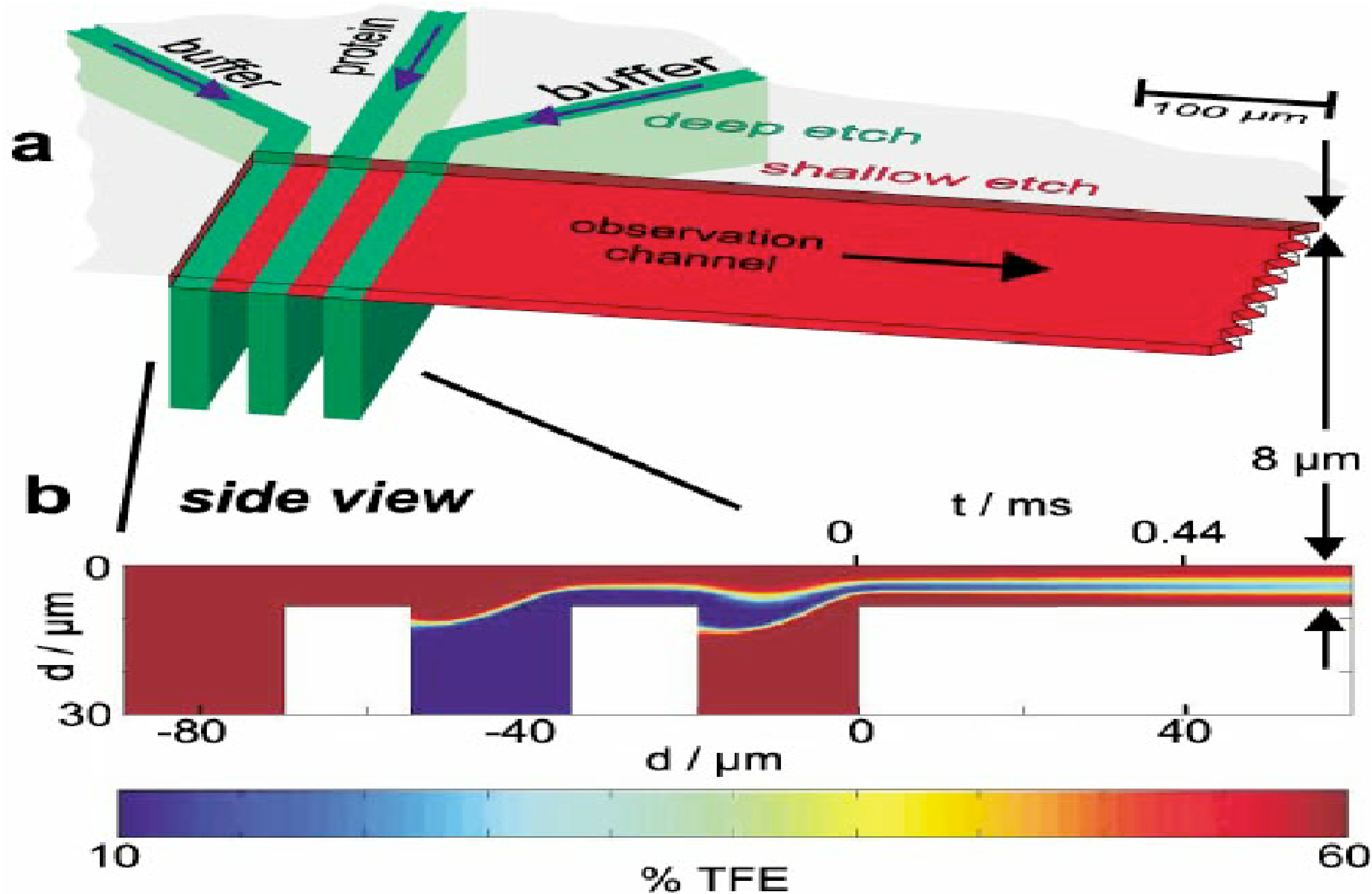


Sometimes h>>x,y. Lois Pollack (CU) has driven a very ambitious time-resolved small angle X-ray scattering experiment using focussed X-ray beam lines at CHESS and APS.



DEEP etched mixer for X-ray experiments. 400 um vertical etch (Lois P.)

Sometimes h<<x,y. This is our IR mixer.



The equations governing the flow are very different in the limits of $h>>x,y$ or $h<<x,y$

My student Nick Darnton has written elegant solutions to the not well known case of $h<<x,y$. It isn't clear that anybody has ever done the following analysis. It isn't my analysis, it's Nick's.

Nick Darnton, Olgicia Bakajin, Richard Huang, Ben North, Jonas Tegenfeldt, Edward Cox, James Sturm and Robert H. Austin (2001) Hydrodynamics in 2.5 Dimensions: Making Jets in a Plane, J. Physics: Condensed Matter 13: 4891-4902

Even the N-S equation with advection thrown out:

$$\rho \frac{\partial \vec{v}}{\partial t} \sim \nabla P + \eta \nabla^2 \vec{v}$$

is NOT easy to solve since it is not
a potential problem (scalar) but instead a
vector equation. There is one simplification
you can make: all of the complex boundaries
are in the x-y plane, but in the z axis ("vertical") the
flow is a simple parabola and we can separate
variables:

$V(x,y,z) = V(x,y)\, f(z)$

$f(z) = [1 - (2z/h)^2]$

Substitution of this form for $\vec{v}$ into equation (4) gives

$$\nabla^2 \vec{v}(x,y) \cdot f(z) + \frac{2}{h^2}\vec{v}(x,y) = \vec{\nabla} P(x,y), \tag{10}$$

where ∇^2 now refers *only* to the dimensions x and y.

Getting out of three dimensions is important, it allows you to define a stream function which while a vector only points in the z axis whose solution is known, hence it is a scalar function of x and y.

I won't go into the details here, but the upshot of this is that in the x-y plane it is possible to define a potential function to a good approximation, and then you can use boundary values of the flow (walls have no flow into them, and currents exist only through openings) to find the velocities of the fluid everywhere in our devices.

What I learned from this is that if you make your device thin enough that the Z-etch is « xy dimensions, you can in fact predict flow patterns quite well, and this became very important in the next work I did.

A brilliant Electrical Engineering student, Richard Huang, realized that if you want to inject narrow or well controlled fluid jets across wide areas the key, learned from our playing with the N-S equation for low Re, is to set the boundary conditions EVERYWHERE by putting in very narrow and long channels EVERYWHERE. They thus act as current sources, not voltage sources (in analogy to electrical circuits) and this sets the boundary conditions in a hard manner.

It may seem obvious, but it really changed the way we did our micro/nanofluidics!

Active area

1 micron wide feeder channels

Injector
Jet

Now, why would you ever do such a stupid thing?

Norbert Weiner coined the name
"Maxwell's Demon" for the imaginary beast who could sit at a (massless) door and only let molecules of higher than average velocity pass from the left to the right side. Since the door has no mass, the demon does no work, yet with time the right side gets hotter than the left.

This would appear to violate the 2nd law of thermodynamics (http://www.slvhs.slv.k12.ca.us/~pboomer/physicslectures/maxwell.html) More on this later!

However, if you do work on the system it IS possible to separate objects based on size using a combination of micromachining and a knowledge of microfluidics.

Tom Duke, a theorist friend of mine, figured out how to do this.

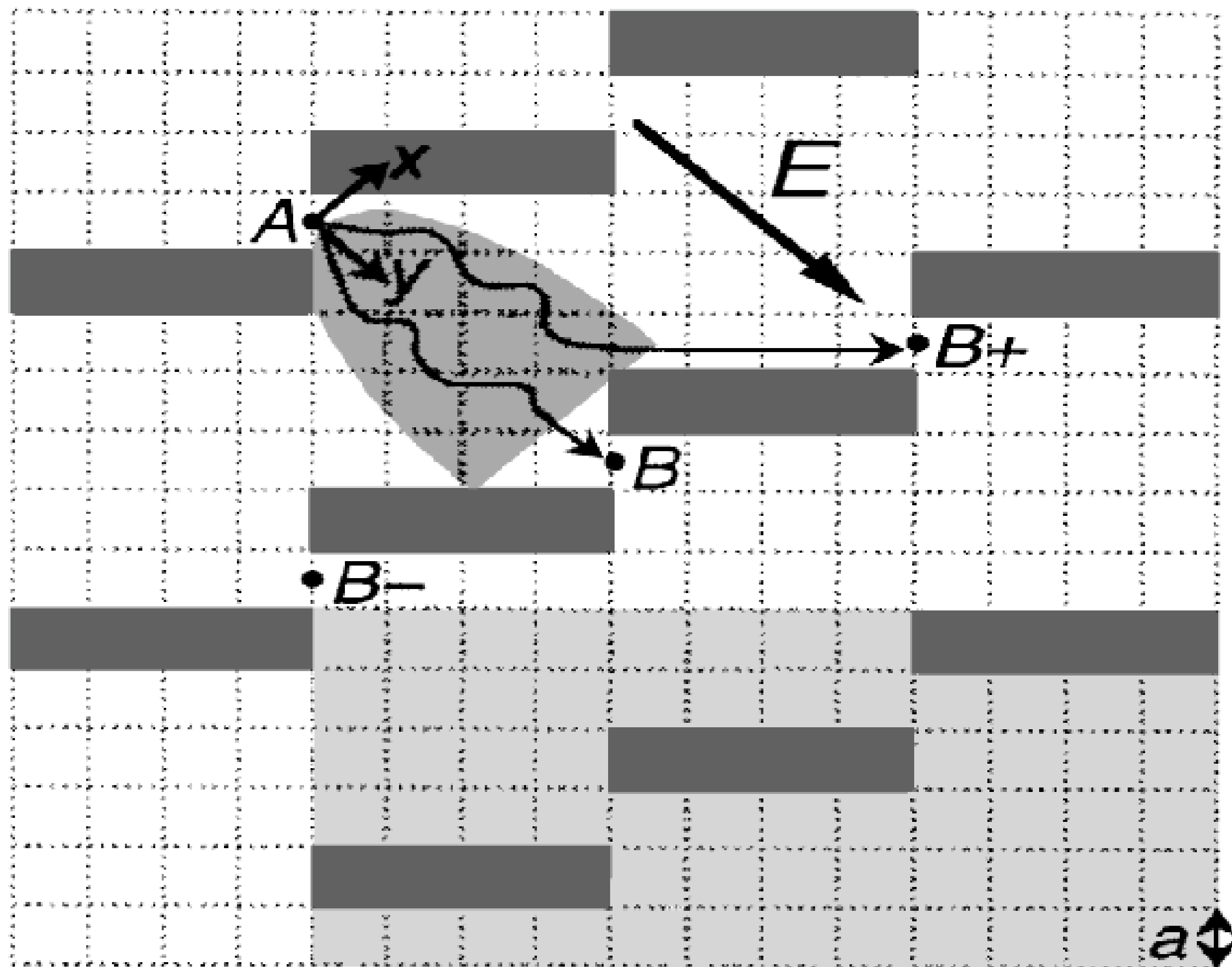
That is, it is possible to have random
forces work for you, if you are willing to invest some energy. This is the origin of so-called brownian ratchet schemes which aim to separate molecules using heat (kT) and what physicists call grandly "broken symmetry", that is, objects which are not
left-right symmetric.

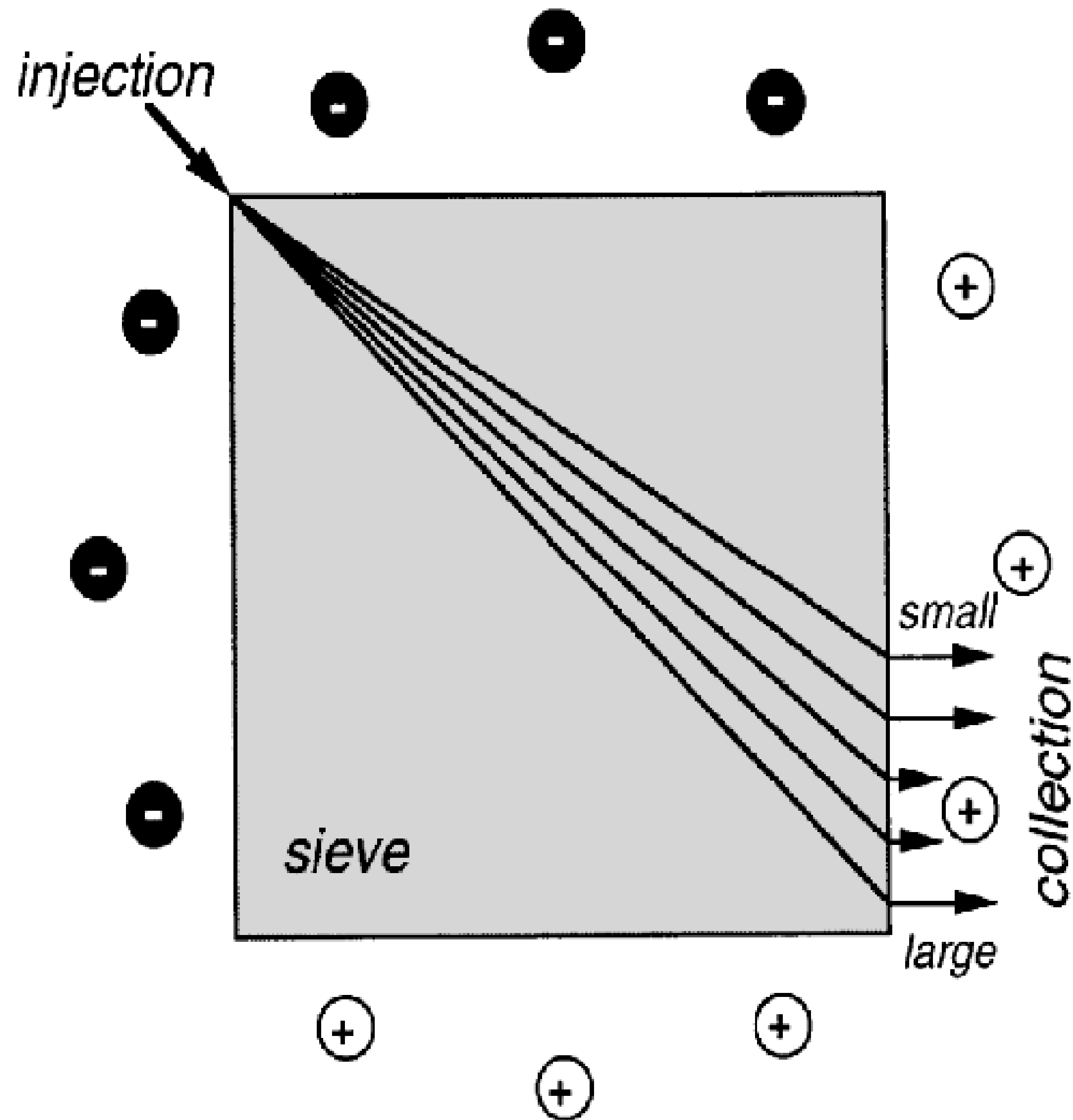
It turns out it is easy to make such structures using microfabrication.

Here's the basic idea, from a pair of theory papers:

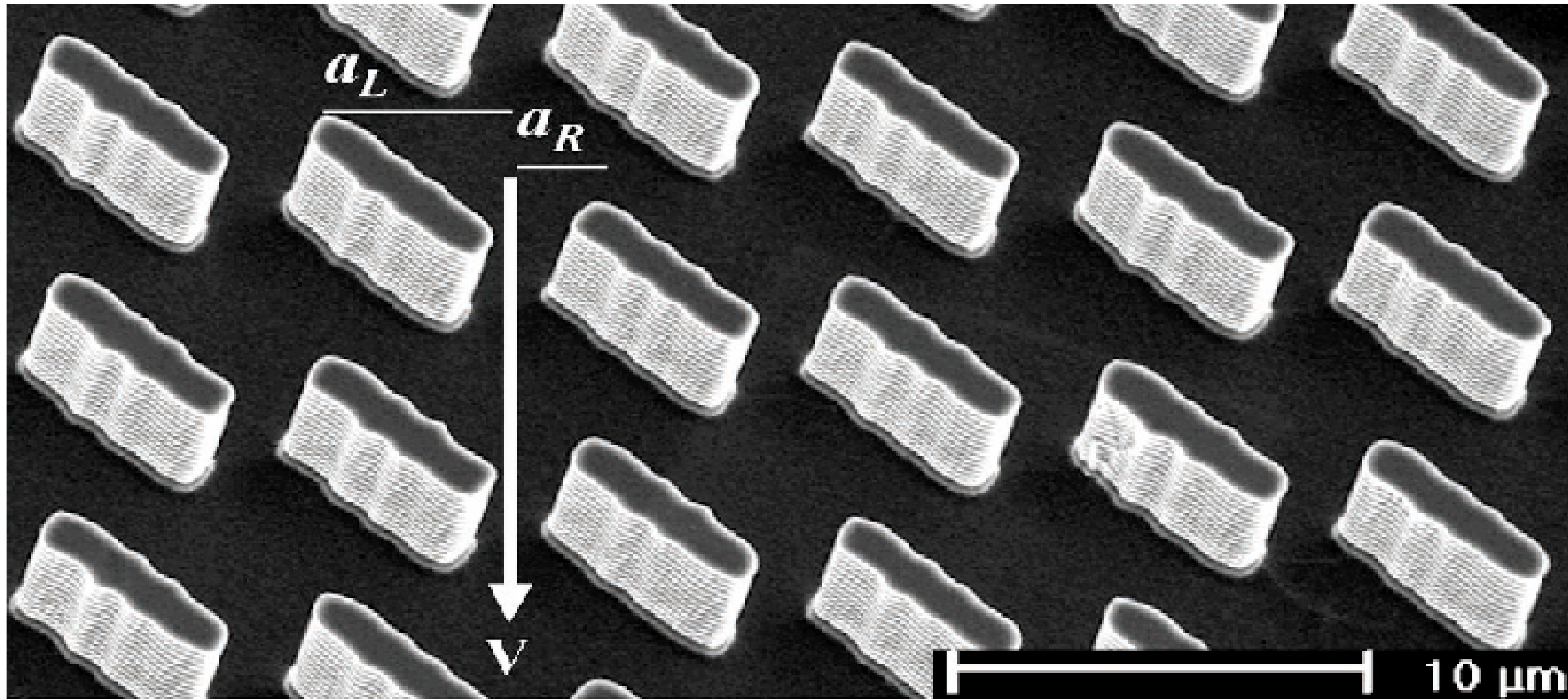
1. T. A. Duke, R. H. Austin, Phys. Rev. Lett. 80, 1552, (1998)

2. D. Ertas Phys. Rev. Lett. 80 1548, (1998)

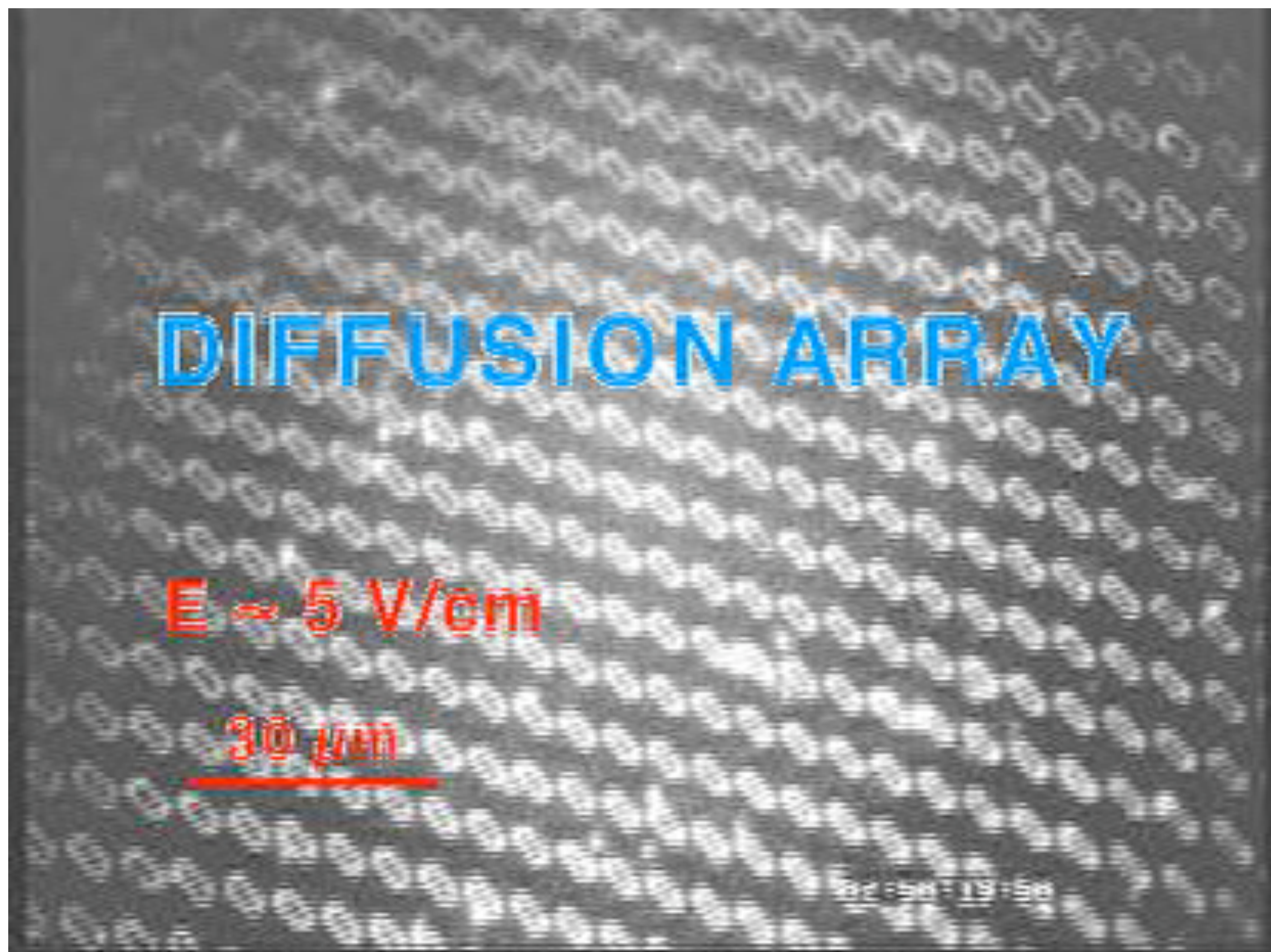


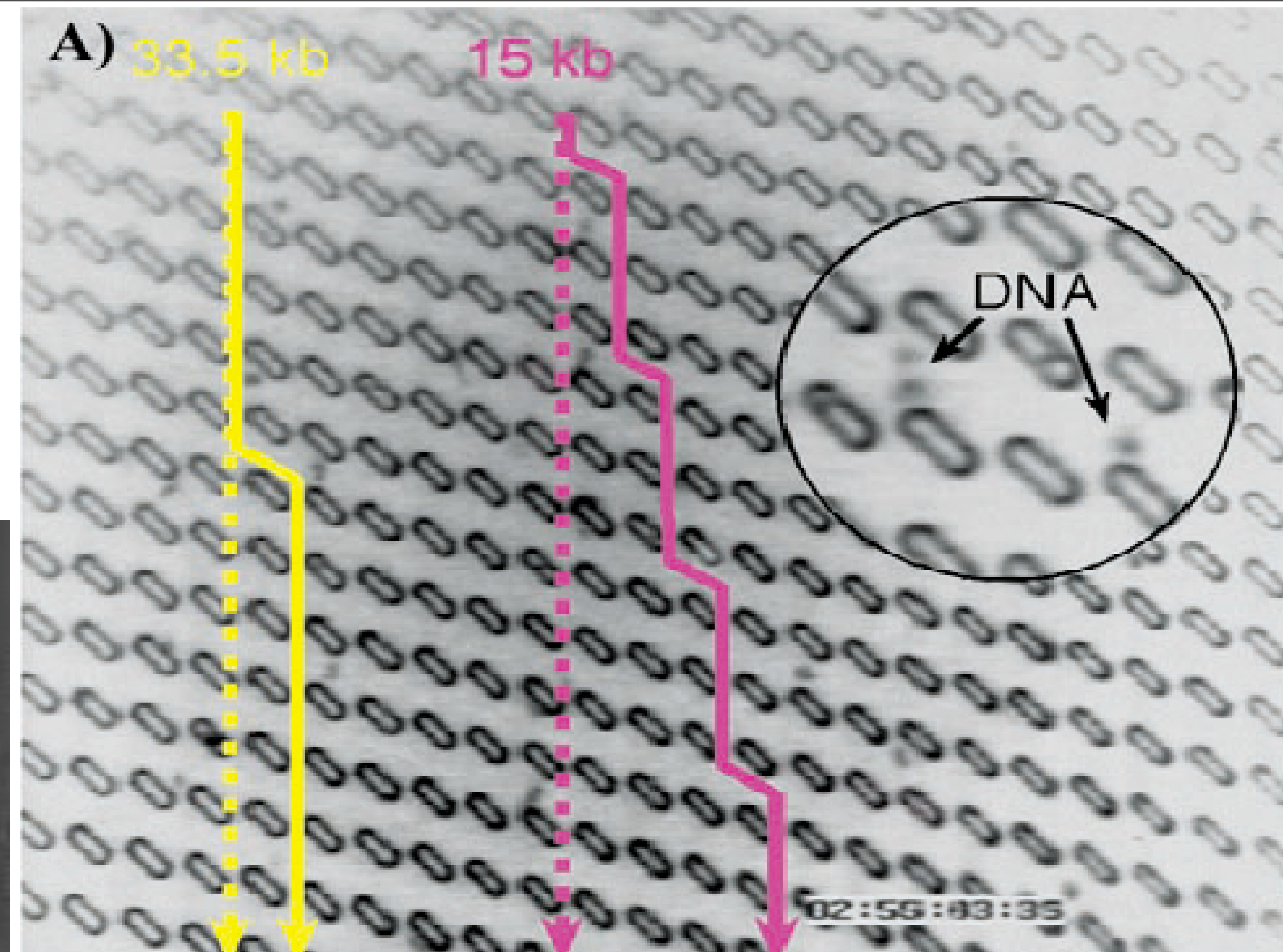


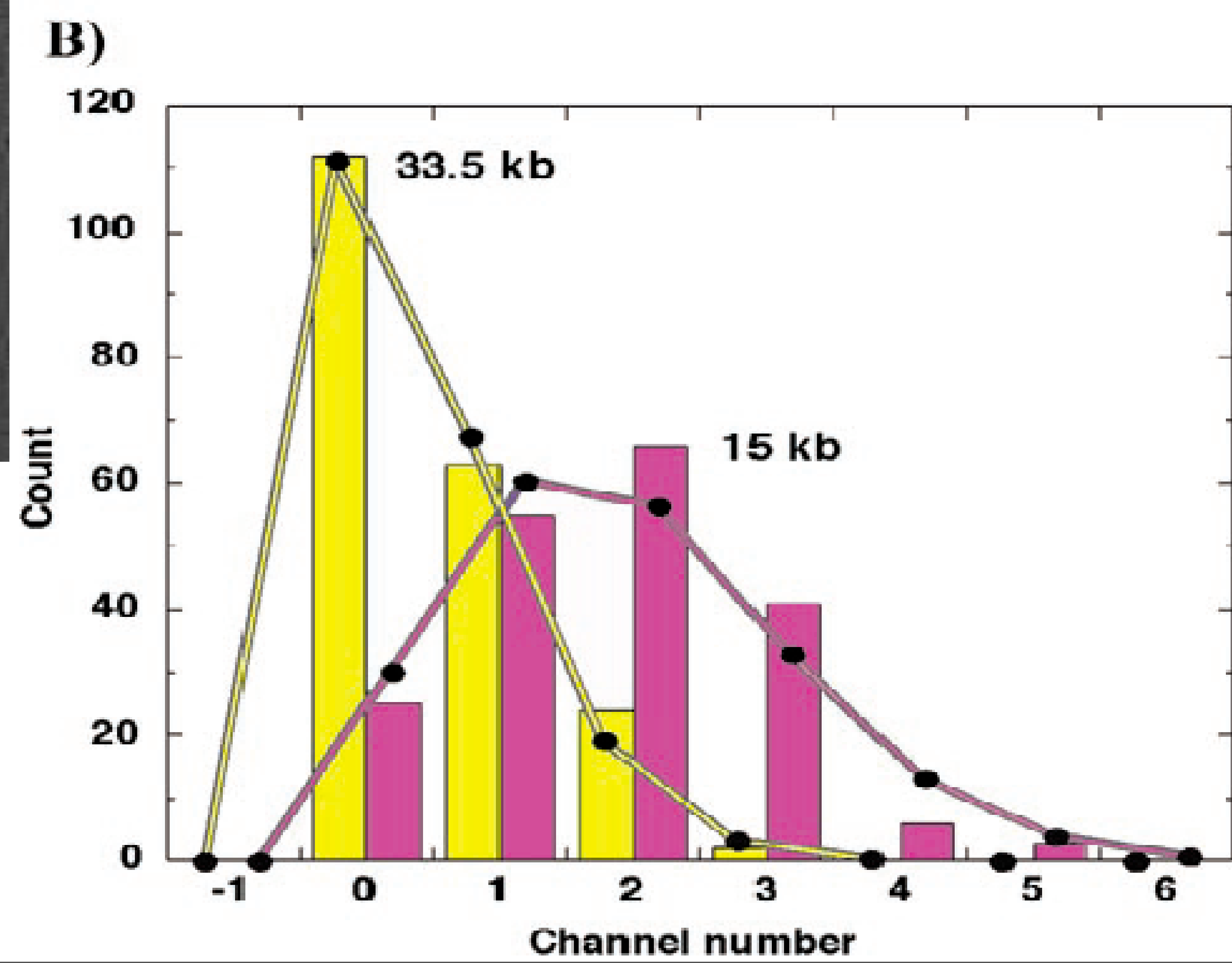
The big idea here is continuous injection and extraction, using a "demon"



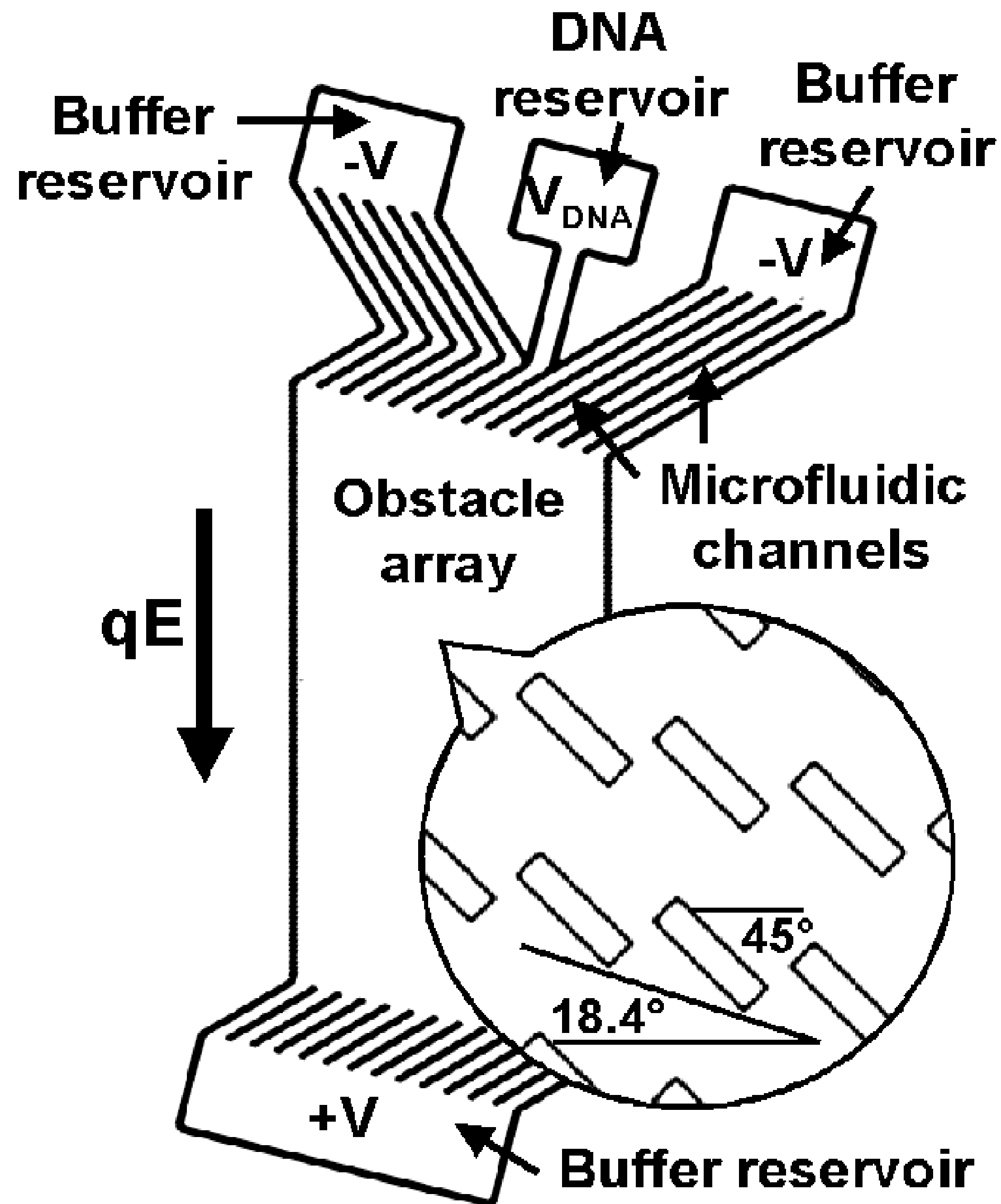
Question: what RIE process did we use to make these asymmeteric structures?

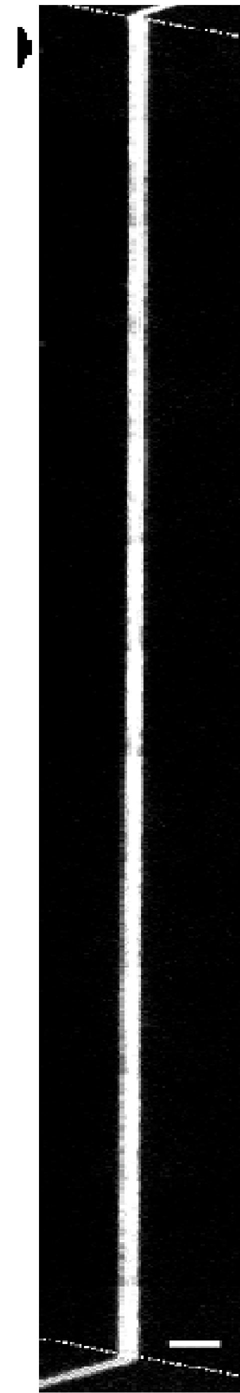

DIFFUSION ARRAY
E ~ 5 V/cm
30 μm


A)
33.5 kb
15 kb
DNA

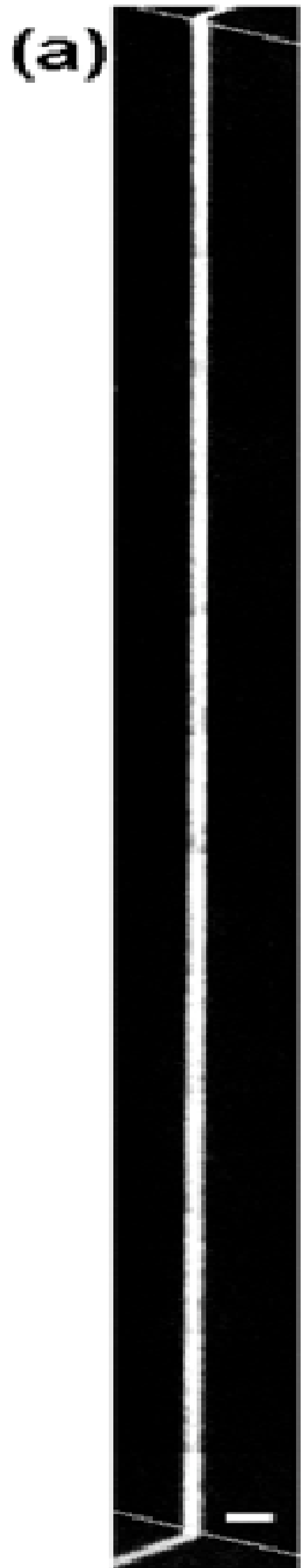

B)
33.5 kb
15 kb
Count
Channel number

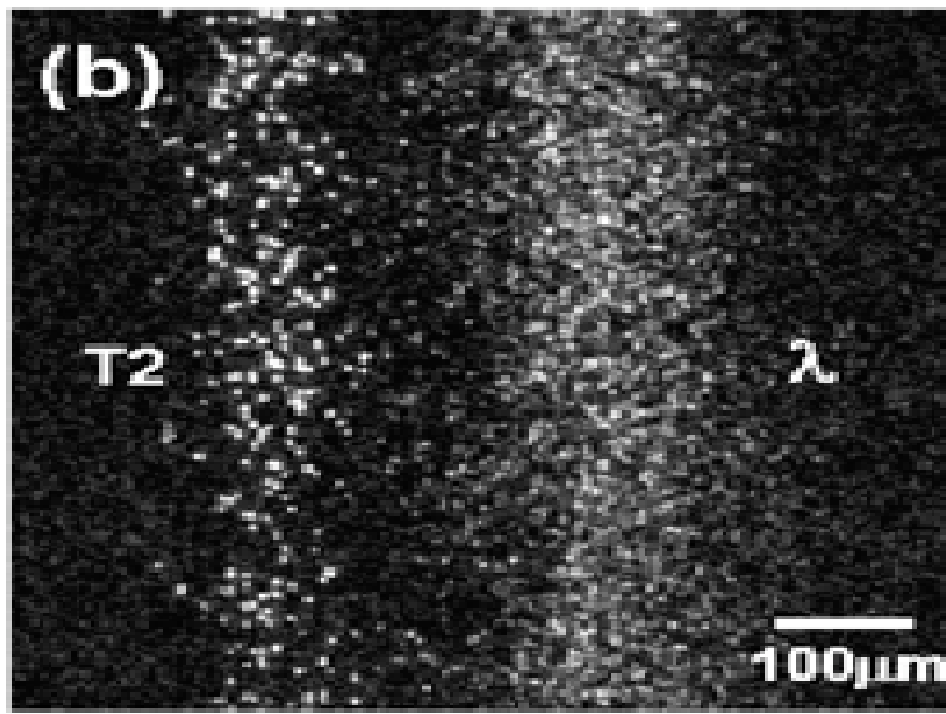
Richard made his trick of the current sheet to get jets.....

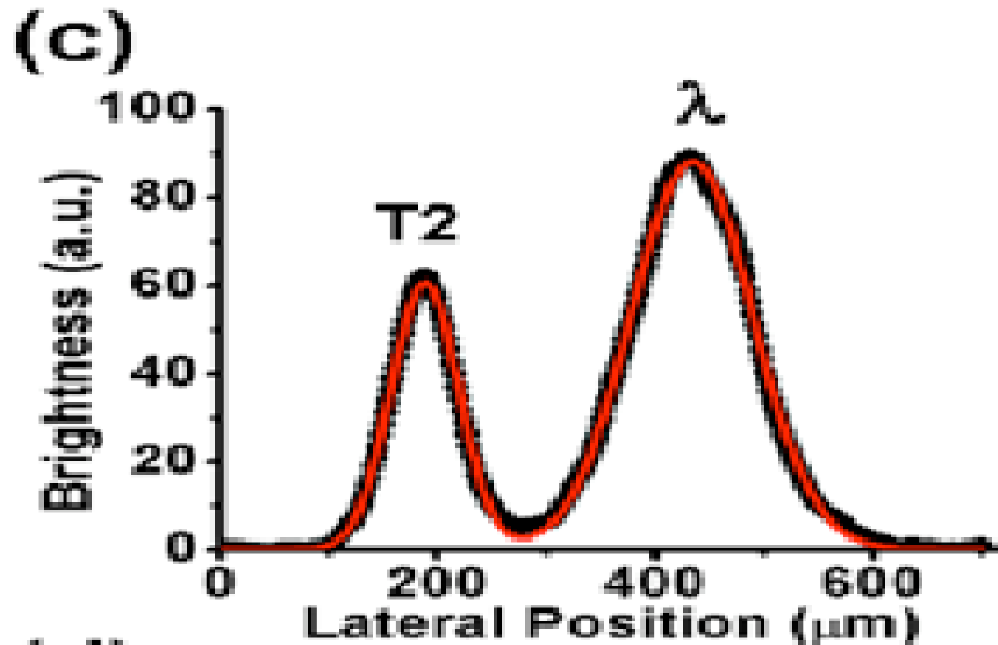


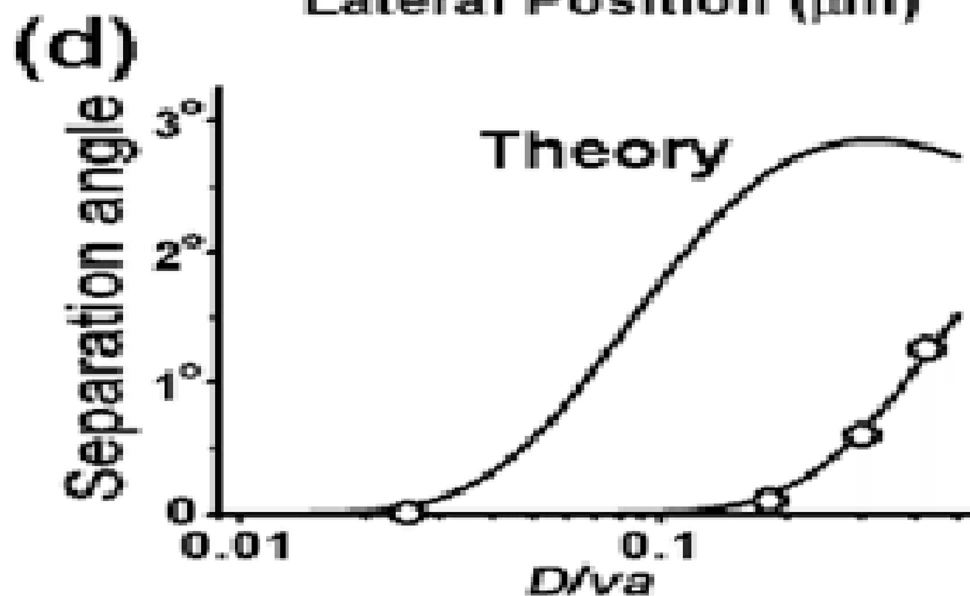


notice the angle of the array edge to get straight isobars..





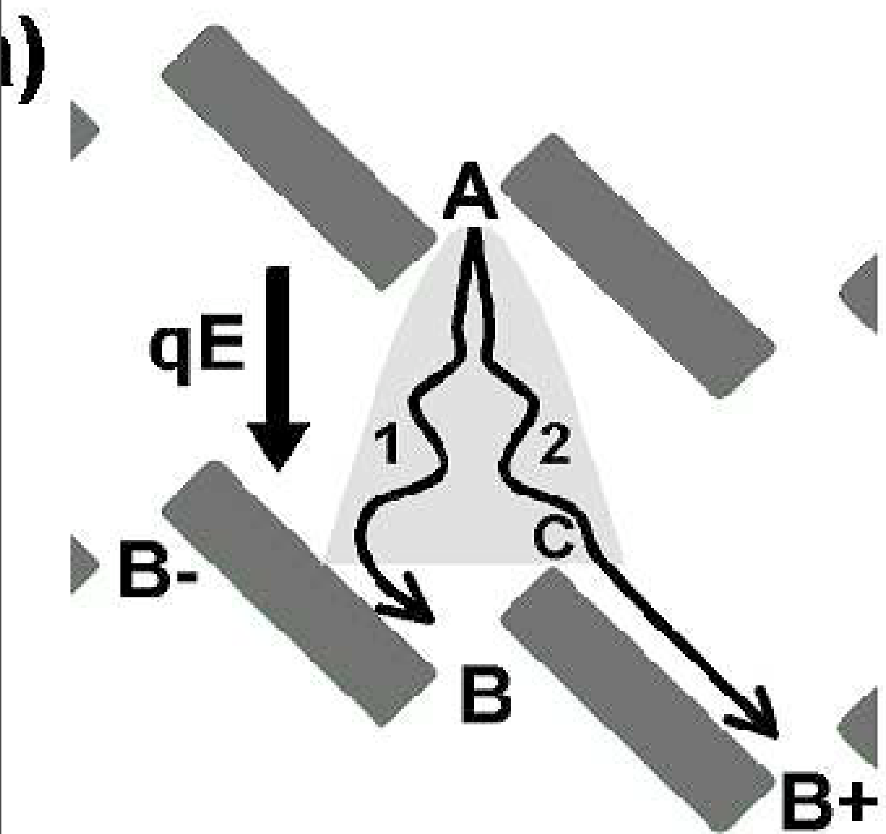


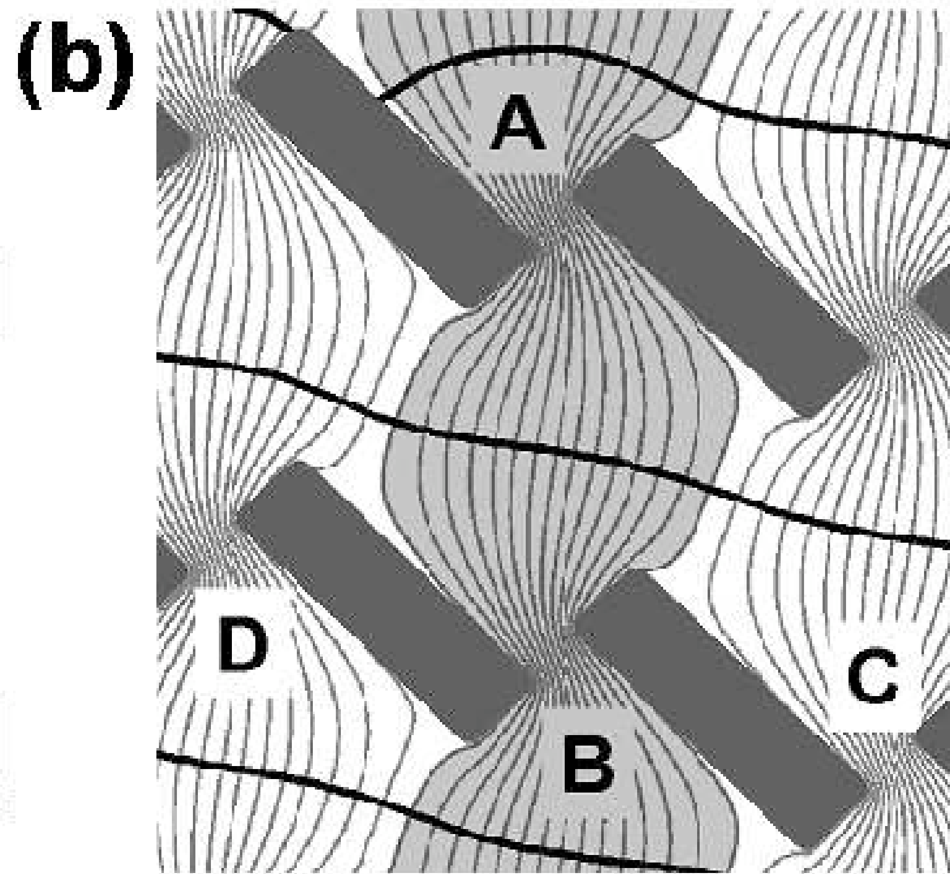


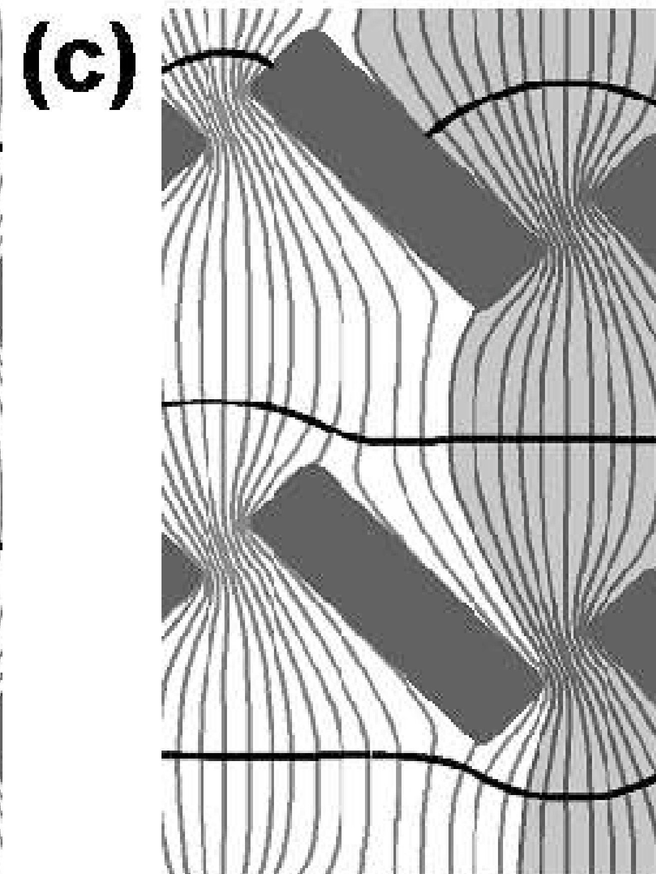
So, can you REALLY

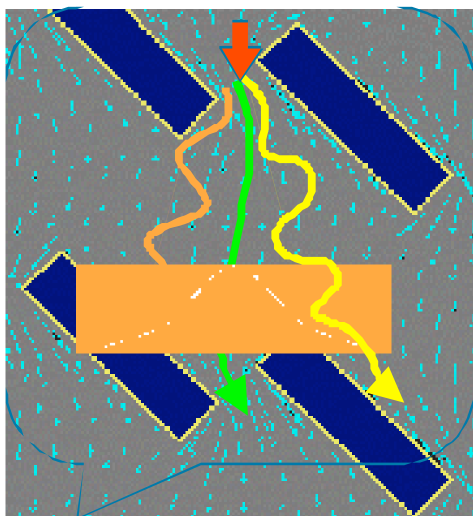
Beat the Demon?

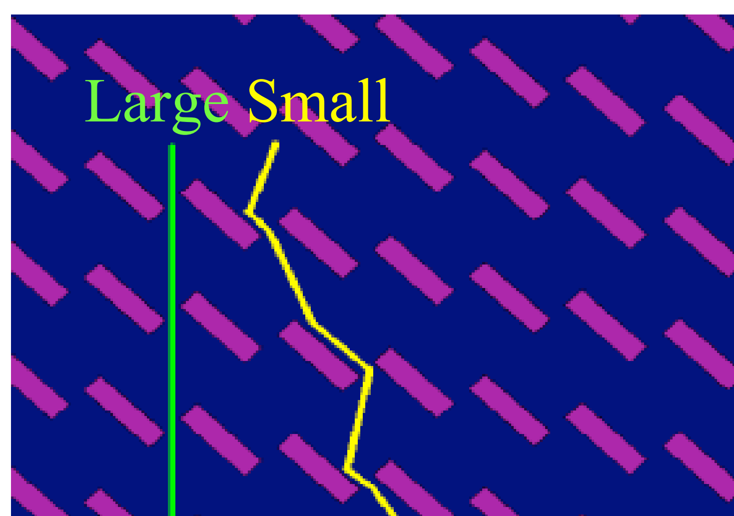
Sort of, but not so interesting to biologists. They have little patience with this. The fractionation
is well under the theoretical value.
Note the 1/Pe in (d).





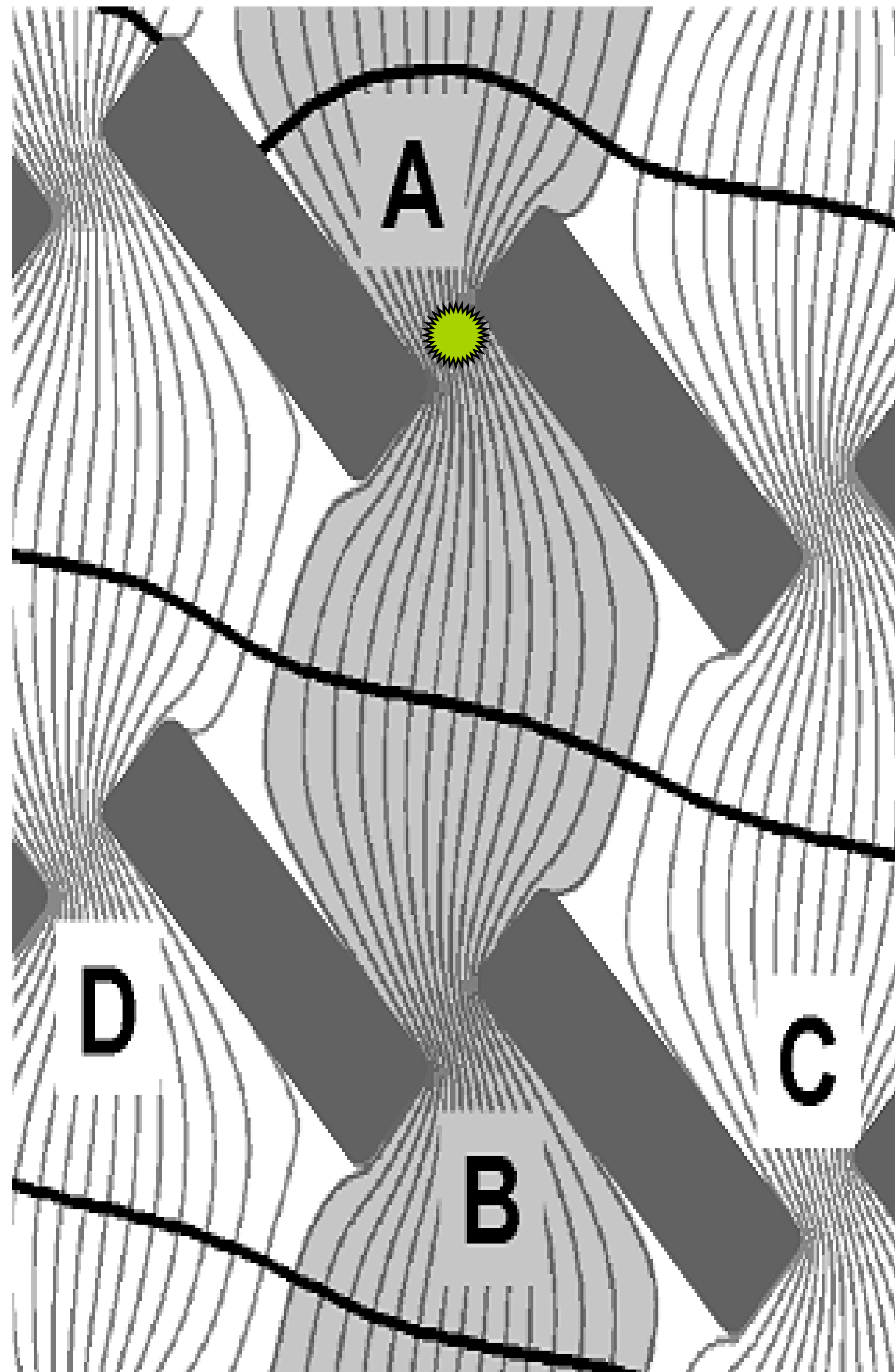






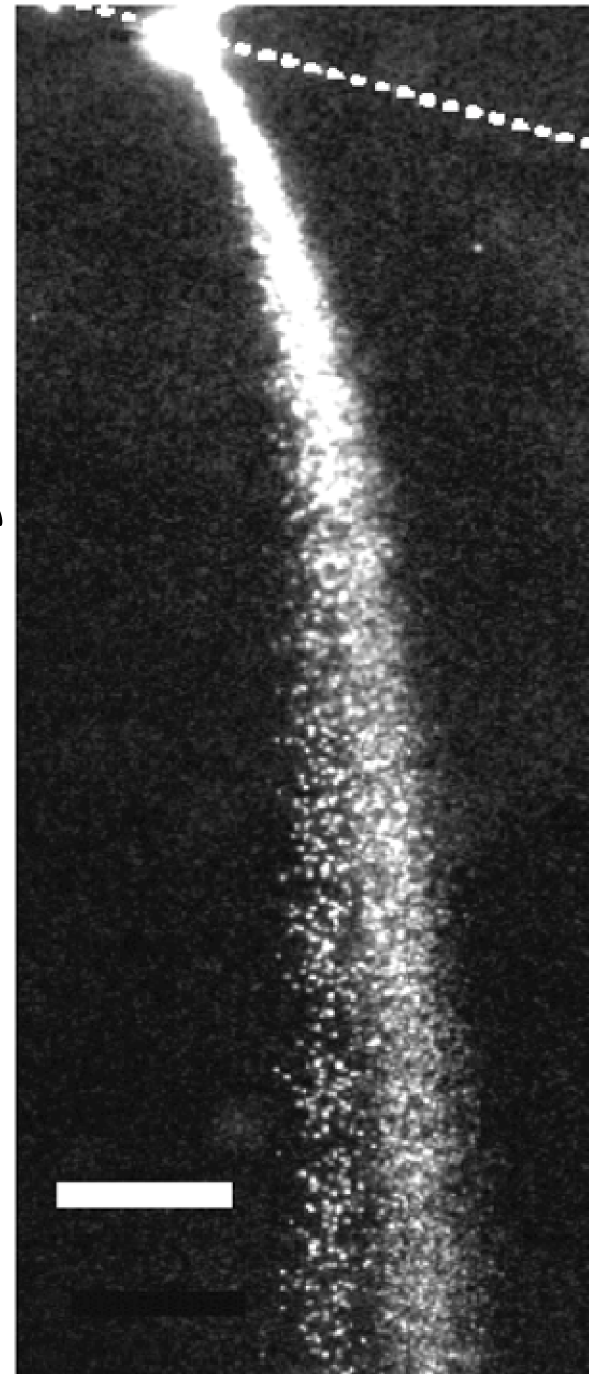
This device WORKS, but only for Pe = 1, transverse diffusion makes it go.

Why do we fail so miserably? Because we forgot that charge can't flow thru silicon dioxide, and insulator (like DNA!). The result of that is that the E field lines have to squeeze back through the gaps, and our statistics get all screwed up because the diffusion distances are much smaller than expected.

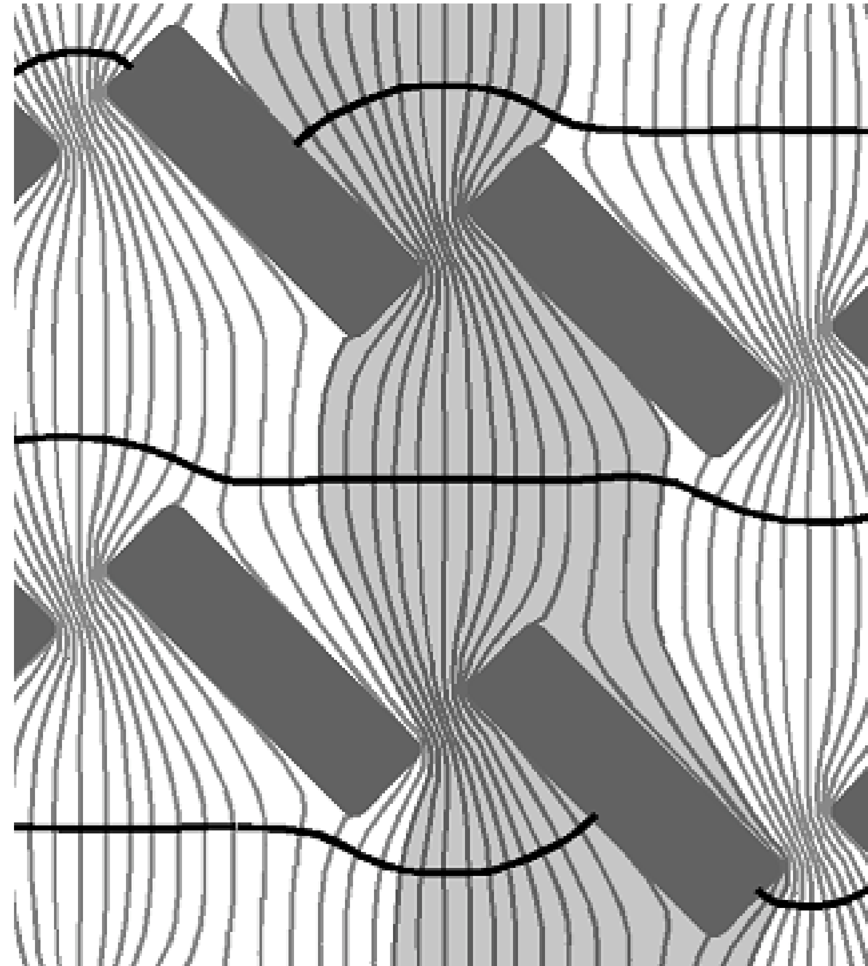


In fact, the device can't work at all unless the particle size is on the order of the gap: "Bigger IS better". The particle has to average over the field lines through the gap.

Is all lost? A good student watches his experiments to spot unexplained puzzles, unlike the silly statement I said earlier. When Richard ran his chip with fluid flow NOT along the clear array axis, he saw something funny: the fractionation went temporarily way up.



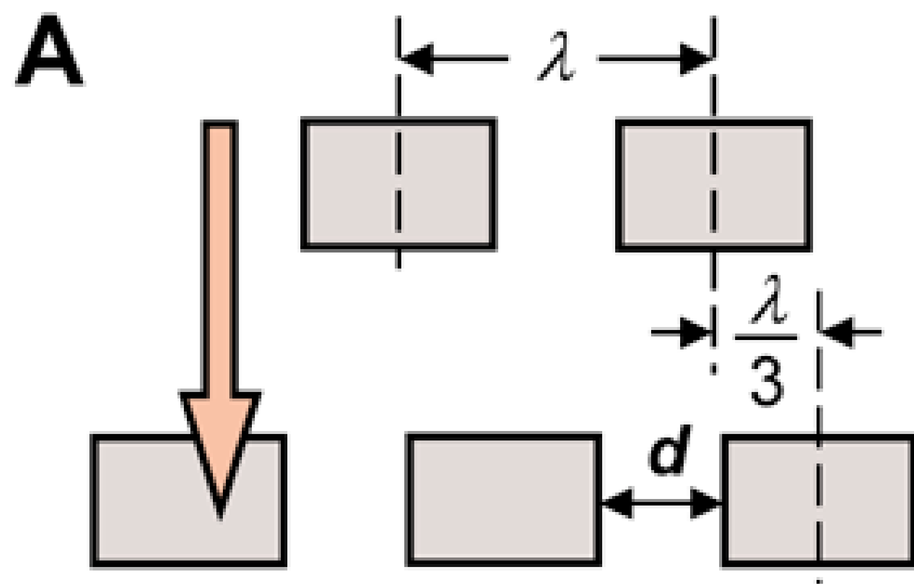
Ne
Buvez
Jamais
d'Eau

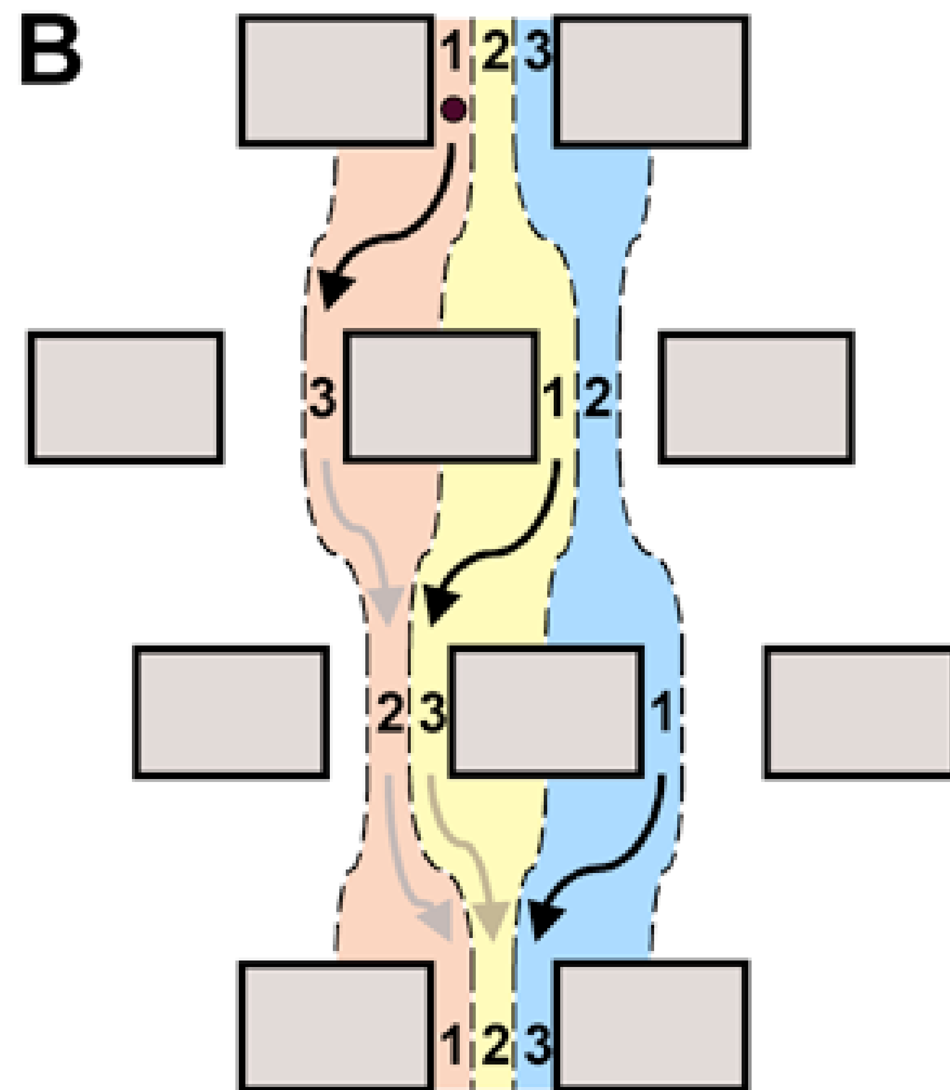


We didn't quite understand this at the start, but it had something with setting the fields deliberately set at an angle to the straight axis.

Somehow, as the flow moves through a mis-alignment to the clear axis of the structure the fractionation dispersion goes up by a factor of 10!

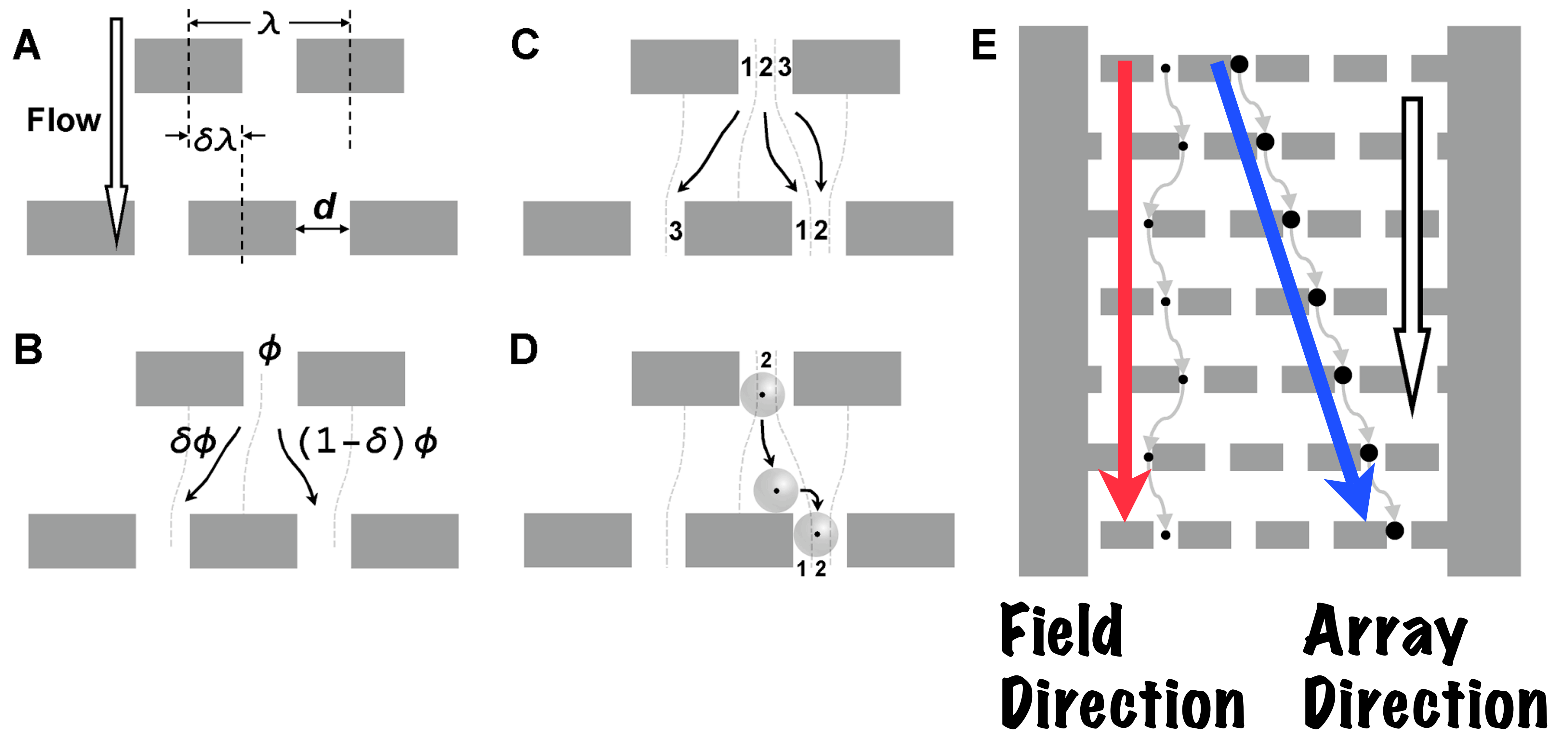
Why? You would think that if anything mis-alignment would screw up the brownian ratchet. In fact you would be right. What is happening has nothing to do with brownian ratchets and everything to do with microfluidics, incompressible fluid flow and what happens when particles intercept multiple streamlines due to finite size.





This is an array created by Richard Huang, it is NOT a brownian ratchet array, there is no direct path straight down the array as we had for the brownian array.

You have to dance step down the array, 1-3-2-1, etc. A step in the tango. This is tricky. If you get it, you are doing well.



Now, here is the really tricky part. Large particles are moved by a sum of streamlines, like a sailboat or a woman surrounded by men (or visa versa) and if the net drag is big enough the particle can move not 3-1-2-3 etc. but rather 1-1-1-1 etc.: along the clear axis, at an angle to the flow direction. We call that process "bumping".

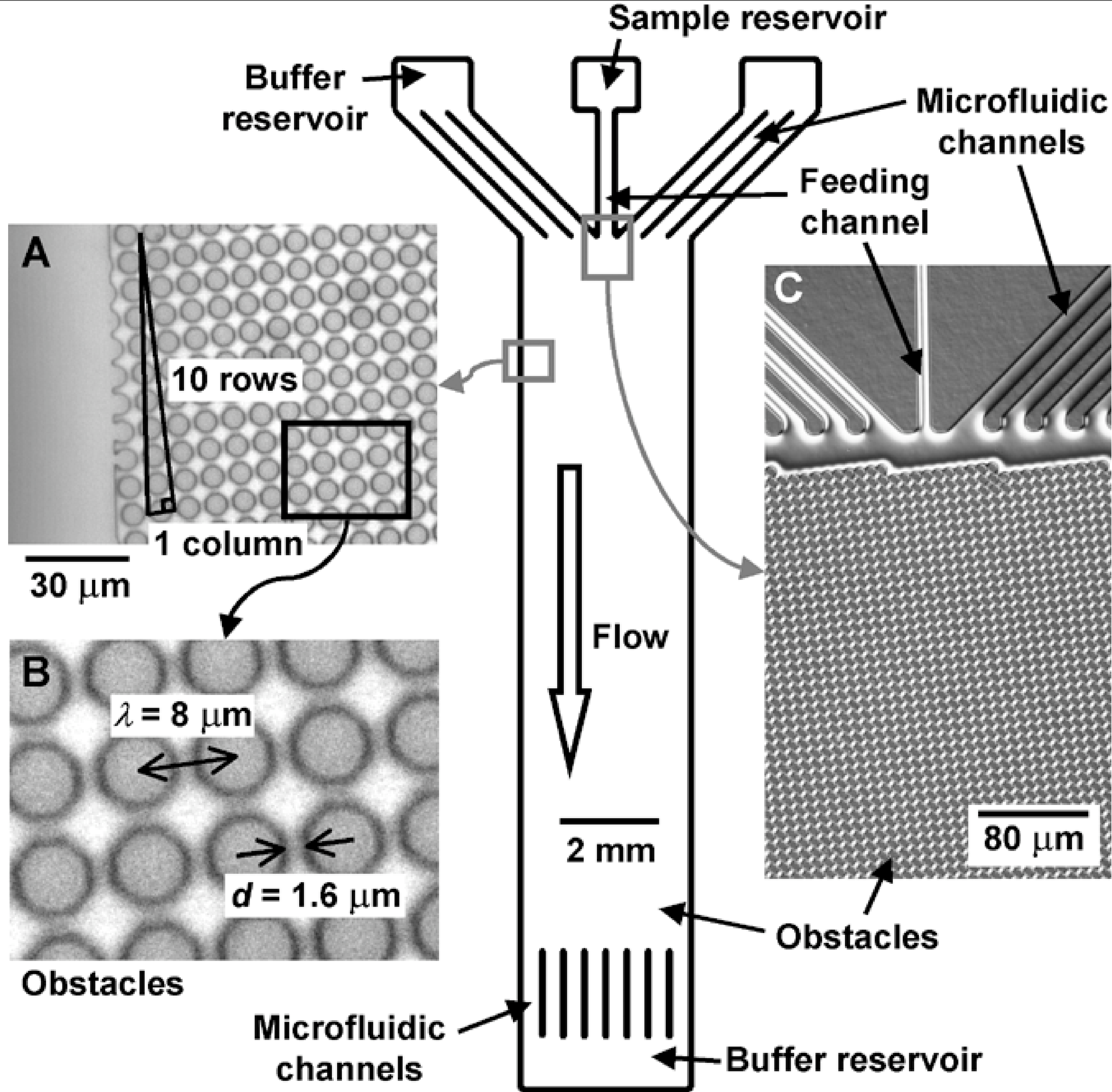
A
Small
Large
Flow
Zigzag mode
Sacada mode

B
λ
Flow
$\Delta\lambda$
d

C
Φ
$\varepsilon\Phi$
$(1-\varepsilon)\Phi$

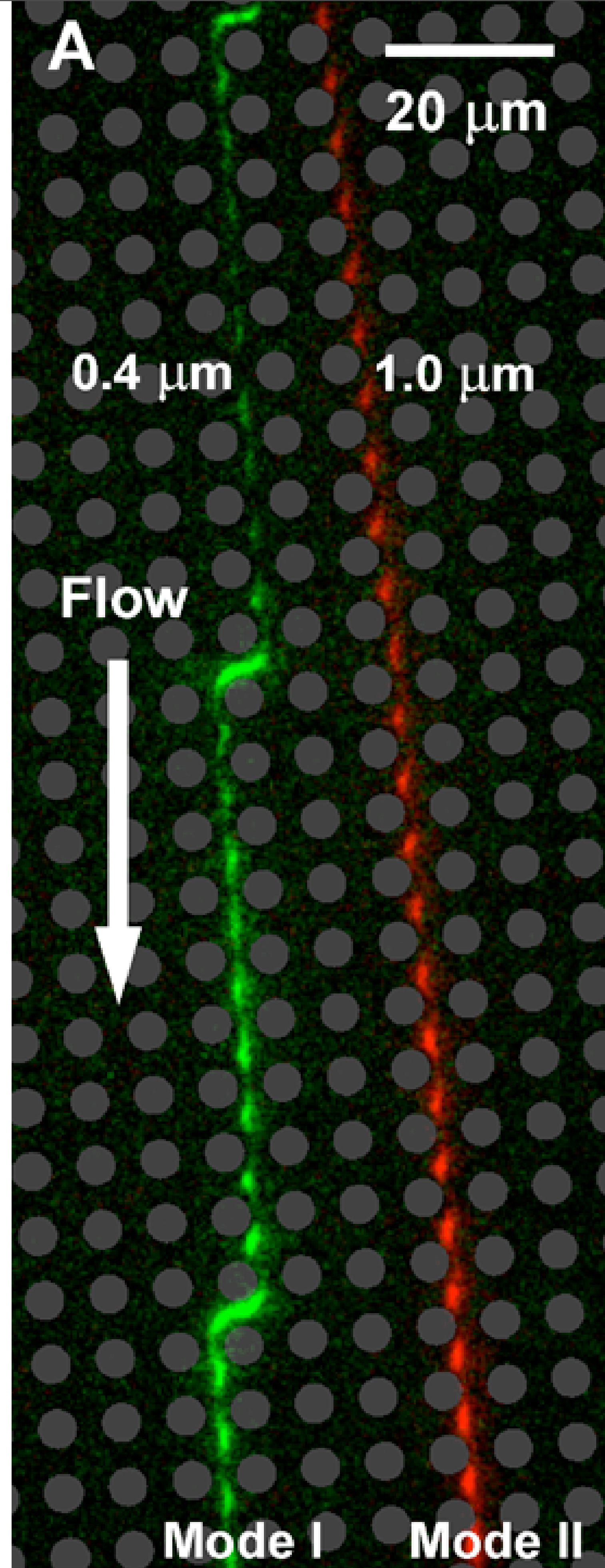
D
1 2 3
3
1 2

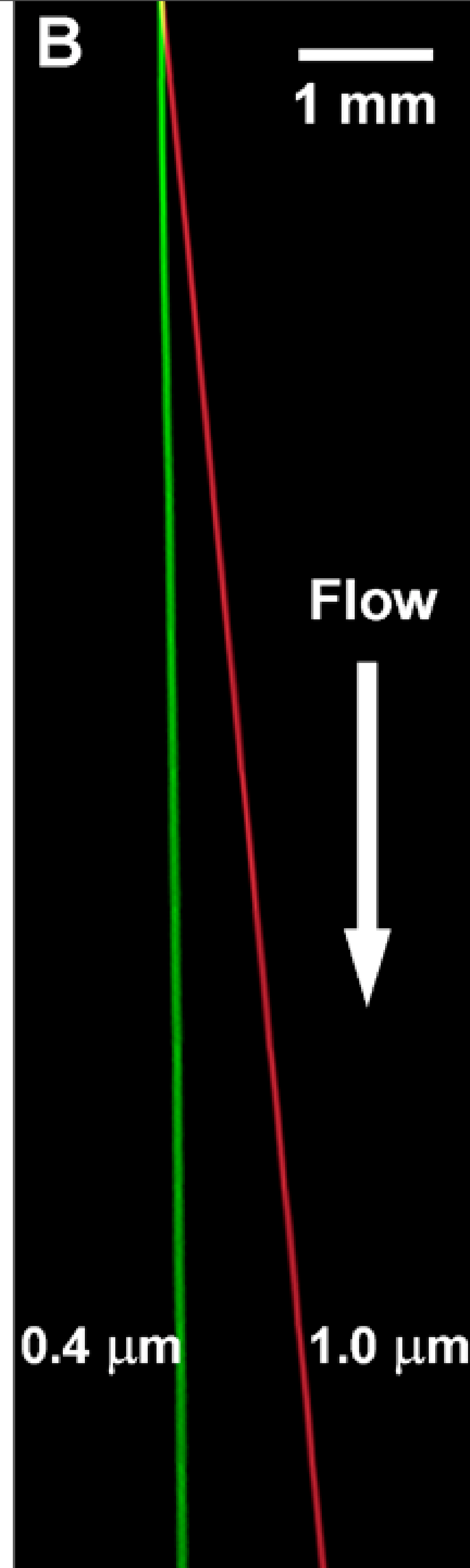
E
2
1 2

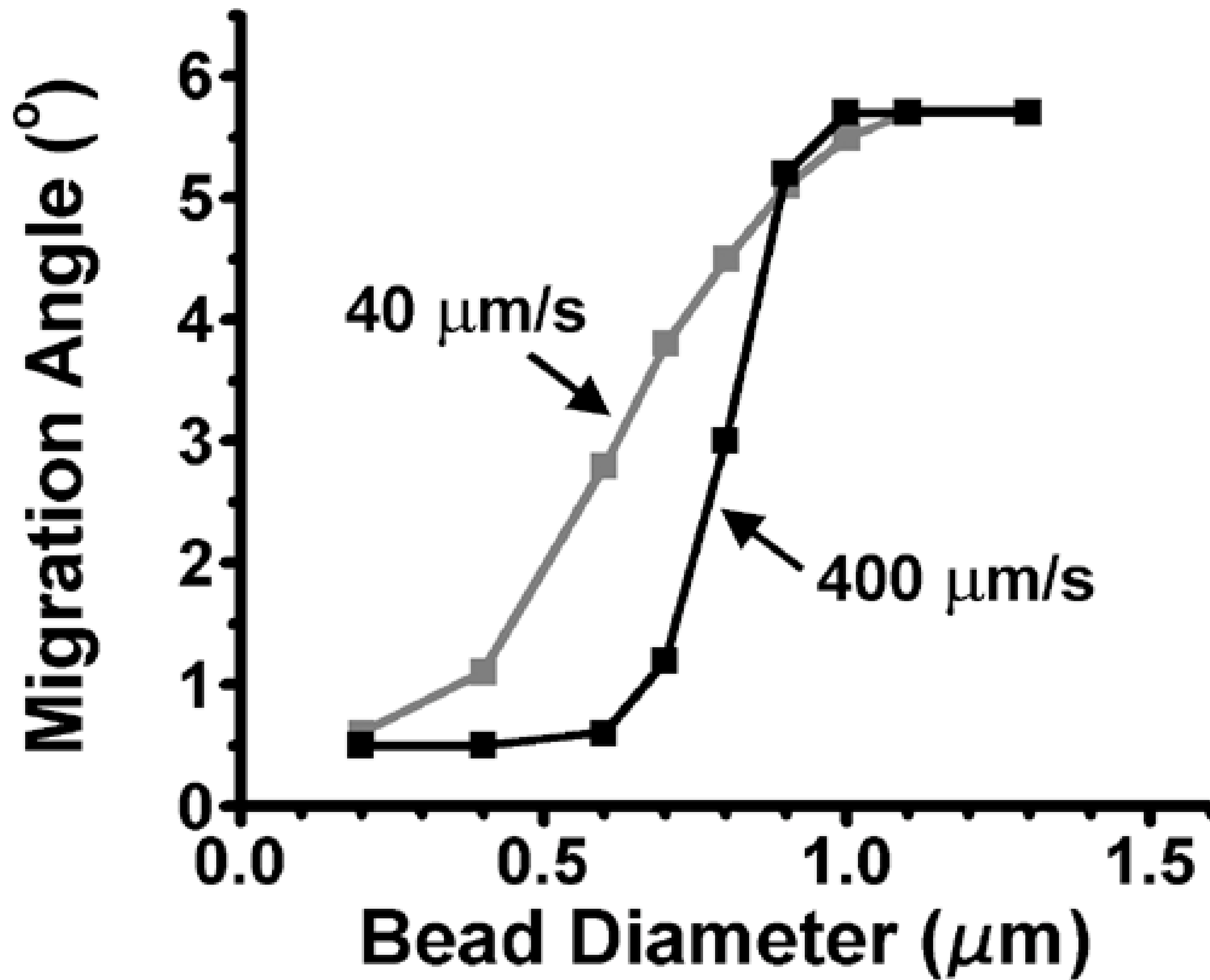


Once we realized what was happening, built misalignment into the device.

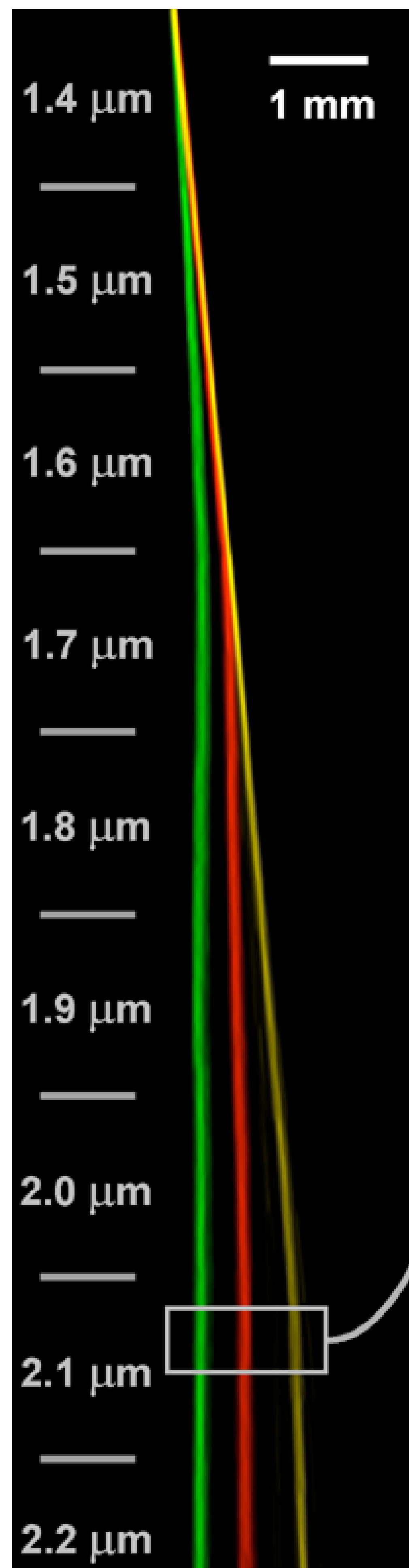
$$\varepsilon = \frac{\delta\lambda}{\lambda} = 1/10$$

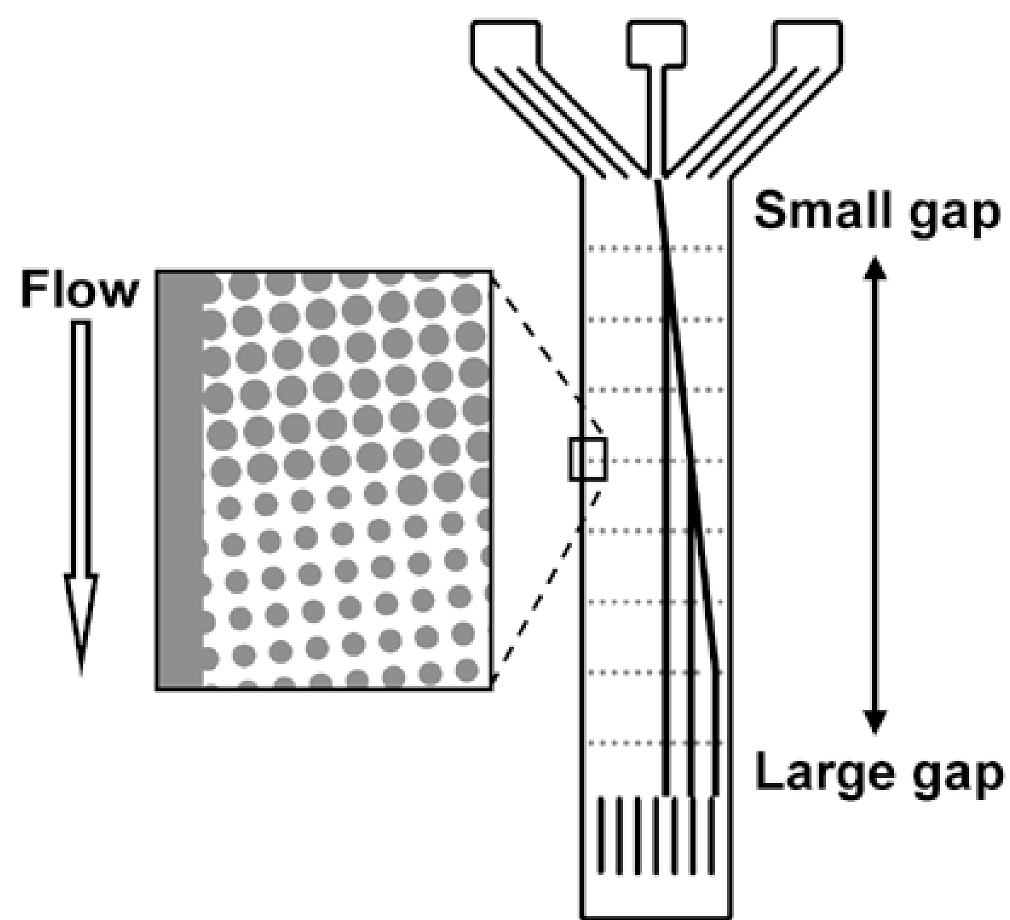


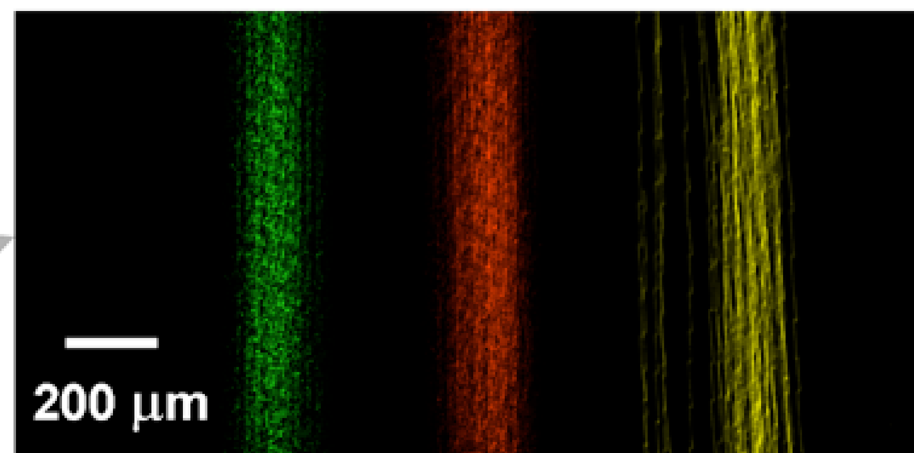


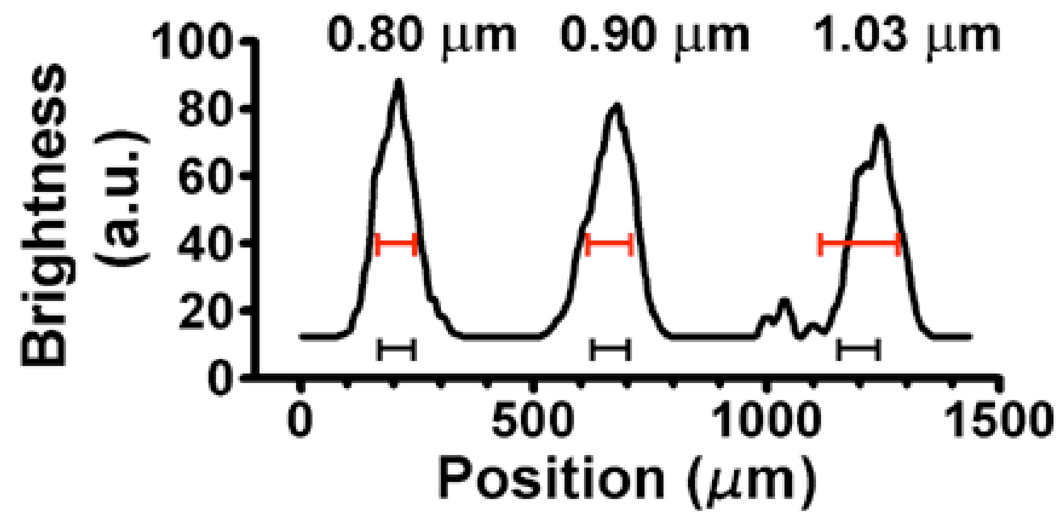


The FASTER the flow, the SHARPER the edge. This is the opposite of a diffusion array. This device wants Pe to be infinity.


1.4 μm
1 mm
1.5 μm
1.6 μm
1.7 μm
1.8 μm
1.9 μm
2.0 μm
2.1 μm
2.2 μm


Flow
Small gap
Large gap


200 μm


0.80 μm
0.90 μm
1.03 μm
Brightness (a.u.)
Position (μm)
0
20
40
60
80
100
0
500
1000
1500

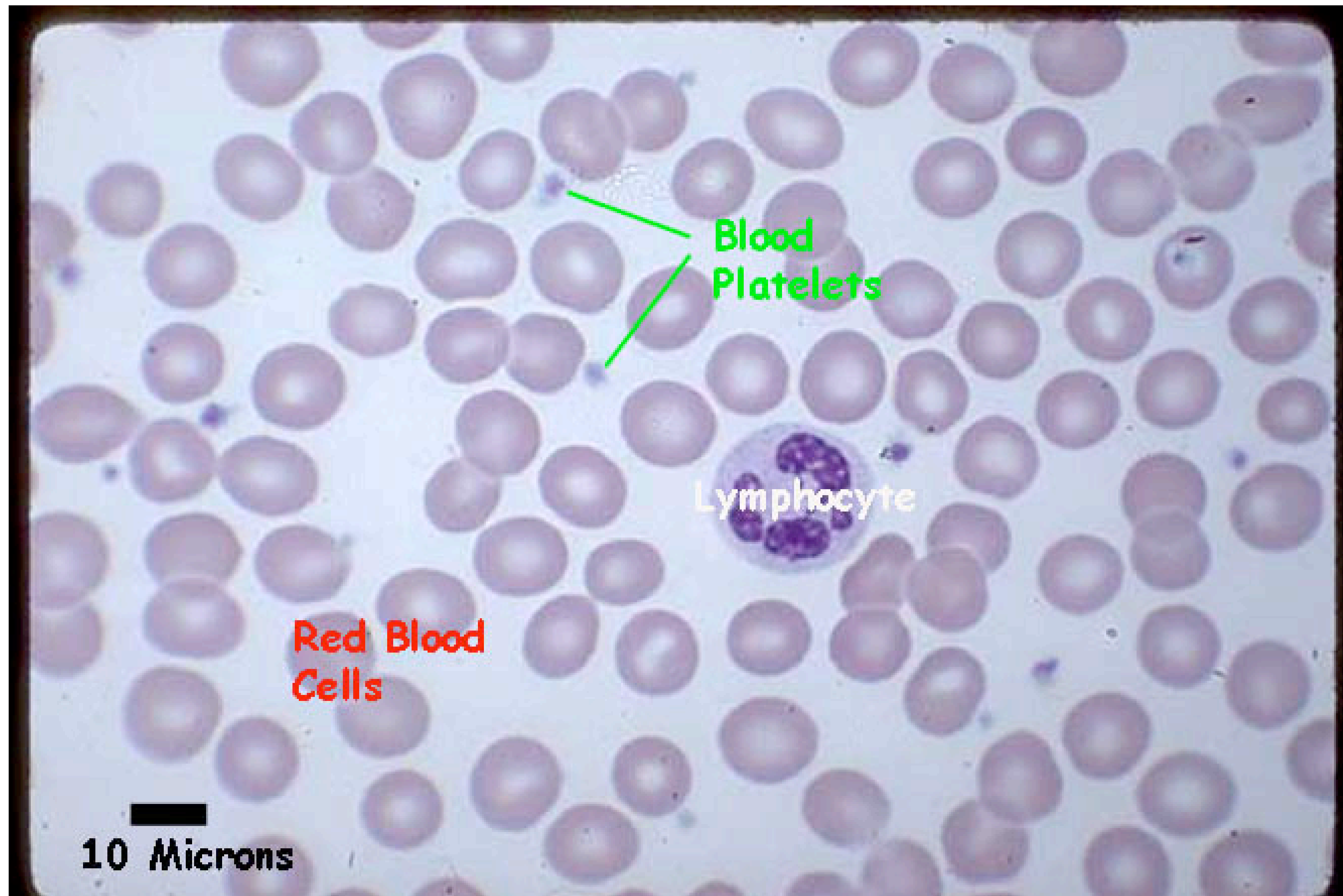
But...it is just DAMN boring and anal to sort micron beads to less than 1% (10 nm!) resolution.

We have two projects right now trying to exploit this "hydrodynamic microscope":

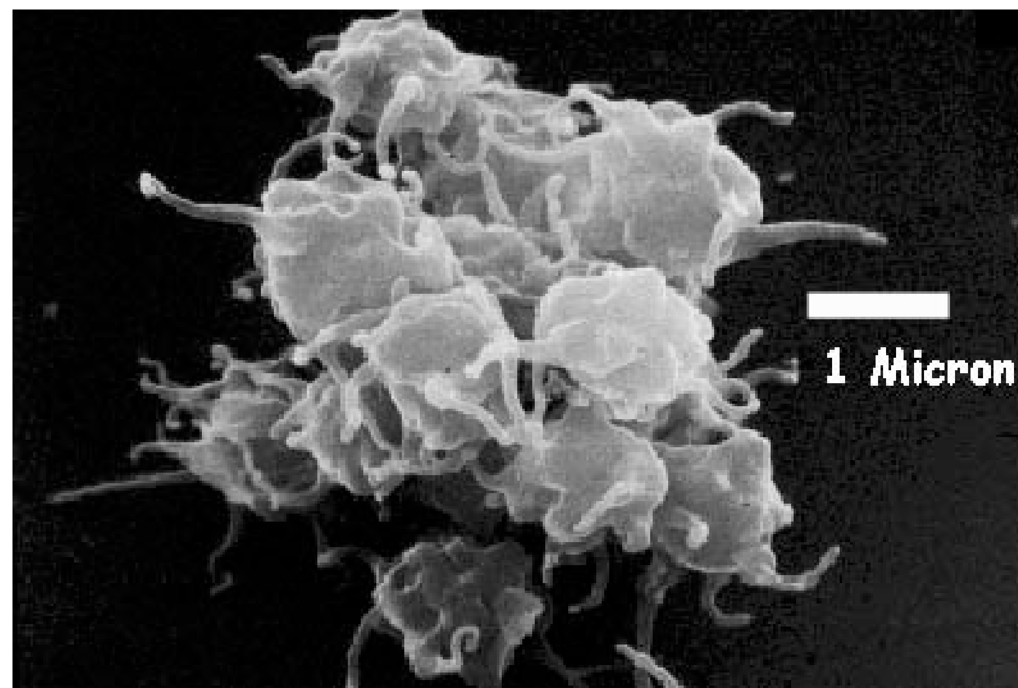
1) Sorting activated blood and blood cell platelets, at the micron level (pretty easy)

2) Sort single molecules (proteins of protein-DNA complexes) at the 10 nm (100 A) hydrodynamic scale with 1 A resolution (really, really hard).

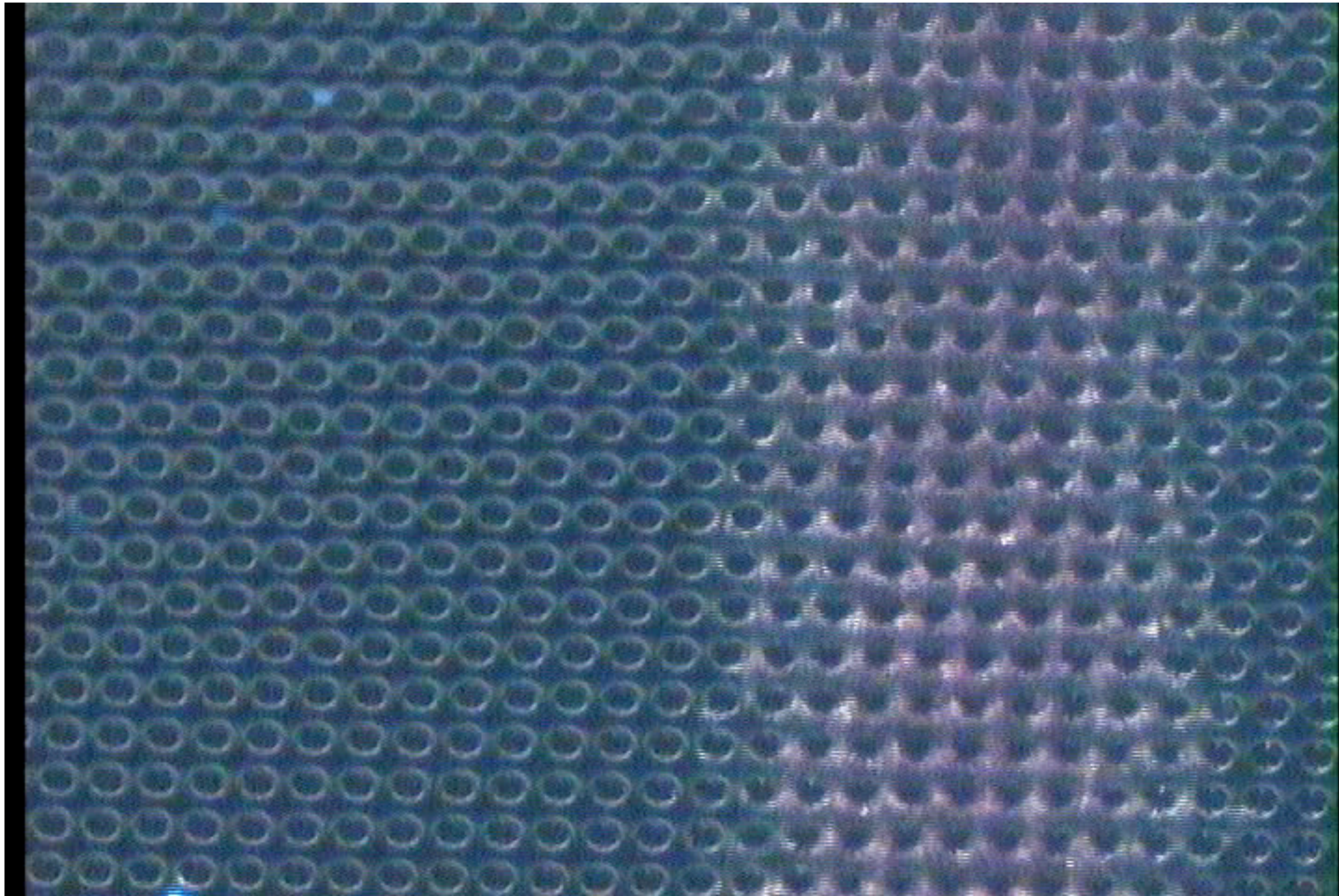
We are machines, and blood is the super-complex fluid that keeps us feed, immune and not leaky.



“resting” platelet, fragile state



Activated platelet, triggers clotting response.



John Davis data on Red Blood Cell/White Blood Cell separation

2) Scaling down to the nm resolution level. Harder problem but of great importance : Can we scale down to getting critical radius to 10 nm, that is separation of proteins or measuring protein-protein interactions at the single molecule scale, or from a single cell?

It is all in the Peclet number and how it scales with a and D:

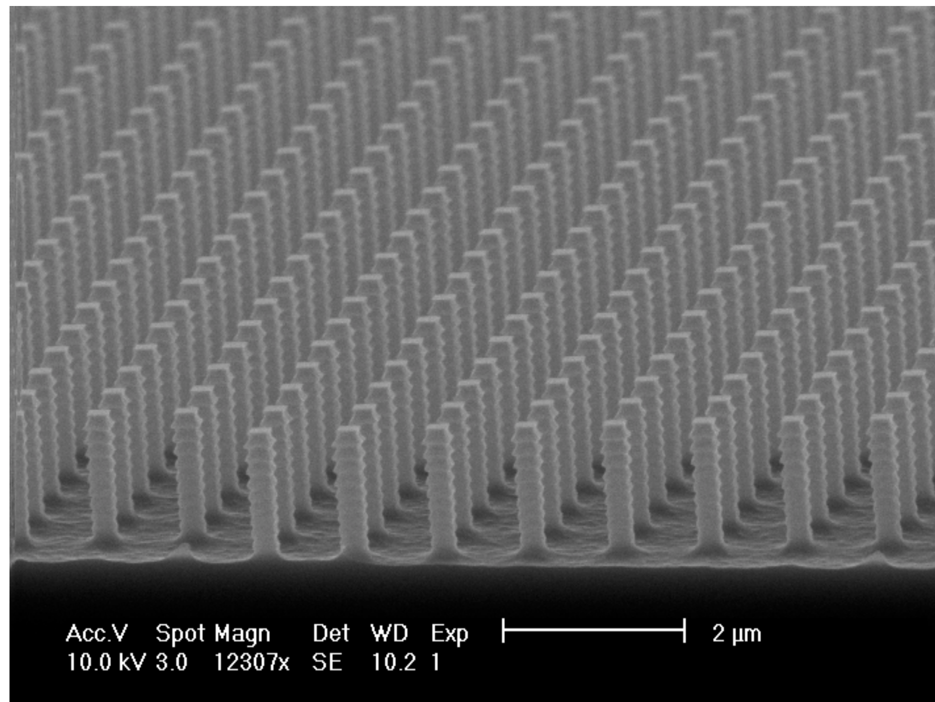
$$P_e \sim \frac{va}{D} \sim \frac{6\pi\eta v^2 a^2}{k_B T}$$

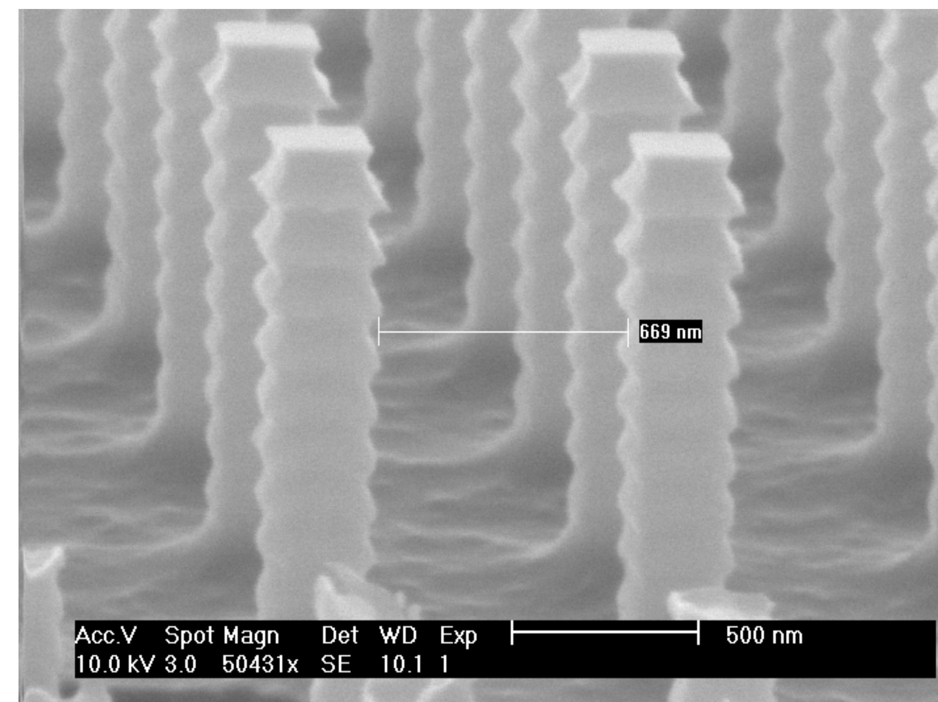
So, to keep Pe high as "a" shrinks v has to go up.

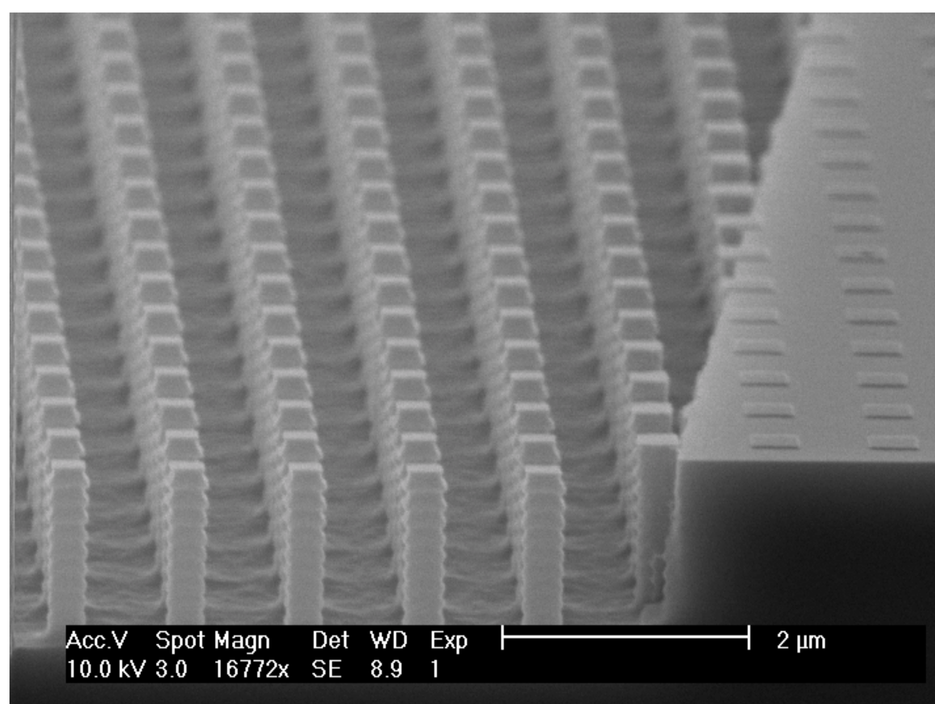
At a= 10 nm and 0.1 nm resolution, v becomes 1 meter/second. This is possible, but requires 1000 bar/cm pressure gradient.

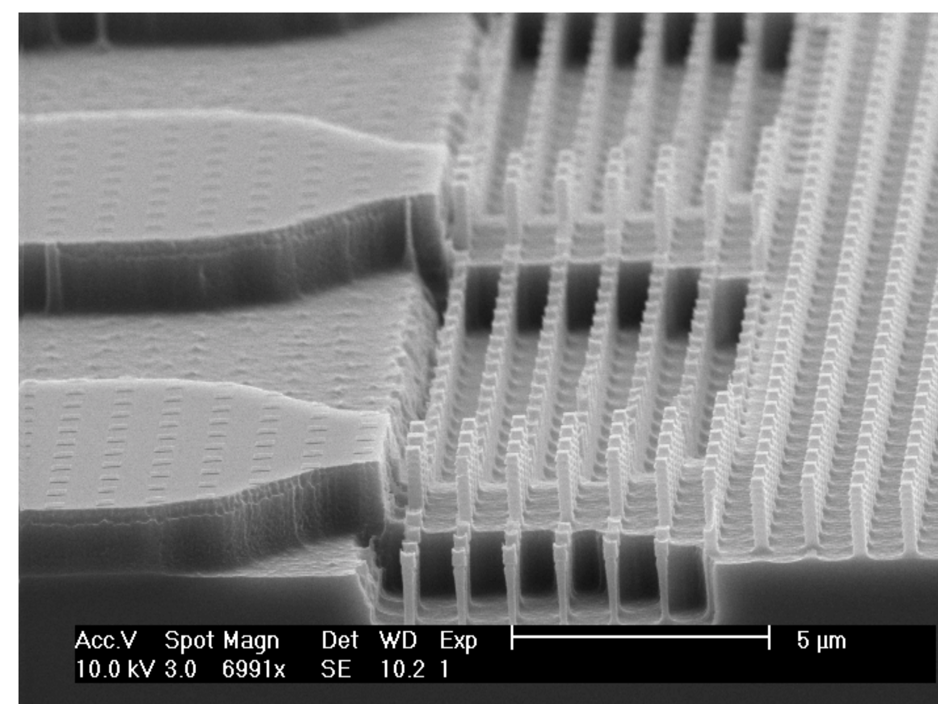
Quite spectacular “real nano” bump structures (not, “it’s micro but we want to call it nano”), by Keith Morton in Steve Chou’s lab.

Keith Morton
Nanostructures Lab
09.26.05



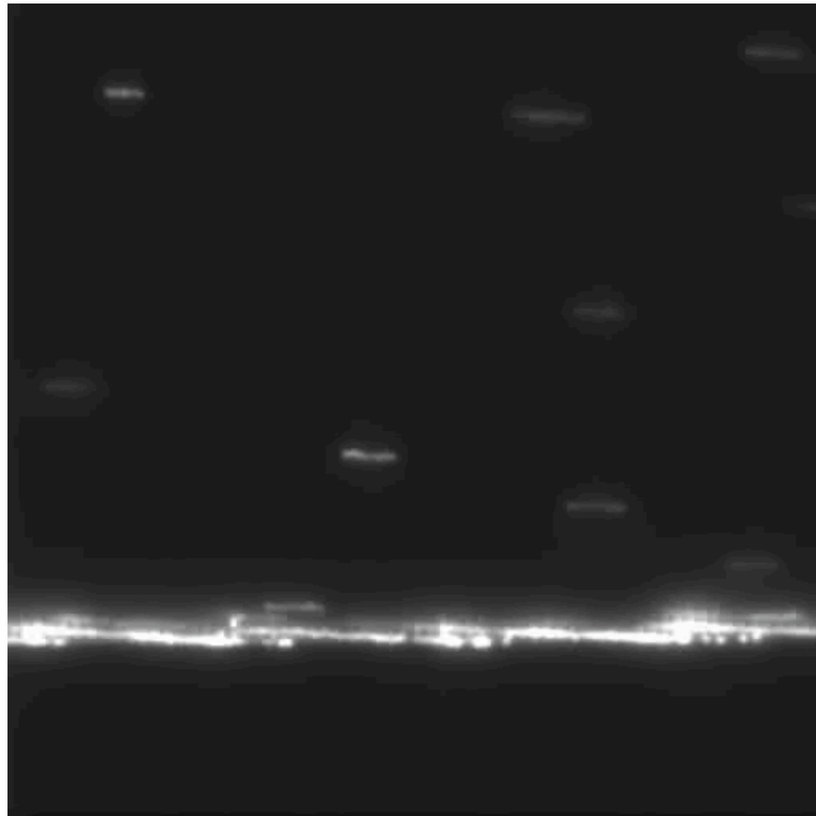


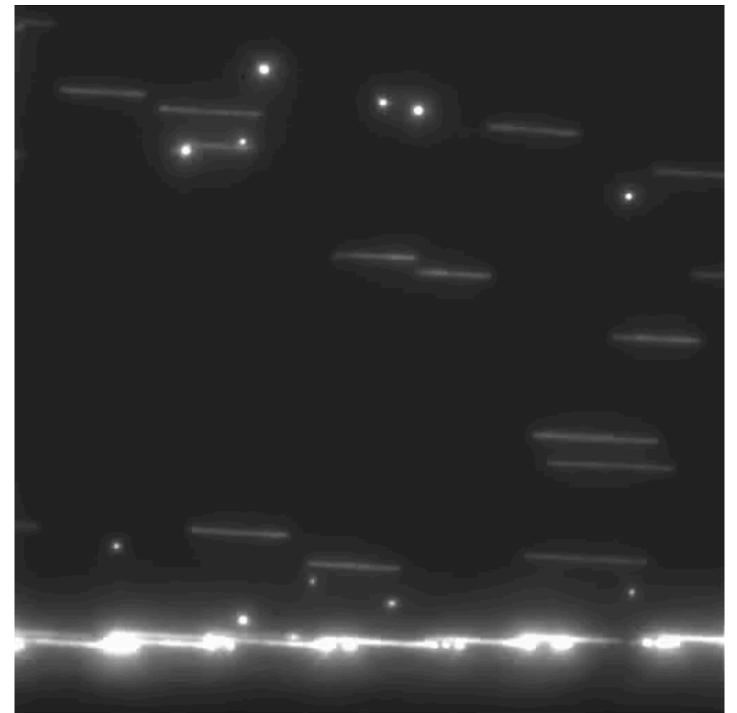




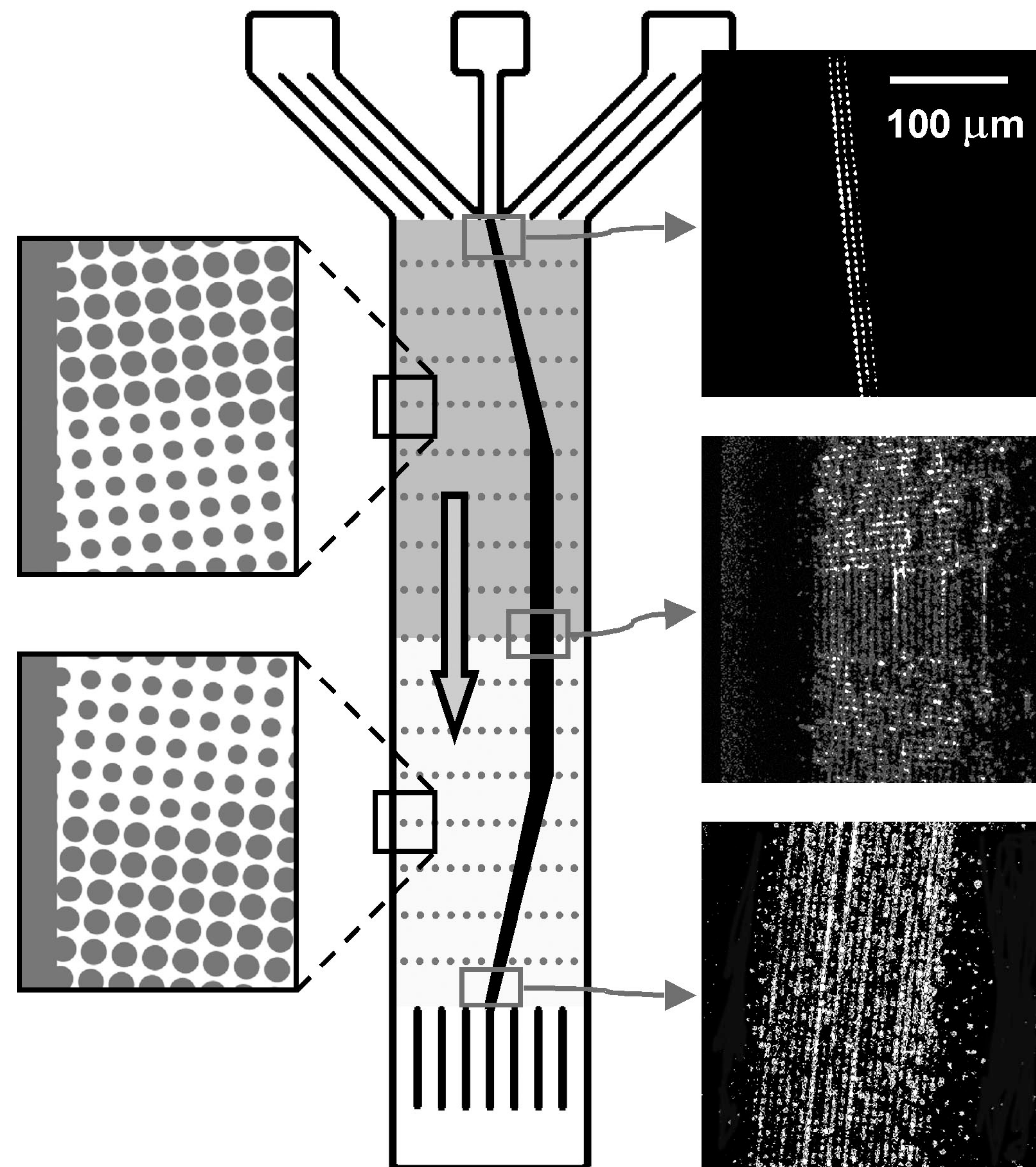
These are 400 nm beads, above the critical bumping threshold. At low pressure gradients, the Pa is small and diffusion competes quite well with bumping.

As we increase the pressure gradient, bumping is increasingly more effective against diffusional smearing.





An interesting thing about this bump technology is that by changing the shift of the posts from right to left you change the sign of the particle displacement (if they have greater than the critical size). It is like optics, where you have positive and negative indices of refraction.



Pressure gradients are an interesting aspect of this technology as we go nano. High pressures and high pressure gradients and nanofeatures require that these structures be made not out of PDMS, which is too soft, but of hard materials such as quartz (fused quartz actually) or silicon.

Several problems arise:

1) SEALING such structures to maintain high pressures

2) Wetting nanostructured sealed devices, and the heartbreak of bubbles.

Tomorrow, we'll talk about my attempts to fractionate DNA in arrays, an introduction to the problem of not small objects but soft polymers in nanofluidics.

Thanks!