

FLUIDIC scaling in MEMS

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Fluidics scaling: table of contents

1. Intro: “Life at low Reynolds number” (key paper by E. Purcell)
2. Reynolds number
3. Drag and sedimentation
4. Flow profile in small channels
5. Forces on particles in liquid flow
6. Diffusion and Mixing
7. Knudsen number and low-pressure regime
8. Surface Tension and capillary pressure

T. M. Squires and S. R. Quake: Microfluidics:
Fluid physics at the nanoliter scale, Rev Mod Phys, 2005

Key fluidic concepts

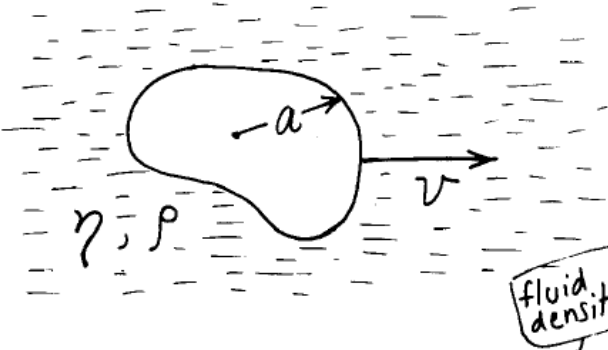
- Reynolds number Re .
 - How do fluids flow when $Re < 10$? what is different from flow at higher Re ?
 - Drag and sedimentation of particles in a liquid
 - Flow in a circular and rectangular channel of multiple liquids - sheath flow
- How do particles behave in a laminar flow. Near walls?
- Diffusion in liquids: scaling? When is diffusion relevant
- Mixing by diffusion: different ways this can be exploited or accelerated for laminar flows
- Knudsen number: rarified gas regime
 - Damping, Q: different regimes
 - Squeeze film damping: what phenomena take place?
- Surface tension
 - Scaling of capillary pressure, Washburn eq, capillary stop valves
 - Electrowetting
 - Droplet formation

Life at Low Reynolds Number (1976) E.M. Purcell

Edward Mills Purcell

- Professor of Physics at Harvard
- Nobel Prize winner for NMR

Reynolds Number ($\mathcal{R}$ or Re)

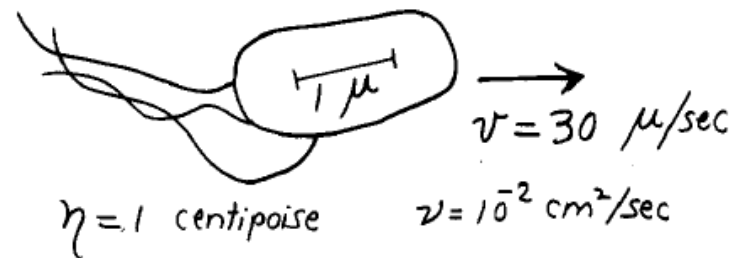
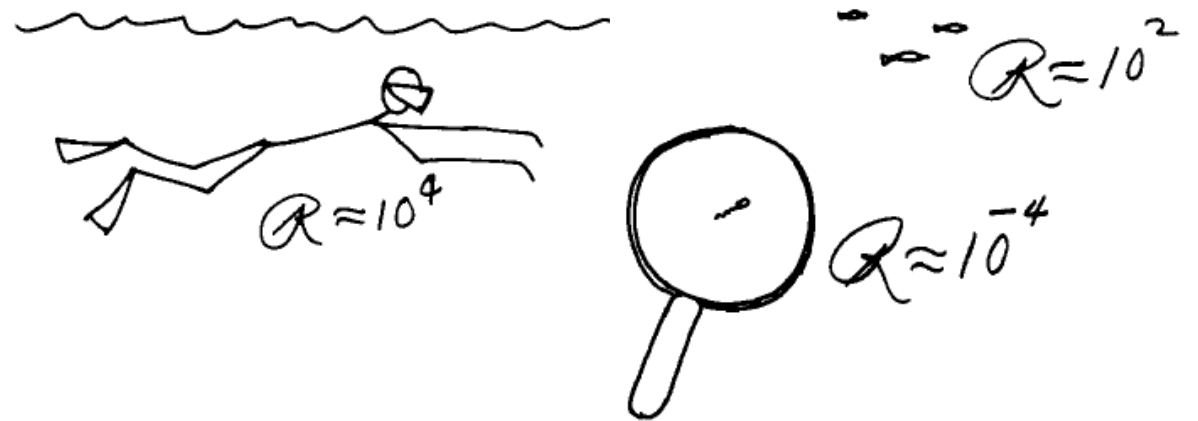


$$\mathcal{R} = \frac{\text{inertial forces}}{\text{viscous forces}} \approx \frac{av\rho}{\eta}$$

fluid density ρ

fluid viscosity η

- Low Re = laminar flow = viscous forces dominate
- High Re = turbulent flow = inertia dominates

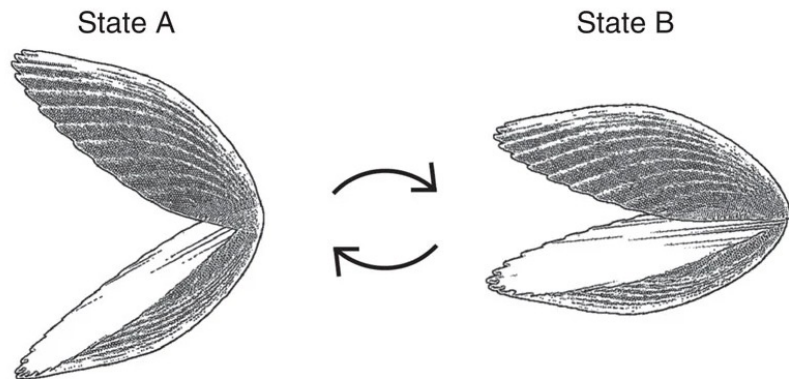


$$\mathcal{R} = 3 \times 10^{-5}$$

$Re = 10^{-5}$: "human in a pool of molasses with arms moving at 1 cm/minute)"
(Purcell, 1997)

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

Simple micro-swimmers



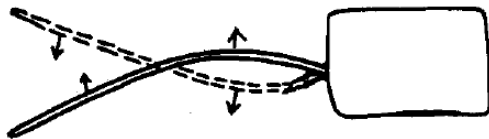
The Scallop Theorem

Reciprocal motion => at low Re , will return to original position

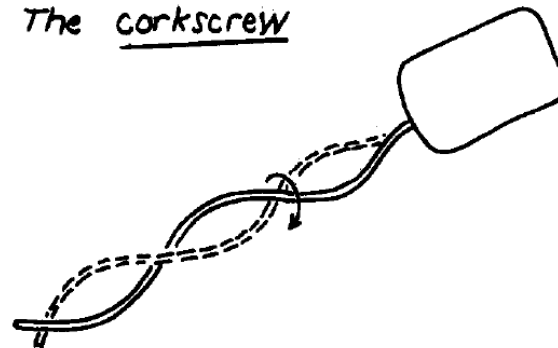
→ Closing faster than you open doesn't work

Solutions

The flexible oar

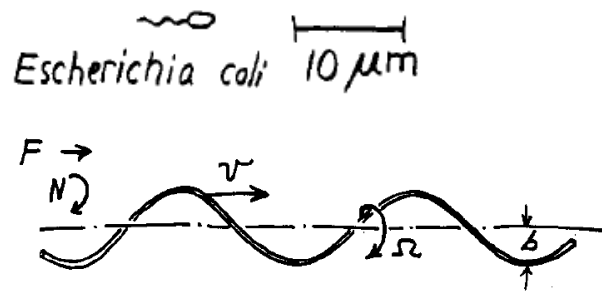


The corkscrew



Real-world micro-swimmers use **flagella**

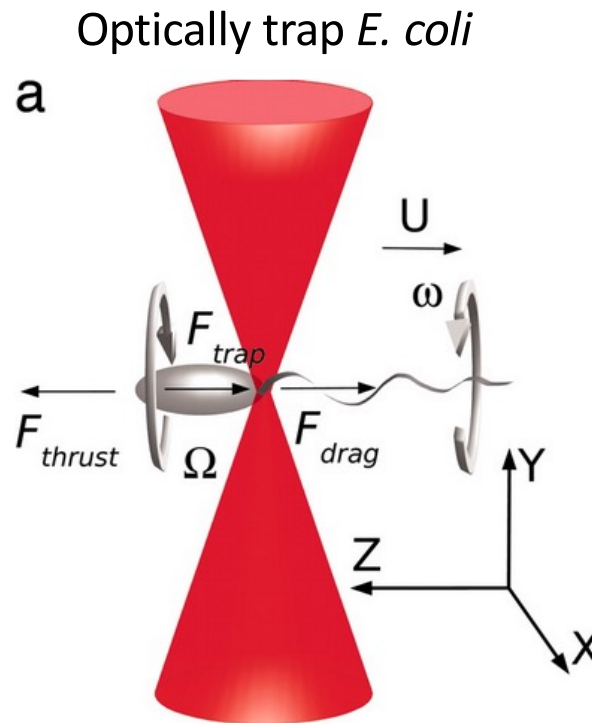
Efficiency of micro-swimmers



Propulsive efficiency $\propto B^2$

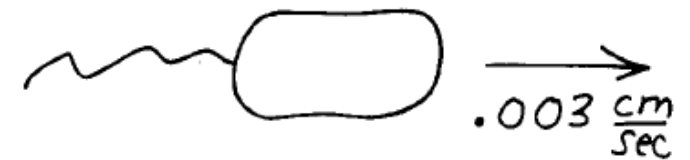
$$B \propto \left(\frac{\text{transverse drag}}{\text{longitudinal drag}} - 1 \right)$$

Theoretical efficiency = ~1%



(Chattopadhyay, et al., 2006)

Experimental efficiency = ~2%



Energy required, if
efficiency of propulsion is 1%:

$$2 \times 10^{-8} \text{ erg/sec,}$$

$$\text{or } \frac{1}{2} \text{ watt/kilogram}$$

Human on a bike = ~5 W/kg

Car = ~100 W/kg

The significance of diffusion

0.5 W/kg → diffusion is enough to feed if density of [energetic molecules] = 10^{-9} M

Stirring vs. Diffusion

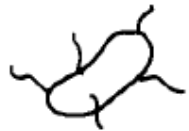
→ Sherwood number (S) =

$\frac{t_{\text{diffusion}}}{t_{\text{stirring}}}$

t_{stirring}

"S" = $\frac{lv}{D}$
 $\swarrow$
 $10^{-5} \text{ cm}^2/\text{sec}$

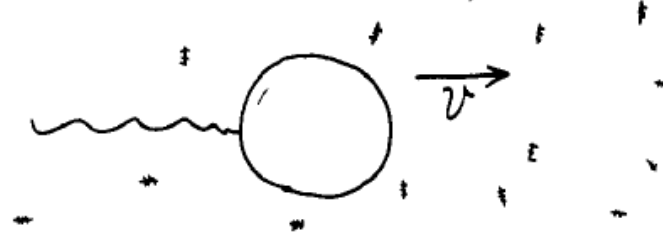
$\left[R = \frac{lv}{v} \right]$
 $\swarrow$
 $10^{-2} \text{ cm}^2/\text{sec}$



$S \approx 10^{-2}$

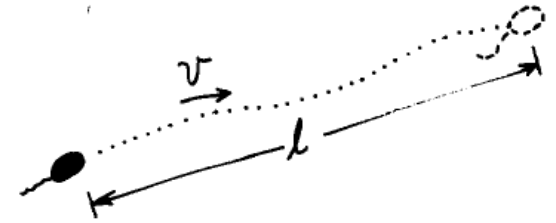
local stirring accomplishes nothing

to increase supply by 10%:



$v = 1.4 D/a = 700 \mu/\text{sec}$

Actual top speed = $\sim 35 \mu\text{m/s}$



to out-swim diffusion:

$l \geq D/v$

if $D = 10^{-5} \text{ cm}^2/\text{sec}$, $v = .003 \text{ cm/sec}$

$l \geq 30 \mu$

Table 2. Time required for diffusion of O_2 over a range of distances.

Distance of Diffusion	Approximate Time Required
10 nm	23.8 ns
50 nm	595 ns
100 nm	2.38 μs
1 μm	238 μs
10 μm	23.8 ms
100 μm	2.38 s
1 mm	3.97 min
1 cm	6.61 hours
10 cm	27.56 days

"If you don't swim that far you haven't gone anywhere."

$t \approx \frac{x^2}{2D}$

Summary – Life at Low Re

1. In low Re situations, inertia is irrelevant and viscosity dominates

→ Only the forces present at the moment matter—the past doesn't matter

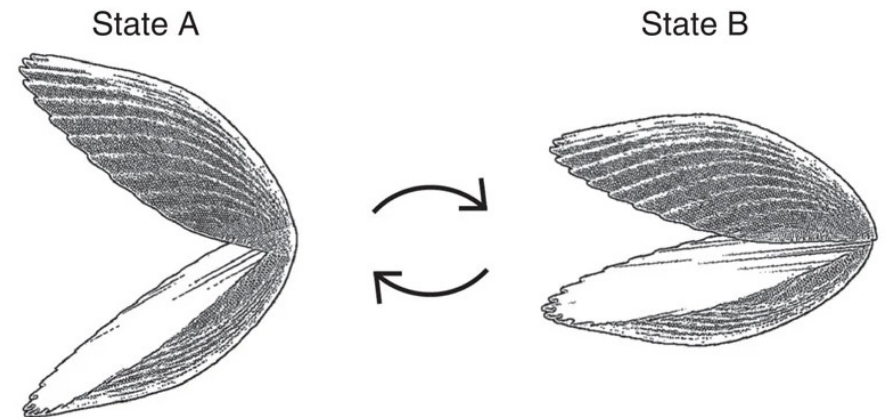


$\left\{ \begin{array}{l} \text{coasting distance} = 0.1 \text{ \AA} \\ \text{coasting time} = 0.3 \text{ microsec.} \end{array} \right\}$

2. Microorganisms swim by different rules – low efficiency, cyclic configurations

3. Diffusion is powerful: need to swim a minimum distance to benefit

$$t_{\text{diffusion}} \propto x^2$$



2. Reynolds number Re

The Reynolds number Re

Reynolds number

$$Re = \frac{\rho \bar{v} D}{\eta} \propto v L$$

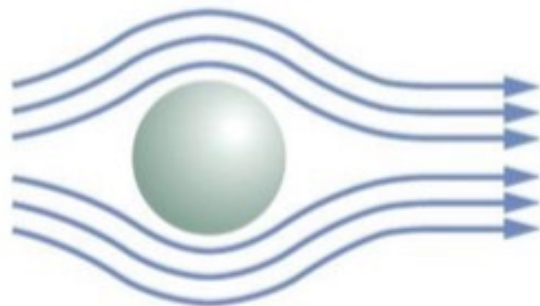
$\frac{\text{inertial forces}}{\text{viscous forces}}$

- ρ : density [kg m^{-3}]
- D : typical size [m]
- v : speed [m s^{-1}]
- η : dynamic viscosity [Pa.s]

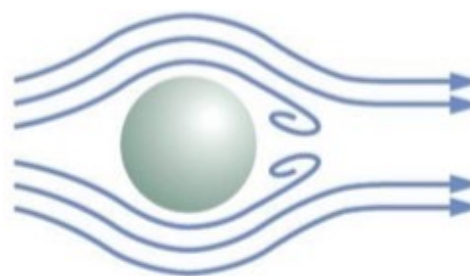
Microfluidics: D and v are small $\rightarrow$ small Reynolds number $\rightarrow$ laminar flow

Numerical: channel dia. $20 \mu\text{m}$, $v = 1 \text{ mm/s}$, water ($\eta = 10^{-3} \text{ Pa.s}$) $\rightarrow Re = 0.04$

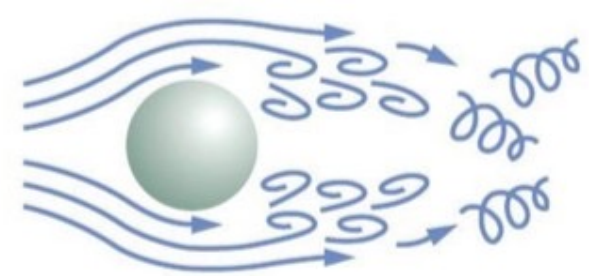
- Small Re : No turbulence, but stable vortices are possible
- Stokes equation: reversibility in time (... if no diffusion or chemical reactions take place)



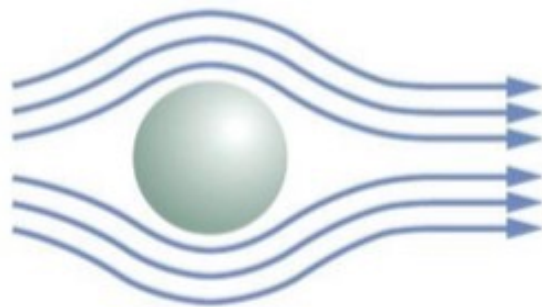
$Re < 10$
Laminar flow



$Re 10-40$
Vortices form and
are maintained



$Re 40-20,000$
Vortices form and are
periodically shed
chaotic

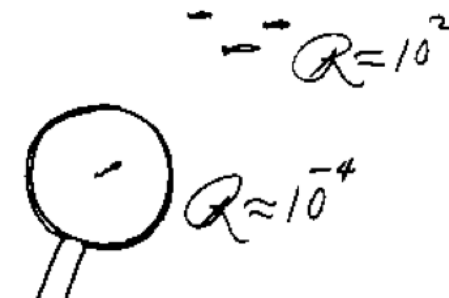
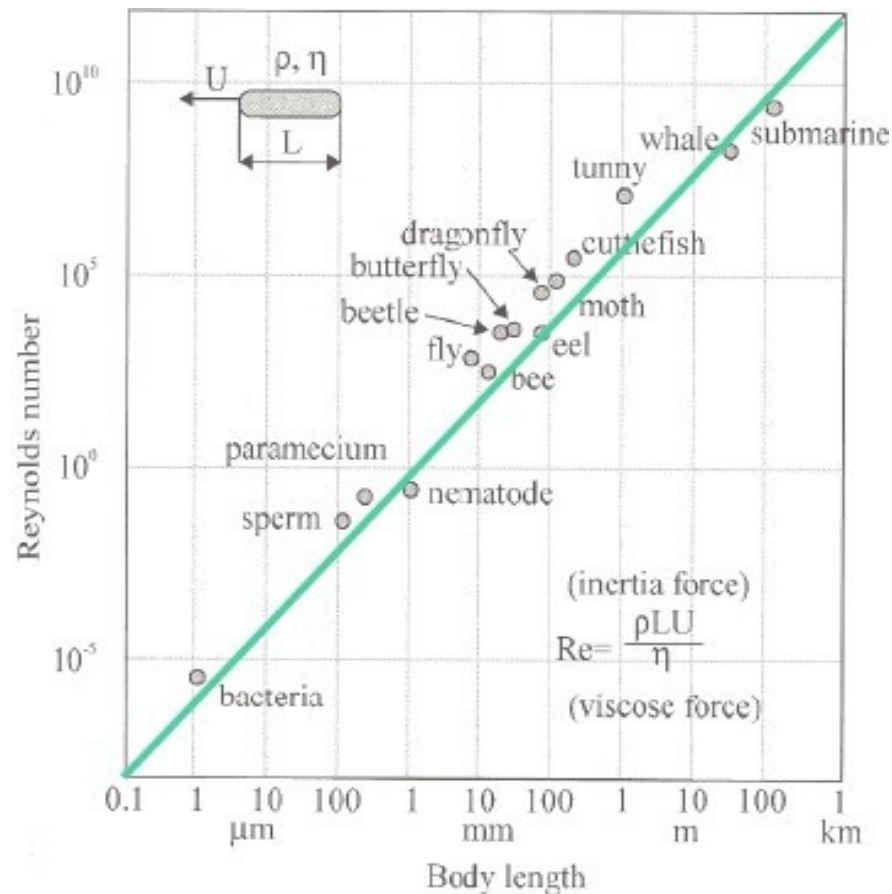


$Re < 10$
Laminar flow



when the flow is laminar: reversibility in time
(when low/no diffusion)

Reynolds number of objects and animals



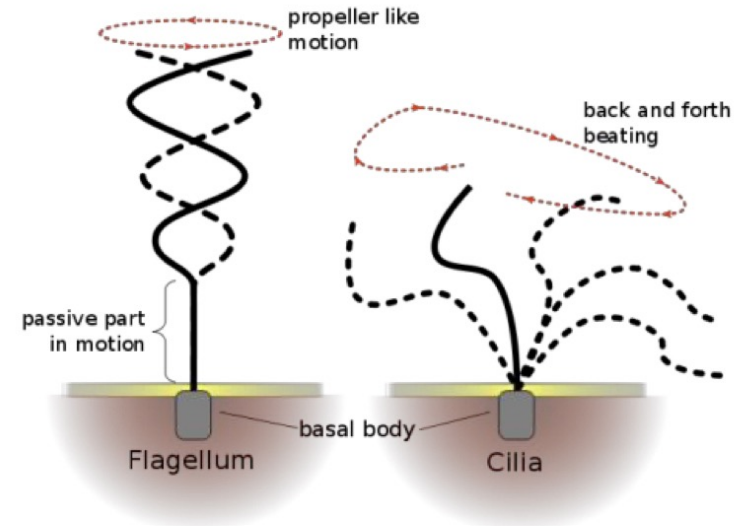
- «Micromachines: A New Era in Mechanical Engineering» by Iwao Fujimasa, Oxford University Press, 1996
- "Life at Low Reynolds Number", E.M. Purcell, 1976

Bacteria swimming in water:

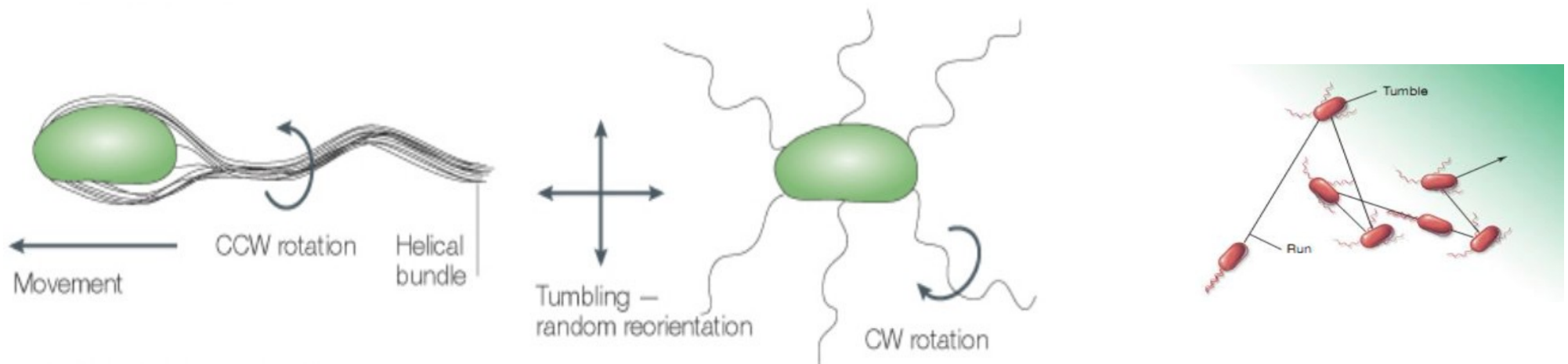
Speed $\sim 30 \times 10^{-6} \text{ m/s}$; size $\sim 1 \times 10^{-6} \text{ m}$

$Re \sim 1 \times 10^{-5} = \text{laminar}$

So bacteria swimming in water is like us in honey

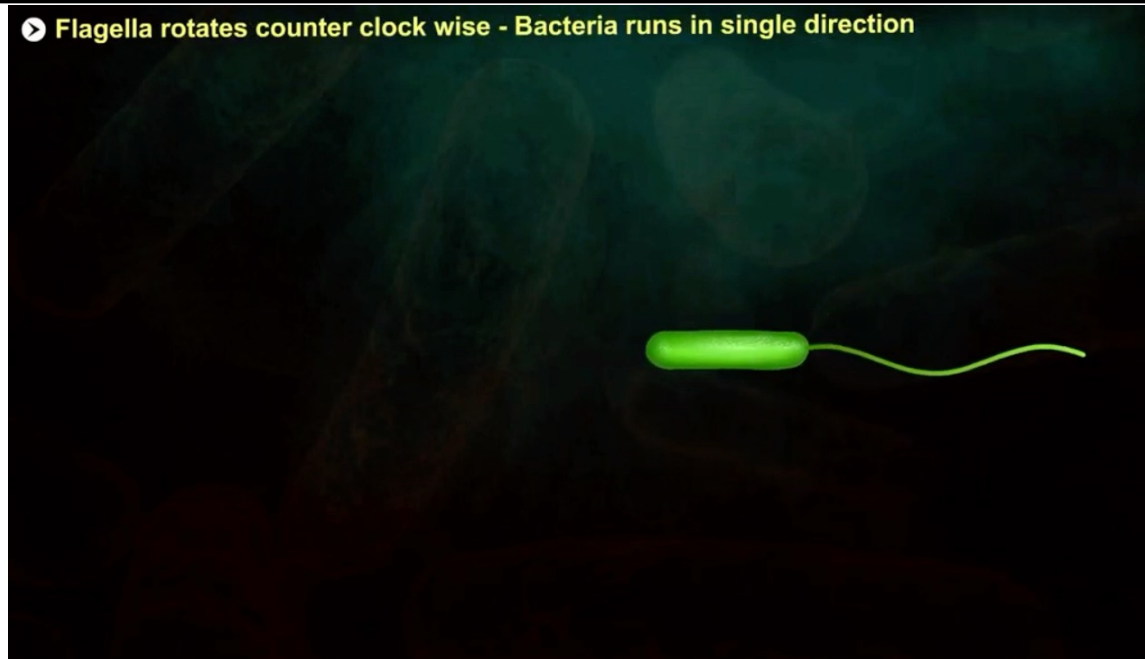


Flagellum and cilia. The former has a rotatory motion while the latter move from side to side
(from Wikipedia <http://en.wikipedia.org/wiki/Flagellum>).



Swimming

► Flagella rotates counter clock wise - Bacteria runs in single direction



Selman Sakar, EPFL
Magnetic actuation

3. Viscous drag and particle sedimentation

Viscous drag on objects in liquids

Stop distance x_0 of small objects in viscous media (*low Re*)

$$F_{\text{stoke}} = 6\pi R \eta v(t)$$

Stoke's drag for sphere radius R in a liquid
 η : Dynamic viscosity [Pa.s]

$$m \frac{dv(t)}{dt} = 6\pi R \eta v(t)$$

$$v(t) = v_0 e^{-t/\tau} \quad \text{where} \quad \tau = \frac{\rho R^2}{3\eta}$$

$$\Rightarrow \text{stop distance } x_0 = \frac{v_0 \rho R^2}{3\eta} \quad \propto R^2 \propto L^2$$

Numerical application: a particle of radius r , moving at a speed of 10 times its radius per second, in water, particle has the same density as water to ignore buoyancy

$$r = 10 \mu\text{m}, v = 100 \mu\text{m/s} \Rightarrow x_0 = \frac{10^{-4} \cdot 10^3 \cdot 10^{-10}}{3 \cdot 10^{-3}} = 3 \text{ nm} \quad \text{Re} = 0.00002$$

$$r = 1 \text{ mm}, v = 10 \text{ mm/s} \Rightarrow x_0 = \frac{10^{-2} \cdot 10^3 \cdot 10^{-6}}{3 \cdot 10^{-3}} = 3 \text{ mm} \quad \text{Re} = 0.2$$

$$r = 33 \text{ m}, v = 5 \text{ m/s} \quad x_0 = 10^6 \text{ km} ! \quad \text{Re} = 3 \cdot 10^8. \text{ so not applicable!}$$

Sedimentation of particles

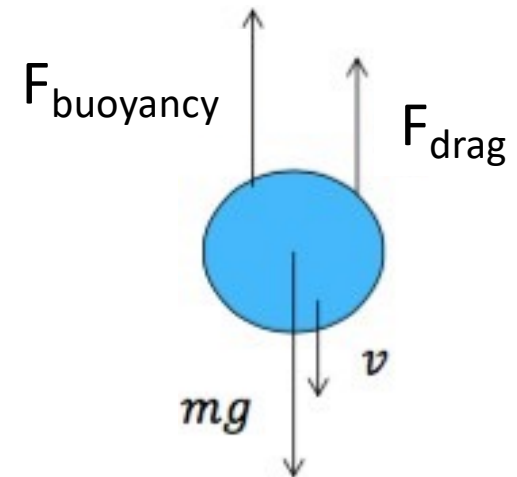
Equilibrium speed v_{sed} : **drag force** = **weight**

$$6\pi r\eta v_{sed} = \Delta\rho \cdot V \cdot g$$

Sedimentation speed
$$v_{sed} = \frac{\Delta\rho V g}{6\pi r\eta} = \frac{2}{9} \frac{\Delta\rho g}{\eta} r^2$$

$$v_{sed} \propto r^2 \propto L^2$$

Small objects settle more slowly

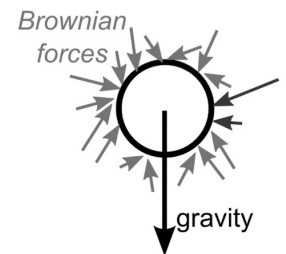


Size limit for particles in suspension: diffusion (Brownian)

The diffusional force exerted on a particle can be approximated by

$$F_{diff} \approx \frac{k_B T}{2r} \propto L^{-1}$$

The particle sediments **much more slowly** when the Brownian motion force is approx equal to buoyancy force, because of diffusional broadening.



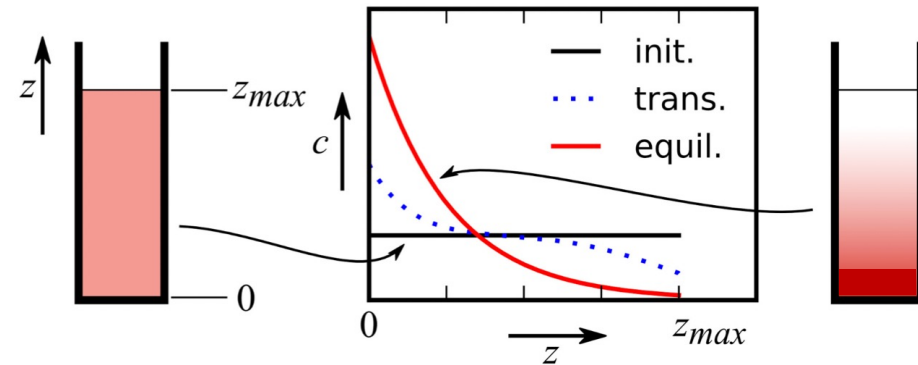
Brownian forces dominate when
$$\frac{k_B T}{2r} > \frac{4}{3} \pi r^3 \Delta\rho g \quad \text{i.e. when} \quad r^4 < \frac{3k_B T}{8\pi \Delta\rho g}$$

r_{crit} approx **2 μm** diameter for a particle of density 2000 kg/m³

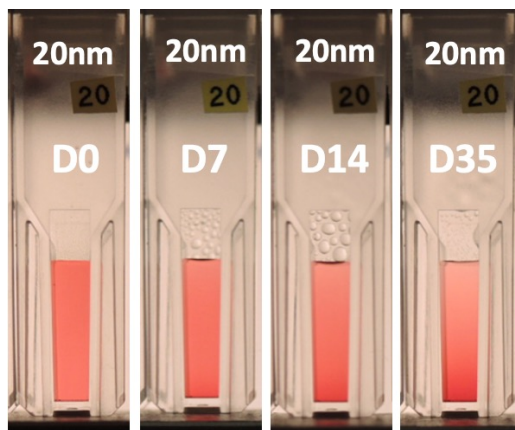
Sedimentation of particles when dominated by Brownian motion

$$\frac{k_B T}{2r} > \frac{4}{3} \pi r^3 \Delta \rho g$$

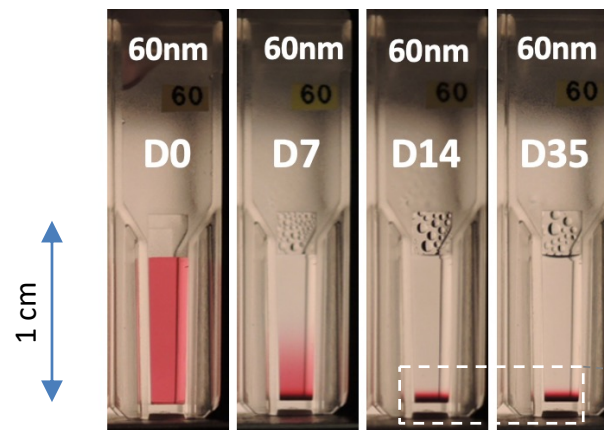
characteristic height of the equilibrium gradient, $z_0 = \frac{k_B T}{m_b g}$



Gold nanoparticles, 35 days of observation



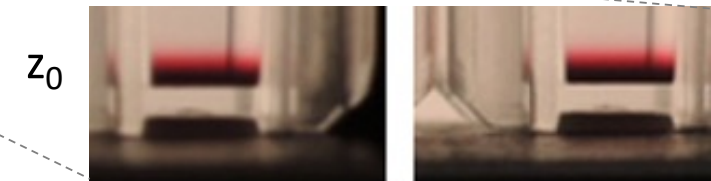
20nm = 1cm / 45days
 $z_0 = 5 \text{ mm}$



60nm = 1cm / 5days
 $z_0 = 0.18 \text{ mm}$

Gold nanospheres in water

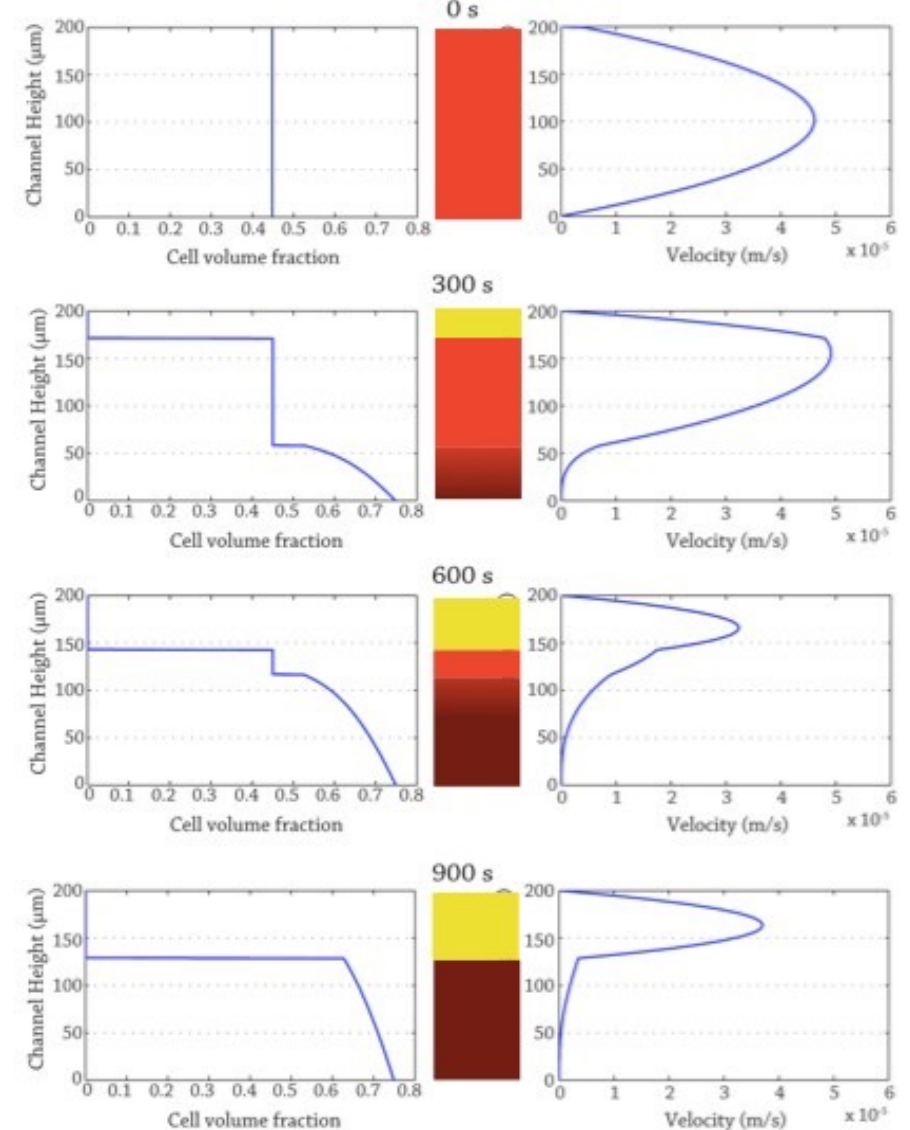
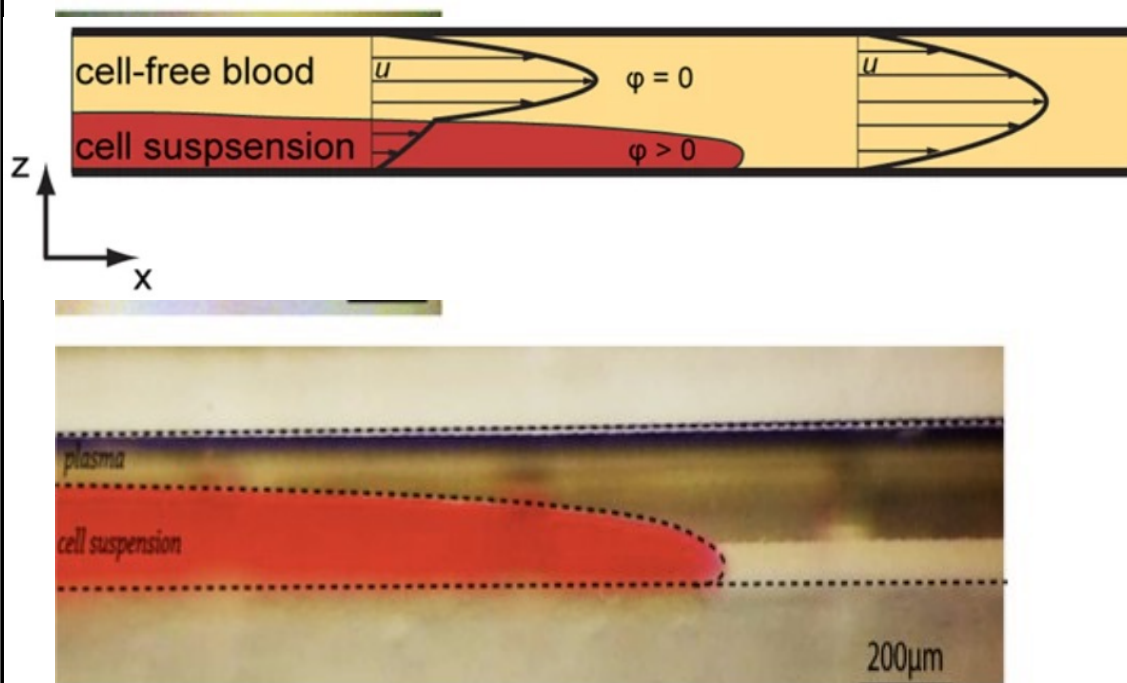
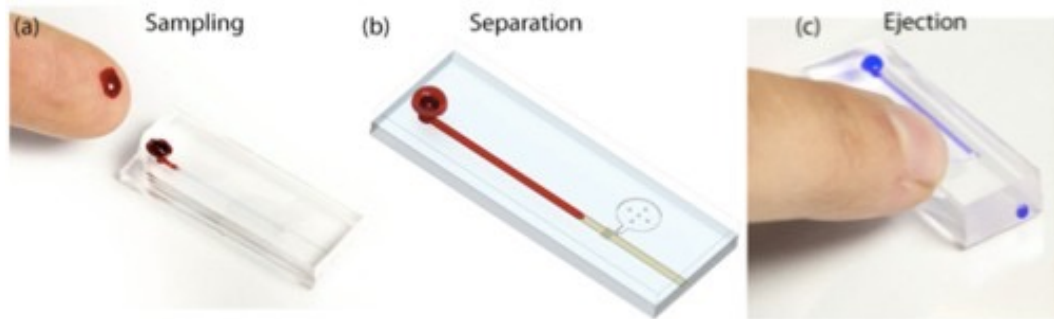
diam. nm	D $\mu\text{m}^2\text{s}^{-1}$	s 10^{-9} s	z_0 mm	$t_{\text{sed}}^{1\text{cm}}$ hours
13	19.9	0.110	18.5	2579
20	13.0	0.260	5.08	1090
40	6.48	1.04	0.636	272
50	5.18	1.62	0.325	174
60	4.32	2.34	0.188	121



Midelet et al, Part. Part. Syst. Charact. 2017 <https://doi.org/10.1002/ppsc.201700095>

Plasma extraction by local sedimentation

capillary-driven microfluidic device that separates blood microsamples collected from finger-pricks and delivers 2 μL of metered serum for bench-top analysis



D. Forchelet, PhD thesis EPFL 2017

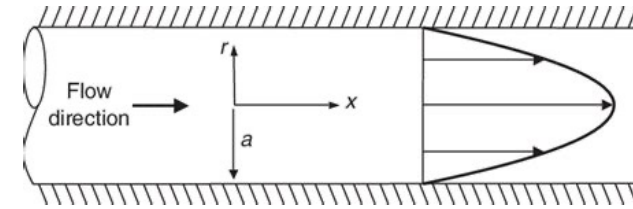
D. Forchelet et al, Sci. Rep. 2018
Doi: 10.1038/s41598-018-32314-4

4. Flow profile in small channels

Pressure drop and flowrate

For a circular cross-section, assuming

- Parabolic velocity profile
- zero flow at the wall



Length l
Radius r
Viscosity η

average Fluid velocity $v = \frac{r^2}{8\eta l} \Delta p$

$$v \propto \frac{r^2}{l} \propto L$$

Pressure drop $\Delta p = \frac{8\eta l}{r^2} v$

$$\frac{\Delta p}{\Delta x} \propto \frac{1}{r^2} \propto L^{-2}$$

Flow rate $Q = \pi r^2 v = \frac{\pi r^4}{8\eta l} \Delta p$

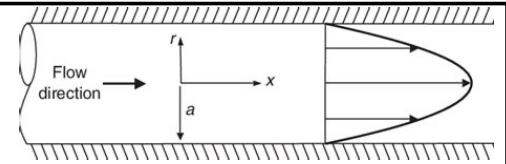
$$Q \propto \frac{r^4}{l} \propto L^3$$

eg Channel: diameter $2r=20 \mu\text{m}$, $l=10 \text{ mm}$, water

$v = 0.1 \text{ mm/s}$	$\Rightarrow$	$\Delta p = 0.8 \text{ mbar}$	$Q = 0.03 \text{ nl/s}$
$\Delta p = 100 \text{ mbar}$	$\Rightarrow$	$v = 12.5 \text{ mm/s}$	$Q = 66 \text{ nl/s}$

Microfluidics are only suited to small volumes...

Flow profile in a rectangular channel as we often have in microfluidics



If w : width $\gg$ h : height : i) parabolic profile in y direction, ii) flat velocity profile in x

$$\Delta p = \frac{12\eta l}{h^2} \bar{v} \quad \Delta p \propto \frac{1}{h^2}$$

Flow rate $Q = w \cdot h \cdot \bar{v} = \frac{w \cdot h^3}{12\eta l} \Delta p$

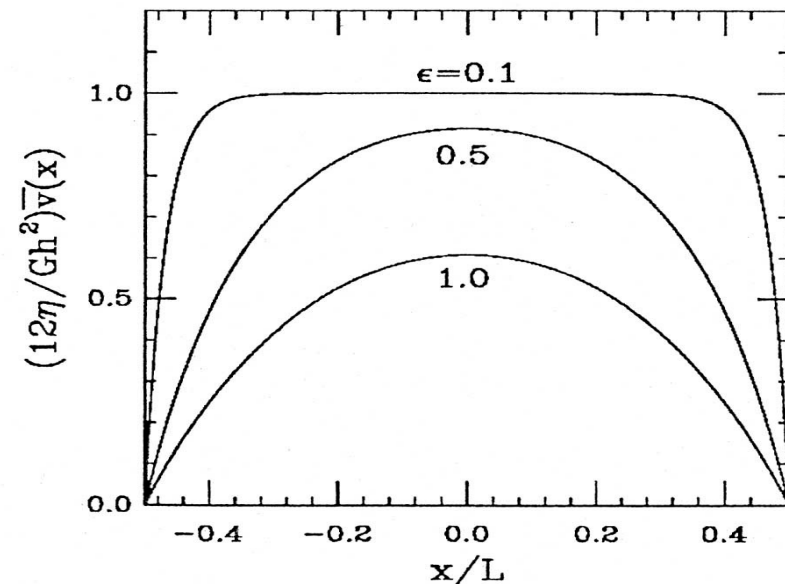
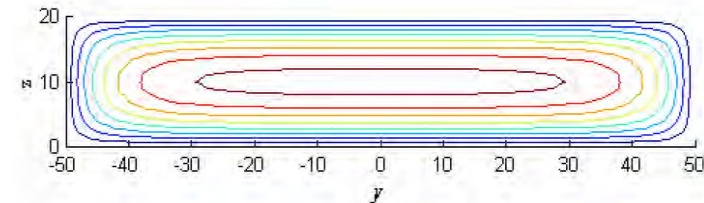
Fluidic resistance $R_f = \frac{12\eta l}{wh^3} \propto L^{-3}$

For w/h ratio not too large (eg 5): non-flat profile in x

$$Q \approx \frac{h^3 w \Delta p}{12\eta L} \left(1 - 0.630 \frac{h}{w} \right)$$

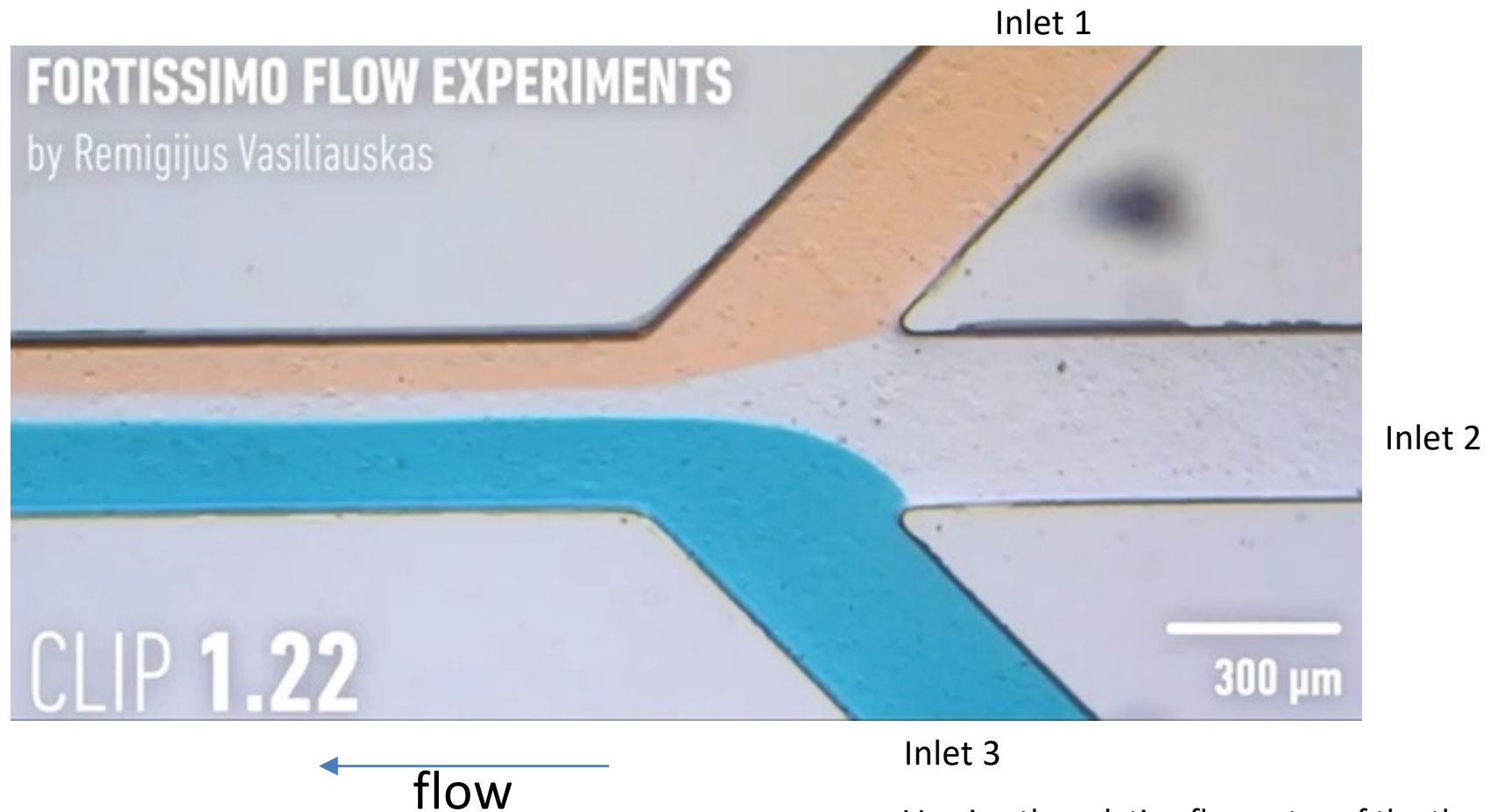
Numerical: Water at $\Delta p = 1$ bar
example $h = 50$ nm , $w = 2$ μ m , $l = 10$ μ m ,

Then $v = 1$ mm/s
 $Q = 0.05$ nl/s



Sheath flow

- To create narrow flow line
- To focus stream (and particles)



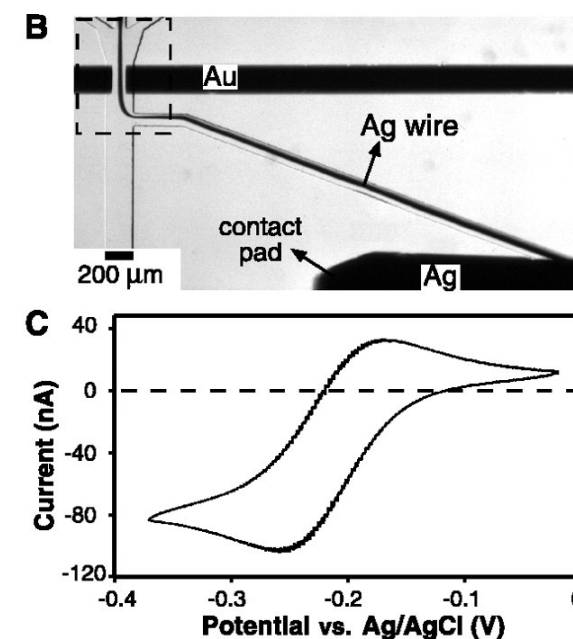
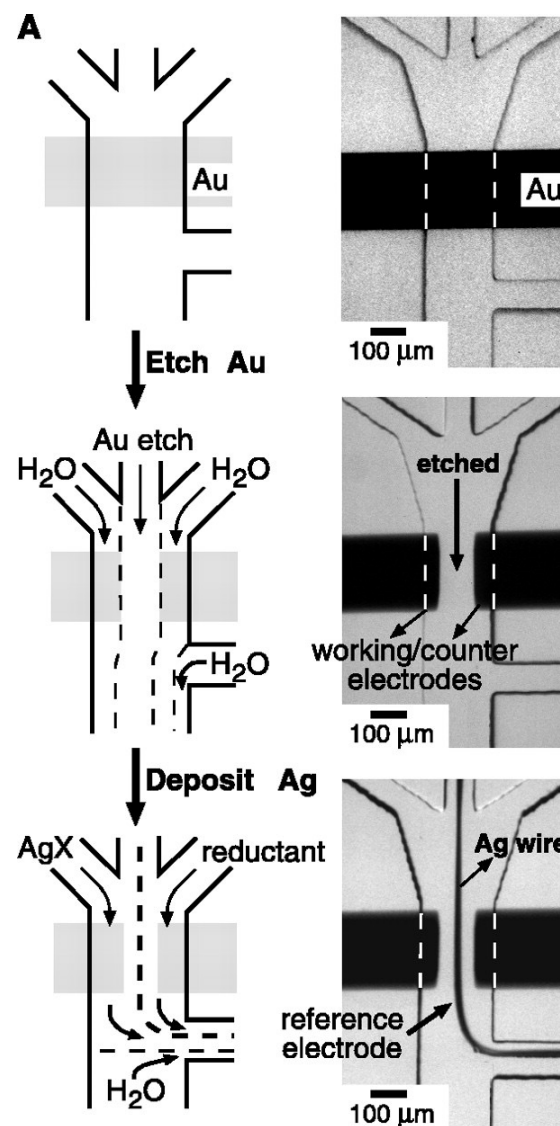
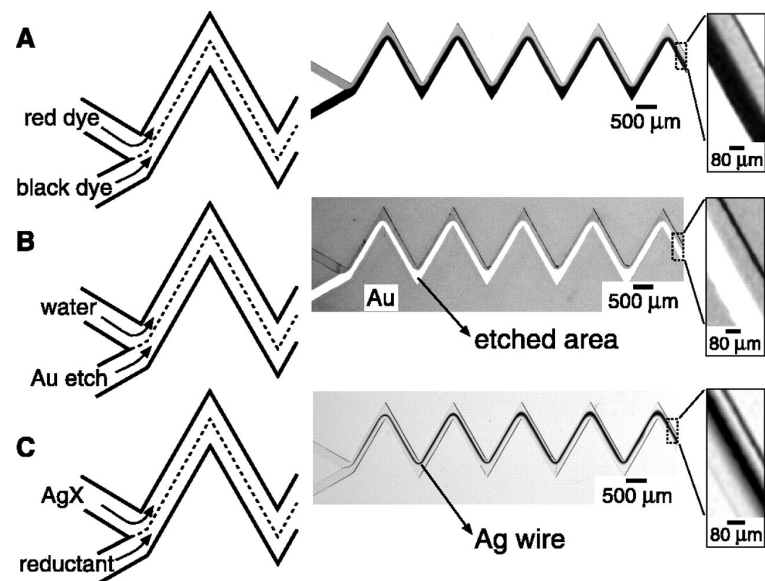
Varying the relative flow rates of the three inlets

Particles will stay with flow lines of the liquid

Sheath flow: an example application

Sheath flow

- To create narrow flow line
- To focus stream (and particles)

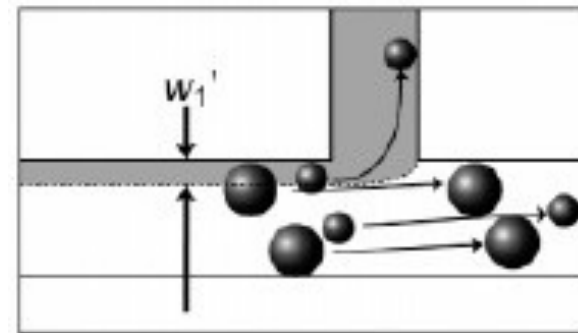
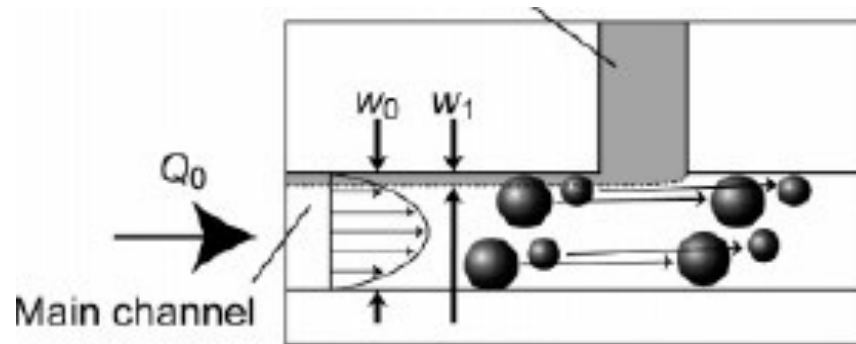


5. Particles in laminar flows

Particles in laminar flows

Filters that never clog: When the size of particles becomes commensurable with the channel size, the particles can be deviated from their flux line by contact with a wall or an obstacle.

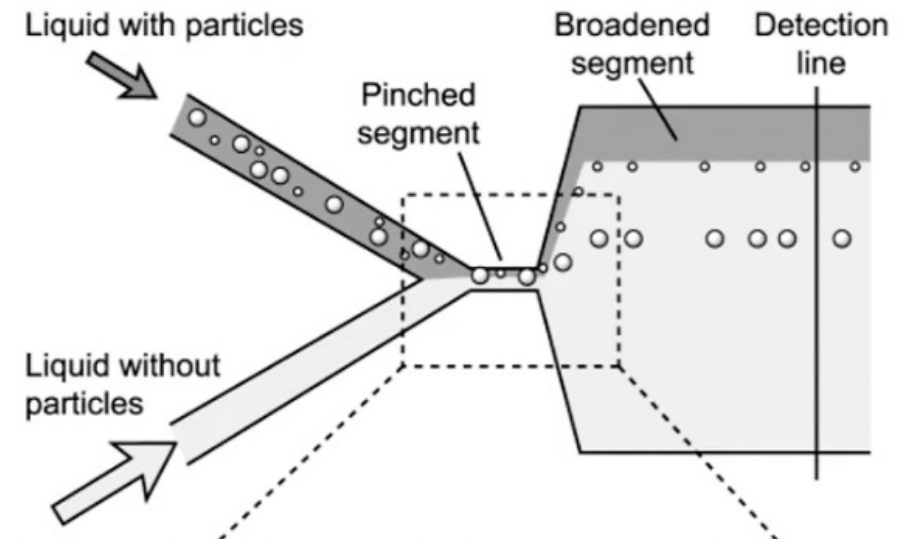
In the example below, only small particles will be extracted. Tune size by tuning flow rates



Yamada et al, Anal. Chem. **2006**, 78,1357-1362

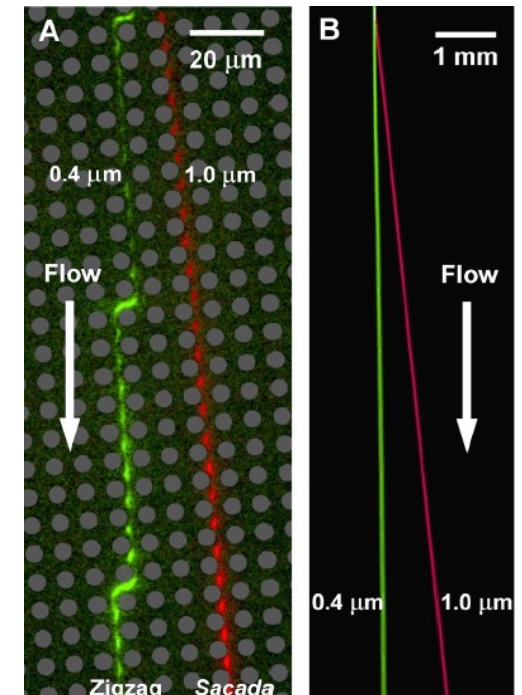
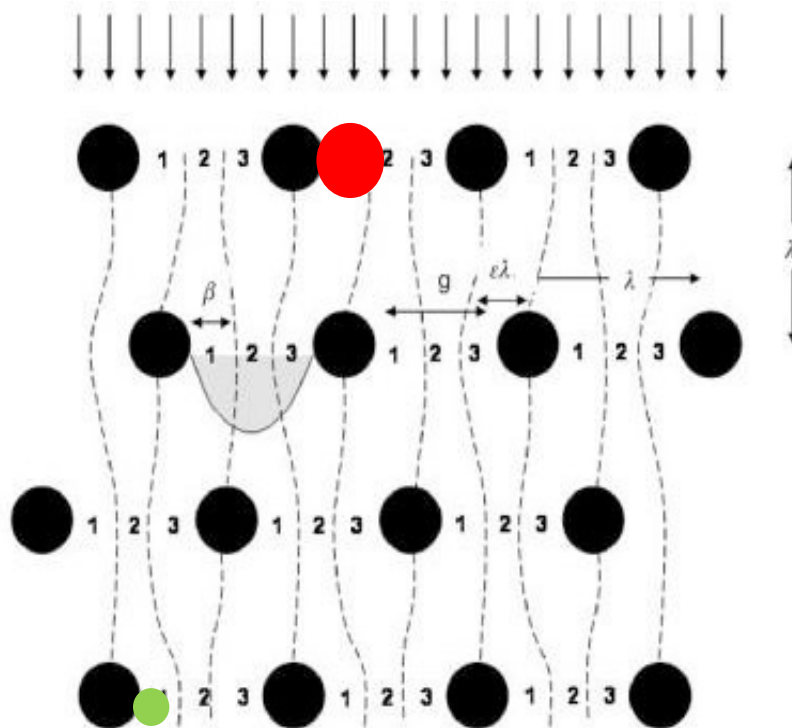
Pinched flow fractionation (PFF): By merging two flows, it is also possible to push particles against the wall and so use this effect for separating particles by size

M Yamada, et al,
Analytical Chemistry **2004** 76 (18), 5465-5471
DOI: 10.1021/ac049863r



Particle in laminar flows – Tango array: sort particles by size

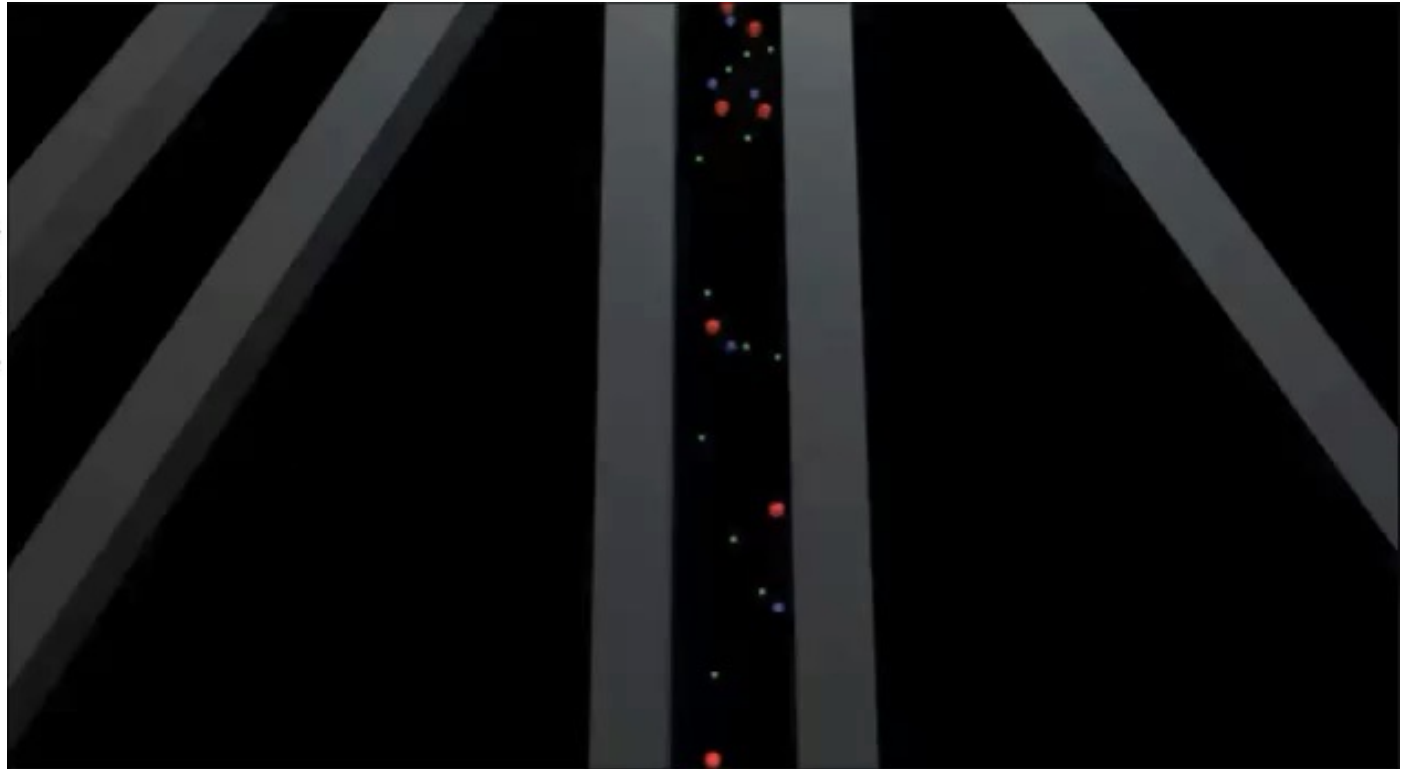
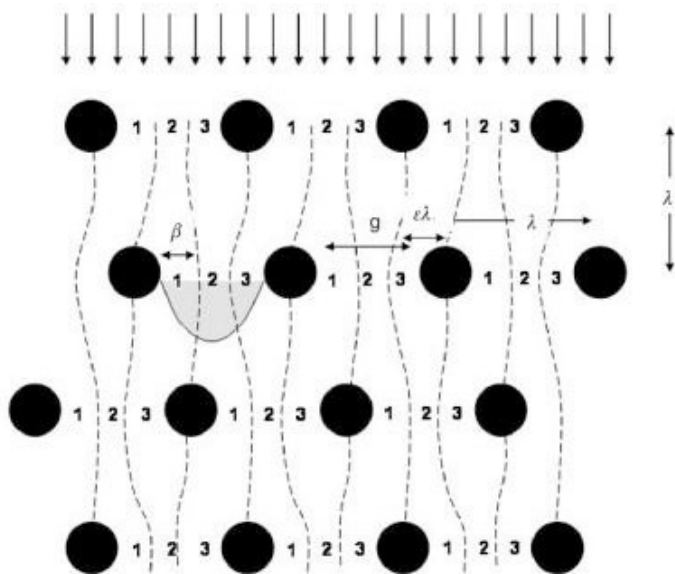
By placing obstacles in a flow with a lateral shift in each row, it is possible to sort particles by size in an efficient manner. In the following example, the displacement is 1/3 of obstacle spacing.



The critical particle radius r where all particle bigger than that are systematically displaced is $r=g/3$

Huang LR, Cox EC, Austin RH, Sturm JC (2004) *Science* 304:987–989

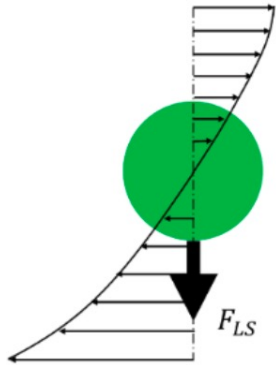
Particle in laminar flows – Tango array



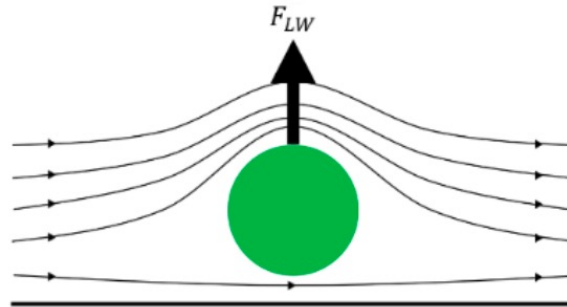
Huang LR, Cox EC, Austin RH, Sturm JC (2004) *Science* 304:987–989

Focusing of particles due to Wall-induced lift force (if flow is fast enough)

When particles are in a fast flow, the shear gradient creates hydrodynamic effects.



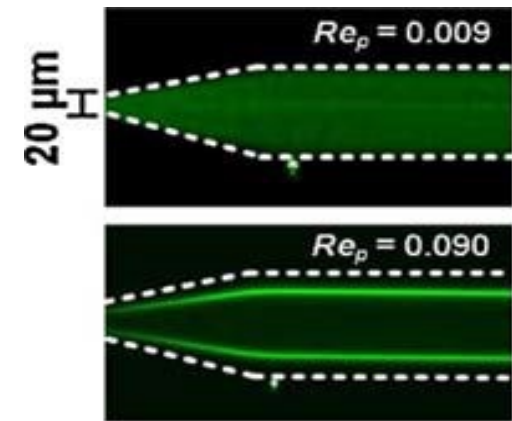
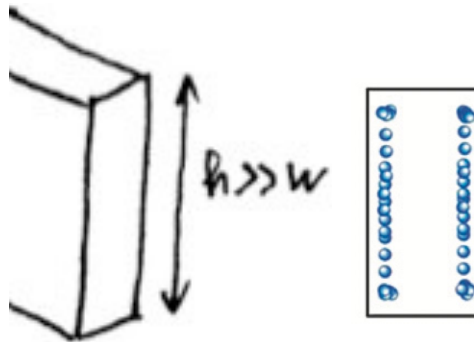
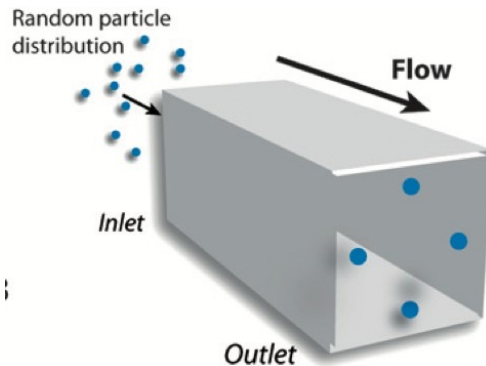
Rotation due to different speeds generates Magnus force pushes towards walls



asymmetric wake induced around particles generates a wall-induced lift force

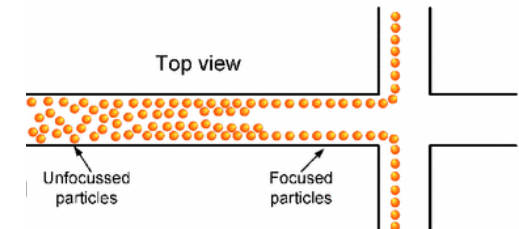
Equilibrium positions when sum of lift forces is zero

$$F_{lift}(z) = \frac{2 \cdot \rho \cdot v_0^2}{h^2} r^4 \bullet f(z) \propto r^4$$



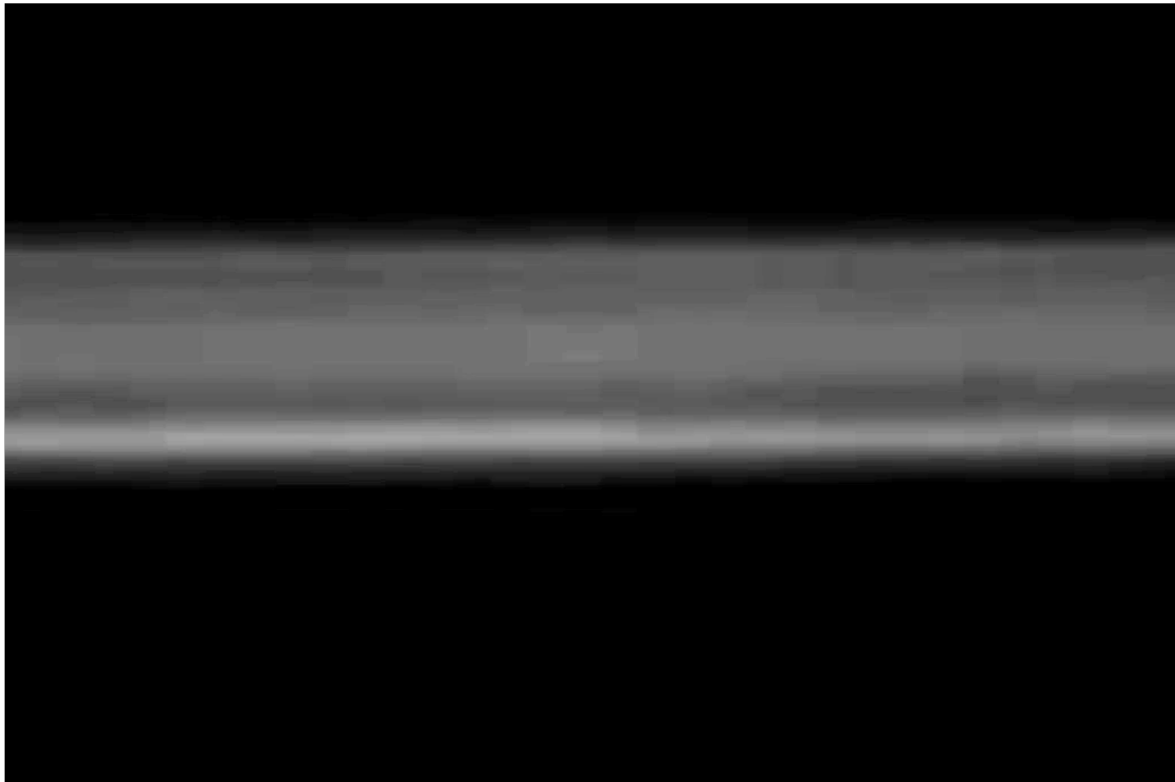
For a rectangular channel, the four equilibrium positions are situated at the center of the walls

Bhagat et al, Microfluid Nanofluid (2008) 7:217–226

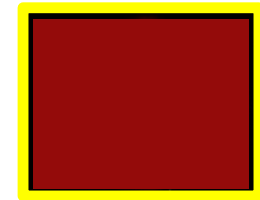
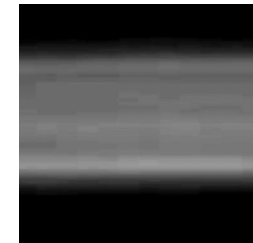


***Shear- and wall-induced forces on particles, at high speed
when inertia and shear become important***

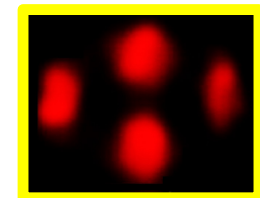
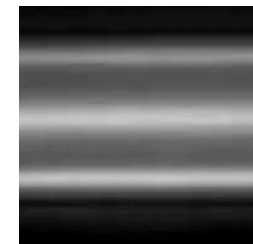
Increasing flow rate (increasing Re)



Low flowrate



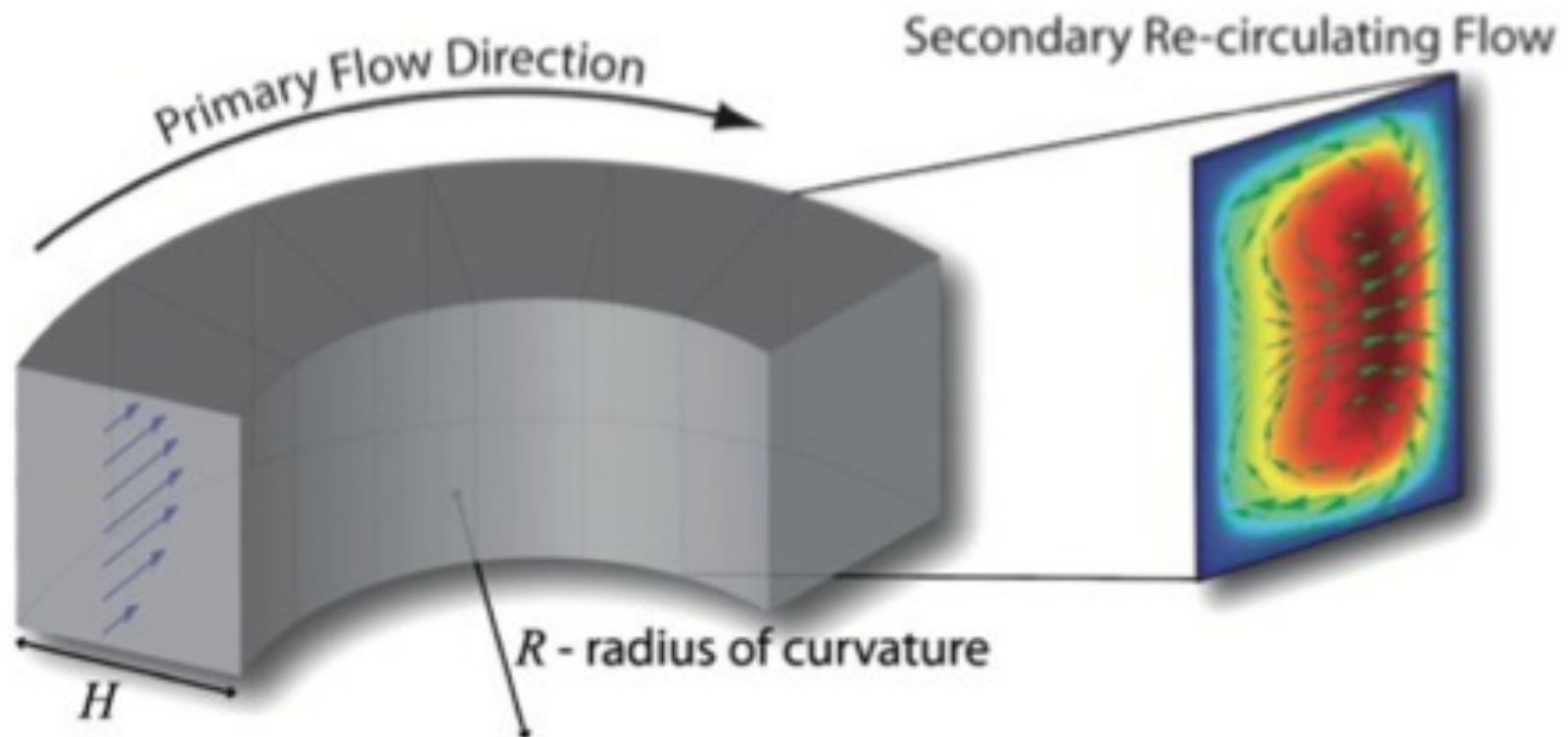
High flowrate



“Inertial microfluidic devices work within an intermediate Reynolds number range ($1 < Re < 100$) between Stokes and turbulent regimes.”

J. Zhang, W. Li, G. Alici, “Inertial Microfluidics: Mechanisms and Applications” (2017), pp. 563–593.

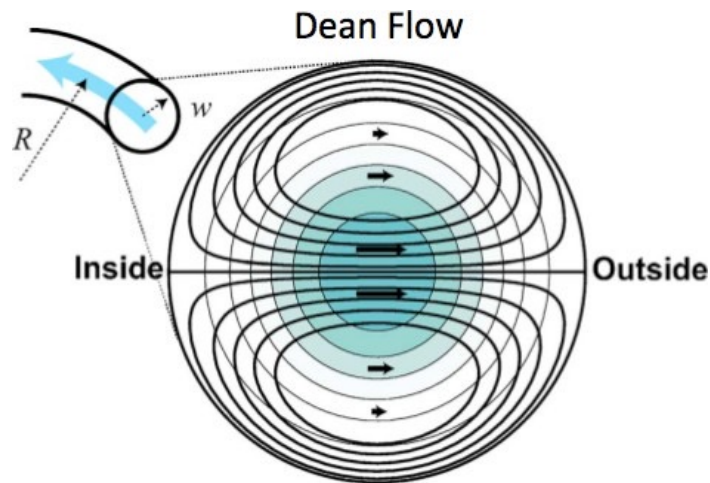
Inertial effects in curved channels: Dean flow



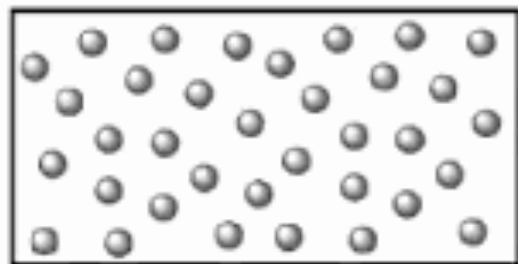
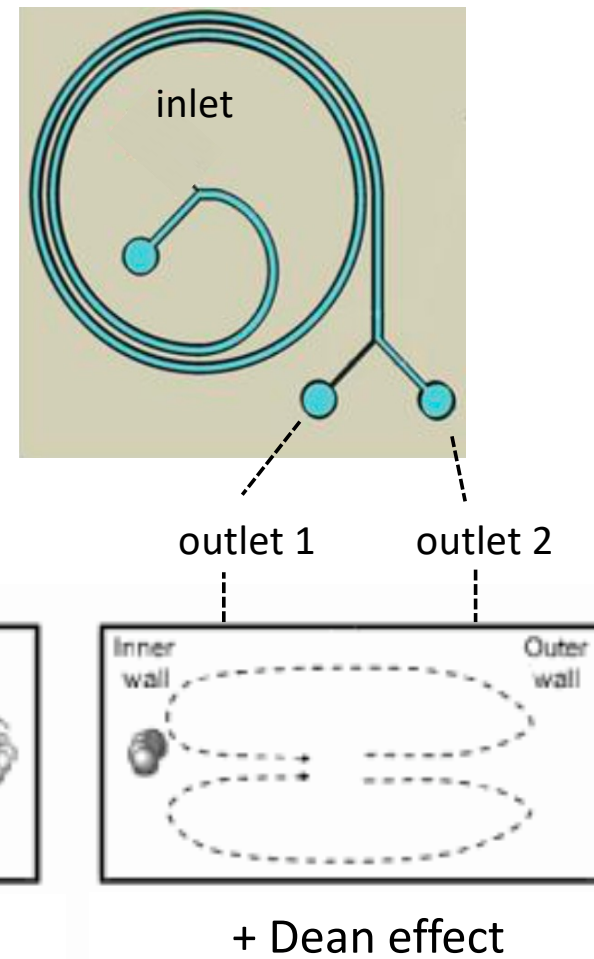
Di Carlo, "Inertial Microfluidics", Lab on a Chip (2009) 3038

Flow in curved channels: Dean effect

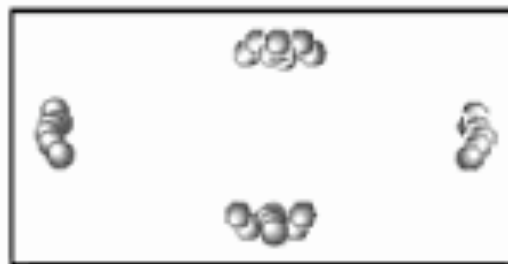
If the channel is running in a curve, a recirculating flow vortex is created. The particles that are in equilibrium positions of the lift force are pushed on the inner side position by the vortex.



T. M. Squires and S. R. Quake: "Microfluidics: Fluid physics at the nanoliter scale", Rev Mod Phys, 2005



inlet



Inertial focusing



+ Dean effect

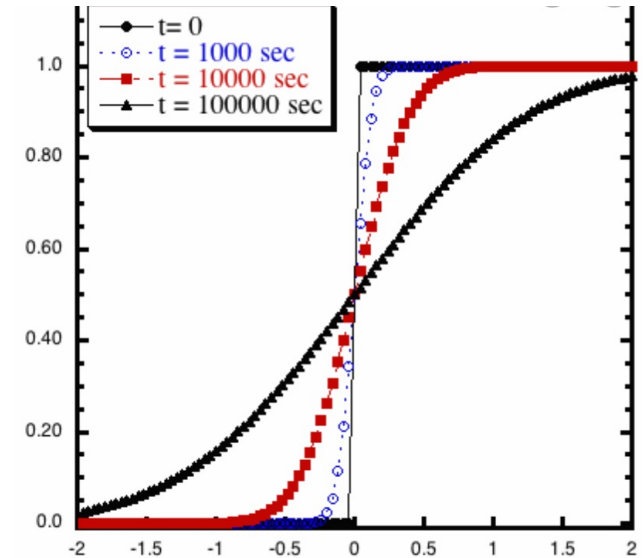
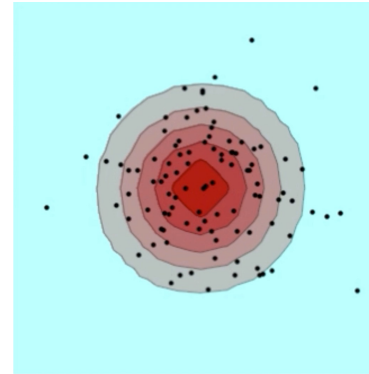
6. Diffusion and Mixing

Diffusion of molecules in liquids

Diffusion: Fick's law

$$J = -D_c \frac{\partial C}{\partial x}$$

J: particle flux in #/m²s
 C: concentration
 D_c: diffusion coefficient in m²/s
 η: viscosity



Diffusion coefficient

$$D_c = \frac{k_B T}{6\pi\eta r}$$

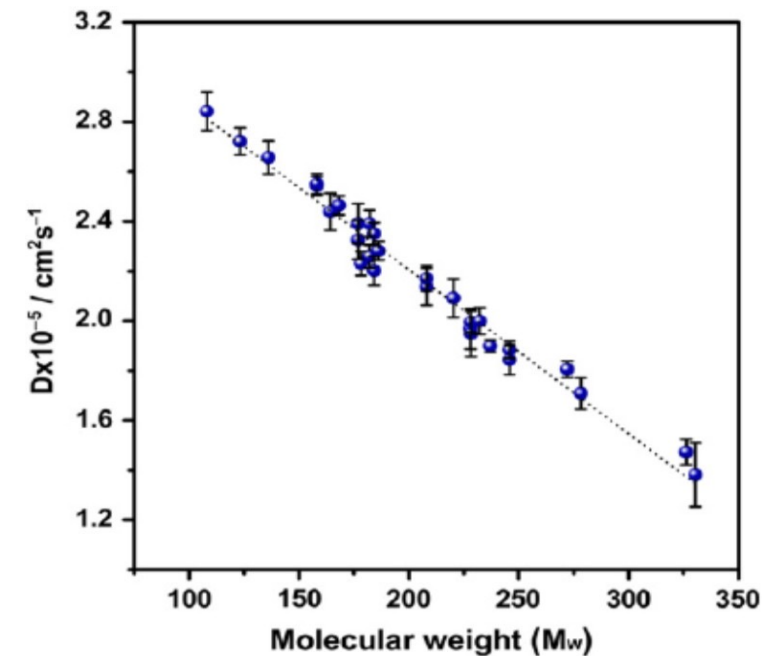
$$D_c \propto L^{-1}$$

Diffusion distance and time:

$$x_D = \sqrt{2D_c t}$$

$$t_D = \frac{l^2}{2D_c}$$

$$D_c \propto l_d^2$$



Diffusion of molecules in liquids

<i>Molecule / particle</i>	<i>Typical size</i>	<i>Diffusion coeff. in water</i>	<i>x_D in 1s</i>	<i>t_D for 50 μm</i>
Solute ion	0.1 nm	2000 $\mu\text{m}^2/\text{s}$	45 μm	0.6 sec
Small protein	5 nm	40 $\mu\text{m}^2/\text{s}$	9 μm	30 sec
Virus	100 nm	2 $\mu\text{m}^2/\text{s}$	3 μm	10 min
Bacterium	1 μm	0.2 $\mu\text{m}^2/\text{s}$	0.6 μm	104 min
Cell	10 μm	0.02 $\mu\text{m}^2/\text{s}$	0.2 μm	1000 min

Heat diffusivity in water	-	$D_{\text{th}} = 1.4 \cdot 10^5 \mu\text{m}^2/\text{s}$	530 microns	0.01 sec
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Diffusion layer in microelectrodes for electrochemical sensors (eg glucose, dissolved O₂)

Electrochemical (amperometric) sensors consume molecules in the surroundings. These are then replenished by diffusion. The goal is to measure concentration of a species C_{species}, by measuring an electrical current.

Charge transfer current at the surface of an electrode with redox reaction taking place:

$$I = n \cdot F \cdot A \cdot J_{mol}$$

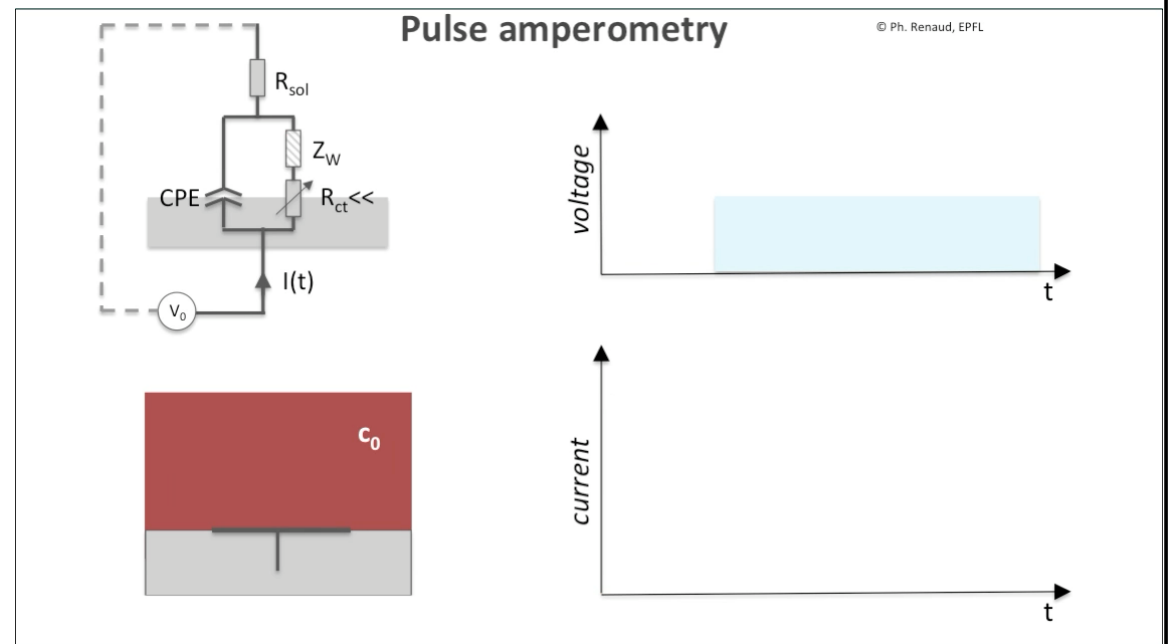
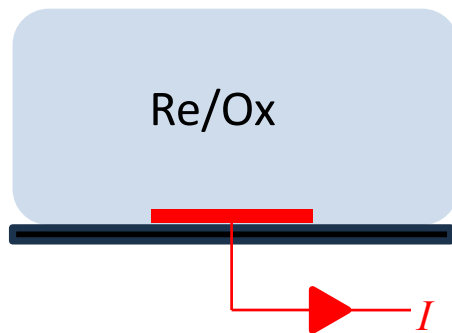
n : # electron in the reaction

A : area of electrode

F : Faraday constant

The measured electrochemical current is directly related to the molecular flux J_{mol} (that feed the redox reaction)

$$J_{mol} = D_{diff} \frac{\partial C(x,t)}{\partial x}$$



Diffusion layer in microelectrodes

1. For a single **large** circular **electrode**:

$$J_{mol} = D_{diff} \frac{\partial C(x,t)}{\partial x}$$

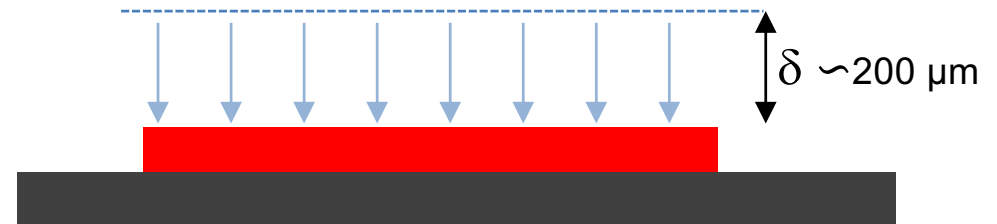
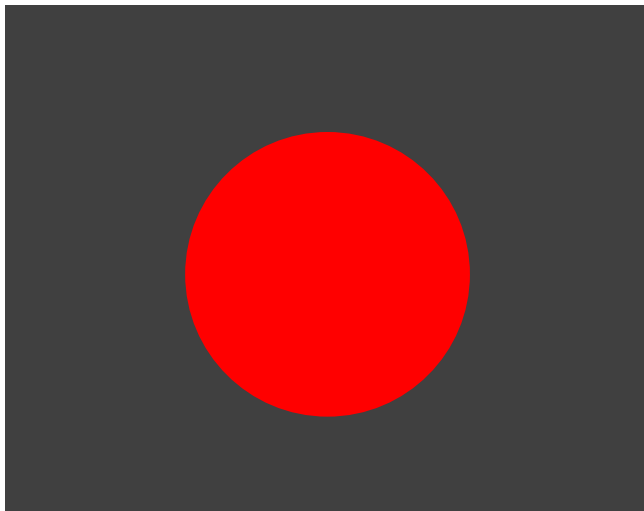
Concentration gradient at electrode surface: $\left. \frac{dC}{dx} \right|_{x=0} = \frac{C_0}{\delta}$

δ is the thickness of the **diffusion layer** (about 0.2 mm)

$$I_{lim} = n \cdot F \cdot \pi r^2 \cdot D_{diff} \frac{C_{\infty}}{\delta}$$

$$\frac{I}{A} \propto \frac{1}{\delta}$$

$$I \propto A \frac{1}{\delta}$$



Diffusion layer in microelectrodes

2. For array of circular **micro-electrode**
(radius $r \ll$ diffusion layer δ)

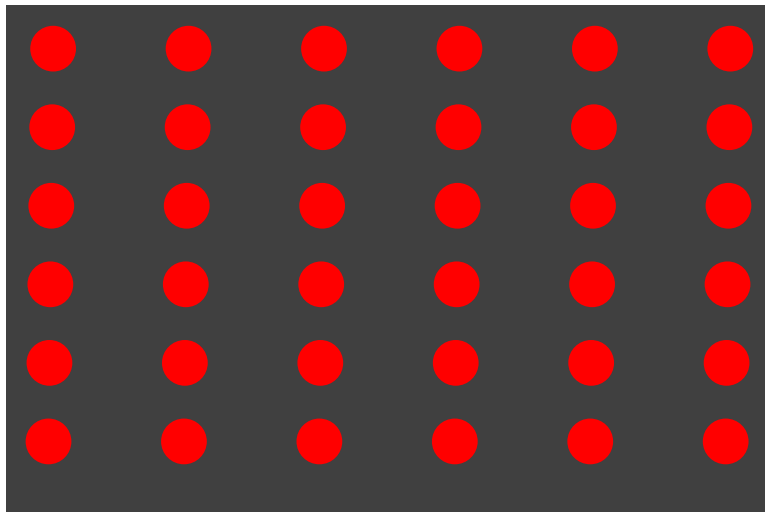
$$J_{mol} = D_{diff} \frac{\partial C(x,t)}{\partial x}$$



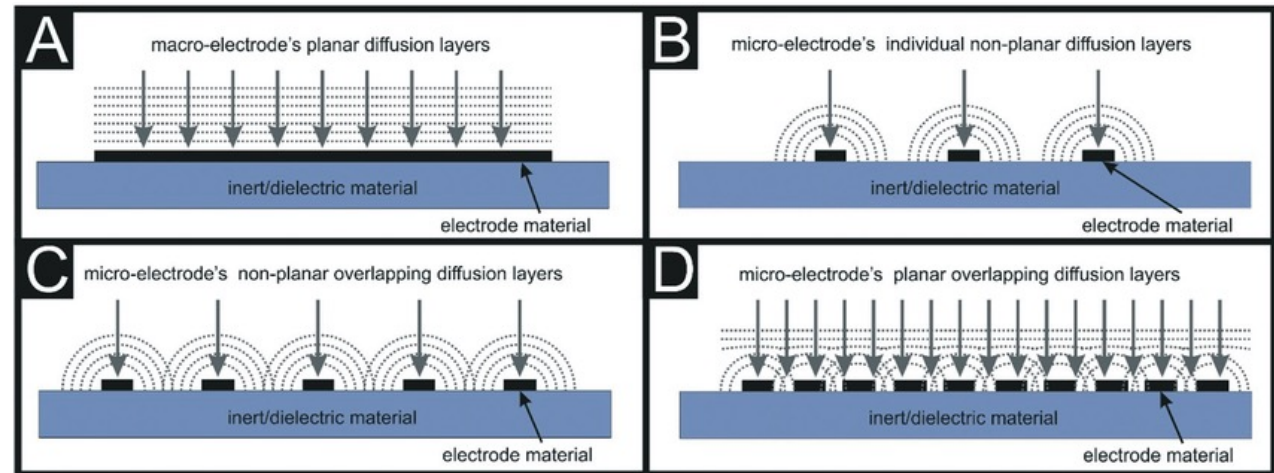
$$I_{lim} = n \cdot F \cdot \pi r^2 \cdot D_{diff} \frac{C_0}{r}$$

$$\frac{I}{A} \propto \frac{1}{r}$$

$$I \propto A \frac{1}{r}$$



$r \ll d$, so Current is much larger with many small electrodes of total area A than with a single large electrode of area A !

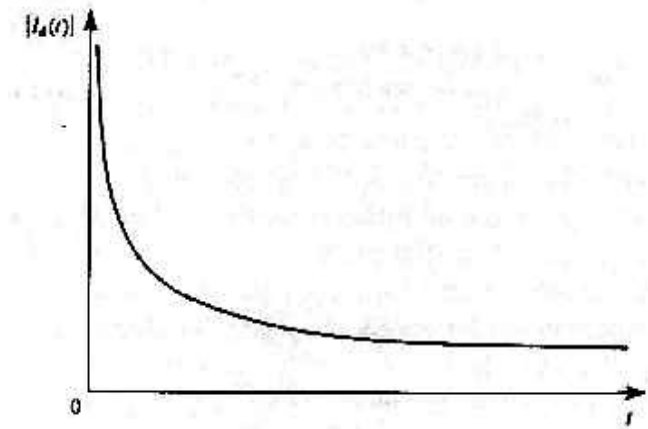


<https://doi.org/10.1039/D0EW00407C>

Response time of microelectrodes

The current around a macroscopic electrode is given by the Cottrell equation:

$$I(t) = nFAD_c C_0 \left(\frac{1}{(\pi D_c \cdot t)^{1/2}} + \frac{1}{\delta} \right)$$



Time evolution of electrochemical current

There are two regimes:

- Initially, when V is turned on, the current is very high until a **steady diffusion layer** is formed
- Then the current is diffusion limited (better for steady measurements)

With micro-electrodes, the diffusion layer thickness is limited to the **radius of the electrode**. Thus the **time** to reach the limiting current is much faster than for macro electrodes (and the **current density** is higher!)

The related time to reach this layer is given by

$$x_{\text{max}} = \sqrt{2D_{\text{diff}} \cdot \tau} \quad \text{then} \quad \tau \approx \frac{r^2}{2D_{\text{diff}}} \quad \tau \propto r^2$$

Numerical: $D_{\text{diff}} = 10^{-9} \text{ m}^2/\text{s}$

$r_0 = 10 \text{ } \mu\text{m}$	$\tau = 50 \text{ ms}$
$r_0 = 5 \text{ } \mu\text{m}$	$\tau = 12.5 \text{ ms}$
$r_0 = 1 \text{ } \mu\text{m}$	$\tau = 0.5 \text{ ms}$

How to Mix fluids in Laminar Flow conditions?

At low Reynolds numbers, mixing occurs only by *diffusion*, not by convection (turbulence)

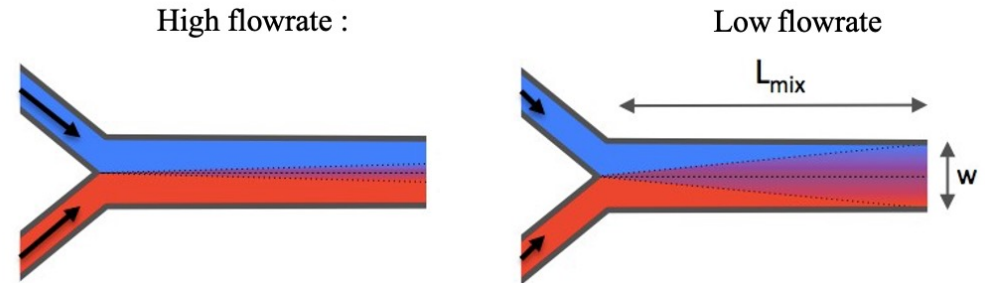
So: need to make *flows thinner* so that ***diffusion times are shorter***

Good overview:

https://ocw.mit.edu/courses/2-674-micro-nano-engineering-laboratory-spring-2016/f28f8672e6386d65276d2e6776ae8611_MIT2_674S16_MicrofluidcMix.pdf

Mixing in laminar flow conditions

Time for stirring (mass transport): $t = \frac{l}{v}$



At low Reynolds numbers, mixing occurs only by diffusion, not by convection (turbulence)

Time to diffuse across the channel width:

$$\tau_D \sim \frac{w^2}{D}$$

In this time, the fluid moves a distance:

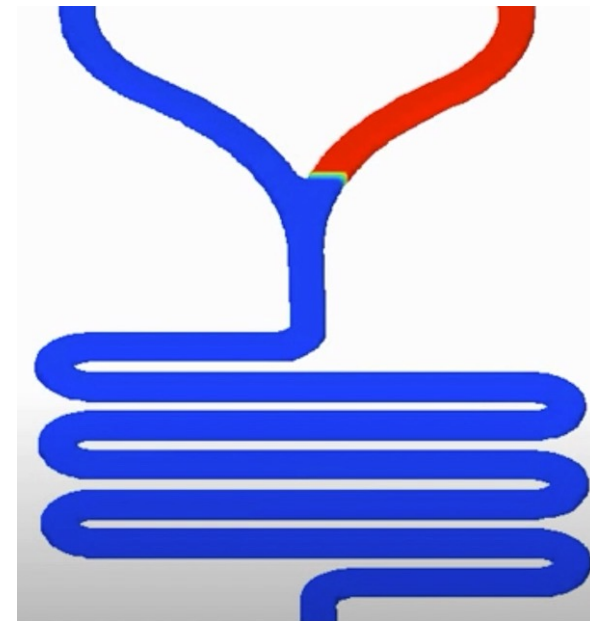
$$Z \sim \frac{v w^2}{D}$$

$$\frac{Z}{w} \sim \frac{v w}{D} \equiv Pe$$

w channel width

D diffusivity

U_0 velocity



Peclet Number: $Pe = \frac{l v}{2D_C}$

Ratio : convection trsp. / diffusion trsp.

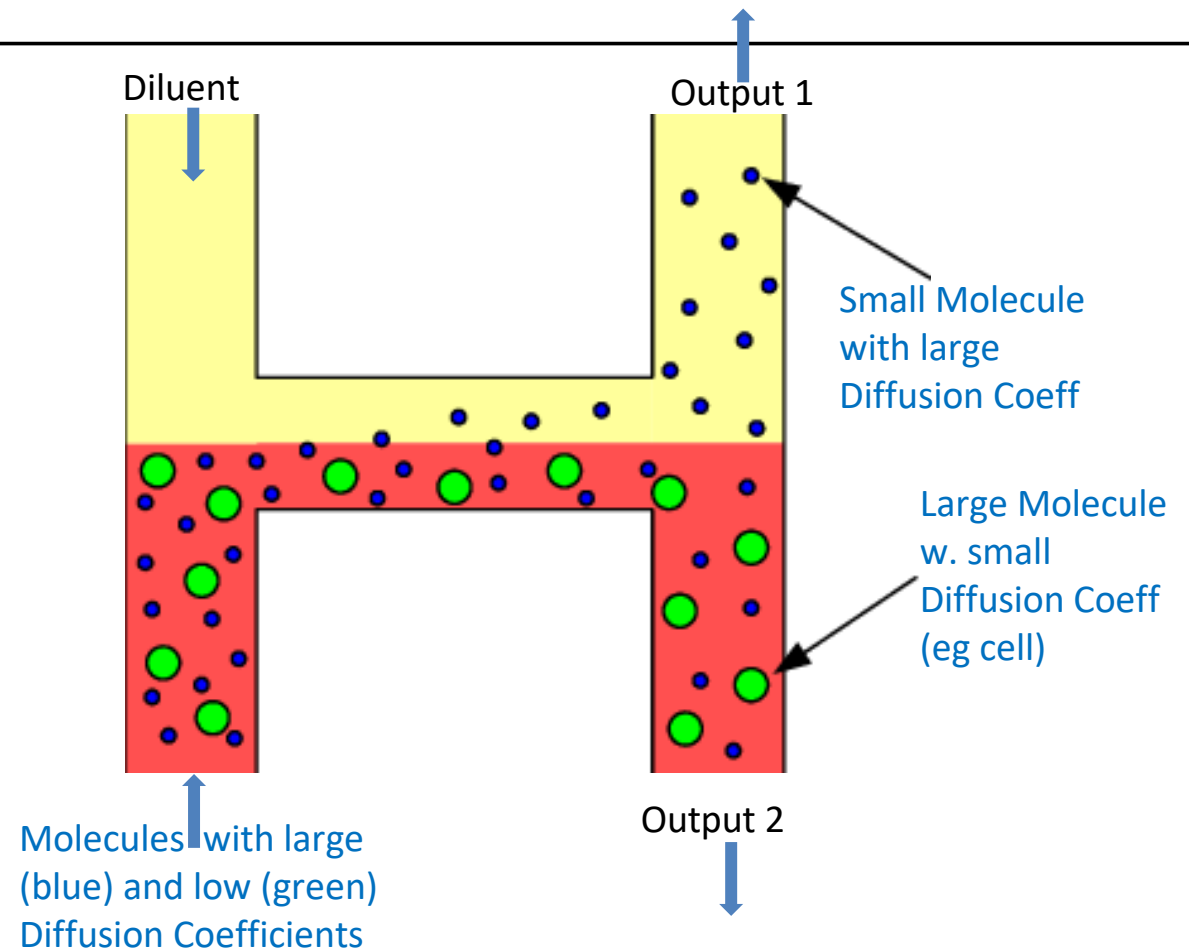
High Peclet #: dominated by convection.

Low Peclet #: dominated by diffusion

The H-filter: exploiting diffusion and laminar flow

Principle: filtration without membrane

- Two laminar flows are put in contact
- High diffusion coefficient molecules/ particles will diffuse laterally
- Low diffusion coefficient particles mostly remain in initial flow
- The two flows are then separated

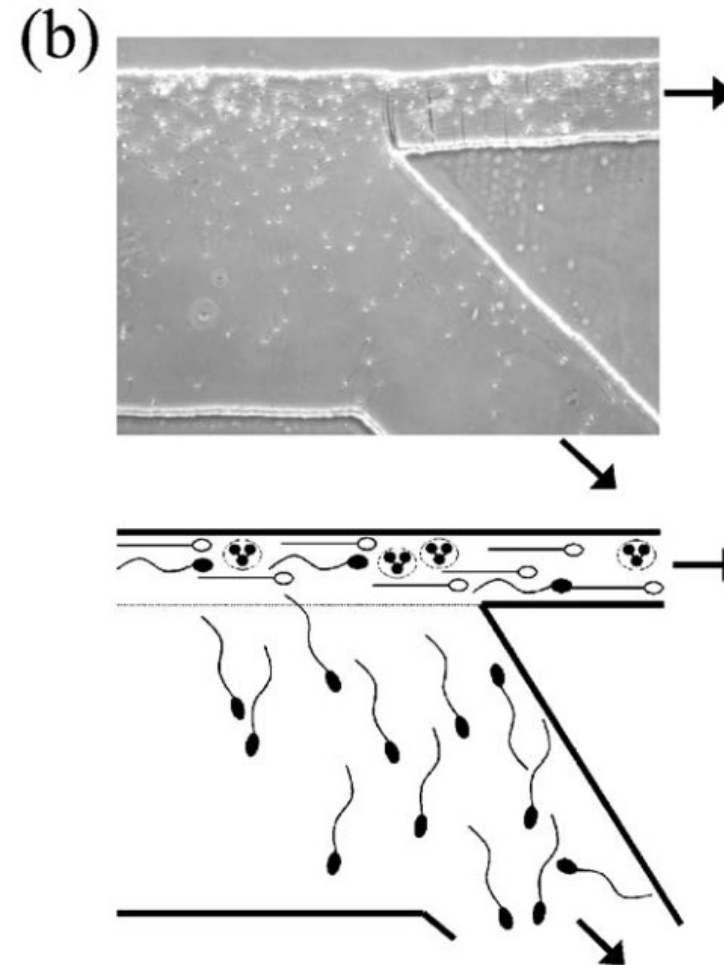
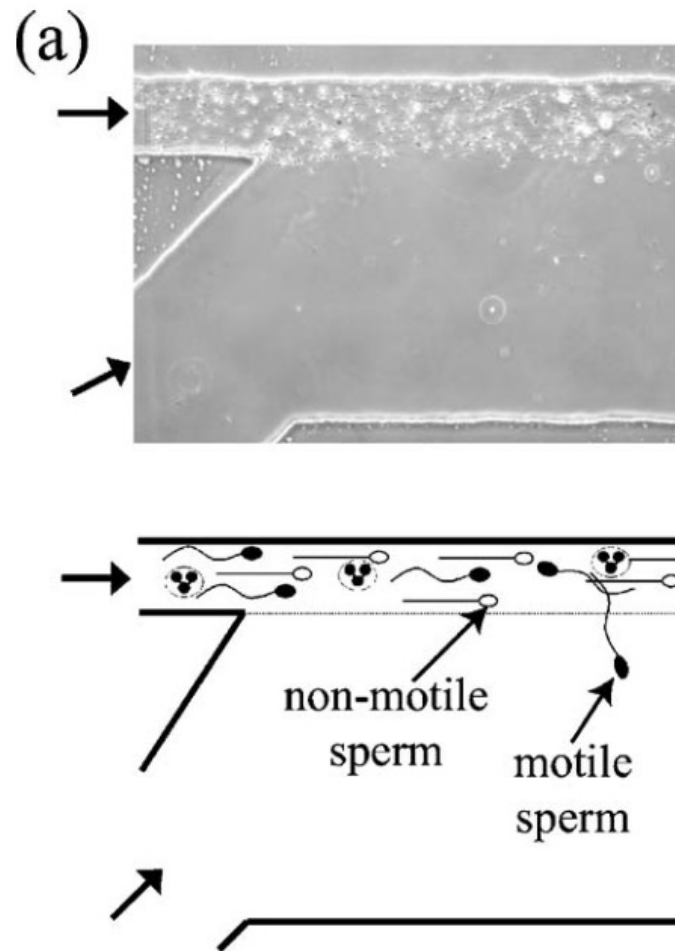


Contact length
 $l = 10 \mu\text{m}$
 $l = 100 \mu\text{m}$

small molecule ($D_c = 1000 \mu\text{m}^2/\text{s}$)
 $t_d = 0.01\text{s}$
 $t_d = 1\text{s}$

20 μm cell ($D_c = 10^{-2} \mu\text{m}^2/\text{s}$)
 $t_d = 1 \text{ min}$
 $t_d = 100 \text{ min}$

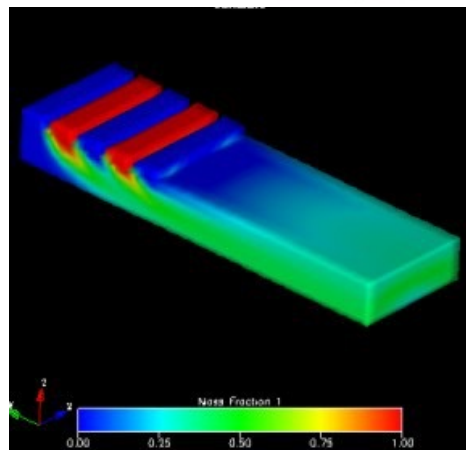
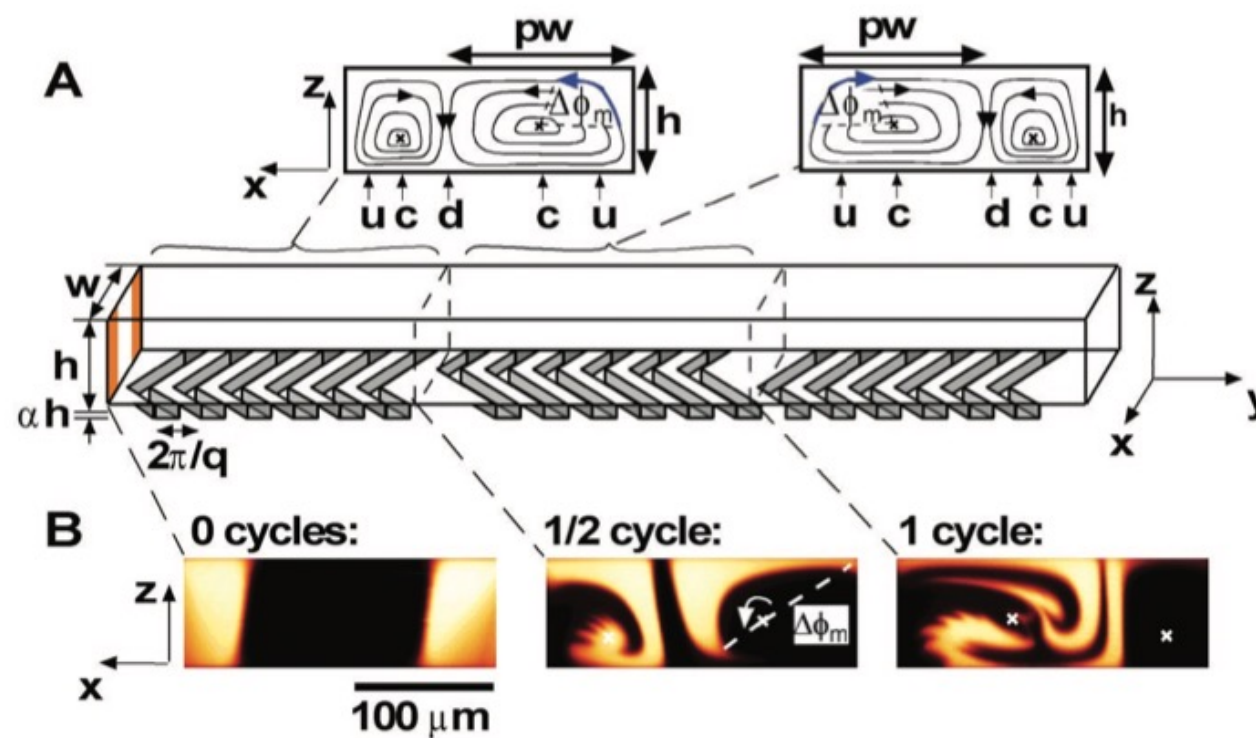
- «Applying microfluidic chemical analytical systems to imperfect samples», P. Yager et al., MicroTAS 98
- Brody et al., 1996; Brody and Yager, 1997
- "Cell sorting in microfluidic systems", P. Tellemar et al, MicroTAS 98
- Commercialized by Micronics



“While the traditional H filter relies upon particle diffusivity differences for differentiation, this device exploits the fact that motile sperm disperse across and homogenize the channel much more rapidly than nonmotile ones, which spread via diffusion alone.”

B. Co, Schuster *et al.*, 2003
Anal. Chem.2003,75,1671-1675

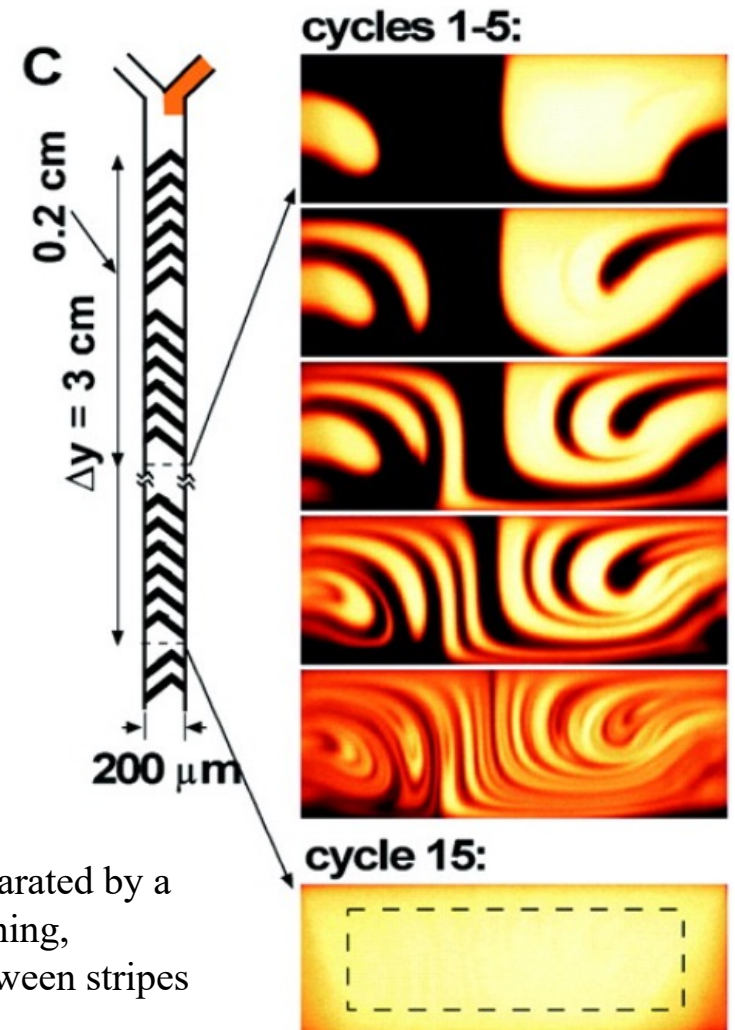
Mixing by chaotic advection



After N cycles requiring $_{\text{cyc}}NL_{\text{cyc}}/U$, where L_{cyc} is the cycle length, stripes are separated by a distance $h_{\text{eff}}h/2^N$. Following the above reasoning, mixing occurs when the time to diffuse between stripes h_{eff}/D is comparable to the cycle time ,

$$N_{\text{chaotic}} = \ln \text{Pe}$$

Induce recirculation between sections, so then diffusion can be more effective

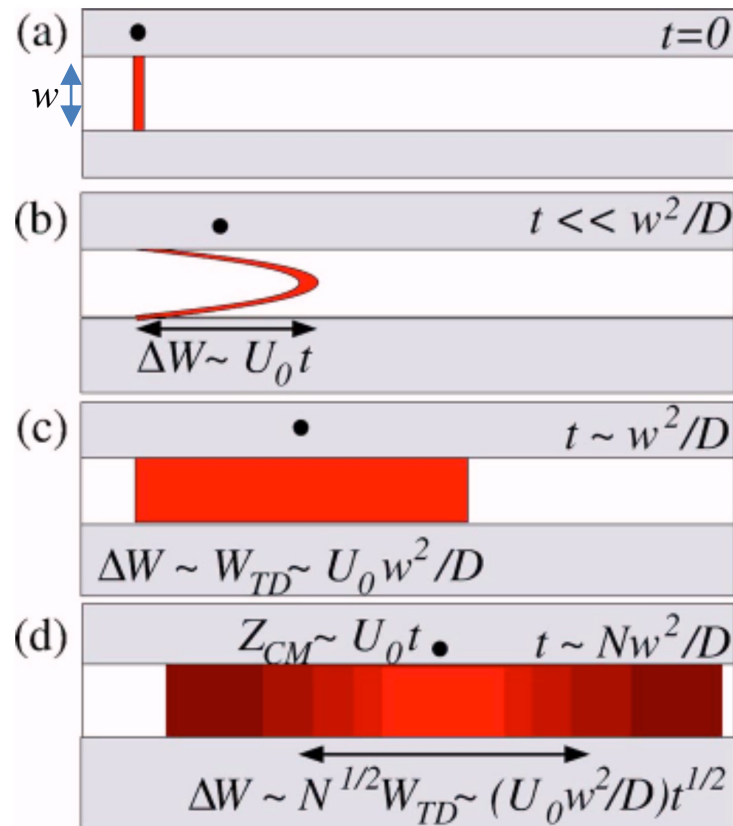


Stroock, Science 2002

Microfluidic mixing

Taylor dispersion (acts in the direction of flow)

The role of convection in dispersing inhomogeneous flows



- Thin stripe of tracer spans circular channel of radius w
- Pressure driven flow stretches it into a parabola
- Molecular diffusion then smears the parabolic stripe into a plug of width $W_{TD} \sim \frac{U_0 w^2}{D}$ after a time τ_D
- Each stripe within the plug goes through the same process: convectively stretched and diffusively smeared.
- After N steps, the initially thin stripe evolves to a Gaussian with width:

$$\sqrt{\langle W^2 \rangle} \sim \sqrt{N} \quad W_{TD} \sim \sqrt{\frac{U_0^2 w^2}{D} t}$$

Effective **long-time** axial diffusivity

$$D_z \sim \frac{U_0^2 w^2}{D} \sim Pe^2 D$$

T. M. Squires and S. R. Quake: Microfluidics:
 Fluid physics at the nanoliter scale, Rev Mod Phys, 2005

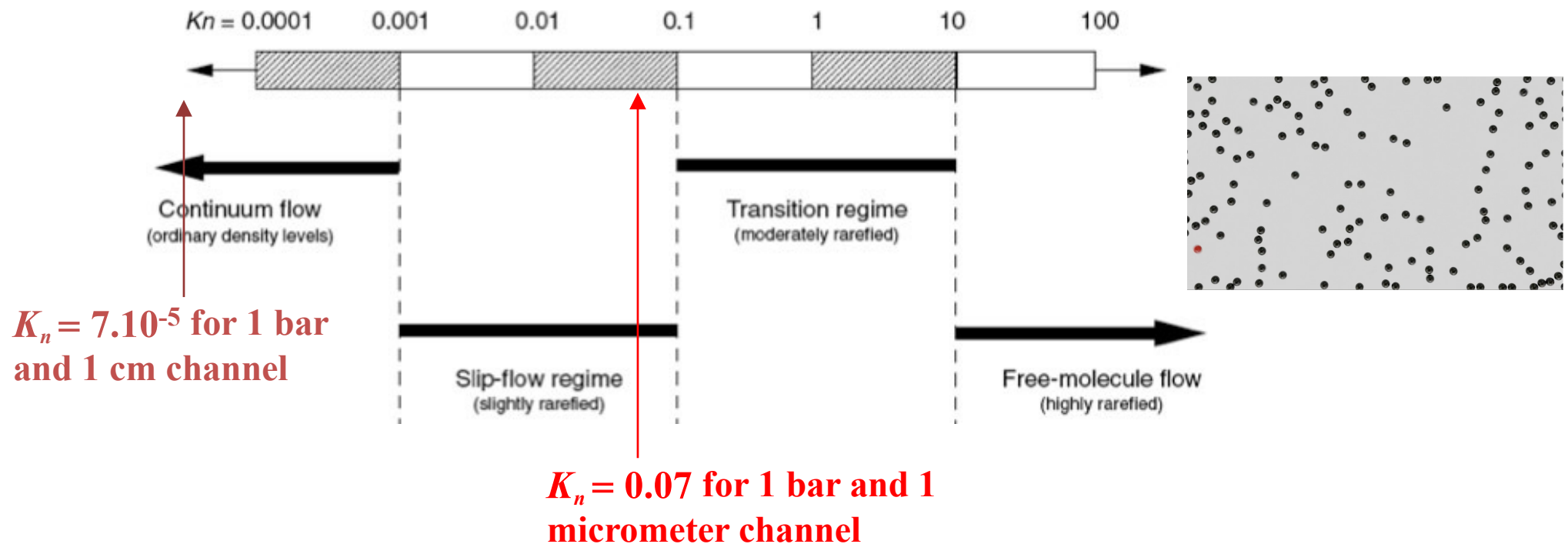
7. Gas flow – Knudsen number

Transitions from fluid to discrete molecules

Gas flow - Knudsen number – transition from fluid to discrete molecules

Mean free path of gas molecules : $\lambda = \frac{\eta}{\rho} \sqrt{\frac{\pi}{2R_0T}}$ air, 20°C, 1 atm: $\lambda = 66 \text{ nm}$

The Knudsen number is defined as : $K_n = \frac{\lambda}{d}$ d : hydraulic diameter, or height of slit



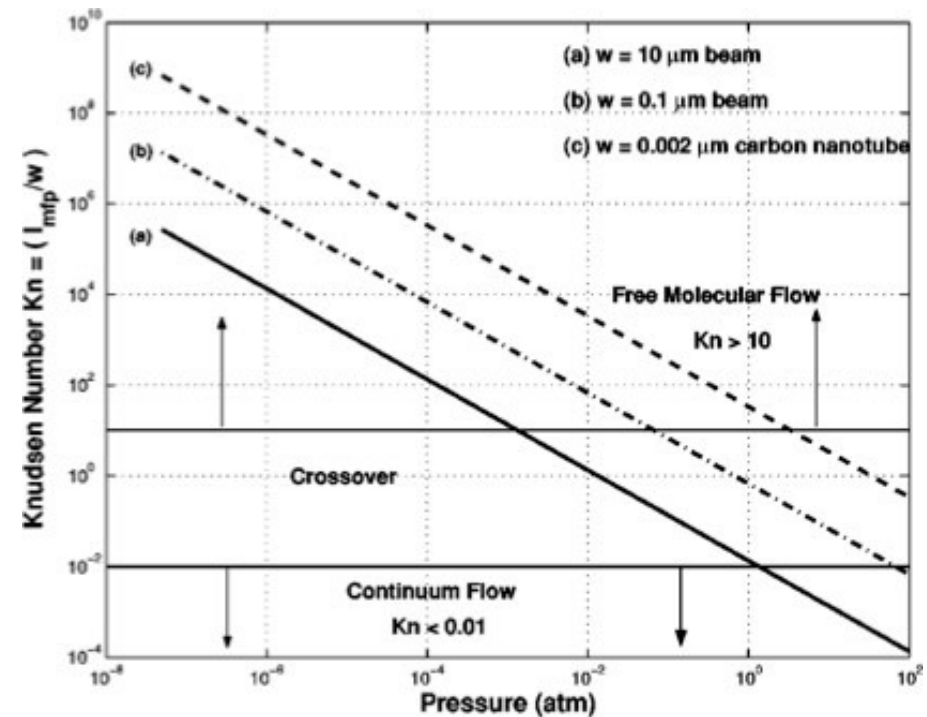
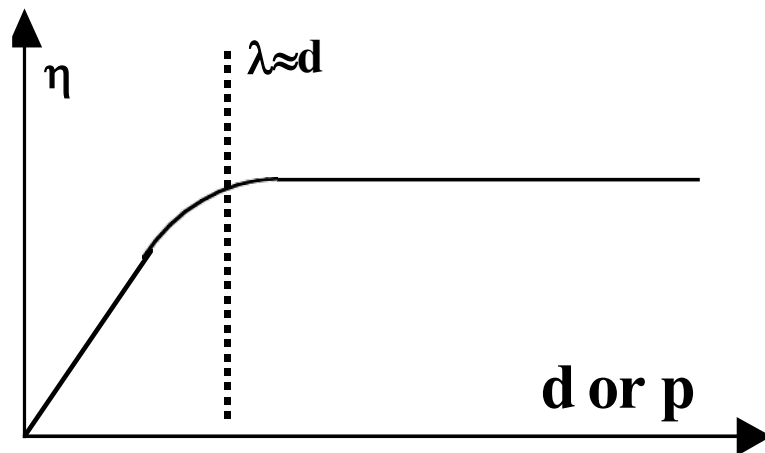
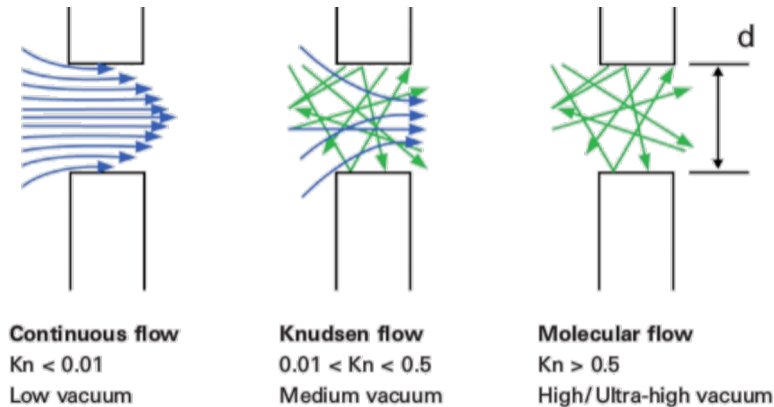
- At low K_n , the gas can be considered as a fluid => normal fluid dynamics (Navier-Stokes) and gas theory
- At high K_n numbers, the gas can no longer be considered as a continuum

Effective viscosity in molecular regime

When entering the molecular regime, the gas viscosity drops because of sparse distribution of molecules in the volume of interest. The effective viscosity η_{eff} deviates from bulk viscosity η :

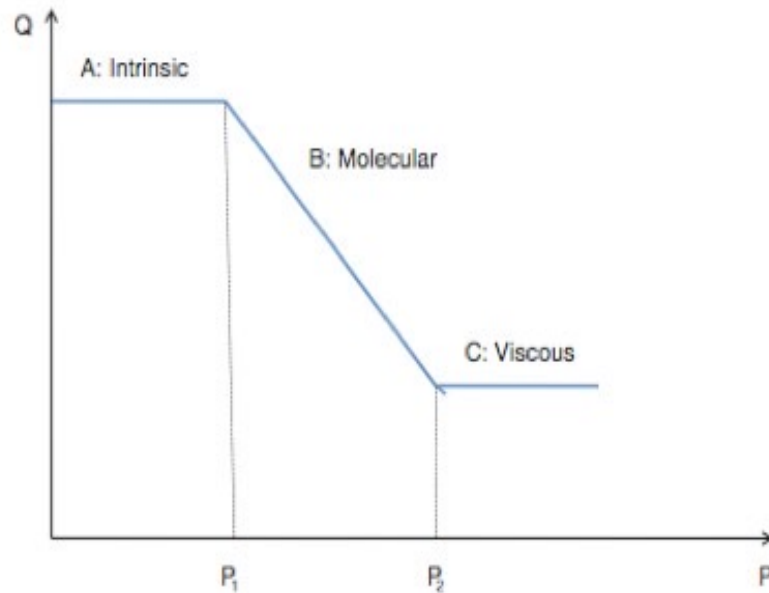
$$\eta_{eff} = \frac{\eta}{1 + 9.6 K_n^{1.2}}$$

- Down to about 10 μm (objects or channels) the continuum approximation applies at atmospheric pressure



- A Knudsen number can be associated to the air surrounding an object. For a beam of width w moving in the vertical direction, $K_n = \lambda / w$
- A **nanosized beam is thus in the molecular regime** (Bhiladvala, Phys Rev. E 69, 036307, 2004)

Gas damping – quality factor Q as a function of pressure



Quality factor vs pressure for a resonator in air

Regime A: the pressure is very low, below 10 Pa. The quality factor is limited by intrinsic mechanical losses (anchor, thermo-elastic, etc)

Regime B: the pressure is in the range from 10 to 1000 Pa. In this regime, air damping is dominant and the quality factor is very sensitive to pressure. Air molecules are so apart from each other that they do not interact. Air damping occurs due to momentum transfer during collision of the molecules with the moving structure.

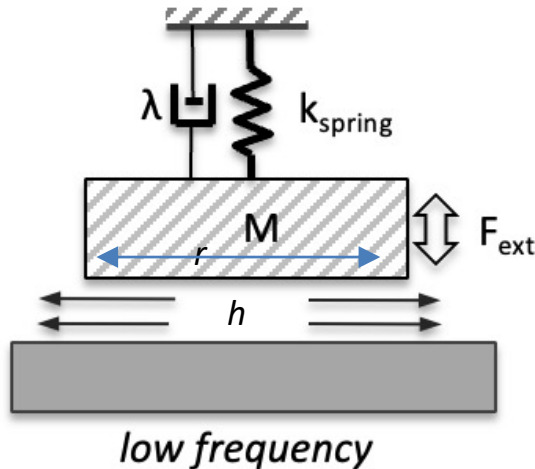
Regime C: the pressure is higher, approximately above a 1000 Pa. In this case, air molecules interact with each other and the air acts as a viscous fluid.

In the molecular regime (B), the quality factor Q scales like $1/P$

In the viscous regime, the Q factor is related to viscosity of gas and geometry of structure

Squeeze film damping in MEMS (e.g. capacitive microphone, accelerometer)

Damping coefficient for two parallel disks of area A and spacing h , need to move air out

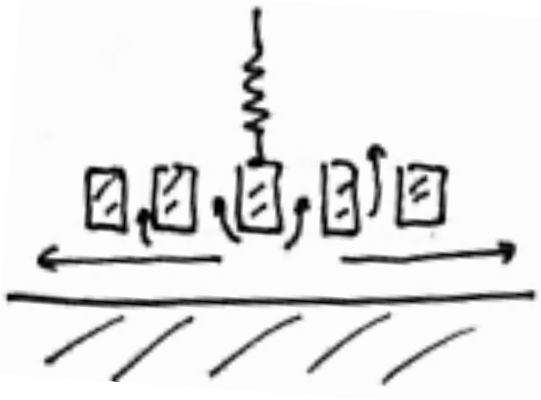


$$\lambda_{film} = \eta \frac{3\pi r^4}{2h^3} \quad [Ns/m]$$

$$\lambda \propto \frac{r^4}{h^3}$$

(if move slowly enough for gas to leave/enter ...)

If one disk is perforated, the damping can be considerably reduced, as the fluid can escape through the perforations instead of being squeezed out of the disk edges.



exact formulation can be found in Veijola papers

“Model for gas damping in silicon accelerometer”, T. Veijola et al., Transducers 97 (1997)

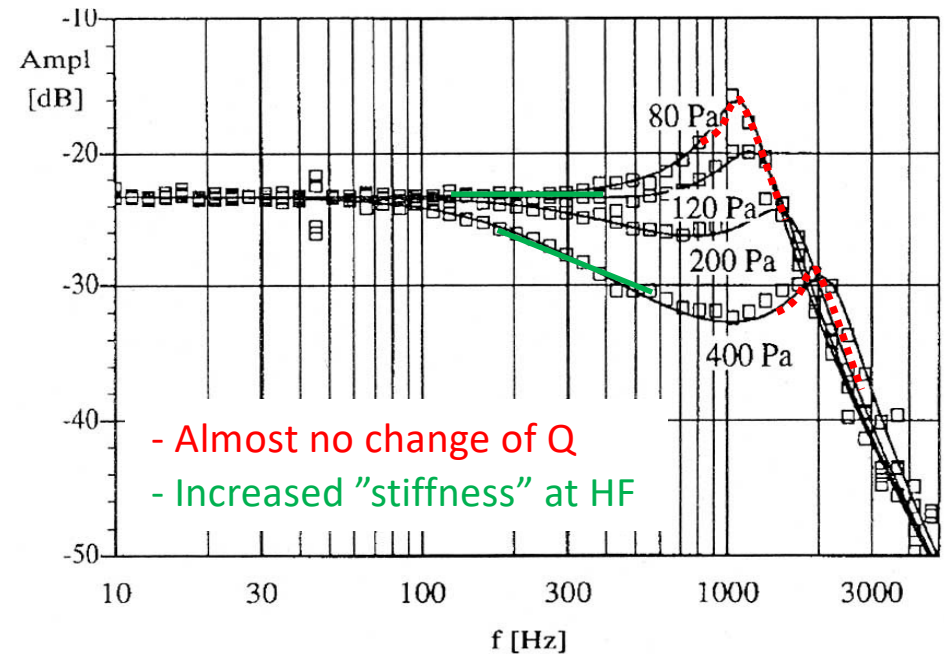
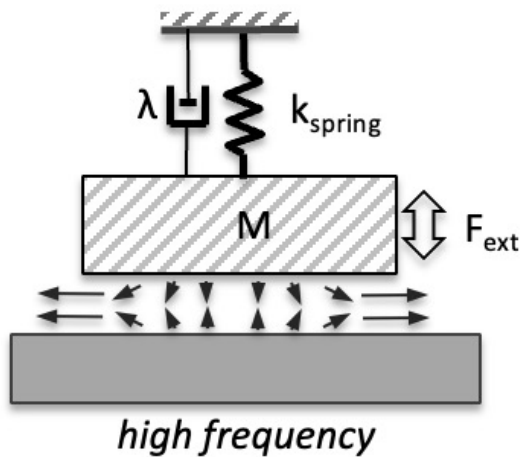
Squeeze film damping at high frequency – “piston” effect

At high oscillation frequencies, the gas does not have time to flow out of the gap. Gas film then acts from the mechanical point of view as a spring. So no damping anymore, but increased stiffness (so lower amplitude)

At high frequency limit, the additional spring force is

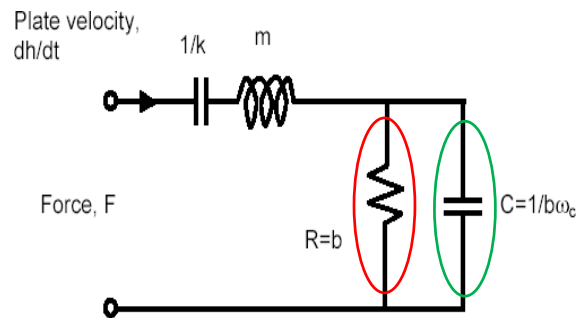
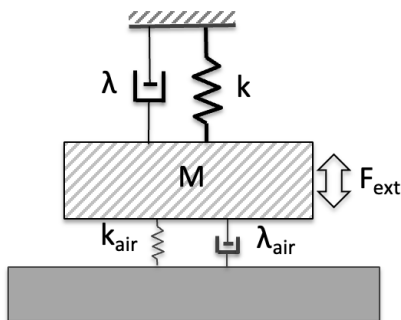
$$k_{air} = \frac{p_0 A}{d}$$

k_{air} depends on frequency!!



- Almost no change of Q
- Increased "stiffness" at HF

Squeeze film damping effect on the frequency response curve of an accelerometer in function of residual pressure

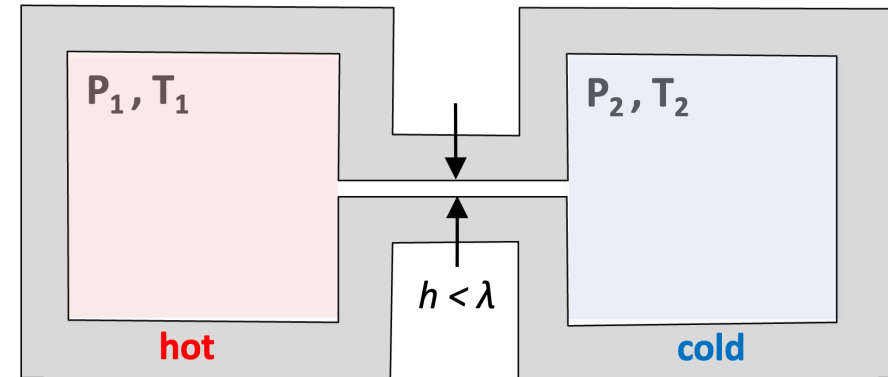


Knudsen pump

When two chambers, at different temperatures, are separated by an aperture of dimension smaller than the mean free path of molecules, there is a pressure gradient at equilibrium.

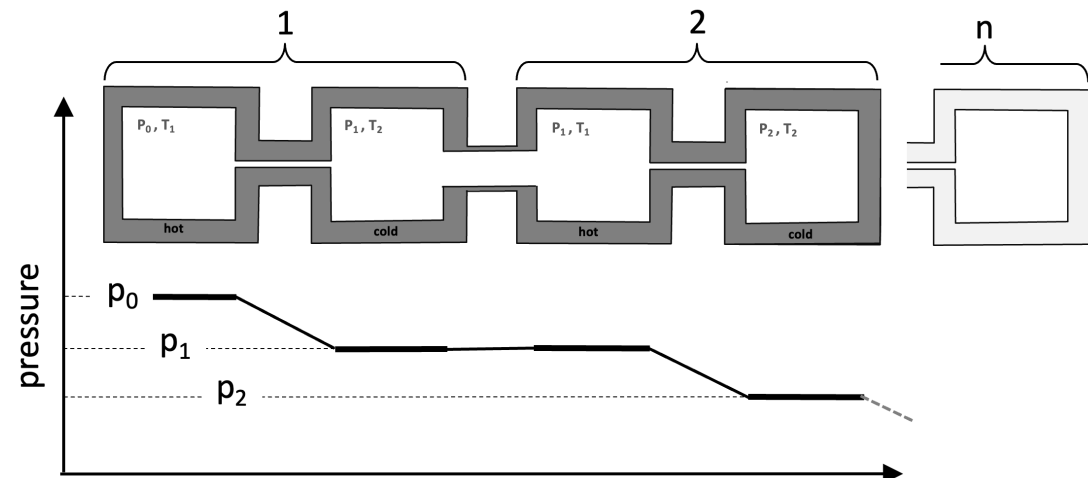
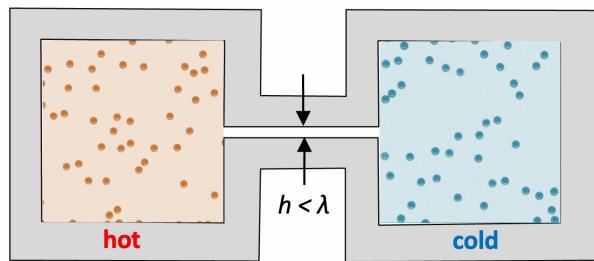
This is known as “thermal transpiration” effect

$$\frac{p_1}{p_2} = \sqrt{\frac{T_1}{T_2}}$$



$$T_1=400, T_2=300 \Rightarrow p_2=0.87 p_1$$

By stacking hot and cold cavities linked by narrow and wide channels, it is possible to make a pump.



- Hobson and Slazman, “Review of pumping by thermal molecular pressure”, *JVST A* 18 (2000) 1758.
- N. Gupta et al., *J Micromech. Microeng.* 22 (2012) p. 105026

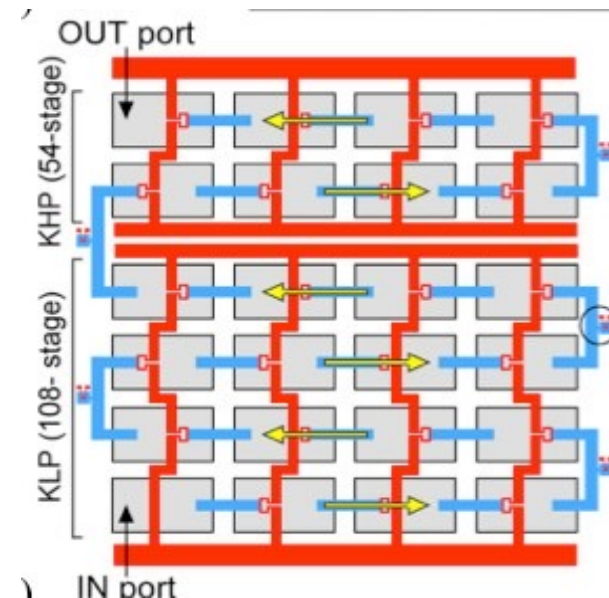
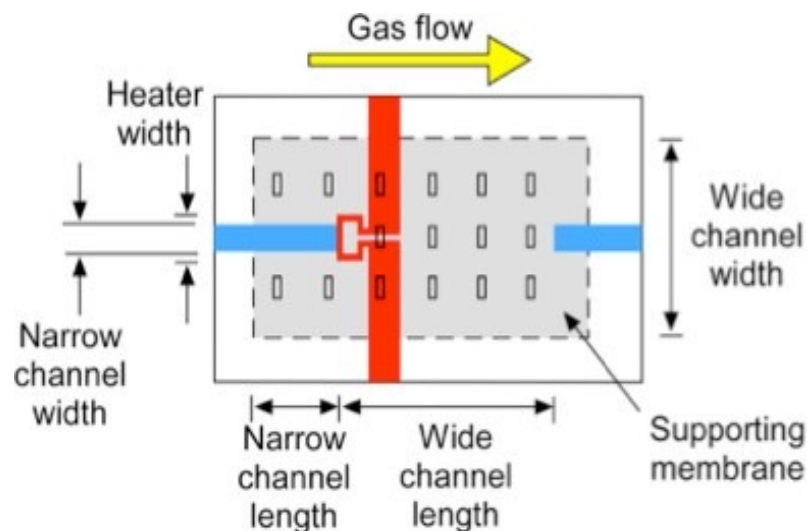
Knudsen pump with 162 stages

Theoretical pressure ratio for N stages:

$$\frac{P_1}{P_2} = \left(\frac{T_1}{T_2} \right)^{\frac{N}{2}}$$

$$T_1=350, T_2=300, N=100 \Rightarrow p_2= 10^{-4} p_1$$

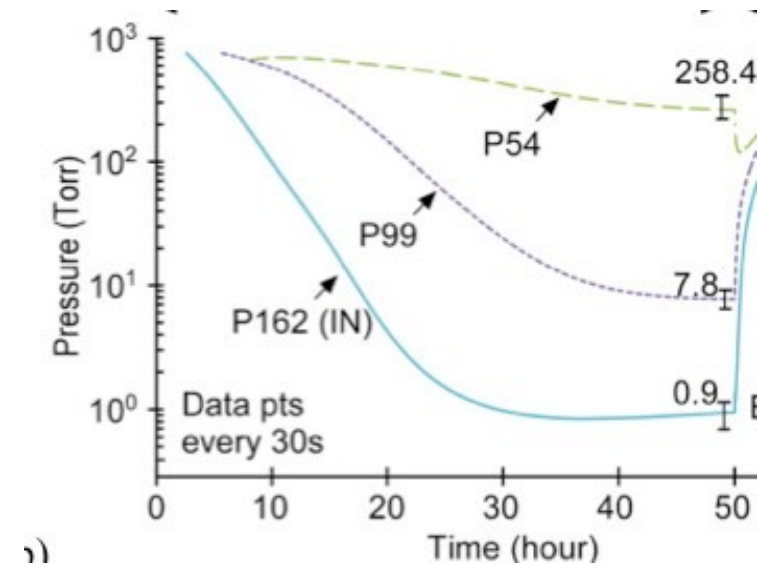
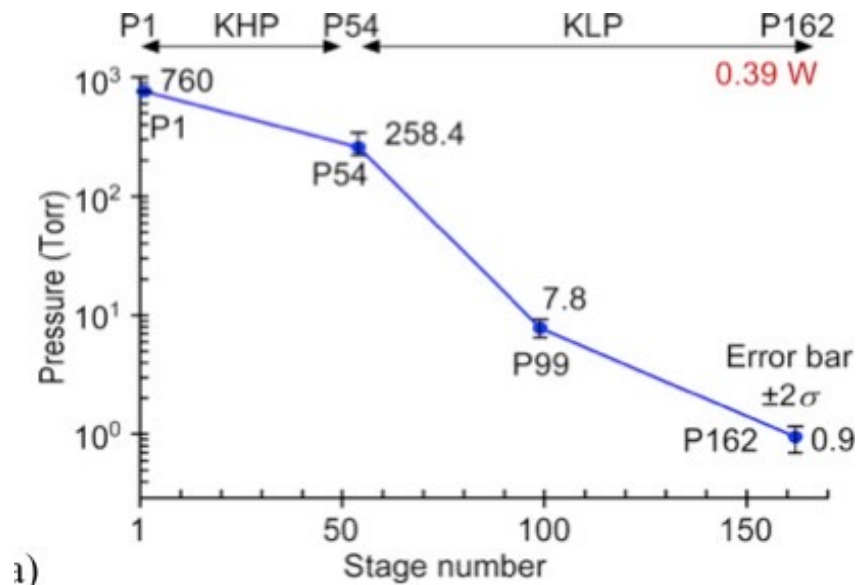
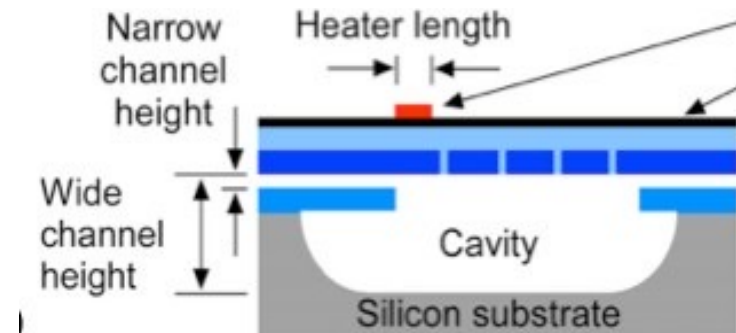
- The narrow channels must have a hydraulic diameter less than 1/10 of the mean free path of the gas and the wide channels must have a hydraulic diameter greater than 20 times the mean free path of the gas.
 - The maximum operating pressure is defined by the diameter of the narrow channels
 - The lowest attainable pressure (best vacuum) is defined by the diameter of the wide channels.
- 162 stages are cascaded: 54 stages designed for the pressure range from 760 to ≈ 50 Torr,
108 stages designed for lower pressures (longer mean free path, so larger channels)



S. An et al., JMEMS, 23,2, 2014 p. 406

Knudsen pump with 162 stages

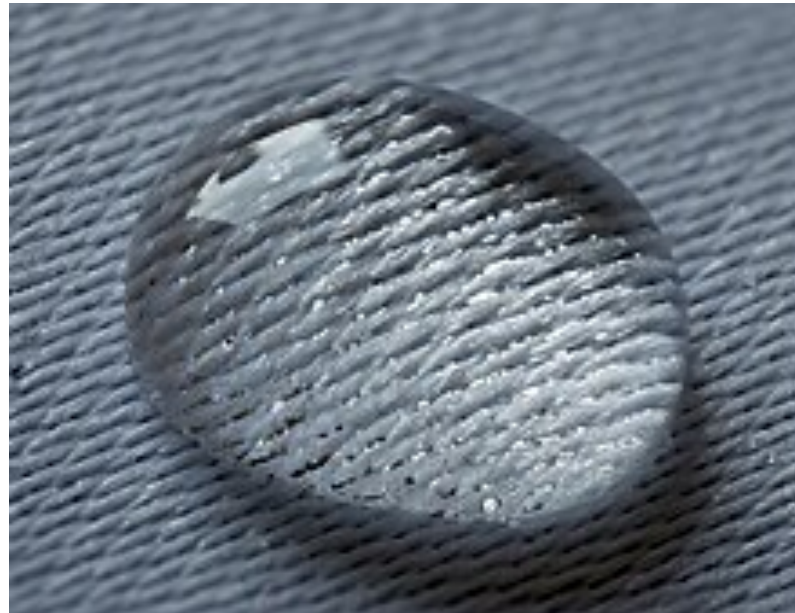
Part	Narrow channel height (μm)	Wide channel height (μm)	Number of stages	Pressure (Torr)	λ (μm) at 300 K
KHP (760Torr - 50Torr)	0.1	30	54	760	0.07
				200	0.28
				50	1.12
KLP (≤ 50 Torr)	1.0	100	108	1	49
				0.1	511



S. An et al., JMEMS, 23,2, 2014 p. 406

Review on Knudsen pumps: Wang et al. Microsystems & Nanoengineering (2020)6:26
<https://doi.org/10.1038/s41378-020-0135-5>

8. Surface tension and capillary pressure



https://en.wikipedia.org/wiki/Surface_tension

Surface tension

The surface tension at the surface of a liquid and a gas (or at the interface between immiscible liquids) originates from the difference of internal adhesion energy of the liquids and adhesion energy at the interfaces.

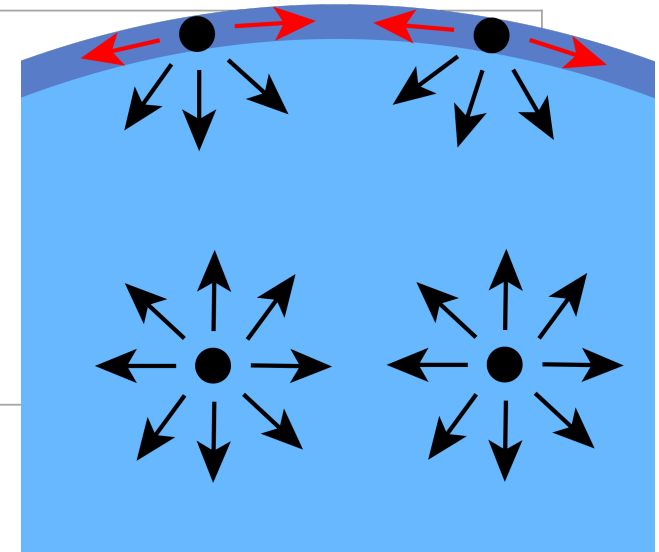
It a measure of the excess energy (unrealized bonding energy) present at the surface of a material, compared to the bulk.

Surface tension definition :

$$\gamma_{lg} = dE_{pot} / dS$$

Water in air $\gamma_{lg} = 73 \cdot 10^{-3} \text{ N/m}$

Ethanol in air $\gamma_{lg} = 22 \cdot 10^{-3} \text{ N/m}$



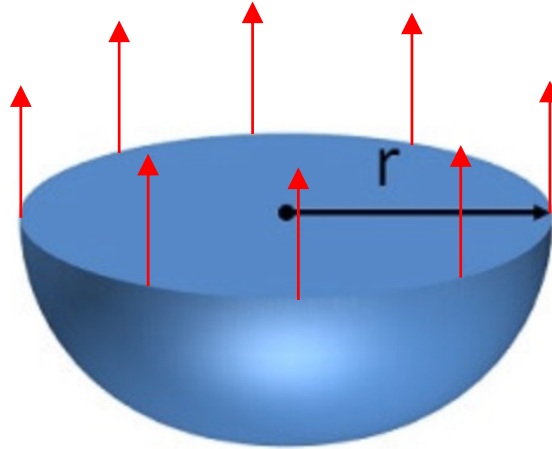
https://en.wikipedia.org/wiki/Surface_tension

Remark: ordinary tap water has only a surface tension of about $40 \cdot 10^{-3} \text{ N/m}$, because of impurities

What is the pressure p inside a droplet in air (or inside an air bubble in water) ?

$$F_{\text{tot}} = \gamma 2\pi r$$

$$p = \frac{F_{\text{tot}}}{\text{Area}} = \frac{2\gamma}{r}$$



$$r = 100 \mu\text{m} \quad P = 14.6 \text{ mbar}$$

$$r = 10 \mu\text{m} \quad P = 146 \text{ mbar}$$

$$r = 1 \mu\text{m} \quad P = 1.46 \text{ bar}$$

Another derivation of p (based on work)

- A bubble is at mechanical equilibrium.
- An increase of internal pressure must be compensated by an increase of surface energy.

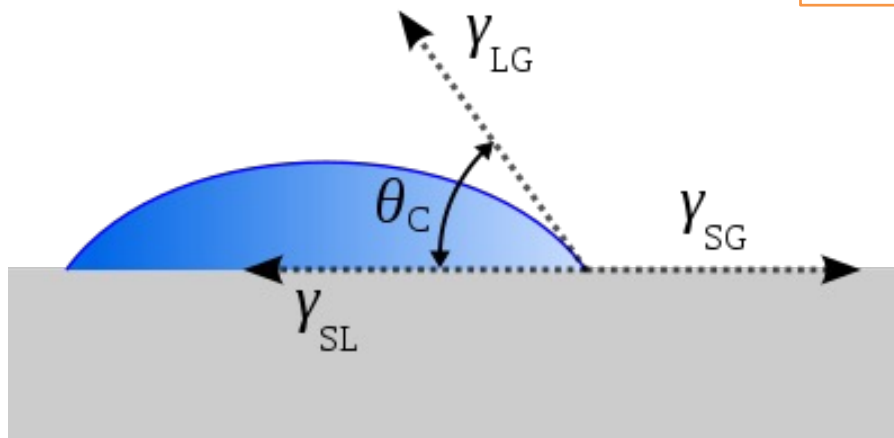
$$\Delta P \cdot dV = \gamma_{\text{lg}} \cdot dA$$

$$\Delta P = \frac{2\gamma_{\text{lg}}}{r}$$

Surface tension - contact angle (Young-Laplace equ.)

Contact angle between liquid and surface :

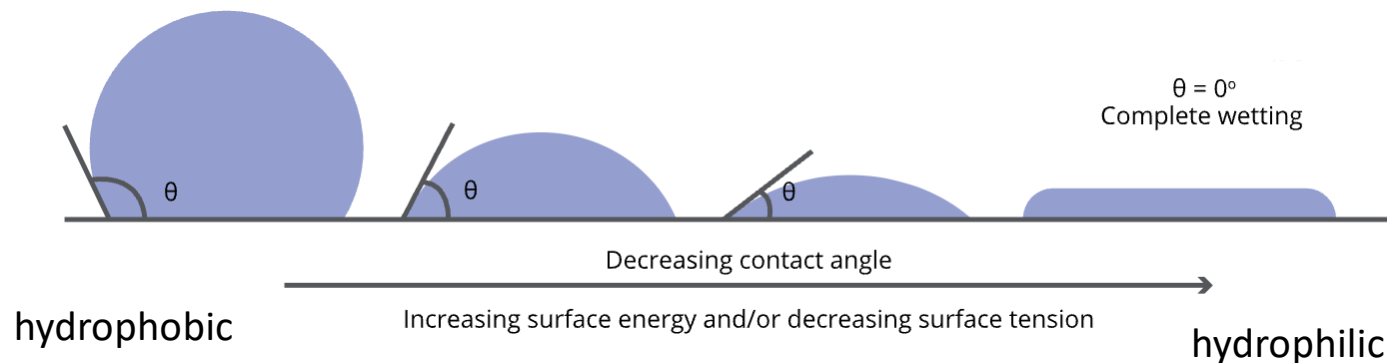
$$\cos \theta = \frac{\gamma_{sg} - \gamma_{sl}}{\gamma_{lg}}$$



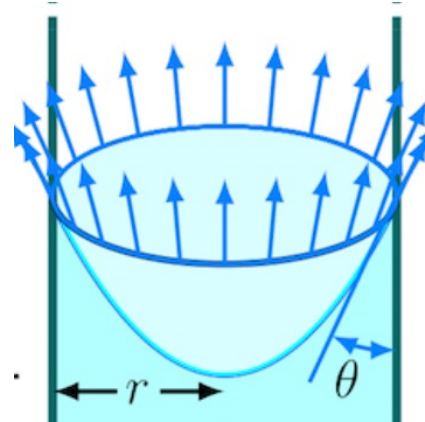
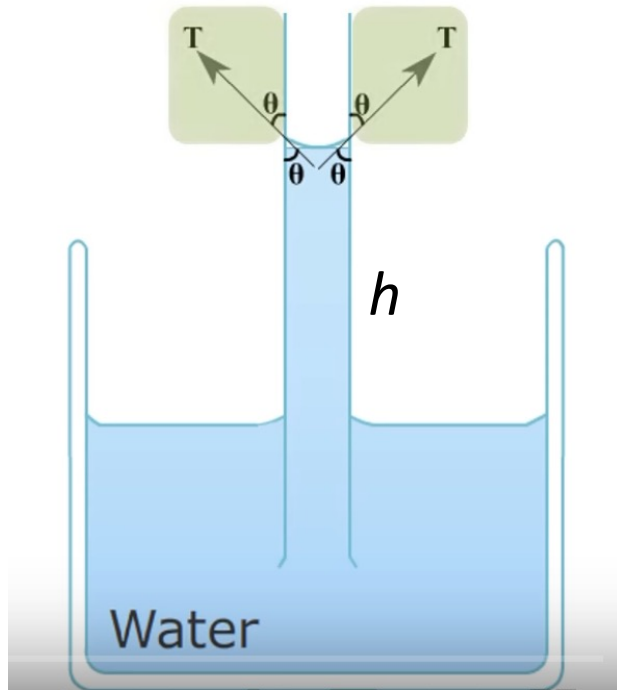
polystyrene	water	86°
glass	water	14°
silicone	water	110°

For perfectly wetting surface $\theta = 0^\circ$

For perfectly non wetting surface $\theta = 180^\circ$



Capillary pressure in a tube



$$\cos \theta = \frac{\gamma_{sg} - \gamma_{sl}}{\gamma_{lg}}$$

$$p = -\frac{2\gamma}{r} \cos \theta$$

If $\theta = 45^\circ$

$r = 100 \mu\text{m}$ $p = 0.01 \text{ bar}$

$r = 10 \mu\text{m}$ $p = 0.1 \text{ bar}$

$r = 1 \mu\text{m}$ $p = 1 \text{ bar}$

$$h = \frac{2 \gamma \cos(\theta)}{\rho g r}$$

Filling of a capillary – Washburn equation. Time to self-fill a capillary, ignoring inertia

Capillary pressure in a channel:

$$\Delta p_{cap}(t) = \frac{2\gamma_{gl} \cos \theta}{r}$$

$$\Delta P_{friction}(t) = \frac{\bar{v} \eta x}{8r^2} = \frac{\eta}{8r^2} \cdot x(t) \frac{dx(t)}{dt}$$

Equation of motion:

$$x \frac{dx}{dt} = \frac{r \cdot \gamma_{gl} \cos \theta}{\eta}$$

Solution :

$$x(t) = \sqrt{\frac{\gamma r t \cos \theta}{2\eta}}$$

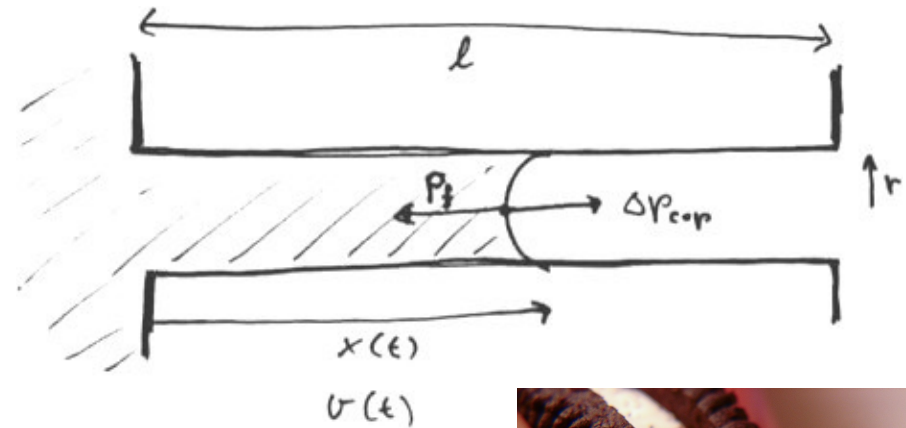
$$x(t) = \sqrt{C t}$$

$$C = \frac{\gamma r \cos \theta}{2\eta}$$

Time to fill a length l_0

$$t_w(l_0) = \frac{\eta}{r \cdot \gamma_{gl} \cos \theta} \cdot l_0^2$$

$$t_w \propto \frac{l^2}{r}$$

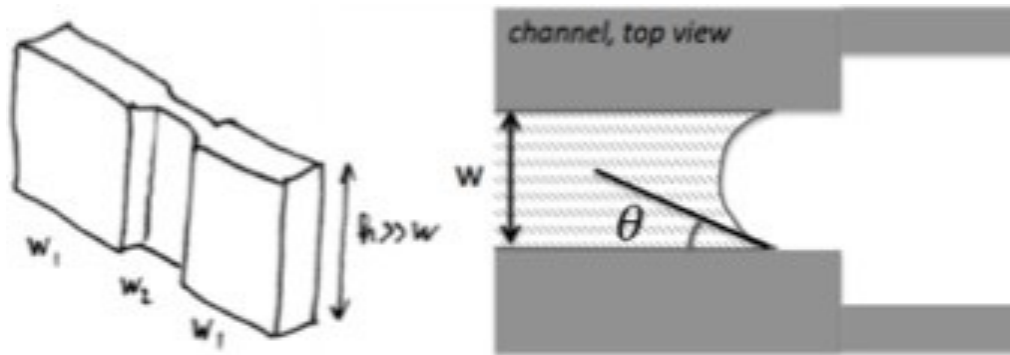


- Does the wetting front goes faster when increasing the radius r ?

Yes... but eventually no longer true because of inertial effects !

Capillary stop valve by channel restriction

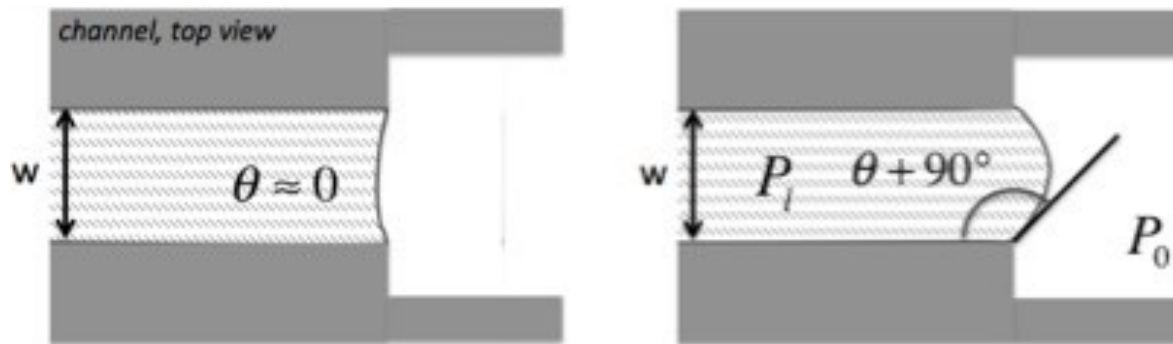
Here we discuss capillary pressure in hydrophilic rectangular channels where $h \gg w$. In this case, the capillary pressure is dominated by the lateral walls:



$$\Delta P_{cap} = -2\gamma \left(\frac{\cos \theta_h}{h} + \frac{\cos \theta_w}{w} \right)$$

$$\text{for } h \gg w \quad \Delta P_{cap} = -2\gamma \frac{\cos \theta_h}{w}$$

When the liquid front reaches the **end of the small section**, the “effective” contact angle opens up and thus decreases the capillary pressure. This **stops** the capillary flow. An additional **pressure pulse** is needed to restart the flow, until the contact angle on orthogonal walls is less than 90° (for the case of sharp 90° side walls)



$$\Delta P_{break} = P_0 - P_l = -2\gamma \frac{\cos(\theta + 90)}{w}$$

$$\Delta P_{break} = 2\gamma \frac{\sin \theta}{w}$$

Biosensors **2021**, 11(10), 405;

<https://doi.org/10.3390/bios11100405>

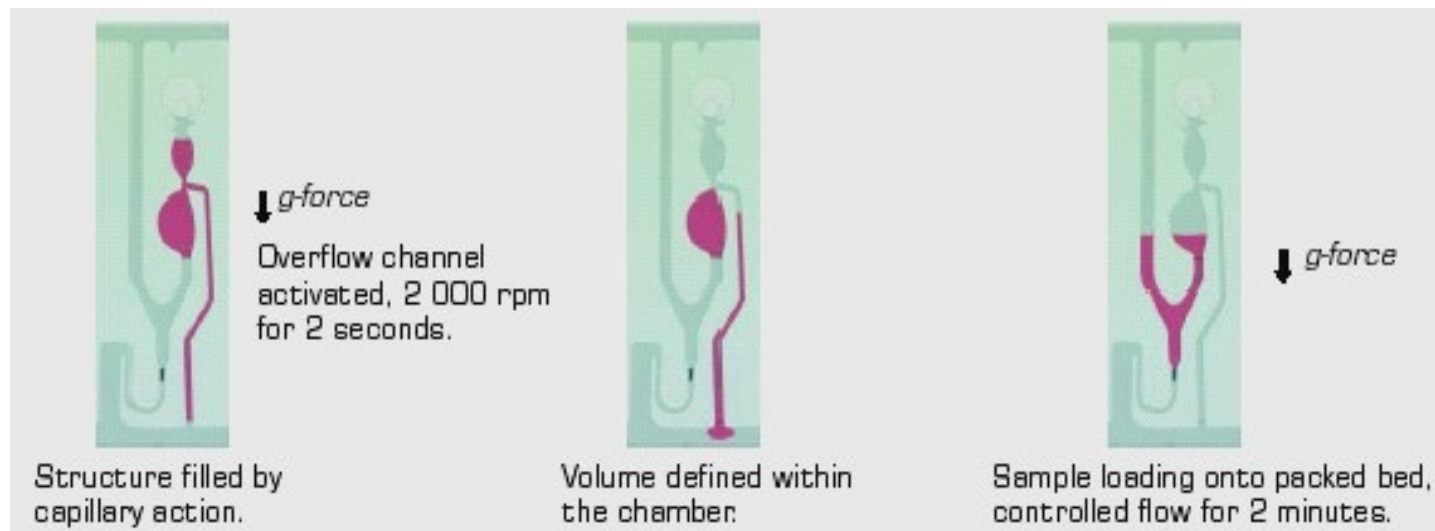
Centrifuge fluidics and capillary barriers

- Use centrifugal force to create pressure.
- Use capillary stops to control progression of liquid in compartments

Equivalent pressure on a liquid plug (length l) $p_{eq} = \frac{F}{A} = \frac{\rho \cdot l \cdot A \omega^2 R}{A} = \rho \cdot l \cdot \omega^2 \cdot R$

Displacement speed: $\rho l \omega^2 R = \frac{\bar{v} \eta l}{8 r^2} \Rightarrow \bar{v} = \frac{8 \rho \omega^2 R}{\eta} r^2 \quad v \propto r^2$

- The plug speed is independent of its length (not as in pressure driven flow)



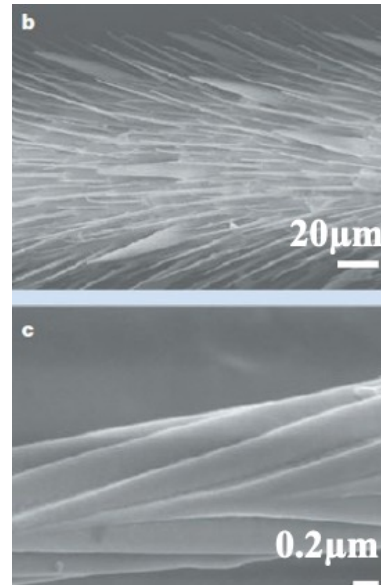
Comparison: pressure driven plug: $\Delta p = \frac{\bar{v} \eta l}{8 r^2} \Rightarrow \bar{v} = \frac{8 \Delta p}{\eta} \frac{r^2}{l}$

Water striders (Gerris remigis)



Surface tension – hydrophobic object “resting on water”

Water striders (Gerris remigis)



A single leg can support 15 times the weight of the insect

Floatability criterion ($f > 1$ to float):

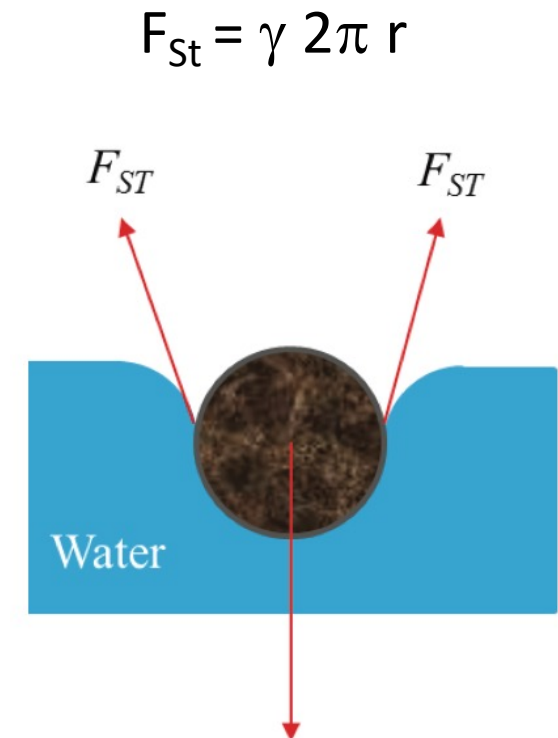
$$f = \frac{F_{st}}{F_{grav}}$$

$$f \propto r^{-2} \propto L^{-2}$$

$$F_{grav} = \frac{4}{3} \pi r^3 \Delta \rho g$$

$$r_{crit} = \sqrt{\frac{3}{2} \frac{\gamma}{\Delta \rho g}}$$

= 2 mm for glass bead on water

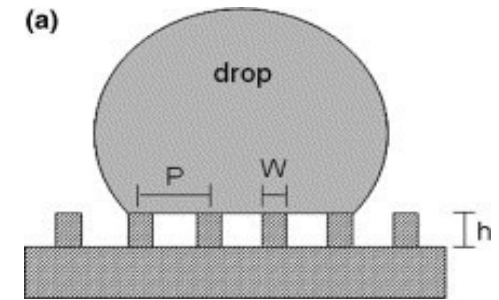


Lotus leaf effect (super-hydrophobic) effective contact angle

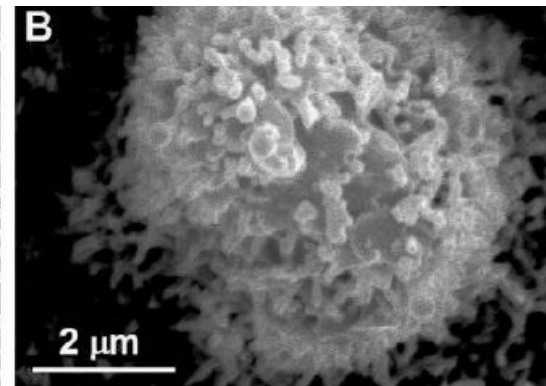
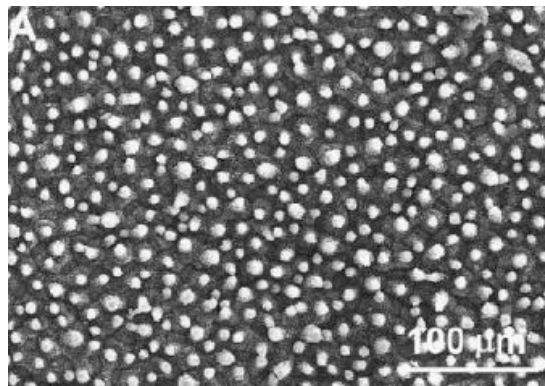
$$\cos \theta_c = \sigma_1 \cos \theta_1 + \sigma_2 \cos \theta_2$$

$$\cos \theta_{cb} = \sigma_1 \cos \theta_1 - \sigma_2$$

Superhydrophobic behaviour is due to surface corrugation:



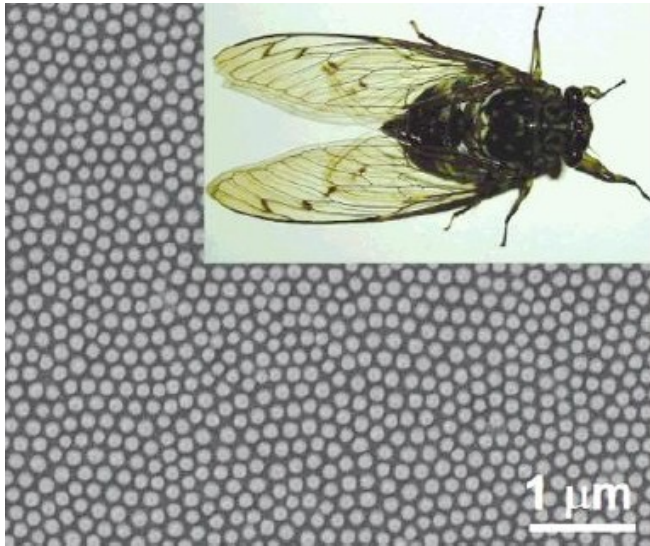
Very high local curvature



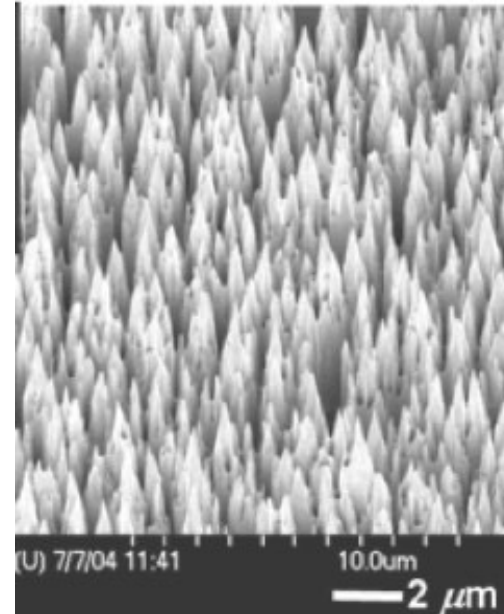
Self-cleaning effect :



Superhydrophobic surfaces

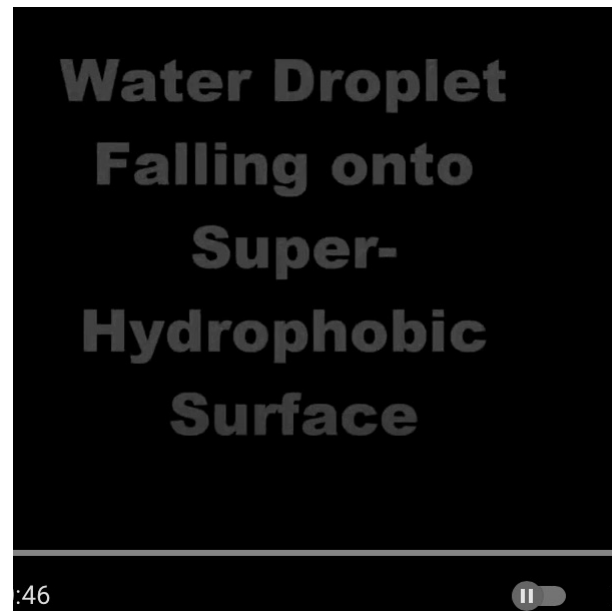


Cicada fly (*Cicada orni*)



Sun et al., *Acc. Chem Res.* 2005, 38, 644

Rebounding of falling droplets on
superhydrophobic surface:



<https://doi.org/10.1021/la8003504>

Electrowetting at surfaces

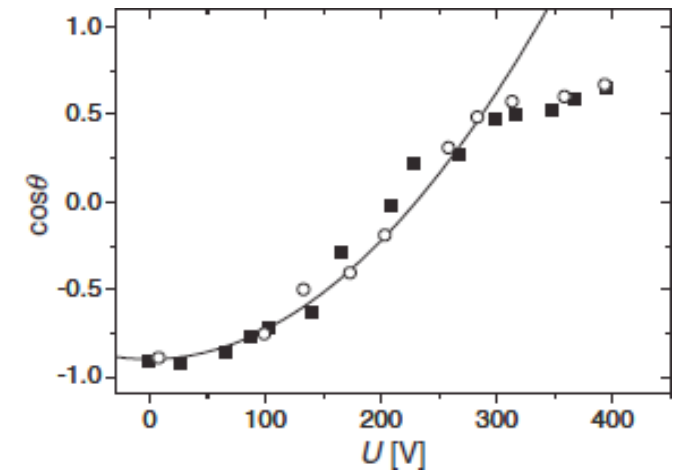
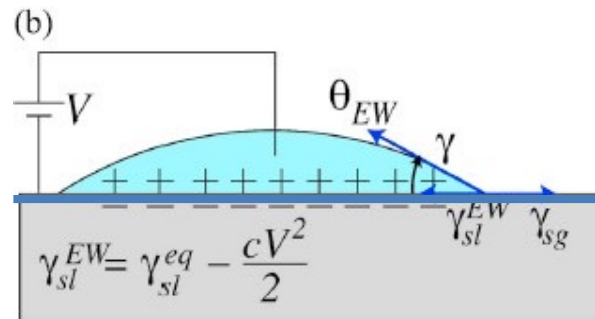
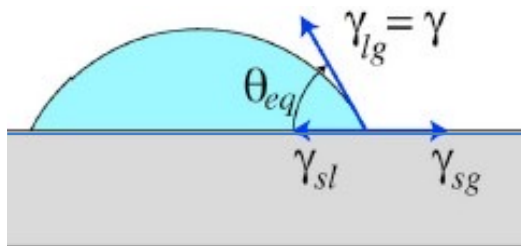
The contact angle can be modified by electrostatic surface energy. The additional electrostatic surface energy is given by the capacitance energy $\frac{1}{2}cV^2$

where

c is the capacitance per unit area $c = \frac{C}{A} = \frac{\epsilon_0 \epsilon_r}{d}$

ϵ_r, d dielectric constant and thickness of the insulator

V voltage on the electrode



$$\gamma_{sg} - \gamma_{sl} - \gamma \cos \theta = 0$$

$$\gamma_{sg} - \left(\gamma_{sl} - \frac{1}{2}cV^2 \right) - \gamma \cos \theta = 0$$

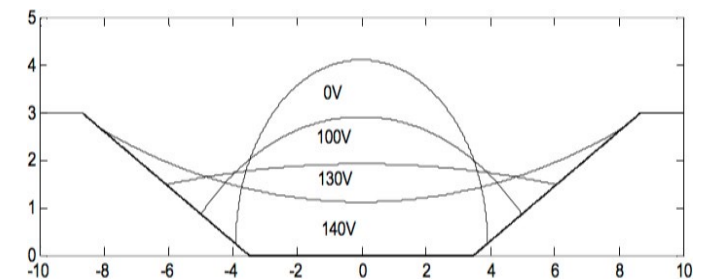
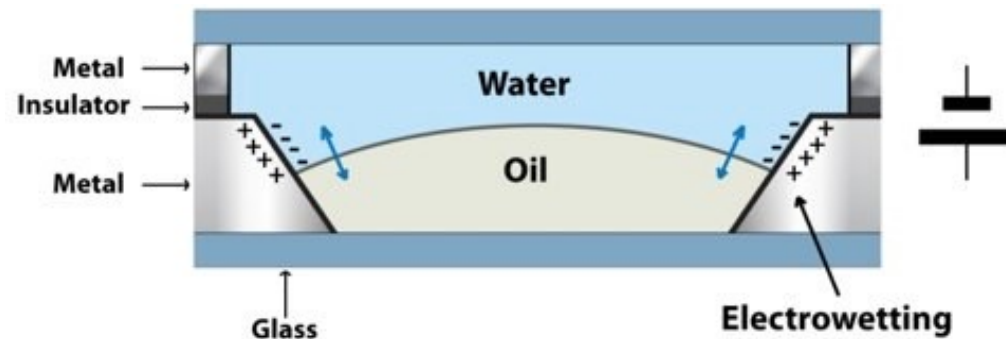
Electrowetting optics

Idea: a liquid drop forms a refractive lens

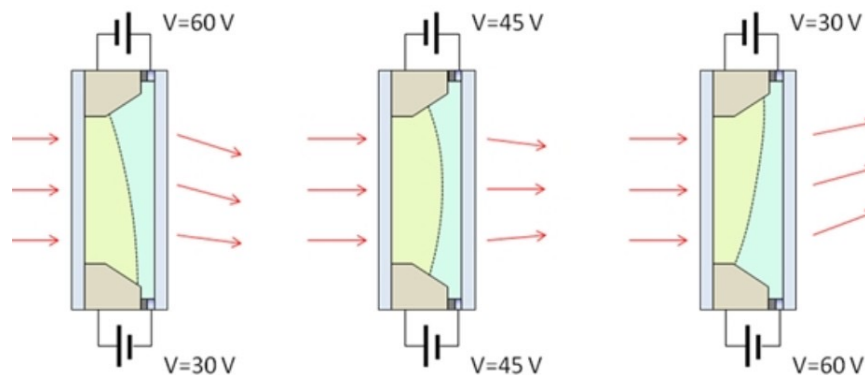
The the radius of curvature can be changed by electrowetting on the contact line of the liquid

In practice, the interface is made between water and oil

Liquid lens for autofocus:



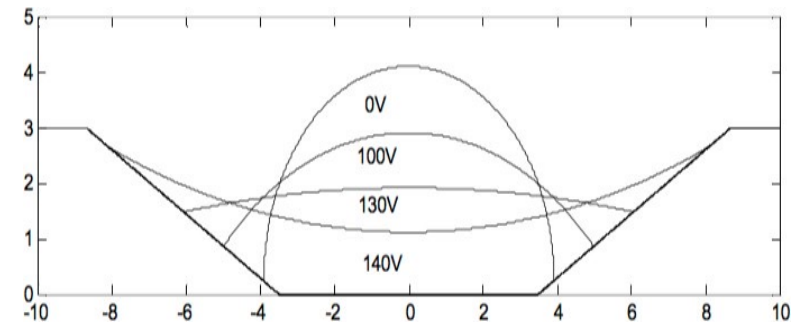
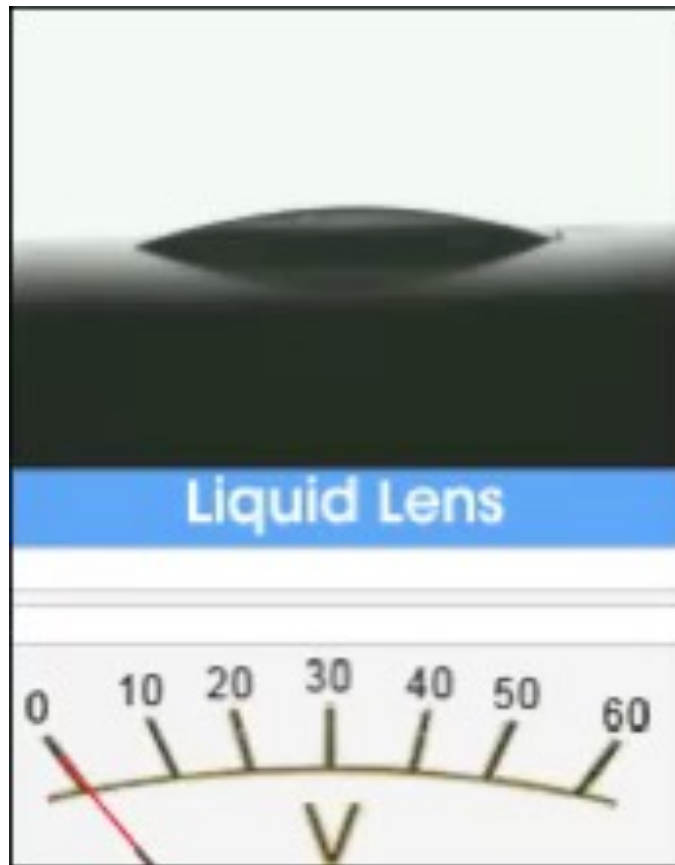
Liquid lens for image stabilization:



B. Berge, J. Peseux, “Variable focal lens controlled by an external voltage: an application of electrowetting”, Eur. Phys. J. E. 3, pp159-163, 2000.

www.varioptic.com

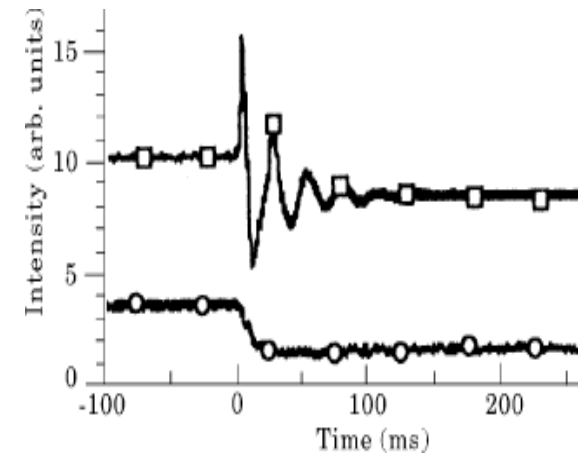
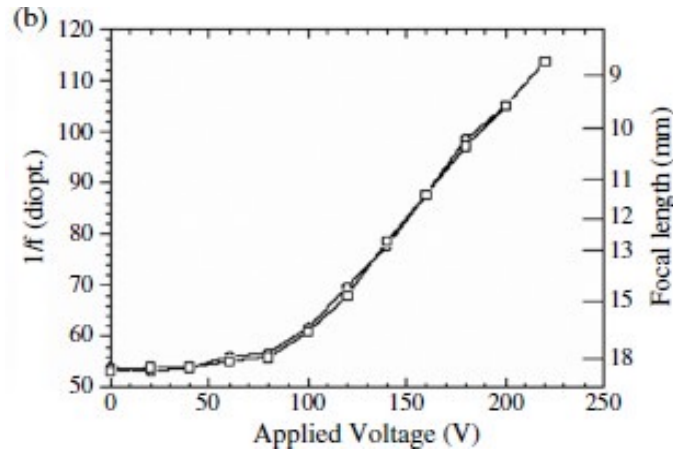
Electrowetting optics



B. Berge, J. Peseux, “Variable focal lens controlled by an external voltage: an application of electrowetting”, Eur. Phys. J. E. 3, pp159-163, 2000.

www.varioptic.com (now Corning)

Liquid lens



- The contact angle is proportional to V^2 , but due to the shape of the electrode, the optical power is almost linear with voltage in the range between 100 V and 250 V
- Because of small size: fast response. Damping can be increased by adding polymer molecules in water.

Scaling: how large a liquid lens can be ?

The capillary length is a characteristic length scale for an interface between two fluids which is subject to gravitational acceleration and to surface tension.

It is defined as :

$$\lambda_c = \sqrt{\frac{\gamma}{\rho g}}$$

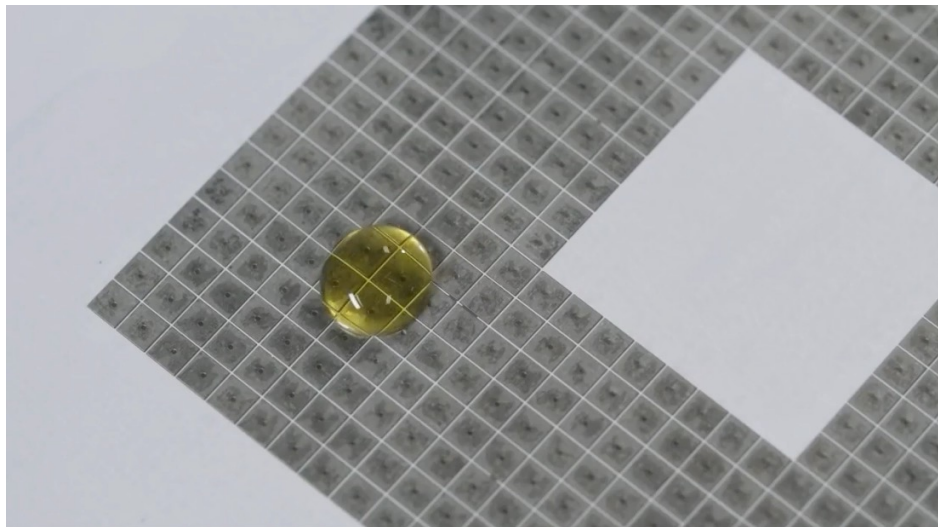
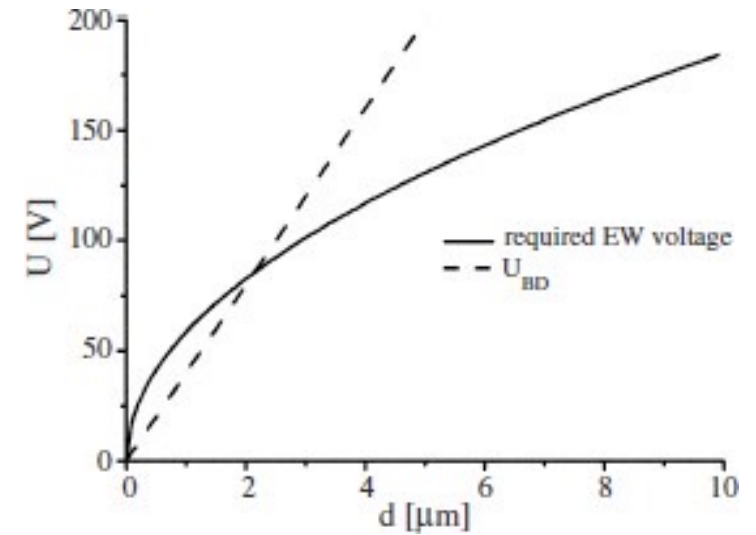
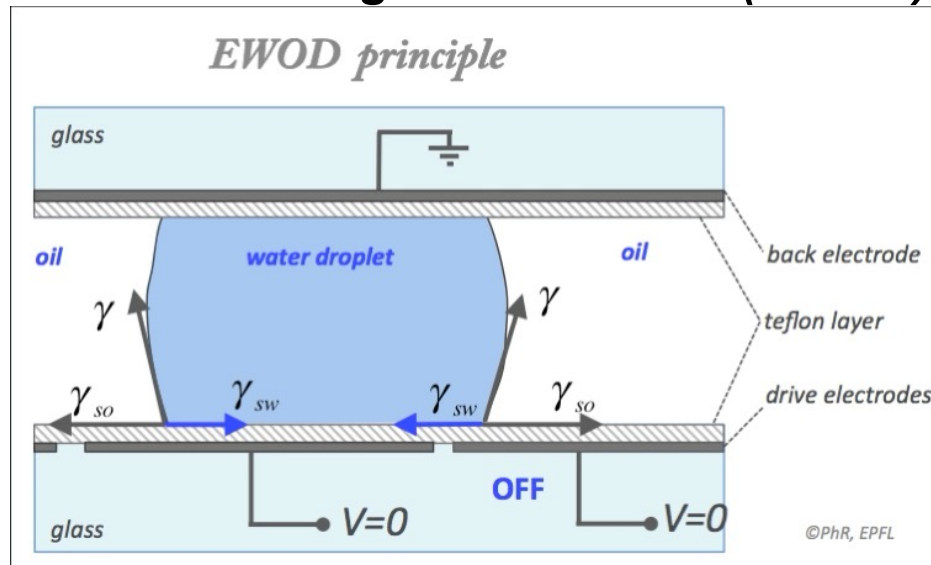
γ : surface tension of interface between fluids
 ρ : density, g : gravity acceleration

For water-air interface, the capillary length is around 2.7 mm.

Sessile drops with a radius smaller than the capillary length are almost spherical.

In liquid lens, the capillary length is much increased by choosing **two liquids with same density**

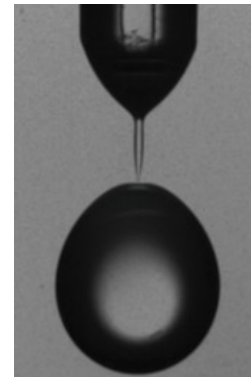
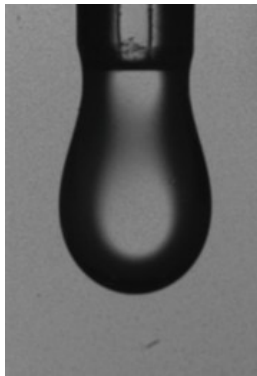
Electrowetting on dielectrics (EWOD)



A good review on electrowetting:

F. Mugele et al., J. Phys:condens. Mater 17 (2005) R705-R774

The hanging drop



The force due to surface tension is proportional to the length of the boundary between the liquid and the tube = equal the circumference. The force due to surface tension is given by :

$$F_\gamma = \pi d \gamma$$

Gravity force : $F_g \propto \frac{4}{3} \pi r^3 \cdot \rho g$

The vertical component of the capillary force is equal to the weight of the drop:

$$mg = \pi d \gamma \cdot \sin \alpha \quad \text{where } \alpha \text{ is the angle of contact with the tube,}$$

At the limit: $mg = \pi d \gamma$ or $\rho \frac{4}{3} \pi r^3 g = \pi d \gamma \quad r \propto d^{1/3}$

It is difficult to make very small drops by simple gravity detachment because of capillary pressure increase.

Ideas : - drop ejection for pressure pulse
- using shear flow

=> drop-on-demand dispensers, inkjet
=> droplets microfluidic

The pitch drop experiment (goutte de poix)

- Extremely viscous fluid. One drop falls every 8 to 10 years !
- Started at Queensland University in 1927
- Measured viscosity of pitch: 1012 time that of water

Date	Event	Years
1927	Hot pitch poured	
October 1930	Stem cut	
December 1938	1st drop fell	8.1
February 1947	2nd drop fell	8.2
April 1954	3rd drop fell	7.2
May 1962	4th drop fell	8.1
August 1970	5th drop fell	8.3
April 1979	6th drop fell	8.7
July 1988	7th drop fell	9.2
November 2000	8th drop fell	12.3
April 2014	9th drop	13.4



webcam: <http://www.thetenthwatch.com>

Drop formation by Rayleigh–Plateau instability



Plateau-Rayleigh instability is a physics phenomenon where a column of liquid breaks up into droplets in order to minimize its surface energy.

The breakup distance depends on the speed of ejection and is roughly proportional to $r^{3/2}$

Drop formation by viscous shear forces (in biphasic flows)

When a fluid A arrives from a perpendicular branch in a main channel, droplets of this fluid can be detached if a fluid B is flowing. The size is given by a balance between the capillary pressure necessary to form a droplet and the viscous stress from the fluid B flowing in a channel.

The Capillary number is defined as:

$$C_A = \frac{\eta \cdot v}{\gamma}$$

High capillary number: behavior is dominated by shear viscous forces

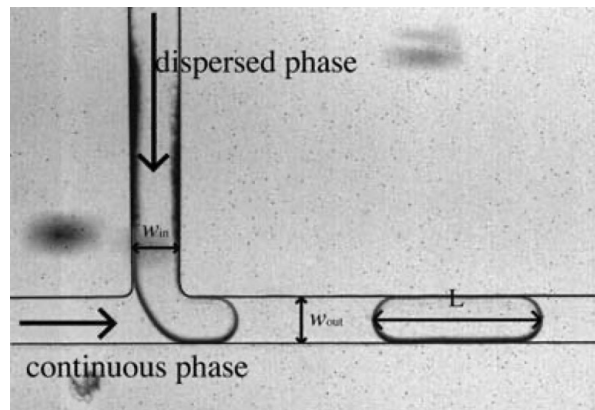
Small capillary number: behavior is dominated by surface tension

Droplets formation by breakup

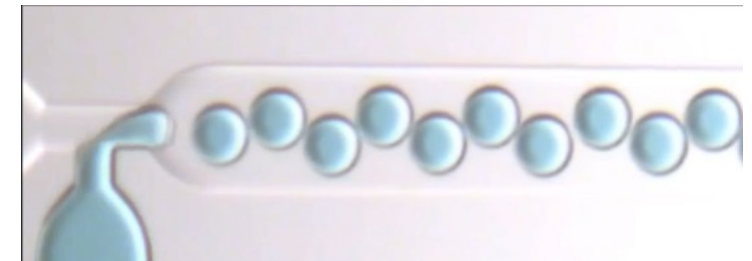


Microfluidic confinement allows the creation of **small** droplets with, very **homogeneous** size distribution

Water in oil droplets require hydrophobic walls and a surfactant



$$\frac{L}{a} \approx 1 + \frac{Q_w}{Q_{oil}}$$



Surfactants:

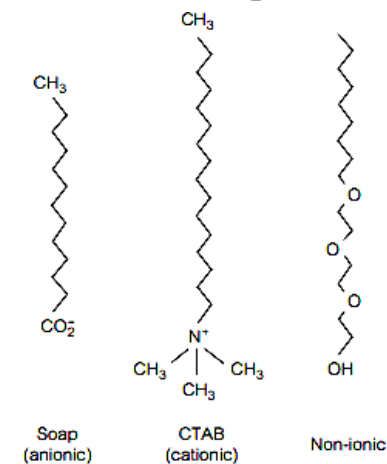
The stability of droplets is maintained by **surfactants**.

Molecules made of two parts:

hydrophilic part 'likes' water

hydrophobic part does not like water

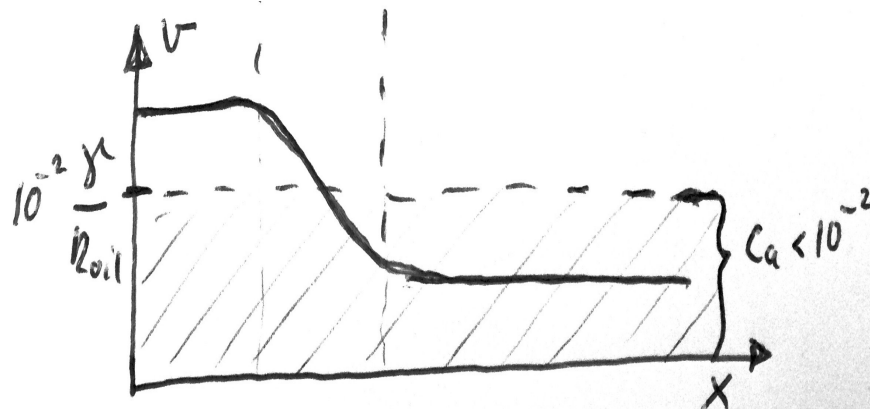
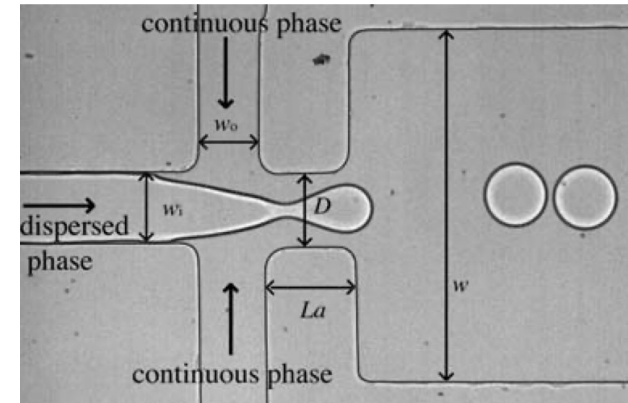
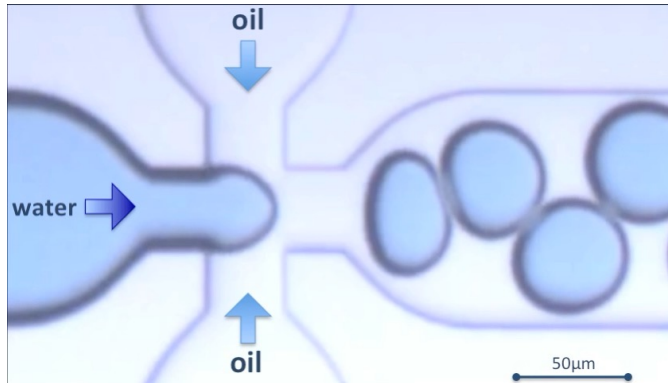
Berthier, p. 175



Tabeling, p.110

Droplets – formation by capillary instability

The droplets are formed by **breaking** the jet by capillary forces (surface tension).



$$Ca_{crit} = \frac{\eta_{oil} v}{\gamma} < 10^{-2}$$

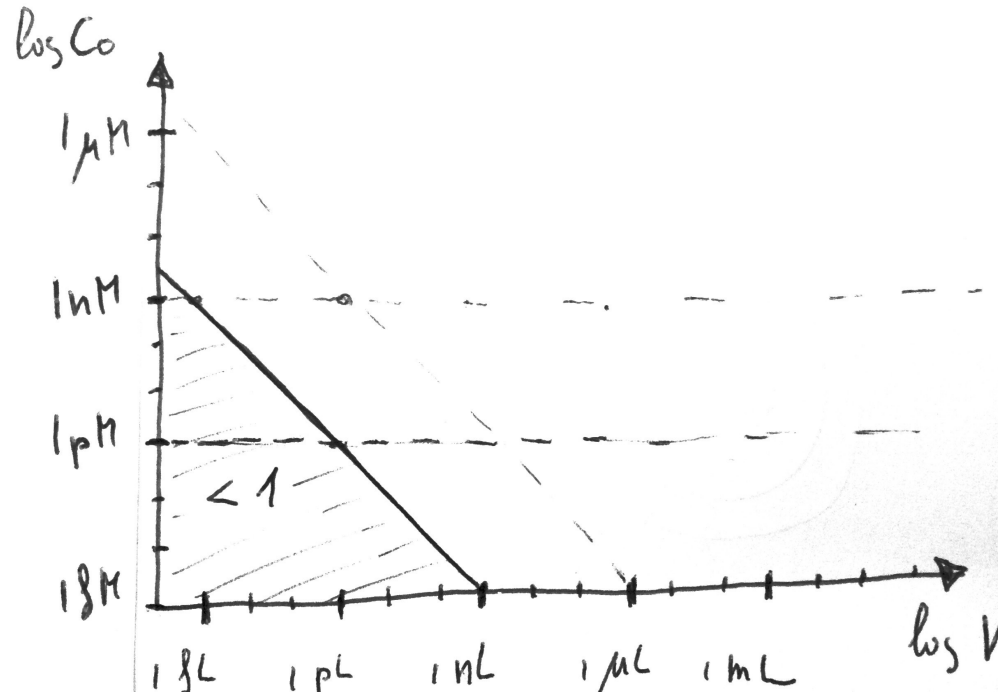
The jet is broken when Ca number is below 10^{-2} (η : viscosity of continuous phase, γ : surface tension)

The Capillary number represents the ratio of **viscous** forces to **surfaces** forces.

Gunther and Jensen, *Lab Chip*, 2006, 6, 1487–1503 and Berthier, p. 183

The dilution (homeopathic) limit

In very small droplet volume, we reach conditions where less than one molecule is present per droplet



Conc.: Nb of molec/mL

1M	$n = 6.10^{20}$ molec/mL
1mM	$n = 6.10^{17}$ molec/mL
1μM	$n = 6.10^{14}$ molec/mL
1nM	$n = 6.10^{11}$ molec/mL
1pM	$n = 6.10^8$ molec/mL
1fM	$n = 6.10^5$ molec/mL

For 1nM concentration :

Volume	1μL	1nL	1pL	1 fL
Size (cube)	1mm	100μm	10μm	1μm
Nb of molecules	6.10^8	6.10^5	600	0.6

Concentration: $1 M = 1 \text{ Mol/liter}$

$1 \text{ Mol} = 6.10^{23} \text{ molecules}$

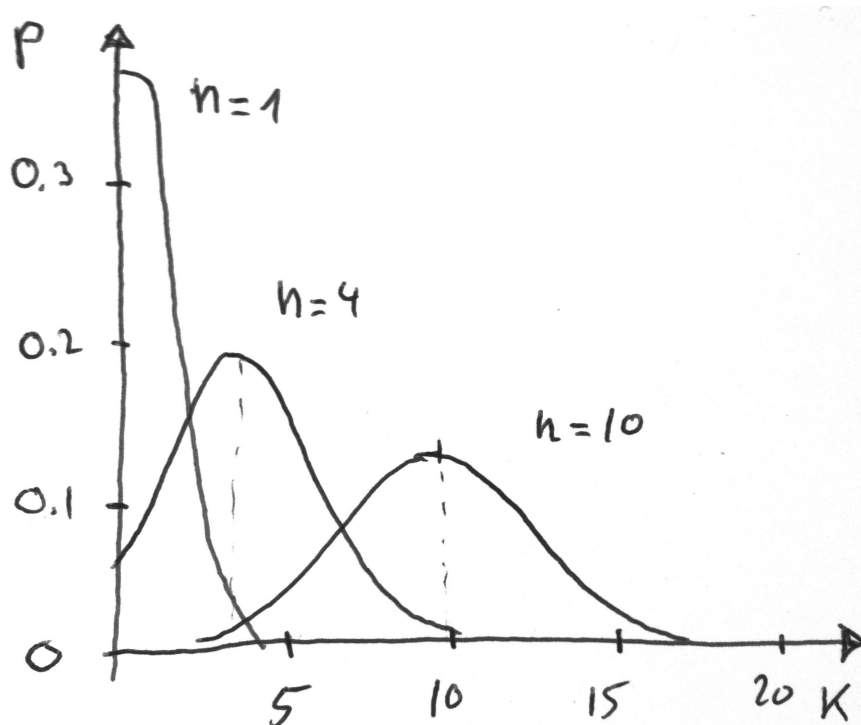
Occupancy statistics at low concentrations in small volumes

The probability distribution of molecules in the well obeys **Poisson** law:

$$p(k;n) = \frac{n^k \cdot e^{-n}}{k!}$$

n : average number of molecules in the volume ($n = C_0 \cdot V \cdot 1000 \cdot N_A$)

$p(k)$: probability of having k molecules in a volume



Probability distribution for different average numbers n

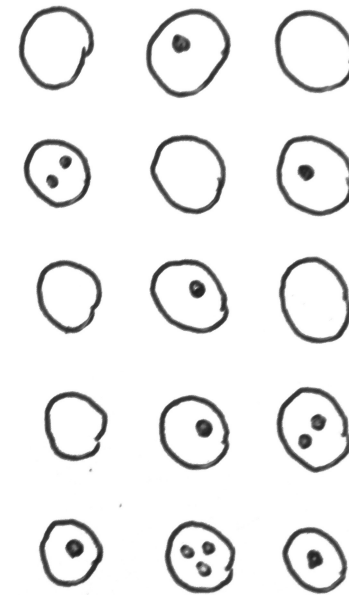
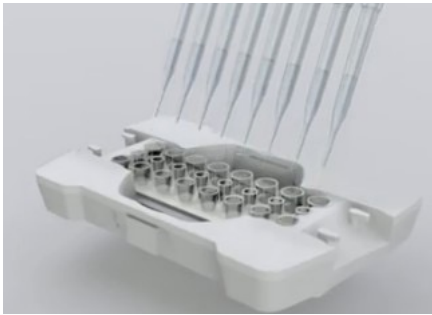
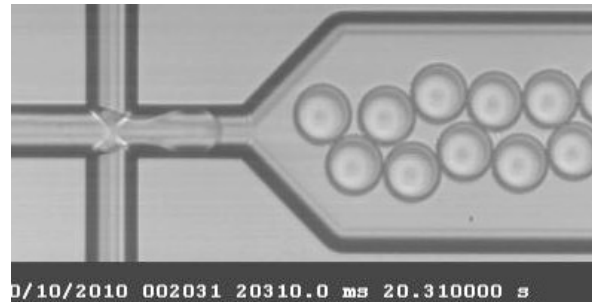


Illustration for for $n=1$

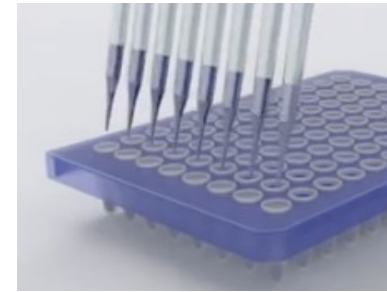
Digital PCR in droplet format (example: Bio-rad, ex QuantaLife)



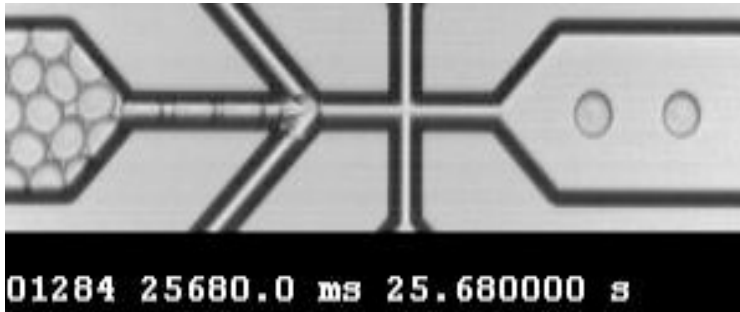
(1) Load samples in chip



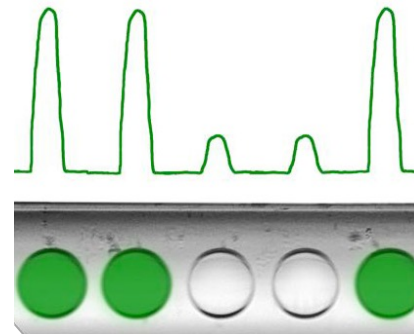
(2) **Partition** into droplets



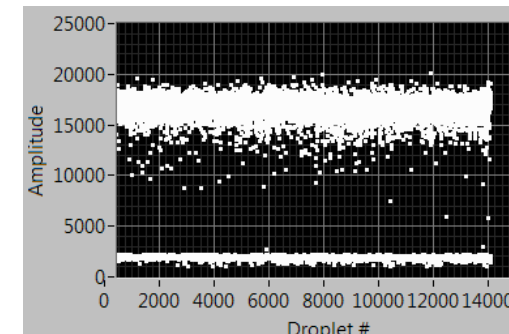
(3) **off-chip** PCR cycles



(4) **Reload** in chip and **align** the droplets



(5) **Read** in flow



(6) **Analysis**

Measured probability of **zeros**

$$p_- = (1 - p_+) = 1 - \frac{2'000}{20'000} = 0.1$$

Number of molecules per chamber

$$n = -\ln(1 - p_+) = 0.10535$$

Calculated concentration of DNA

$$C = \frac{n}{V_0} = \frac{0.10535}{10^{-9} \cdot 1000 \cdot N_A}$$