Lab on a Chip and Microfluidics

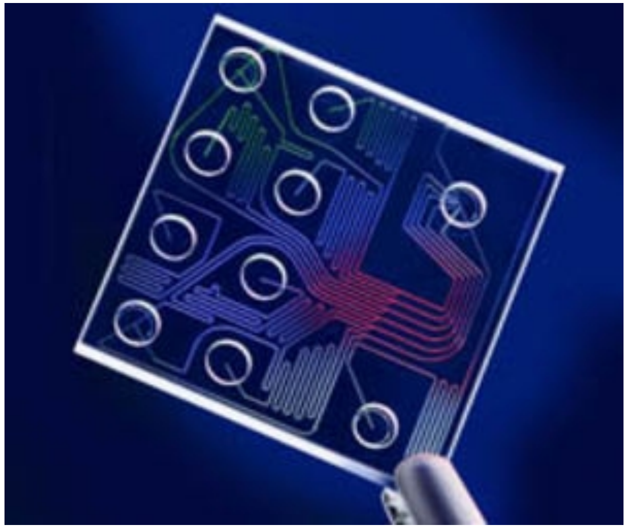
Benoît CHARLOT

http://www.ies.univ-montp2.fr/~charlot/

l'institut d'électronique

Part V. Mixing, Diffusion, Separation

Introduction : Lab On a Chip



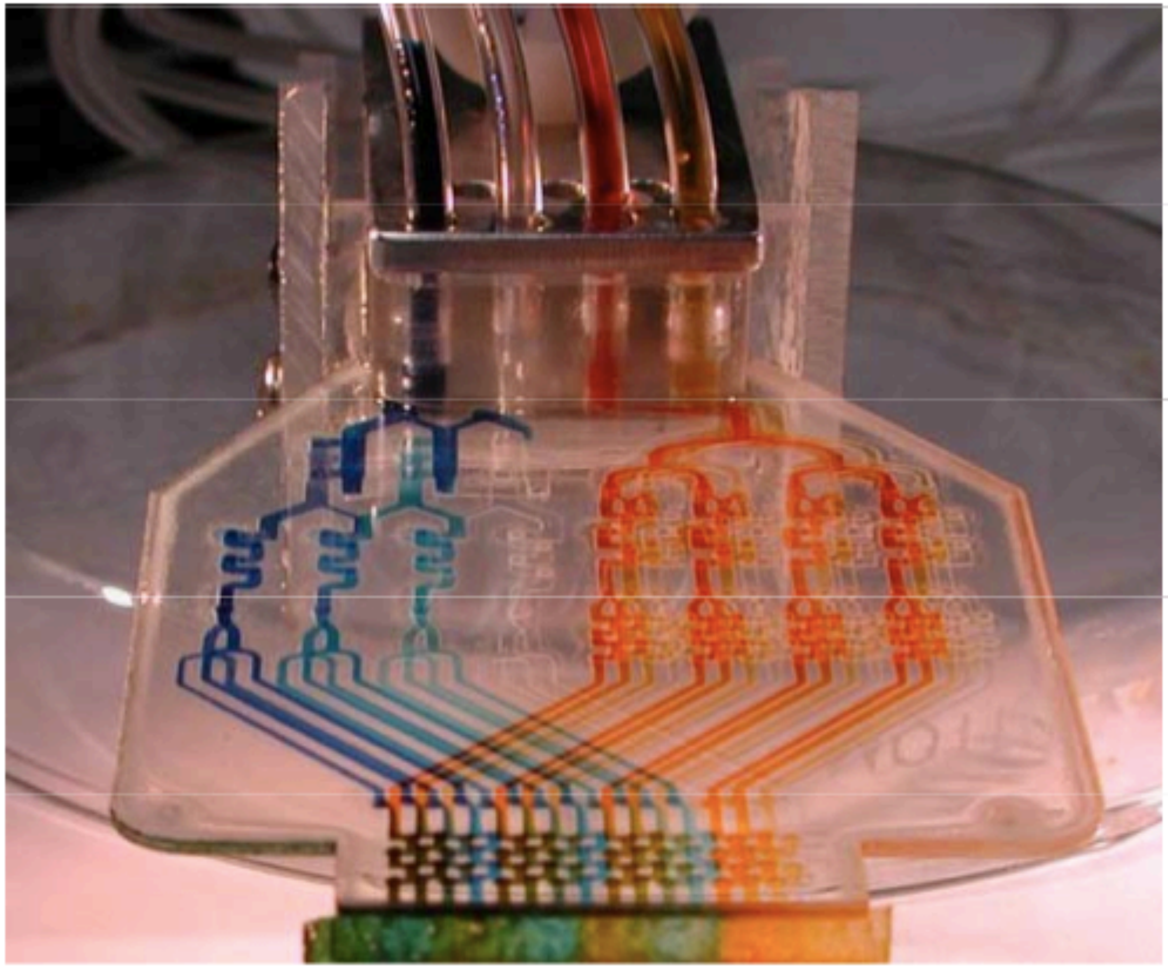
Lab On a Chip (laboratories on chip) LOC
µTAS (micro Total Analysis System)
Point of Care

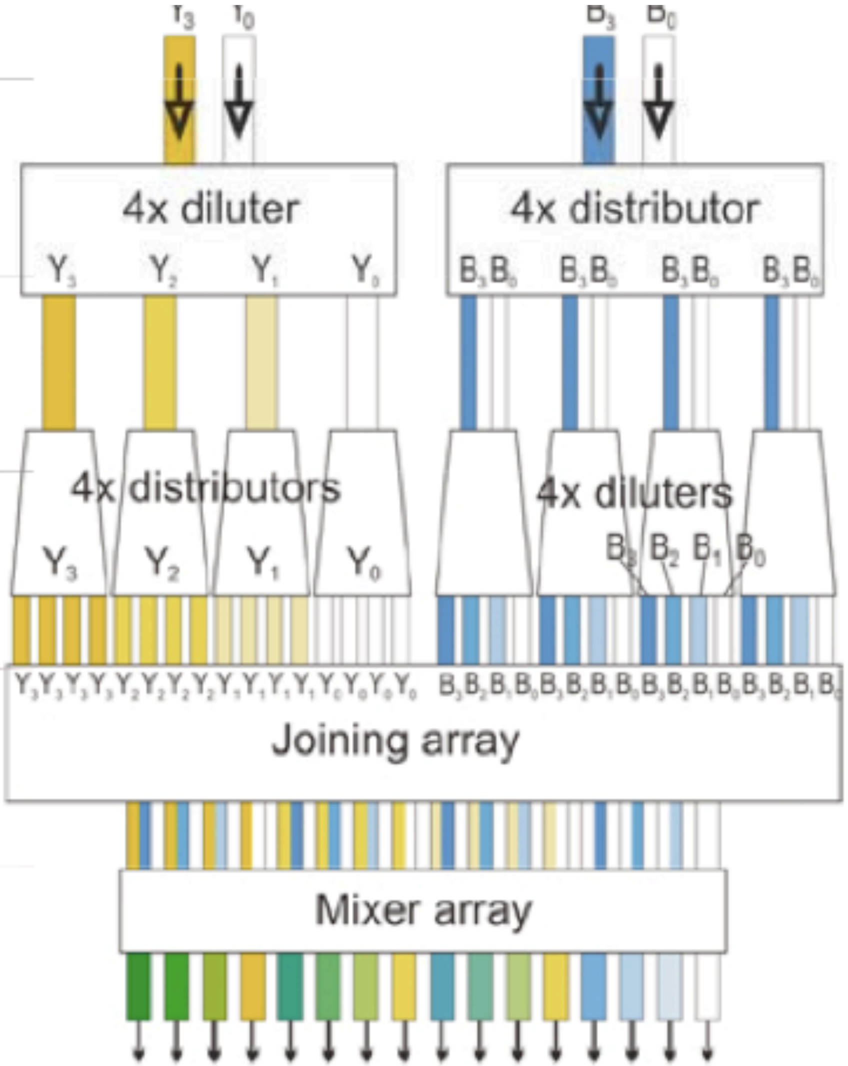
A lab-on-a-chip (LOC) is a device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters to achieve automation and high-throughput screening

Functions operated on a Lab On Chip

- **Fluid transport** (Electro-osmosis, Electro-phoresis, Hydrostatic pressure)
- **Preparation** (Heating, Filtration, Extraction)
- **Separation** (diffusion, electrophoresis, isoelectric focusing)
- **Mixing** (diffusion, forced mixing)
- **Reaction** (culture chambers, markers)
- **Detection** (Chemiluminescence, electrochemiluminescence, fluorescence, Electrochemical detection, mass spectroscopy, Surface Plasmon Resonance)

Dilution

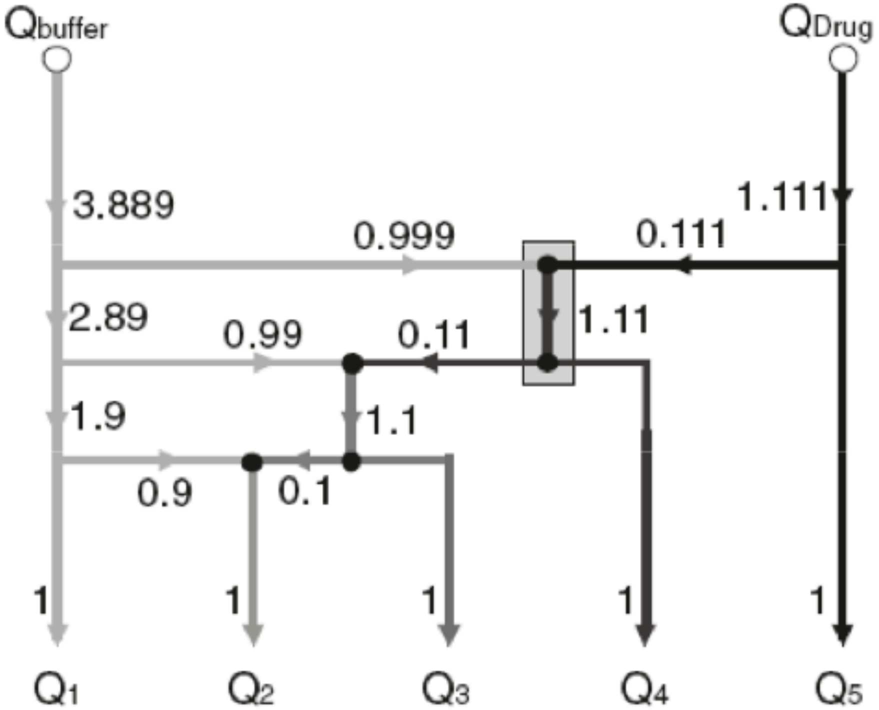


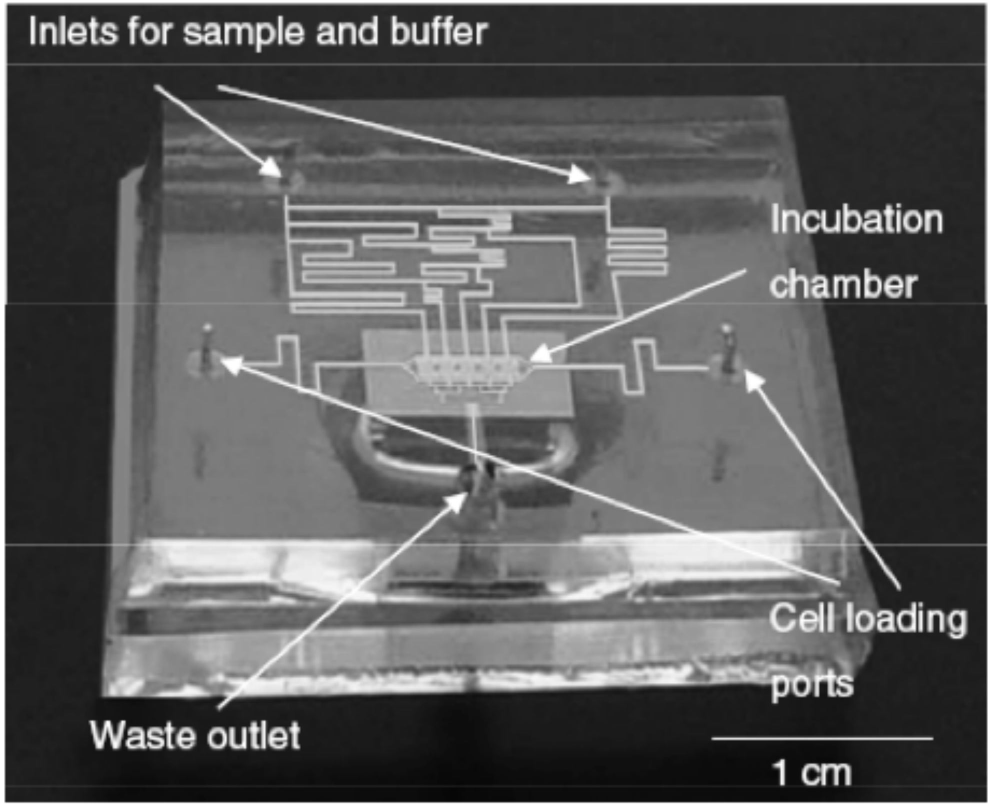


¶ http://faculty.washington.edu/afolch/FolchLabResearchProjects.htm, ¶ Lab Chip, 4 , 342–350, 2004

Dilution

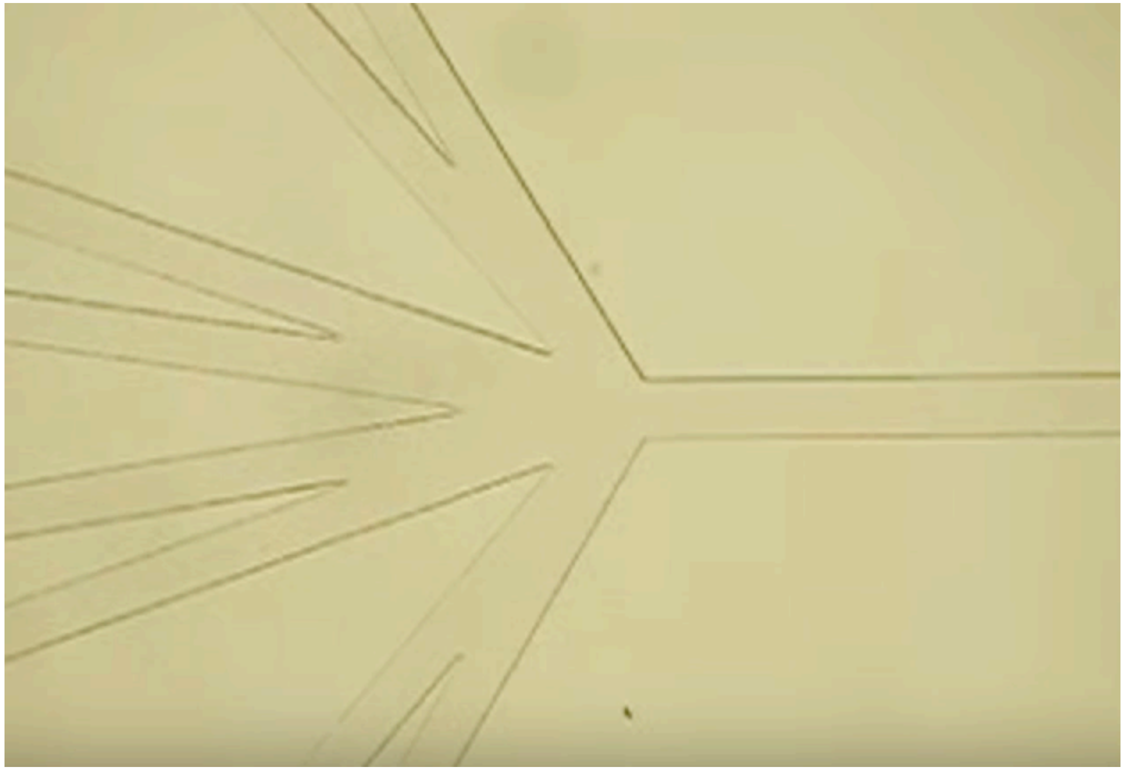
Logarithmic Dilution
Equivalence with Kirchoff law in electricity



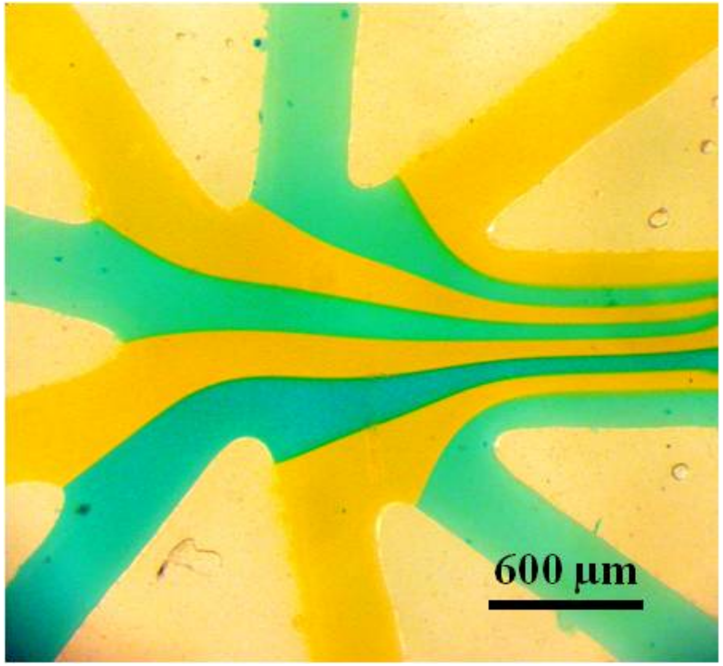


Mixing

In microfluidics, low R_e : highly laminar flow, no transport in between liquids

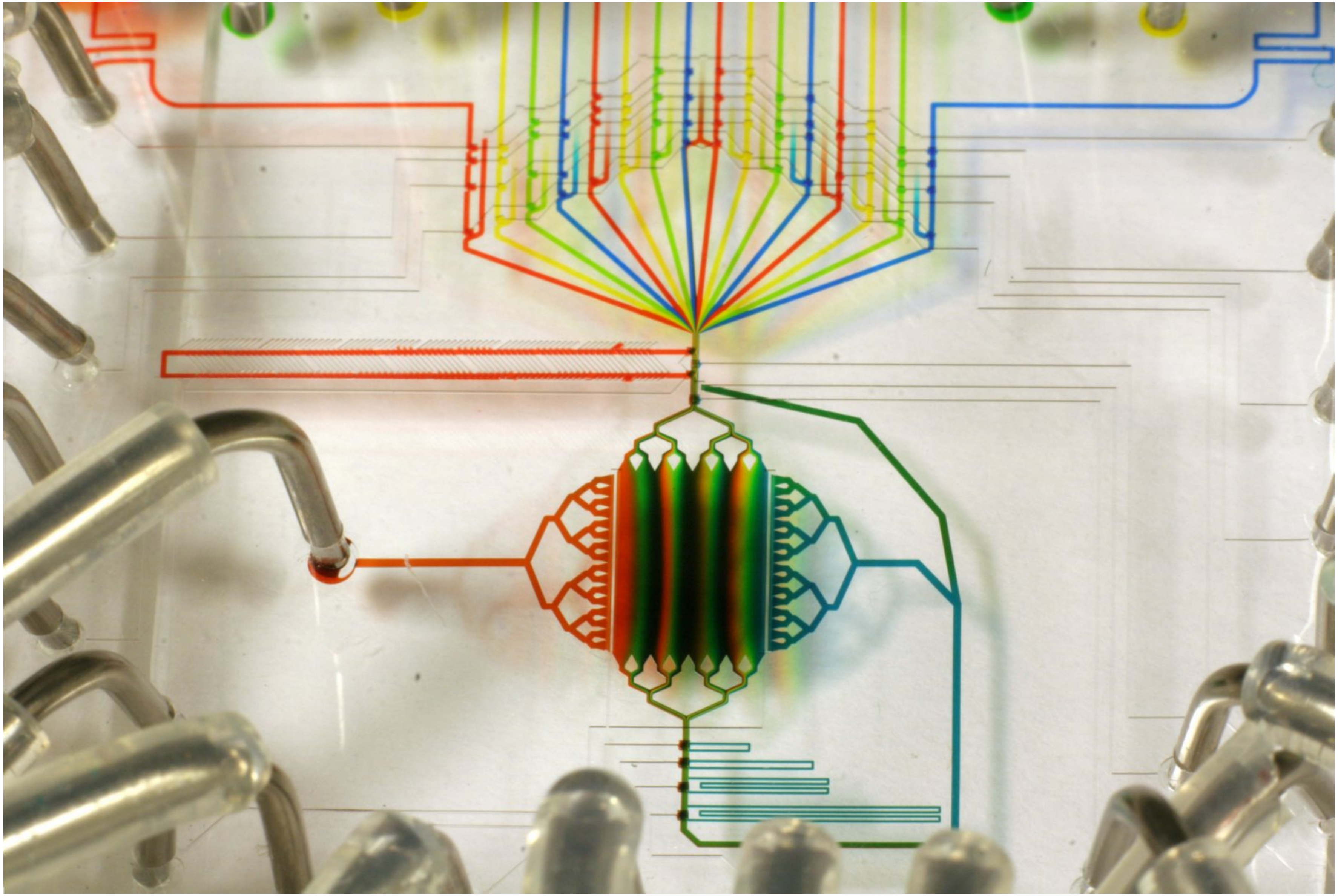


Albert Folch, Univ. Washington



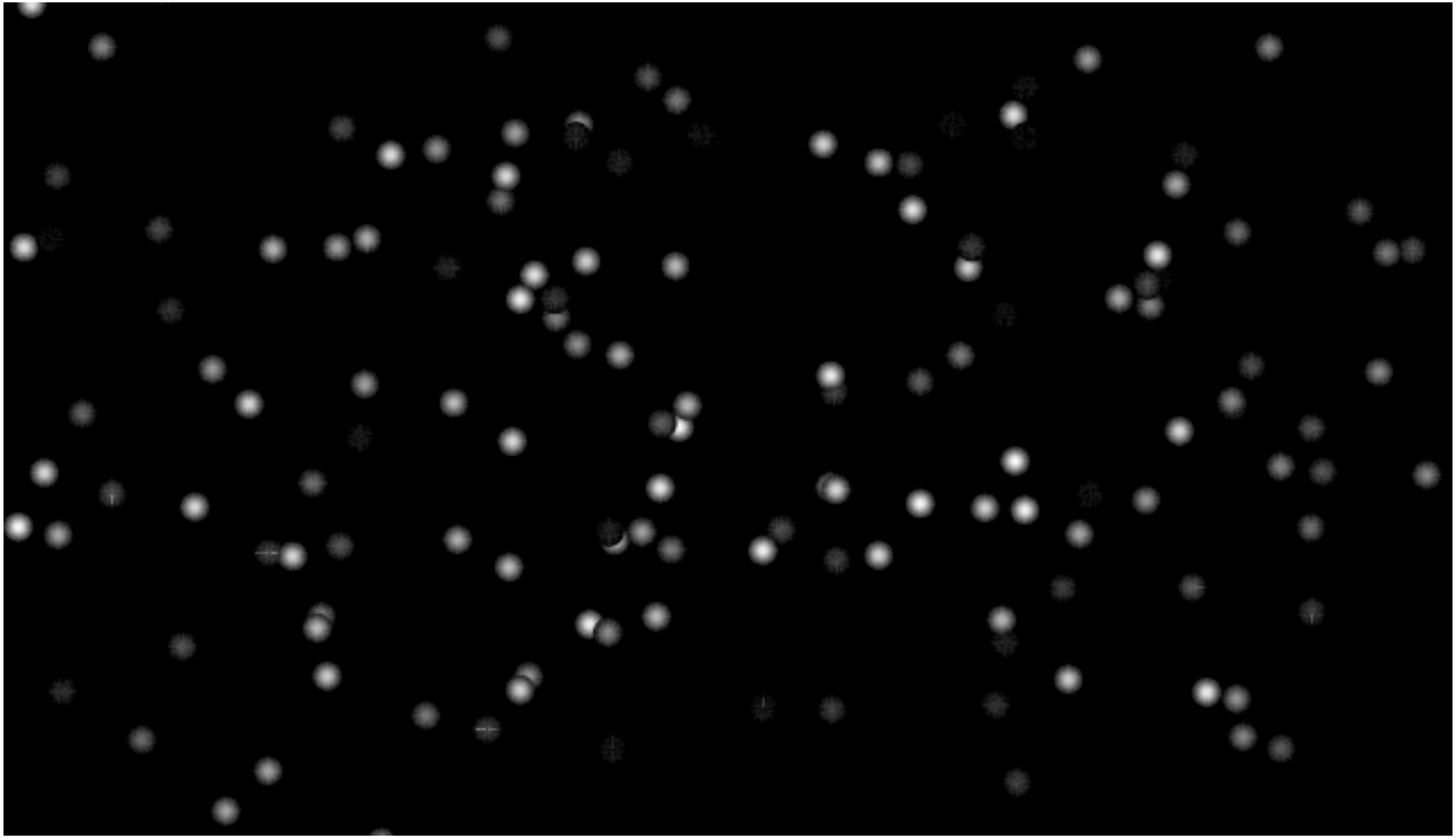
How to mix liquids?

Mixing



Albert Folch, Univ. Washington

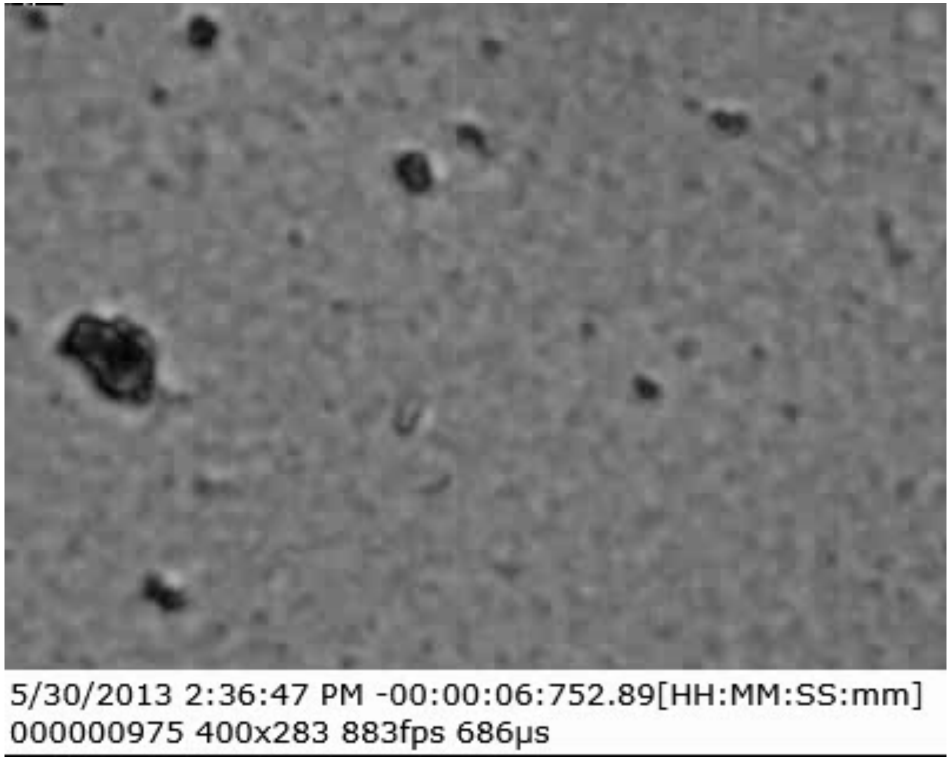
Brownian motion

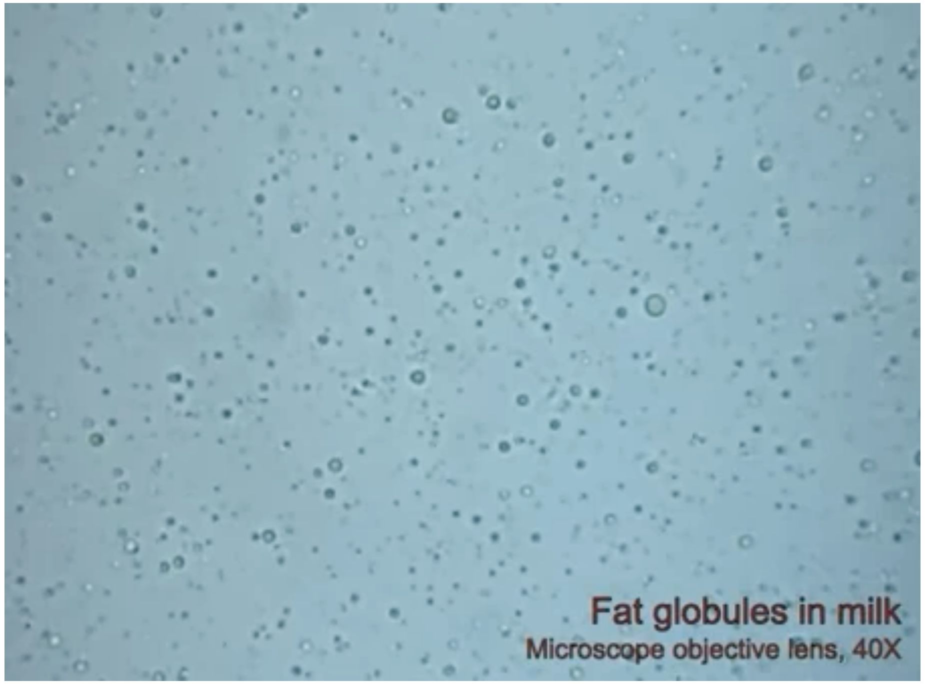


μ is the mobility (not viscosity)

$$D = \mu k_b T$$

Brownian motion





µ is the mobility (not viscosity)

$$D = \mu k_b T$$

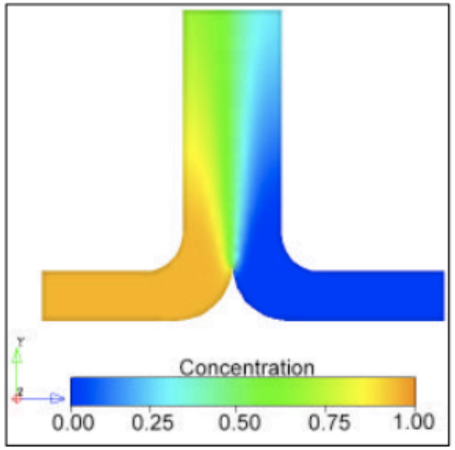
Diffusion

Diffusion is the net movement of molecules or atoms from a region of **high** concentration to a region of **low** concentration.

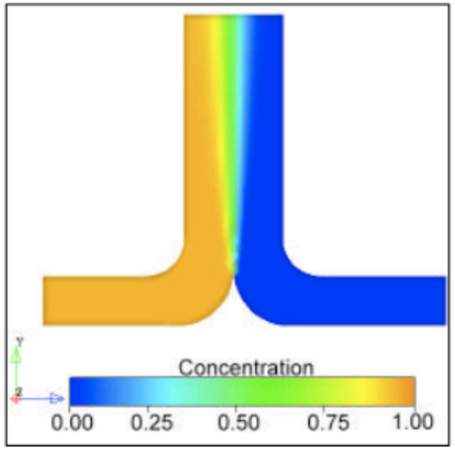
Fick's law

$$\vec{j}_{diff} = -D\vec{\nabla}C$$

$$\vec{j}_{diff} = -D.gr\vec{a}dC$$



biotin (D ~ 350 $\mu m^2/s$)



albumin (D ~ 65 $\mu m^2/s$)

Diffusion

A distribution of a quantity $\varphi(r,t)$

Fick's law

$$\vec{j}_{diff} = -D\vec{\nabla}C$$

$$\vec{j}_{diff} = -D.gr\vec{a}dC$$

Particules conservation

$$\vec{\nabla}.\vec{j} + \frac{\partial \varphi}{\partial t} = 0$$

$$div\vec{j} + \frac{\partial \varphi}{\partial t} = 0$$

$$\frac{\partial \varphi}{\partial t} = D\Delta\varphi$$

3D diffusion equation

The same as heat diffusion equation

$$\rho c \frac{\partial T}{\partial t} = \lambda \nabla^2 \varphi$$

density

Specific heat

Thermal conductivity

Diffusion

Some Diffusion coeficients

Molecule in a gaz	D= $2.10^{7}\ \mu m^{2}.s^{-1}$
Water molecule in water	D= $2000\ \mu m^{2}.s^{-1}$
Ion in water	D= $200\ \mu m^{2}.s^{-1}$
DNA 30pb	D= $40\ \mu m^{2}.s^{-1}$
DNA 5Kbp	D= $1\ \mu m^{2}.s^{-1}$
Al in Cu (solid solid)	D= $1,3.10^{-18}\ \mu m^{2}.s^{-1}$

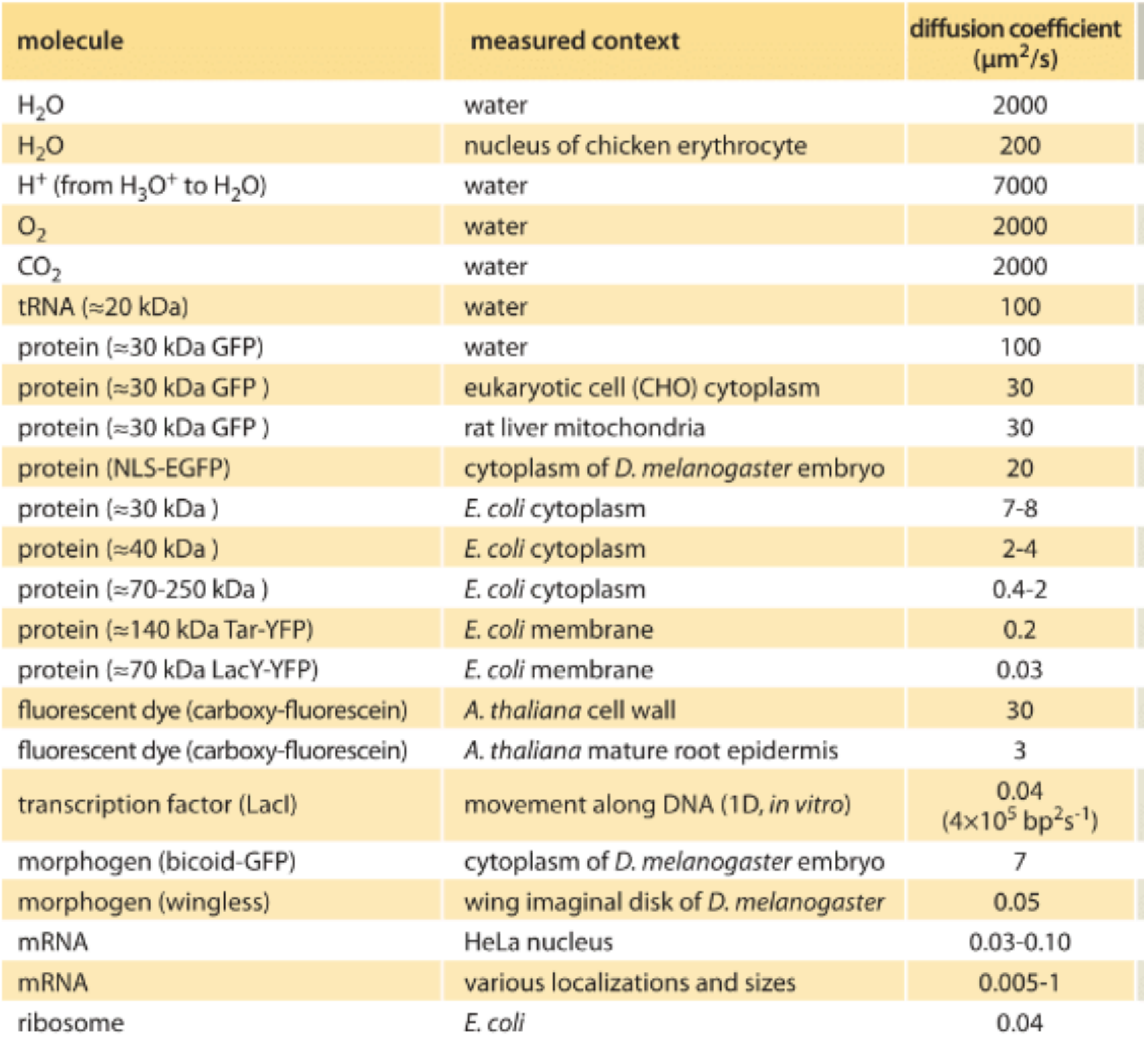
Stokes Einstein equation

Diffusion coeficient for a particule of radius r in a liquid with a viscosity μ (low Reynolds)

$$D = \frac{k_b T}{6\pi\mu r}$$

Diffusion

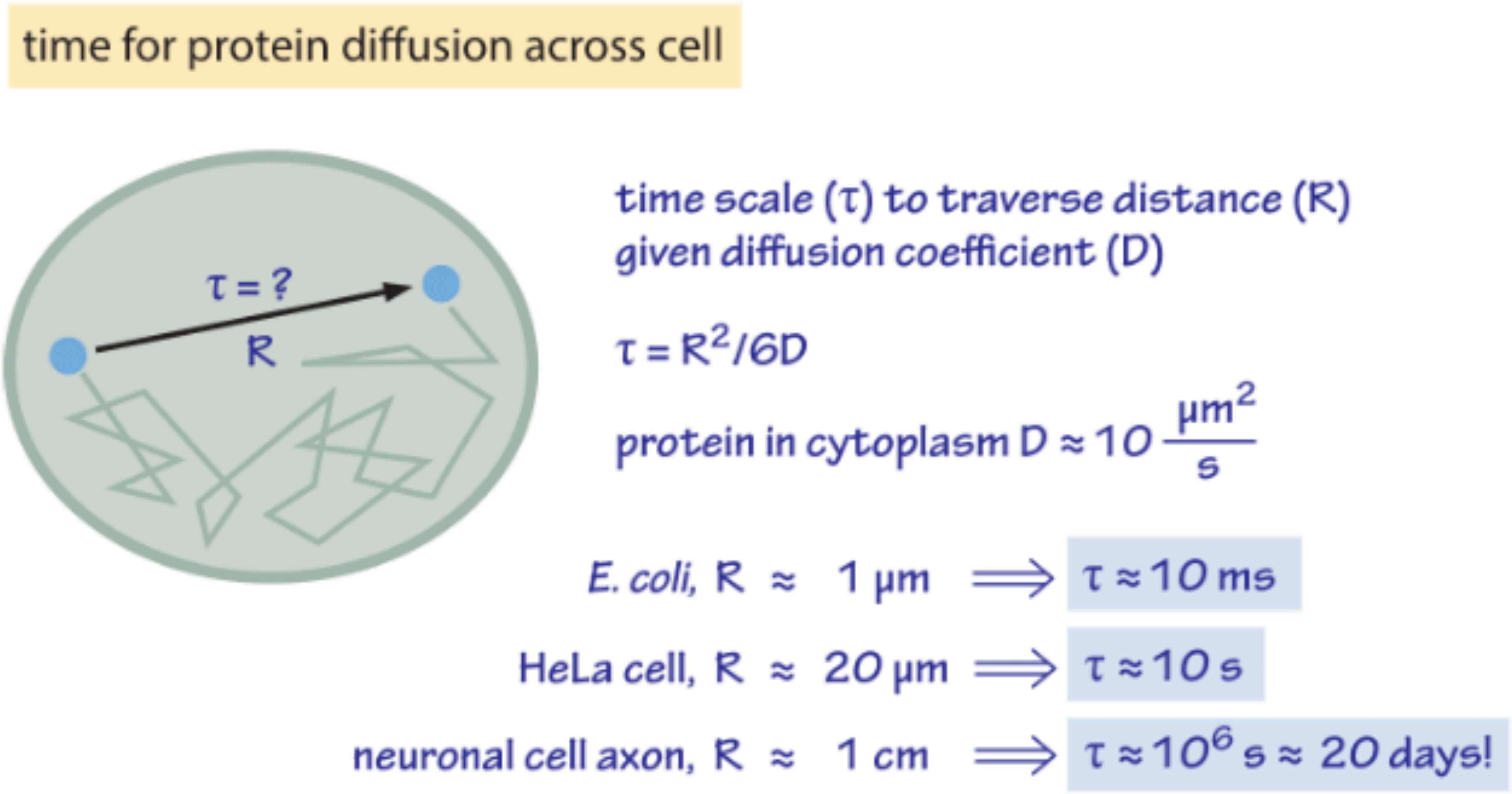
More diffusion coefficients



molecule	measured context	diffusion coefficient ($\mu m^2/s$)
H_2O	water	2000
H_2O	nucleus of chicken erythrocyte	200
H^+ (from H_3O^+ to H_2O)	water	7000
O_2	water	2000
CO_2	water	2000
tRNA (≈20 kDa)	water	100
protein (≈30 kDa GFP)	water	100
protein (≈30 kDa GFP)	eukaryotic cell (CHO) cytoplasm	30
protein (≈30 kDa GFP)	rat liver mitochondria	30
protein (NLS-EGFP)	cytoplasm of *D. melanogaster* embryo	20
protein (≈30 kDa)	*E. coli* cytoplasm	7-8
protein (≈40 kDa)	*E. coli* cytoplasm	2-4
protein (≈70-250 kDa)	*E. coli* cytoplasm	0.4-2
protein (≈140 kDa Tar-YFP)	*E. coli* membrane	0.2
protein (≈70 kDa LacY-YFP)	*E. coli* membrane	0.03
fluorescent dye (carboxy-fluorescein)	*A. thaliana* cell wall	30
fluorescent dye (carboxy-fluorescein)	*A. thaliana* mature root epidermis	3
transcription factor (LacI)	movement along DNA (1D, *in vitro*)	0.04 (4×10^5 bp^2s^{-1})
morphogen (bicoid-GFP)	cytoplasm of *D. melanogaster* embryo	7
morphogen (wingless)	wing imaginal disk of *D. melanogaster*	0.05
mRNA	HeLa nucleus	0.03-0.10
mRNA	various localizations and sizes	0.005-1
ribosome	*E. coli*	0.04

Diffusion

In cells



time for protein diffusion across cell

time scale (τ) to traverse distance (R) given diffusion coefficient (D)

$\tau = R^2/6D$

protein in cytoplasm $D \approx 10 \, \frac{\mu m^2}{s}$

E. coli, $R \approx 1\ \mu m \implies \tau \approx 10\ ms$

HeLa cell, $R \approx 20\ \mu m \implies \tau \approx 10\ s$

neuronal cell axon, $R \approx 1\ cm \implies \tau \approx 10^6\ s \approx 20$ days!

Ron MILO and Rob PHILLIPS, CELL BIOLOGY by the NUMBERS
http://book.bionumbers.org/

Diffusion

Diffusion time $\tau \approx \frac{l^2}{D}$

Grenadine syrup
l=10cm
D=10^{-9}

τ =10^7s (100 days)

Socks
l=170cm
D=2. 10^{-5}

τ =0,85 10^5s (1 day)

Diffusion Advection

transport of a quantity (scalar or vector) by a vector field

Advection diffusion equation

$$\frac{\partial C}{\partial t} = \nabla.(D\nabla C) - \nabla.\vec{v}C + S$$

C interest value (concentration, temperature...)
D diffusivity (coefficient of diffusion)
V velocity

$$\frac{\partial C}{\partial t} = div(D.gr\vec{a}dC) - div(\vec{v}C) + S$$

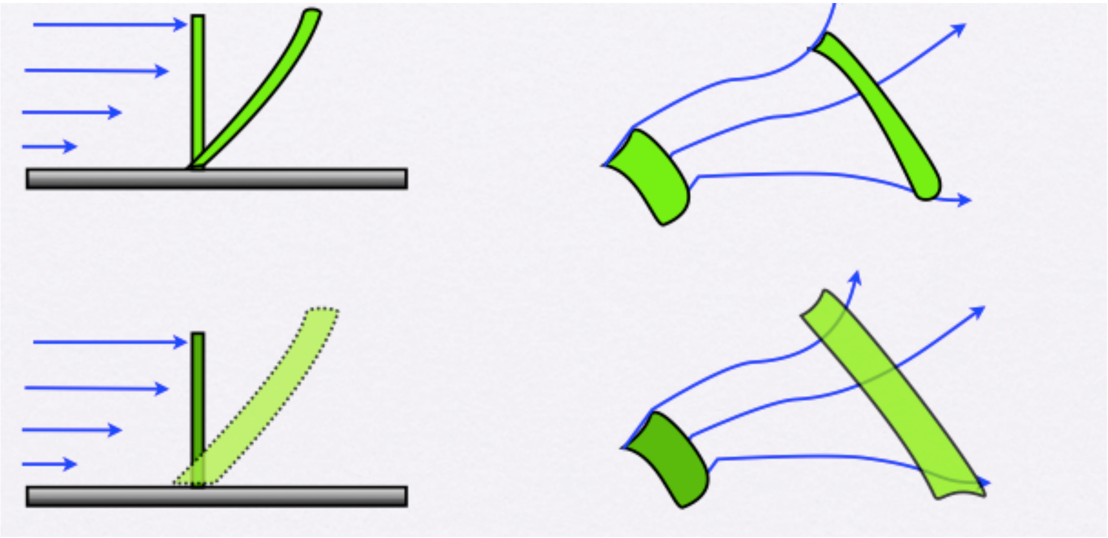
Simplifies in

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \vec{v}.\nabla C$$

$$P_e = \frac{UL}{D}$$

Péclet Number compares the advection time to the diffusion time

If D=0, pure advection



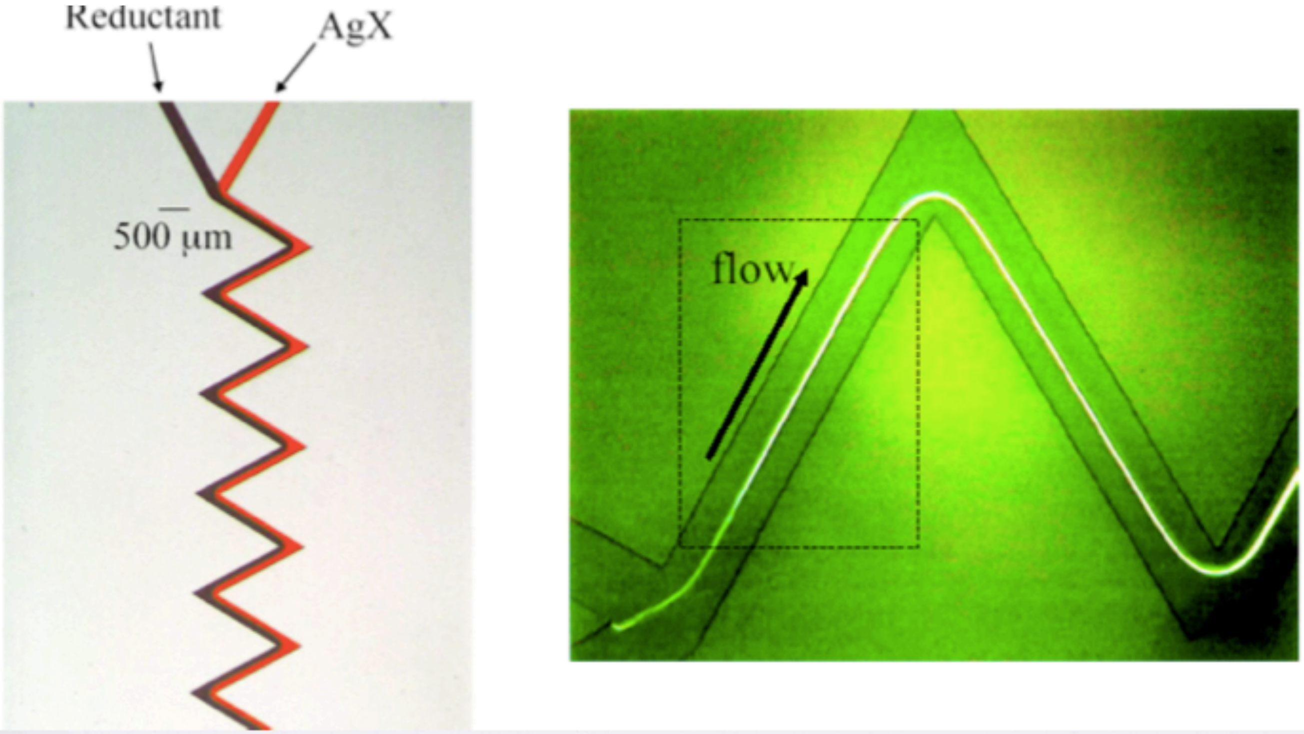
Diffusion Advection

Péclet number in microfluidics?

For D 10^{-5} cm^2/s

100µm wide channel and 1mm/s velocity -> Pe=100
1µm wide channel and 10µm/s velocity -> Pe =0,01

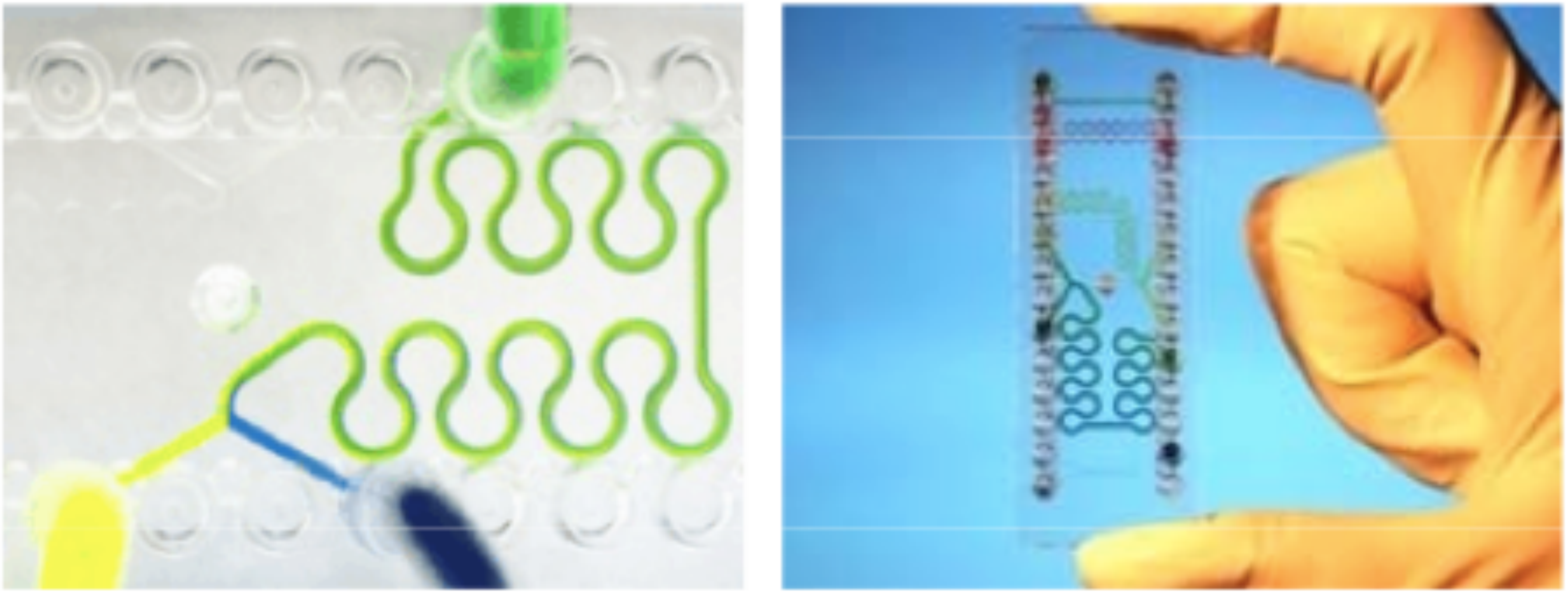
If Pe>> 1 high Péclet regime, advection preponderance



Kenis, P.J.A., Ismagilov, R.F. & Whitesides, G.M. Science 285, 83–85 (1999)

Mixing

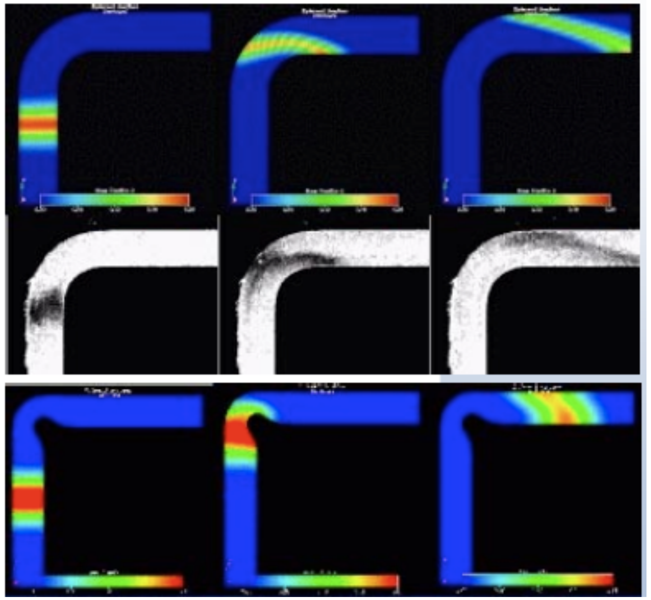
How to improve diffusion in microfluidics?

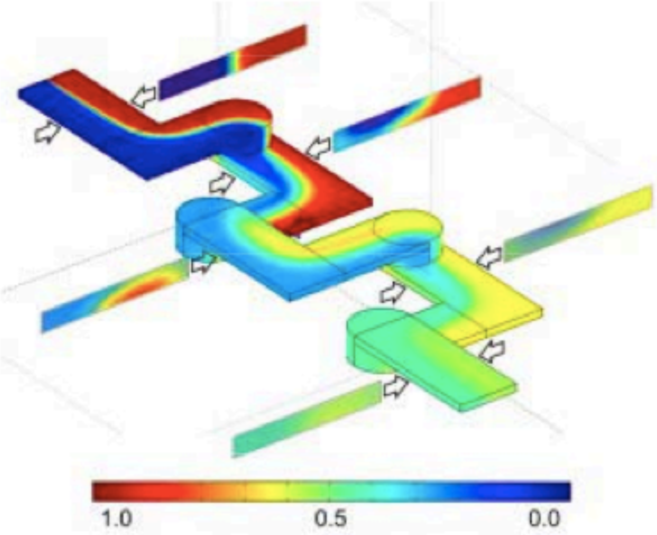


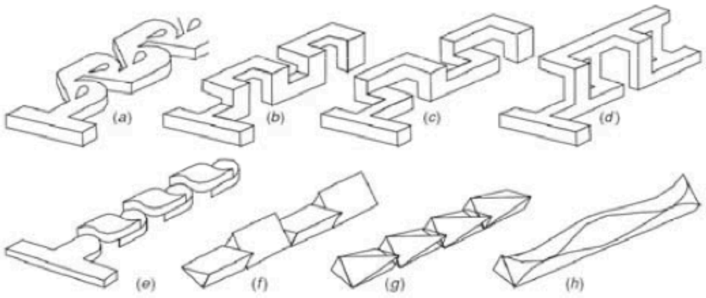
By lengthening the course .... But not only

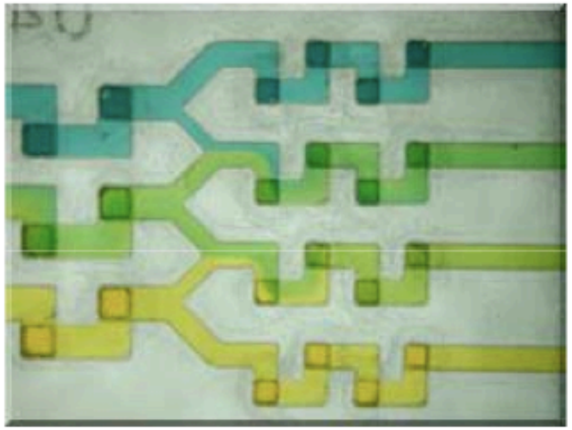
Mixing

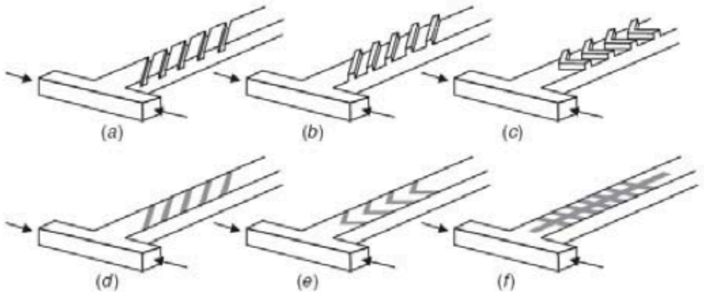
Diffusion + geometric dispersion





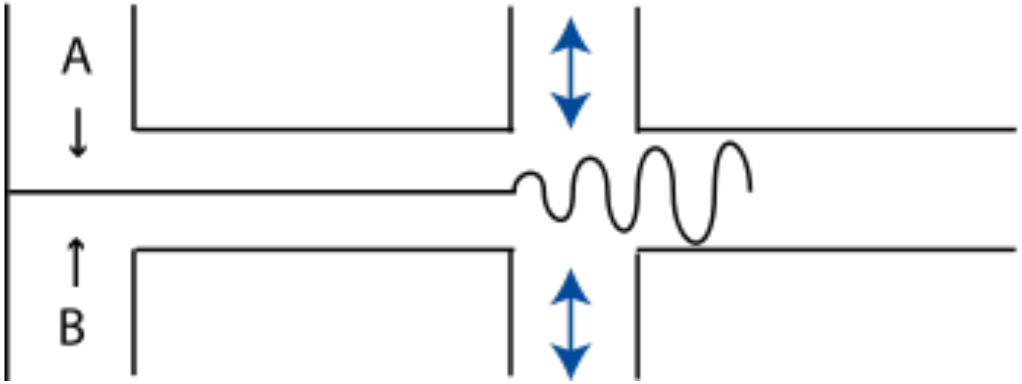


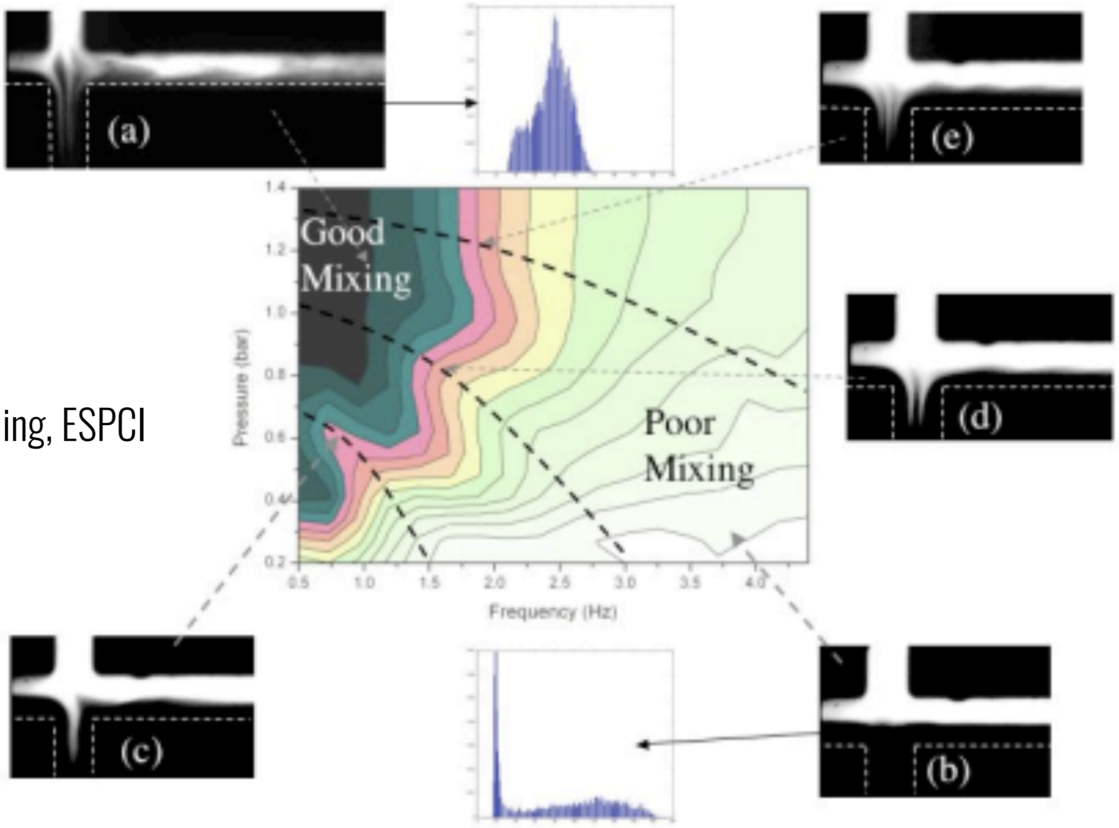




Mixing

Diffusion + geometric dispersion



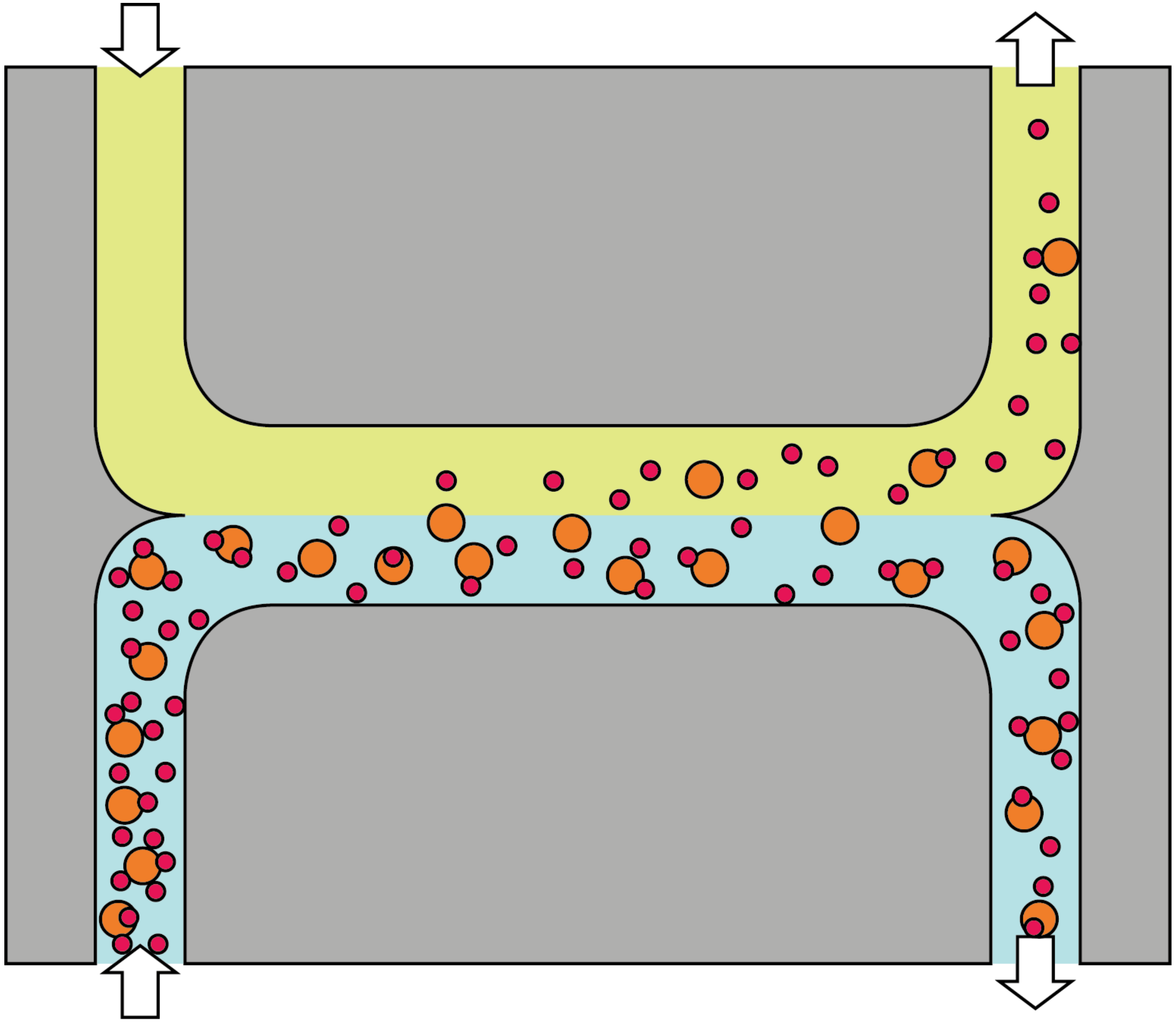


P.Tabeling, ESPCI

Separation

Difference of diffusion can be used to separate species :

difference of diffusivity in a H-shaped bifurcation



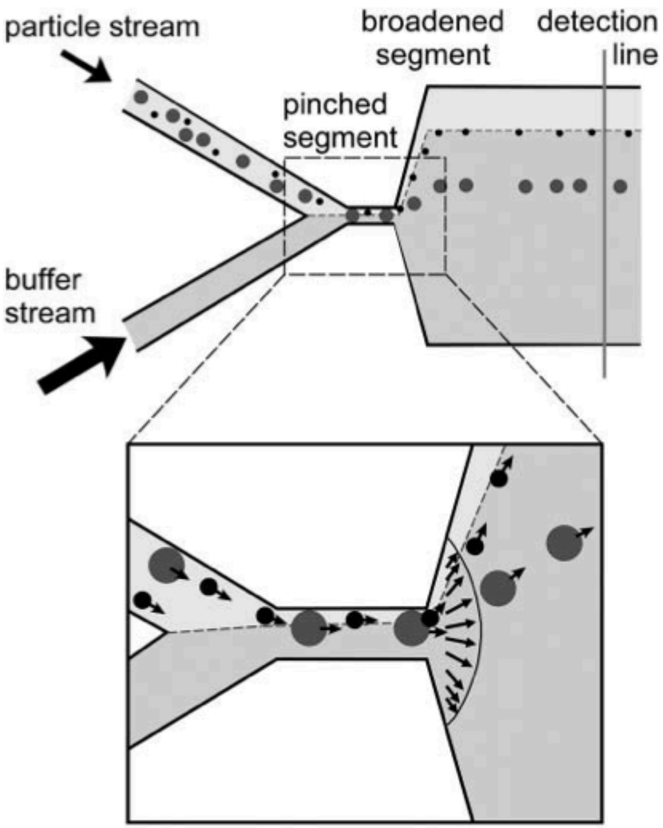
Separation Pinched flow fractionation

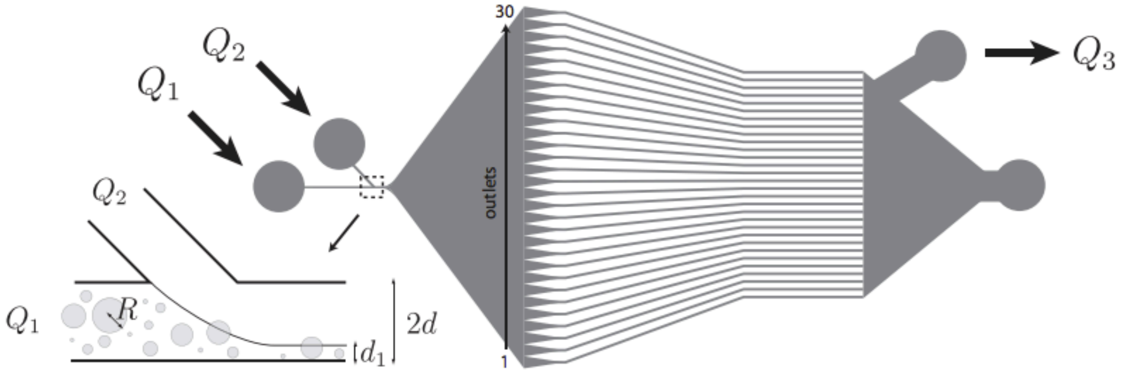
Particles are stucked along one wall by a buffer stream

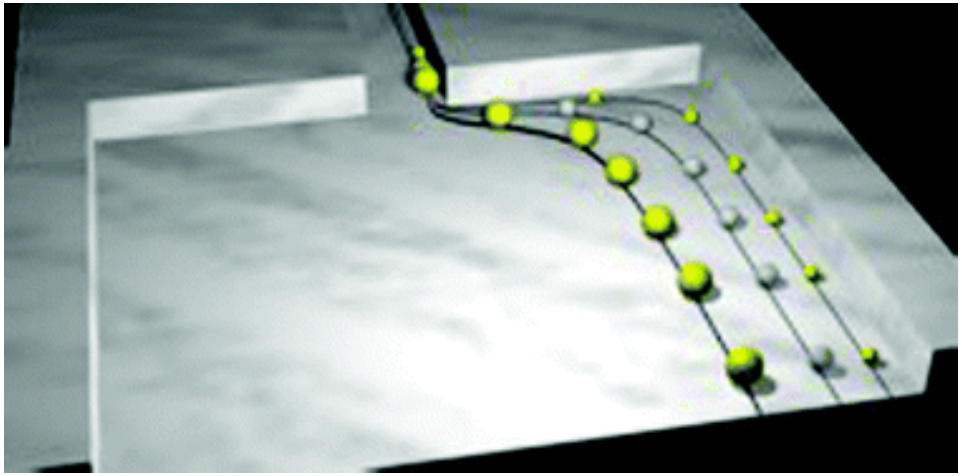
-different particle size = different position regarding the wall

-Expansion of the flow

-Collection of particles by streamlines



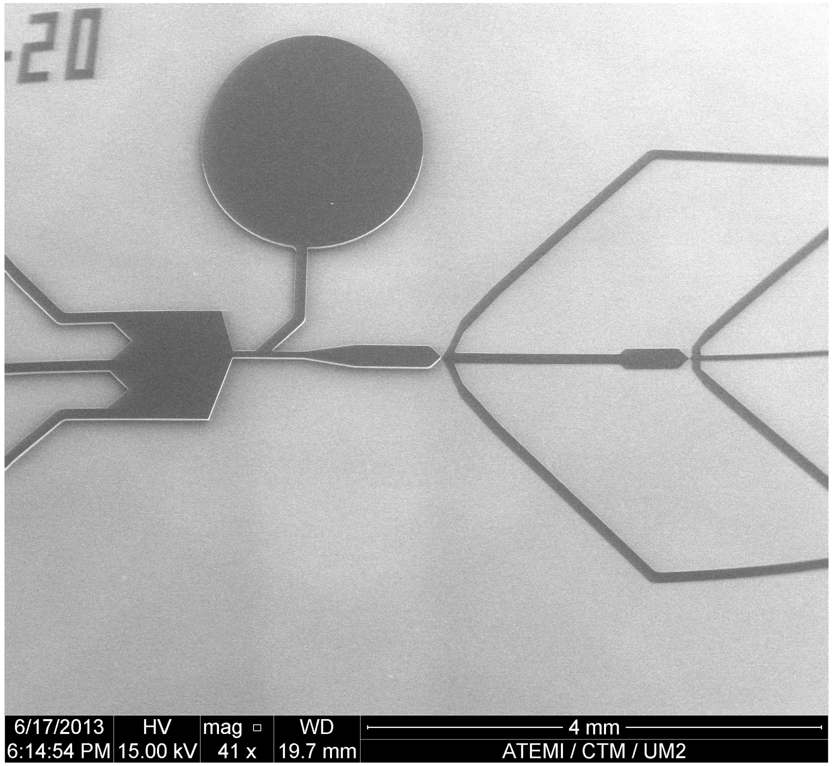


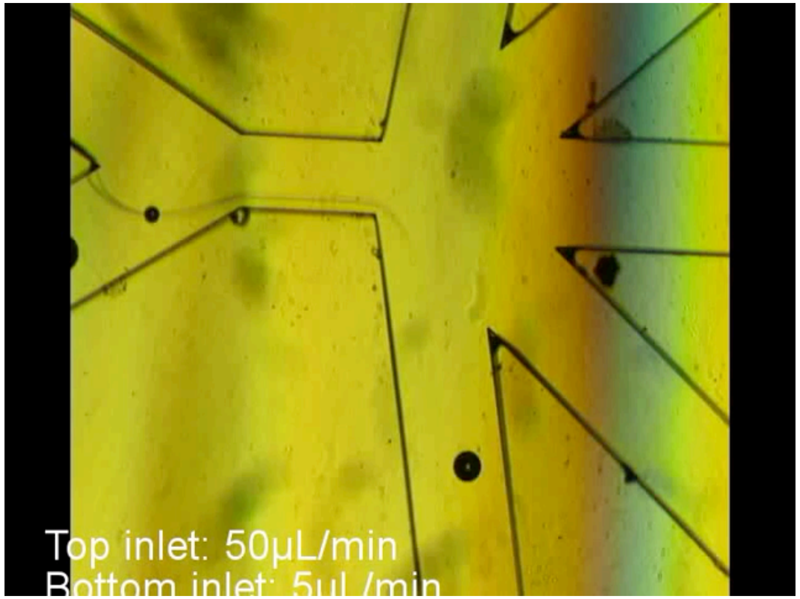


N.Pamme Lab Chip, 2007, 7, 1644–1659

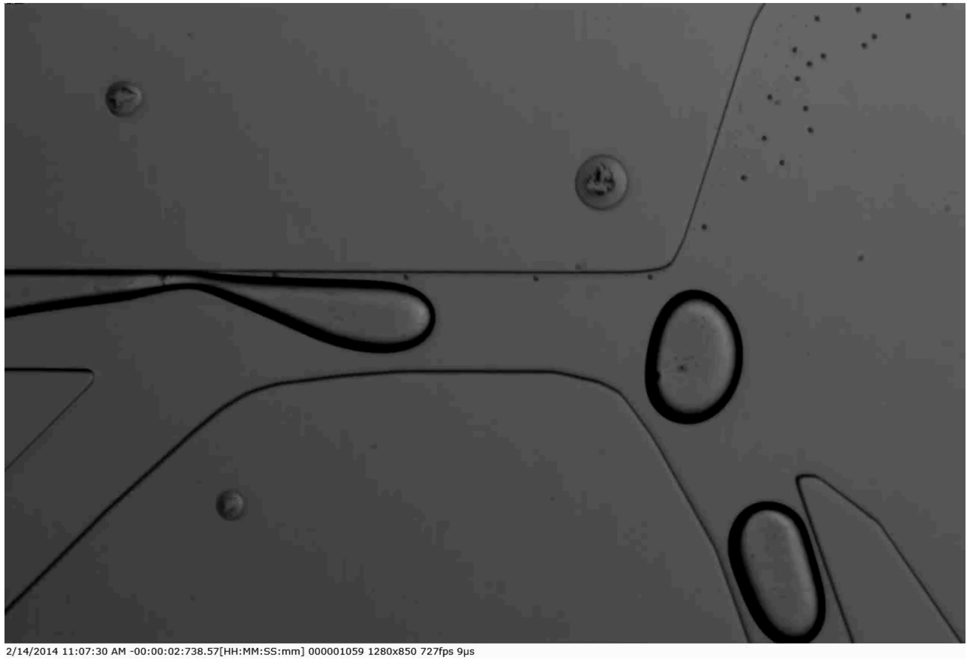
Separation Pinched flow fractionation

Example



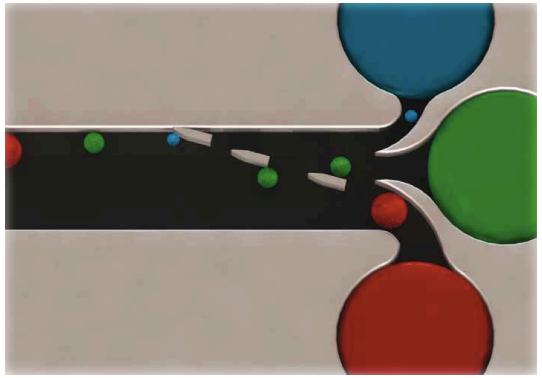


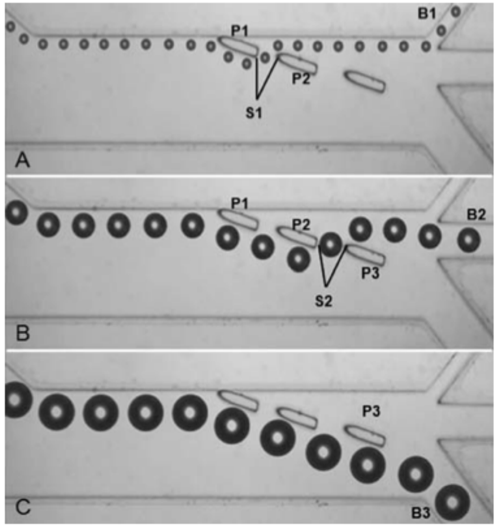
University of Twente and BIOS.

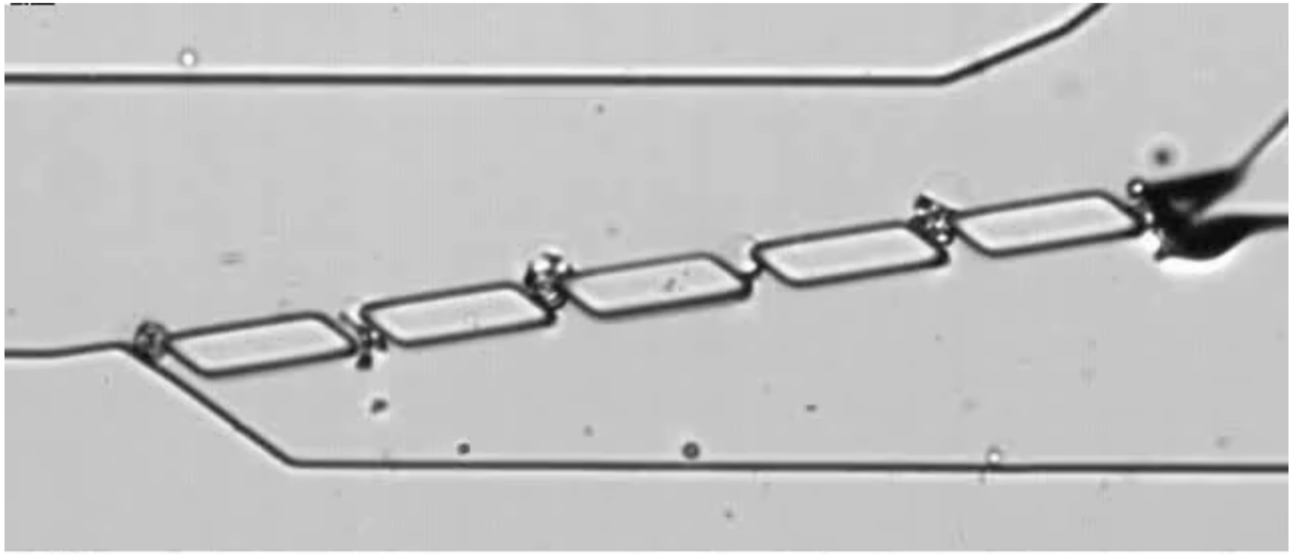


Separation

Separation by filtering



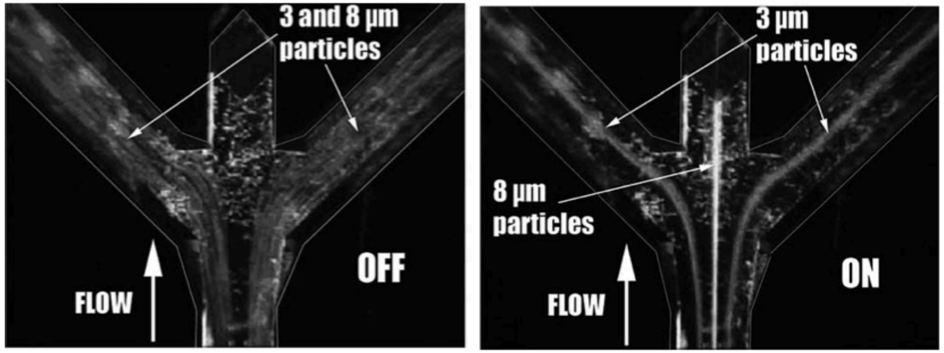




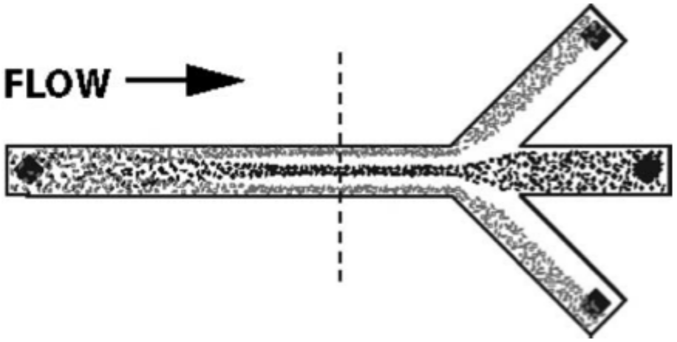
9/16/2013 5:19:03 PM -00:00:03:345.56[HH:MM:SS:mm] 000001552 640x273 4070fps 57µs

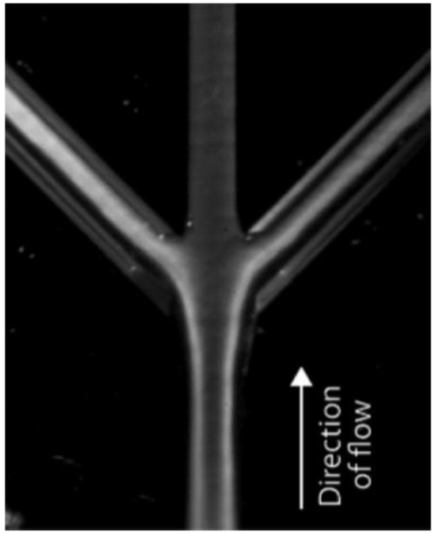
Separation Acousto fluidics

- Creation of ultrasonic standing wave in a fluidic microchannel
- Nodes and anti nodes are created along the channel
- Compressive particles are sorted by size

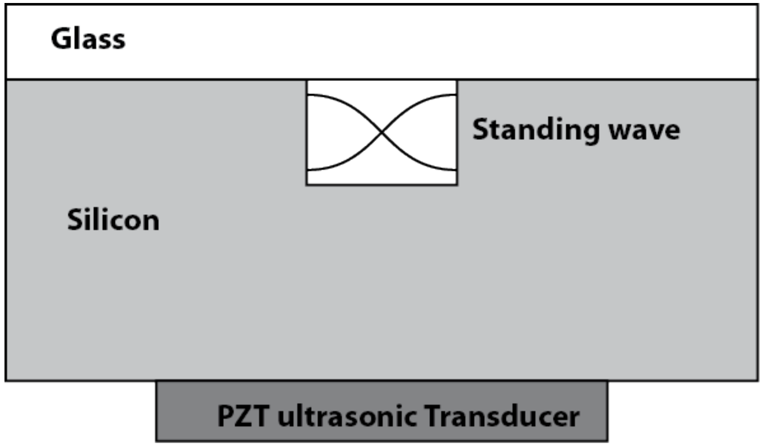


Lenshof et al. Lab Chip, 2012, 12, 1210





Laurell et al. Chem. Soc.
Rev., 2007, 36, 492–506



Lab on a Chip and Microfluidics

Benoît CHARLOT

http://www.ies.univ-montp2.fr/~charlot/

l'institut d'électronique