Polymers in Soft and Biological Matter
2012

MICROFLUIDICS

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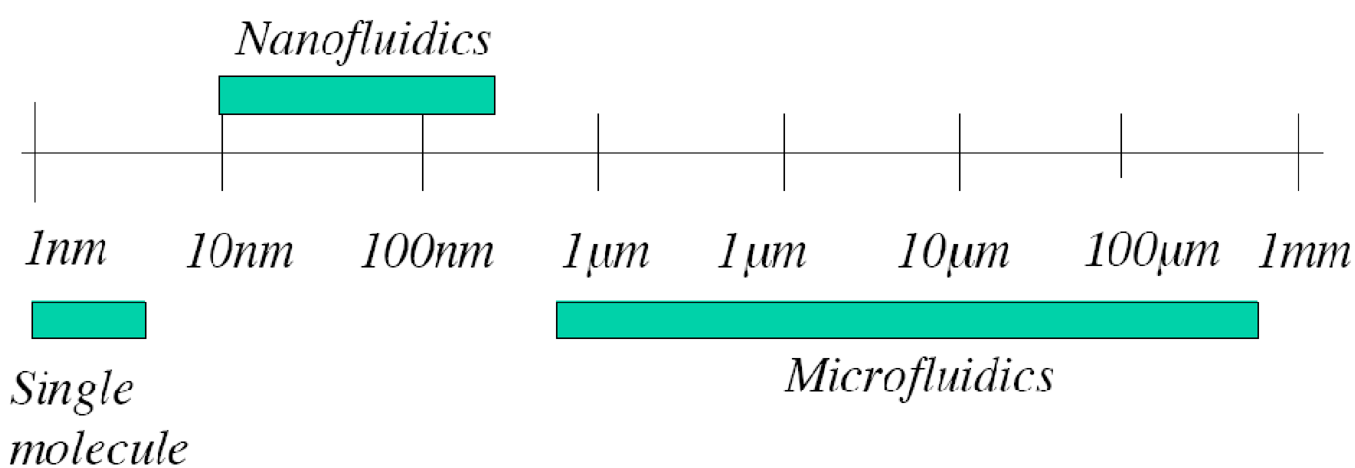
1. Fundamentals of microfludics
2. Topics in microfluidics

Microfluidics is the area of science and technology that is focused on simple or complex, mono- or multiphasic flows that are circulating in natural or artificial ***micro*** systems with at least, one dimension of below 500 μm (sometimes below 1000 μm)



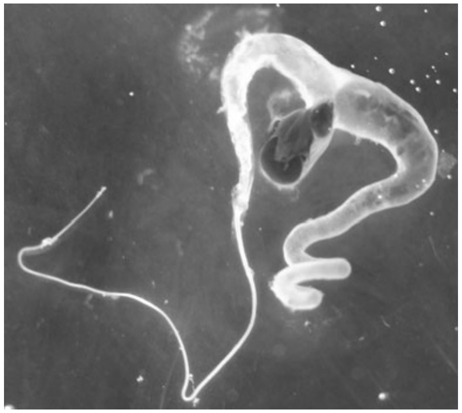
Microfluidic systems in nature

- A tree bringing water and nutrients to the leaves via a complex network of capillaries

A capillary network of hundreds of thousands of microchannels with diameters between 100 μm (in the trunk) and 10's of nm (in the leaf).

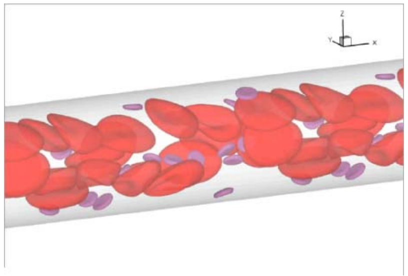
The hydrodynamics of the system: *the ability of the capillaries to deform under the effect* of pressure), the significance of *capillary effects* and *redundancy* (if one capillary dies, another takes its place).

A spider web. The spider produces a long, exceptionally strong silken thread a few dozen μm in diameter. The silken thread is a protein that is synthesized in a gland



One of the silk glands of a *nephila clavipes*

Blood circulation



Vessel	$\bar{V}$ (m/s)	d (mm)	$\dot{\gamma}$ (s^{-1})	Re (–)
Aorta	0.4	25	130	2500
Arteries	0.45	4	900	450
Arterioles	0.05	0.05	8,000	0.5
Capillaries	0.001	0.008	1,000	0.002
Venules	0.002	0.02	800	0.01
Veins	0.1	5	160	125
Vena cava	0.38	30	100	2800

Vennermann et al. ***Exp. Fluids*** (2007) 42, 495

Man-made systems. Why Micro ?

1. **Unique physical and chemical effects, mass and heat transfer characteristics**
2. **Small volumes of expensive and/or dangerous reagents**
3. **Parallel operation**
4. **Portability, integration (reactions, separation, detection)**
5. **Implanting microfluidic devices in biological systems**
6. **Compatibility with other micro/nanoscale devices**

Why Flow? Some of important features

- *Transform time to space*. Instead of absolving subsequent steps in one volume as a function of time, pass through distinct (fixed) sections of a microchannel at different times

- Ability to integrate different subsequent steps

- Dynamically change conditions for each step

- Induce mechanically stimulated events (shear)

- Ability to transport (small/large molecules, nano and microparticles)

- Ability to conduct separations

Focus of Microfluidics

- **Phenomena**
- **Components**
- **Systems**
- **Applications**

Chemical Analysis
Biological Sensing
Chemical sensing
Drug Delivery
Molecular Separation
Amplification, sequencing, synthesis of nucleic acids
Cell biology

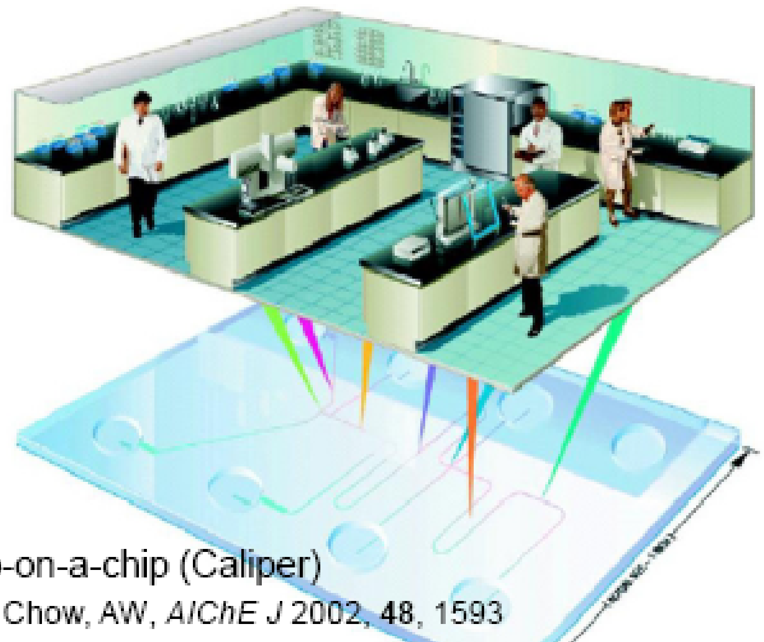
Lab-on-a-Chip Systems

Applications

- Chemical, biological and environmental analysis
- Medical diagnosis
- Therapeutic devices

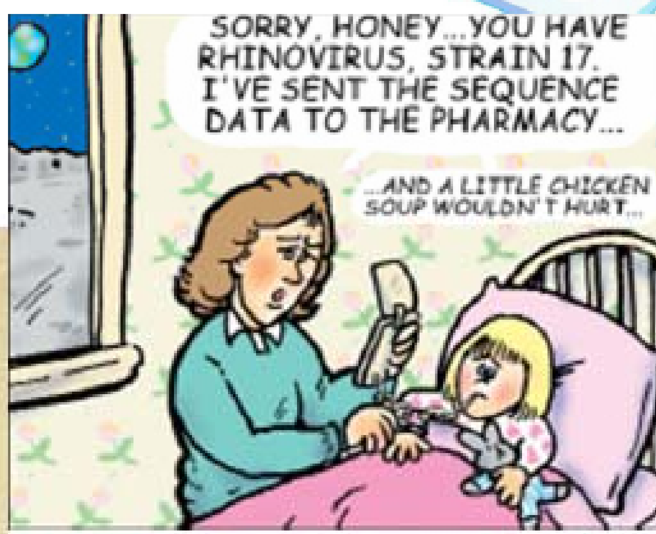
Advantages

- Small volumes of expensive reagents,
- Parallel operation,
- Shorter processing,
- Integration of flow, reactions, separation, and detection
- Integration with information management



Lab-on-a-chip (Caliper)
Chow, AW, *AIChE J* 2002, **48**, 1593

www.biosite.com



Burns, MA, *Science* 2002, **296**

www.mchips.com

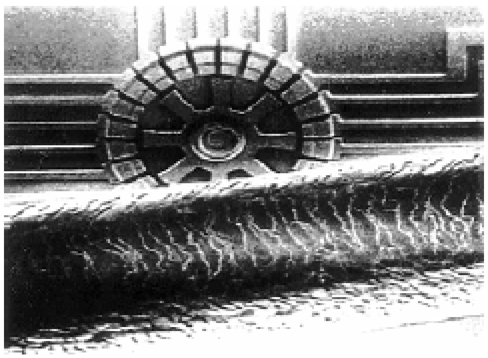
Whitesides Group 2009

MEMS and microfluidics

Miniaturization → micrometer-size mechanical, fluidic, electromechanical, or thermal systems.

1980s

Wheel



Complex objects

1990s: birth of microfluidics

300 μm

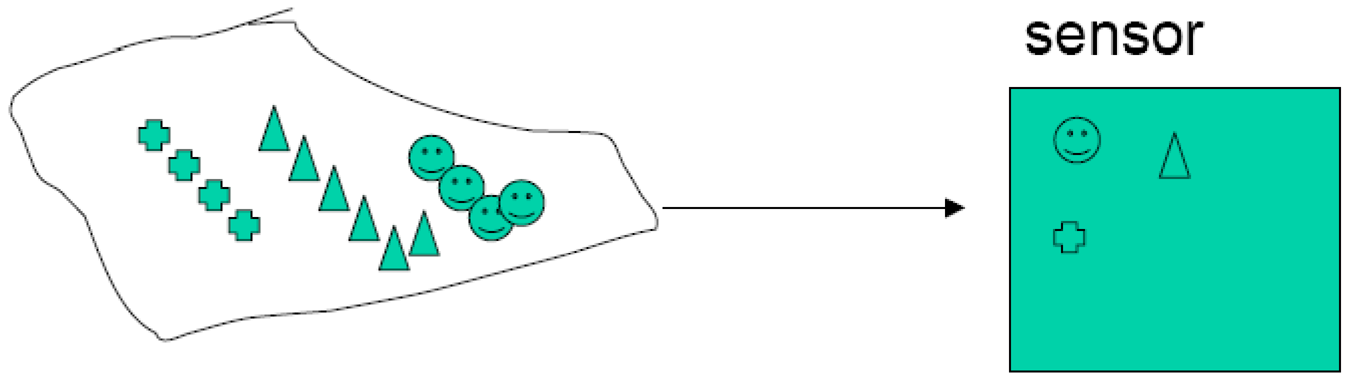
Dimensions: generally, below 500 μm; sometimes 1000 μm

This image was provided by the Karlsruhe group (Germany)

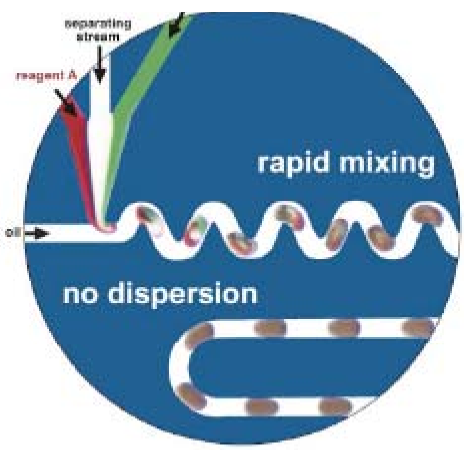
Microfluidics and high throughput screening/separation

Take a sample containing many different objects

High throughput sensor

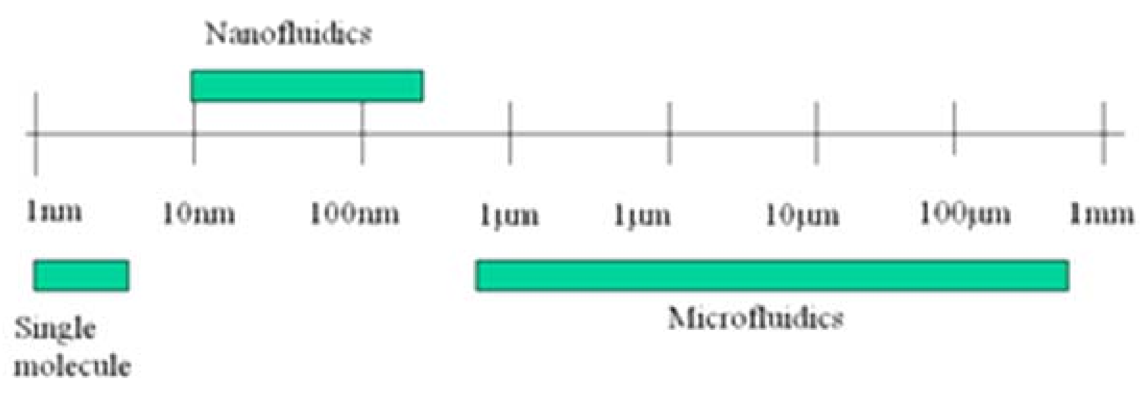


A sensor with high throughput is a sensor that determines a substantial part of the elements present in your sample



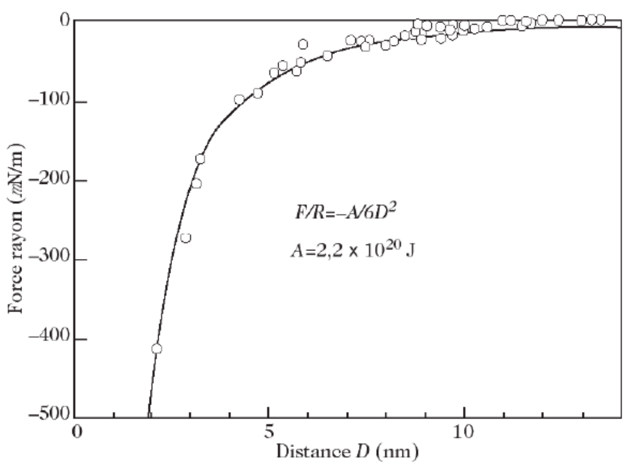
Microfluidic screening

A few words about nanofluidics

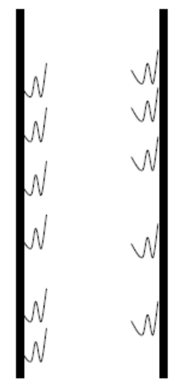


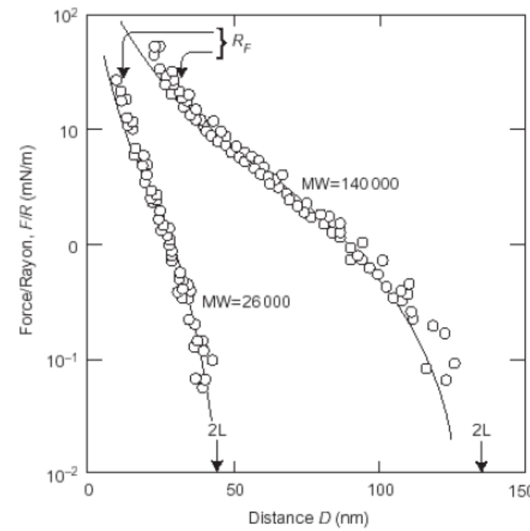
A Surface Forces Balance Technique

Van der Waals forces between surfaces in the vacuum extends over nanometers

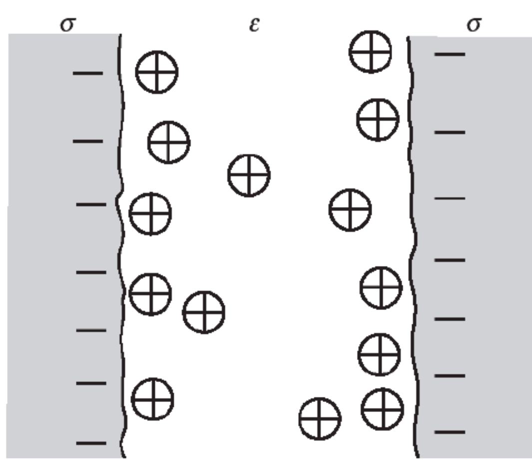


Interactions between adsorbed polymer layers



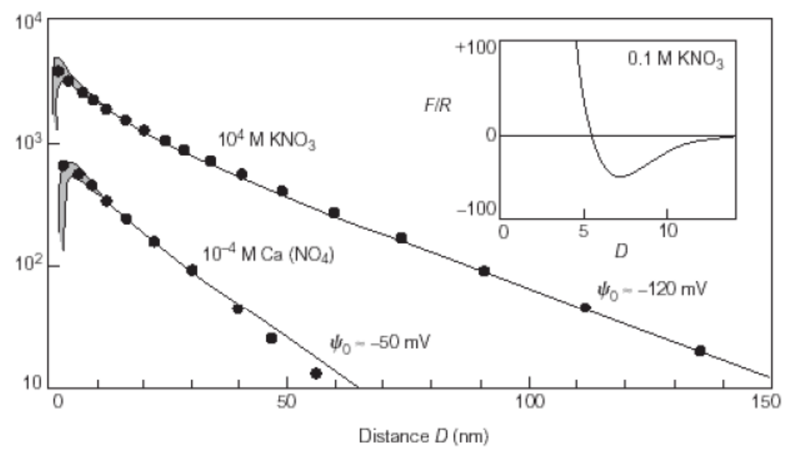


Forces in the presence of electrolyte (Debye layers)



DEBYE-HUCKEL layers - typically 100 nm up to 1 μm thick in pure water

Debye layers may have sizes comparable to Submicrometric channels.



(*Expected*) novel phenomena in nanochannelss

- *The presence of a slip over solid surfaces induces unusual flows.*
- *The dynamics of interfaces in nanochannels is not understood*
- *Hydrodynamic instabilities have specific structures*
- *Ordinary liquids may perhaps adopt unusual states*

……….

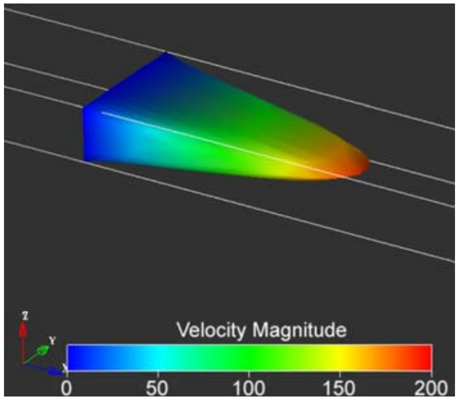
Experimental studies of flow in nanofluidic devices are just beginning

Difficulties in the fabrication of nanodevices and in the measurement techniques tend to slow down the investigation of the domain

How to make liquid move through microfluidic channels?

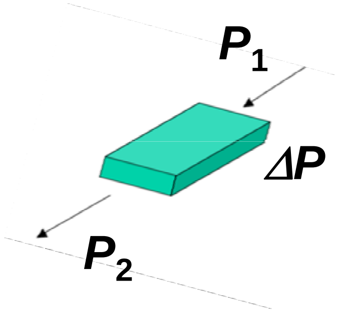
Pressure Driven Flow

The fluid is pumped through the device *via* positive displacement pumps (syringe pumps) or using pressure gauges. One of the basic laws is the so-called *no-slip boundary condition*: the fluid velocity at the walls must be zero. This produces a parabolic velocity profile within the channel.

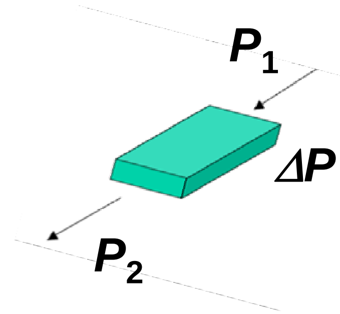


Velocity profile in a microchannel with aspect ratio 2:5 for pressure driven flow (calculation using Coventorware software*.*

http://faculty.washington.edu/yagerp/microfluidicstutorial/basicconcepts/basicconcepts.htm



Hydrodynamic resistance



$$\Delta P = R_h Q$$

Q* is the volumetric flow rate of the liquid, *ΔP* is pressure drop, R_h is the hydrodynamic resistance** (analogous to the electrokinetic law ***U=IR)

Channel with a *circular* cross-section (total length *L*, radius R): $R = \frac{8\mu L}{\pi R^4}$

Channel with a *rectangular* cross-section (width *w* and height *h*, *h*<*w*)

$$R_h \approx \frac{12\mu L}{wh^3(1 - 0.630h/w)}$$

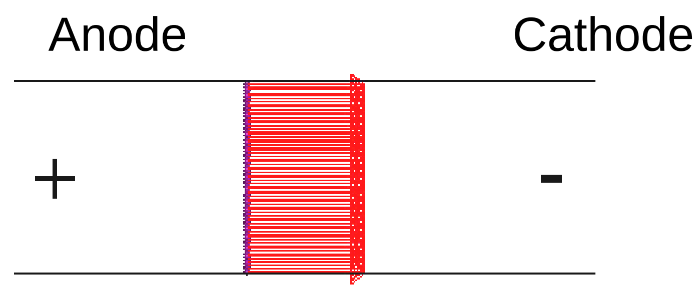
R_h increases as the system size decreases

In a network of channels R_h can be computed as in electrokinetics:

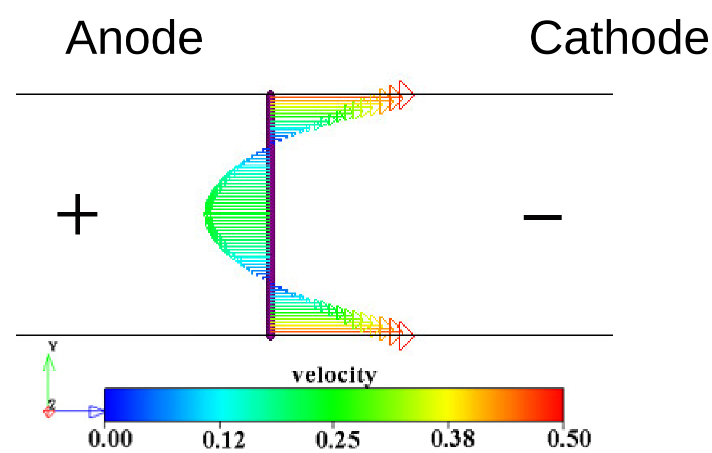
- two channels *in series* have a resistance $R_h = R_{h1} + R_{h2}$
- two channels i*n parallel* have a resistance $1/R_h = 1/R_{h1} + 1/R_{h2}$.

Electrokinetic Flow

If the walls of a microchannel have a charge, an electric double layer of counter ions will form at the walls. When an electric field is applied across the length of the channel, the ions in the double layer move towards the electrode of opposite polarity. This creates motion of the fluid near the walls and transfers *via* viscous forces into convective motion of the bulk fluid.



• For the channel open at the electrodes, the velocity profile is uniform across the entire width of the channel.



• For a closed channel, a recirculation pattern forms, in which a fluid along the center of the channel moves in a direction opposite to that at the walls.

Fluid mechanics of microfluidics

Navier-Stokes equation is the central relationship of fluid dynamics

Basic assumptions

continuous media

continuum mechanics

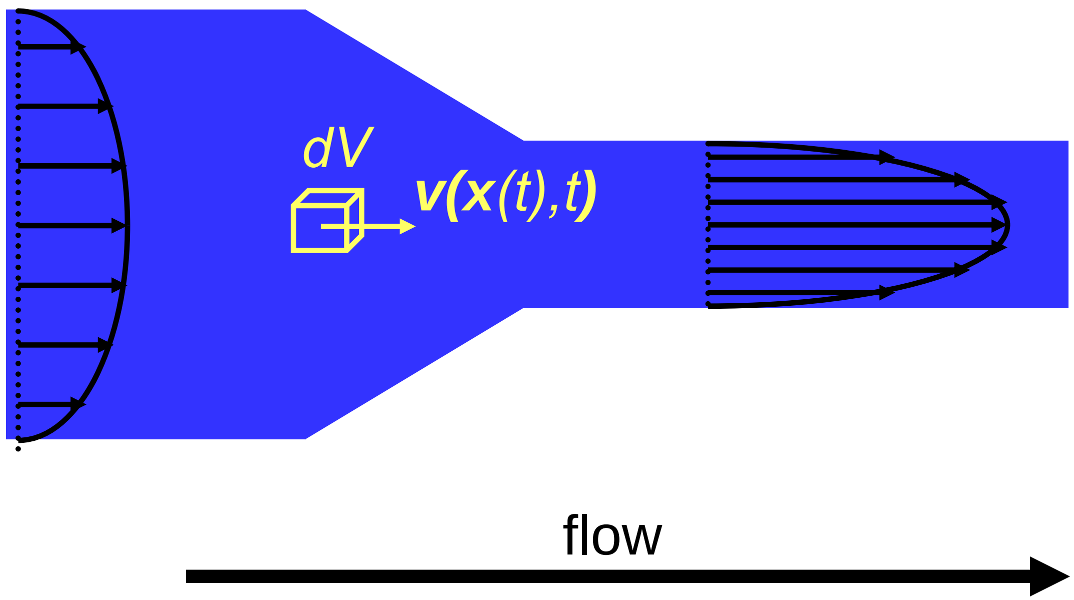
For liquids:

Assumptions made in macrofluidics, work for microfluidics (down to 10-100 nm)

How to describe the motion of a fluid?

- Velocity depends on space and time ***v*** = ***v***(***x***(t),t)
- Consider Newtons law for a infinitesimal volume *V*:

$$\mathbf{F} = m \cdot \mathbf{a} \quad \Longrightarrow \quad \frac{\mathbf{F}}{V} = \mathbf{f}_a = \frac{m}{V} \cdot \mathbf{a} = \rho \cdot \frac{d\mathbf{v}}{dt}$$



$\mathbf{f}_a$ and $\mathbf{v}$ are vectors!!

How to describe the motion of a fluid?

- Momentum equation (acceleration) in **x-direction**:

$$f_{a,x} = \rho \cdot \frac{dv_x}{dt} = \rho \cdot \frac{d}{dt} v_x(x(t), y(t), z(t), t) =$$

$$= \rho \cdot \left(\frac{\partial v_x}{\partial x}\bigg|_{y,z,t} \cdot \frac{dx}{dt} + \frac{\partial v_x}{\partial y}\bigg|_{x,z,t} \cdot \frac{dy}{dt} + \frac{\partial v_x}{\partial z}\bigg|_{x,y,t} \cdot \frac{dz}{dt} + \frac{\partial v_x}{\partial t}\bigg|_{x,y,z} \right) =$$

$$= \rho \cdot \left(\boxed{\frac{\partial v_x}{\partial x}\bigg|_{y,z,t} \cdot v_x + \frac{\partial v_x}{\partial y}\bigg|_{x,z,t} \cdot v_y + \frac{\partial v_x}{\partial z}\bigg|_{x,y,t} \cdot v_z} + \boxed{\frac{\partial v_x}{\partial t}\bigg|_x} \right)$$

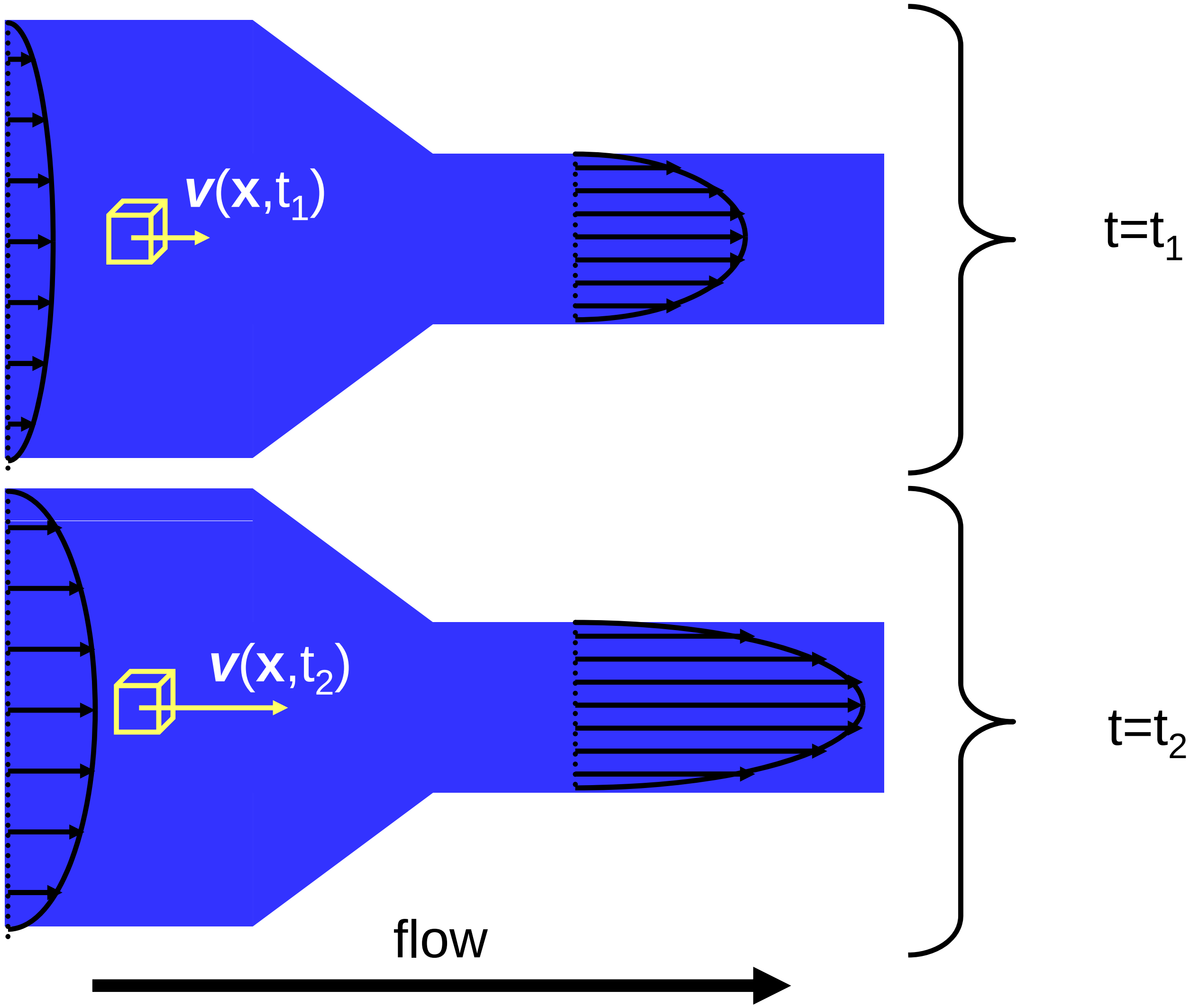
- Momentum equation in 3D (vector notation):

$$\mathbf{f}_a = \rho \cdot \frac{d\mathbf{v}}{dt} = \rho \cdot \left(\boxed{(\mathbf{v} \cdot \nabla)\mathbf{v}} + \boxed{\frac{\partial \mathbf{v}}{\partial t}} \right)$$

$$\vec{\nabla} = \left(\frac{\partial}{\partial x}, \frac{\partial}{\partial y}, \frac{\partial}{\partial z} \right) = \vec{e}_1 \frac{\partial}{\partial x} + \vec{e}_2 \frac{\partial}{\partial y} + \vec{e}_3 \frac{\partial}{\partial z}$$

Nabla operator

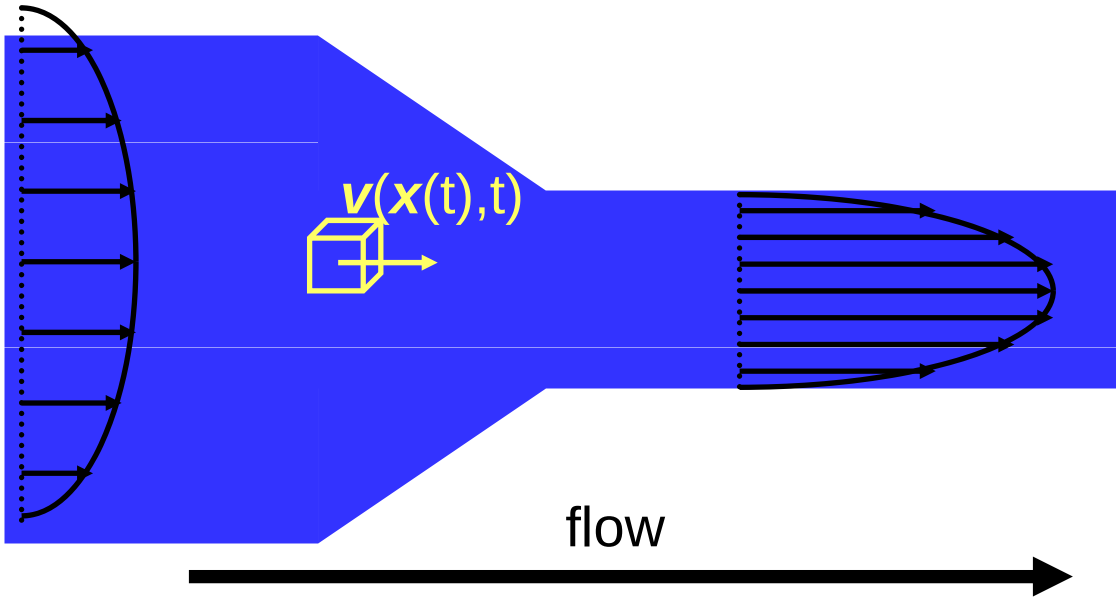
Acceleration over time



$$\mathbf{f}_a = \rho \cdot \frac{\partial \mathbf{v}}{\partial t}$$

Acceleration along a streamline

- Increase of the fluid velocity due to mass conservation
- Fluid has to be accelerated along the streamline



$$\mathbf{f}_a = \rho \cdot \mathbf{v} \cdot \nabla \mathbf{v}$$

The Navier-Stokes equation

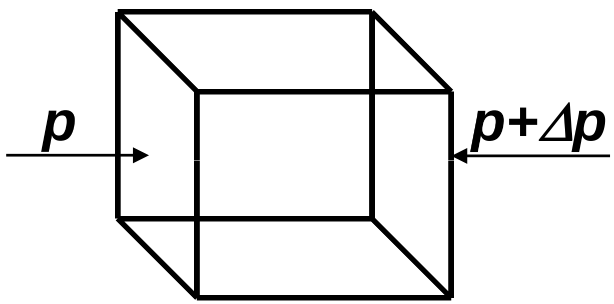
- … for incompressible Newtonian fluids

$$\mathbf{f}_a = \rho\left[\frac{\partial}{\partial t}\mathbf{v} + (\mathbf{v}\cdot\nabla)\mathbf{v}\right] = \mathbf{f}_{pressure} + \mathbf{f}_{friction} + \mathbf{f}_{volume}$$

- **left hand side**
  - **Change in momentum (Newton)**
    - due to change of velocity over time at a given location
    - due to acceleration of fluid e.g. when moving into smaller flow channel cross-sections (also in stationary cases)
- right hand side
  - **Forces acting on fluid**
    - pressure gradient
    - friction forces
    - volume forces

Pressure gradient

$$\mathbf{f}_a = \mathbf{f}_{pressure} + \mathbf{f}_{friction} + \mathbf{f}_{volume}$$



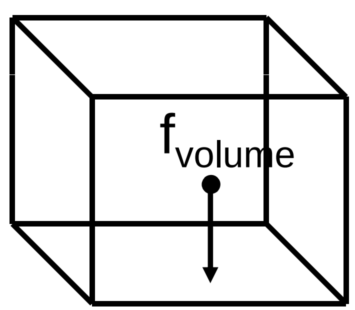
$$\mathbf{f}_{pressure} = \frac{d\mathbf{F}_{pressure}}{dV} = -\nabla p$$

Body force (= volume force)

$$\mathbf{f}_a = \mathbf{f}_{pressure} + \mathbf{f}_{friction} + \mathbf{f}_{volume}$$

- Actuation of fluid by the body force:

force $\boldsymbol{f}_{\text{volume}}$ acts in the volume itself



Body forces: centrifugal forces
gravity forces
electrostatic forces

Example 1: static pressure under gravity

– Only gravity is considered in NS-equation

$$\mathbf{f}_{volume} = \mathbf{f}_{\mathbf{g}} = \rho\mathbf{g}$$

– Stationary flow (v=const.):

- friction is zero (no motion)
- acceleration is zero (dv/dt=0)

$$\cancel{\mathbf{f}_a} = \mathbf{f}_{pressure} + \cancel{\mathbf{f}_{friction}} + \mathbf{f}_{volume} \quad \Rightarrow \quad -\mathbf{f}_{pressure} = \mathbf{f}_{volume}$$

– Result:

$$\nabla p = \rho_\infty \mathbf{g} \qquad \frac{dp}{dy} = \rho_\infty g \quad \Rightarrow \quad p_{\max} = \rho_\infty g h + p_0$$

- ***Example* 1:** for water in a microchannel:

  $\rho = 1000$ kg/m^3

  $g = 9.81$ m/ s^2

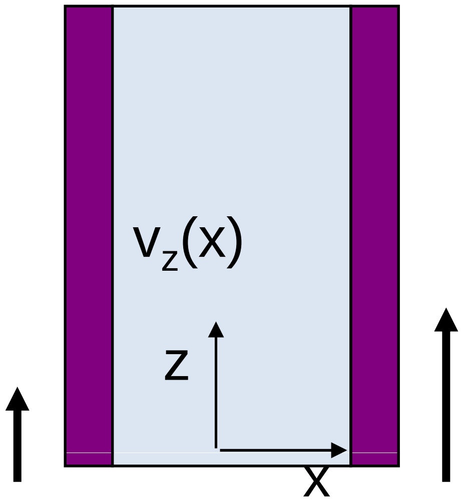
  $h = 100$ μm

$$\Rightarrow \quad p_{\max} = 0.981 Pa = 9.81 \cdot 10^{-6}\,\text{bar}$$

Gravitational effects are negligible in microfluidics

Friction

– Friction affects the motion (velocity) of the fluid



$$f_{friction,z} = \frac{\mathrm{d}F_\eta}{\mathrm{d}V} = \eta \frac{\partial^2 v_z}{\partial x^2}$$

$$\mathbf{f}_{friction} = \eta \nabla^2 \mathbf{v}$$

The motion is damped by the friction force

Reynolds number (*Re*)

- Approximate friction energy $$E_{friction} \propto \left\| \mathbf{F}_{friction} \right\| \cdot l = \eta \frac{v}{l} A \cdot l = \eta \frac{v}{l} V$$
- Approximate kinetic energy $$E_{kin} \propto mv^2$$

$$\frac{E_{kin}}{E_{friction}} = \frac{mv^2 l}{\eta v V} = \frac{\rho l v}{\eta} = \boxed{Re}$$

$$\boxed{Re = \frac{\rho l v}{\eta}}$$

Reynolds number is the ratio of work spent on acceleration to energy dissipated by friction

(A more general definition: ***Re*** a dimensionless number that gives the ratio of inertial forces (characterizing how much a particular fluid resists to motion) to viscous forces.

- the *Re*-number is the most important dimensionless number in microfluidics
- low *Re*-numbers, i.e. **viscous forces dominate, are typical for microfluidics**
- ***l*** is a characteristic length scale

Simplifications in microfluidics

$$\rho_\infty \left[\frac{\partial}{\partial t}\mathbf{v} + (\mathbf{v}\cdot\nabla)\mathbf{v} \right] = -\nabla p + \eta \nabla^2 \mathbf{v} + \mathbf{f}_{volume,g}$$

- Gravity is neglected
- Influence of convection is small, $\rho(\boldsymbol{v}\cdot\nabla)\boldsymbol{v} \rightarrow \mathbf{0}$, i.e. we assume that there is no convective momentum transport
- If additionally a stationary flow is considered …

- Poisson equation (driving pressure and friction are balanced in a stationary laminar flow):

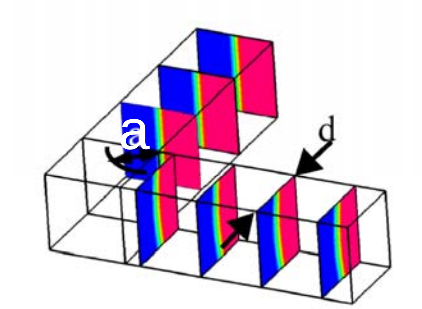
$$\rho_\infty \left[\frac{\partial}{\partial t}\mathbf{v} + (\mathbf{v}\cdot\nabla)\mathbf{v} \right] = -\nabla p + \eta \nabla^2 \mathbf{v} + \rho_\infty \mathbf{g}$$

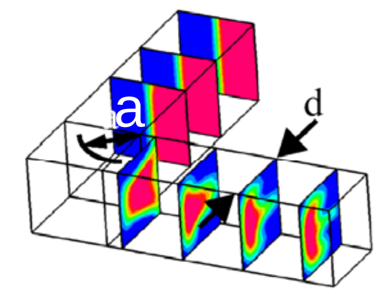
$$\boxed{\nabla p = \eta \nabla^2 \mathbf{v}} \Rightarrow \boxed{\mathbf{f}_{pressure} = -\mathbf{f}_{friction}}$$

Flow Regimes

- ***Re*<1 (Stokes regime)**
  - No lateral convection
  - Adjacent layers (lamellae) do not "interfere" (lamellae do not mix)
  - inertial terms are neglected
- **1 < *Re* < *Re*** * (Intermediate)
  - Lateral convection becomes increasingly important
- ***Re*>*Re*** * (Turbulent)
  - Perturbations are amplified
  - Curling of field lines
  - „Unpredictable" development of field of velocity vectors over time

Re*<*Re *
laminar flow





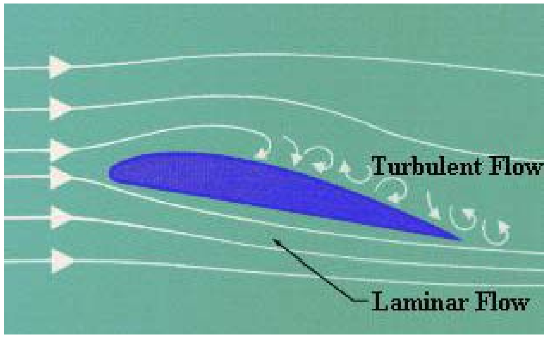
Re*>*Re *
turbulent fow

***Re** ~ 2300**

Critical Reynolds number

– Critical ***Re**** corresponds to a critical velocity ***v****

$$v^* = Re^* \frac{\eta}{\rho l}$$

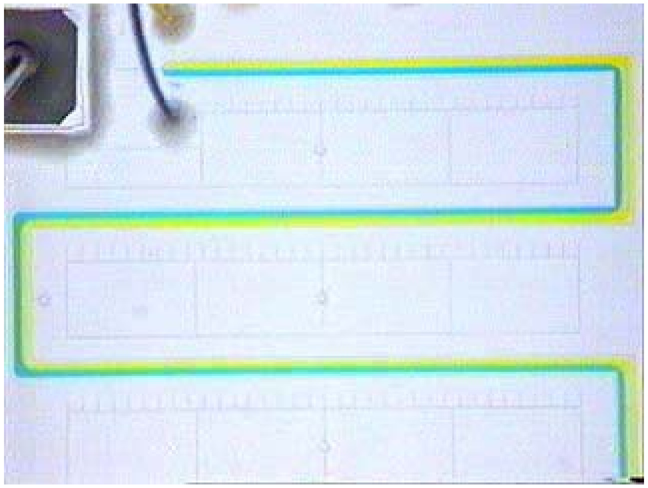


– Typically ***Re**** is in the range of **2300**

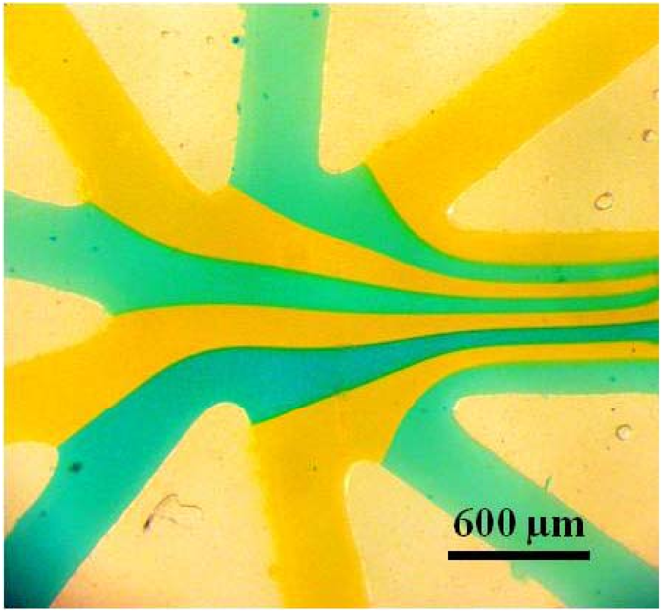
– For a **microdevice** ***v**** is hardly reached (l = 100 µm → $v^* \approx$ 25 m/s)

– As ***Re*** increases further, the turbulent character of flow increases

Examples of laminar flow



http://strc.herts.ac.uk/mm/micromixers.html



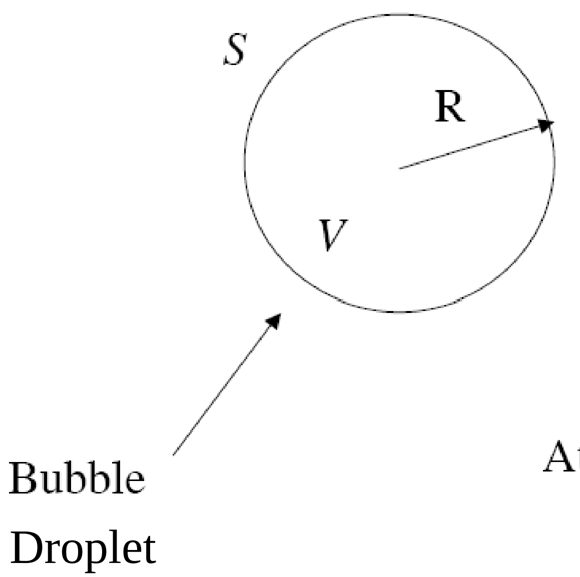
http://alcheme.tamu.edu/?page_id=6720

Laminar flow means that diffusion is the only mechanism to achieve mixing between parallel fluid streams. This is a slow process.

Other dimensionless numbers

Capillary phenomena are extremely important in microsystems

Laplace law



$$\delta E = -p\delta V + \gamma \delta S$$

$$V = \frac{4}{3}\pi R^{3} \Rightarrow \delta V = 4\pi R^{3}\delta R$$

$$S = 4\pi R^{2} \Rightarrow \delta S = 8\pi R\,\delta R$$

At mechanical equilibrium : $\delta E=0$

$$p = \frac{2\gamma}{R}$$

Pressure drops caused by capillarity are ~ l^{-1} while those due to viscosity scale as l^{0}

The capillary number, ***Ca***, represents the relative effect of viscous forces versus surface tension acting across an interface between a liquid and a gas, or between two immiscible liquids

$$Ca = \frac{\mu U}{\gamma}$$

μ is the viscosity of the liquid, ***U*** is a characteristic velocity and γ is the surface or interfacial tension between the two fluid phases

Microfluidics: $Ca \approx 10^{-1} - 10^{-3}$

Summary

- NS-equation is derived by a momentum balance for a continuum element
- For **Newtonian**, **incompressible** fluids the NS equation is

$$\rho_\infty\left[\frac{\partial}{\partial t}\mathbf{v}+(\mathbf{v}\cdot\nabla)\mathbf{v}\right]=-\nabla p+\eta\nabla^2\mathbf{v}+\rho_\infty\mathbf{g}$$

- Momentum change (right-hand side) can be caused by:
  - Pressure gradients
  - Viscous losses
  - Body forces
- ***Re*** number characterizes the damping of disturbances → laminar and turbulent flow)

$$Re=\frac{\rho l v}{\eta}$$

Summary (cont)

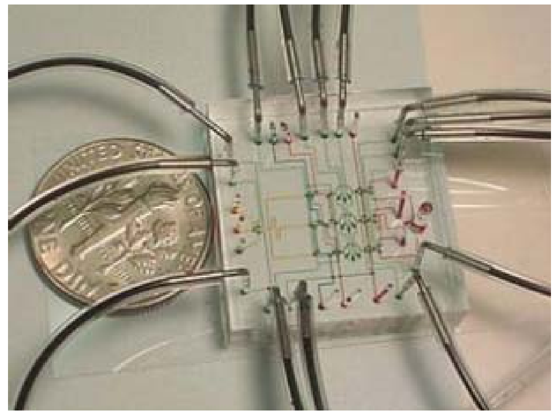
- For *Re* < *Re* * the flow is laminar
- For *Re* > *Re* * the flow is turbulent

- In microfluidics we (usually) assume
  - No gravity
  - Incompressibility
  - Dominance of viscous forces

- Capillarity plays an important role in microfluidics, as represented nu small Capillary numbers

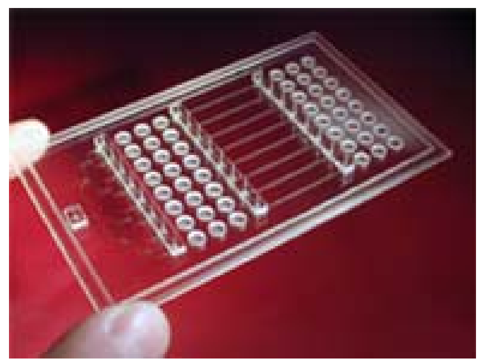
How to make a microfluidic device?

- **Thermoembossing**
- **Wet and dry etching**
- **Moulding**
- **Laser ablation**
- **Photolithography**
- **Soft lithography**
- **…. other clever methods**

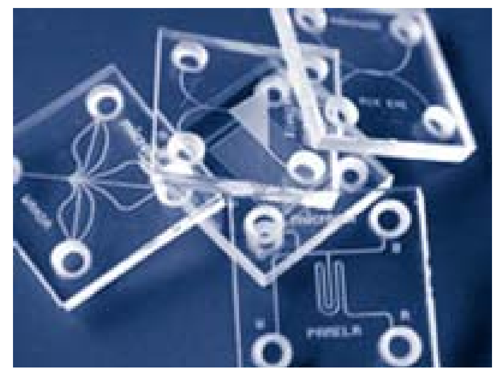


http://www.zzz.com.ru/data/users/arhines/mf3.jpg

http://www.smalltimes.com/images/microfluidics_inside_1.jpg



http://www.epigem.co.uk/images/fluidics-intro3.jpg



http://www.micronit.com/images/Cust_chips.jpg

EFFECT OF SURFACE ENERGY OF MICROCHANNELS

design ~ 1 hour
print out ~ 1 day
fab master ~ 3 hours ~ 2 days

----

make copies of the device ~ 2 hours each

Speed matters!

Fabrication of Microfluidic Device: Soft Lithography

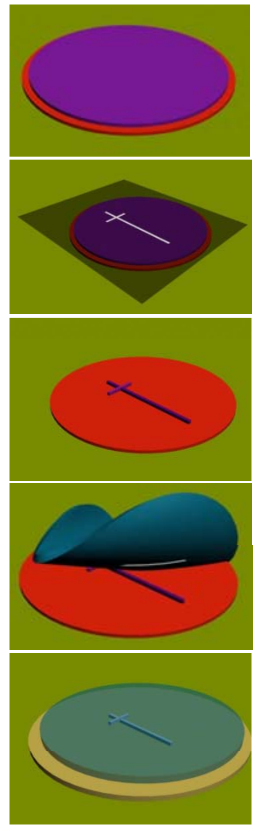
1) Spincoat photoresist

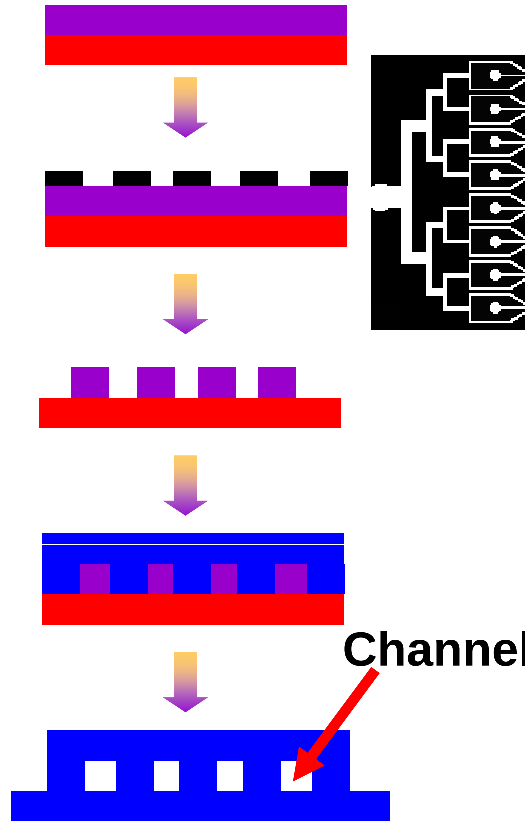
2) UV Exposure

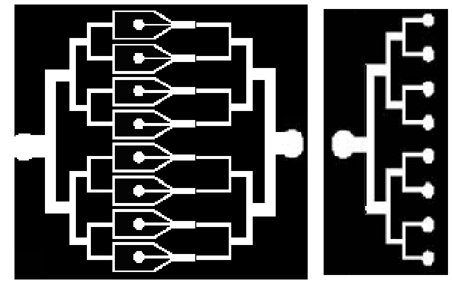
3) Develop photoresist

4) Prepare mold

5) Seal to substrate







SU-8 | Si Wafer | Photomask | PDMS prepolymer

Y. Xia, G. M. Whitesides, *Angew. Chemie Int. Ed.* 1998, 37, 550

MIXING IN MICROFLUIDICS

Mixing in microfluidics

- No turbulence in microfluidics. Mixing occurs by diffusion. Little or no mixing.

- A dimensionless number, analogous to the Reynolds number, is ***Peclet number***

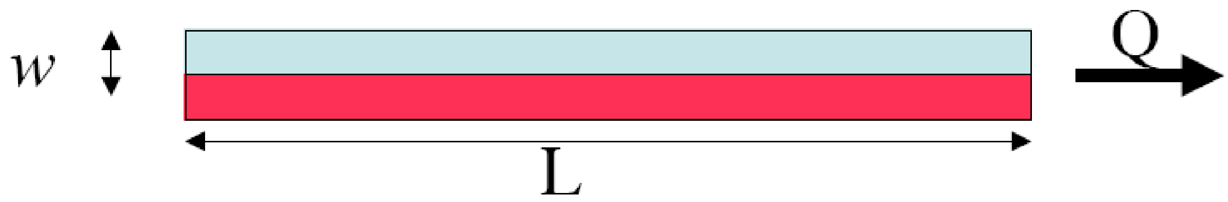
$$Pe = Ul/D \sim \frac{\text{advection}}{\text{diffusion}}$$

Diffusion time for a 100 µm wide channel (for a molecule such as fluorescein):

$$\tau = \frac{l^2}{D} \sim 100\,s$$

This time may be too long, especially if one develops several chemical reactions on the same chip

Mixing by diffusion



Residence time : $t_R = L/U = Lwb/Q$

Mixing time : $t_D = w^2/D$

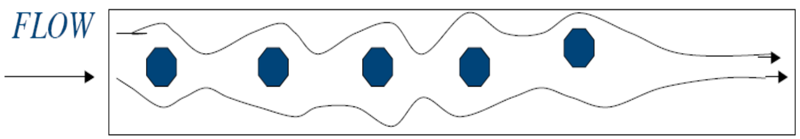
In order to achieve mixing, one must have $t_R >> t_D$; this implies:

$$L >> Qw/bD$$

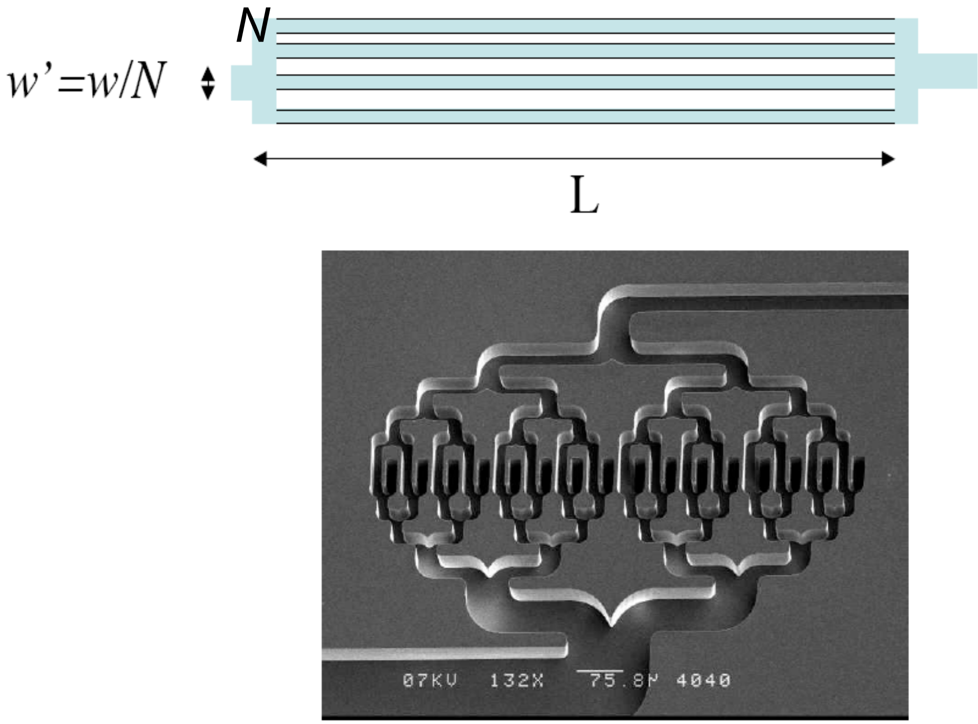
In practice, one reaches lengths on the order of centimeters

Clever solutions

Posts

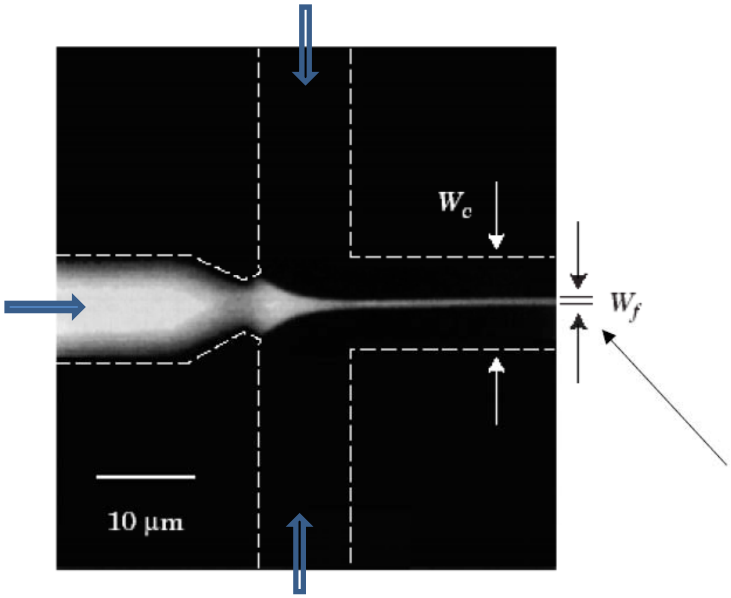


The distributive micromixer



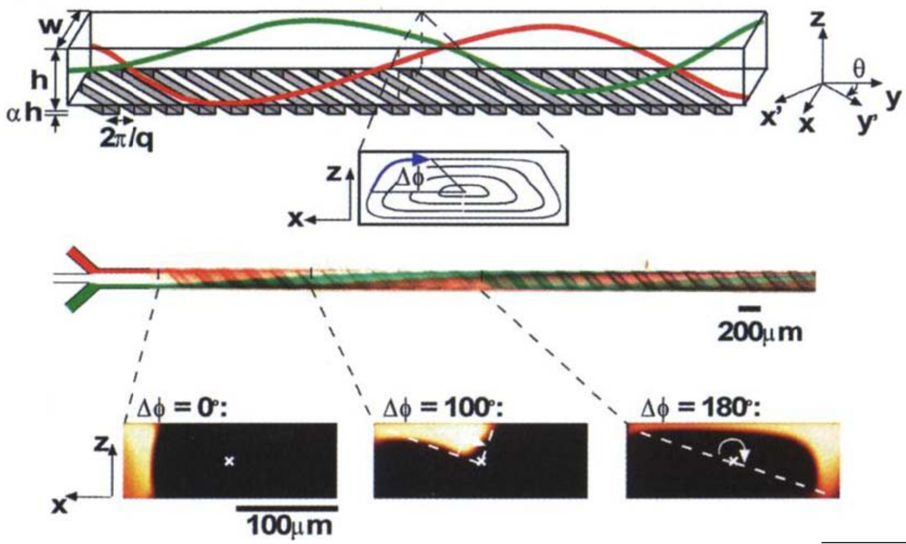
From A. Manz (2004)

Hydrodynamic focusing



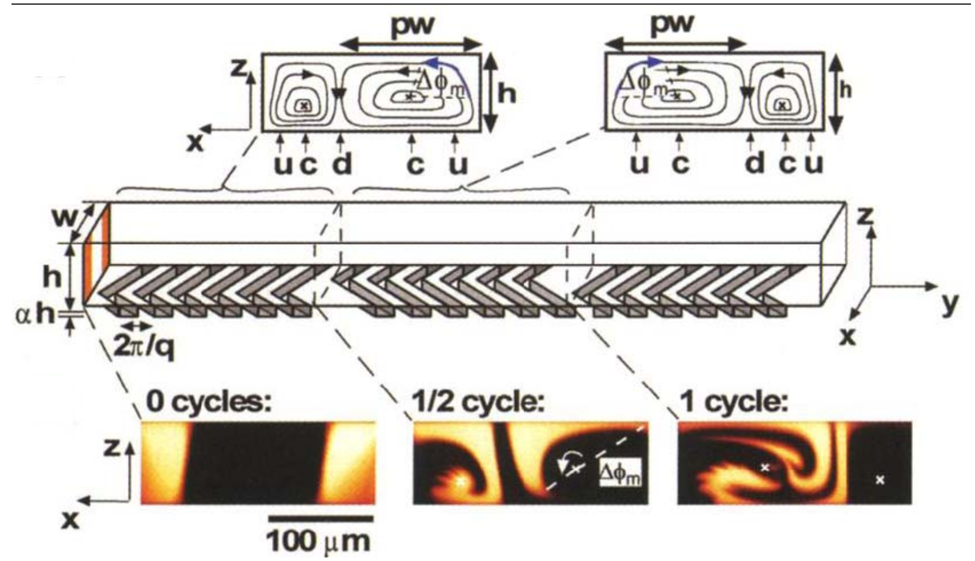
Mixing in tens of microseconds
Austin et al, PRL (2002)

Chaotic mixer for microchannels

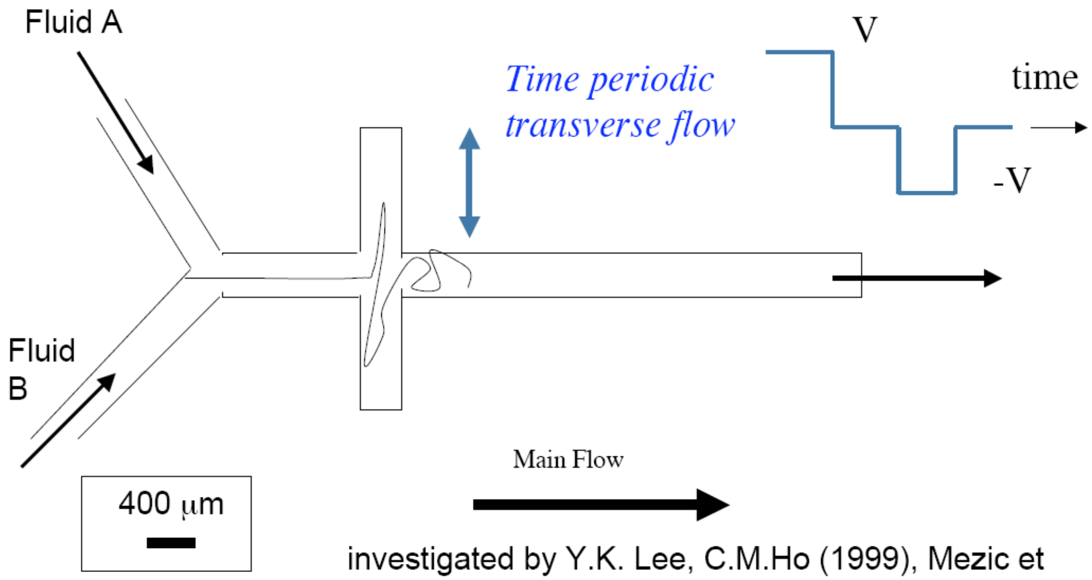


Whitesides et al. ***Science***, 295, 647 (2002)

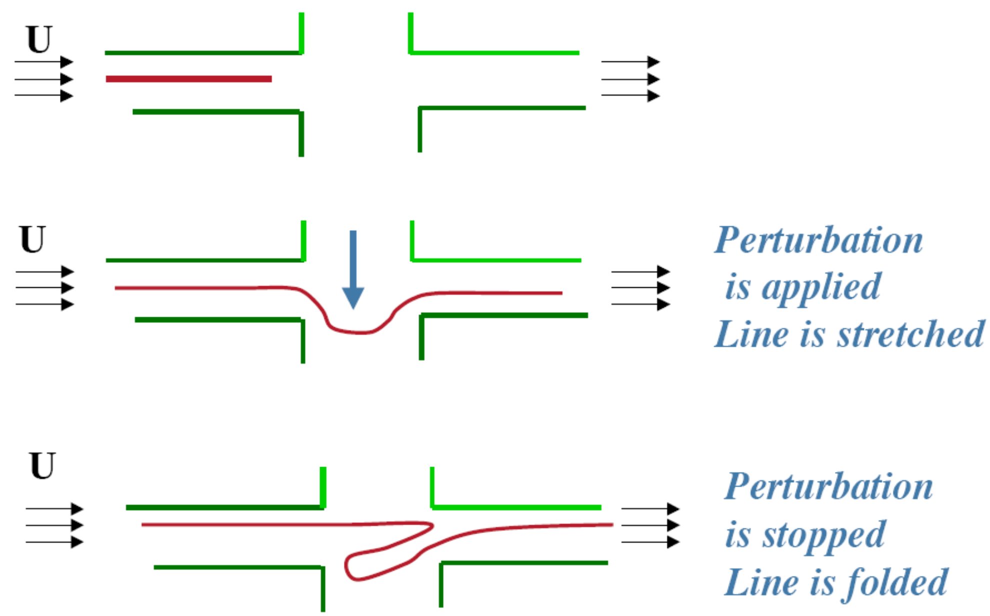
To generate transverse flows in microchannels, ridges were placed on the floor of the channel at an oblique angle, with respect to the long axis (y) of the channel



Cross-channel mixer

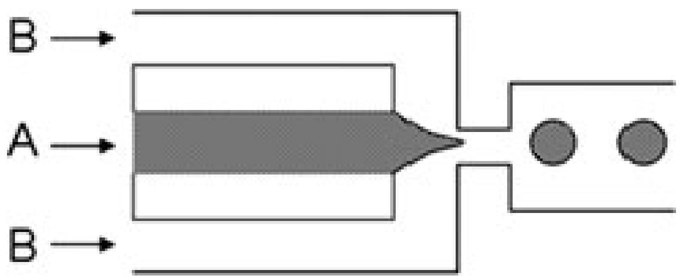


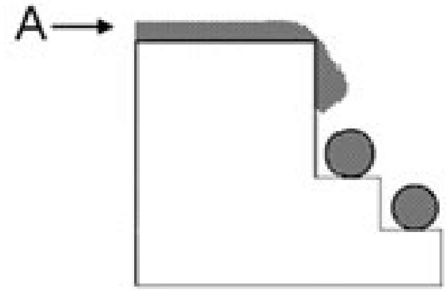
investigated by Y.K. Lee, C.M.Ho (1999), Mezic et al (1999)

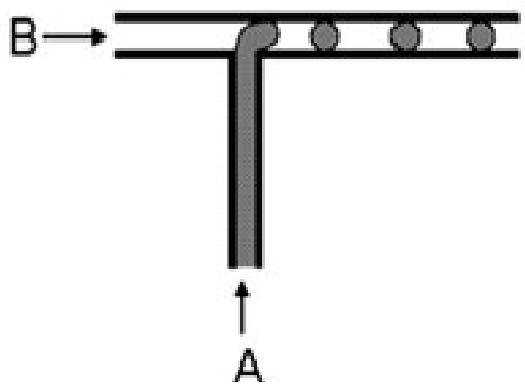


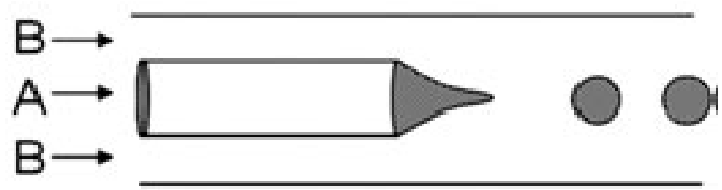
Droplet microfluidics

Generation of droplets





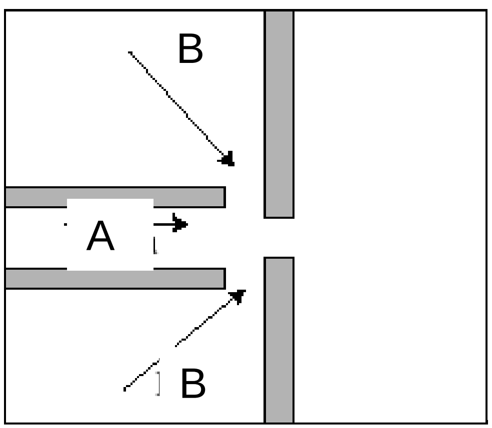


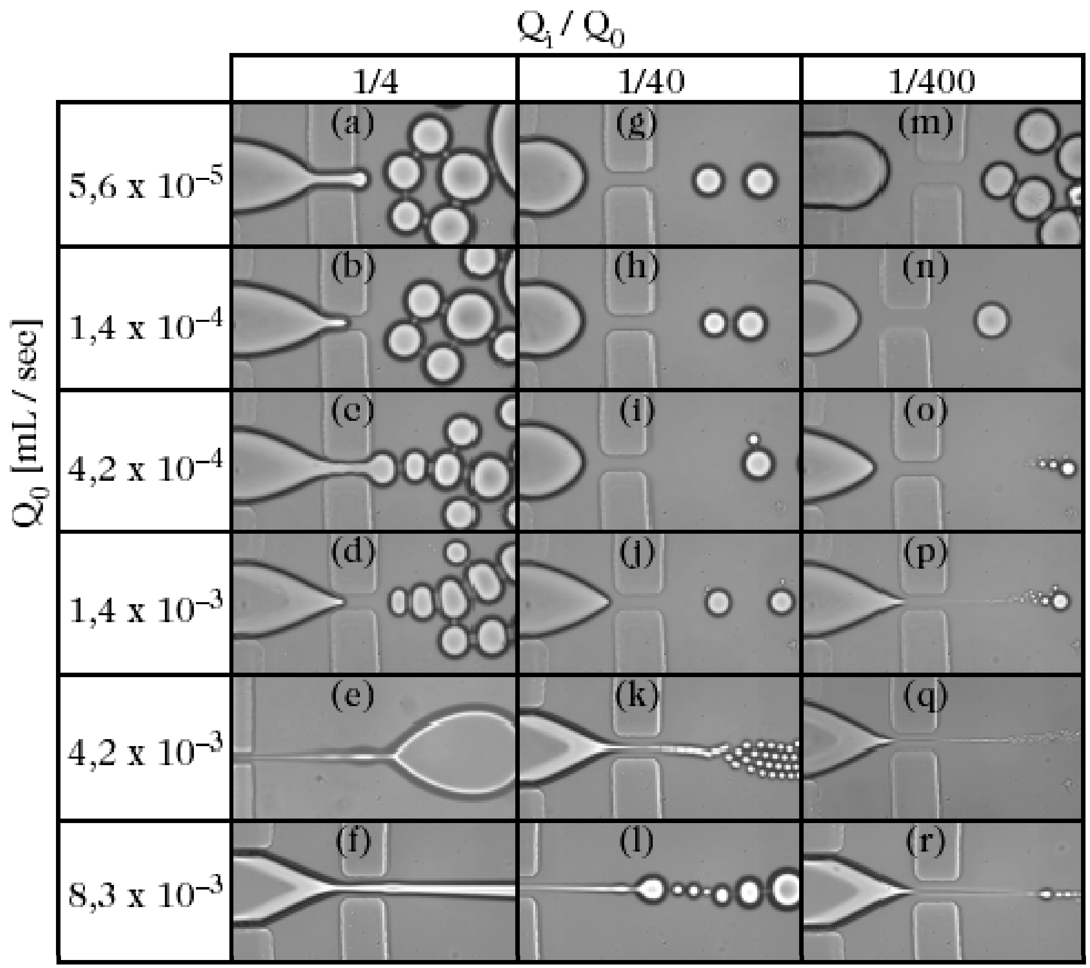


A and B are two immiscible liquids

Narrow size distribution
High frequency of droplet generation
Control of droplet morphology (double emulsions)

Flow-focusing

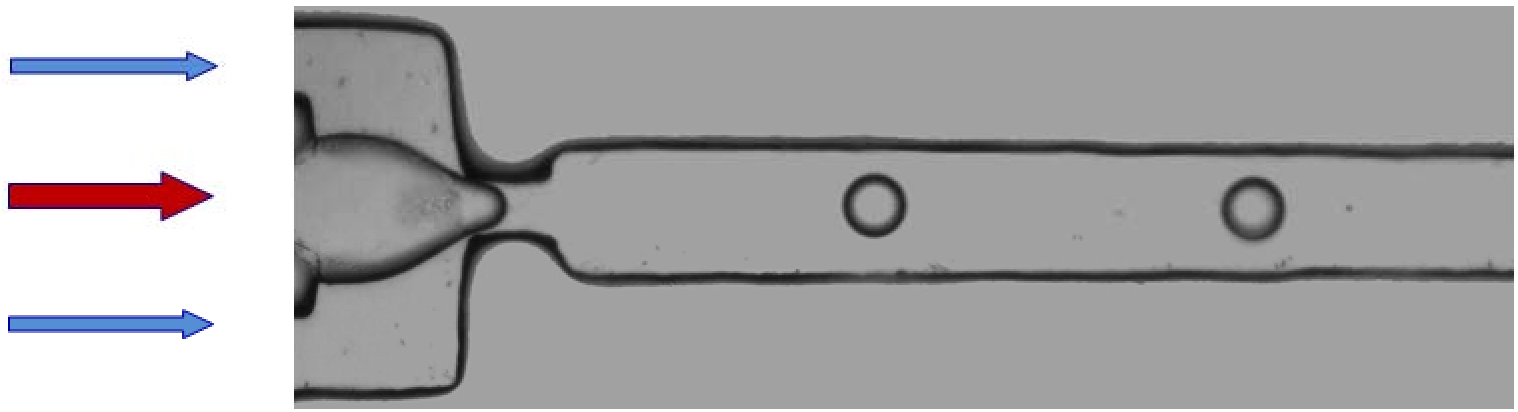




Stone, APL, 2002

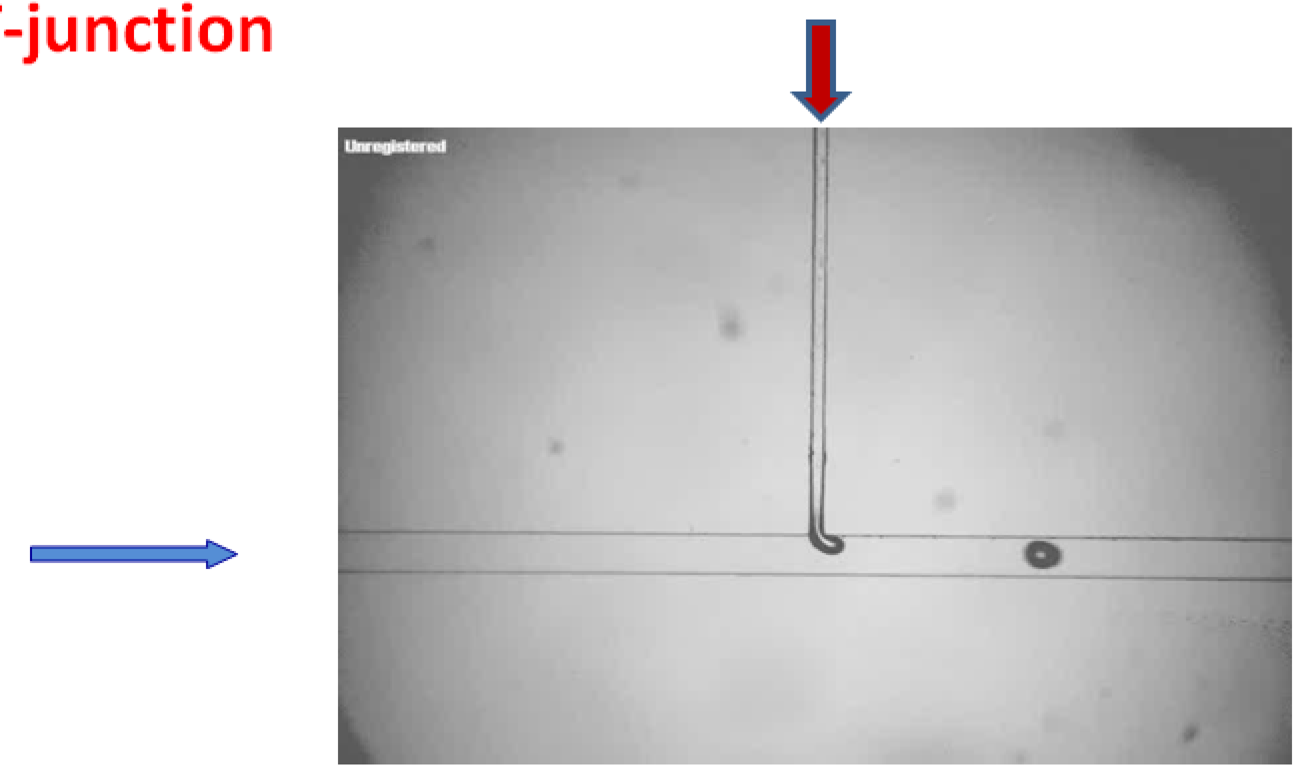
Flow-focusing

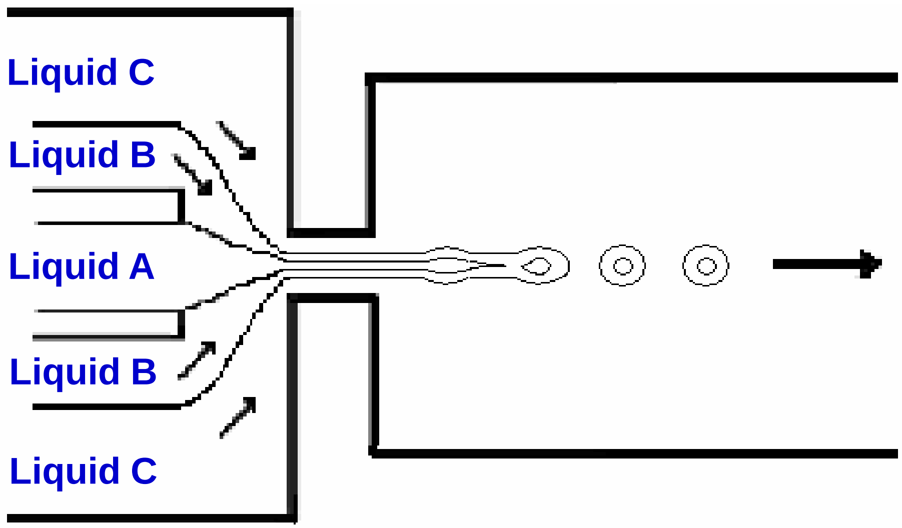
A 100-fold reduced speed

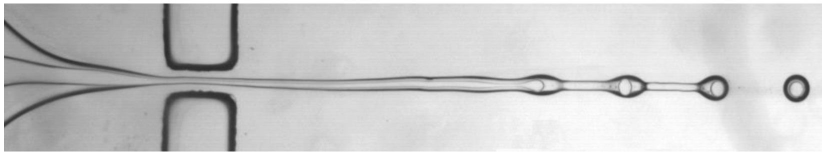


T-junction

100 µm





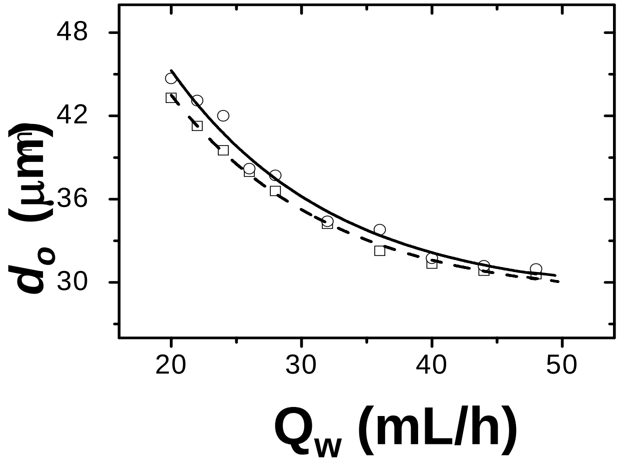


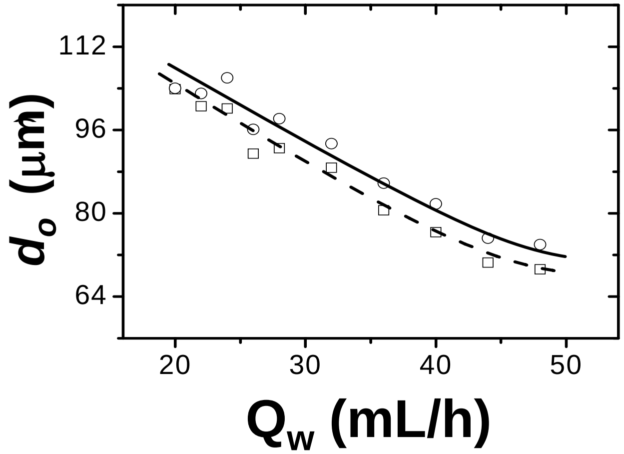
$$d = [(4/\pi)\,(Q_{drop}/v_{x,\,cont})]^{1/2}$$

***d* is the average diameter of the coaxial jet**

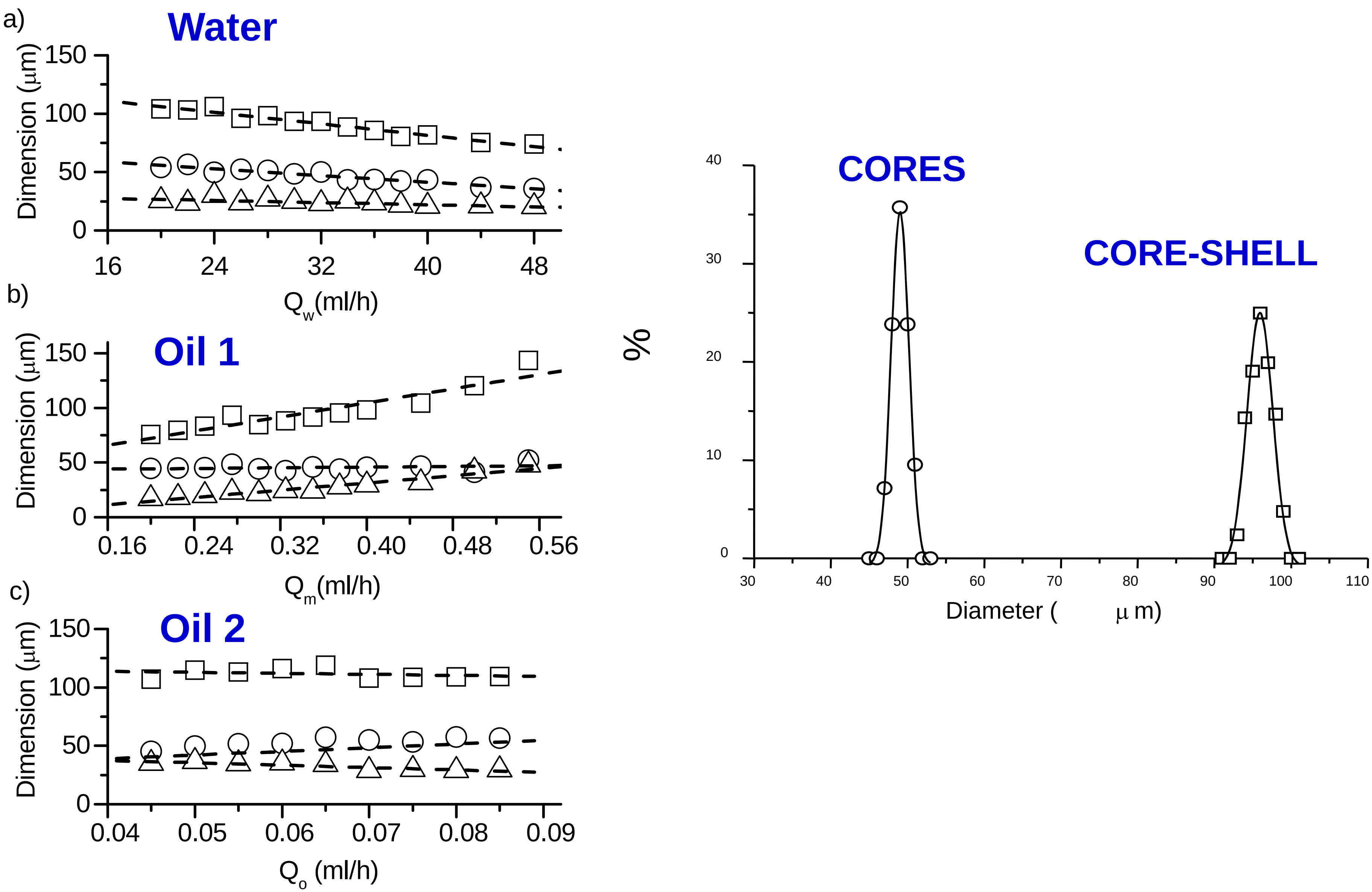
$$d_0 = (1.5\lambda_{\,breakup}\; d^2)^{1/3}$$

***d_0* is the average diameter of droplets**



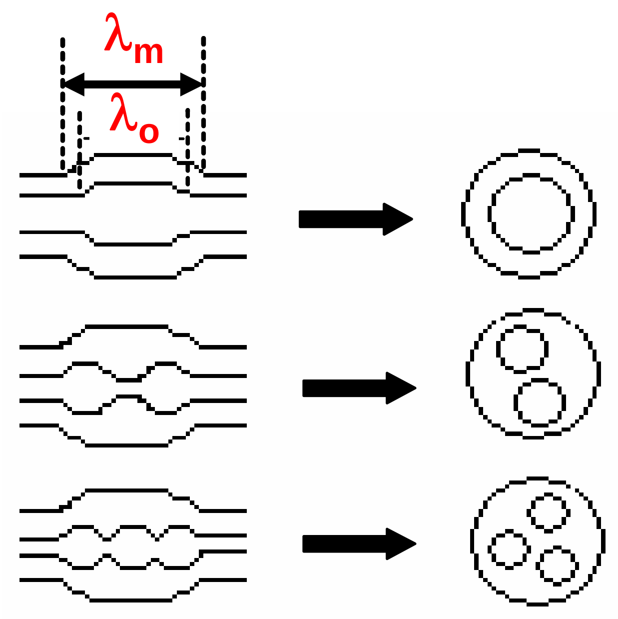


Z. Nie *et al*. *J. Am. Chem. Soc.* *127*, 8058 (2005)



a)
Water
Dimension (µm)
150
100
50
0
16
24
32
40
48
Qw(ml/h)
b)
Oil 1
Dimension (µm)
150
100
50
0
0.16
0.24
0.32
0.40
0.48
0.56
Qm(ml/h)
c)
Oil 2
Dimension (µm)
150
100
50
0
0.04
0.05
0.06
0.07
0.08
0.09
Qo (ml/h)
CORES
CORE-SHELL
%
40
30
20
10
0
30
40
50
60
70
80
90
100
110
Diameter (µ m)

Multicore Capsules: Hypothesis



Interfacial wavelength

$$\lambda \approx 9.02\boldsymbol{d}_{jet}$$

$$\lambda \sim (\boldsymbol{Q}_{disp} / \boldsymbol{Q}_{cont})^{1/2}$$

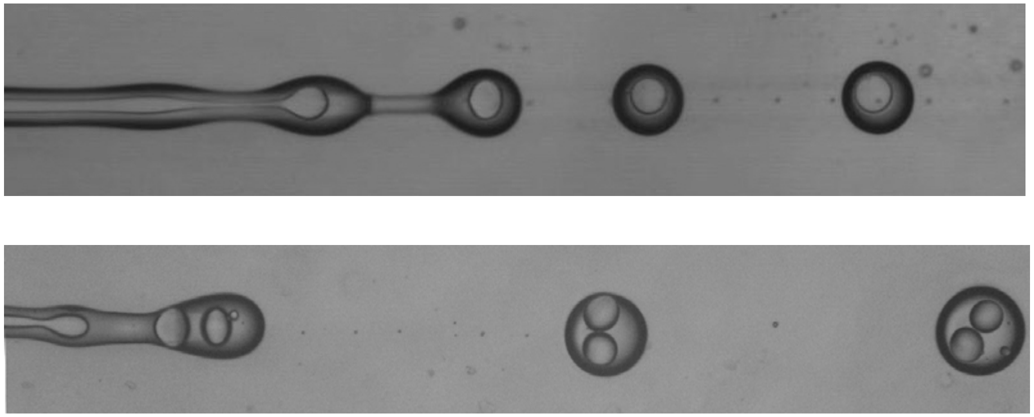
$$\lambda_m / \lambda_o \cong n$$

n is the number of **monodisperse** oil cores per capsule

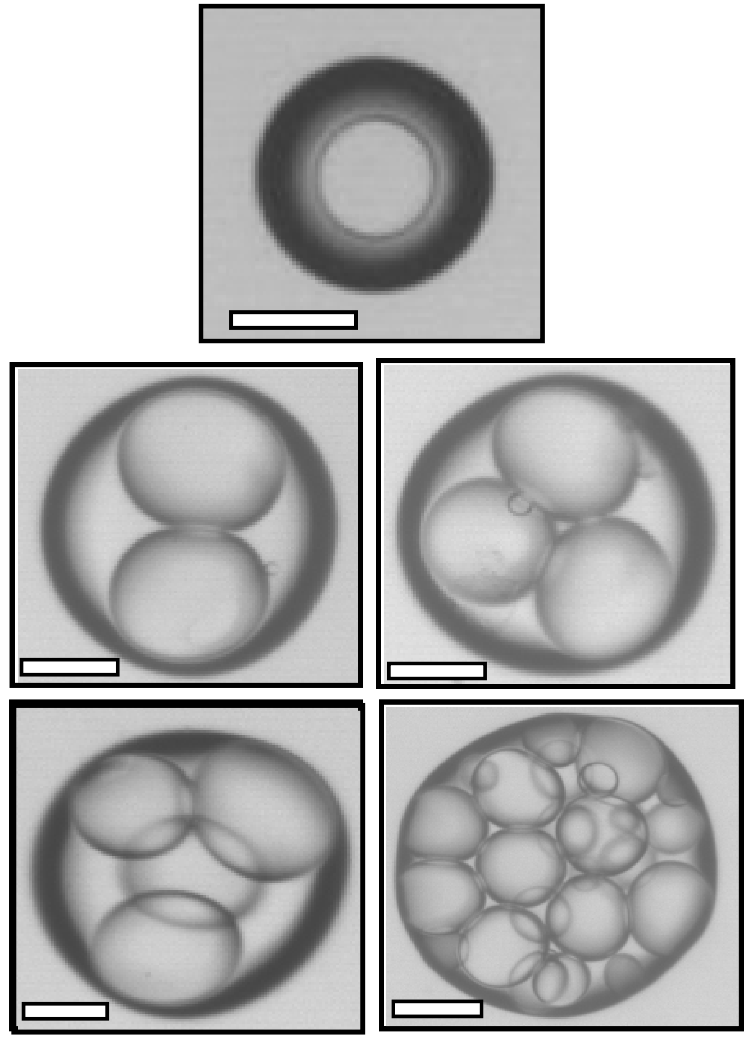
$$n - 1 < \lambda_m / \lambda_o < n$$

n is the number of **polydisperse** oil cores per capsule

λ_o is breakup wavelength of oil jet; λ_m is breakup wavelength of monomer jet

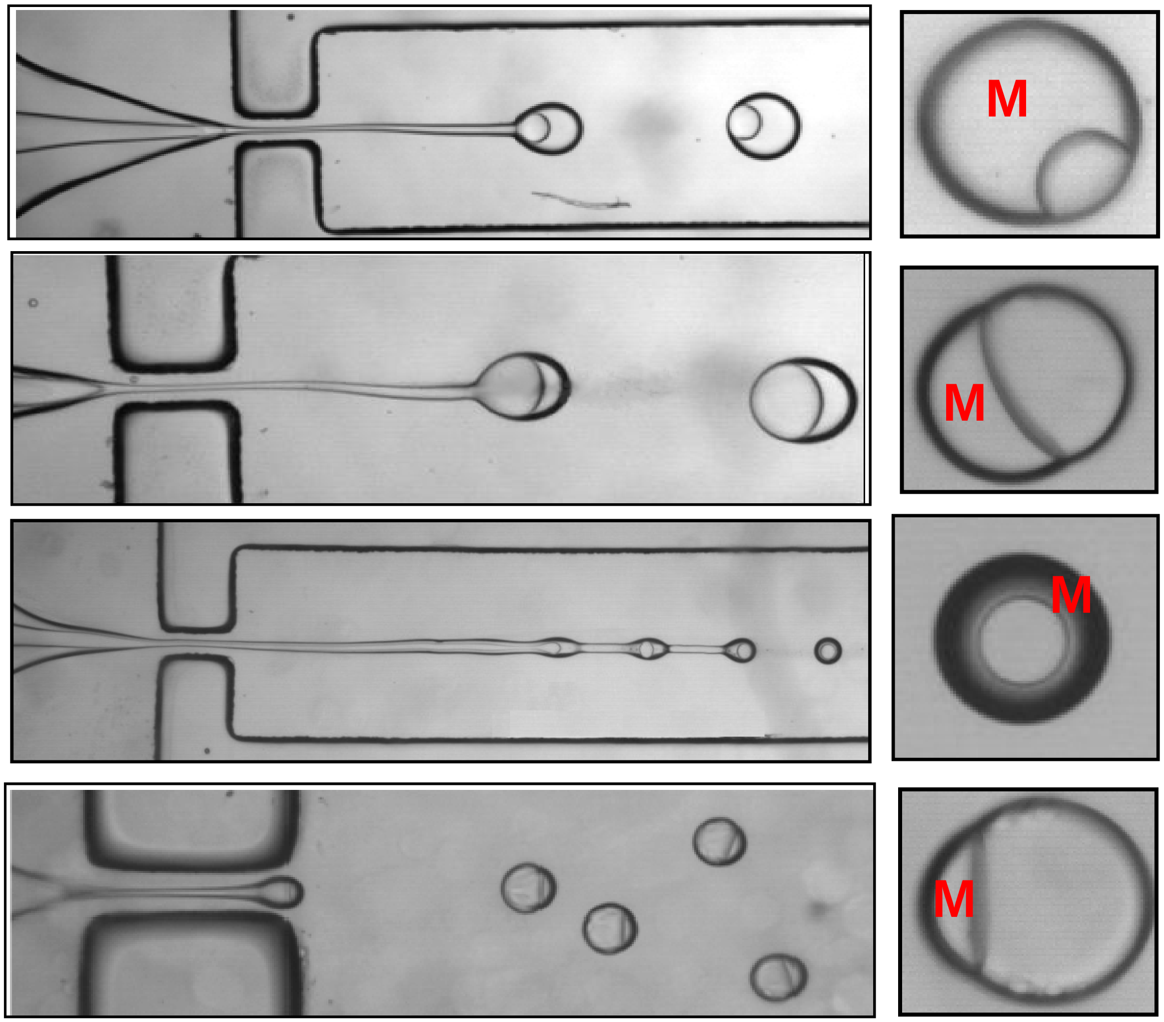


Stable breakup of coaxial jet

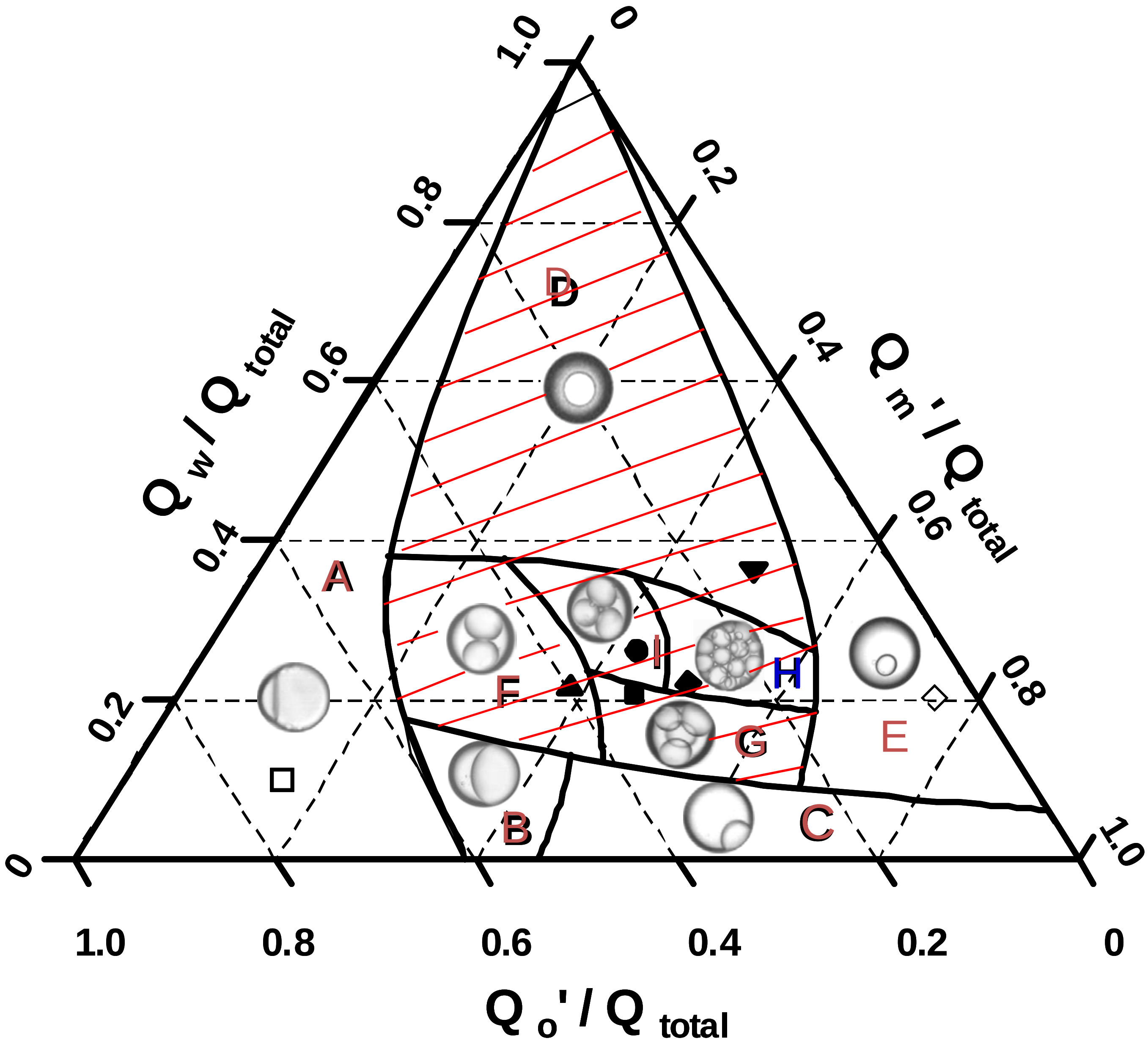


Z. Nie *et al*. *J. Am. Chem. Soc.* *127*, 8058 (2005)

$$n-1 < \lambda_m / \lambda_o < n$$

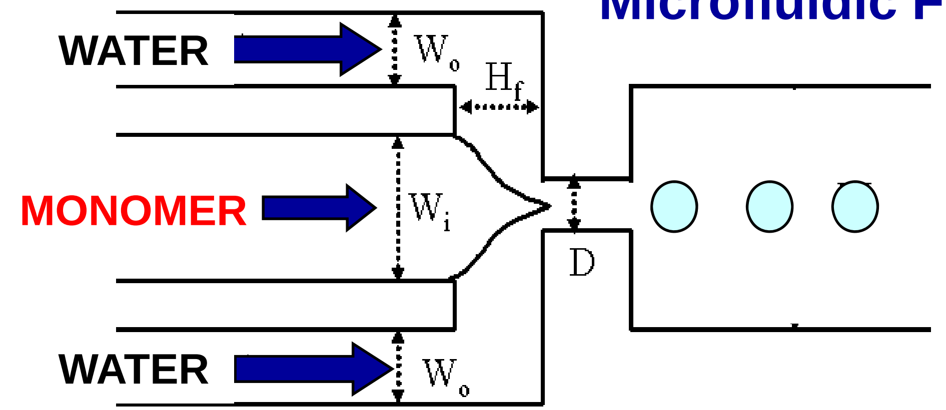


Synthesis of Polymer Capsules

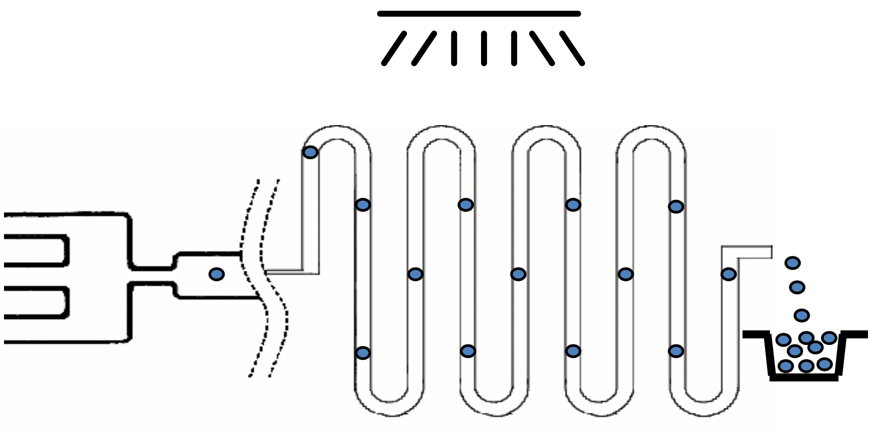


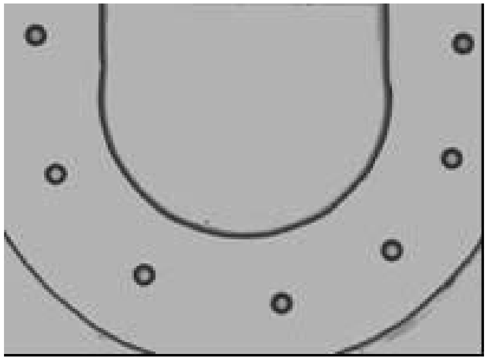
Continuous **Microfludic Reactors**

Microfluidic Flow-Focusing Device

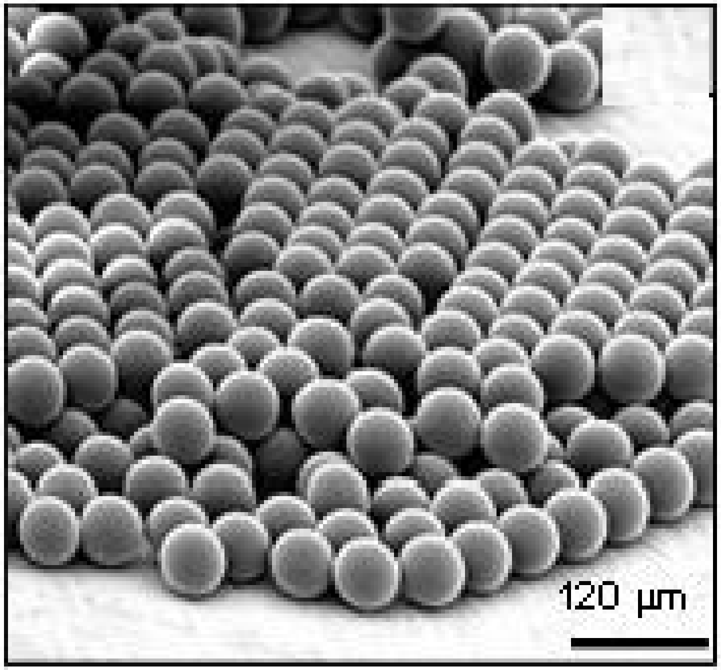


UV-irradiation



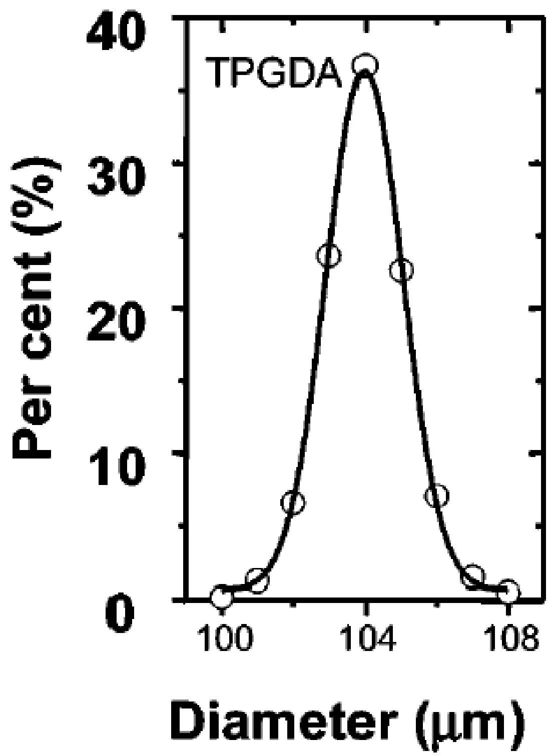


H. A. Stone et al. ***Appl. Phys. Lett.*** **361,** 51-515 (2001)



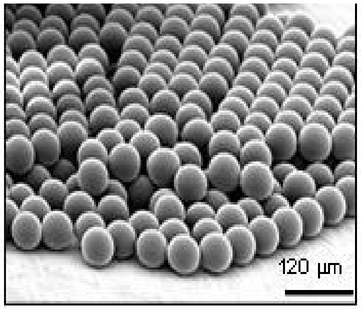
Poly(tripropylene glycole diacrylate)

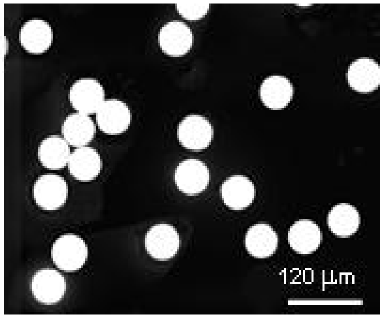
Polyacrylates
Polystyrene
Polyurethane
Biopolymer gels

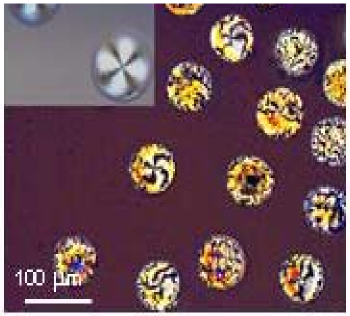


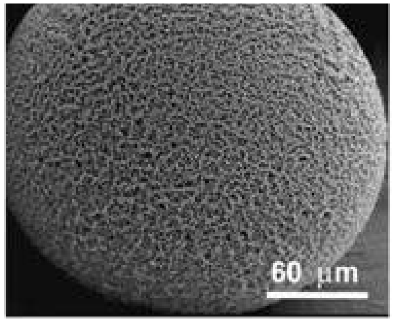
0.5 % < CV < 3 %

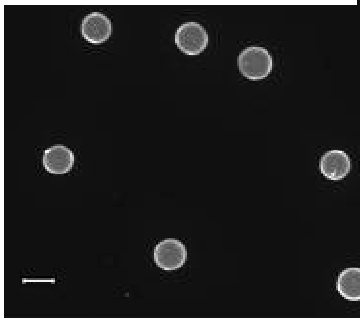
S. Xu et al. ***Angew. Chem. Intnl. Ed.*** **44, 724 (2005)**











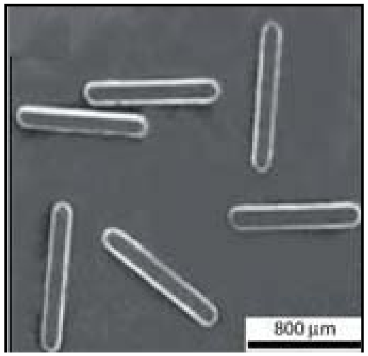
Polymer microbeads

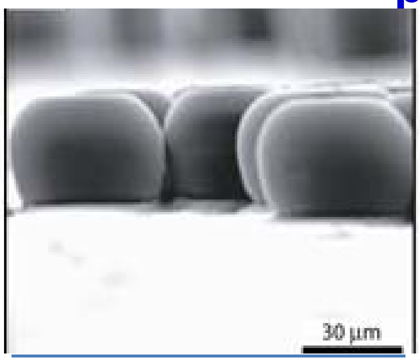
Nanoparticle-loaded beads

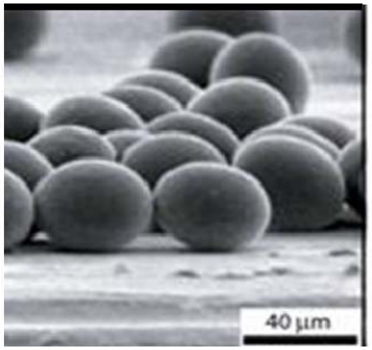
Liquid Crystal-polymer particles

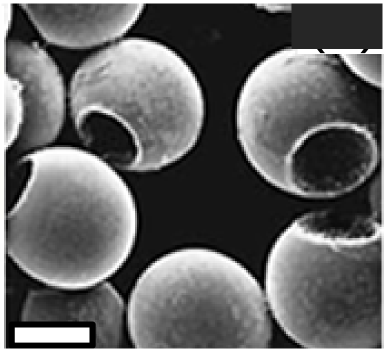
Porous microbeads

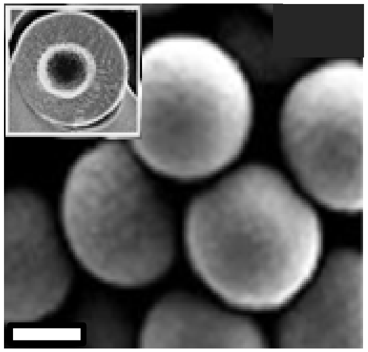
FITC-BSA-conjugated beads



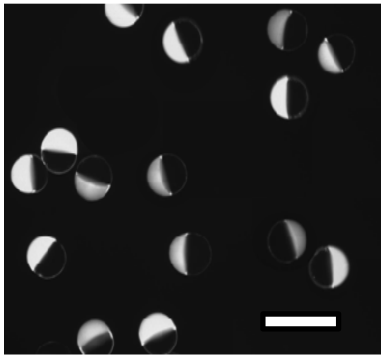


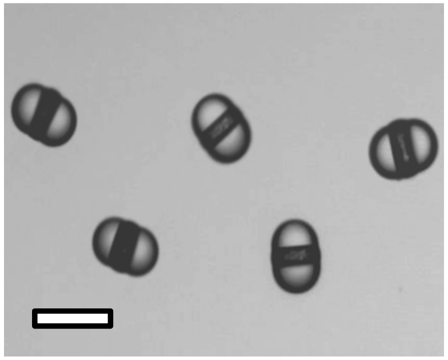


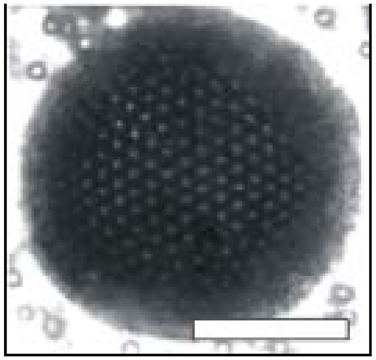




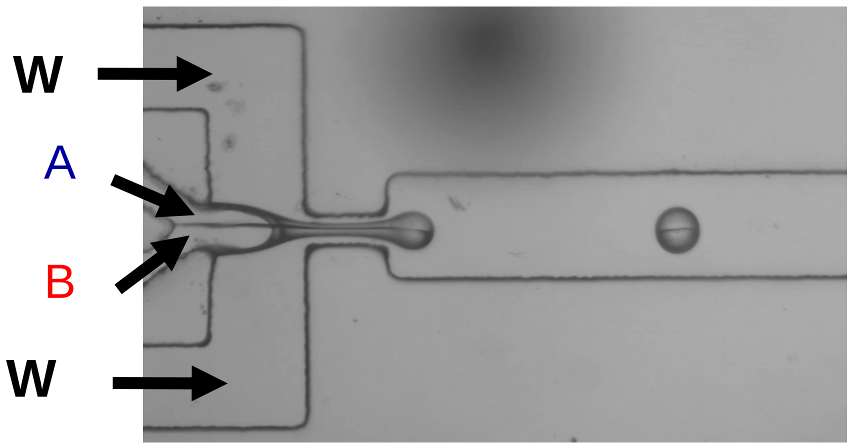
Shape and morphology control



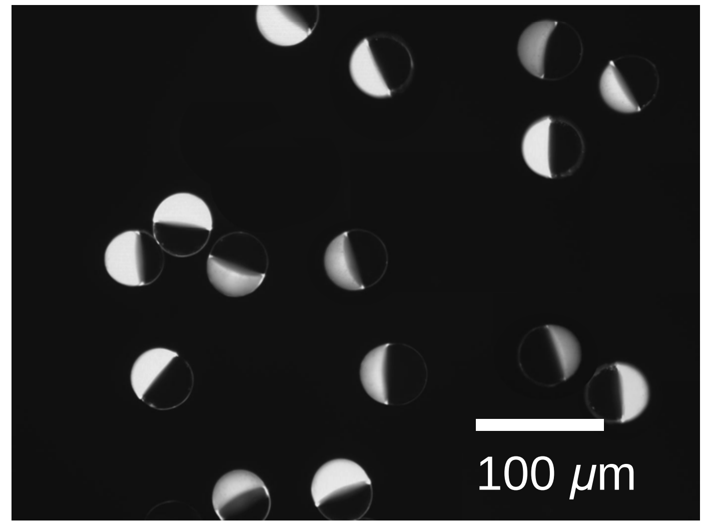


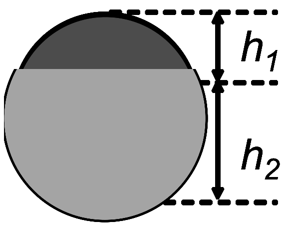


Synthesis of Janus particles



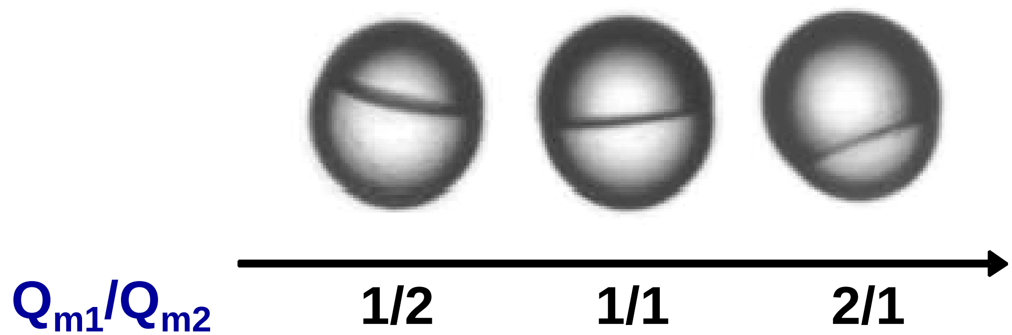
A: MAOP-DMS + **dye**
B: PETA-3/AA



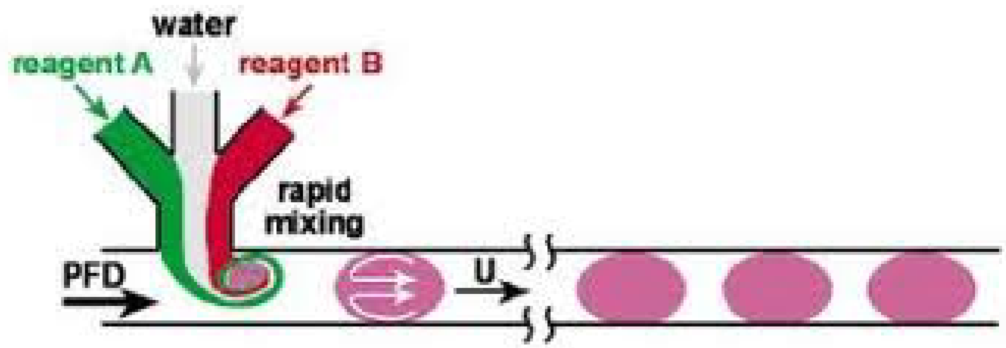


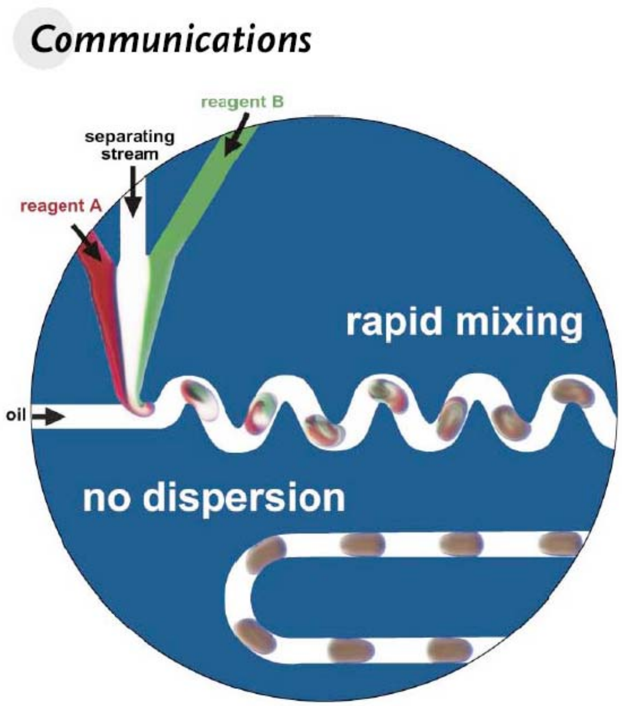
$$V \sim (Q_{m1} + Q_{m2}) / Q_w)$$

$$\frac{Q_{m1}}{Q_{m2}} = \frac{h_1^{\,2}(3R - h_1)}{h_2^{\,2}(3R - h_2)}$$



Exploratory droplet microfluidics





Optimization of chemical reactions

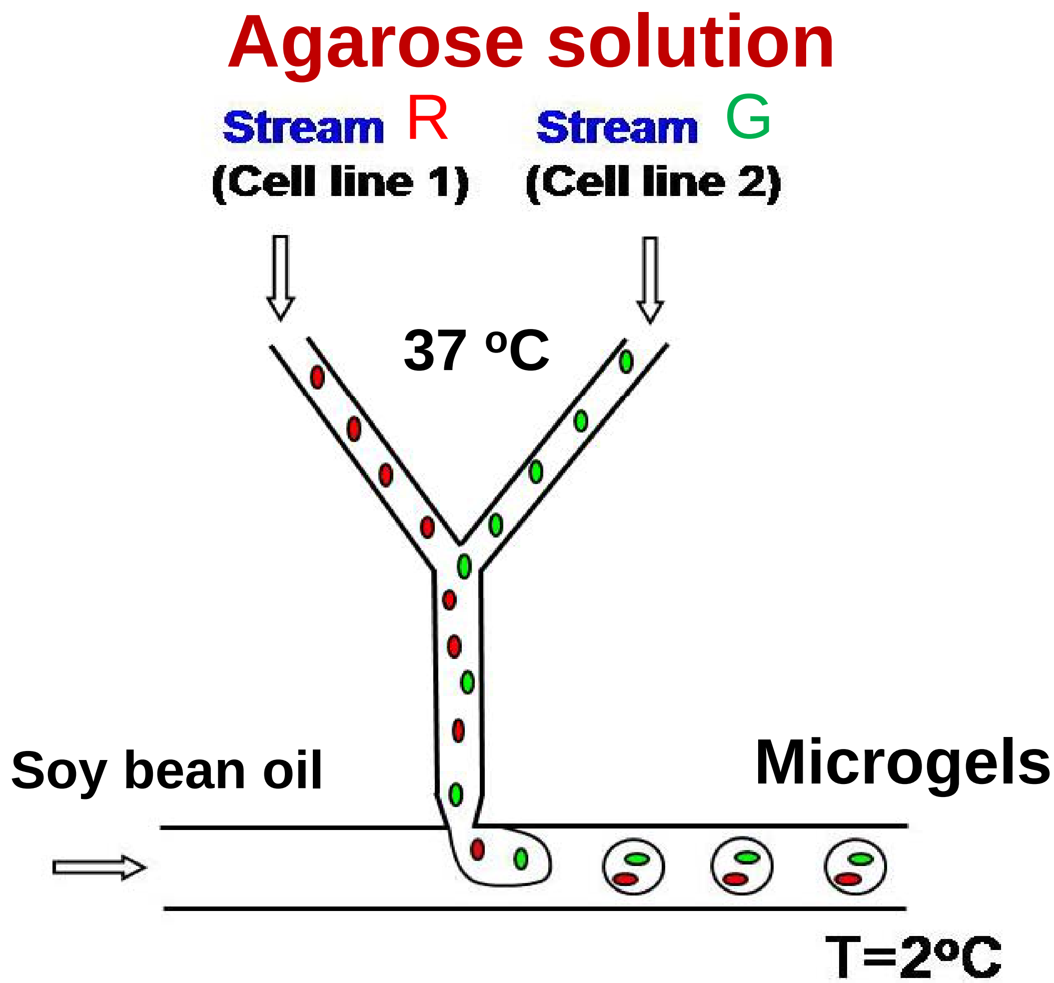
High-throughput generation of cellular microenvironments

Ismagilov, 2005

Microenvironments for cell co-culture

Direct and indirect cell-cell interactions:

proliferation, self-renewal, death or differentiation



Applications:

- wound healing
- tissue engineering
- inhibition of cancer spreading

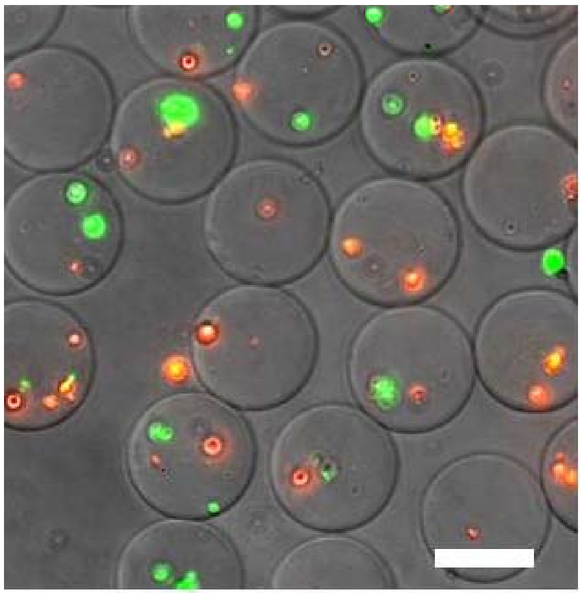
$Q_{tor} = Q_G + Q_R = const$

Change the ratio Q_G/Q_R

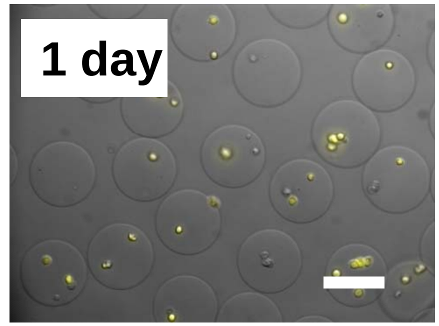
61

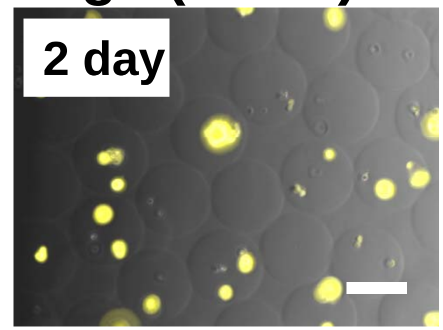
Microenvironments for cell co-culture

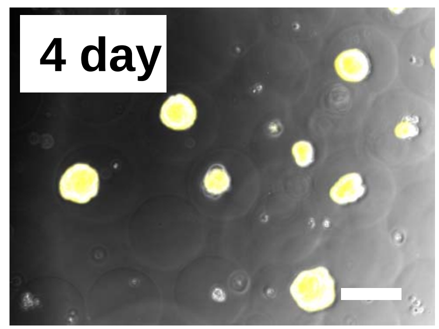
Murine embryonic stem (mES) cells labelled with Vybrant Cell Tracer ("green") and CellTracker Orange ("red")

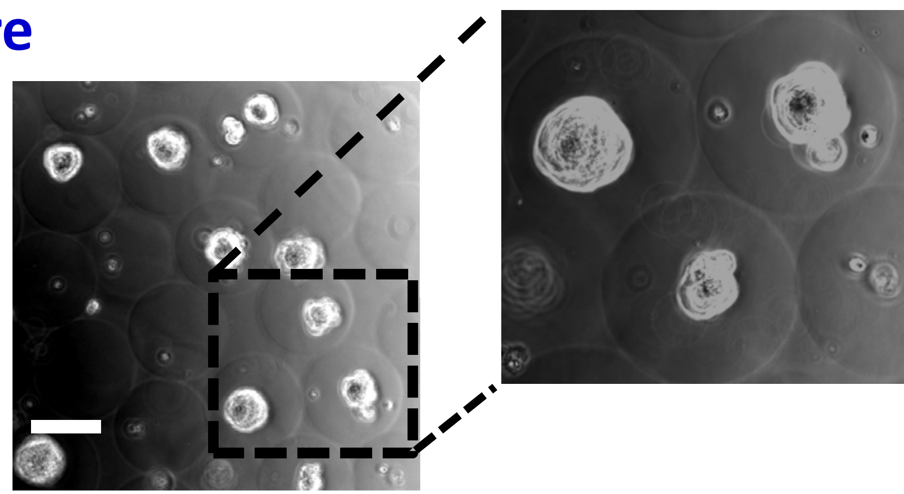


Cell co-culture







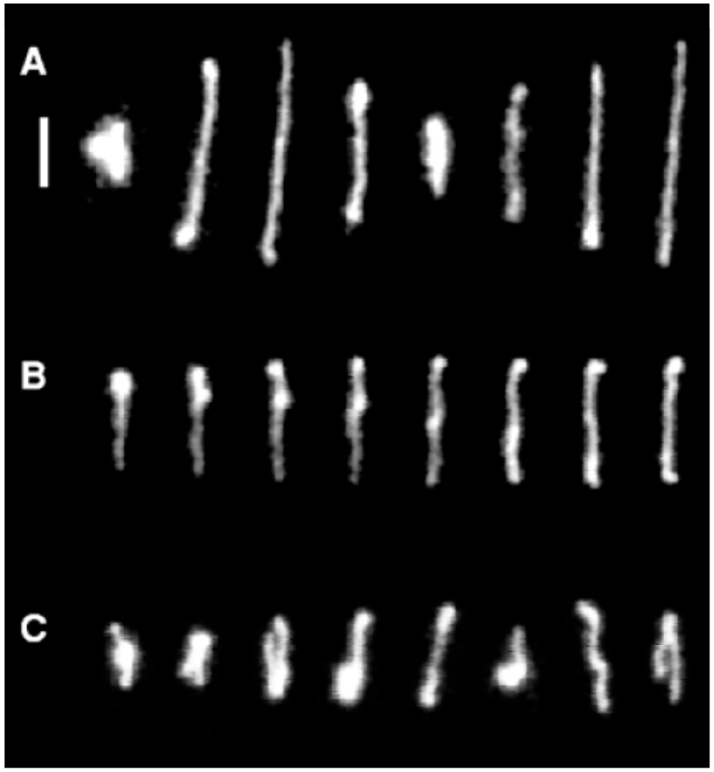


Embryoid bodies

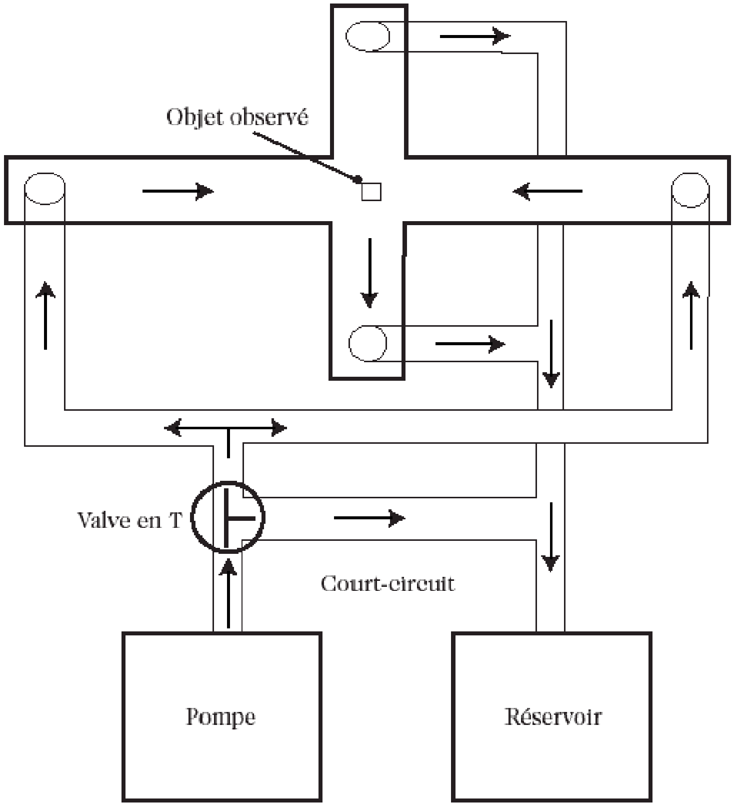
(YC5 Mouse Embryonic Stem cells)

Scale bar is 100 μm

Microfluidics and single molecule studies



Experiment by S. Chu et al (1994)



Books

P. Tabeling. Introduction to Microfluidics.

Microfluidics for Biotechnology *- J.Berthier P.Silberzan*

Micro and NanoFlows *(2-nd edition of Karnadiakis's book)*

Reviews:

-H.Stone, A.Stroock, A.Ajdari, Ann.Rev.Fluid Mech, 36, 381(2004)

- S.Quake, T.Squire, "Microfluidics : Fluid Physics at the microscale"(2005)
-Analytical Chemistry, Lab on a Chip

- P.A.Auroux, D.Iossifids, D.Reyes, A.Manz, Anal.Chem,74, 2637 (2002)

- Huck *et al*. *Angew. Chem. Int. Ed*., 49, 5846-5868 (2010)