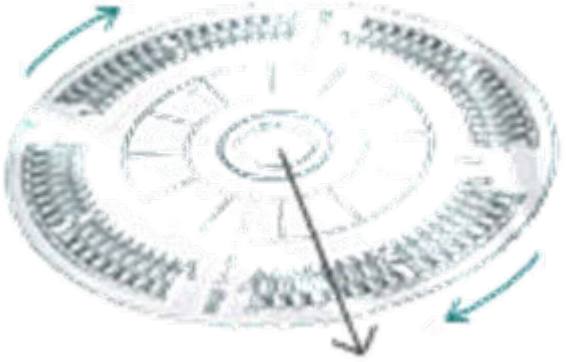
Microsystems Design, 11/11-2008

- Surface tension
- Capillary forces
- Ideal gas law
- Viscosity
- Navier Stokes equation
- Reynolds number
- Poiseuille flow
- Electroosmotic flow
- Electrophoresis
- Mixing

These topics are important for design of well-functioning fluidic microsystems.

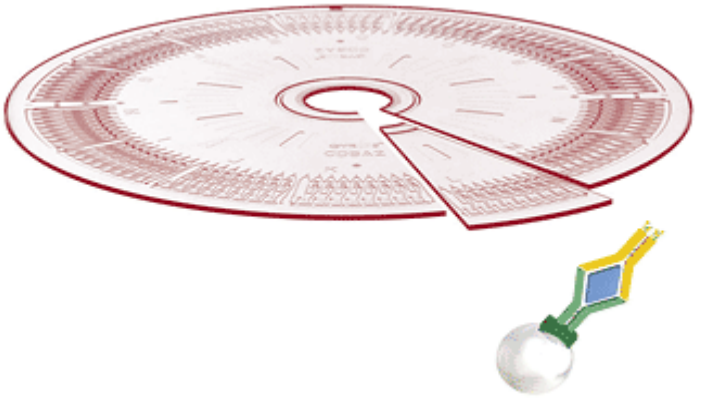
Gyros AB microfluidics platform

- world leader in the miniaturization and integration of laboratory applications through its proprietary microfluidics platform, Gyrolab CD (compact disc) microlaboratory.



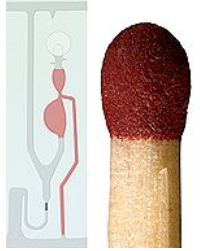
Gyros AB, Sweden
GyroLab CD microlaboratory

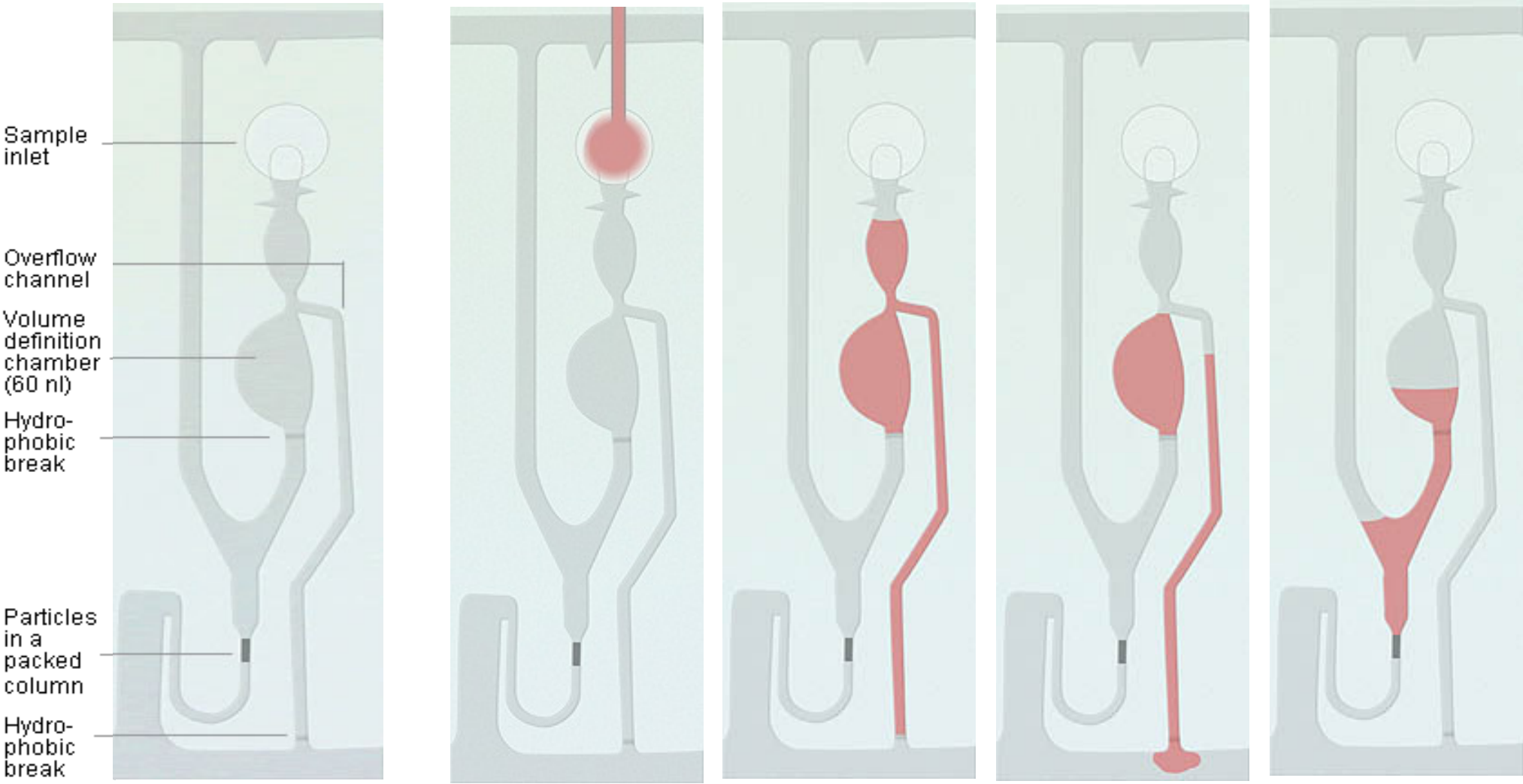
- Protein quantification
- Microchannels in polymer disk
- Multiple analyses
- Centrifugal forces



- Instrument
- Polymer disk

www.gyros.com





Surface modification

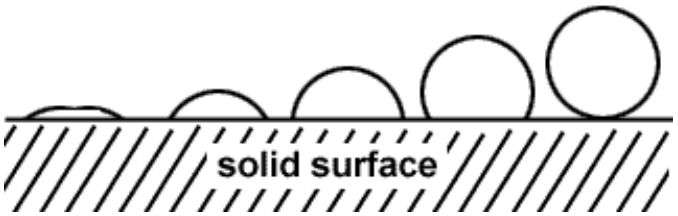
- Hydrophilic / hydrophobic surfaces
- Wetting/non-wetting droplets
- Fuktende/ ikke-fuktende væsker

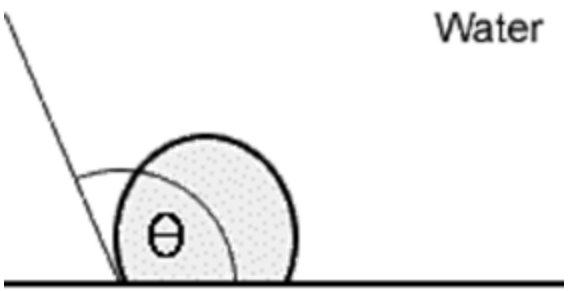
- Lithographic patterning
- E.g. deposition of self-assembled -monolayers

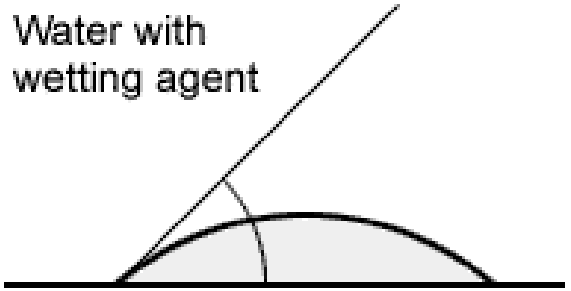
Wetting / Non-wetting

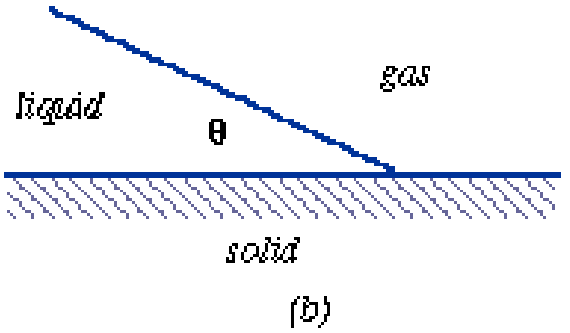
- Contact angle depends on the solid/liquid/gas that meet in one point

- Wetting fluid: Contact angle < 90
- Non-wetting: Contact angle > 90



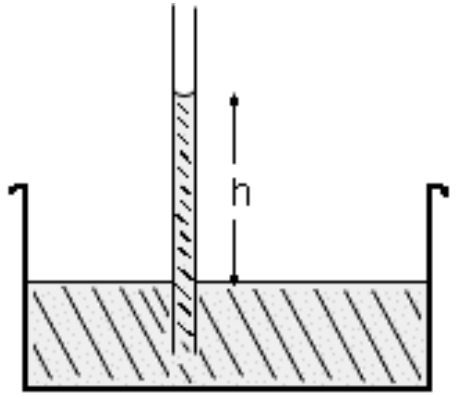


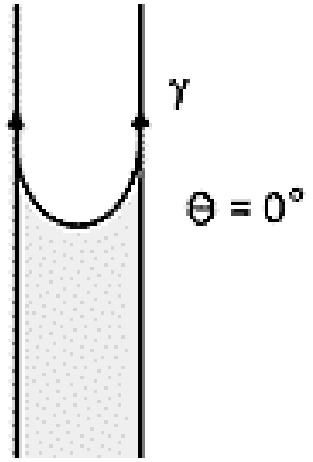


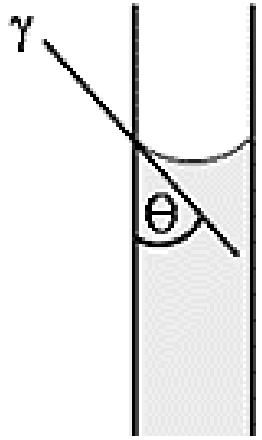


Definition of wetting angle

- Can be modified by (chemical) surface treatment

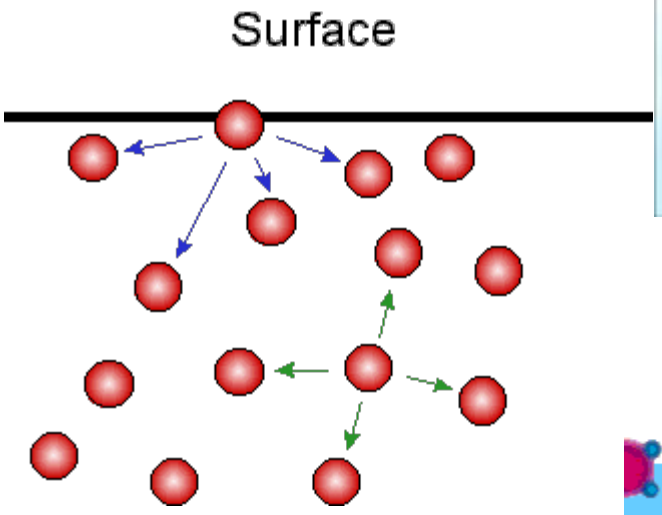


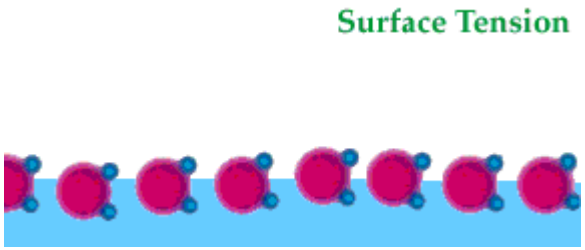




Surface tension

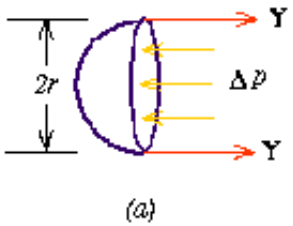
- Surface between two fluids
  - Gas-Liquid
  - Liquid-Liquid
- Energy per surface area
- Force per unit length [N/m]

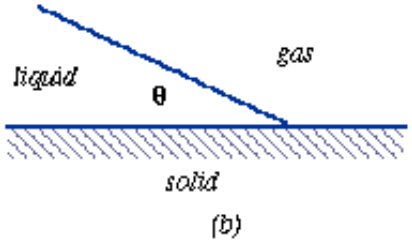




- Surface tension along periphery
- Pressure on section area

$$2\pi r\Gamma = \Delta P \pi r^2$$



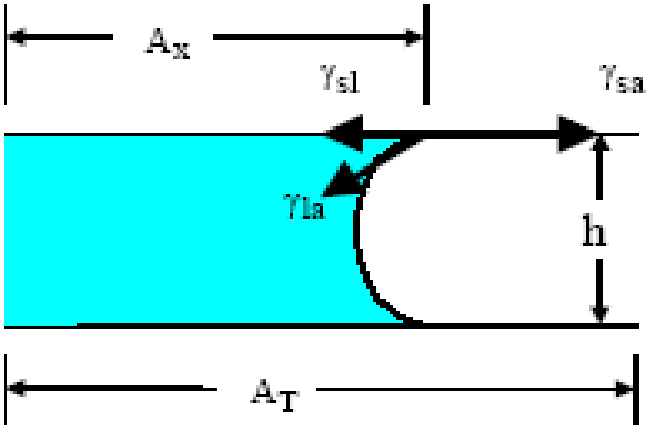


Pressure difference outside/inside drop: $\Delta P = 2\Gamma / r$

Equilibrium pressure difference across meniscus in capillary tube

- Young-Laplace equation, circular capillary tube:

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



Tube radius *r*

- Young-Laplace equation, rectangular capillary tube:

Channel width *w*

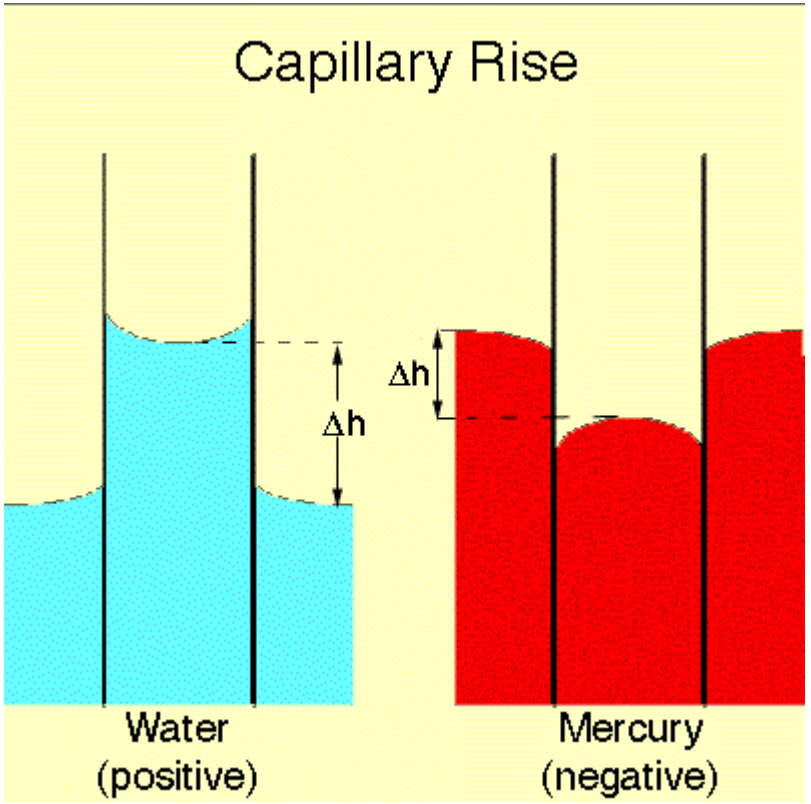
Channel height *h*

$$\Delta p = -2\gamma\left[\frac{\cos\theta_{wall}}{w} + \frac{\cos\theta_{top}}{h}\right]$$

Capillary rise Senturia 13.2.3

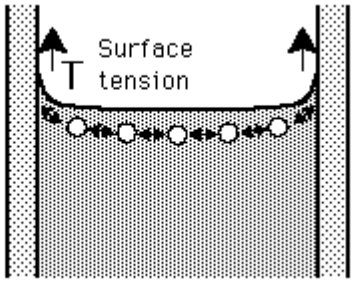
- A liquid that wets the walls will rise to a height *h* in a capillary tube
- Equilibrium is when weight of liquid column equals surface forces that pull meniscus up

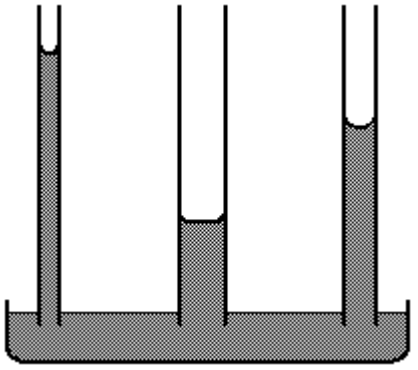
- Forces:
  - Surface forces pull meniscus up $2\pi r\Gamma\cos\Theta$
  - Gravity pull liquid down $\rho g h \pi r^2$



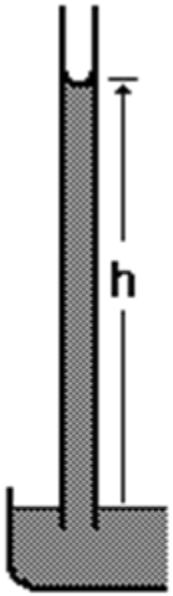
$$\rho g h \pi r^2 = 2\pi\Gamma\cos\Theta$$

Capillary action is the result of adhesion and surface tension. Adhesion of water to the walls of a vessel will cause an upward force on the liquid at the edges and result in a meniscus which turns upward. The surface tension acts to hold the surface intact, so instead of just the edges moving upward, the whole liquid surface is dragged upward.





$$h = \frac{2\Gamma \cos\theta}{\rho g r}$$



Since it is weight limited it will rise higher in a smaller tube

Capillary action occurs when the adhesion to the walls is stronger than the cohesive forces between the liquid molecules. The height to which capillary action will take water in a uniform circular tube is limited by surface tension. Acting around the circumference, the upward force is

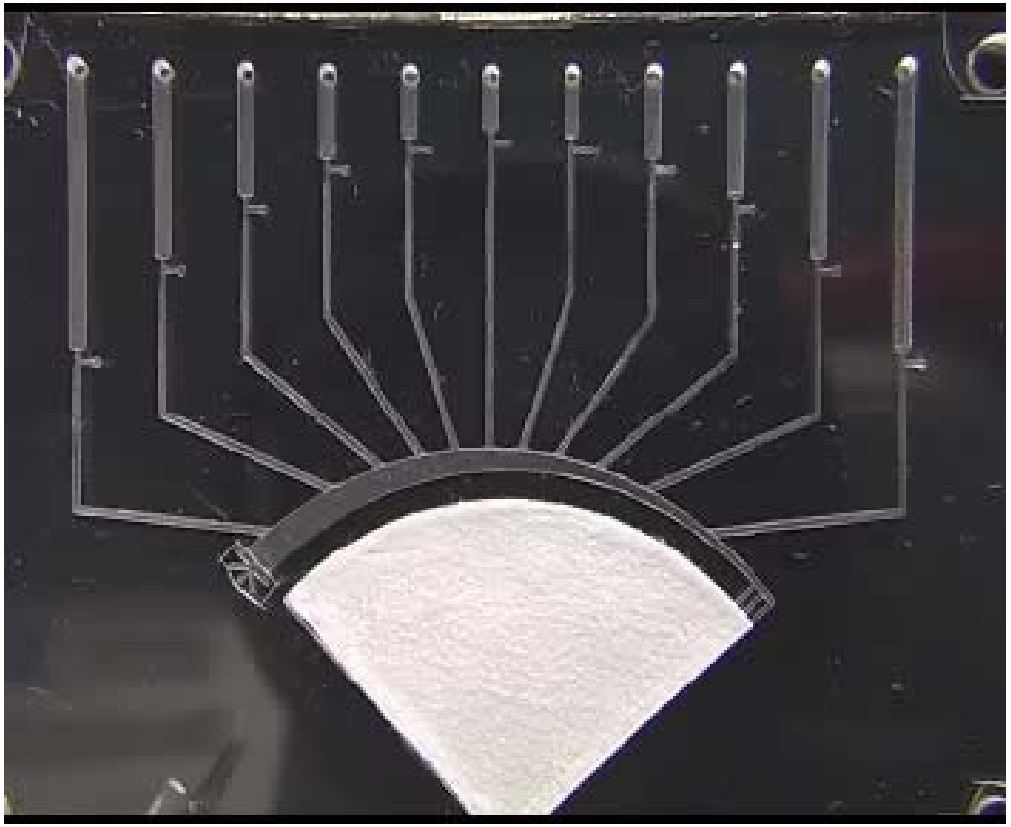
$$T 2\pi r = \rho g (h \pi r^2)$$

The height h to which capillary action will lift water depends upon the weight of water which the surface tension will lift:

The height to which the liquid can be lifted is given by

$$h = \frac{2T}{\rho r g}$$

Capillary filling

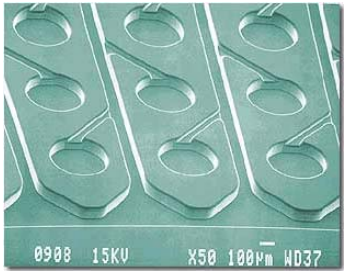


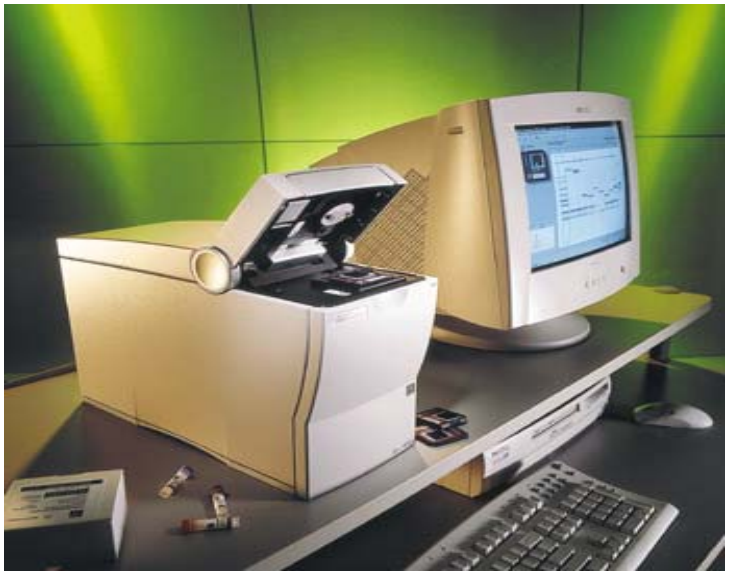
Manufacturing of microfluidic chips

- Plastic
  - Master manufactured in silicon with lithographic methods, then in nickel by electroplating
  - Use foundry (støpeform) for plastic forming
  - Hot embossing
  - Injection moulding
- Glass
  - Lithographic patterning of resist on e.g. gold chromium
  - Wet etch of glass
- Sealed by glass or plastic film -> bonding or lamination

- Typical depth of microfluidic channel: 10-100μm

Mikro-kanaler



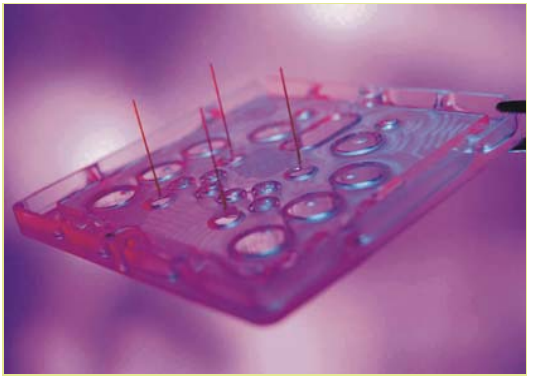


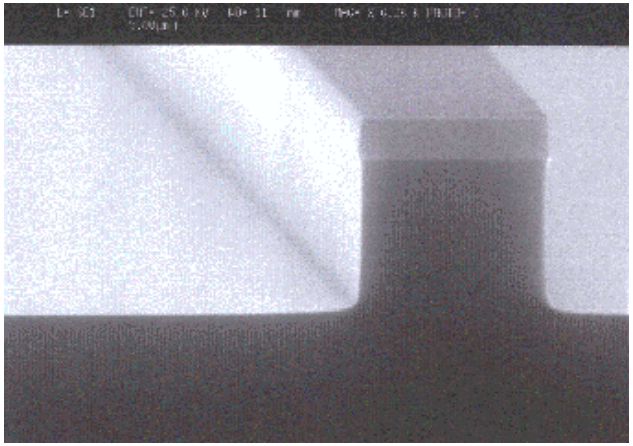
- Kanaler med vertikale vegger i silisium

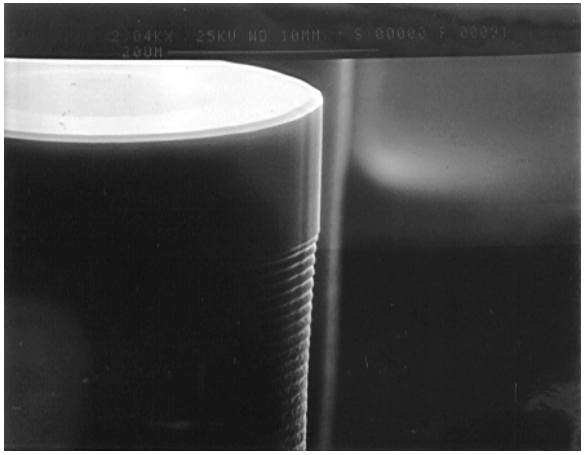
- Sprøytestøping av plast

  Støpeformene generert f.eks. via silisium + elektroplatering

Caliper



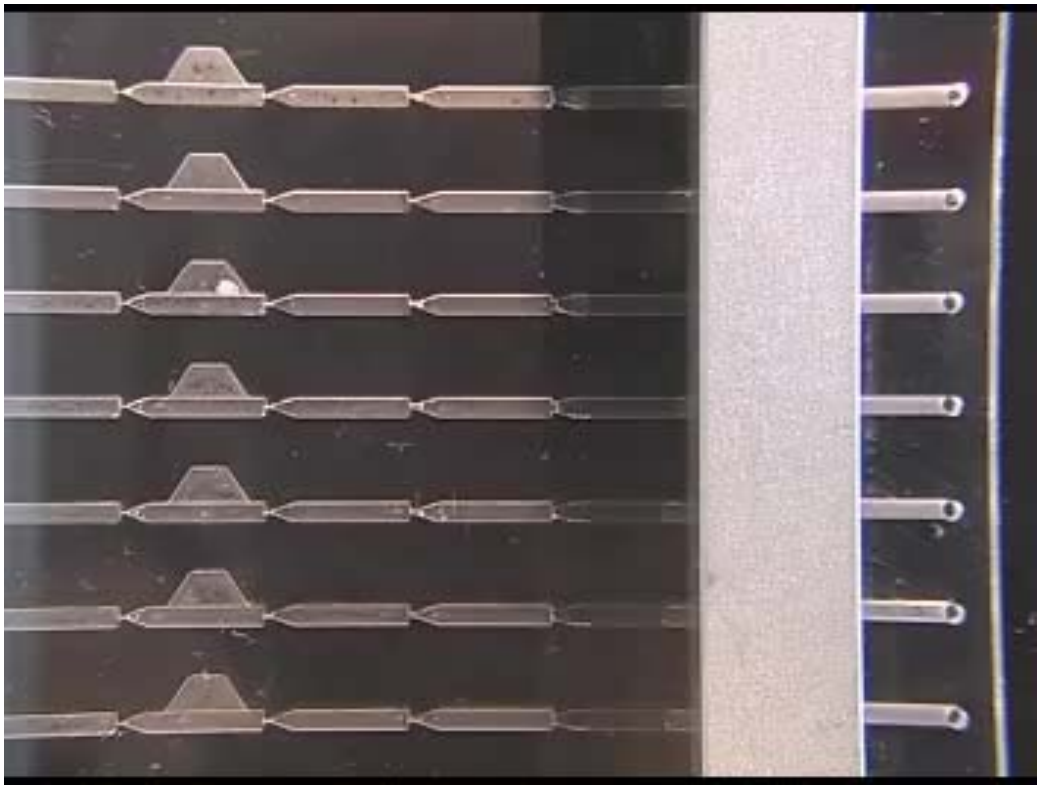




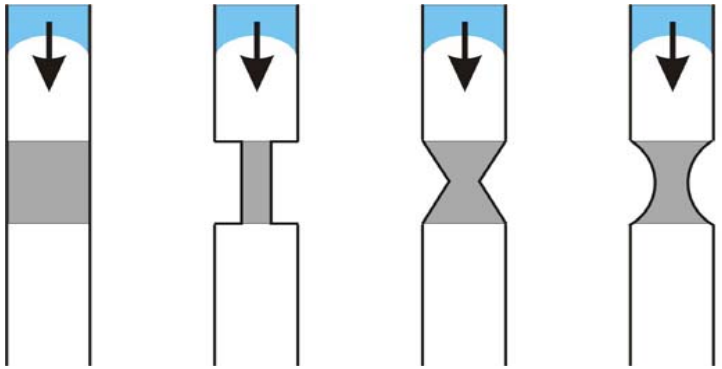
New:
Deep reactive ion etch DRIE, BOSCH process

Parallel plug displacement chip

- 7 liquid plugs in parallel
- Plug volume ~1µl
- Working liquid: DI water
- Teflon spotted hydrophobic valves
- Single pump source, pump velocity 10µl/min

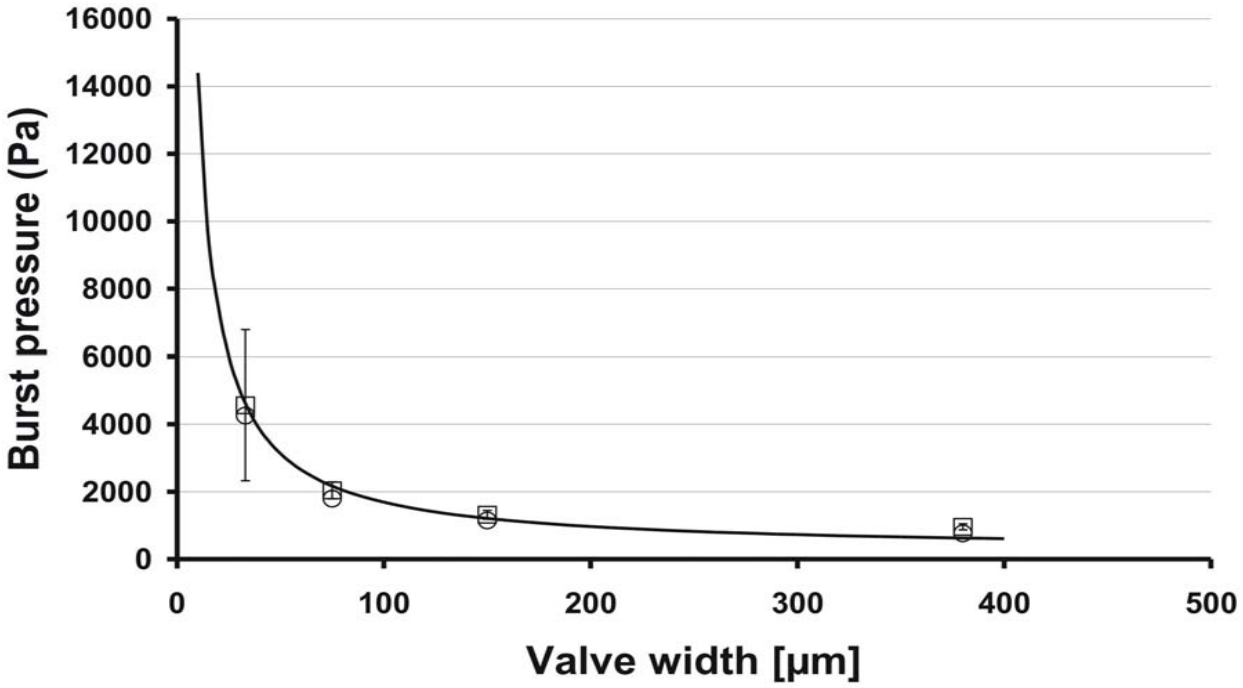


Capillary valving (surface manipulation to change wetting properties



- Grey –teflon
- Hydrophobic valves
- Small restriction – high pressure required to “break” the valve
- Can efficient flow control using a single pressure source for many parallel channels be achieved?

Burst pressures water, reagents



Burst pressures of the capillary valves as function of valve width. Symbols: □ DI water; ○ reagents; solid line represents the analytical values for water. Contact angle of DI water on Teflon was measured to be approx. 110º. The pressure data for each valve represents an average of 35 measurements (5 chips with 7 parallel channels each).

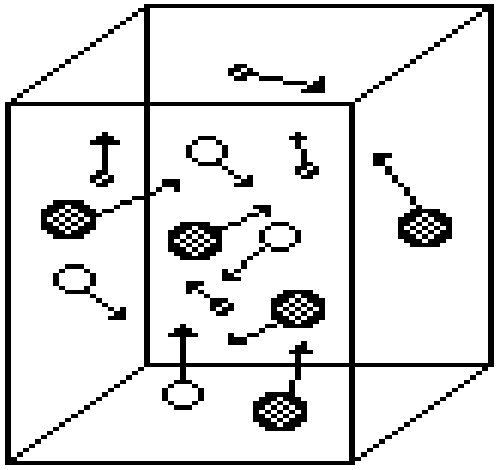
Ideal Gas Law

- Equation of state for (ideal) gases
- pV=NkT
- k=1.38 10^{-23} J/K, Boltzmann constant

- Senturia:

$$P = \rho_m (\frac{R}{M_W})T$$

  - R=8.31 J/(mol K), universal gas constant



State variables

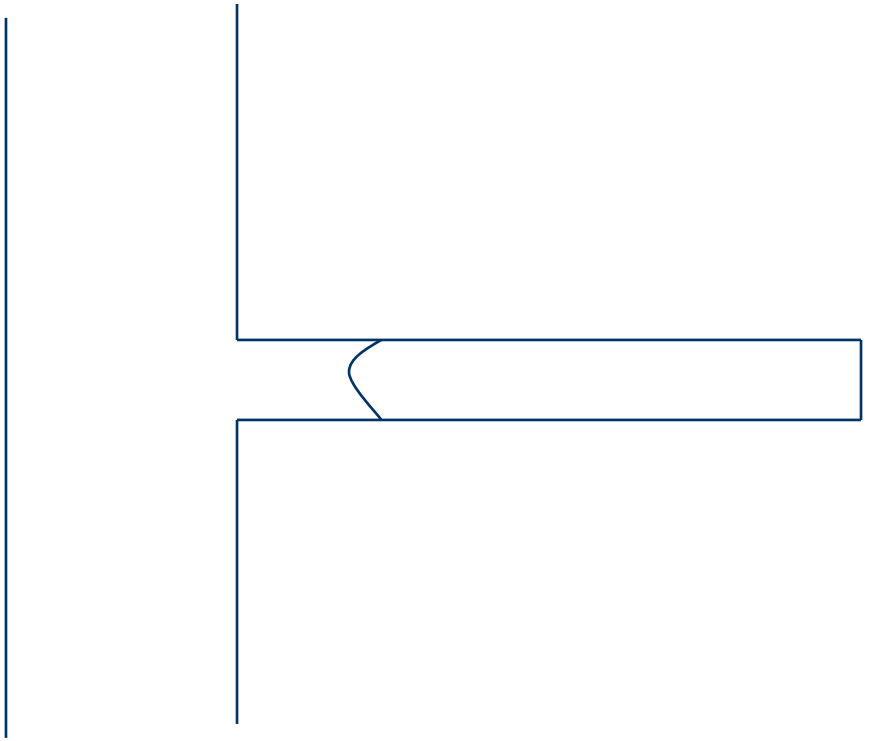
V volume

P absolute pressure

T absolute temperature

Exercise:
Fluid volume in capillary “dead-end”

- Where does the meniscus stop?
- What is the volume that is pulled into the narrow capillary?
- What happens when temperature is increased?



- Molecular diagnostics
  - Cancer
  - Infections (bacteria, virus, parasites)
  - Cardiovascular diseases
- Molecular markers
  - DNA, RNA
  - Proteins; antigens, enzymes, hormones
  - Low molecular compounds

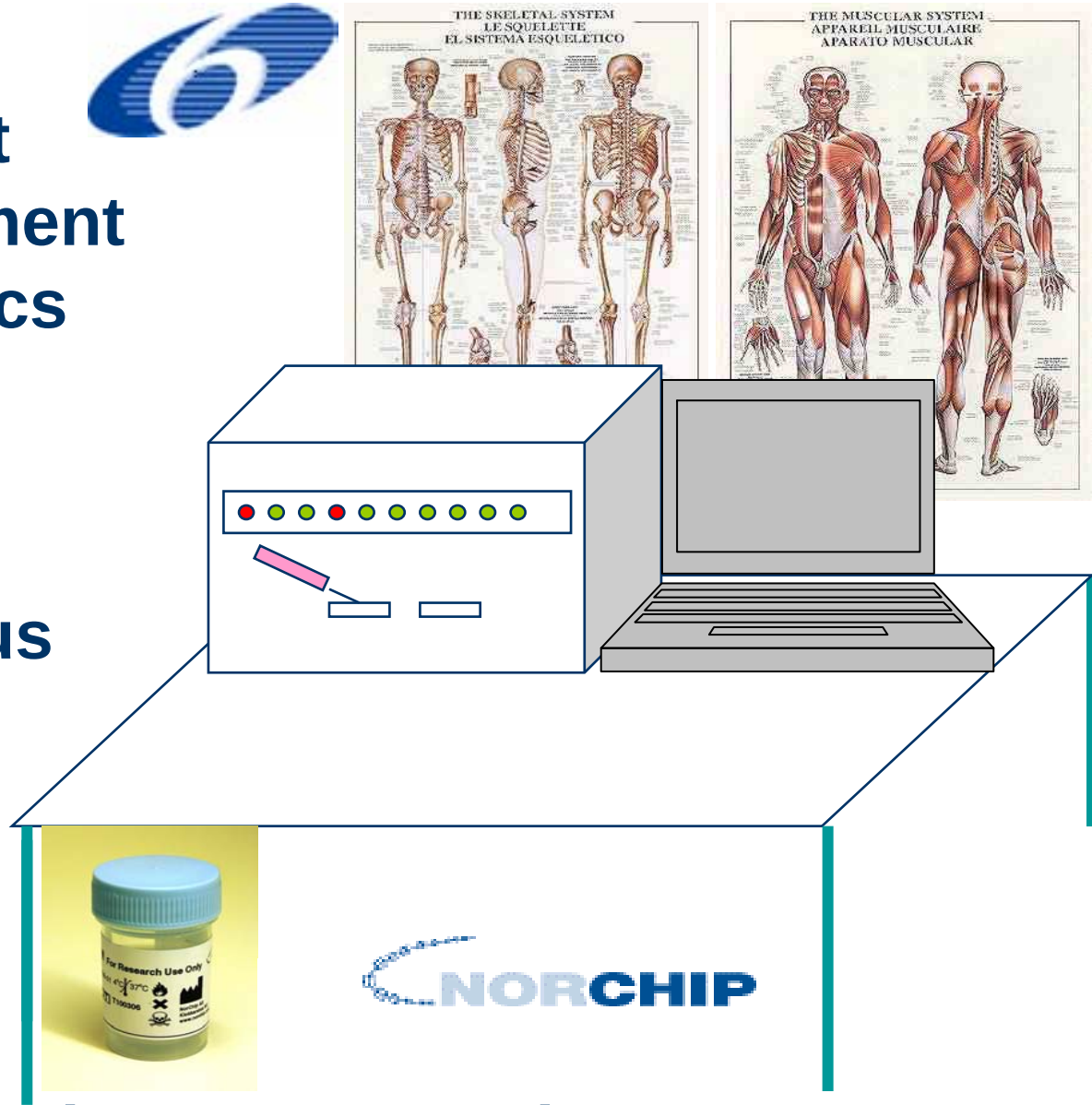
- Sample preparation
  - filters, micro-pillars, magnetic beads, separation
- Washing
- (Amplification e.g. PCR)
- Reactions
  - Immunoreactions
  - Hybridization
- Detection
  - Labels (dye, fluorescent, radioactive)
  - Label-free (impedance, electrochemical, amperometric, cantilevers, evanescent fields)
- Choose methods for all steps:

SENSITIVITY + SPECIFICITY

Cepheid GeneXpert technology

Roche AmpliChip Pharmacogenetic microarray based test

The main objective for The MicroActive project is to develop an instrument for molecular diagnostics intended for use in the doctor's office



- Human papilloma virus
- Cervical cancer
- mRNA
- Two microchips
- Instrument

NORCHIP

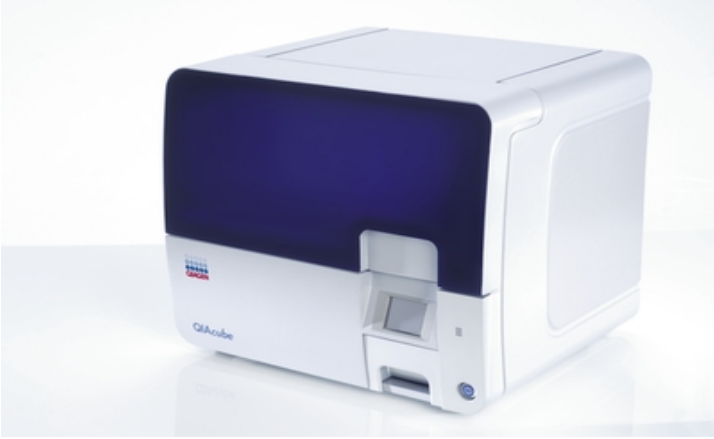
- Cell sample in, diagnosis on 10 HPV viruses out

A sample preparation chip has been manufactured

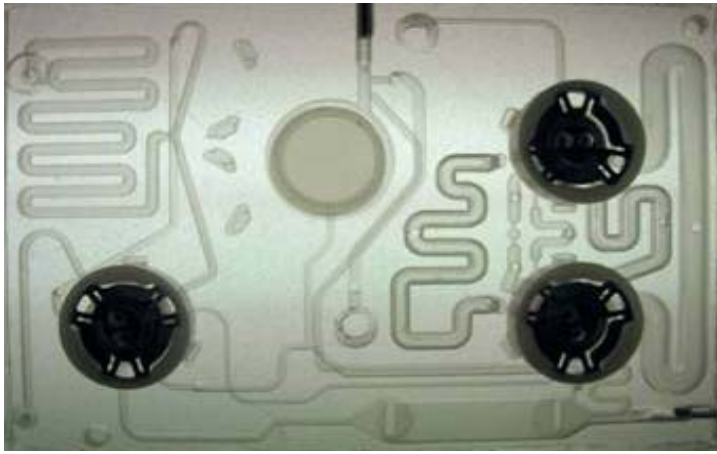
- Purification of nucleic acids
- Start material (5 ml): liquid based cytology
- Output (20 μl): mRNA suitable for NASBA amplification

- Functions
  - Lysis buffer, wash buffers, elution buffer stored on-chip
  - Cell filter
  - Nucleic acid capture filters

- Chip output has successfully been amplified by NASBA

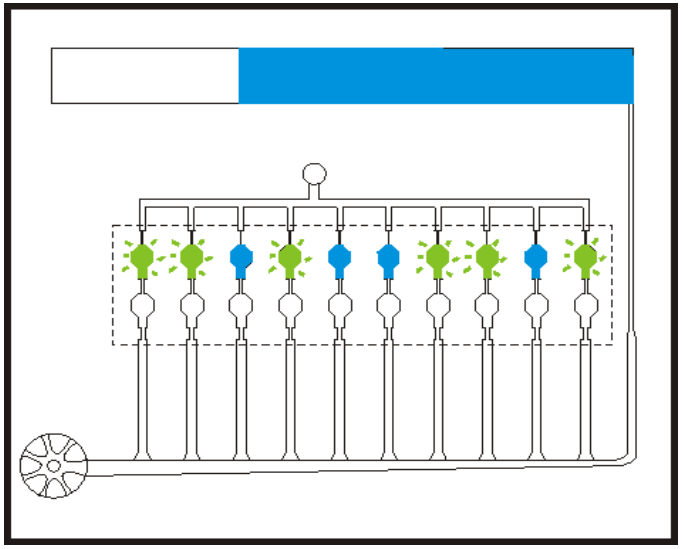


Biomerieux, Qiagen



MicroActive chip (IMM)

A NASBA amplification and fluorescent detection chip has been manufactured



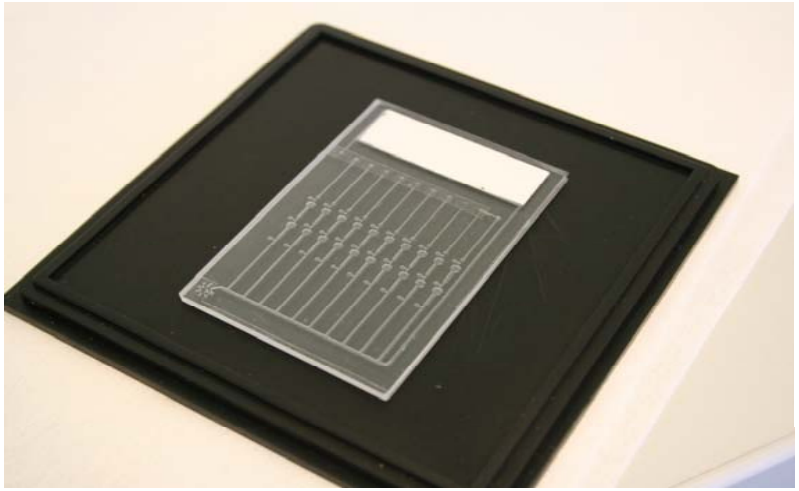
Input: 20 μl of purified nucleic acids

Split fluid volume into 10 droplets of 500 nl

Primers for each HPV type and NASBA enzymes stored in dry state on chip

3 droplet stop positions controlled by hydrophobic patches in channels

- Metering
- Dissolution of master-mix reagents
- Dissolution of enzymes and detection

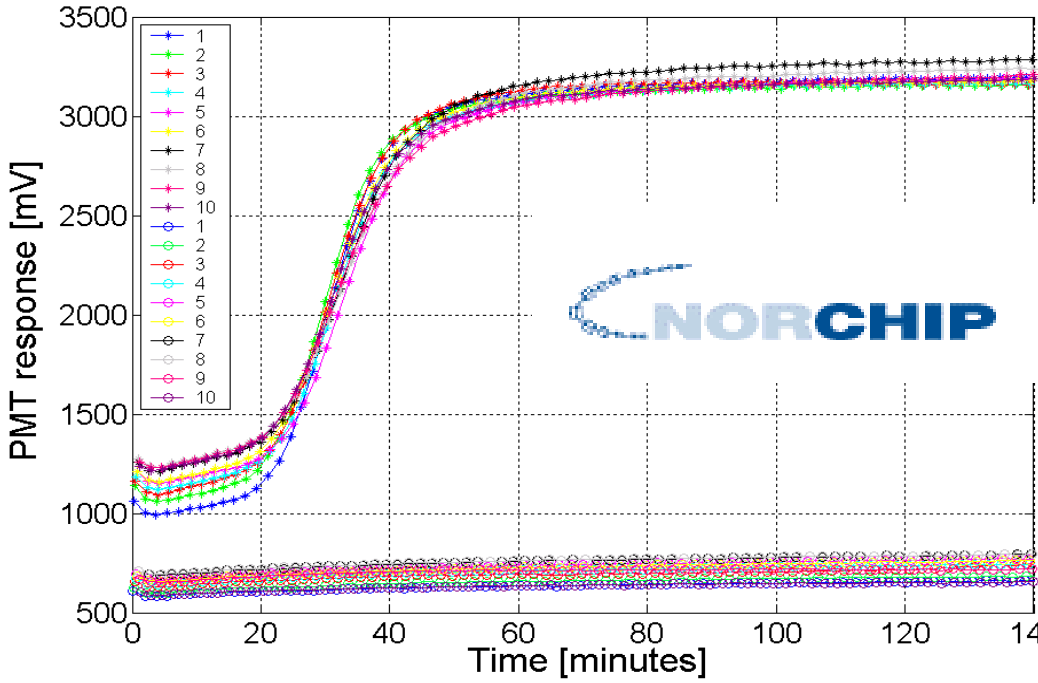


SINTEF injection molded chip

NASBA of HPV-16 mRNA in 500 nl plugs in microchip

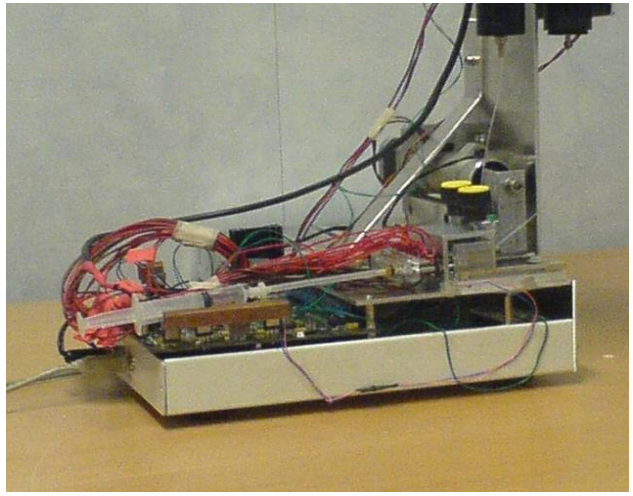
- Optimization of drying agents
- Wall roughness
- Wall coating
- Re-hydration of dried reagents

- NASBA amplification in sample plugs using dried enzymes

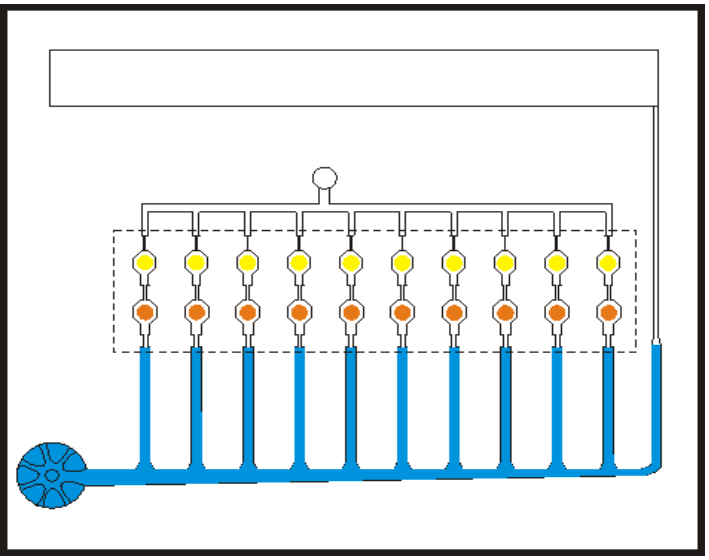


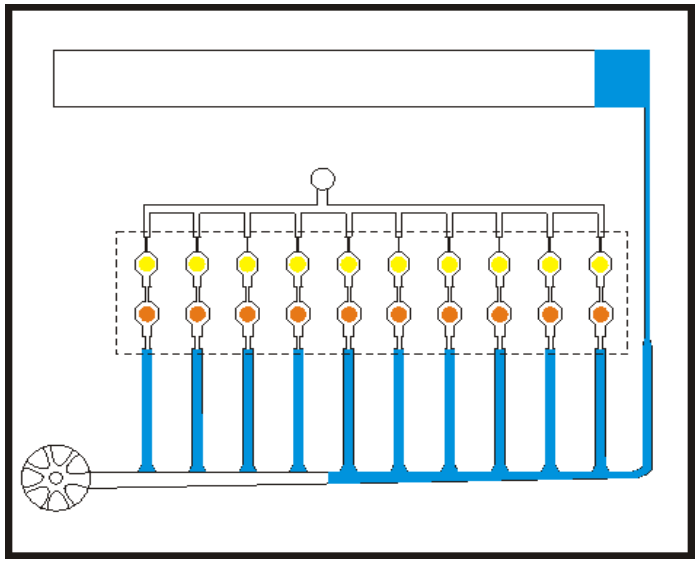
Instrument

- Pump
- Heating (for amplification)
- Fluorescent readout of 10 chambers

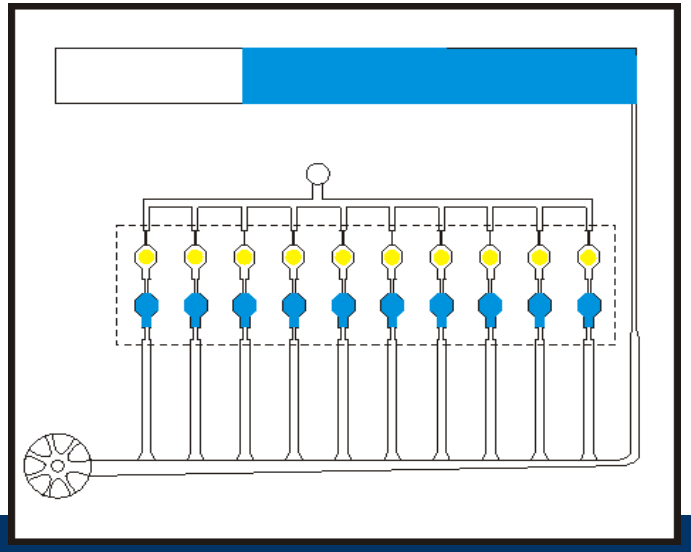


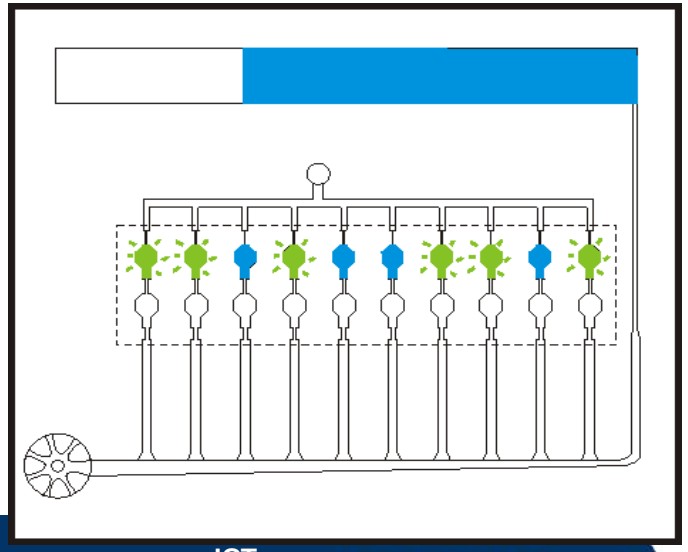
Cartoon of amplification chip function



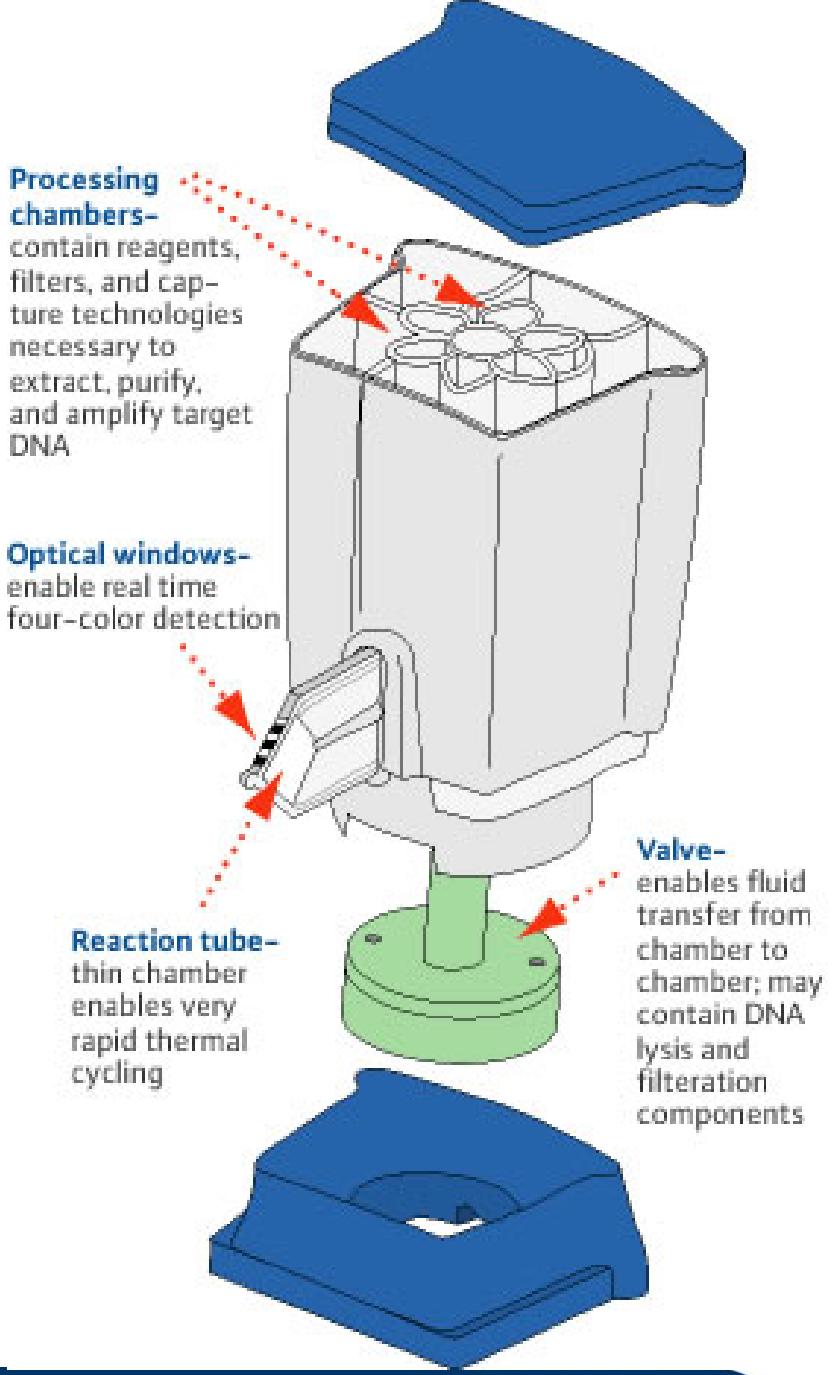


- Sample insertion
- Splitting into channels
- Metering
- Mix reagents 1
- Mix reagents 2
- Amplification
- Detection





Cepheid GeneXpert



Viscosity Senturia 13.2.1

- Deformation of fluids in the presence of shear forces
- The property of a fluid that resists the action of a shear force
- η[Pa s]

- Newtonian fluid:

$$\tau = \eta \frac{U}{h}$$

$$\tau = \eta \frac{\partial U_x}{\partial y}$$

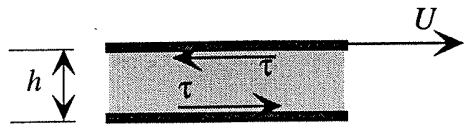
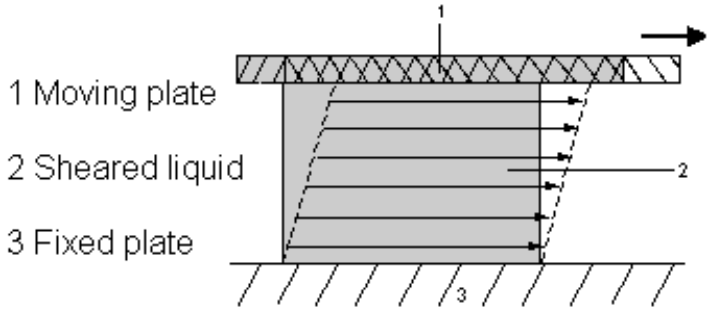


Figure 13.1. Fluid between two plates. The upper plate moves to the right with velocity U, setting up shear forces τ.



Navier-Stokes equation

- Conservation of mass

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \vec{v}) = 0$$

- Newton's 2nd law for a fluid

$$\rho\left(\frac{\partial \vec{v}}{\partial t} + (\vec{v} \cdot \nabla)\vec{v}\right) = \nabla p + \eta \nabla^2 \vec{v}$$

- Incompressible flow

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

Reynolds number

$$\mathrm{Re} = \frac{\rho U L}{\eta}$$

- Laminar or turbulent flow?
- Ratio of inertial forces to viscous forces
- Reynolds number:

ratio of kinetic energy of a volume of fluid in the flow

to

the energy dissipated by the volume in the shear caused by interaction with its solid boundaries

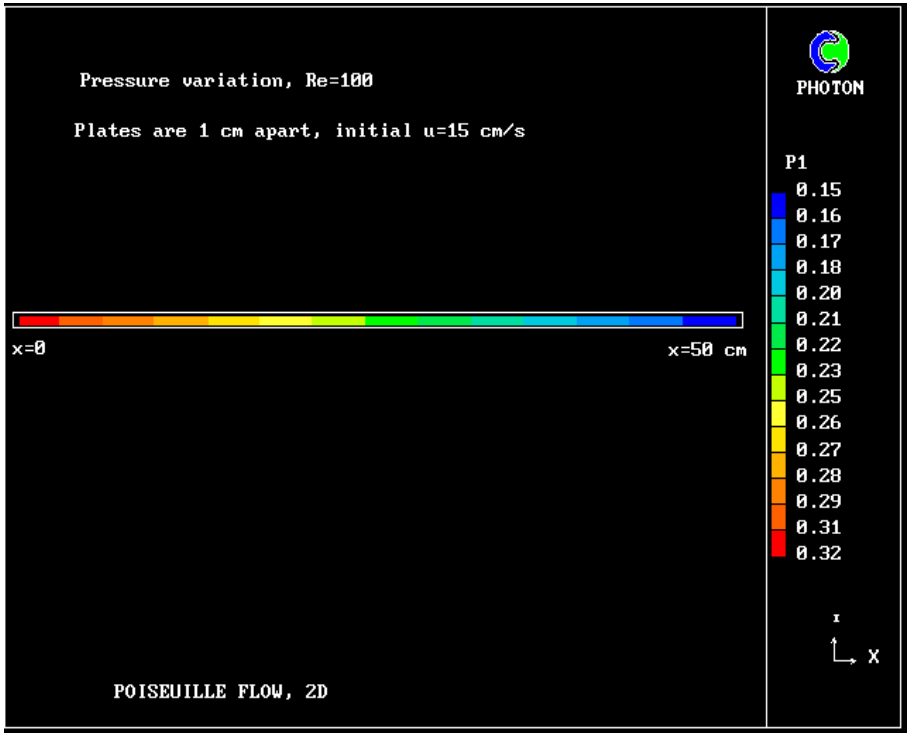
- Microchannel:
- 1 cm long
- 1 mm wide
- 100 μm deep

- L=50 μm
- ρ=1000 kg/m^2
- η=0.001 kg/ms

Laminar for flow speeds less than 10m/s

Poiseuille flow

- Pressure driven flow in channel
- Pressure drop along channel
- Steady flow
- Incompressible flow
- Flow in x-direction, only
- No-slip boundary equations



Poiseuille flow

$$\eta \frac{\partial^2 U_x}{\partial^2 y} + \frac{\Delta p}{L} = 0$$

Integrate twice :

$$U_x(y) = -\frac{1}{2\eta}\frac{\Delta p}{L} y^2 + c1y + c2$$

No slip boundary condition gives :

$$U_x(y) = \frac{1}{2\eta}\frac{\Delta p}{L}\left[(a/2)^2 - y^2\right]$$

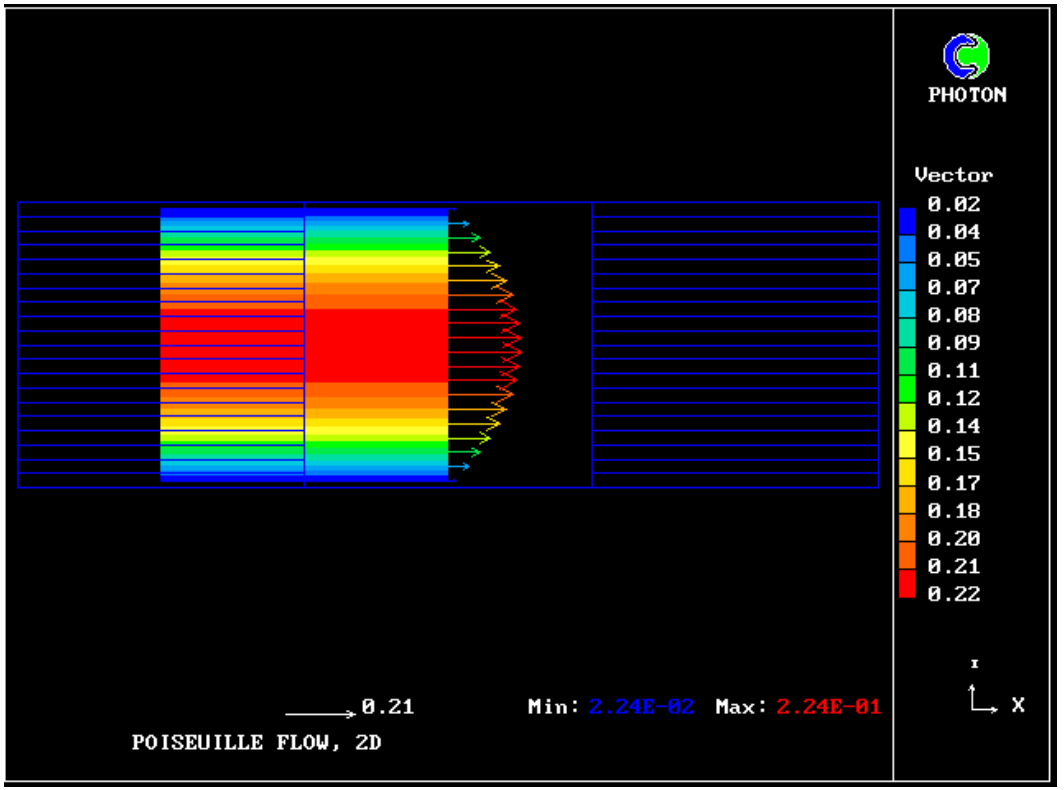
Flow rate :

$$Q = \int_0^{l_z} dz \int_{-a/2}^{a/2} U_x(y)dy$$

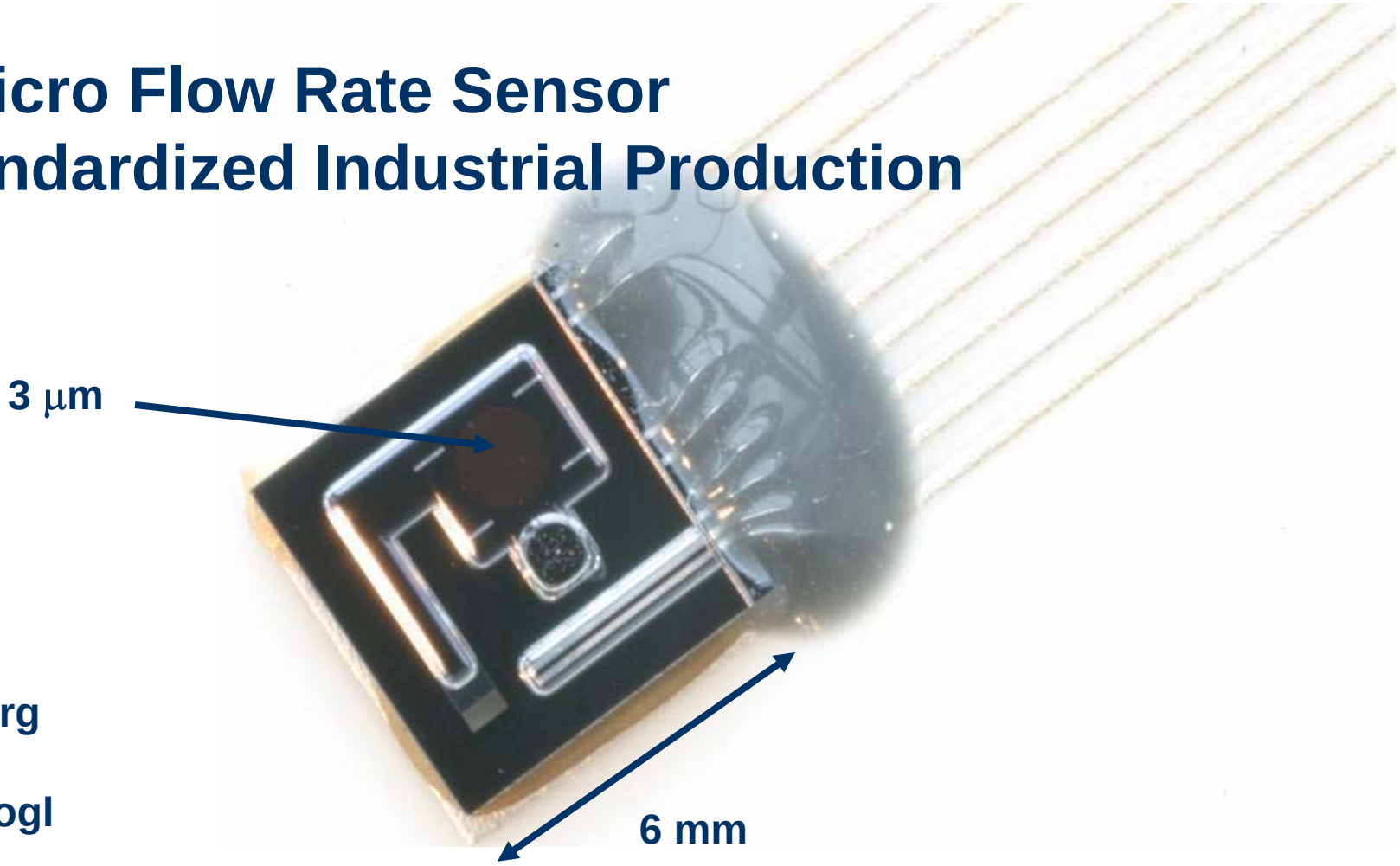
$$Q = \frac{l_z a^3}{12\eta}\frac{\Delta p}{L}$$

Circular pipe :

$$Q = \frac{\pi\, a^4}{8\eta}\frac{\Delta p}{L}$$



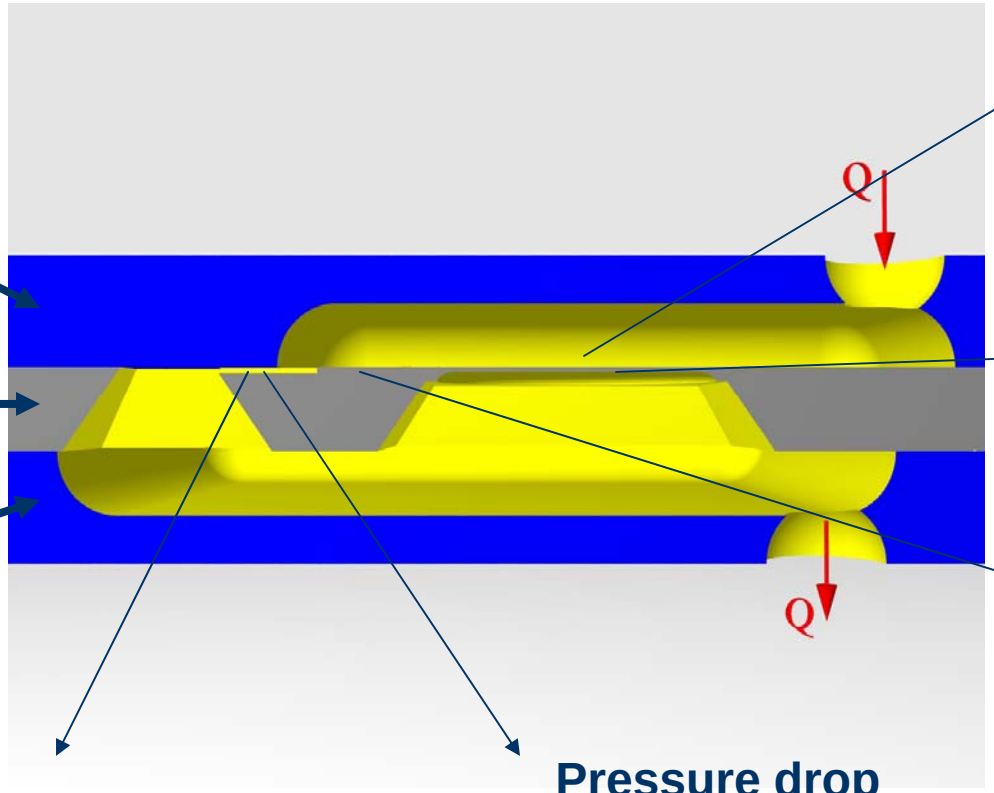
New Micro Flow Rate Sensor for Standardized Industrial Production



Liv Furuberg
Dag Wang
Andreas Vogl

Microsystems and Nanotechnology
SINTEF Information and Communication Technology

The new design suggests a low-noise, mechanically robust flow sensor



Sensitive and strong membrane

Pyrex

Silicon

Pyrex

Protected piezoresistors for stress measurements

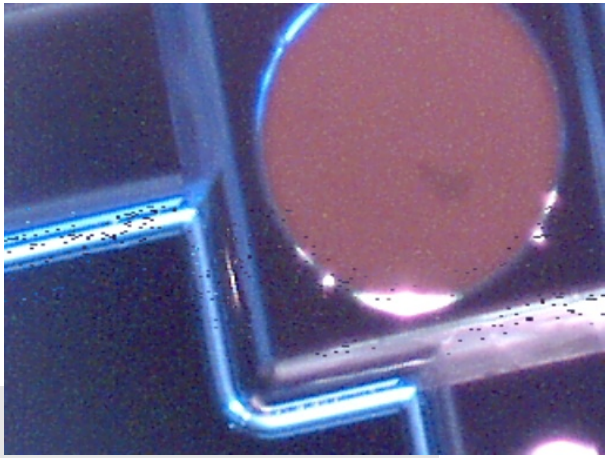
Temperature sensing diode

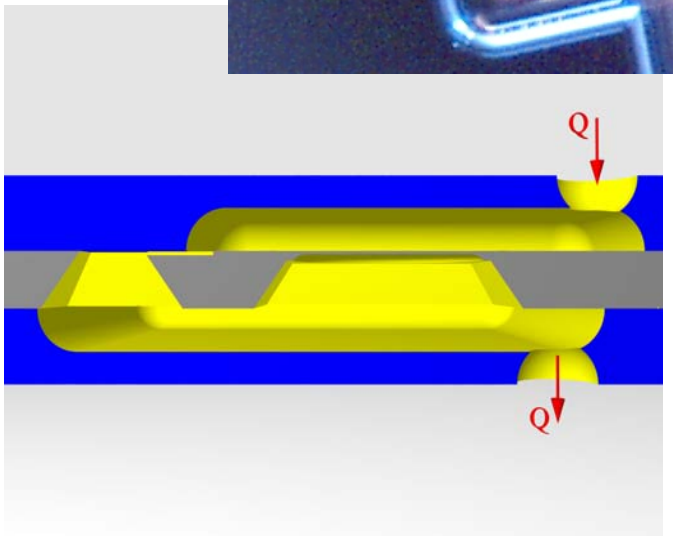
Channel depth 11 μm

Pressure drop proportional to the flow rate

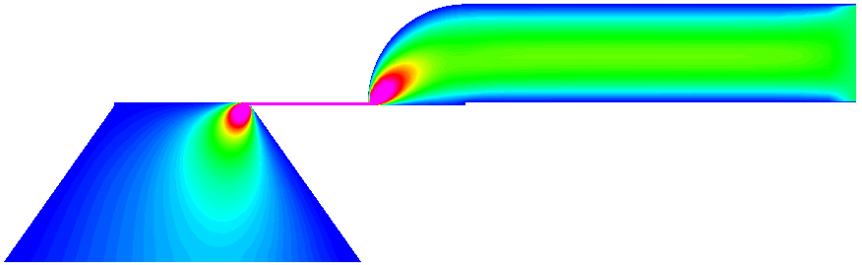
Volum-strømningsmåler

- Applikasjoner: Dosering, tilføring av reagenter, måle flow gjennom analysesystem
- Væskestrøm gjennom brikken
- Glass-silisium-glass brikke
- Laminær strøm, lave Re tall
- Differensiell trykksensor (membran + piezomotstander)
- Trang kanal med trykkfall, Pouseille strøm
- Trykkfall ~ 100 -200 Pa
- Integrert temperaturmåler





- Kanal: 800x1500x10 μm
- Flow rate 2 μl/min



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

Electroosmotic Flow

$$U_0 = \frac{\varepsilon_w \zeta E}{\mu}$$

- Flow driven by electric field
- Voltage applied between electrodes immersed in electrolyte

- Force on fluid near the boundaries, excess of charged particles
- Debye screening layer, typically 10nm

- Disadvantages:

Sensitivity to impurities

Ohmic generation of heat

Need for high voltages

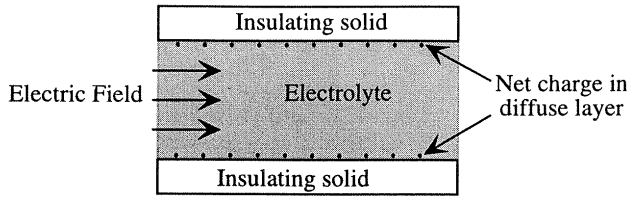


Figure 13.11. Illustrating electroosmotic flow

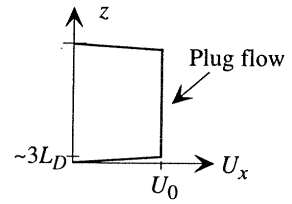


Figure 13.12. Electroosmotic flow profile.

- Advantage:
- Plug flow

Solving Navier Stokes

Poiseuille flow vs. electroosmotic flow

Advantage in 3D visualization/detection

Three pictures after creation of fluorecent molecule:

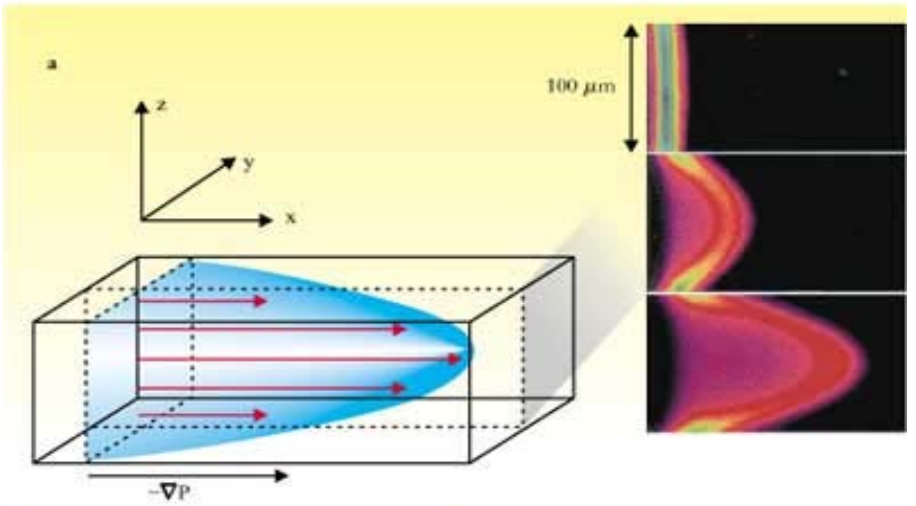
0s

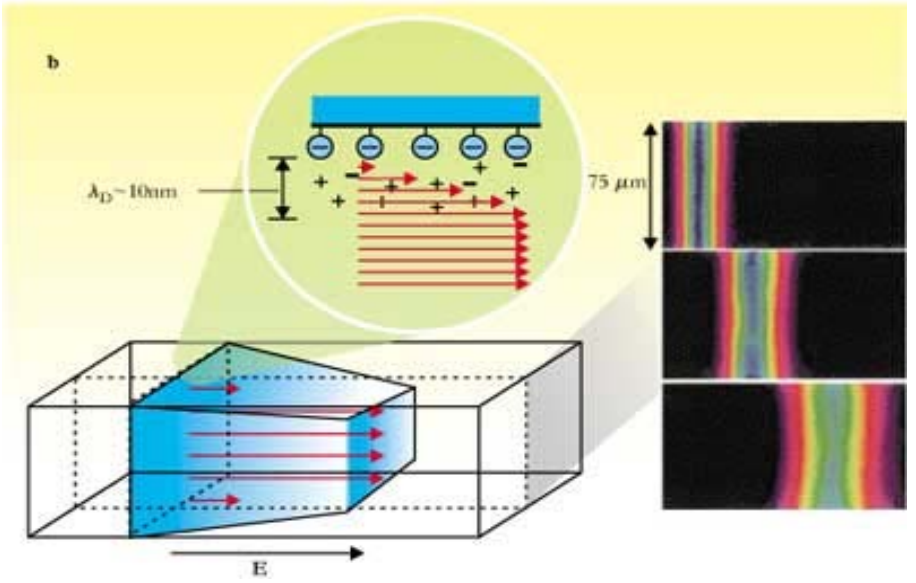
66ms

165ms

Separation based on charge-to-size ratio of molecules.

Separated bands of species





Electrophoresis

- Species carried along with electroosmotic flow
- Drift relative to the moving velocity:

$$v_{ep} = \mu_{ep} \varepsilon_x$$

  - Electrophoretic mobility

  - Apply voltages to channels
  - Create controlled plug of species
  - Separate molecules by charge and volume by electrophoresis

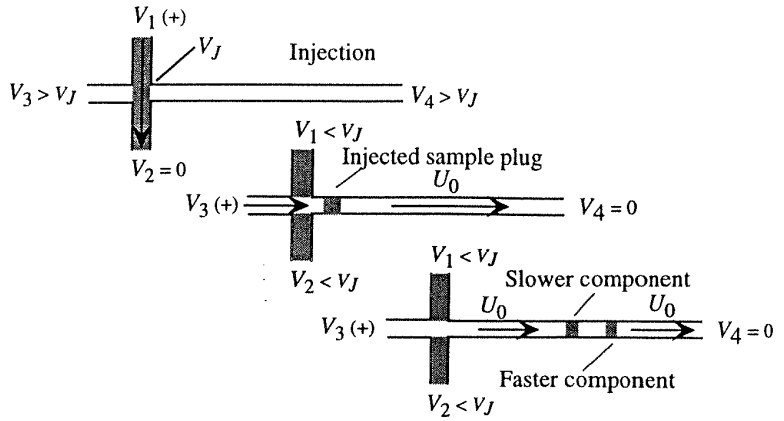
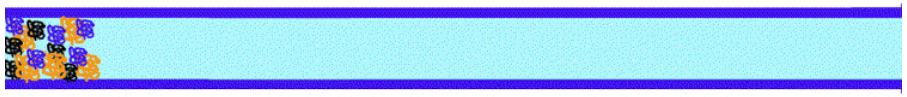
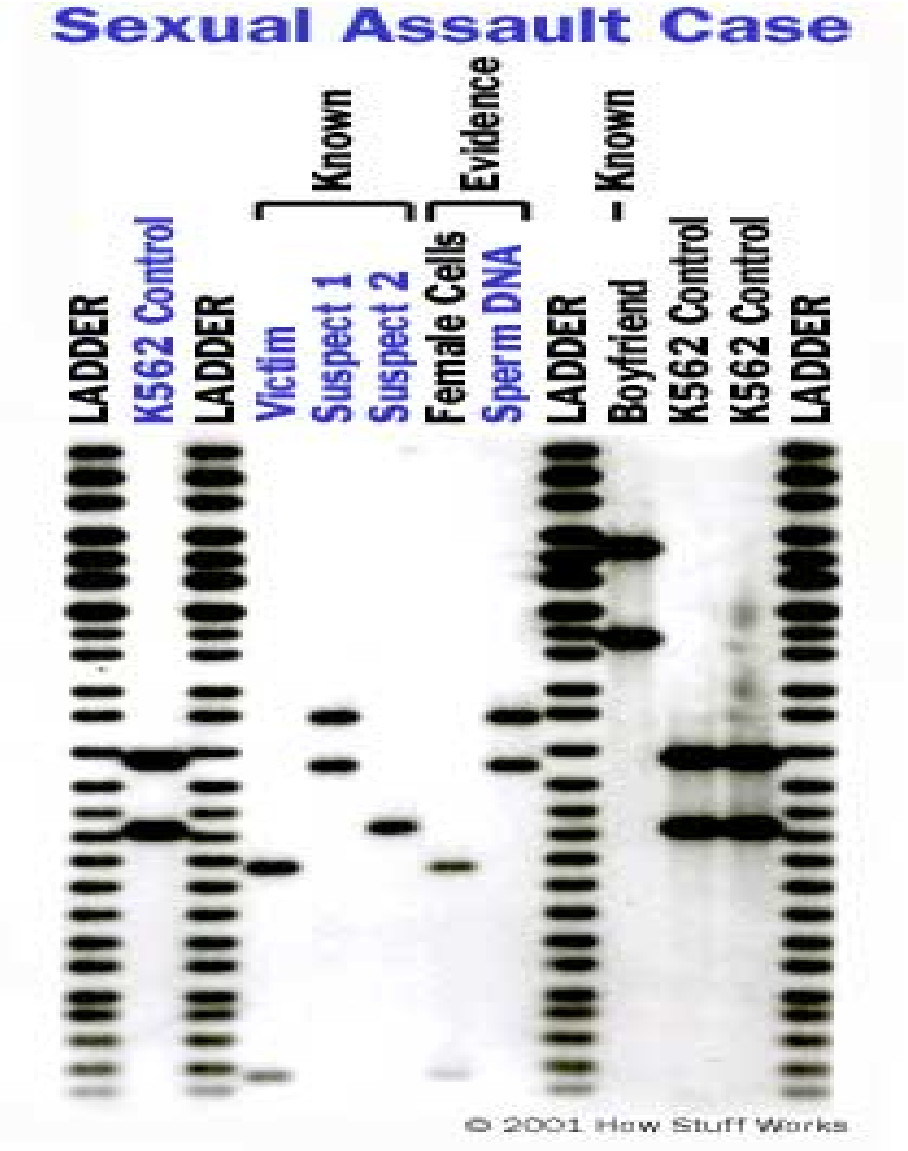


Figure 13.14. Illustrating electrophoretic separation with electroosmotic flow. The voltages used during the injection and separation sequence are described in the text.

Suspect - DNA analysis

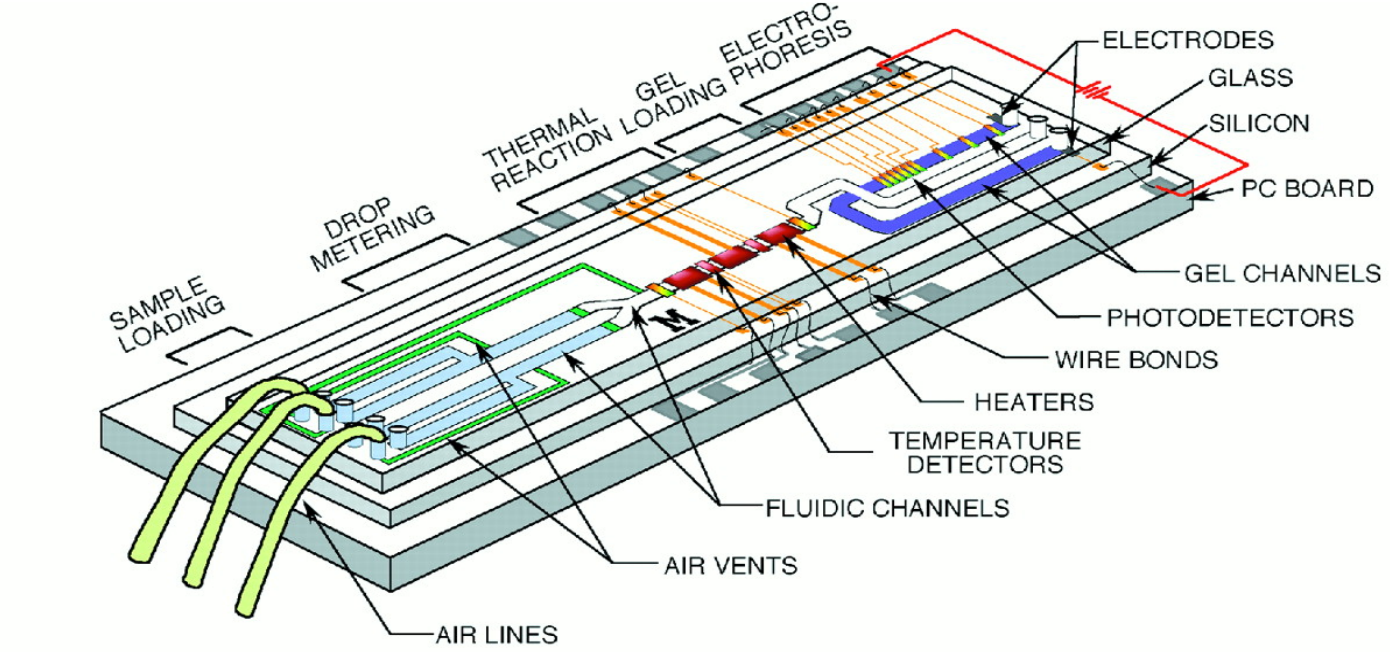
- DNA fingerprint

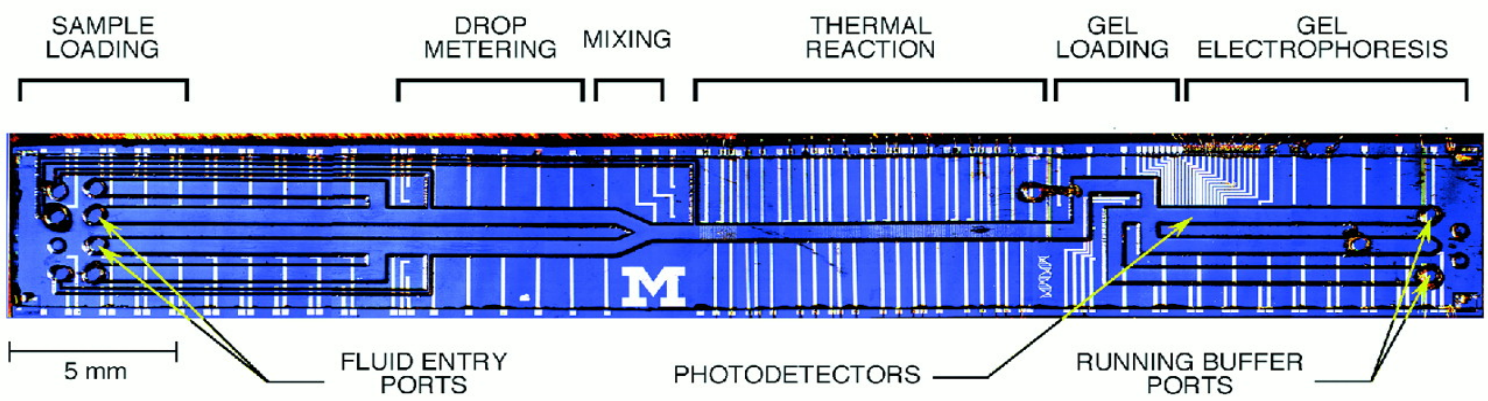




Burns et al., droplet based total analysis system

"An Integrated Nanoliter DNA Analysis Device"
Science 16 October 1998: Vol. 282. no. 5388, pp. 484 - 487





Mixing

- Laminar flow
- Mixing by diffusion only

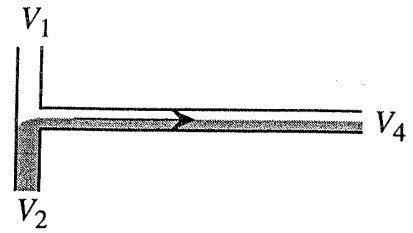


Figure 13.16. Illustrating laminar flow when two streams are combined. Mixing occurs only by diffusion.

- Diffusion equation

$$\frac{\partial C(r,t)}{\partial t} = D\nabla^2 C(r,t)$$

  - Average displacement of diffusing particle:

$$l = \sqrt{4Dt}$$

  - Diffusion constant for water

$$D = 2.3 \cdot 10^{-9}\,\mathrm{m}^2 / s$$

- Water: Diffusion length after 1 s: 90μm
- On the other hand:
- Characteristic lines become blurred…
- What about larger molecules?

Diffusion of ink

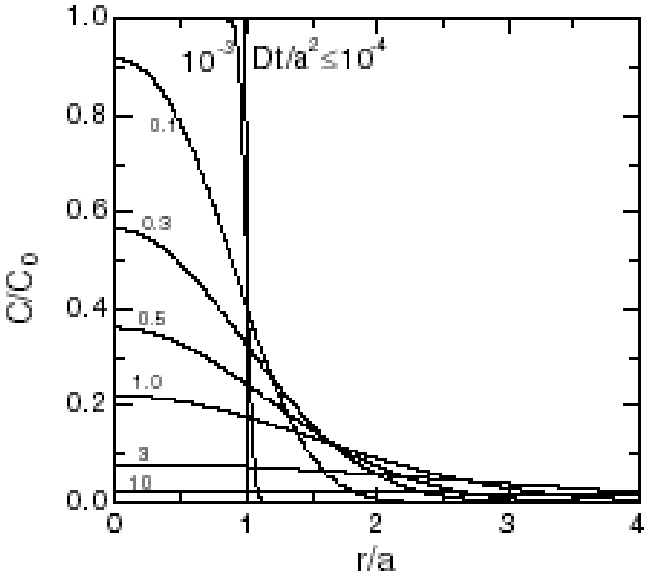


Figure 1. The concentration distribution at various times.

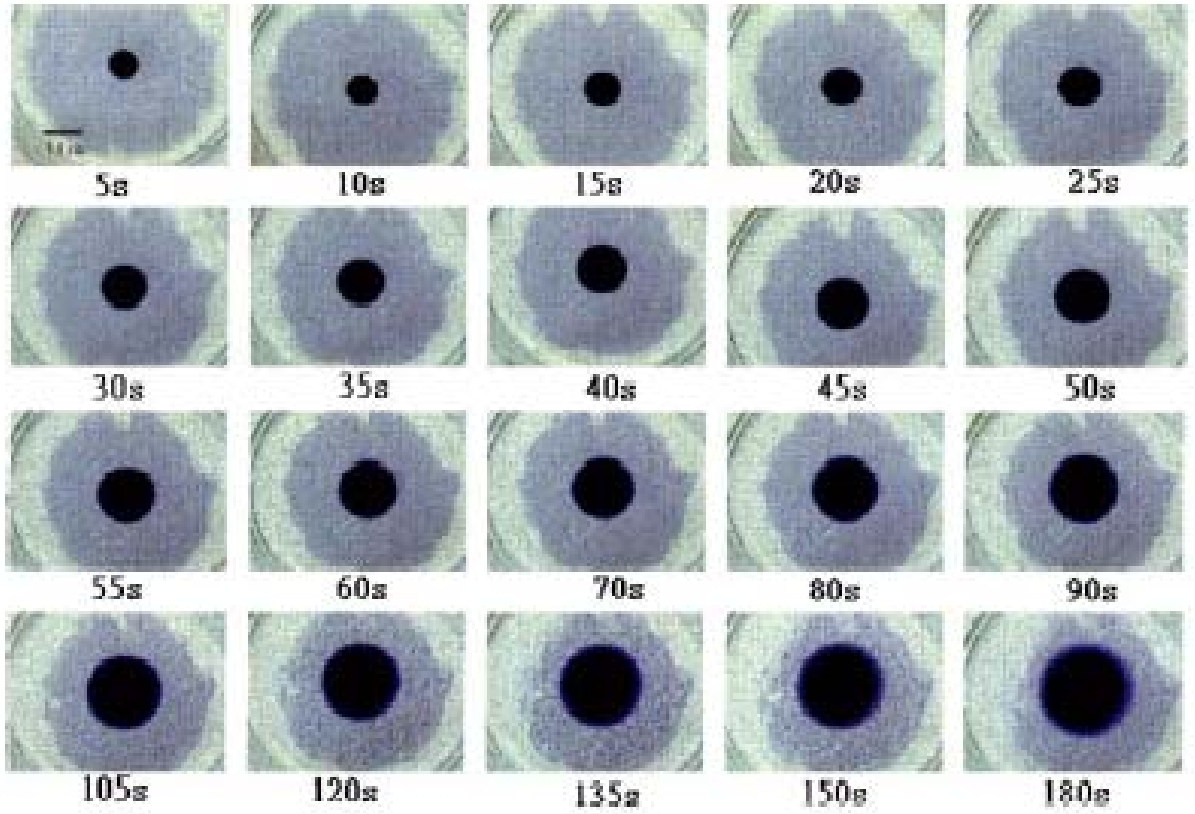


Figure 2. Sequential pictures of stamp ink diffusing in water.

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Eur. J. Phys. 25 (2004) 331–336 — PII: S0143-0807(04)58976-6

A simple diffusion-based filter, the H-filter

Micronics.net

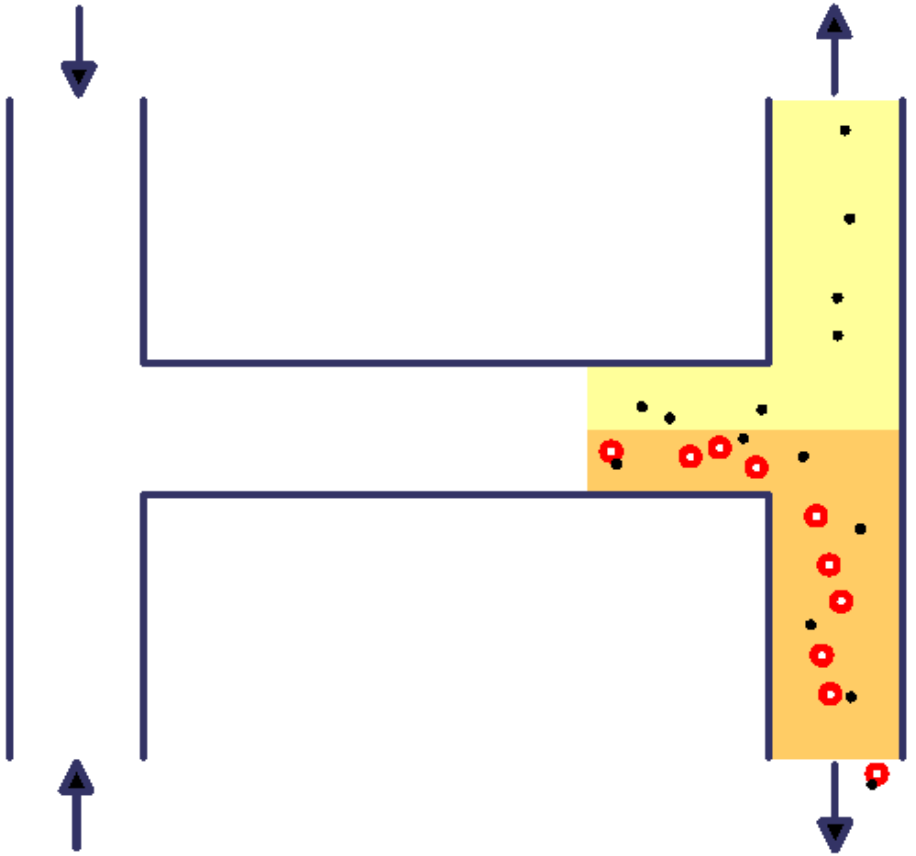
Large and small molecules in via lower channel

Clean solvent in via upper channel

Large molecules have a smaller average diffusion distance than small

More small molecules will go up

Repeat



Mixing

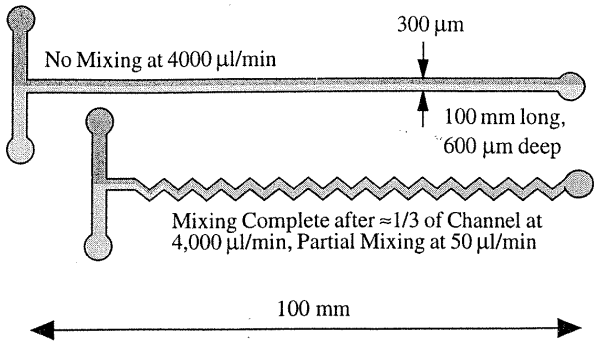


Illustration of miniature fluidic channels used to compare mixing in macroscopic and microscale fluidics. After Branebjerg, et al. (1994).