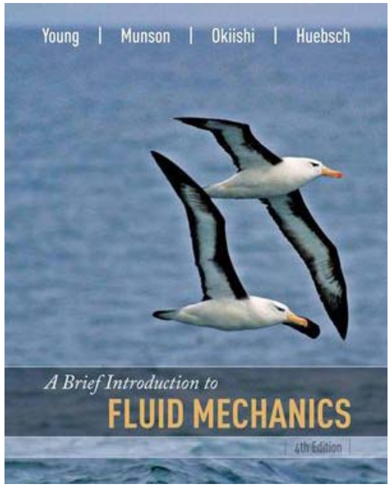
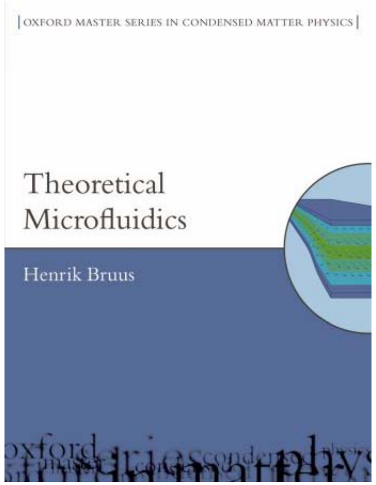
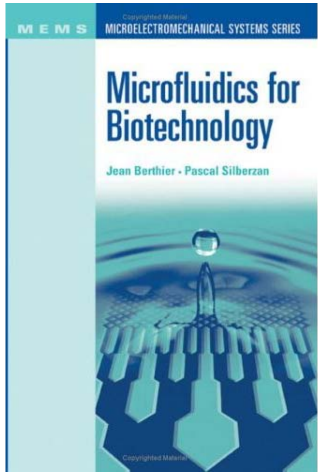
Lab-on-a-Chip







<u>Synopsys</u>

- Introduction to Lab-on-Chip. Basic properties of fluids. Digital microfluidics.
- Statics of fluids
- Fluid dynamics. Bernoulli equation
- Navier-Stokes equations
- Dynamic Similarity. Laminar and turbulent flow
- Experimental flow characterisation
- Numerical flow simulation (COMSOL)
- Electrofluidics
- Flow with Diffusion. Two phase flow.
- Nanofluidics.
- Microfabrication and design examples.

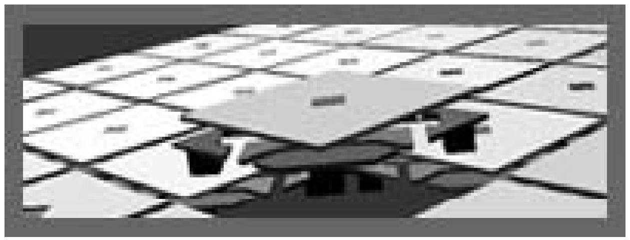
Lecture plan

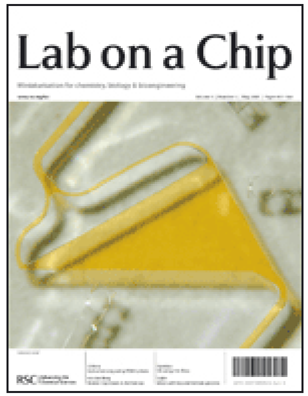
- Introduction to Lab-on-a-Chip: concept, applications and challenges
- Continuum hypothesis and fluid particles
- Properties of liquids:
  - Compressibility
  - Viscosity and No-Slip condition
  - Surface tension
- Wetting phenomena and digital microfluidics
- Problem session

Introduction

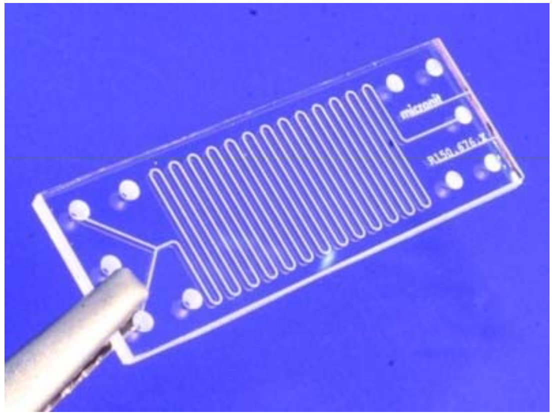
- **Miniaturization in microelectronics** – Moor’s Law, doubling integration density every 18 monthy. According to Intel who currently uses 50nm features they will be able to follow Moor’s Law for another 10 years at least (32nm and 15nm lithography is under development)

- **Miniaturization of non-electronics** devices started in late 70s as MEMS (MicroElectroMechanical Systems) but also extends to fluidics and optical components.



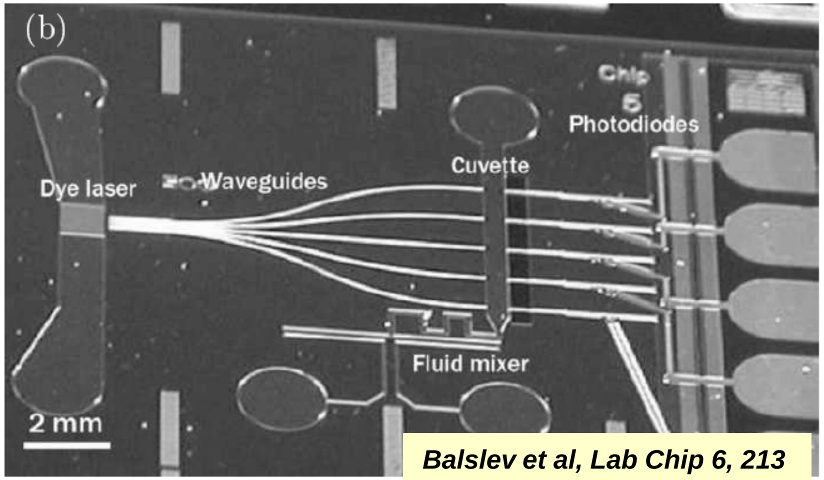


Lab-on-a-Chip

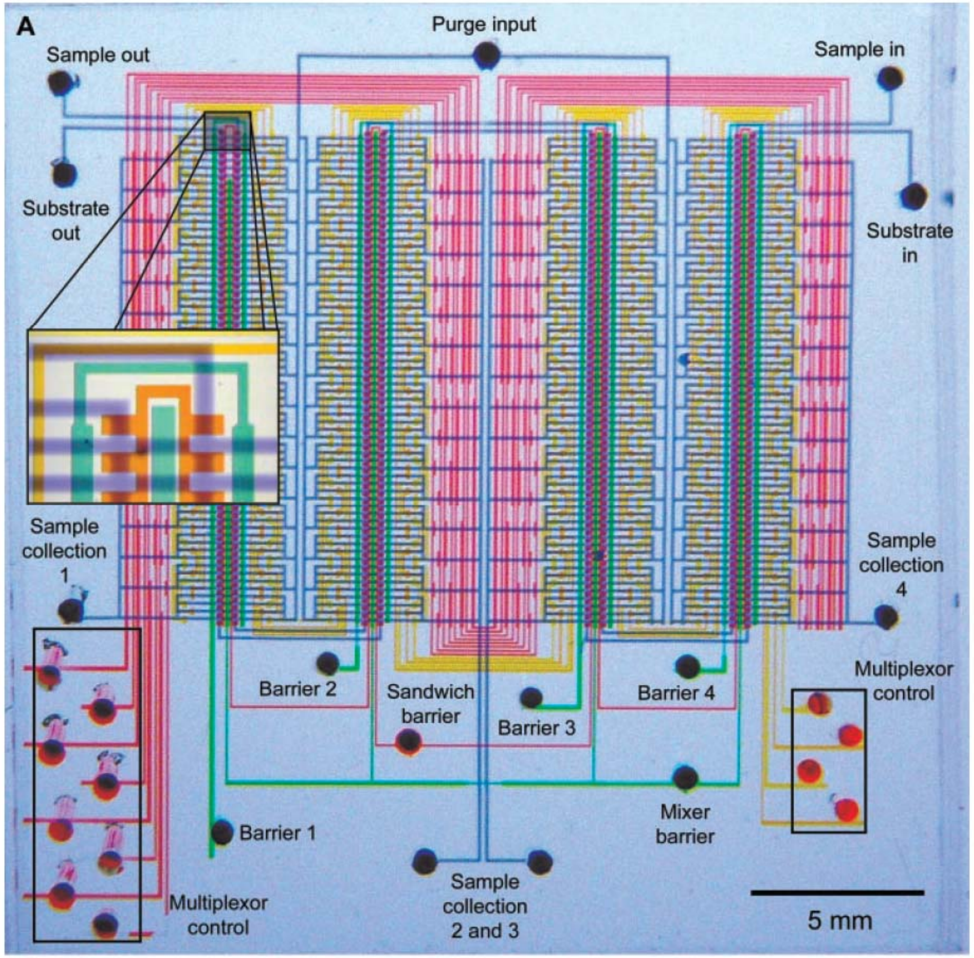


- A **lab-on-a-chip** (LOC) is a device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters in size.
- LOCs deal with the handling of extremely small fluid volumes down to less than pico liters.
- Lab-on-a-chip devices are a subset of MEMS devices and often indicated by "Micro Total Analysis Systems" (µTAS) as well. Microfluidics is a broader term that describes also mechanical flow control devices like pumps and valves or sensors like flowmeters and viscometers. However, strictly regarded
- "Lab-on-a-Chip" indicates generally the scaling of single or multiple lab processes down to chip-format, whereas "µTAS" is dedicated to the integration of the total sequence of lab processes to perform chemical analysis. The term "Lab-on-a-Chip" was introduced later on when it turned out that µTAS technologies were more widely applicable than only for analysis

Microfluidics circuits



Balslev et al, Lab Chip 6, 213



S. Quake et al, Science 298, 580

- Can include active and passive elements: pumps, mixers, reaction chamber
- Range of sensors
- Light sources
- Electronic circuitry

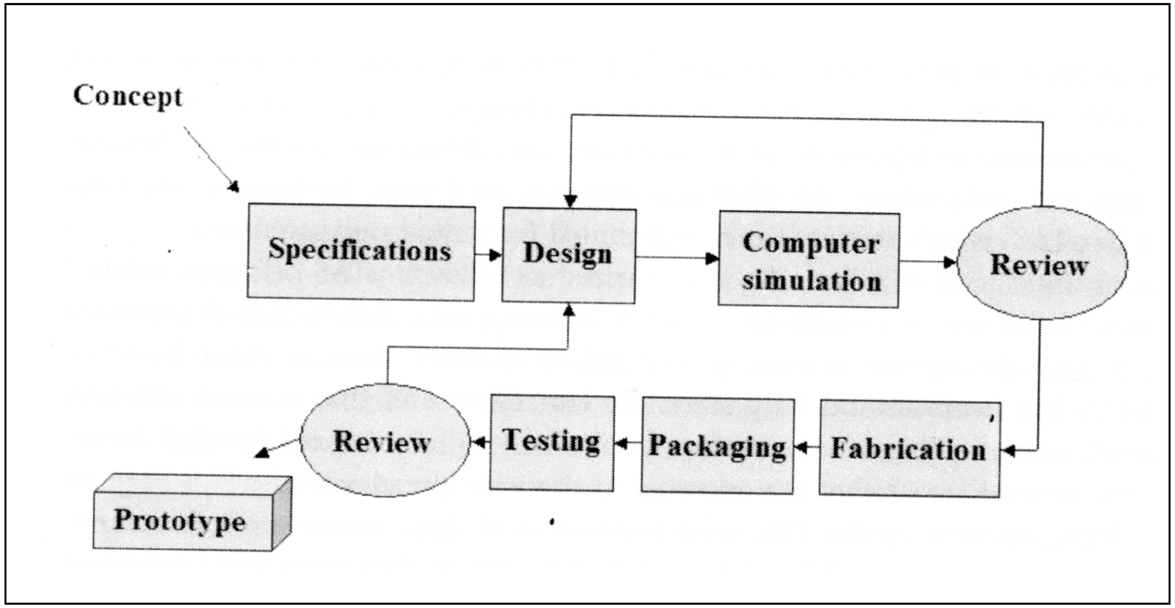
Why Lab-on-a-Chip

- small amount of sample and reagents
- portability, small size
- low power consumption
- low cost
- multiple analysis on the same chip (μTAS)
- Devices that can be used as a “black box”, no special training required
- reliability: exactly the same analysis can be performed number of times

→

- Move analysis to the customer
- Performing analysis in the field

The Aspects of Lab-on-a-Chip Design



- Where the system will be used
- How to perform the analysis?
- What volumes do we need?

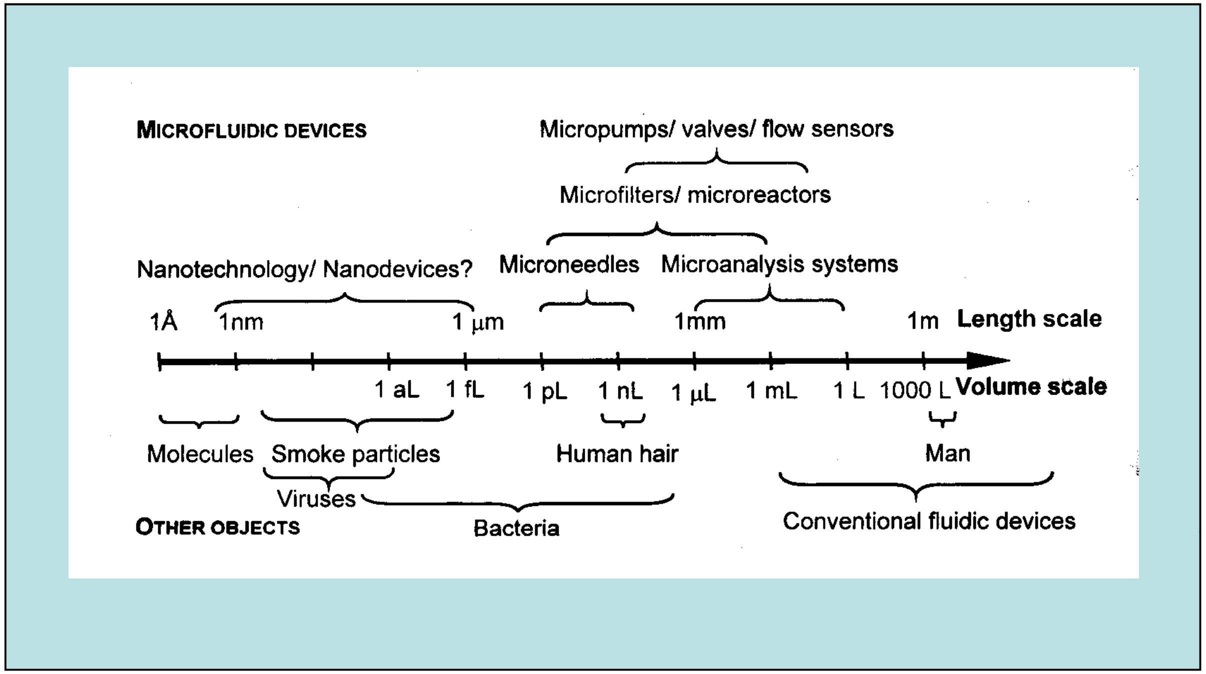
- How to input and propel the sample and reagents? What components are required?

- What materials to use and how to fabricate?

- How to package and interface?

What size we are speaking about?

- Volume goes as L^3, so fairly small decrease in size leads to dramatic reduction of sample volume

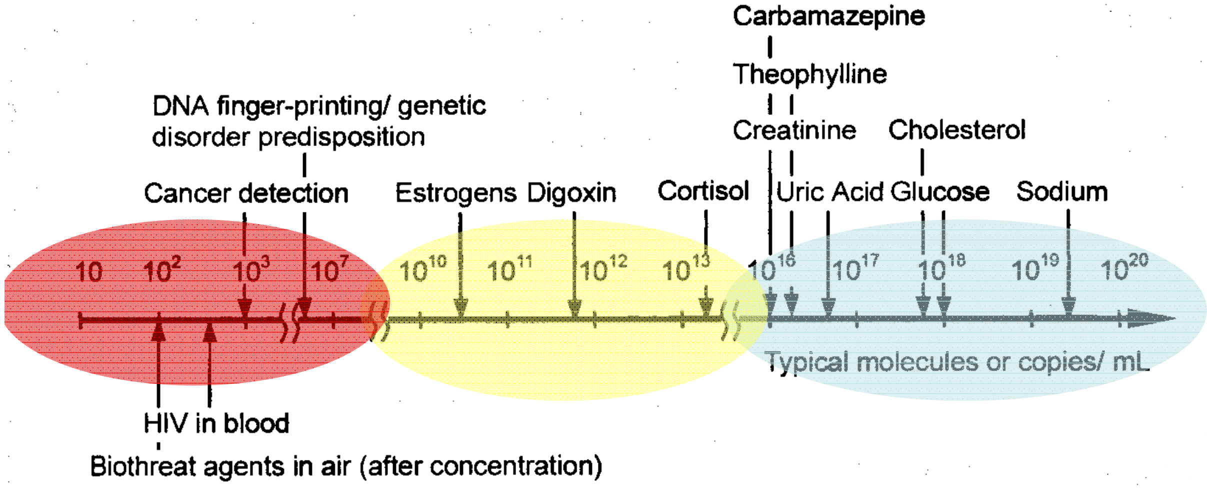


Unit Prefixes

Atto	Femto	Pico	Nano	Micro	Milli	Centi	Deka	Hecto	Kilo	Mega	Giga
10^{-18}	10^{-15}	10^{-12}	10^{-9}	10^{-6}	10^{-3}	10^{-2}	10	10^{2}	10^{3}	10^{6}	10^{9}

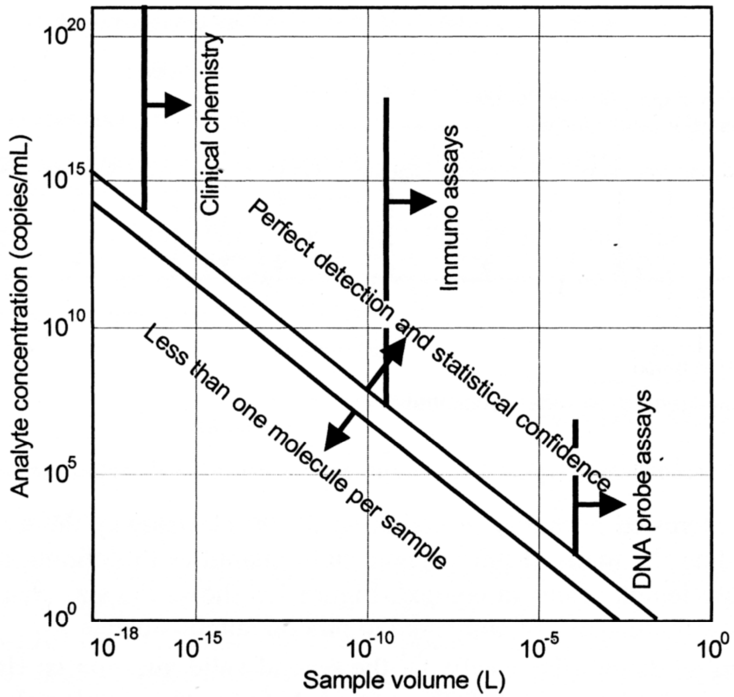
zepto 10^{-21}

What amount do we need



$$V = \frac{1}{\eta_s N_A A_i}$$

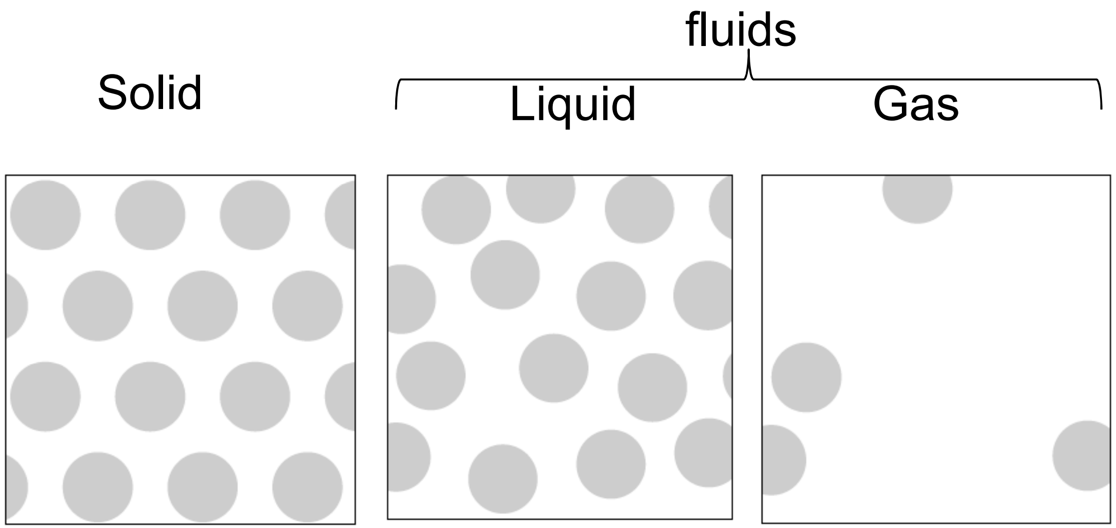
Where
- η_s – is sensor efficiency
- N_A – Avogadro number
- A_i – concentration of analyte



Samples volumes that are too small may contain not enough target molecules!

Validity of continuum approach

- Standard approach in fluid mechanics is based on the breaking the flow into a sufficient number of fluid particles.
- We need to ensure that the macroscopical properties of the fluidic particles are the same as the bulk

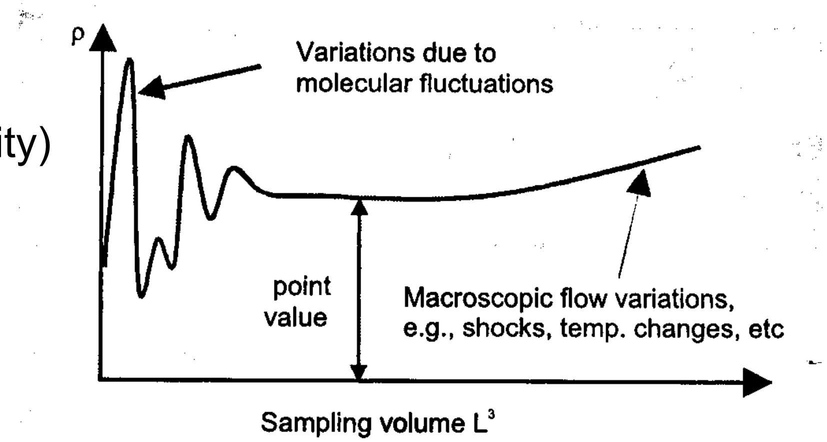


we expect large fluctuation at the atomistic scale
due to molecular structure of matter

Validity of continuum approach

Thought experiment:

1. measuring density (or any other thermodynamic quantity)



Due to random thermal fluctuations the amount of molecules will fluctuate.
The standard deviation:

$$\sigma \propto \sqrt{N}$$

The relative uncertainty:

$$\propto \sqrt{N} / N$$

2. measuring transport properties (diffusion, heat transfer, viscosity) – mean free path related

Properties of a Typical Gas and Liquid at Standard Conditions (After [10])

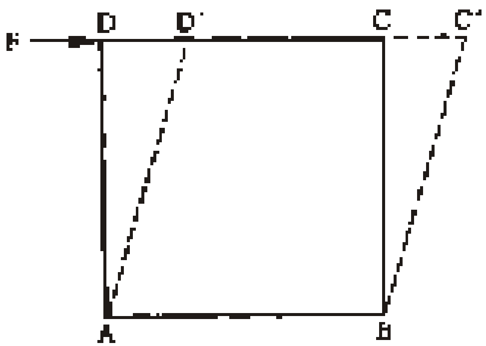
Property	*Gas (N_2)*	*Liquid (H_2O)*
Molecular diameter	0.3 nm	0.3 nm
Number density	3×10^{25} m^{-3}	2×10^{28} m^{-3}
Intermolecular spacing	3 nm	0.4 nm
Displacement distance	100 nm	0.001 nm
Molecular velocity	500 m/s	1,000 m/s

Basic Properties of Flowing Fluids

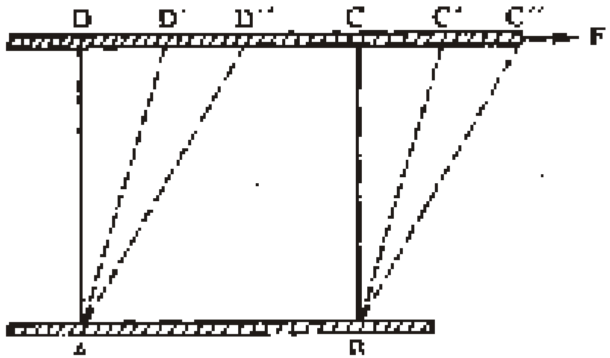
- Thermodynamic properties (e.g.pressure, temperature, density, surface tension)
- Transport properties (e.g.viscosity, thermal conductivity, diffusivity)
- Kinematic properties (e.g.linear and angular velocity, vorticity, acceleration, strain rate)

Definition of fluid

”a substance that deforms continuosly under the application of shear (tangential) stress, no matter how small the stress may be”

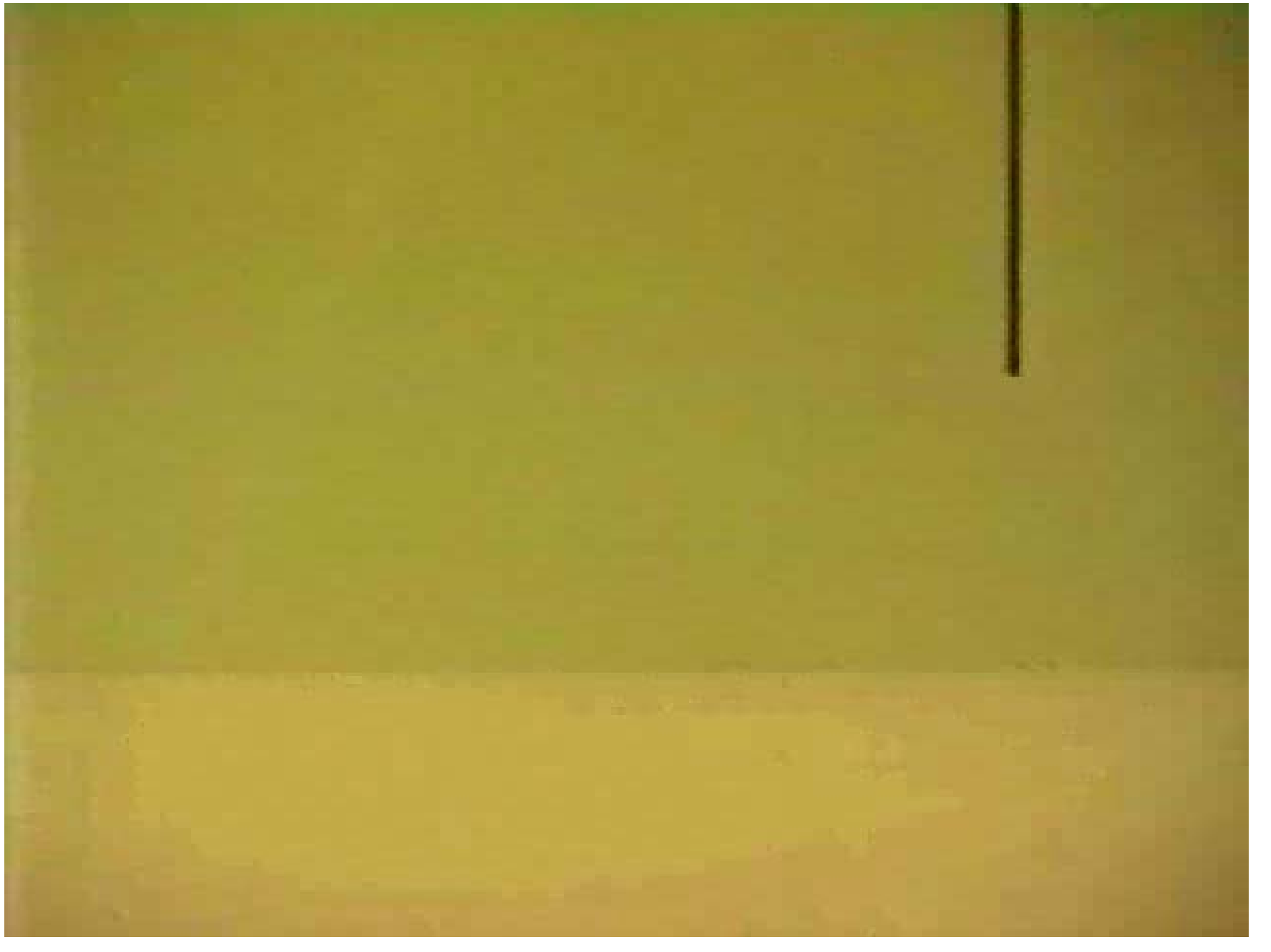


Solid



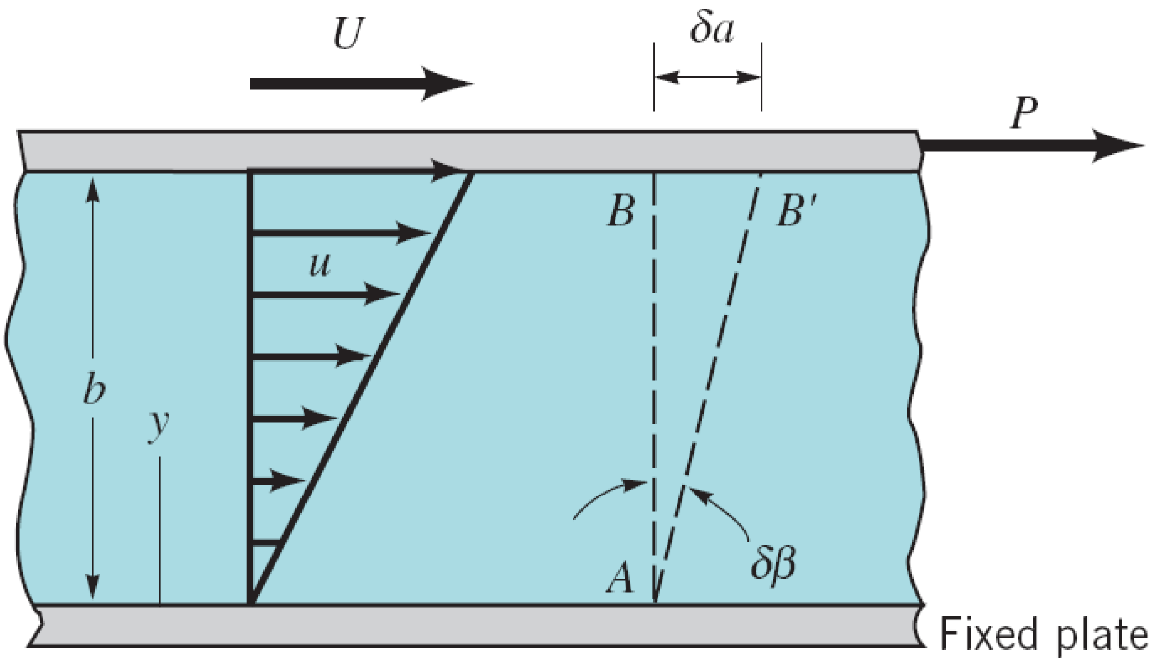
Fluid

No-slip condition



- As a fluid flows near a solid surface, it "sticks" to the surface, i.e., the fluid matches the velocity of the surface. This so-called **"no-slip"** condition is a very important one that must be satisfied in any accurate analysis of fluid flow phenomena.

Viscosity



Shearing stress, t:

$$\tau = F / A \quad [N / m^2]$$

Newtonian fluid:

$$\tau = \mu \frac{du}{dy}$$

Rate of shearing strain
(velocity gradient)

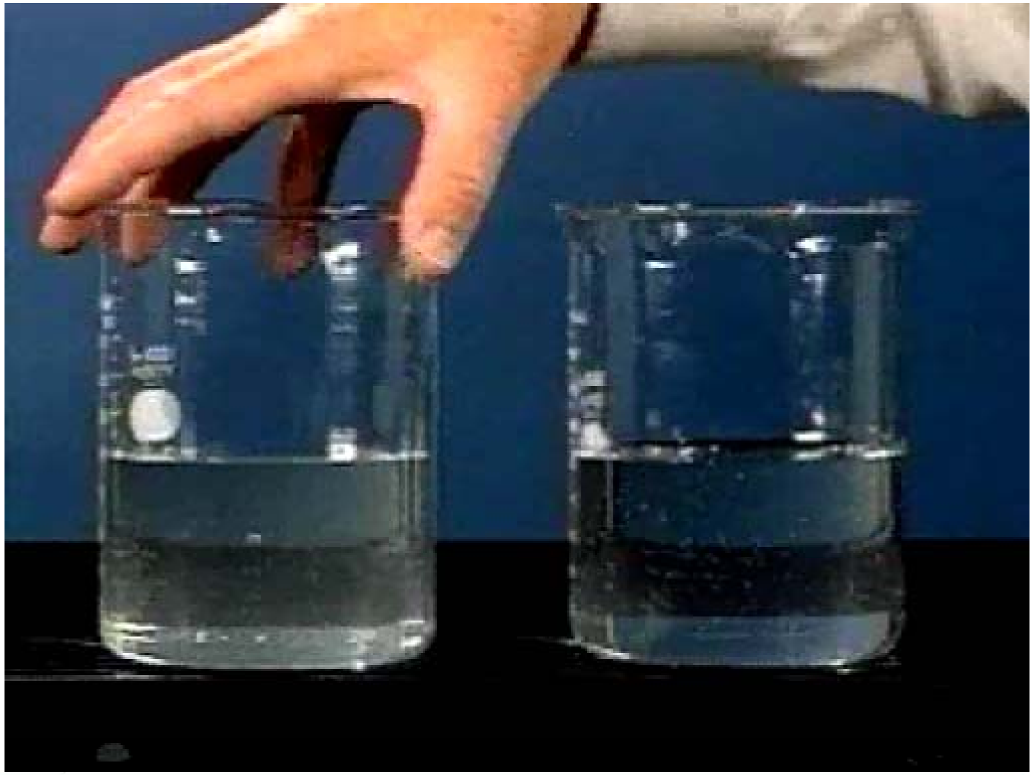
dynamic viscosity [N/m^2 / (m/s / m) = **N s/m^2**]

kinematic viscosity $\upsilon = \tau / \rho$

Viscosity

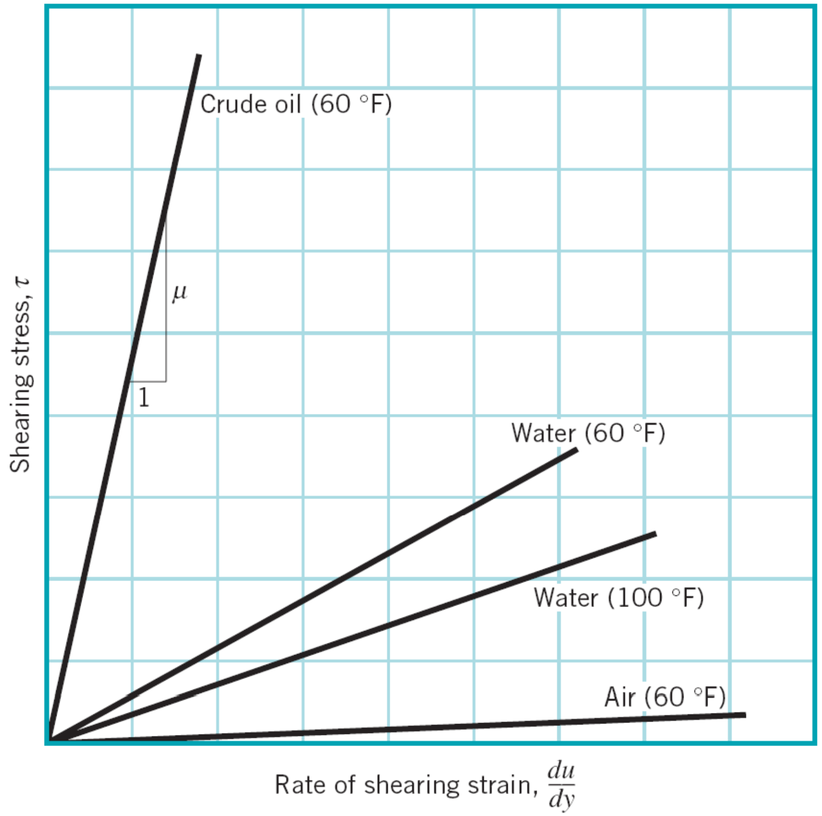
- Viscosity, one of the important properties, is responsible for the shear force produced in a moving fluid.

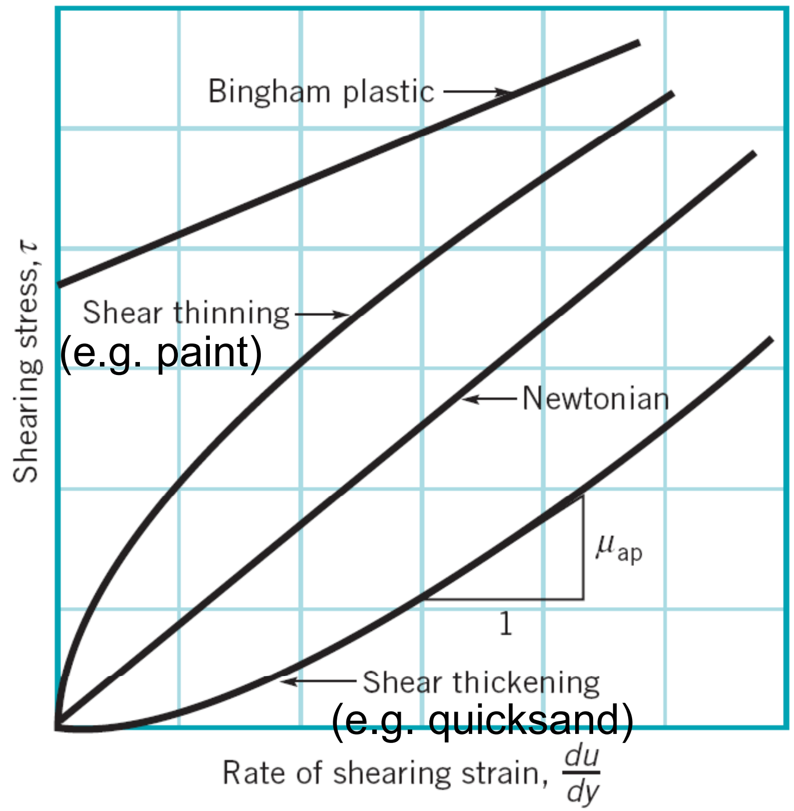
Although the two fluids shown look alike (both are clear liquids and have a specific gravity of 1), they behave very differently when set into motion. The very viscous silicone oil is approximately 10,000 times more viscous than the water



Liquid	Temperature (°C)	Density, ρ (kg/m³)	Specific Weight, γ (kN/m³)	Dynamic Viscosity, μ (N · s/m²)	Kinematic Viscosity, ν (m²/s)	Surface Tension,[a] σ (N/m)	Vapor Pressure, p_v [N/m² (abs)]	Bulk Modulus,[b] E_v (N/m²)
Carbon tetrachloride	20	1,590	15.6	9.58 E − 4	6.03 E − 7	2.69 E − 2	1.3 E + 4	1.31 E + 9
Ethyl alcohol	20	789	7.74	1.19 E − 3	1.51 E − 6	2.28 E − 2	5.9 E + 3	1.06 E + 9
Gasoline[c]	15.6	680	6.67	3.1 E − 4	4.6 E − 7	2.2 E − 2	5.5 E + 4	1.3 E + 9
Glycerin	20	1,260	12.4	1.50 E + 0	1.19 E − 3	6.33 E − 2	1.4 E − 2	4.52 E + 9
Mercury	20	13,600	133	1.57 E − 3	1.15 E − 7	4.66 E − 1	1.6 E − 1	2.85 E + 10
SAE 30 oil[c]	15.6	912	8.95	3.8 E − 1	4.2 E − 4	3.6 E − 2	—	1.5 E + 9
Seawater	15.6	1,030	10.1	1.20 E − 3	1.17 E − 6	7.34 E − 2	1.77 E + 3	2.34 E + 9
Water	15.6	999	9.80	1.12 E − 3	1.12 E − 6	7.34 E − 2	1.77 E + 3	2.15 E + 9

Non-Newtonian fluids





Fluids for which shearing stress is not linearly related to the rate of shearing strain are designated as non-Newtonian fluids.

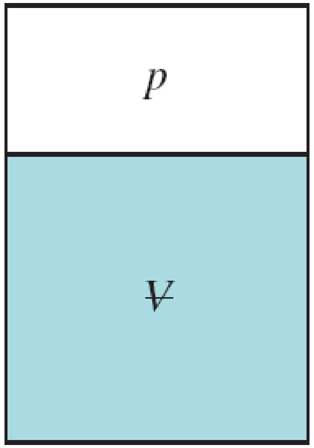
Non-Newtonian Fluids

A mixture of water and corn starch, when placed on a flat surface, flows as a thick, viscous fluid. However, when the mixture is rapidly disturbed, it appears to fracture and behave more like a solid. The mixture is a non-Newtonian shear thickening fluid which becomes more viscous as the shearing rate is suddenly increased through the rapid action of the spoon.

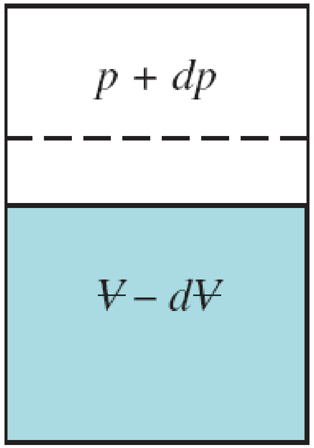
Compressibility of fluids

- Bulk module of elasticity

$$E_v = \frac{dp}{d\forall / \forall} = \frac{dp}{d\rho / \rho}$$



Water: E_v=2.15 *10^9 N/m^2
1% compression would require 2*10^7 N/m^2 =200 atm!!!.



- Speed of sound

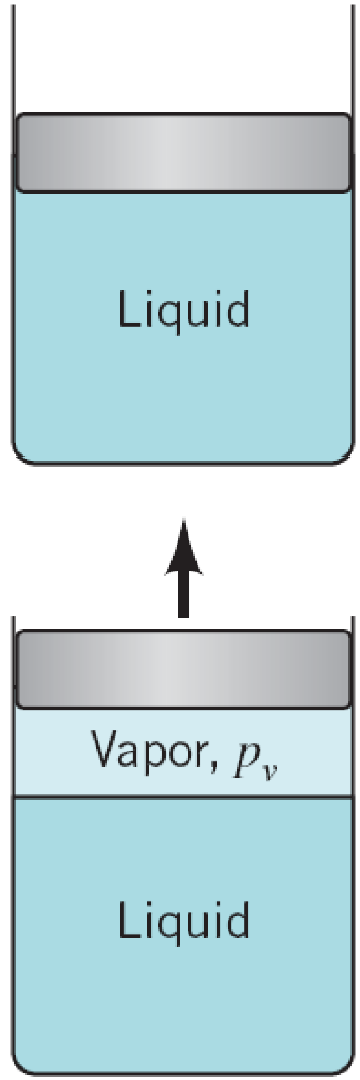
$$c = \sqrt{\frac{E_v}{\rho}}$$

Check the dimension!

Vapour pressure

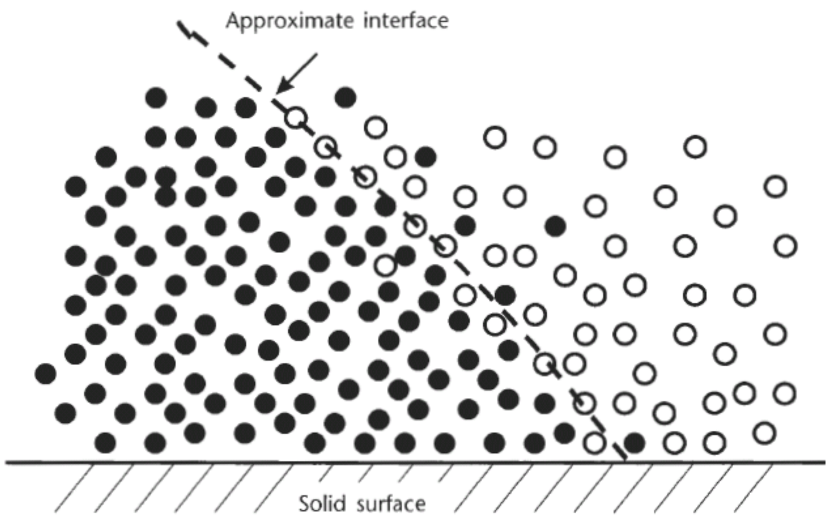
- Pressure of liquid vapour in equilibrium with liquid is called saturated vapour pressure (depends on T!)
- Boiling occurs when the total pressure is equal to the vapour pressure.

Water at 20C: p_v=1.77 10^3 N/m^2



Physics of wetting

- molecules on the interface interact to one half with the molecules of the same material and to the other half with the molecules of other liquid or gas.
- therefore surface possesses extra energy per unit of surface called **surface tension** (units N/m)



$$E = \gamma S$$

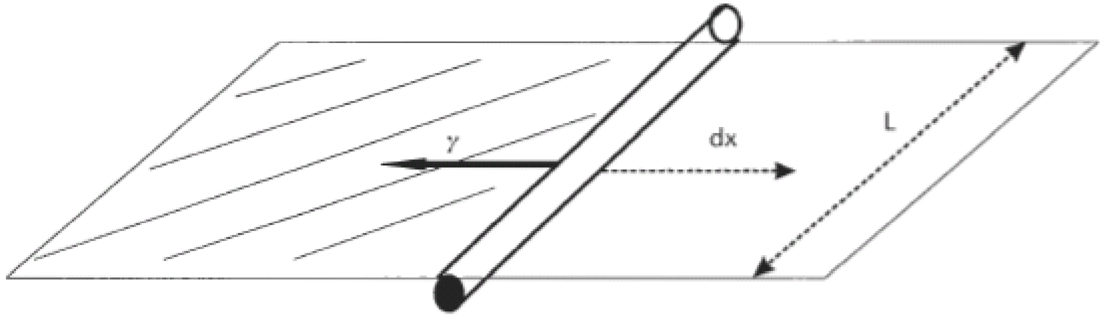
Table 2.1 Typical Values of Surface Tensions at Room Temperature

Type of Components	*Water/Air*	*Water/Oil*	*Glycerol/Air*	*Ethanol/Air*	*Cyclohexan/Air*	*Mercury/Air*
Surface tension [mN/m]	72	50	63	23	25	485

Physics of wetting

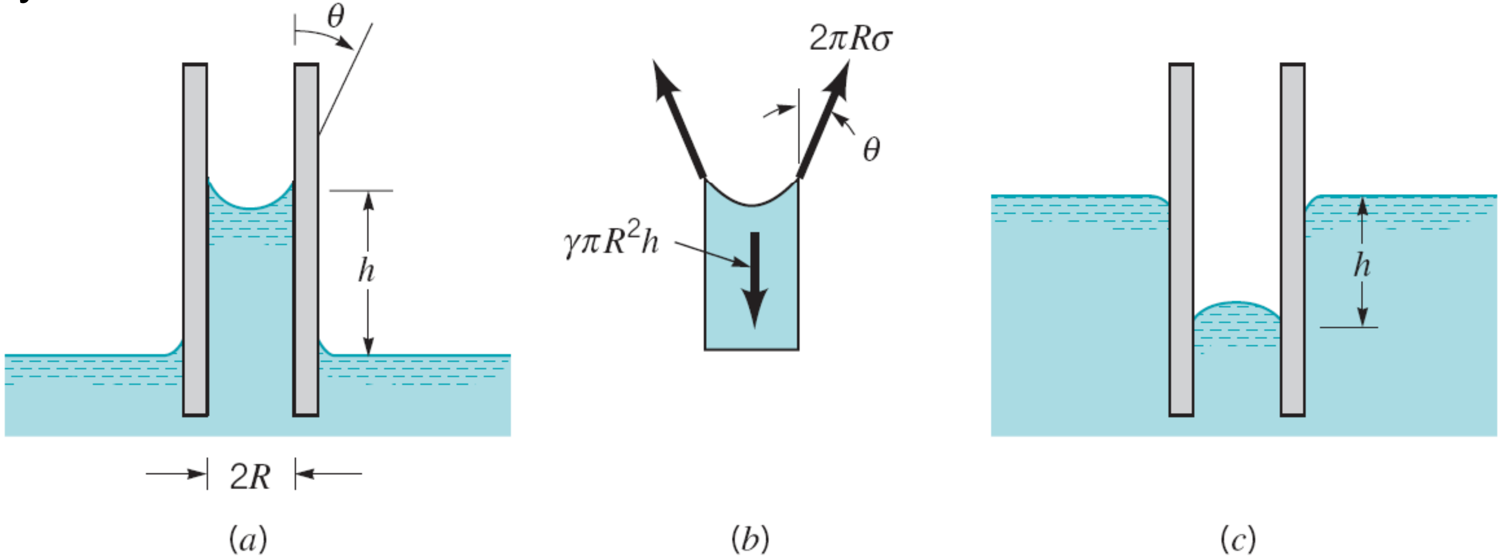
- Surface tension can be treated as force per unit length N/m
- Force on a free boundary:

$$\delta W = F dx = 2\gamma L dx$$



Capillary rise

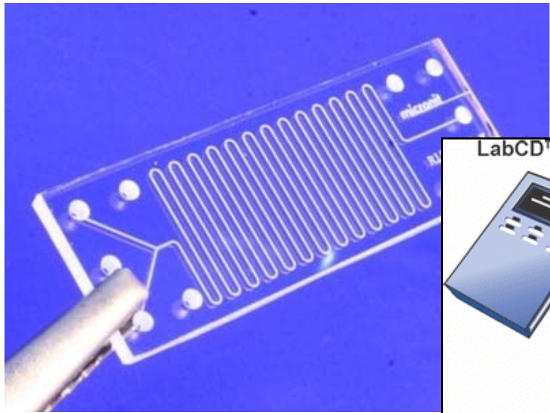
Surface tension causes liquid rise (or depression, depending on wetting) in a thin capillary



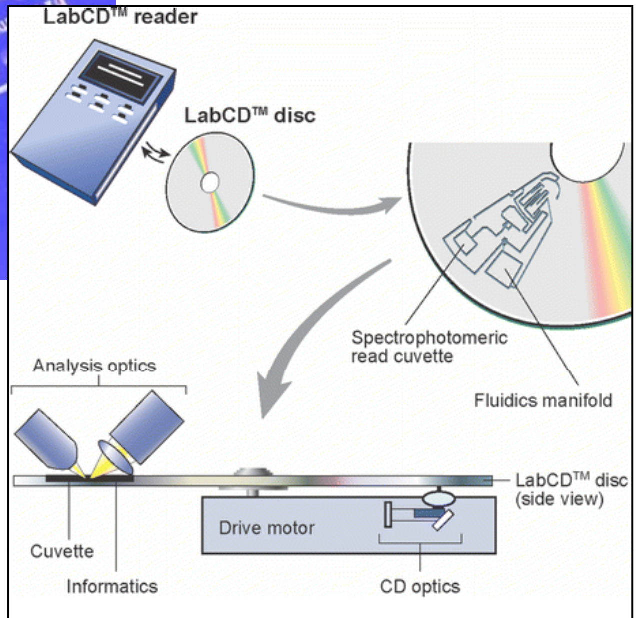
$$\rho g \pi R^2 h = 2\pi R \sigma \cos\theta \;\Rightarrow\; h = \frac{2\sigma\cos\theta}{\rho g R}$$

How to propel the liquid in channels

• pressure driven fluidics



• gravity driven fluidics
("Lab on a CD")



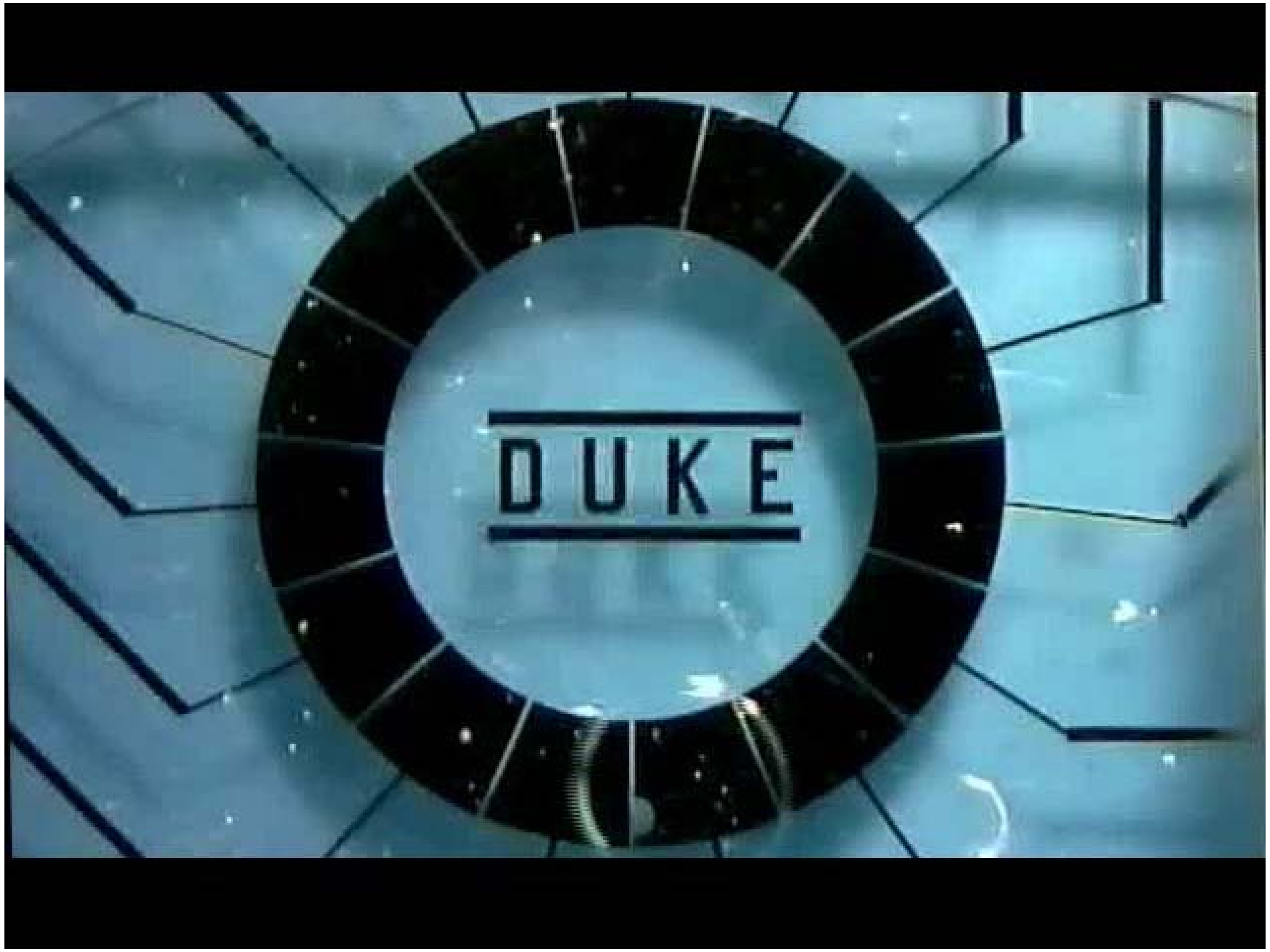
Madou M, et al. 2006.
Annu. Rev. Biomed. Eng. 8:601–28

• electrokinetic pumping

•surface tension driven flow (incl. Electrowetting)

”Digital” microfluidics

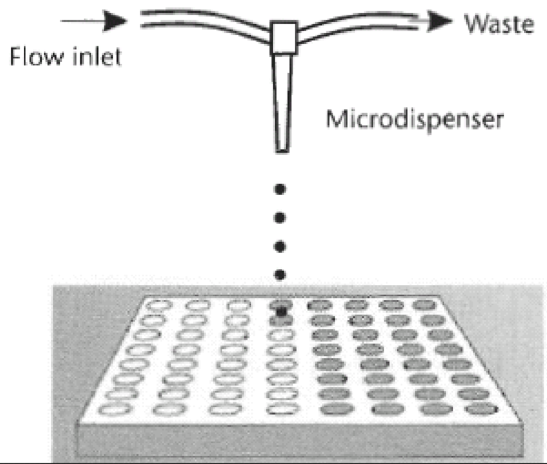
Droplet transport by electrowetting in a ring structure (Duke University, NC)

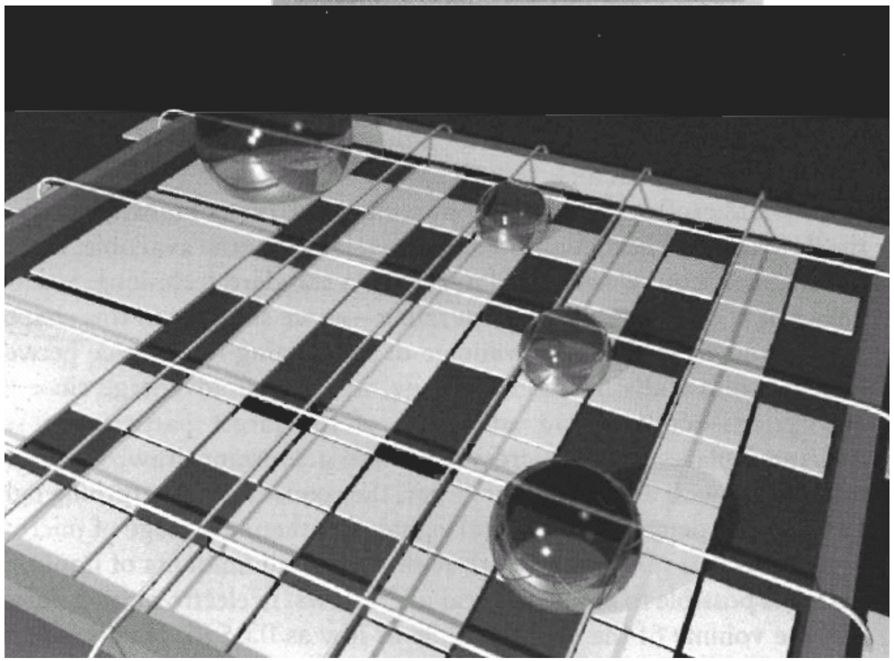


Microdrops in microfluidics

Why microdrops are important?

- Microdrops can be used directly to deliver sample to an array
- Microdrops can be used to transport and manipulate small samples in microfluidics systems:
  <u>Advantages:</u>
  – nonspecific adsorption to the walls is minimized
  – very small sample volumes (as low as 50 nl) can be used without diluting the sample
  – sample can be transported along the chosen trajectory





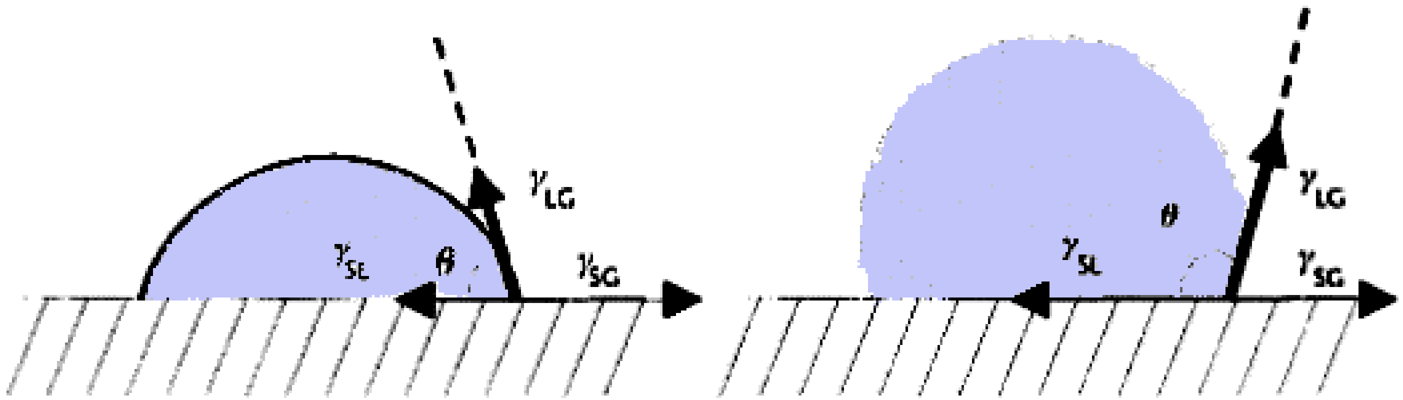
Physics of wetting

- Liquid droplet on solid surface:

partial wetting **total wetting** $S = \gamma_{SG} - (\gamma_{SL} + \gamma_{LG}) > 0$

- In case of partial wetting a triple line is formed. Equilibrium along the triple line is described by **Young's law**

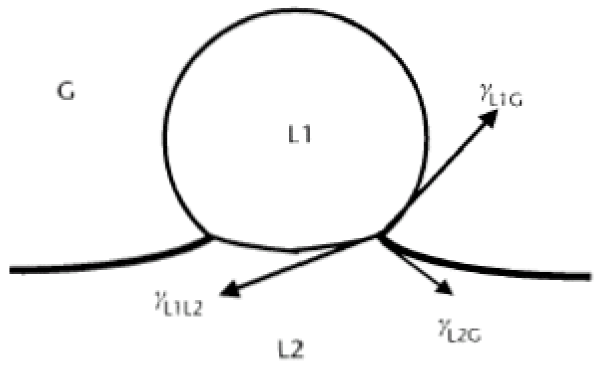
$$\gamma_{LG} \cos\theta = \gamma_{SG} - \gamma_{SL}$$



Hydrophilic contact, $\theta < 90°$ Hydrophobic contact, $\theta > 90°$

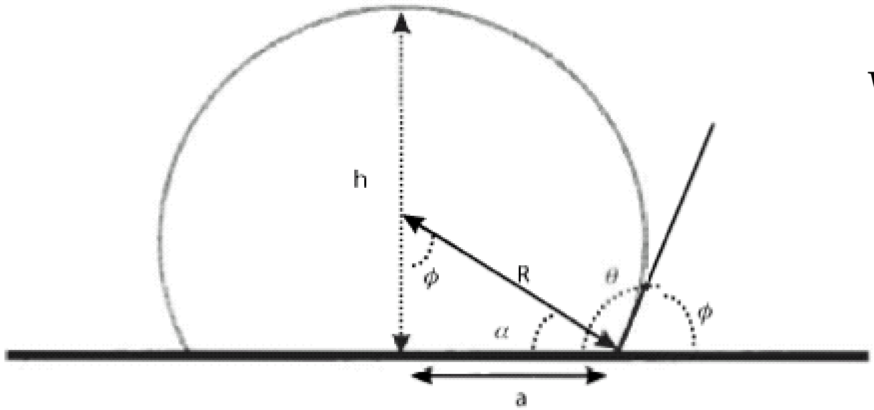
Physics of wetting

- in case of liquid drop on solid vertical force is balanced by the reaction of solid. In case of liquid drop on liquid balance in X and Y direction should be obtained



Equilibrium shape of a droplet

- assuming a spherical droplet (no gravity):



$$V = \pi R^3 \left(\frac{2}{3} - \frac{3\cos\theta}{4} - \frac{\cos 3\theta}{12} \right)$$

- the shape can be determined by minimizing energy with constant volume

$$E = \left(\gamma_{LS} - \gamma_{GS}\right) S_{LS} + \gamma_{LG} S_{LG} =$$

$$= \pi R^2 \left[\left(\gamma_{LS} - \gamma_{GS}\right) \sin^2\theta + 2\gamma_{LG}(1 - \cos\theta) \right]$$

$$dE = \frac{\partial E}{\partial R}(R,\theta)dR + \frac{\partial E}{\partial \theta}(R,\theta)d\theta = 0$$

- minimization will lead to Young’s law

Shape of drops on solid surface

- large drops are not spherical as the gravity flattens the drop. Equilibrium shape can be found by minimization of energy

$$E = \left(\gamma_{LS} - \gamma_{GS}\right)\pi R^2 \sin^2\theta + 2\pi R^2 \gamma_{LG}(1-\cos\theta) + R^4 \rho g \frac{2\pi}{3}(3+\cos\theta)\sin^6\left(\frac{\theta}{2}\right)$$

$$\frac{\partial E}{\partial R}(R,\theta)dR + \frac{\partial E}{\partial \theta}(R,\theta)d\theta = 0$$

$$\cos\theta - \frac{\gamma_{LS} - \gamma_{GS}}{\gamma_{LG}} + \frac{\rho g R^2}{\gamma_{LG}}\left[\frac{\cos\theta}{3} - \frac{\cos 2\theta}{12} - \frac{1}{4}\right] = 0$$

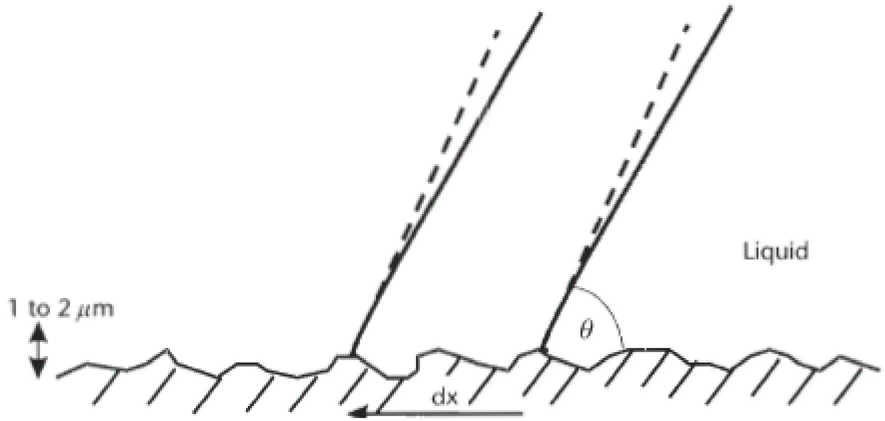
- Bond number represents the ration of gravitational forces and surface tension

$$Bo = \frac{\rho g R^2}{\gamma_{LG}}$$

Typically: r=1000 kg/m^3, g=72 mN/m, R=1mm, so Bo=0.15

Droplet on rough surface: Wenzel's law

- assumption: roughness on a microscopic scale



- work along the contact line:

$$dE = dW = \sum F_x dx = (\gamma_{SL} - \gamma_{SG}) r dx + \gamma_{LG} \cos\theta dx$$

$$\gamma_{LG} \cos\theta = (\gamma_{SL} - \gamma_{SG}) r$$

$$\cos\theta = \frac{(\gamma_{SL} - \gamma_{SG}) r}{\gamma_{LG}} = r \cos\theta^*$$

on smooth surface

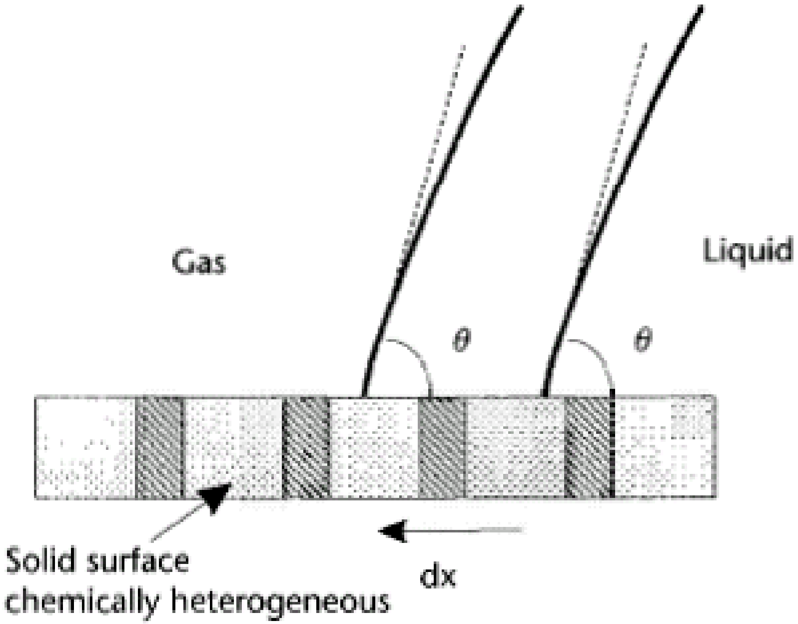
Wenzel's law

$\theta > \theta^*$ for hydrophobic surface ($\theta^* > 90^0$)

$\theta < \theta^*$ for hydrophilic surface ($\theta^* < 90^0$)

Cassie-Baxter law

- droplet on an inhomogeneous surface:

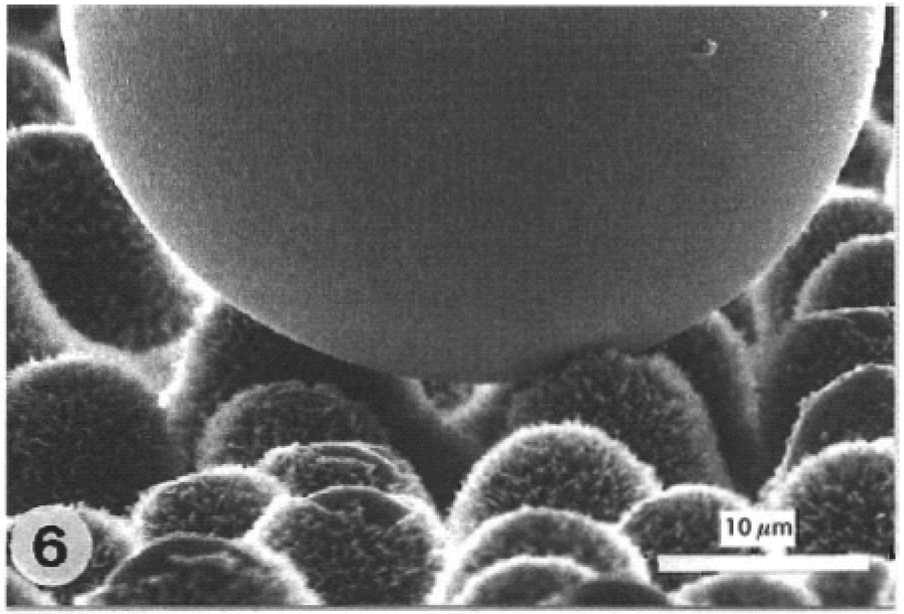


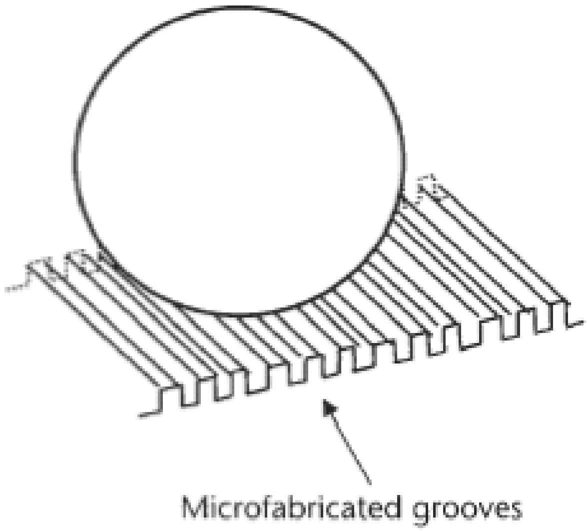
$$dE = dW = \sum F_x dx = (\gamma_{SL1} - \gamma_{SG1}) f_1 dx + (\gamma_{SL2} - \gamma_{SG2}) f_2 dx + \gamma_{LG} \cos\theta dx$$

$$\cos\theta = f_1 \cos\theta_1 + f_2 \cos\theta_2$$

Superhydrophobicity and Superhydrophilicity

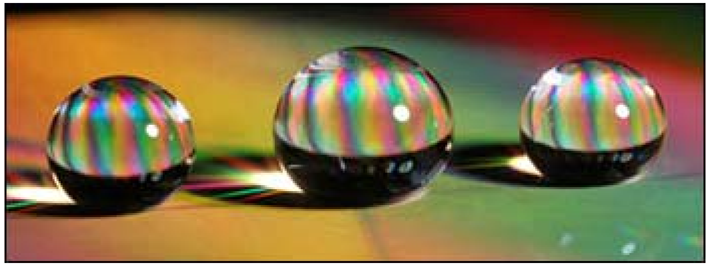
- Wenzel's law: hydrophobocity or hydrophilicity is enhanced by an increase in surface roughness
- In addition inclusion of air pores contributes to the superhydrophobicity $\cos\theta = f_1 \cos\theta_1 - f_2$ as $\theta_{AIR} = 180^0$

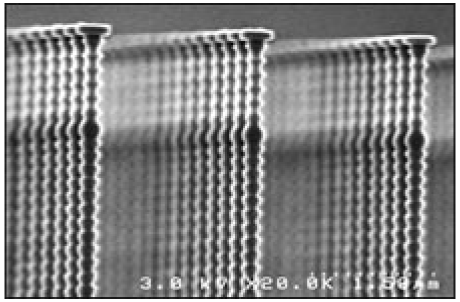




Superhydrophobic surfaces

- Tom Krupenkin and J. Ashley Taylor , Langmuir to be published Feb 2008

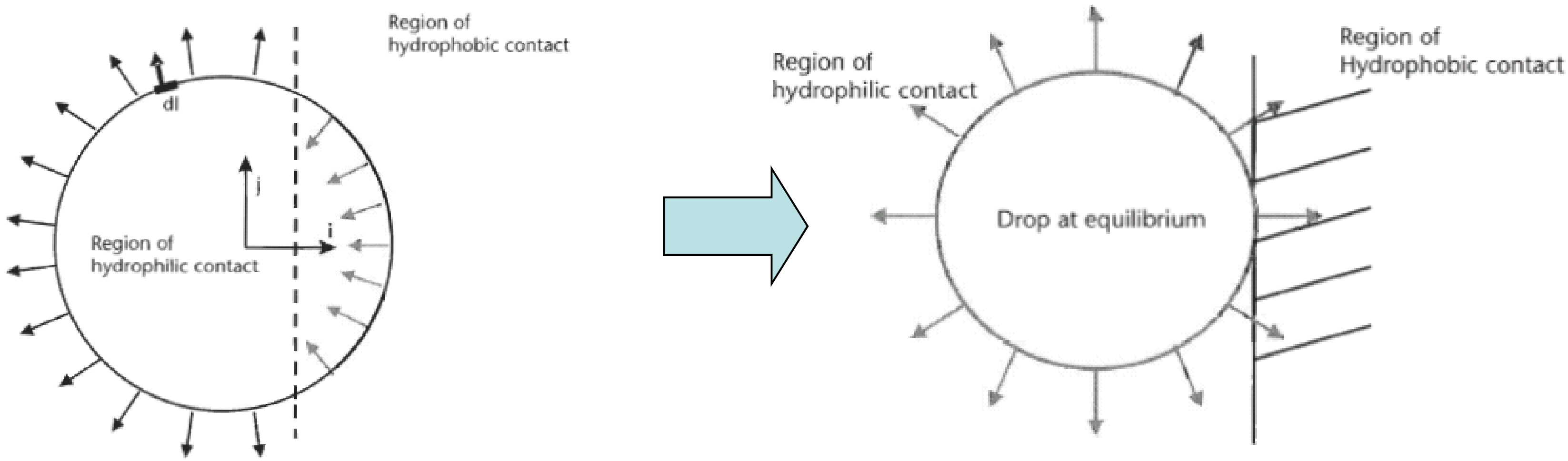


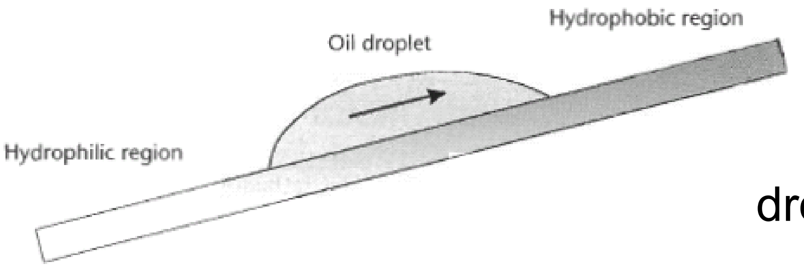


Silicon "nanonails" created by Krupenkin and Taylor form the basis of a novel surface that repels virtually all liquids. The surface may have applications in biomedical devices such as "labs-on-a-chip," chemical microreactors, and in extending battery life.

Motion of drops under action of hydrophilic/Hydrophobic forces

- droplet deposited on a border between hydrophilic/hydrophobic region will move towards hydrophilic region

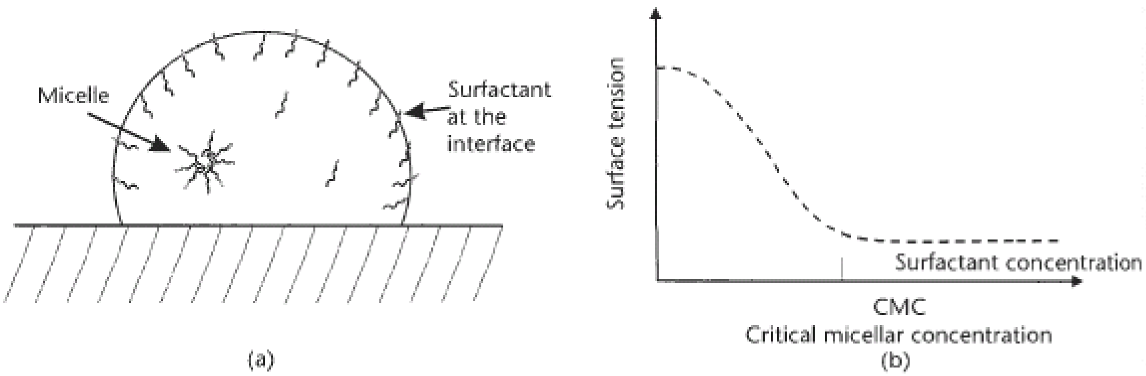




droplet running uphill

The effect of surfactants

- in the presence of surfactants the surface tension will be reduced (e.g. for water from 72 mN/m down to 30 mN/m)



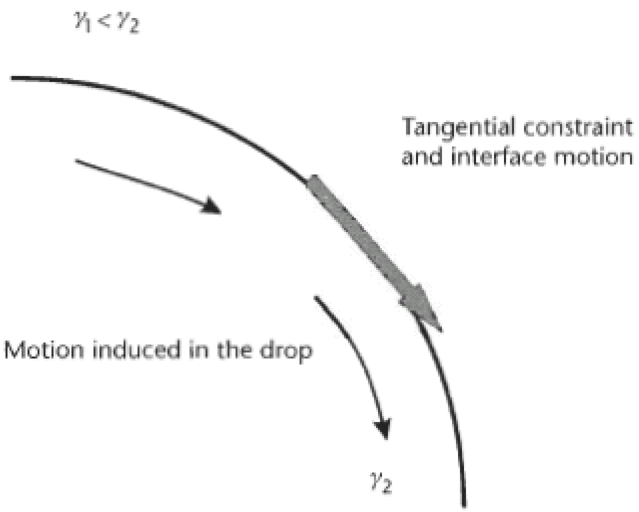
Marangoni effect

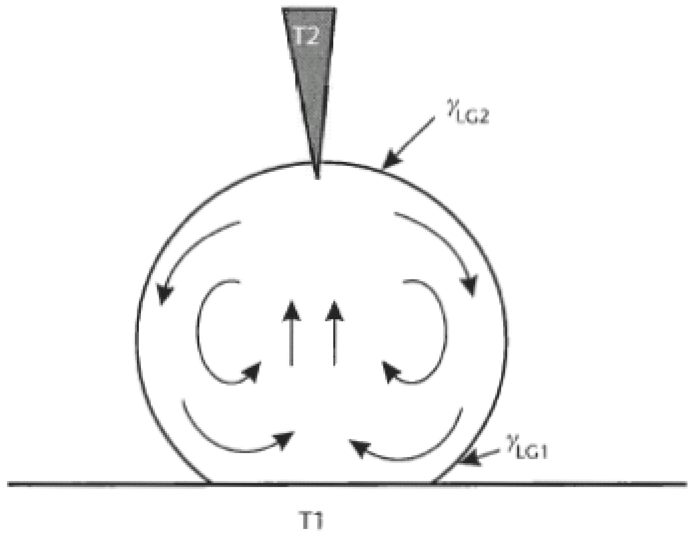
- surface tension depends on temperature as

$$\gamma = \gamma_0 (1 - \beta (T - T_0))$$

for water/air interface: g_0=72mN/m and b=0.1 mN/(m K)

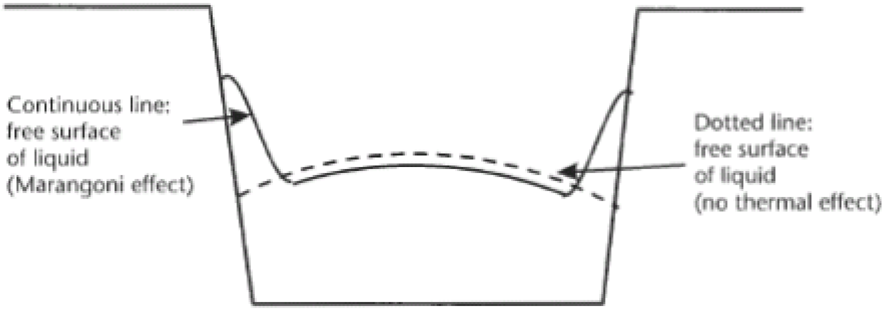
- surface tension distribution induces tangential force distribution on the interface and convective motion inside the droplet



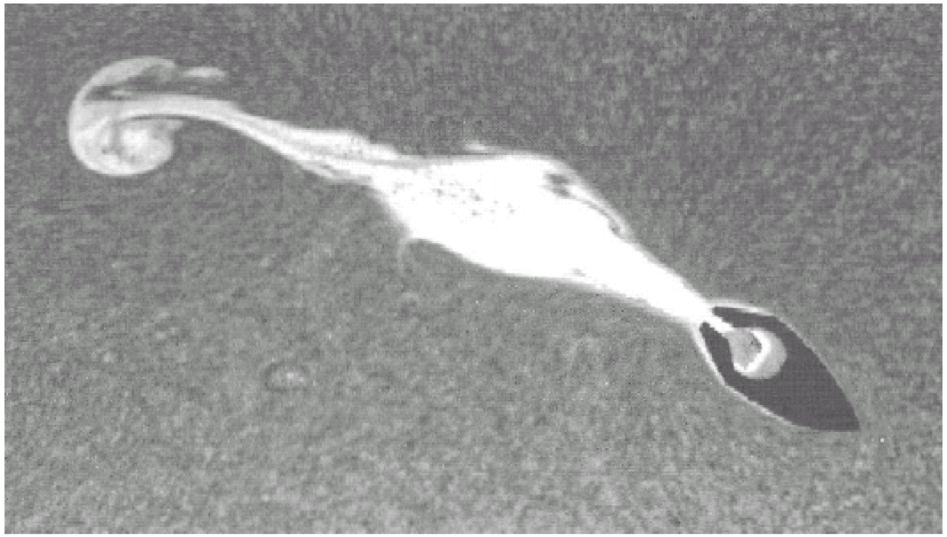


Marangoni effect

- Marangoni effect due to temperature in a microwell

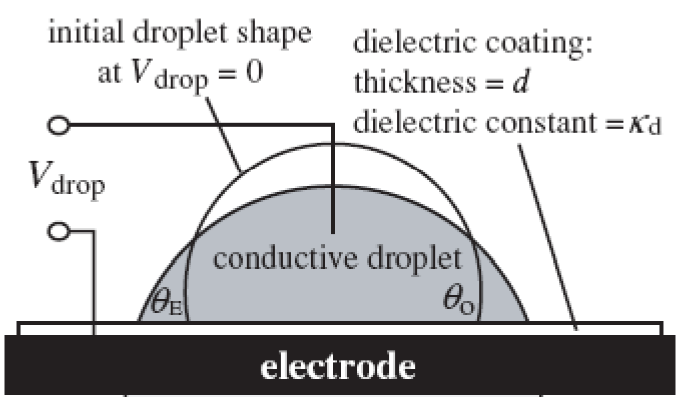


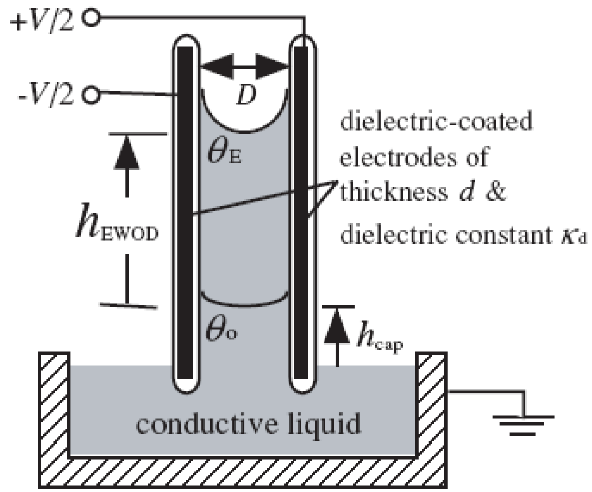
- Marangoni effect due to surfactant concentration



Electrowetting

Electrowetting on Dielectric film is a phenomenon where the surface property of a dielectric film can be modified between hydrophobic and hydrophilic states using an electric field. This process can cause a droplet of liquid to bead or spread out on the surface depending upon its surface state.



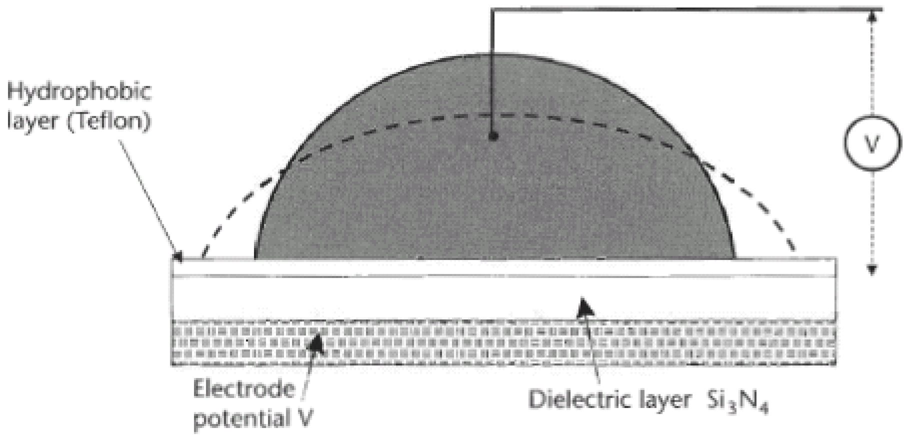


Applications

- liquid dispensers
- voltage-controlled fluidic switches
- laboratory-on-a-chip
- focused liquid lenses
- Optoelectronics couplers
- electronic paper displays

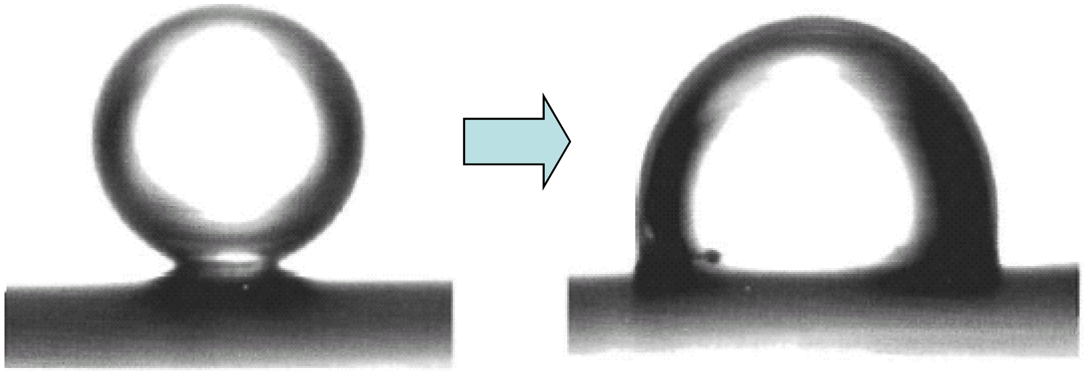
Electrowetting

- redistribution of charges under applied electric field causes change in wetting properties

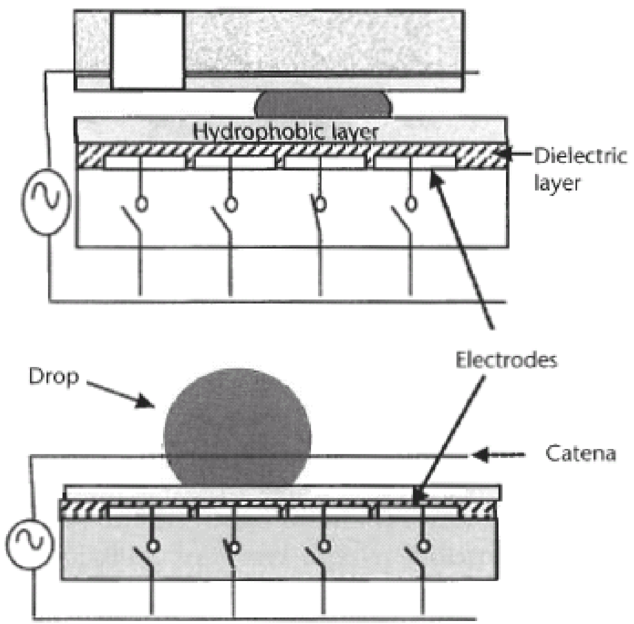


$$\gamma_{SL} = \gamma_{SL,0} + \frac{1}{2} C V^2$$ Lippmann's law

$$\cos\theta = \cos\theta_0 + \frac{1}{2}\frac{C}{\gamma_{LC}} V^2$$



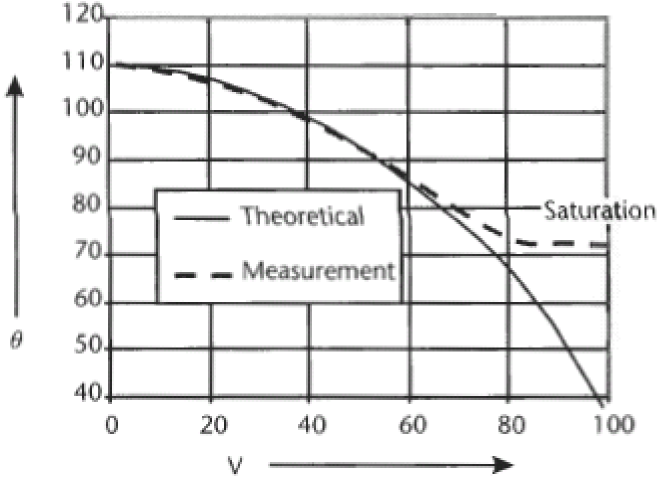
Electrowetting



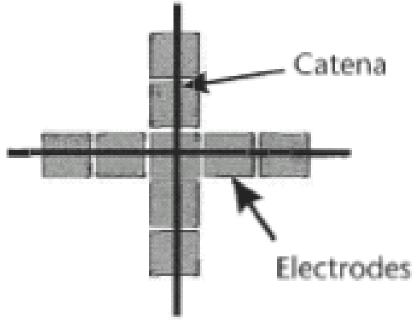
covered EWOD (Electro-Wetting On Dielectric) system

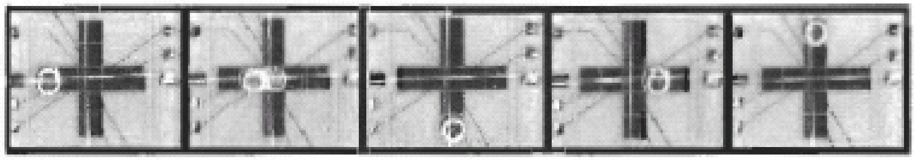
open EWOD system

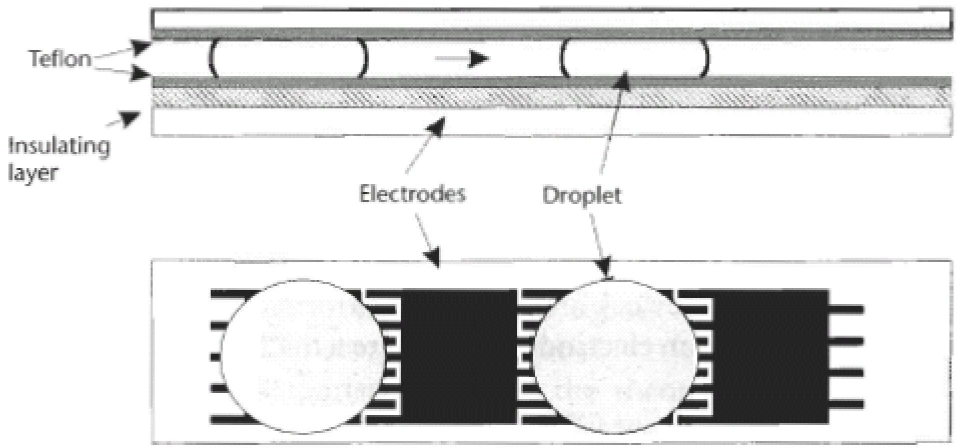
- Experimentally observed a saturation of contact angle vs. applied potential



Electrowetting devices

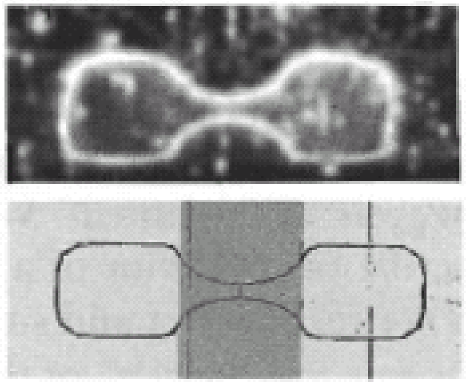




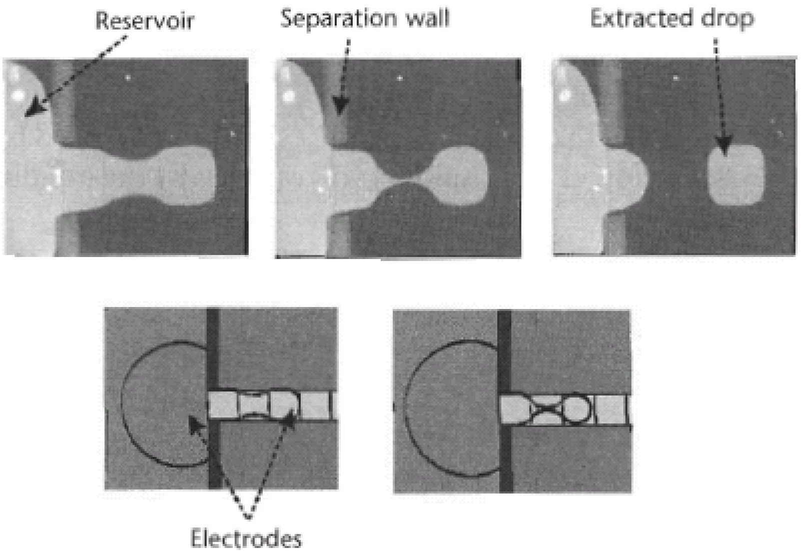


Electrowetting devices

- drop division



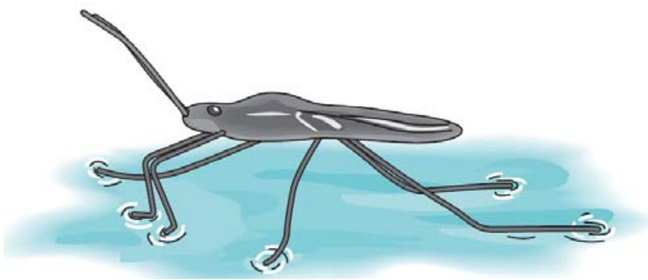
- drop formation by electrowetting



Problems

- Estimate the minimum size of air and water volume where the fluctuation of thermodynamic variables will be less than 0.5%. Assume that air is an ideal gas at atmospheric pressure and the fluctuations go as $\sqrt{N}/N$

- **Munson1.49** Find the minimum length of the interface necessary to support a water strider. Assume the bug weighs 10^{-4} N and surface tension acts vertically upward. Surface tension of water σ=7.3 10^{-2} N/m. What length of the interface would be required to support a person weighing 750N.



- **Munson1.29** As was discussed in the lecture, no-slip condition means that a fluid sticks to a solid surface, both fixed or moving. Determine the ratio between the share stresses acting on the upper and on the bottom plate.