BioMEMS (and Microfluidics)

MEMS Technology

Microfluidics &
Implantable sensors

BioMEMS

'Traditional' MEMS

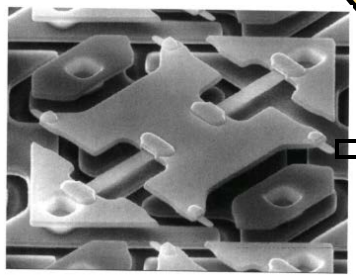
Accelometers &
Inject Heads

RF MEMS

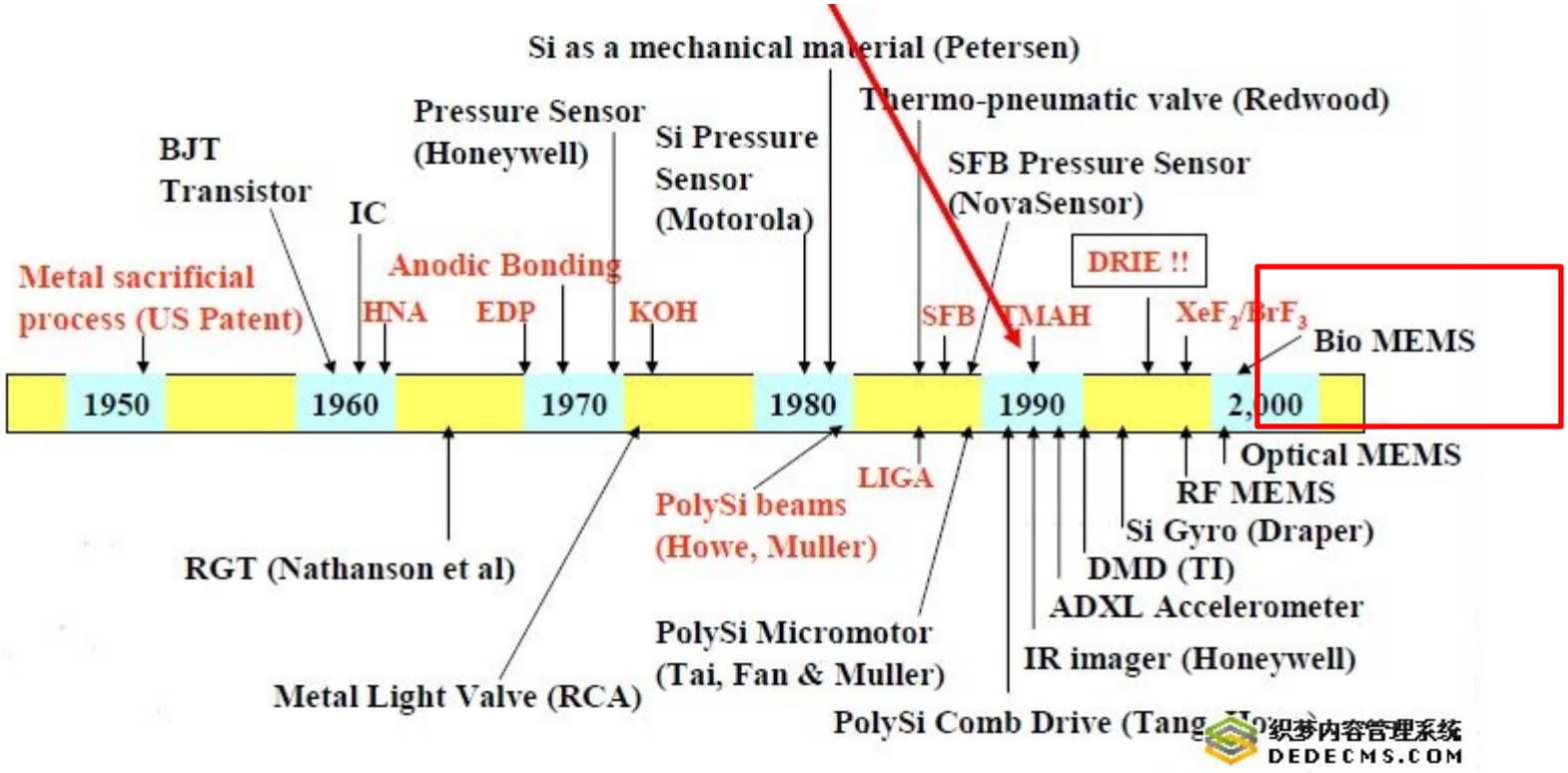
Filters &
Varactors

Optical MEMS (MOEMS)

Mirrors &
Switches



History of MEMS Technology



BioMEMS is a relatively new field…

Image taken from: http://www.rfmems.net/a/MEMS/20100411/58.html

BioMEMS Materials

SILICON & ITS DERIVATIVES

Silicon(Si)
Silicon Dioxide - SiO_2 (glass)
Silicon nitride (Si_xN_y)
....

⇩

- Mechanical Reliability
- Performance
- IC compatibility

POLYMERS

Photosensitive Polymers (e.g. SU-8)
Polydimethylsiloxane (PDMS)
Parylene
PS
PMMA
...

⇩

- Biocompatibility
- Cost
- Surface Modification
- Disposability (e.g. single use devices)
- Rapid Prototyping

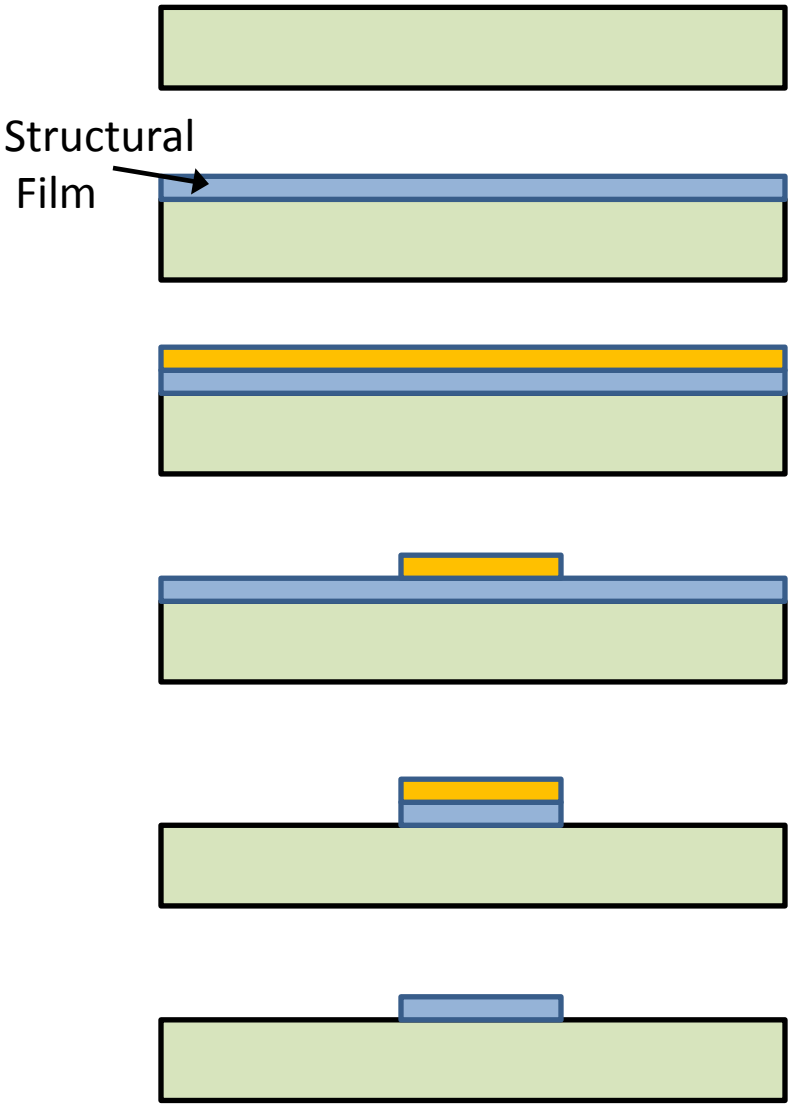
METALS

Platinum
Silver
Chrome and Gold
Indium Tin Oxide (ITO)
...

⇨

- Increased Functionality
- Integration (sensors & actuators)

Microfabrication Consists of 3 Major Steps: Deposition, Patterning, Removal



1. Select a Substrate (e.g. a silicon wafer)

2. DEPOSIT the *Structural* Material
(usually a few-microns thick film)

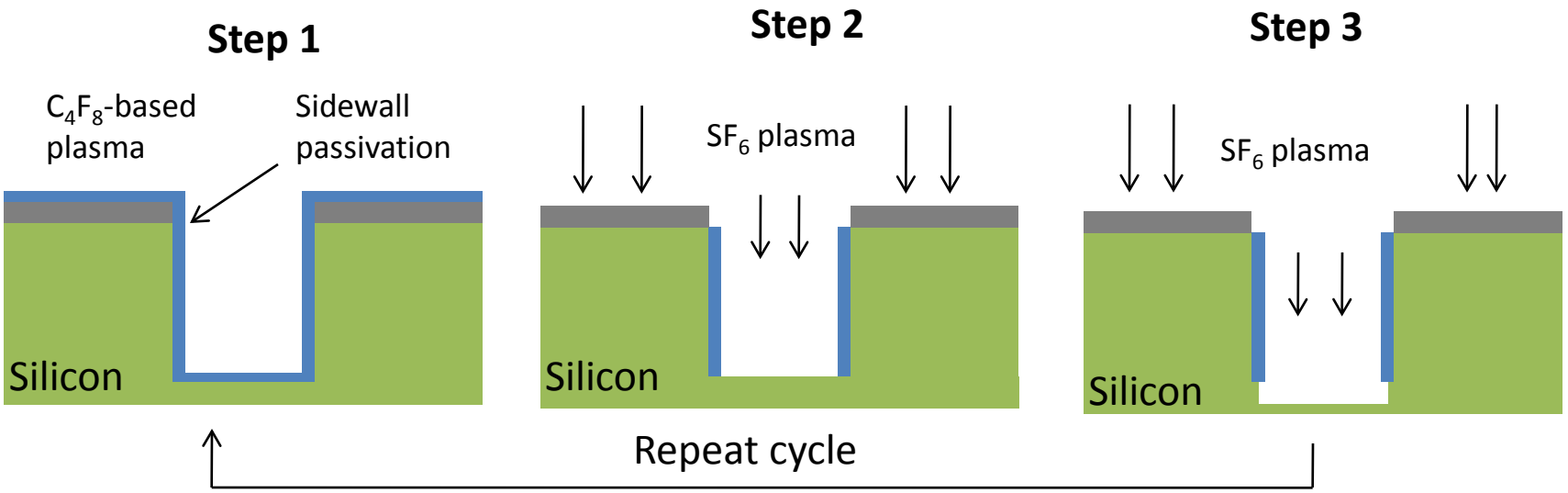
3. DEPOSIT PhotoResist (PR)
(PR is photosensitive to UV radiation)

4. PATTERN PR using light (LITHOGRAPHY)

5. REMOVE the structural material

6. REMOVE PR

DRIE of Si – Operation Principle



Etching is performed in cycles of 3 steps:

Deposit Polymer (step 1) : C_4F_8-based plasma is used to conformally deposit a few monolayers of PTFE-like fluorocarbon polymer across all surfaces

Etch polymer (step 2): The plasma gas is then switched to SF_6 that isotropically etches silicon (like typical RIE). Ions from the plasma bombard the surface of the wafer, removing the polymer. Increased ion energy in the vertical direction results in a much higher rate of removal of fluorocarbon from surfaces parallel to the wafer surface.

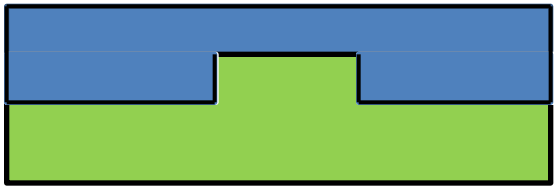
Etch silicon (step 3) : Following selective polymer removal, the silicon surface at the base of the trench is exposed to reactive fluorine-based species that isotropically etch the unprotected silicon. The remaining fluorocarbon polymer protects the vertical walls of the trench from etching.

Soft- Lithography:
Creating a 'Soft' (e.g. PDMS) Mold

1. Start with a Master Mold

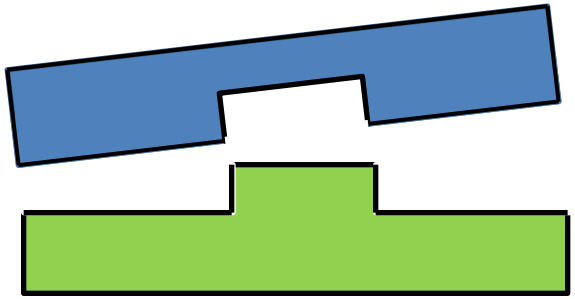
Master Mold

2. Cast and Cure PMDS



e.g. cure at 100°C for 45 min

3. Peel off and u r DONE!

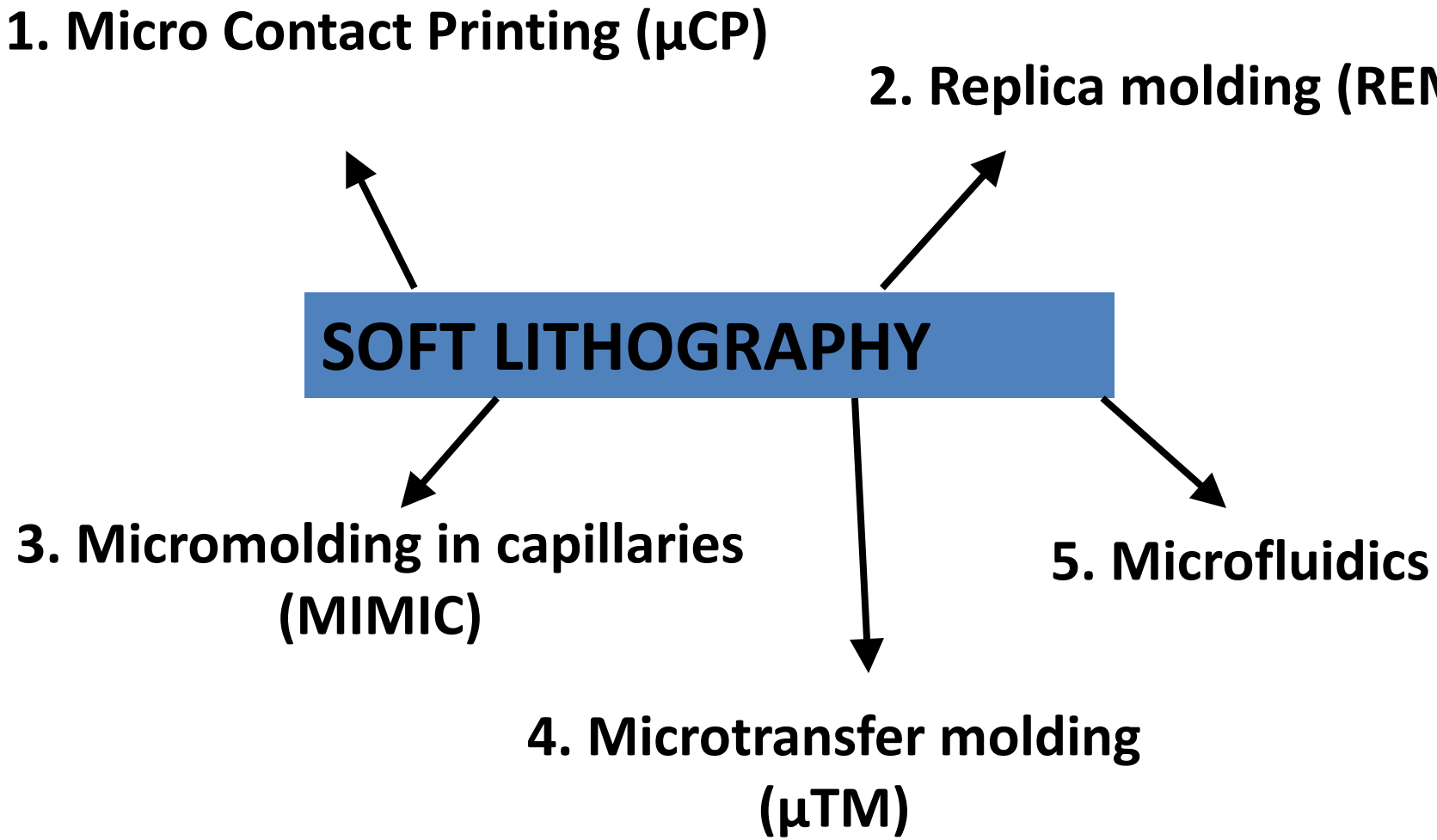


Soft Mold

Master Mold

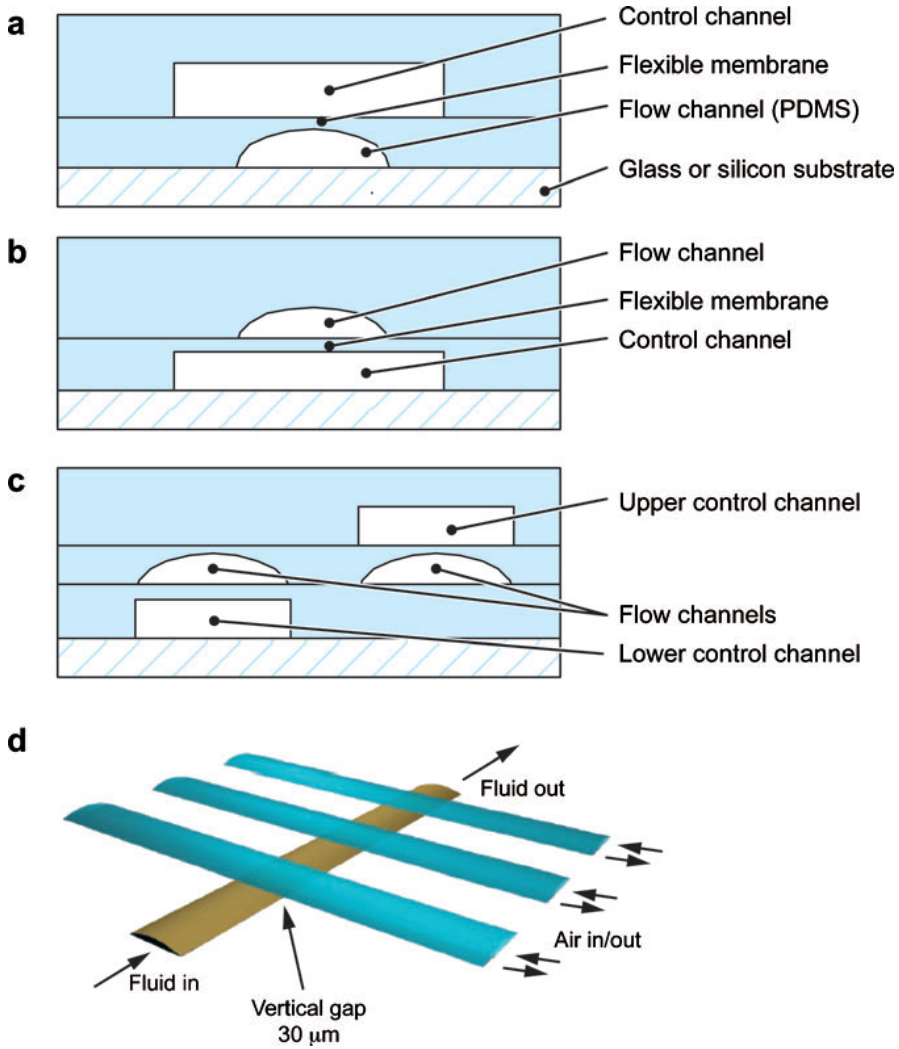
It can be reused

What can you do with the ‘Soft’ Mold?

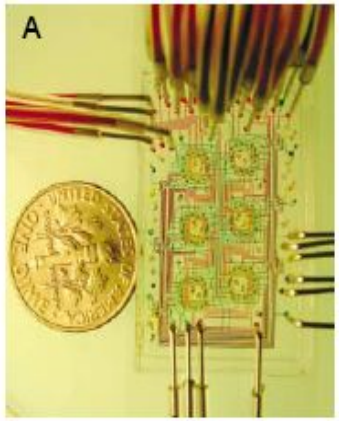


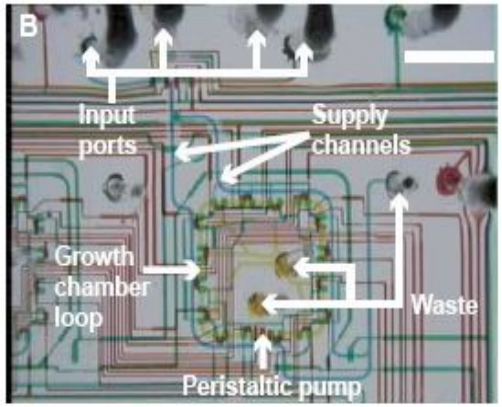
& Multilayer Soft Lithography

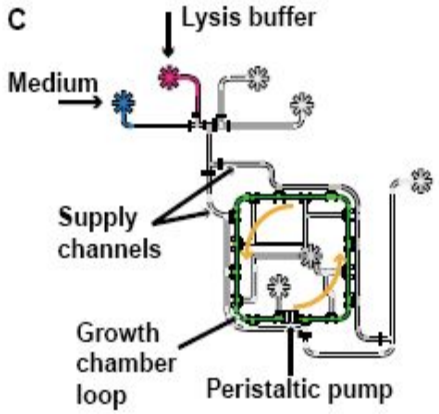
…From Simple Valving…

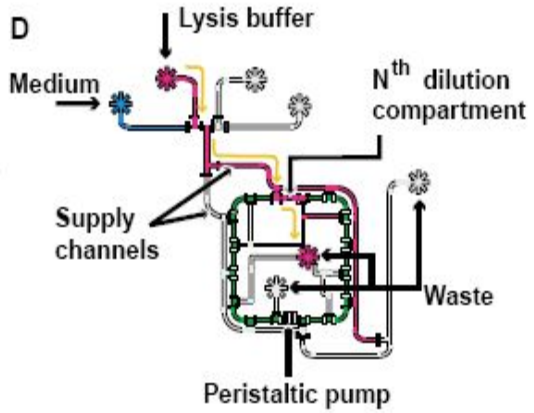


…to Complex Systems: A microfluidic Chemostat



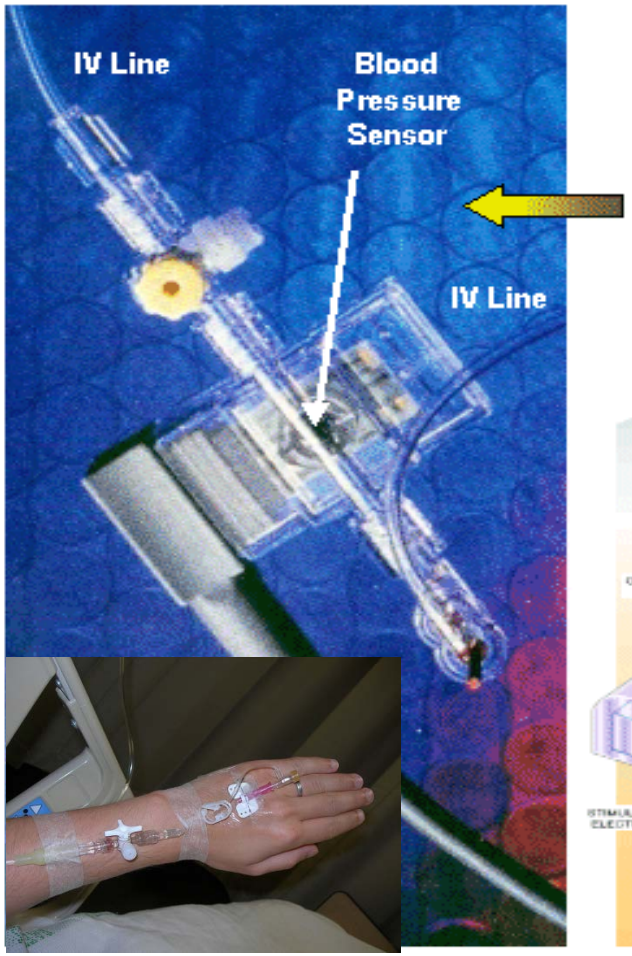






BioMEMS in the Medical Field

Ex vivo…



In vivo…

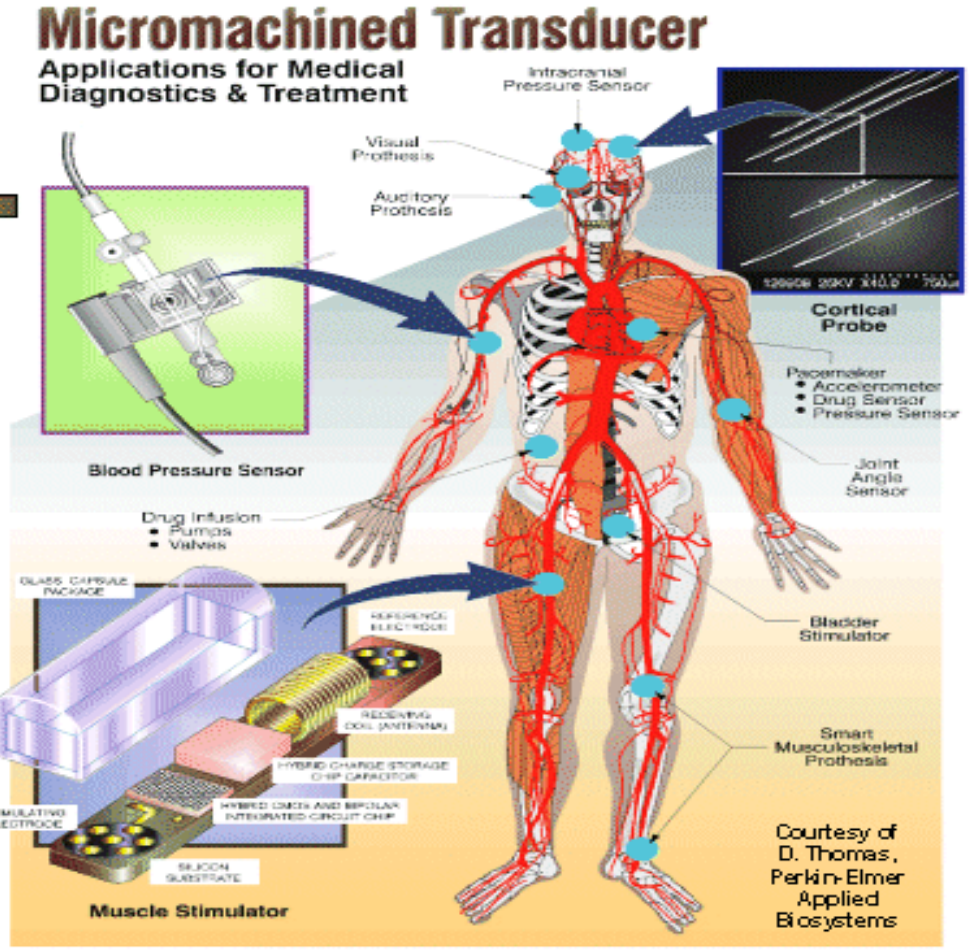
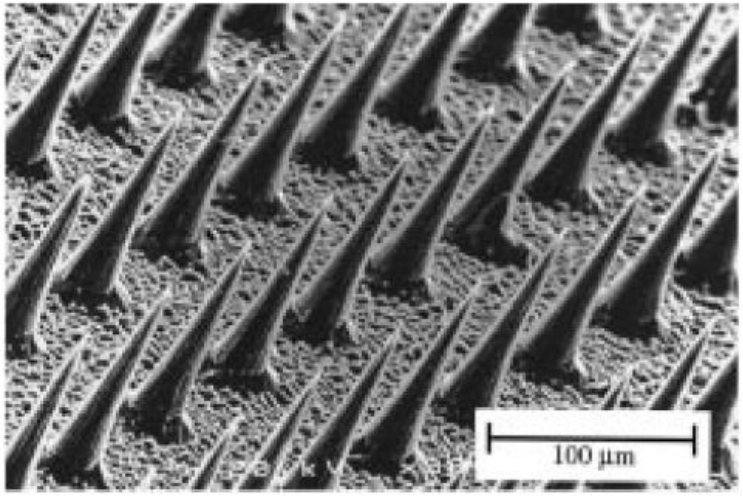


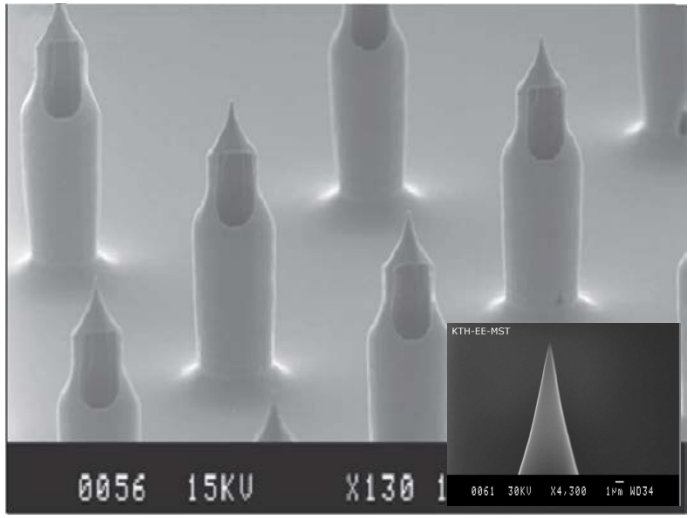
Image taken from : http://mems.colorado.edu/c1.res.ppt/ppt/g.tutorial/ppt.htm

Micro Needles

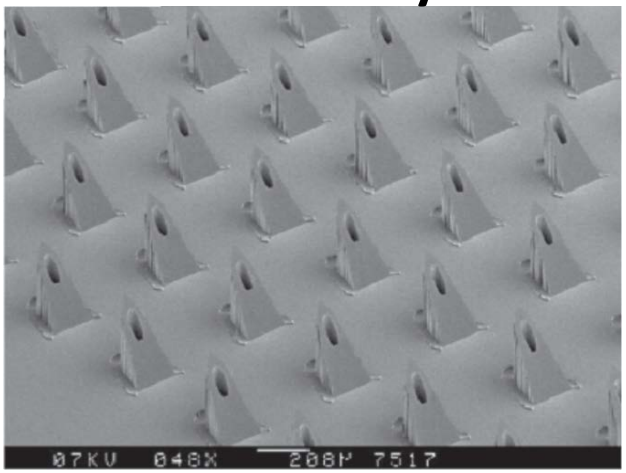
Solid MicroNeedles (coated, first generation)



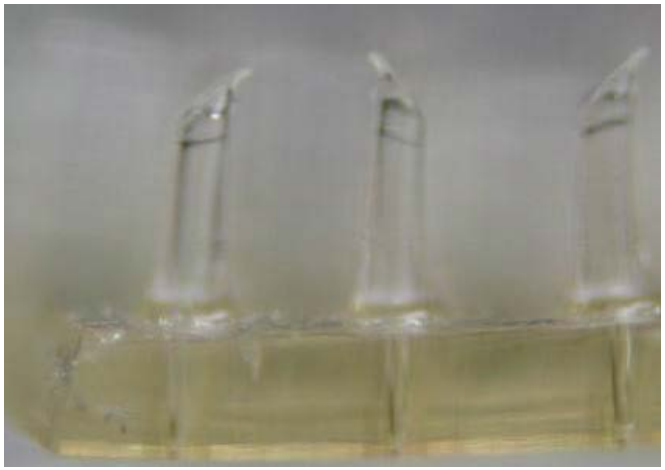
Ultrasharp Si (Citadel style) with a hole at the side



Saw-tooth style

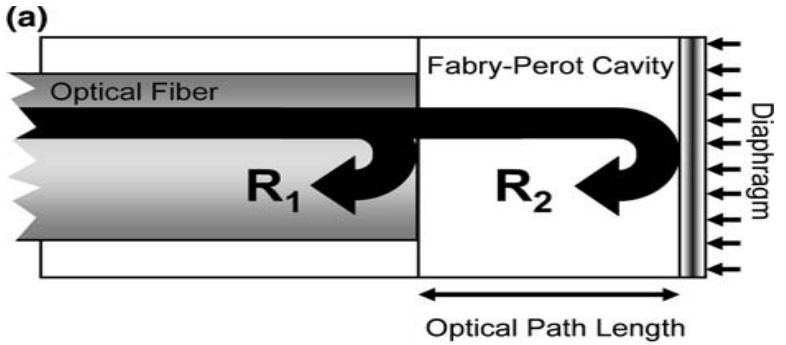


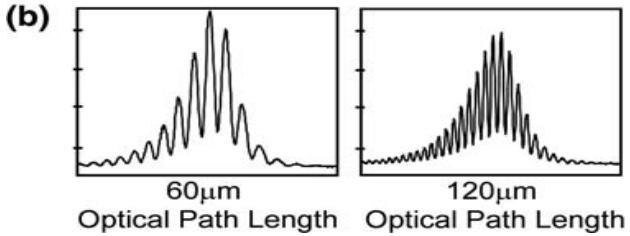
Polymer-based (PDMS)

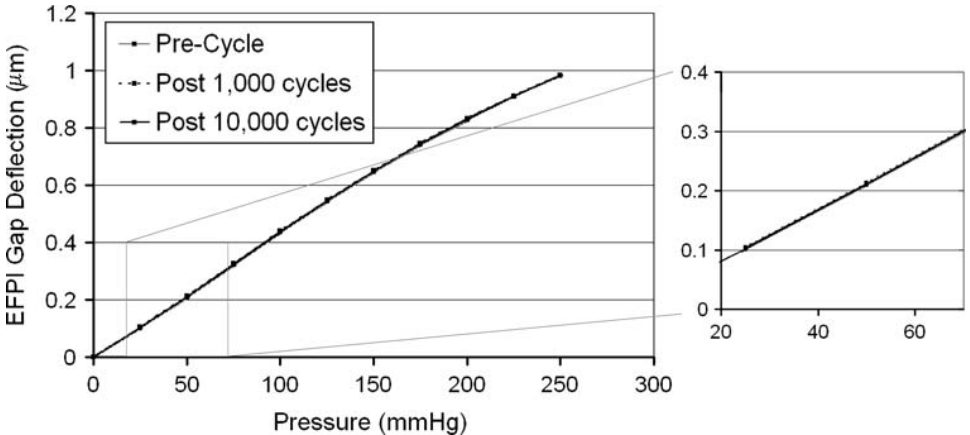


Optical Pressure Sensors

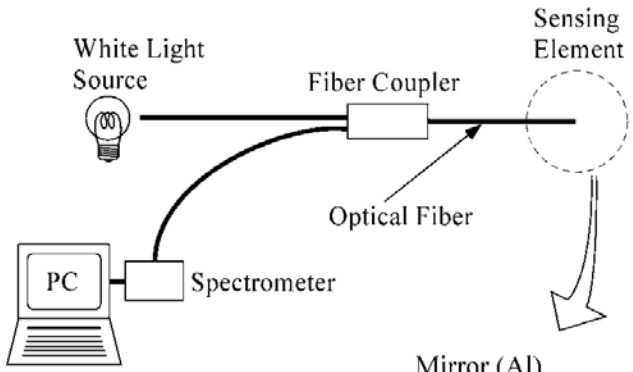
Concept: *A deformable membrane acts as a mirror in a Fabry–Pérot cavity*

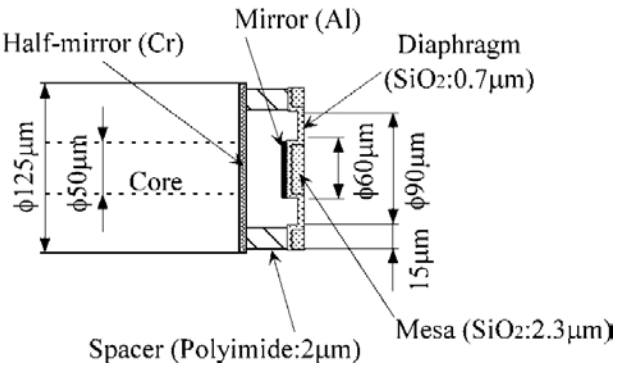






The Measuring Setup

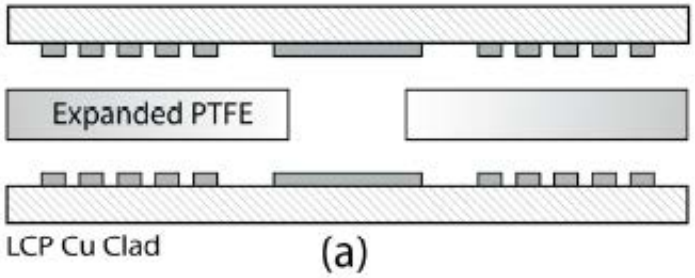




The CardioMEMS Sensor

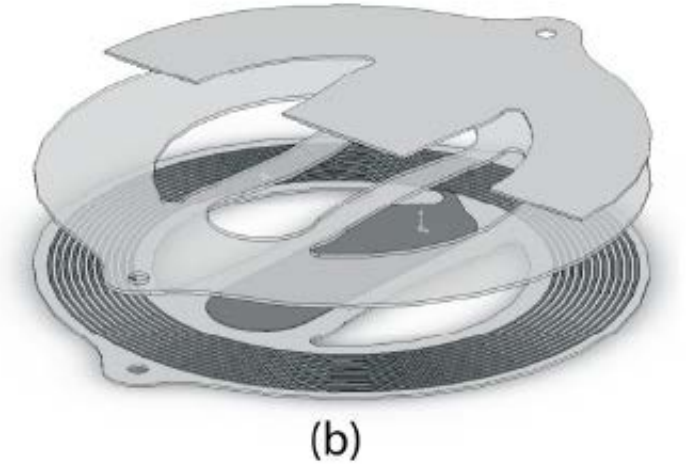
Materials

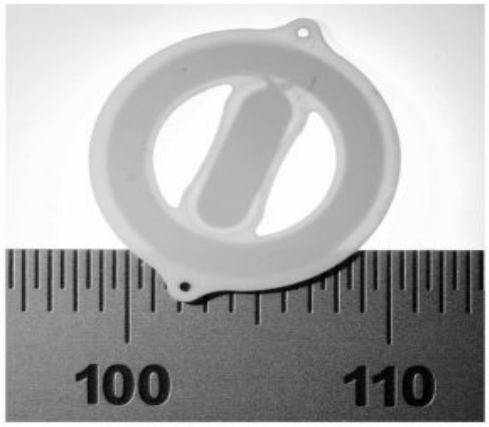
- Copper-clad Liquid Crystal Polymer (LCP)
- Expanded polytetrafluoroethylene (PTFE)



Microfabrication Process

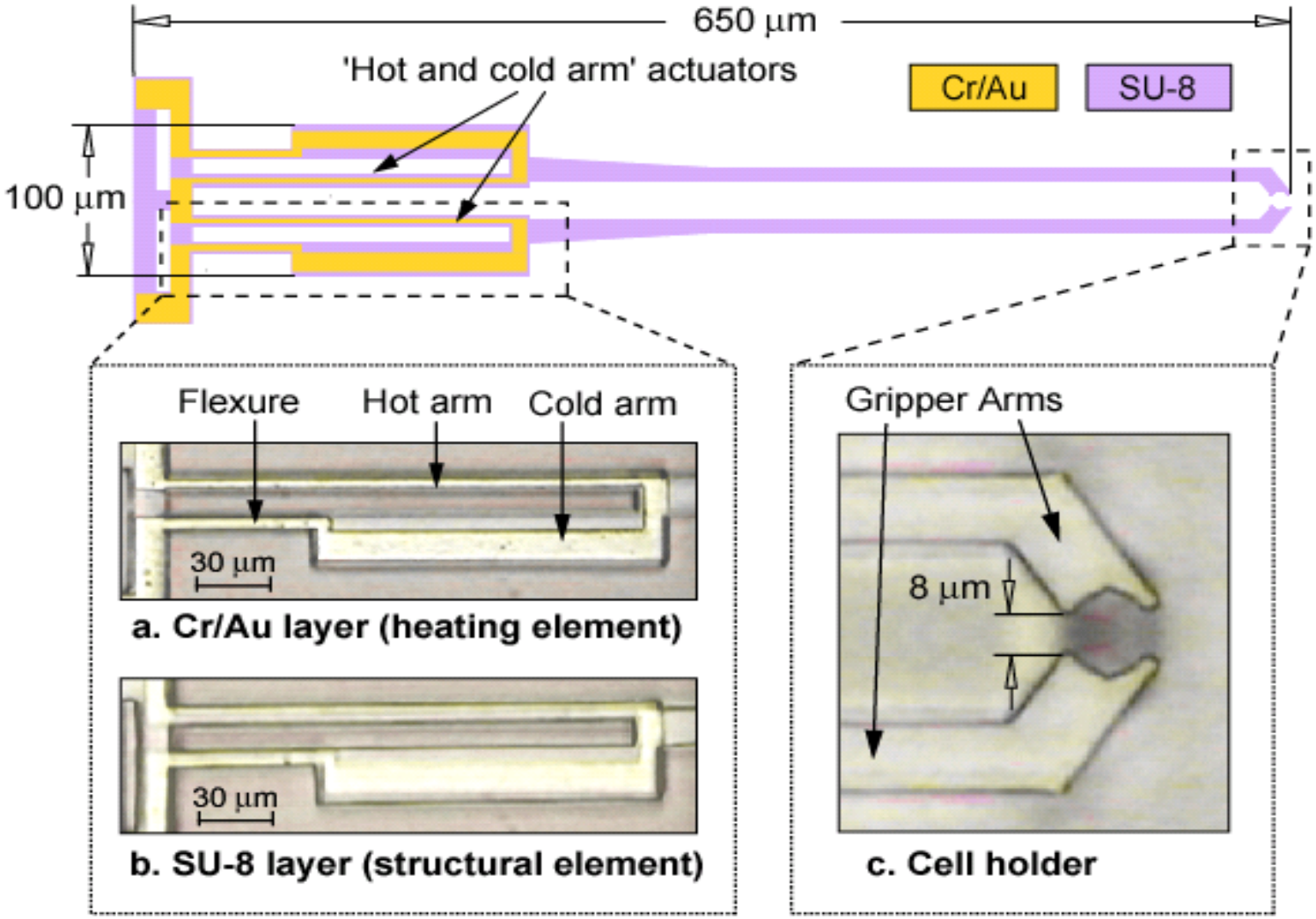
- Photolithography/ Wet Etching
- Bonding: The layers are aligned, assembled and laminated at 180^{o}C under pressure



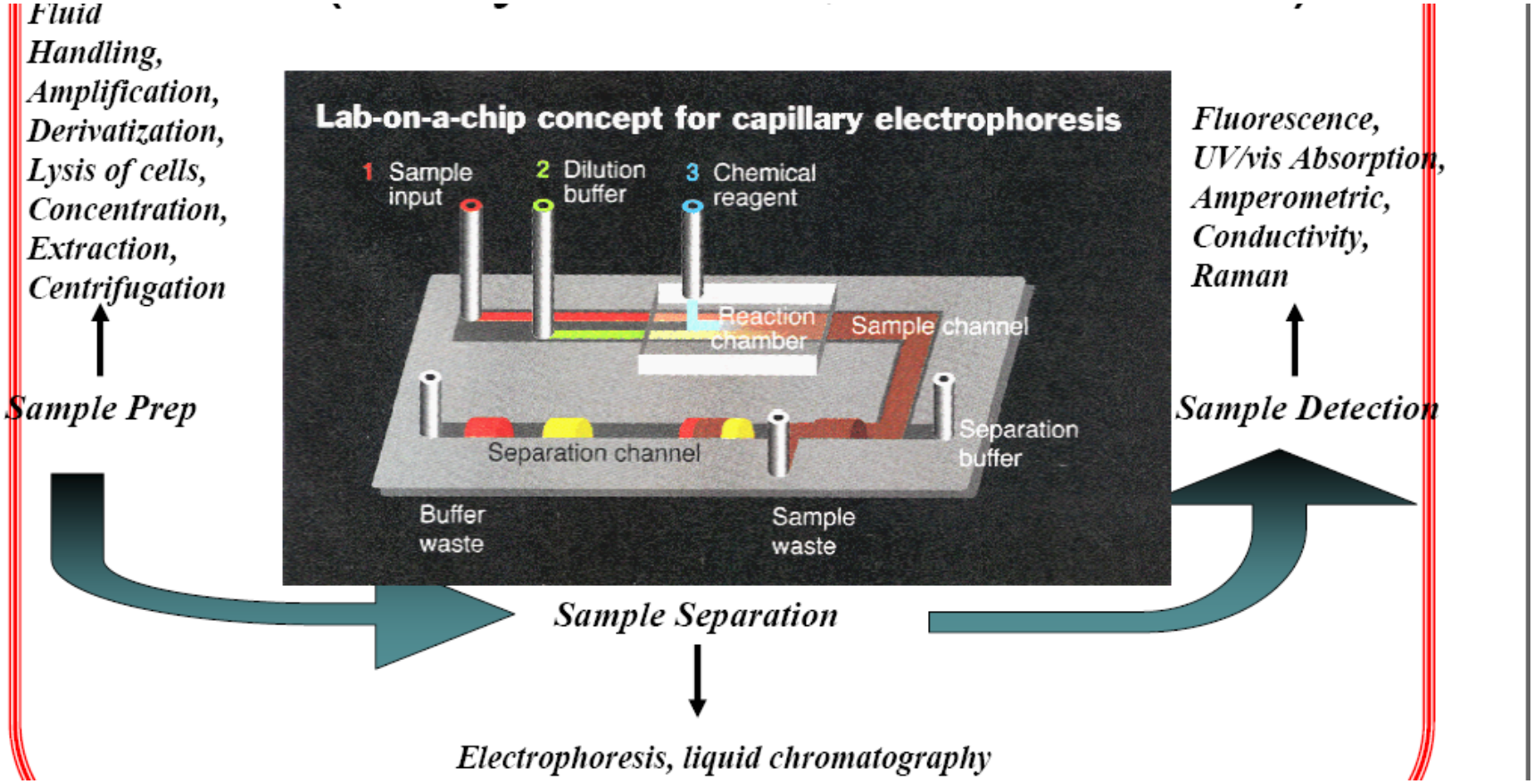


Final Device: A self-packaged structure in which only a polymer outer surface is exposed to the environment

BioMEMS Actuators



Microfluidics/Lab-on-Chip Systems



Navier-Stokes Equations

$$\rho\left(\frac{\partial \vec{V}}{\partial t} + \vec{V}\cdot\nabla\vec{V}\right) = -\nabla p + \rho\vec{g} + \mu\nabla^2\vec{V}$$

Inertial Forces

Pressure Forces

Gravity Forces

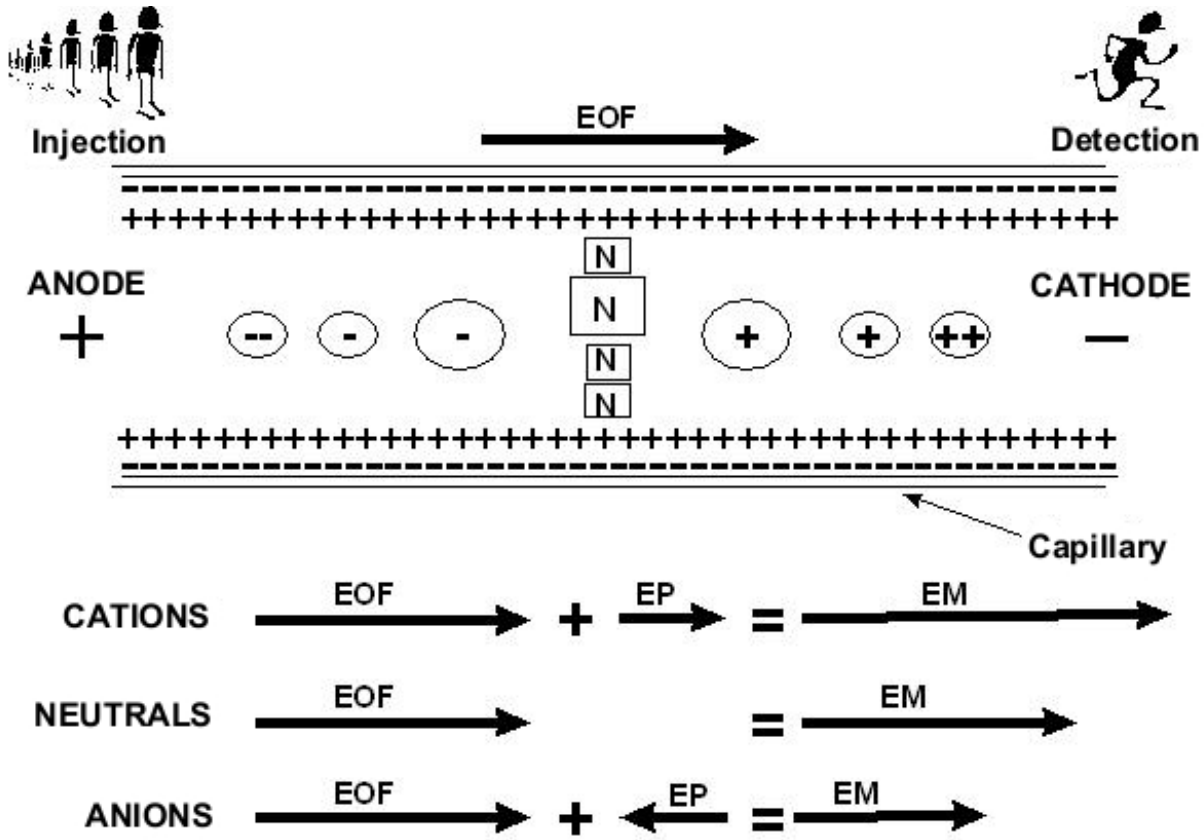
Viscous Forces

In most microfluidic cases, Inertial & Gravity forces are negligible compared to Pressure & Viscous forces

N-S: $0 = -\nabla p + \mu\nabla^2\vec{V}$

EOF and Electrophoresis

EOF and Electrophoresis might compete each other…



Do not forget to calculate absolute velocities:

$$\vec{u}_{abs} = \vec{u}_{ep} + \vec{u}_{EOF}$$

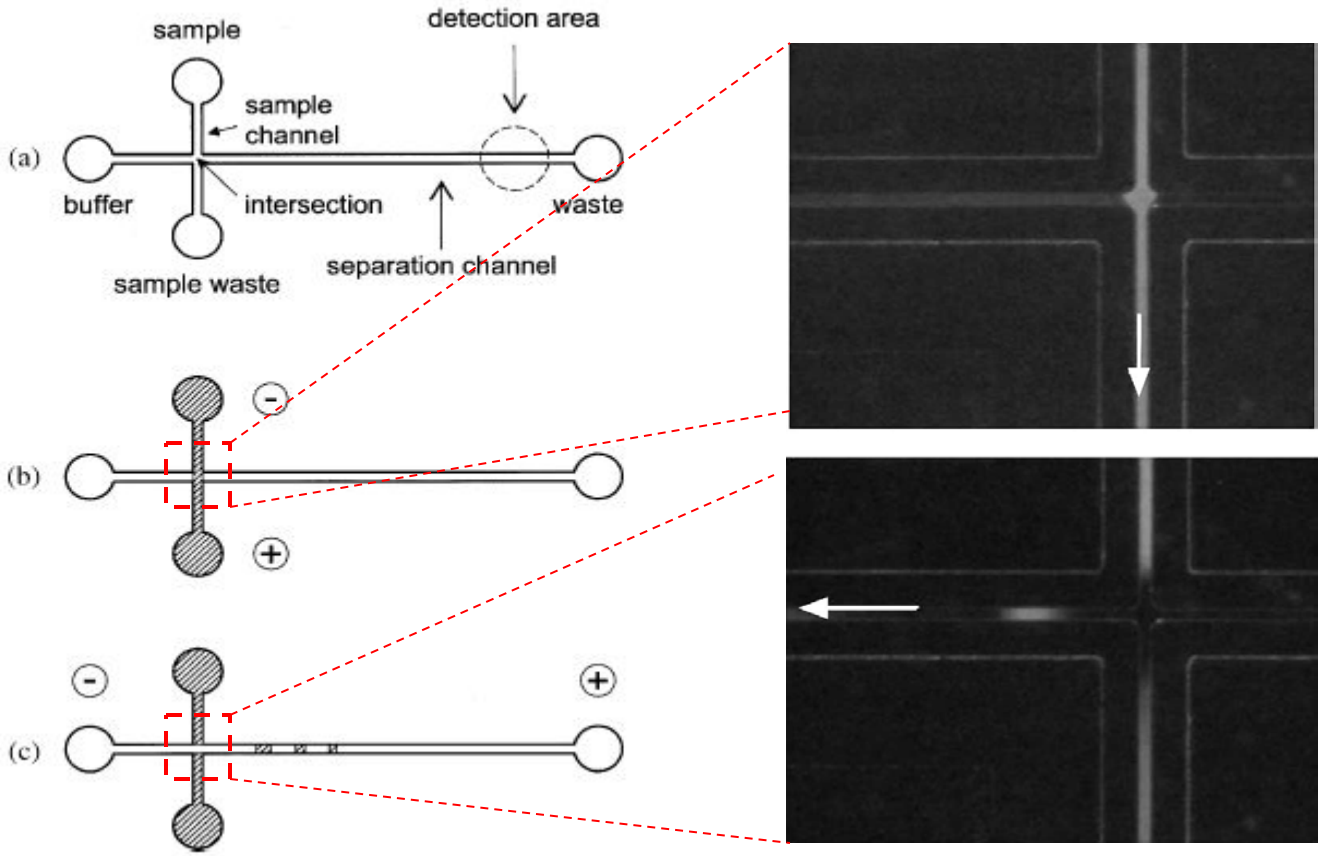
Capillary Electrophoresis for DNA Separation

Concept:

Use microfluidic channels (capillaries) to separate DNA fragments

Operation Principle

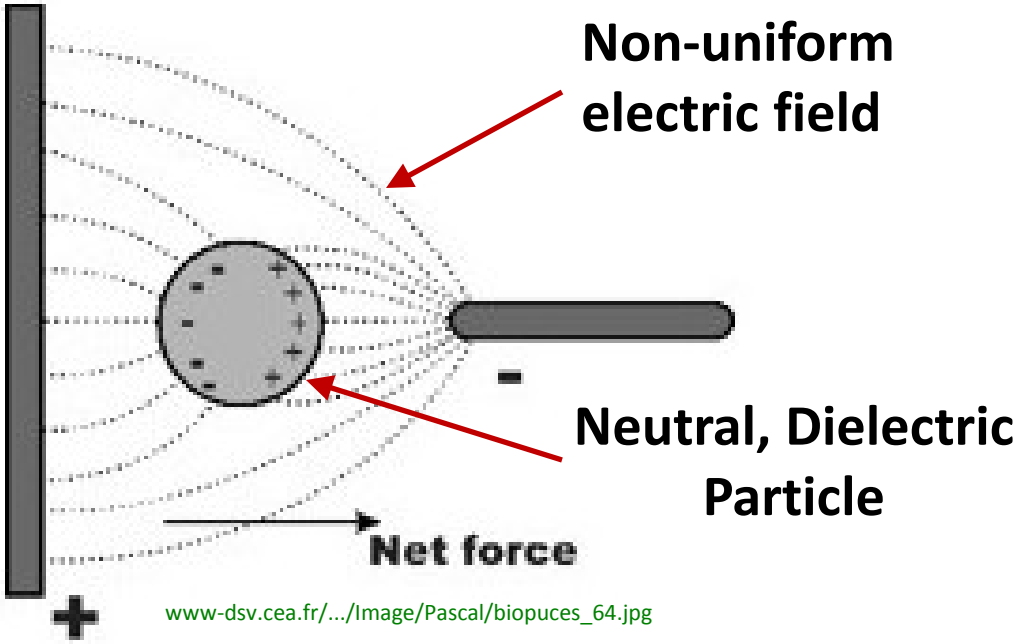
a) Fill the channel intersection with sample solution
b) Apply potential between buffer and waste inlets to initiate electrophoresis



Electric Field applied: 200-400 V/cm, Separation time: 1-2 min, Limiting factor: Joule Heating

Dielectrophoresis

An Non-uniform Electric Field exerts a force on a uncharged, dielectric object (e.g. particle)



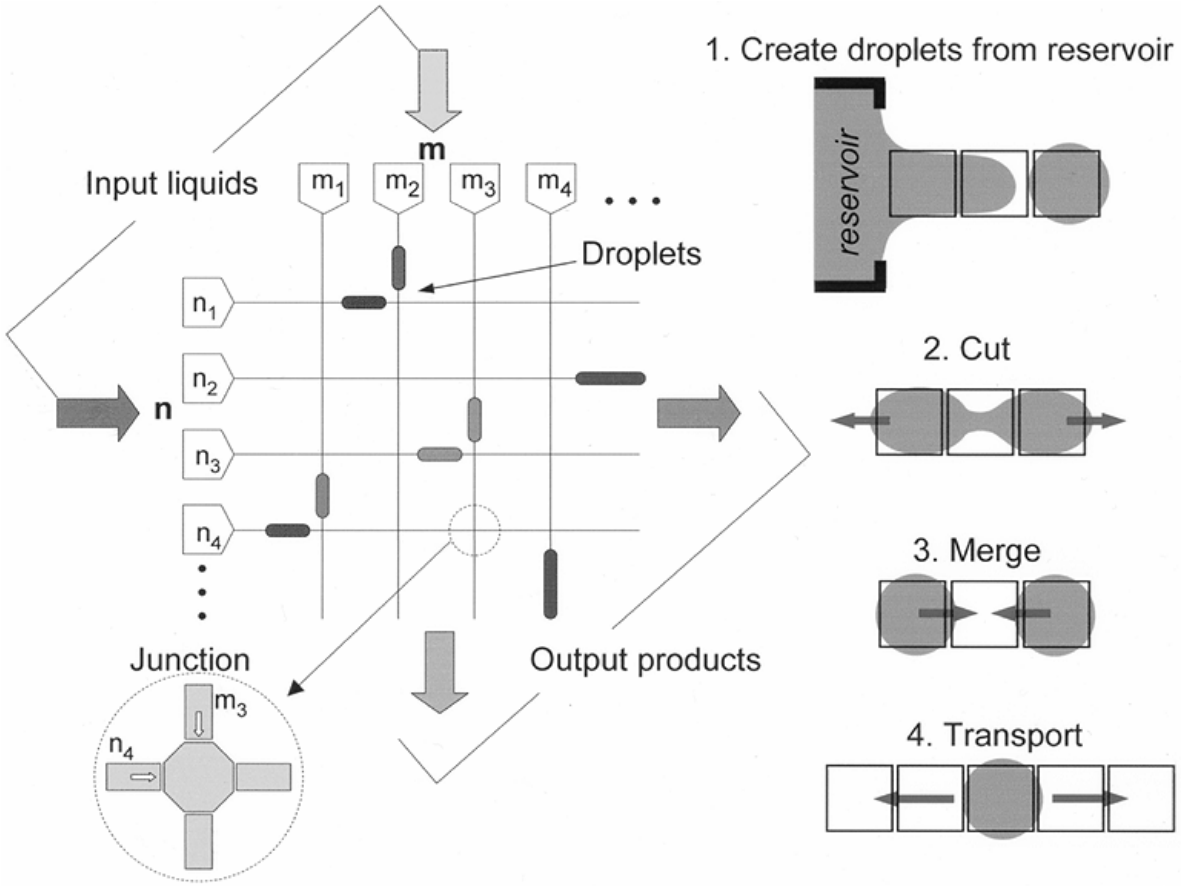
The object does not have to be charged,

All dielectric objects exhibit dielectrophoretic activity!

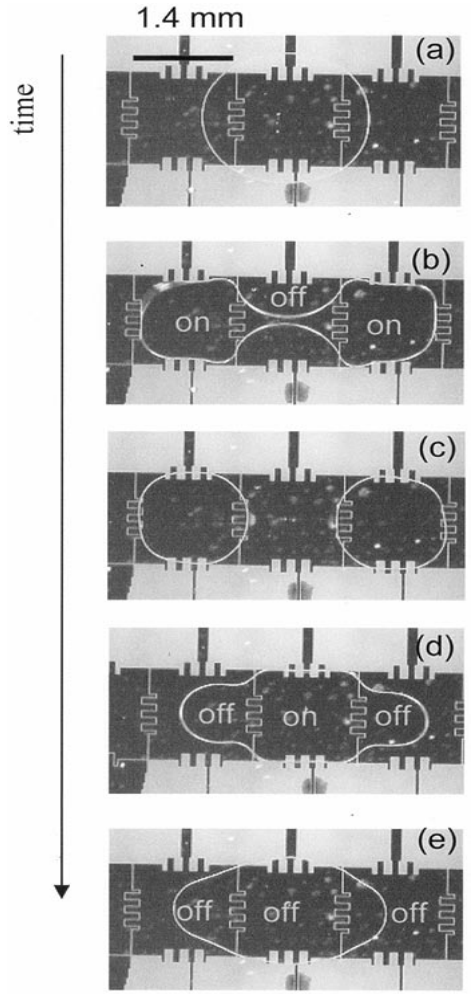
Application

To move, trap, separate, neutral, dielectric objects (e.g. cells)

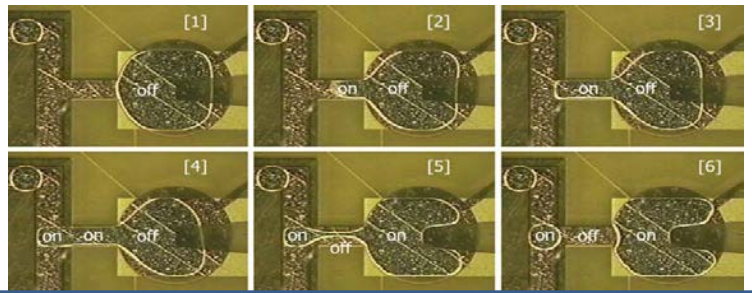
Fluidic Operations in Digital μfluidics



2. Cut & Merge (Split & Mixing)

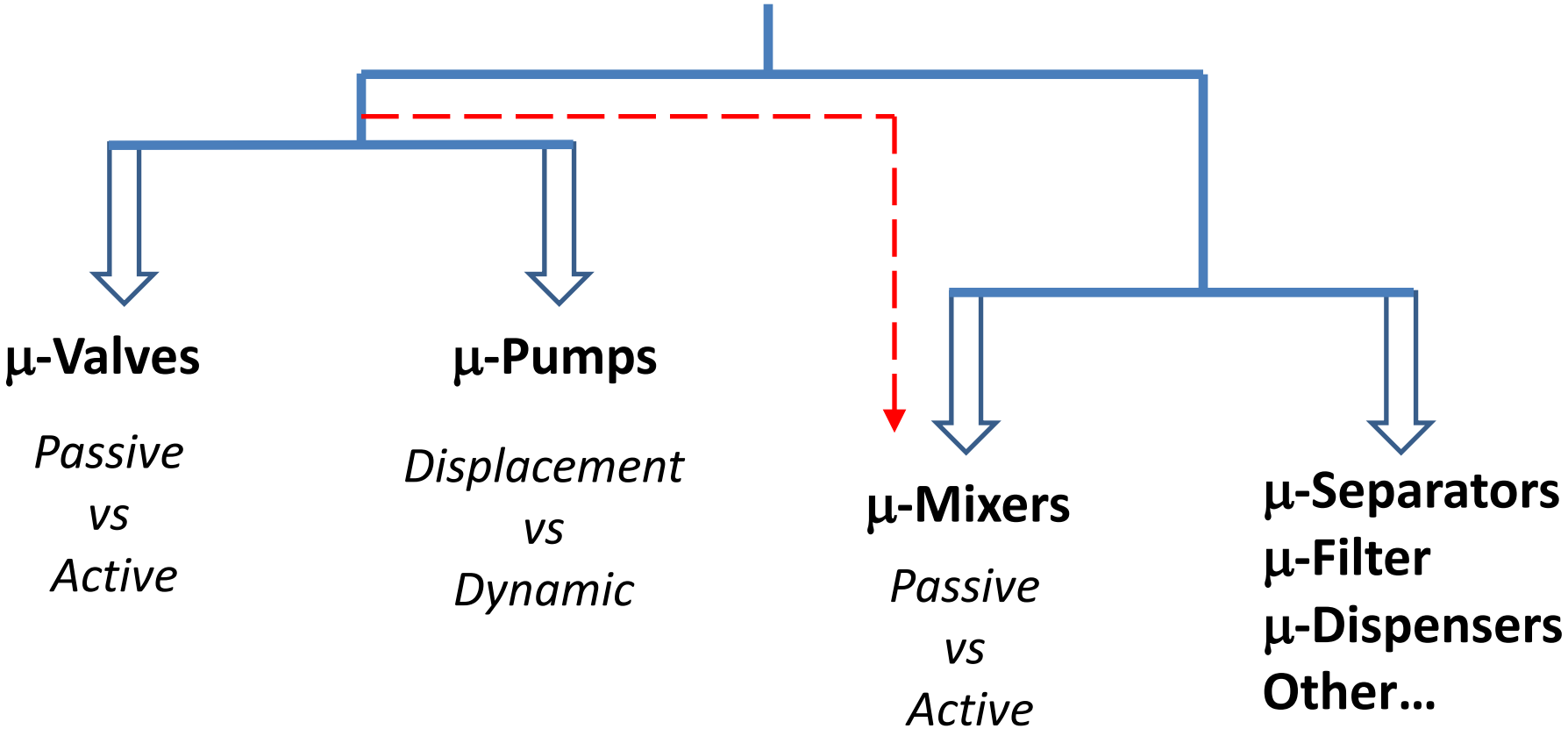


1. Droplet formation/injection



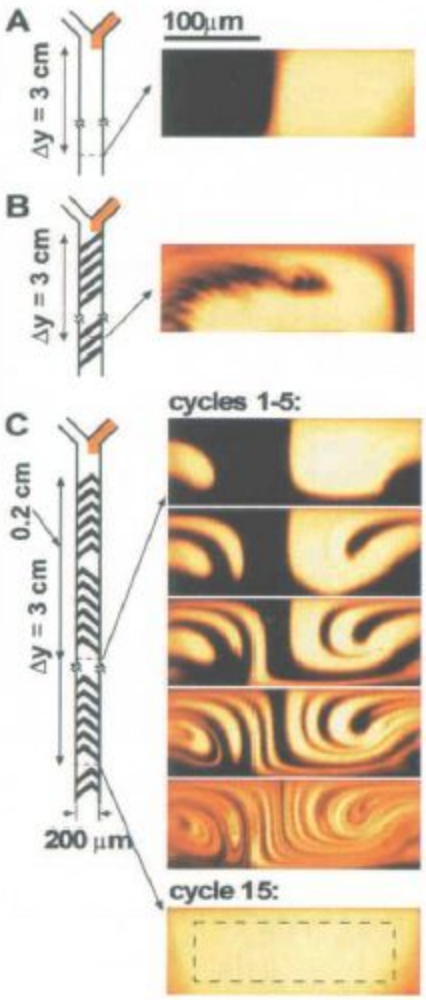
Microfluidic Components

Used to manipulate
(transport, mix, separate, etc) fluids



The Herringbone Mixer

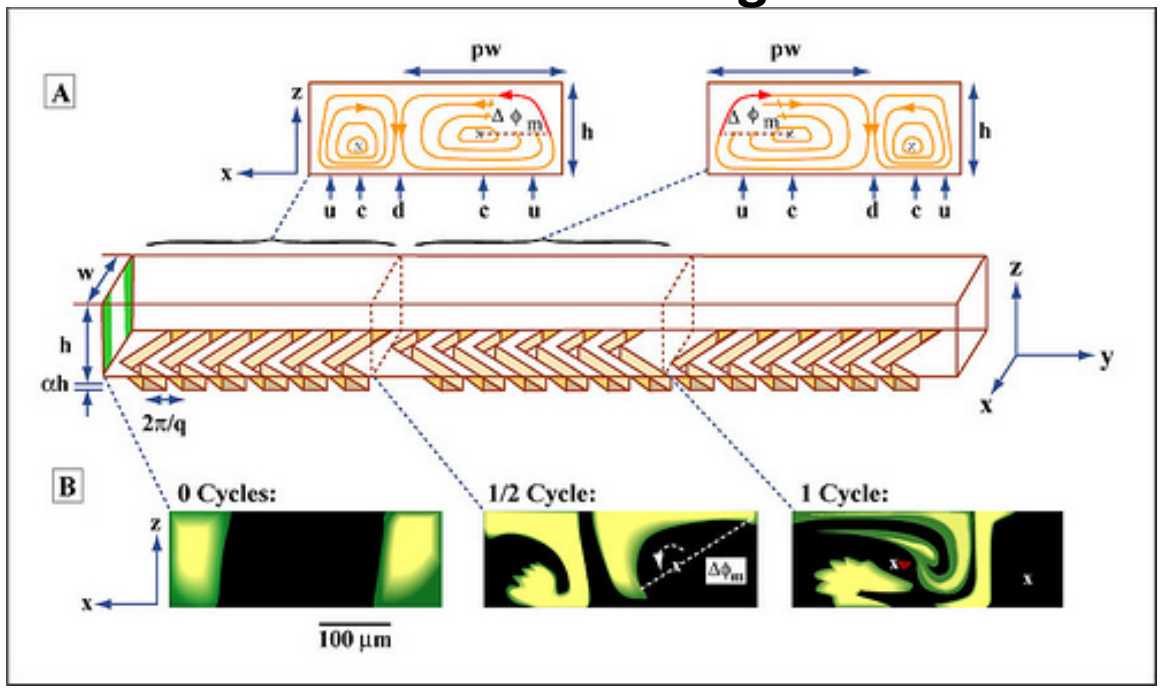
2-Flow Mixing



Concept:

Use set of ridges to create transverse vortices, (parallel to the cross section of the channel

3-Flow Mixing

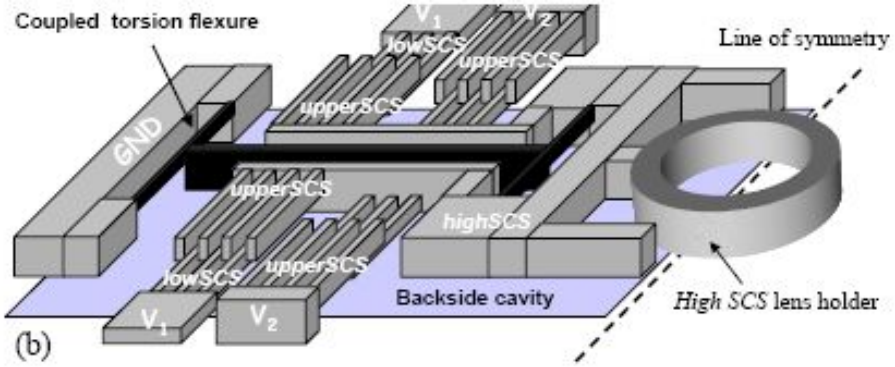


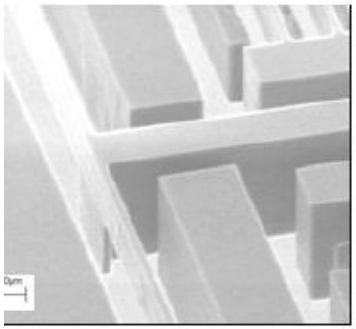
- Channel Width = 200 μm, Channel Height = 70 μm ,Ridge Depth = 40 μm, Ridge Width ridge = 200 μm
- Mixing length 1-3 cm, Re ~ 10^{-2}

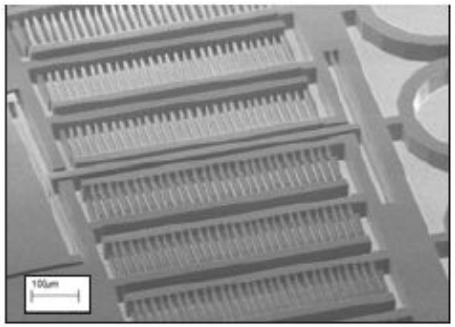
Integration. μ–lenses on μ–Actuators

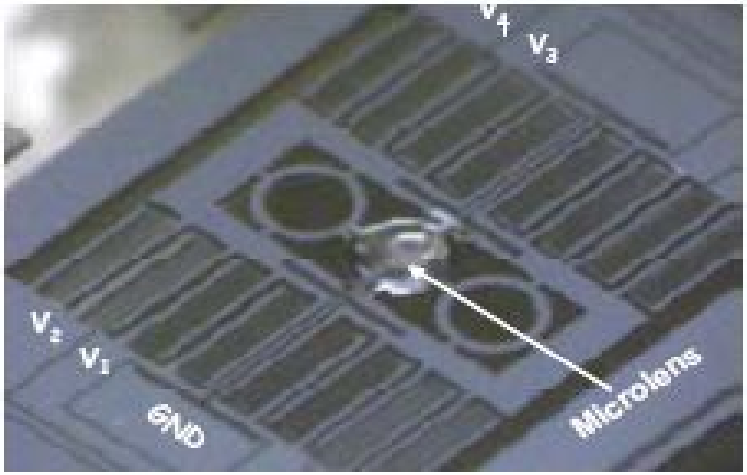
Concept

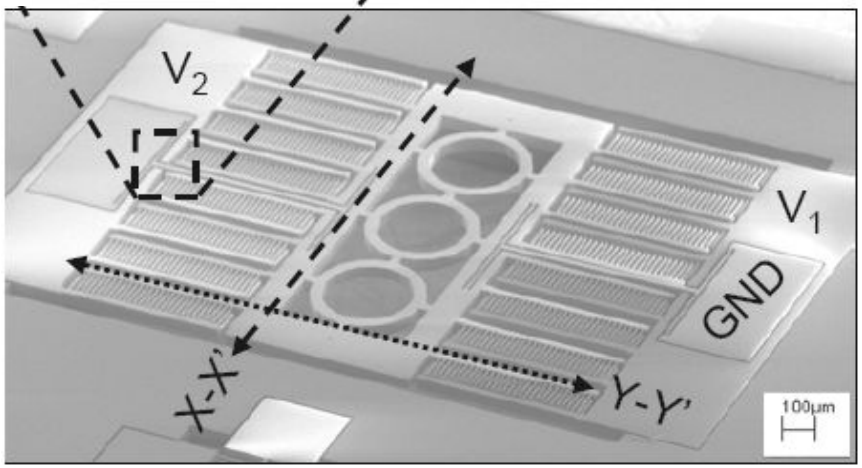
Integrate electrostatic μ-actuators with μ-lenses (e.g. for scanning…)





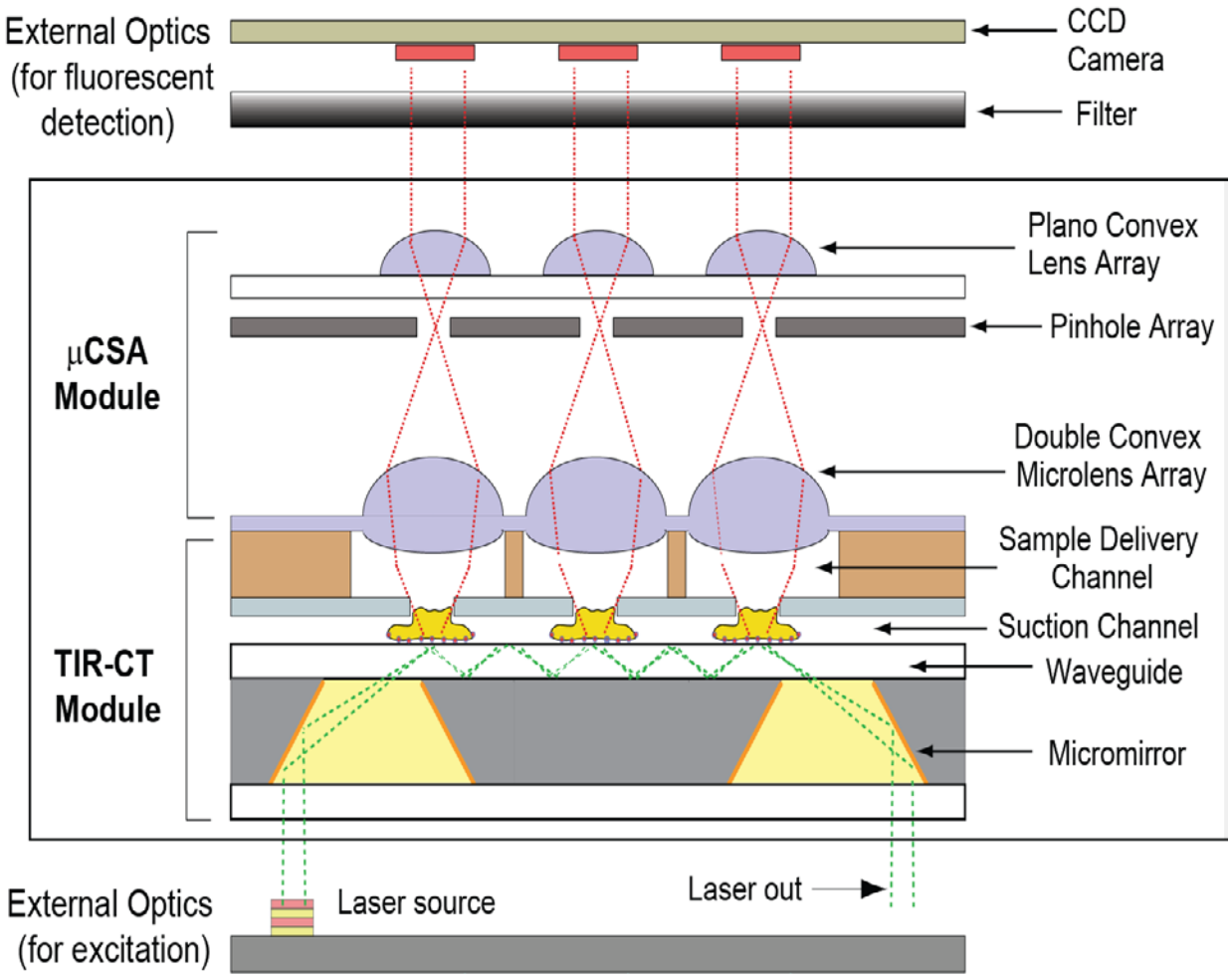






- *μ-lenses are simply dispensed on the actuator ring and UV cured…*
- *Electrostatic actuators (comb drives) are used as they require minimum power*

Integration. Optical Detection and Excitation on-chip



The biochip integrates two modules:

- the **TIR-CT module** for Isolating, Trapping and Illuminating single WBCs
- the **μCSA module** for imaging/counting the trapped WBCs

Some other exciting stories…

1. Single Molecule Real Time (SMRT) Sequencing

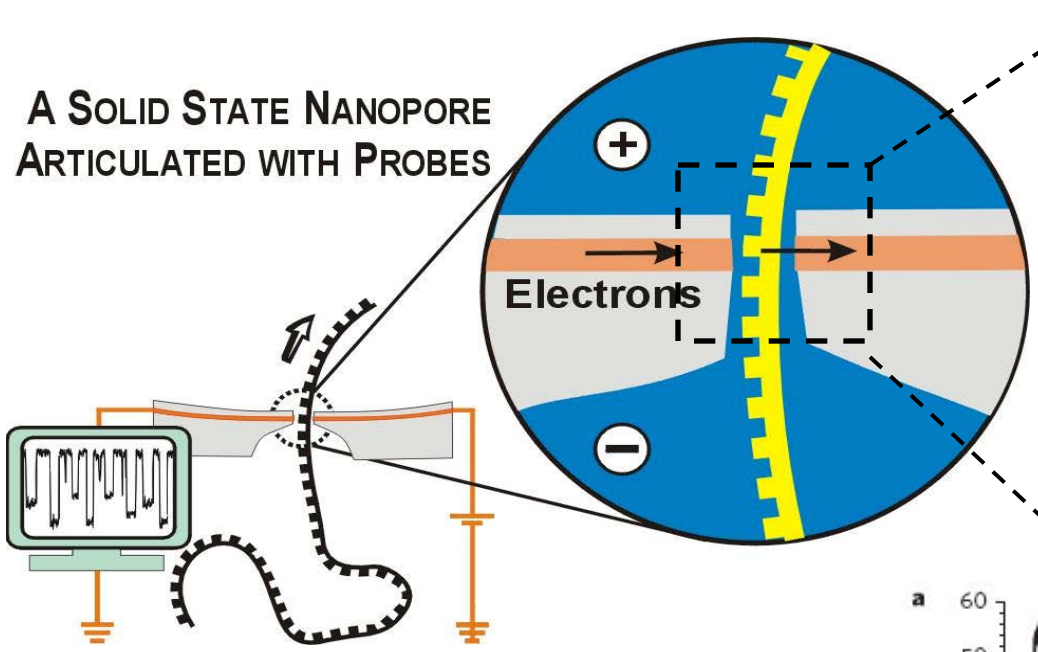
Motivation: The $1,000 Genome Project

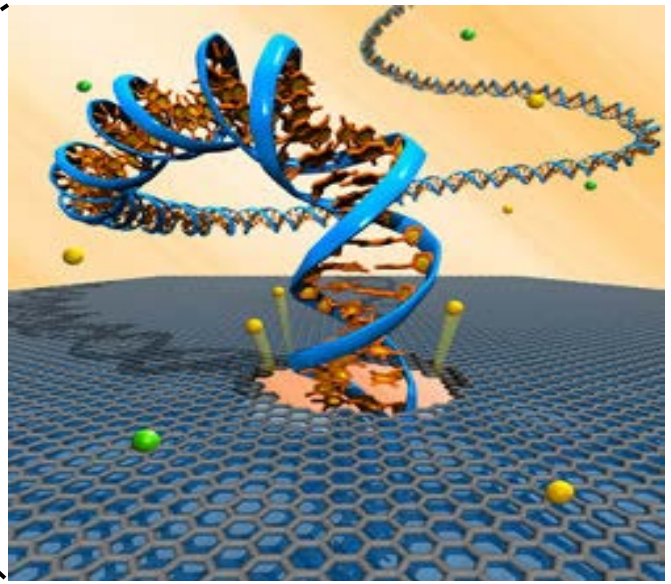
What if you could sequence the entire human genome in a single day, in a single experiment — for less than $1,000?

Nanopores for DNA SMRT Sequencing

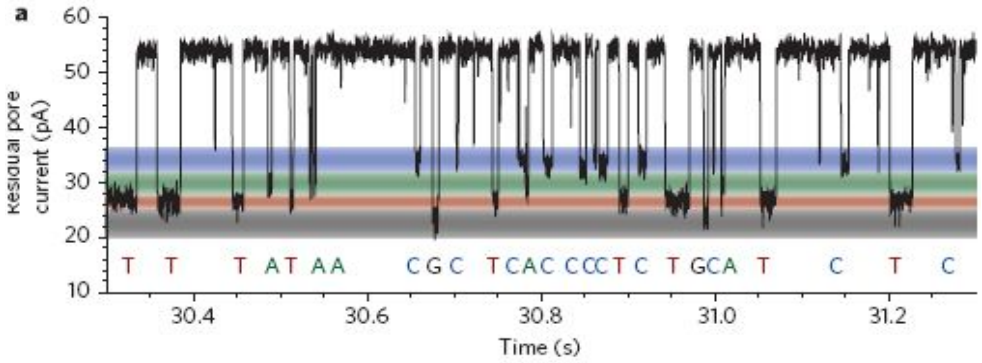
Concept

Flow DNA through a (~1nm) nanopore and measure the electric current



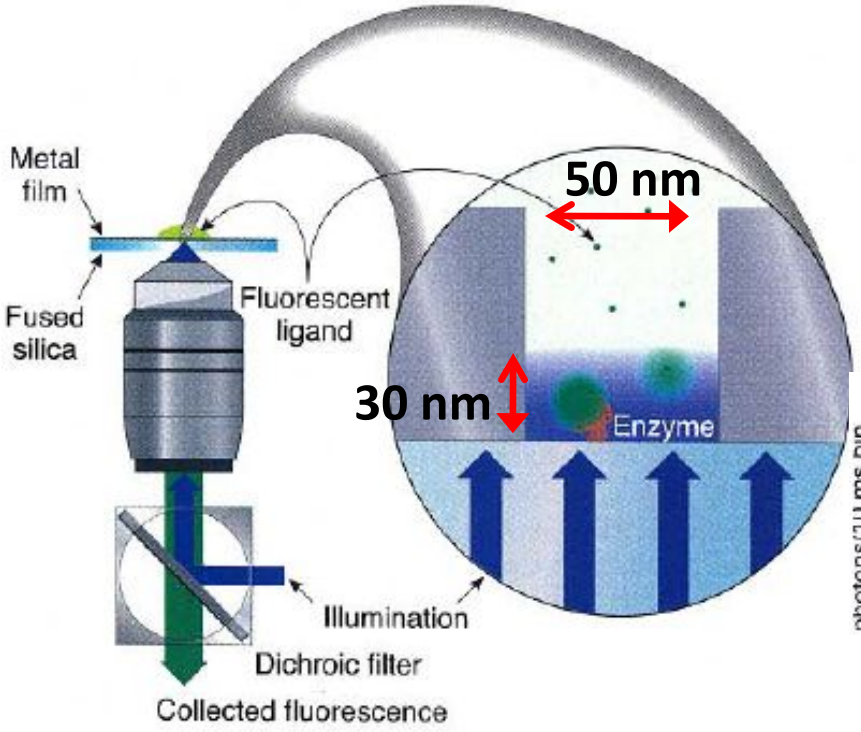


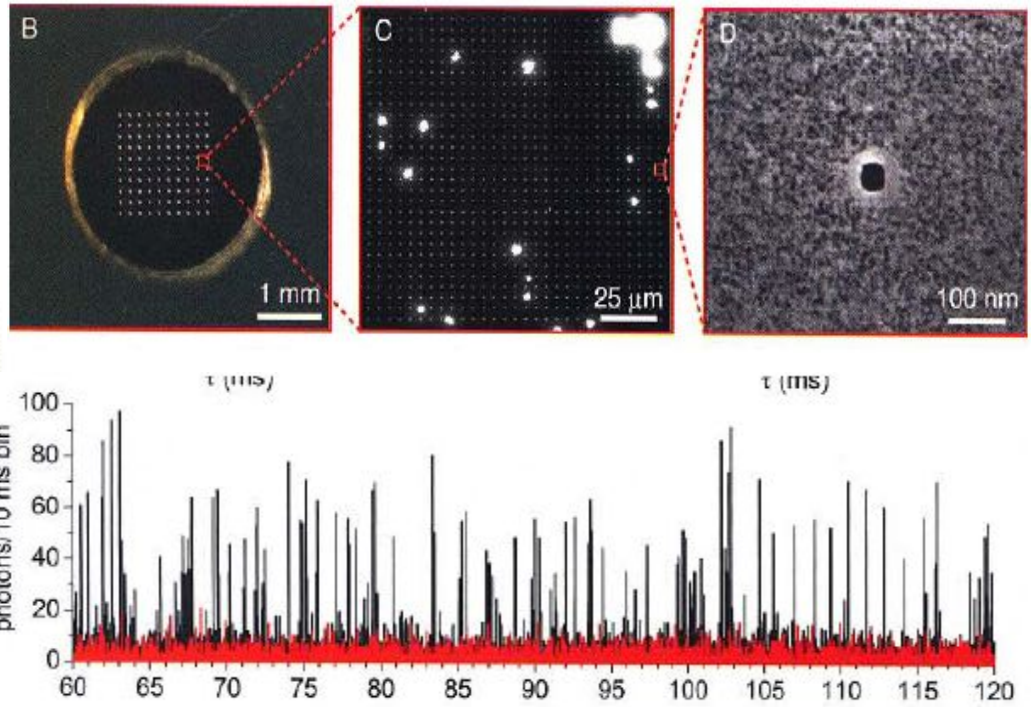
…The amount of current which can pass through the nanopore at any given moment depends on whether the nanopore is blocked by an A, a C, a G or a T



Currently under development by several companies (Oxford Nanopore Technologies, Noblegen)

Zero-mode Waveguides for DNA SMRT Sequencing





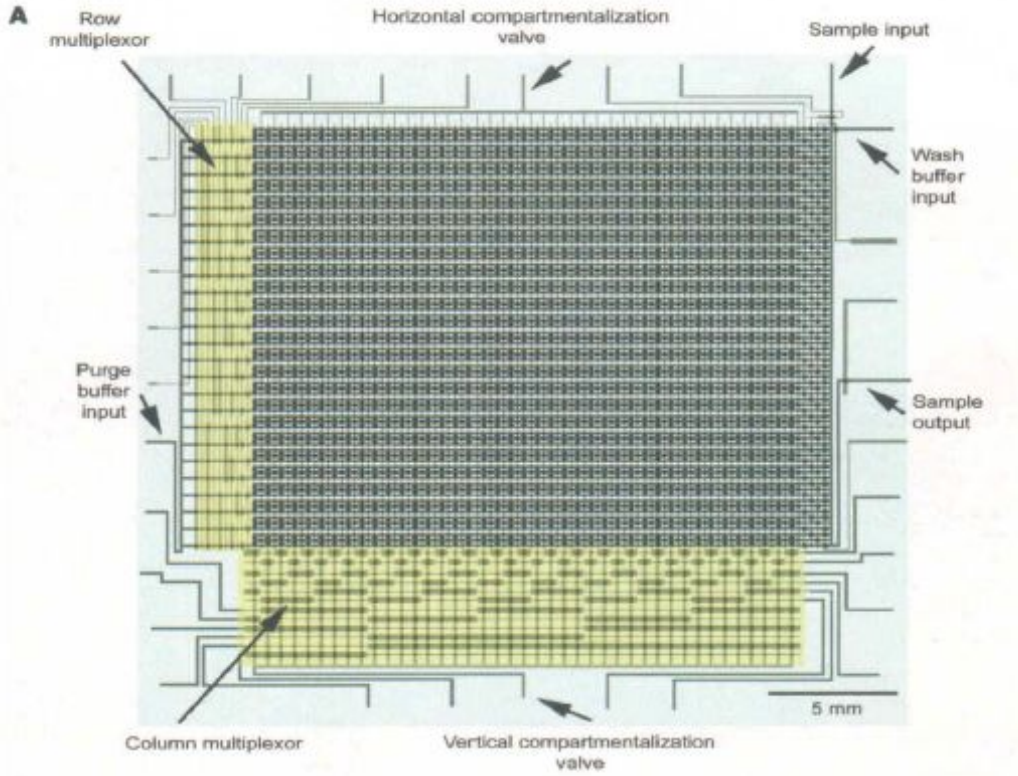
Zero-mode waveguides (ZMW) guides light into a volume that is small in all dimensions compared to the wavelength of the light:

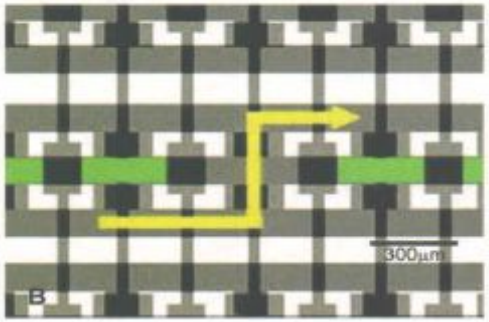
→ **Minimize background noise** → **Single Molecule Imaging**

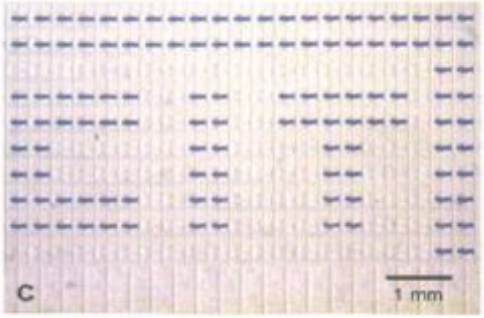
Under development by Pacific Biosciences

2. Large Scale Microfluidic Handling

Large-Scale Integration of μ-valves



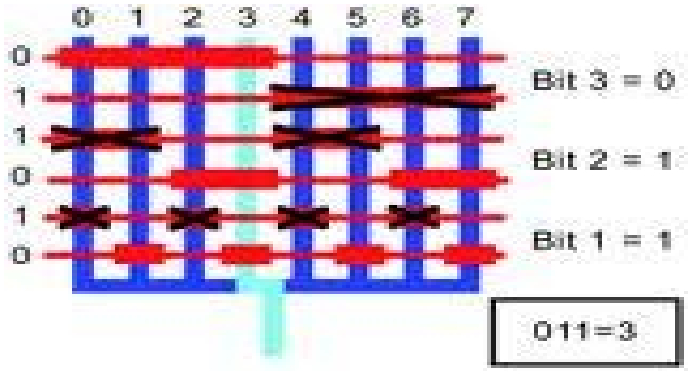




SPECS

- 3574 on-chip μ-valves
- 22 outside control interconnects
- 1,000 individually addressable picoliter reaction chambers
- A column and row multiplexor are used to address each chamber

The microfluidic Multiplexor



Reference: 'Microfluidic Large-Scale Integration', Science, 2002, Vol. 298 no. 5593 pp. 580-584

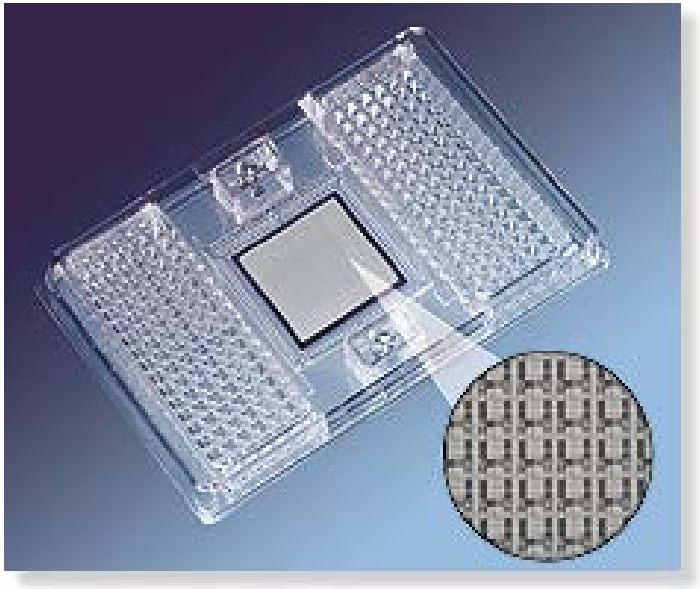
Fluidigm Dynamic Array
Integrated Fluidic Circuits (IFCs)

On-chip High-throughput Polymerase Chain Reaction (PCR)

Fluidigm chips have an on-chip network of microfluidic channels, chambers, and valves that automatically assemble up to 2,304 unique PCR reactions , decreasing the number of pipetting steps required by up to 100 fold.

Applications

- Gene Expression
- SNP Genotyping
- Targeted Resequencing
- Single-Cell Gene Expression
- Protein Crystallization
- …

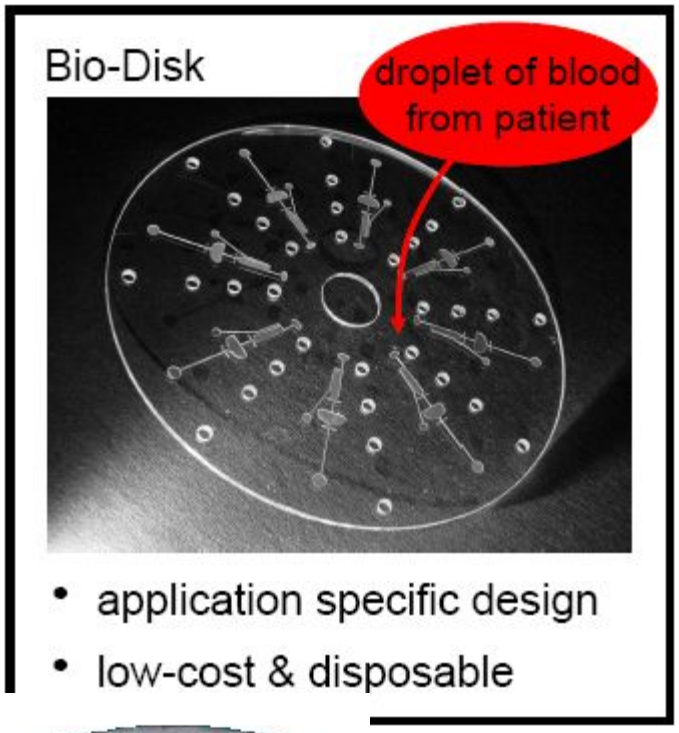


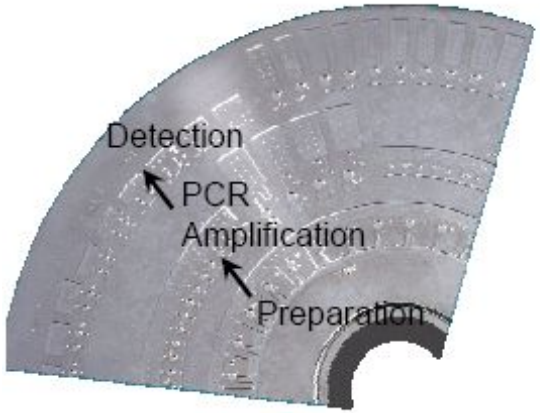
Watch Videos at: http://www.fluidigm.com/biomark-videos.html

3. Centrifugal Microfluidics

Commercialized by GYROS:
http://www.gyros.com/en/company/about_gyros/index.html

The GYROS BioDisk





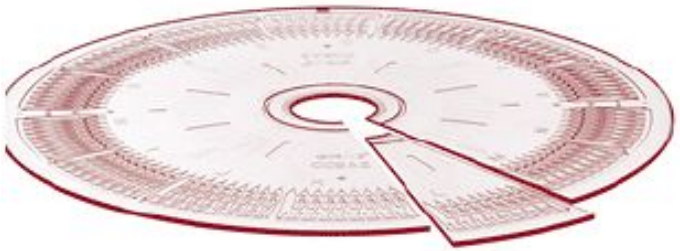
Key Idea:

Use hydrophobic Patches to block fluid flow. Use Centrifugal Forces to overcome these pads

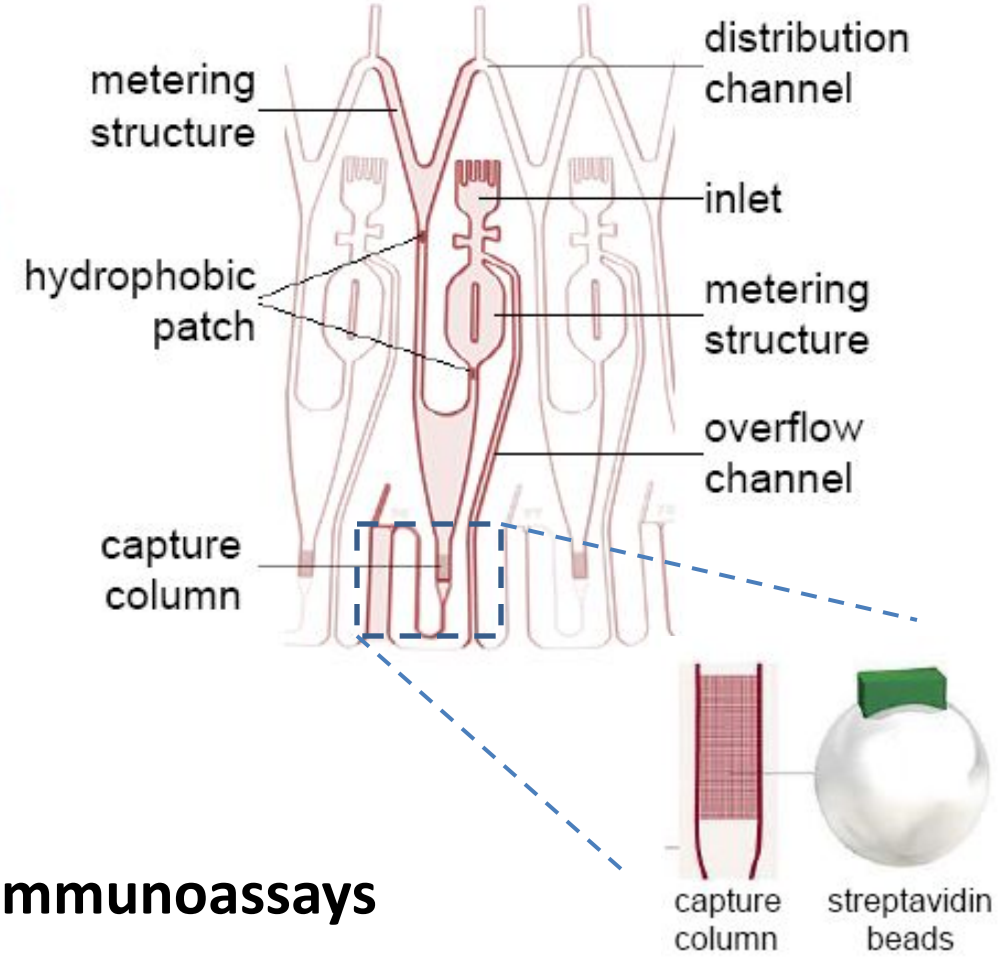
Watch movie: www.gyros.com/en/products/gyrolab_bioaffy_cds/gyrolab_bioaffy_cds/index.html

GYROS for Protein Quantification

CD for protein quantification

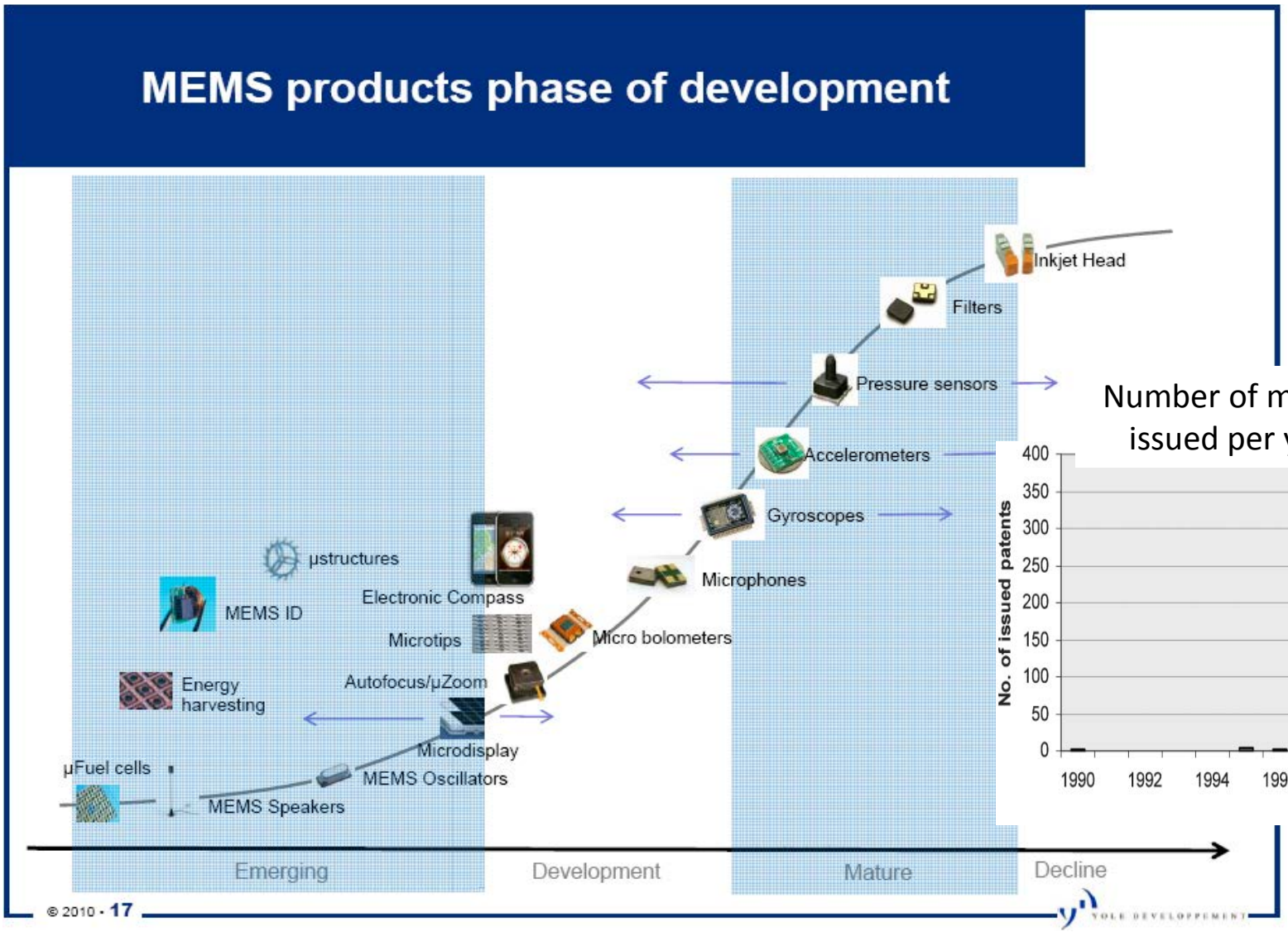


- 112 parallel measuring structures per CD
- 200 nL of sample and reagent per measurement
- time-to-result < 1h



<u>Applications</u>: Point-of-Care Immunoassays

BioMEMS: The future is Bright!



Number of microfluidic patents issued per year (in the USA)

Hope you got Inspired!

…And please do not forget to evaluate the class…