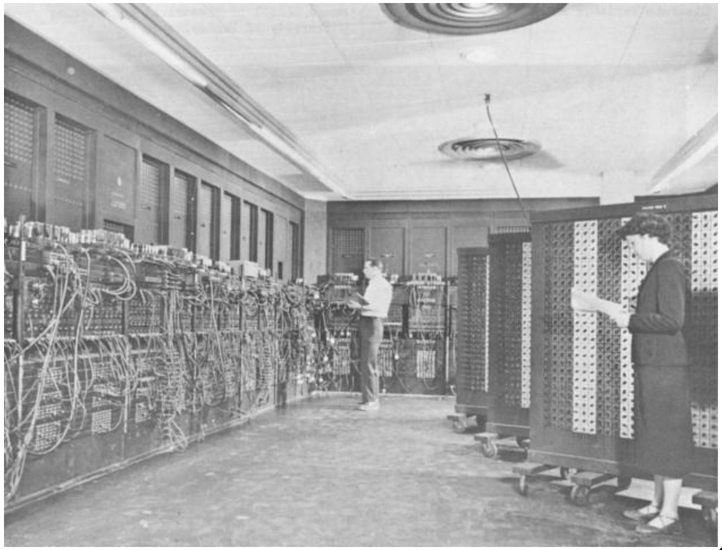
Miniaturization in Electronic Technology



ENIAC: the "Electronic Numerical Integrator and Calculator“, 1943

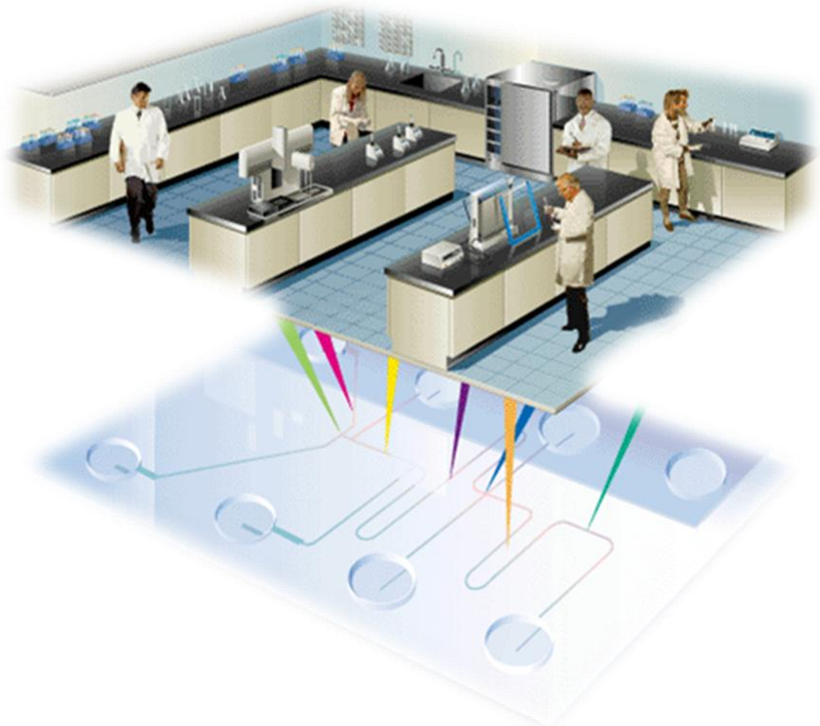
ENIAC filled a 20 by 40 feet room, weighed 30 tons, and used more than 18,000 vacuum tubes.

iPhone 6

A8 Chip, 2014
$>10^9$ transistor

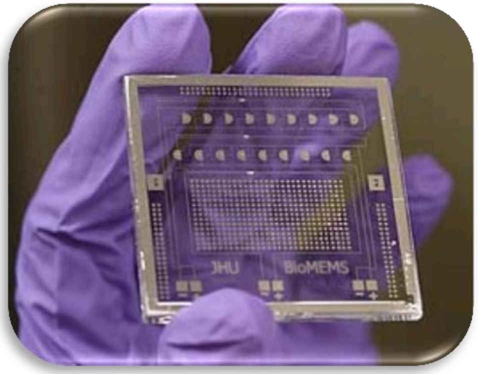
Why Being Small ?

- Savings in time & cost
  - Less materials and samples
  - Short processing time
- Disposable
- Parallel processing
- Integration/Automation



- Gain from the unique microscopic features
  - Laminar Flow
  - High surface to volume ratio

    High single-to-noise ratio in transuding signals
  - Small thermal mass
  - Strong fields such as electric fields

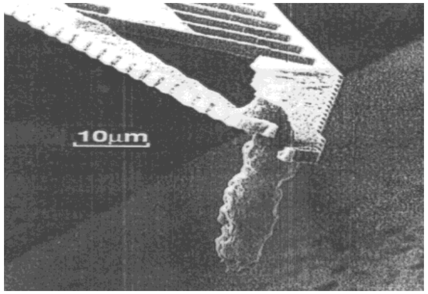


Why Being Small ?

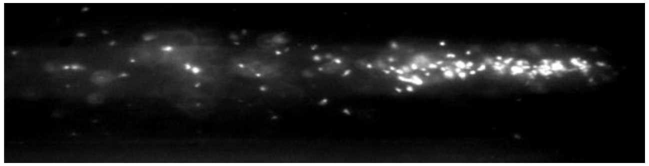
❖ **Length Scale Matching**

- **Manipulation of molecules and cells**
- **High resolution / sensitivity**

e.g. to facilitate single-molecule diagnostics, study of single-cell biology

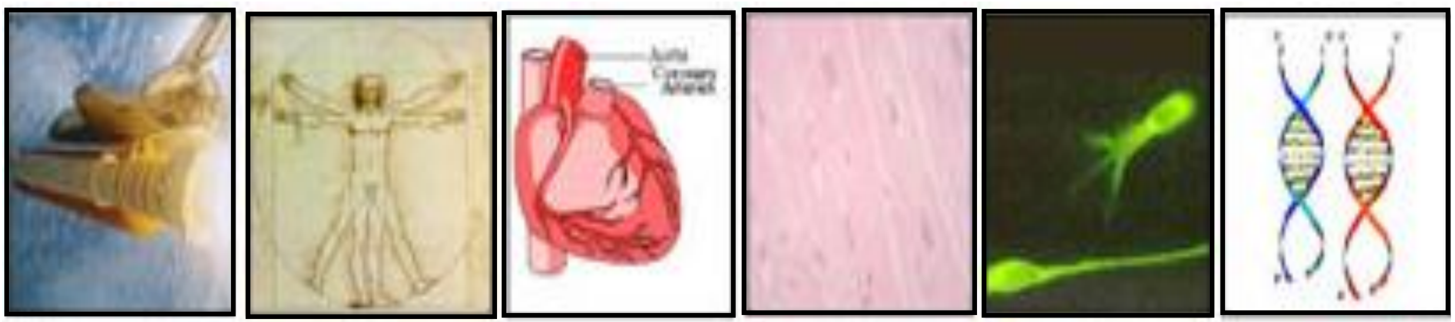


(Kim)



(Wang)

>100 m **1 m** **10^{-2} m** **10^{-6} m** **10^{-9} m**



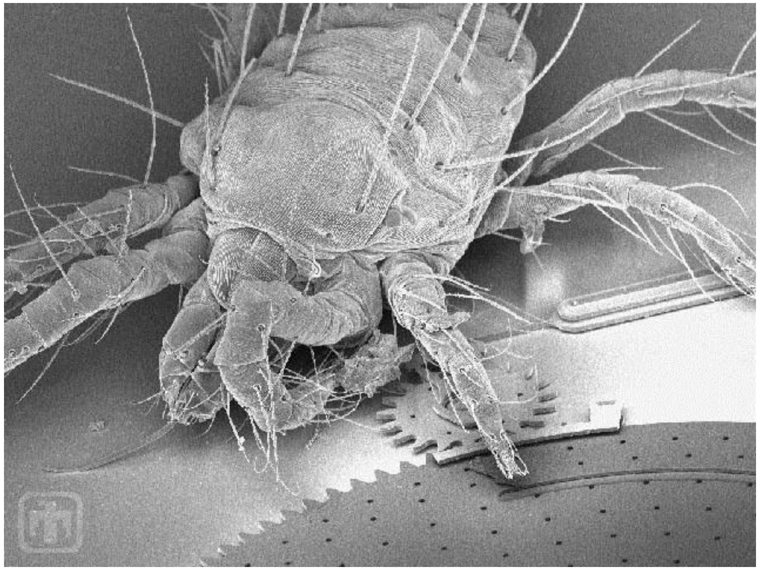
Spacecraft **Human** **Organ** **Tissue** **Cell** **DNA**

Micro/Nano Technology

Classes of BioMEMS (Bio-MicroElectroMechanicalSystem)

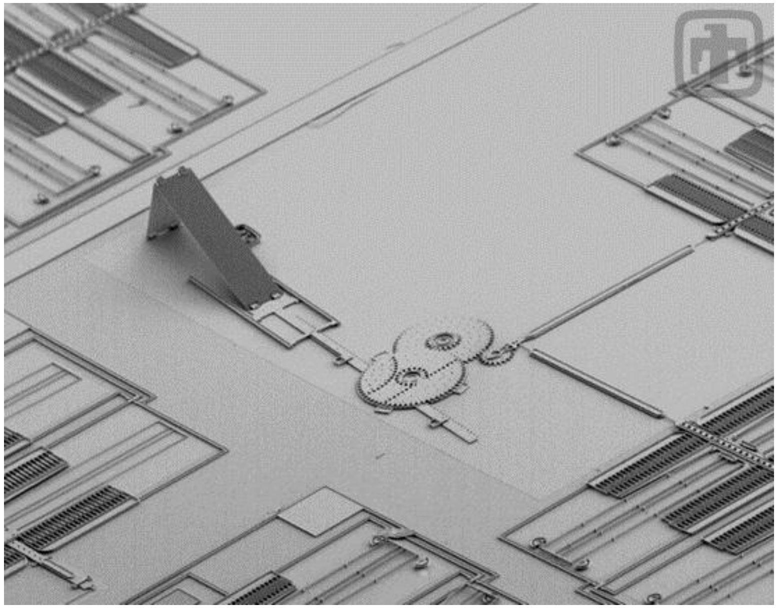
- Microfluidics & Microfluidic Devices
- Biosensors and Bioelectronics
- Neural Interface Devices
- Chromatography /Electrophoresis Devices
- Microsurgical Tools
- Bioreactors
- Tissue Engineering Devices
- Molecule /Cell Handling Devices
- Implantable Devices, Drug Delivery Devices

Examples of MEMS Devices



Spider mite on gears

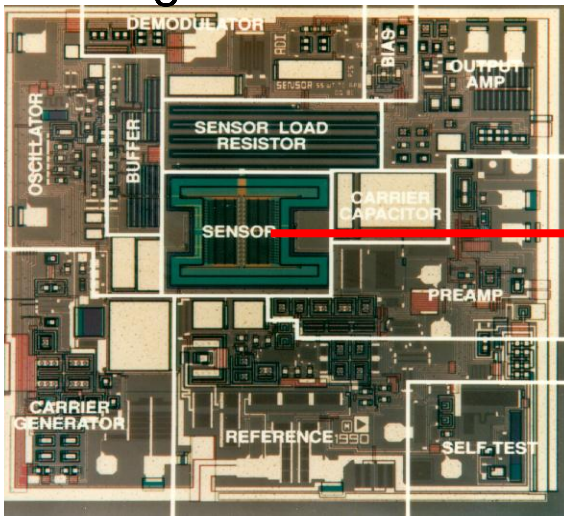
Micro-mirrors

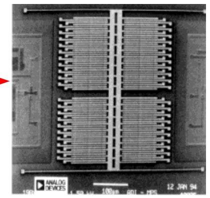


(Sandia)

Examples of Industrial MEMS Devices

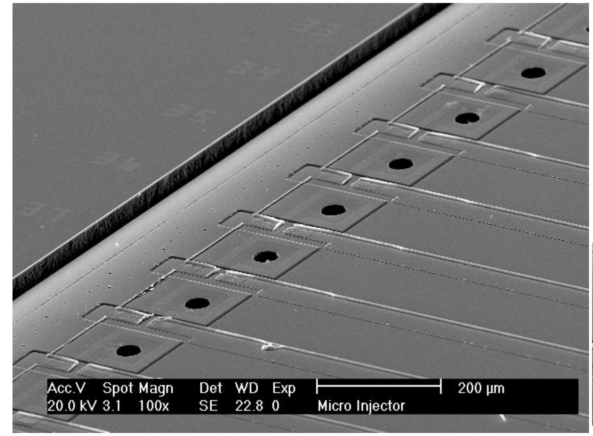
Air Bag Sensor

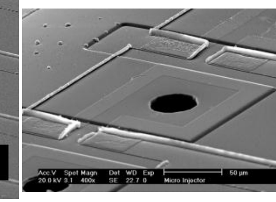




(Analog Device)

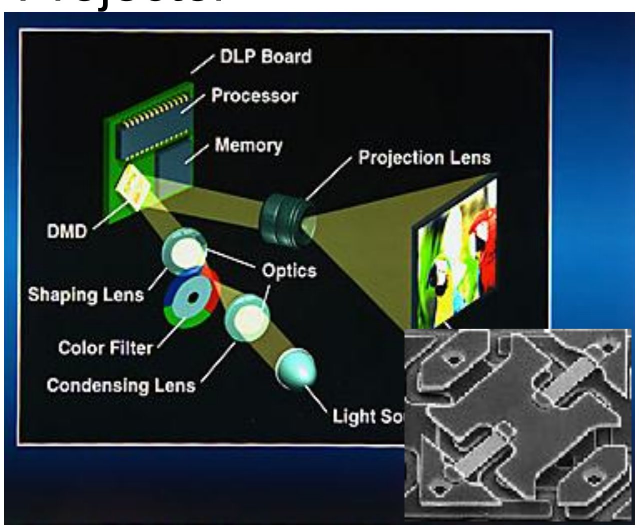
Bubble Inkjet





(HP)

Projector

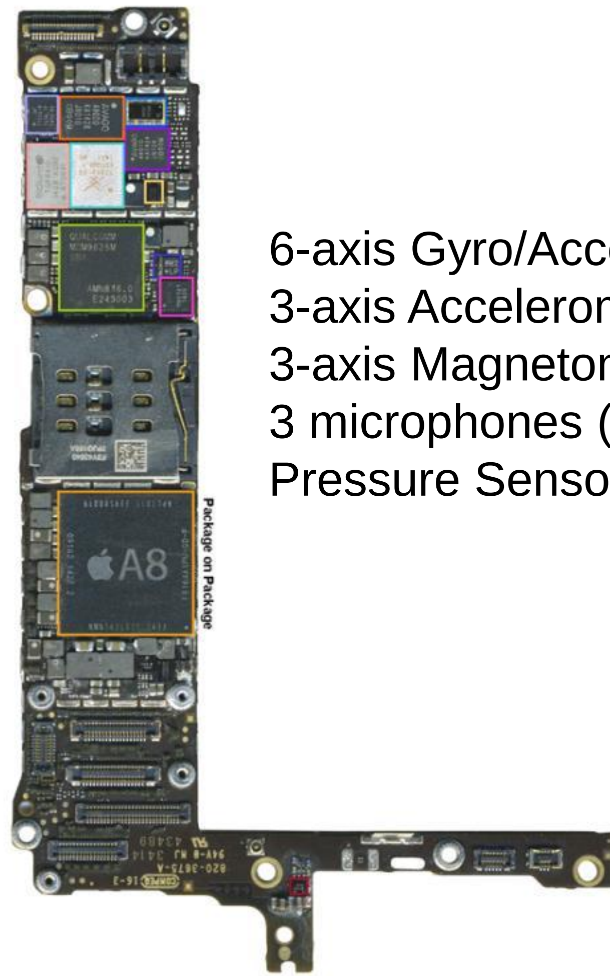


(Texas Instruments)

Motion & Orientation sensor (Wii)

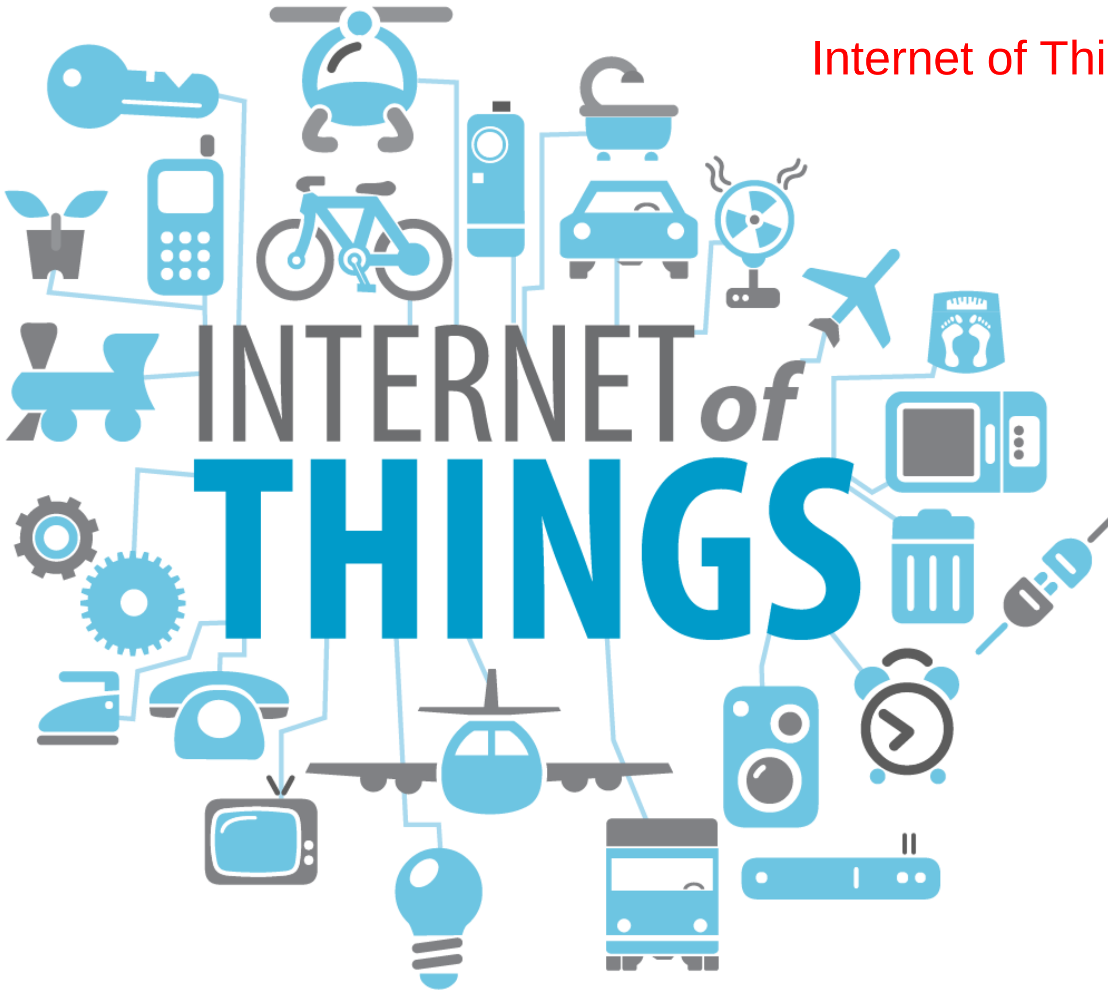
(Nintendo)

Apple iPhone 6



6-axis Gyro/Accel (Invensense)
3-axis Accelerometer(Bosch)
3-axis Magnetometer (AKM)
3 microphones (Knowles)
Pressure Sensors (Bosch)

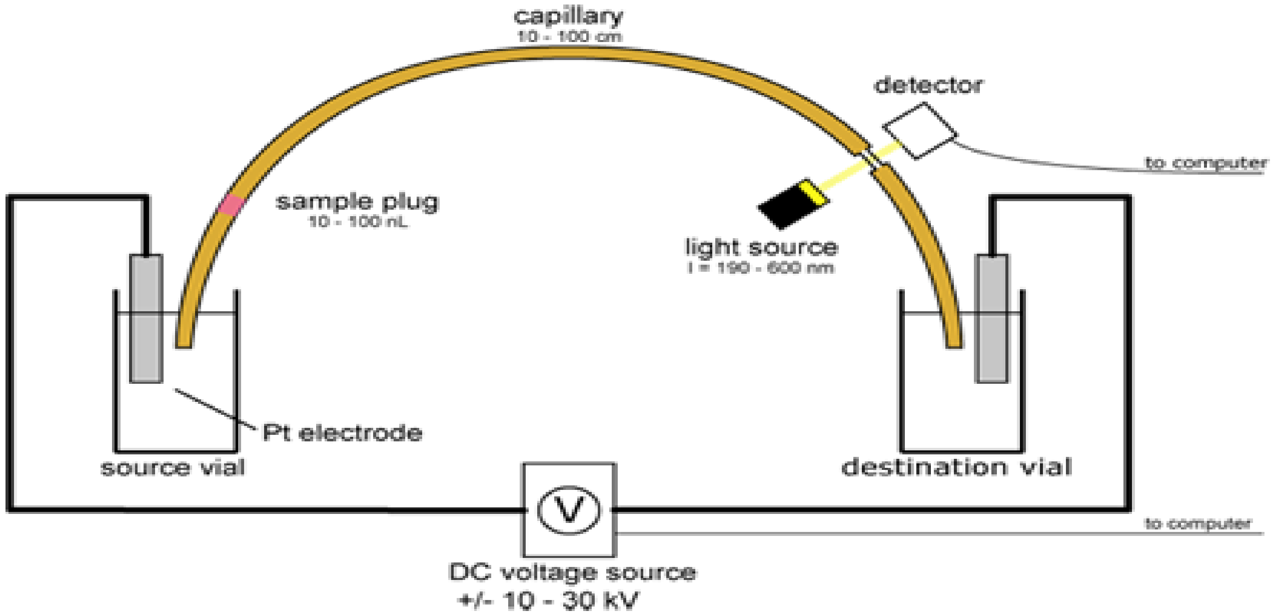
MEMS Is Everywhere in Your Daily Life

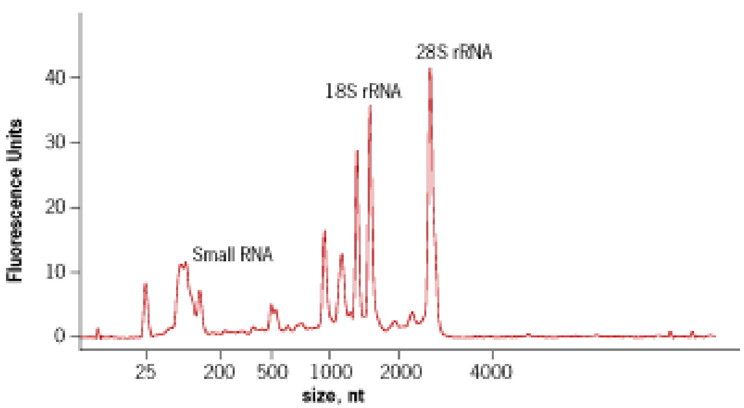


Internet of Things (IoT)

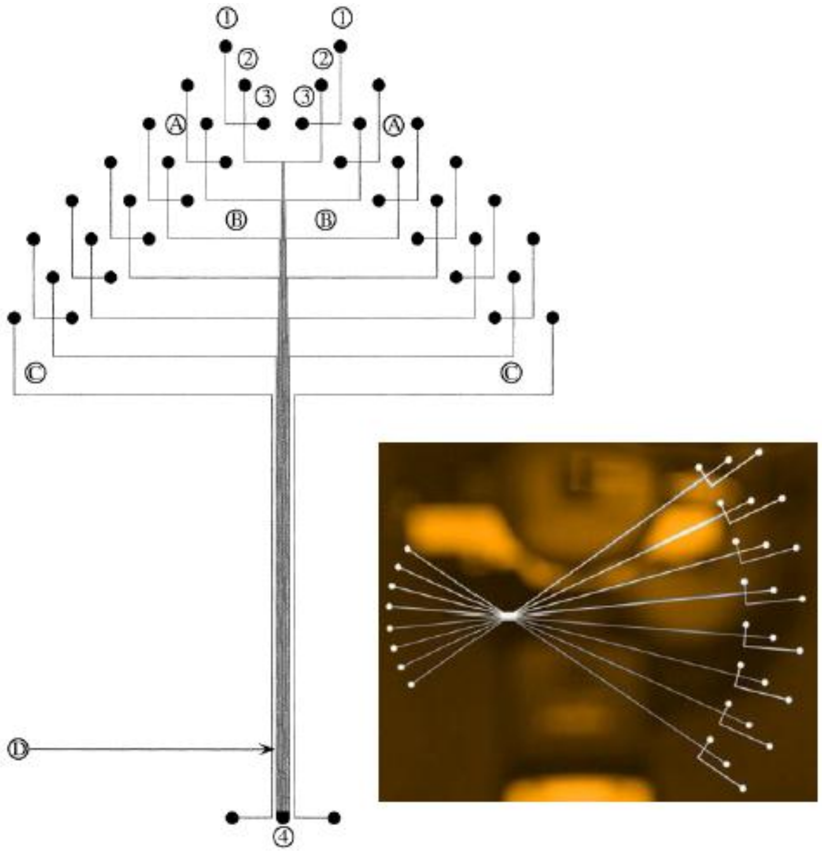
Trillions of MEMS sensors coming soon !

Capillary Electrophoresis

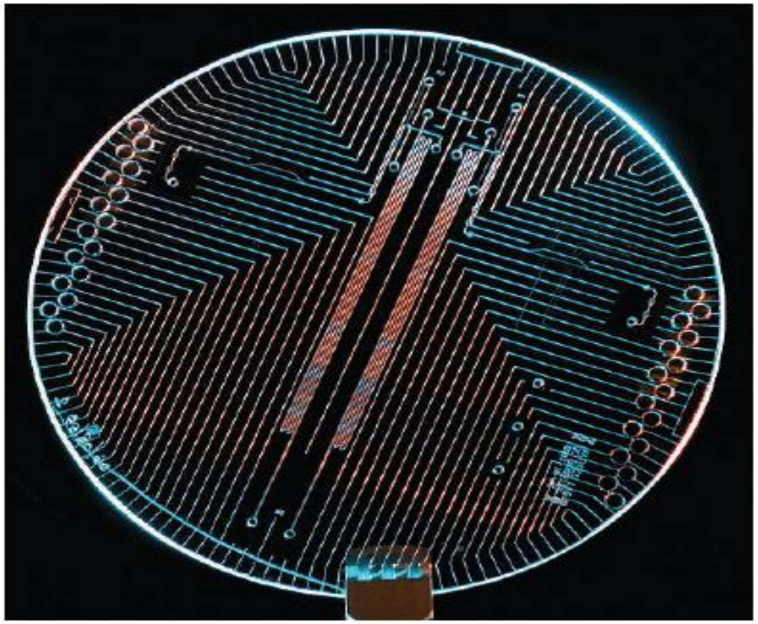




Micromachined Capillary Electrophoresis (μ-CE)



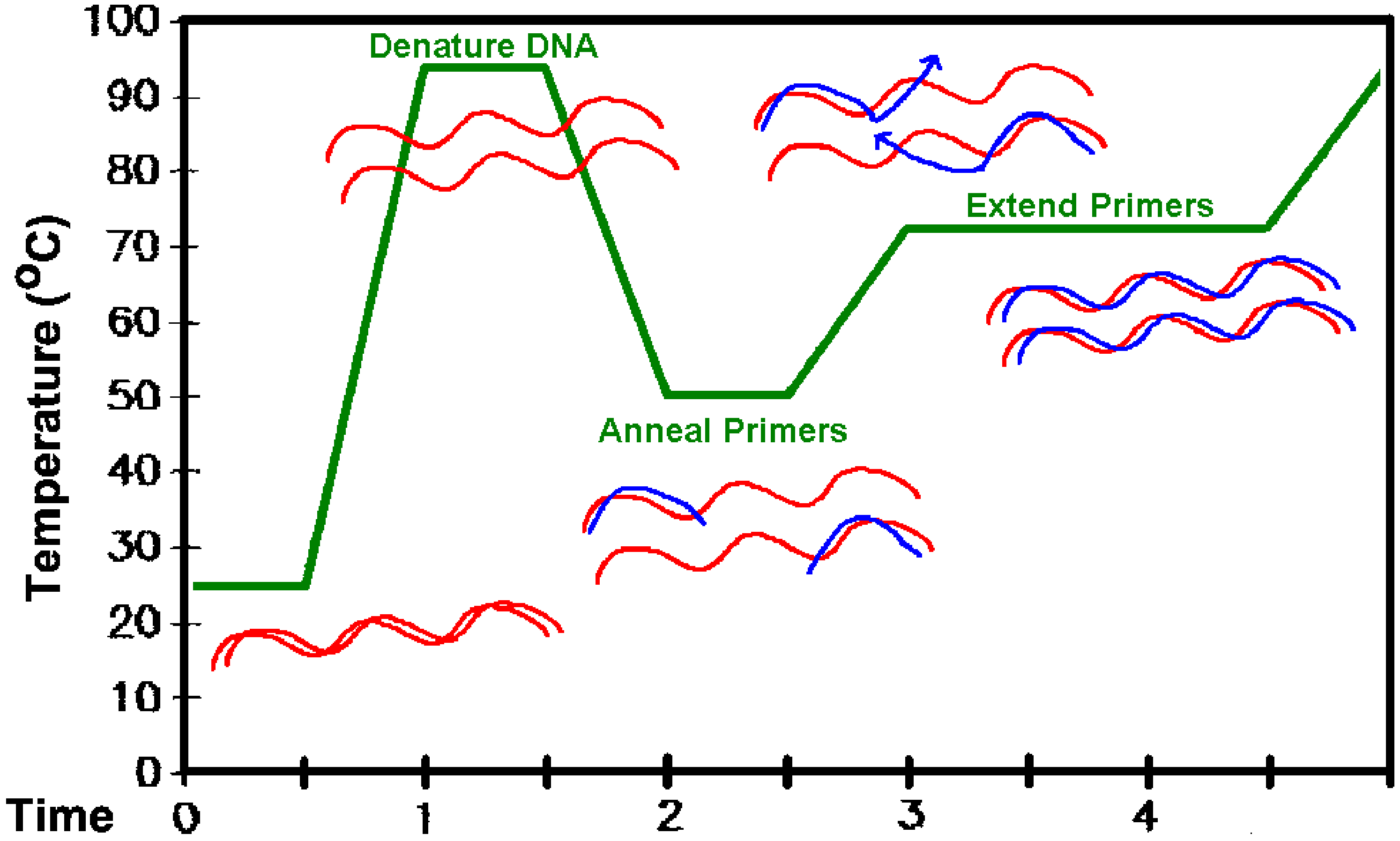
- High throughput
- Low volume
- Rapid analysis



- **Integrated with thermal cycling and CE for Sanger sequencing**
- **Off-chip optical detection**

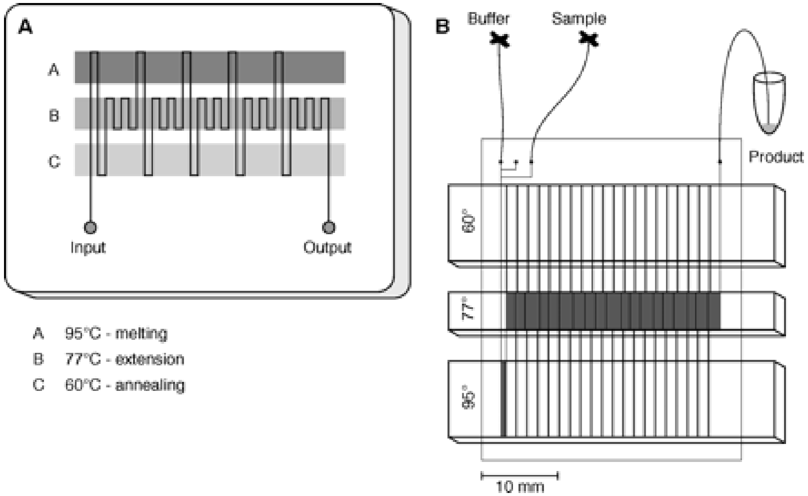
(Ra Mathies, PNAS 2006)

Thermal Cycling for Polymerase Chain Reaction (PCR)

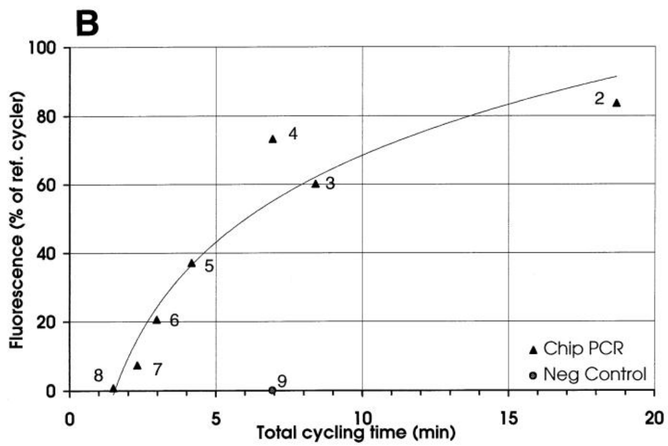


PCR is an expensive and time-consuming technique

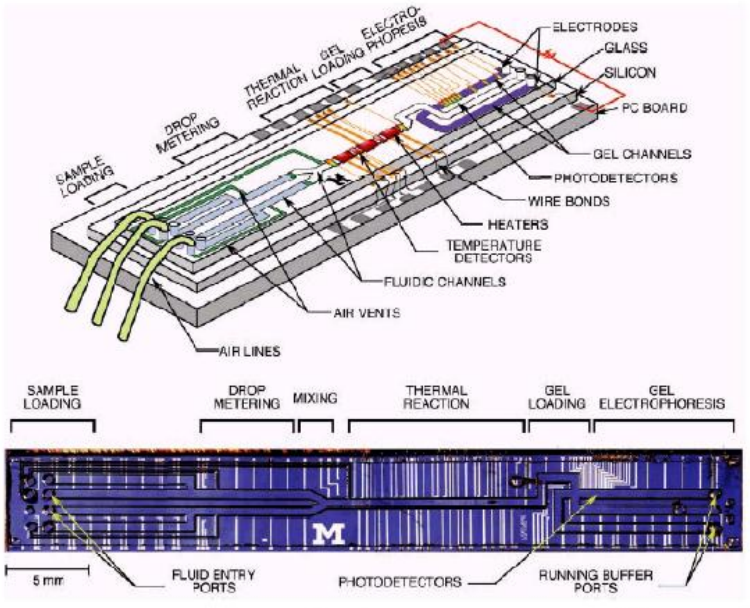
Continuous-flow Micro PCR



(A. Manz, Science 2002)



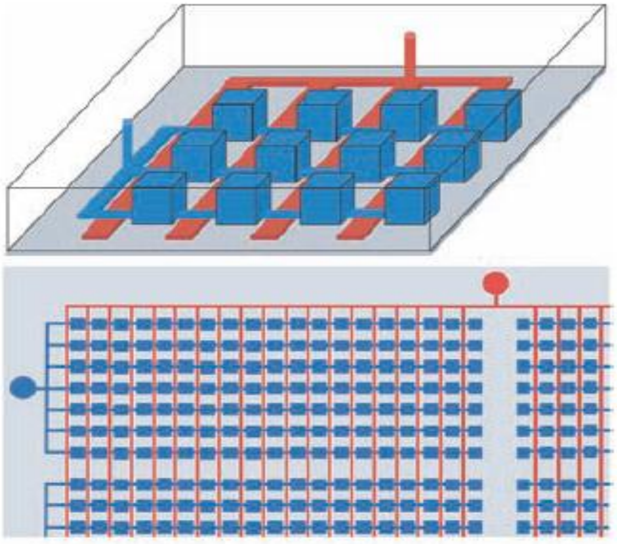
Integration of CE and μ-PCR

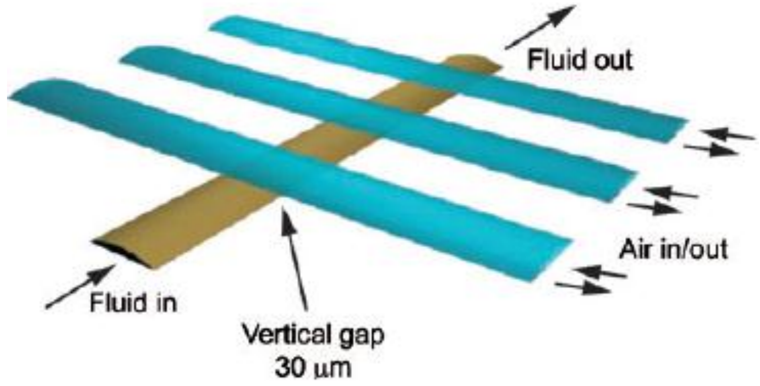


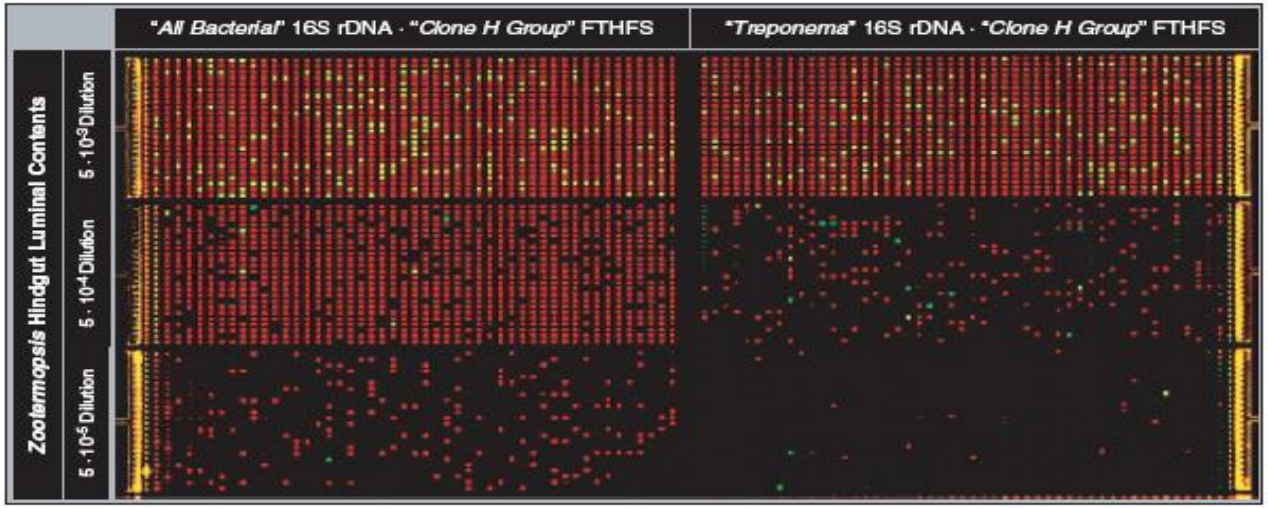
(M.A. Burns U Mich, Science

- PCR reaction
- Gel electrophoresis
- Microfluidics
- On-line electrical detector

Microfluidic Digital PCR : Nanoliter-sized PCR arrays



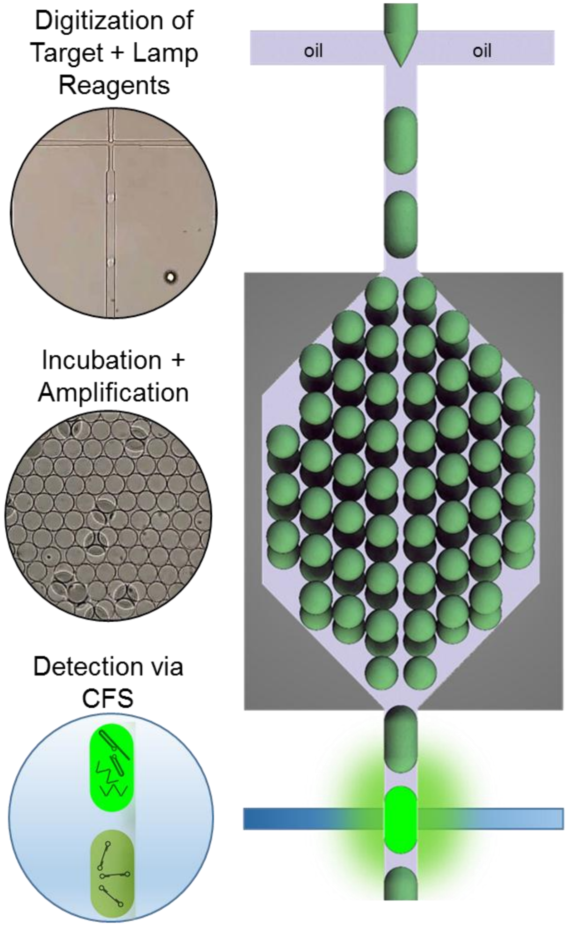


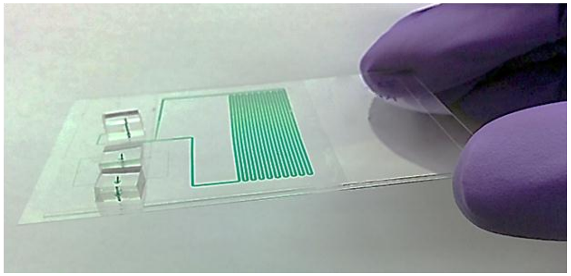


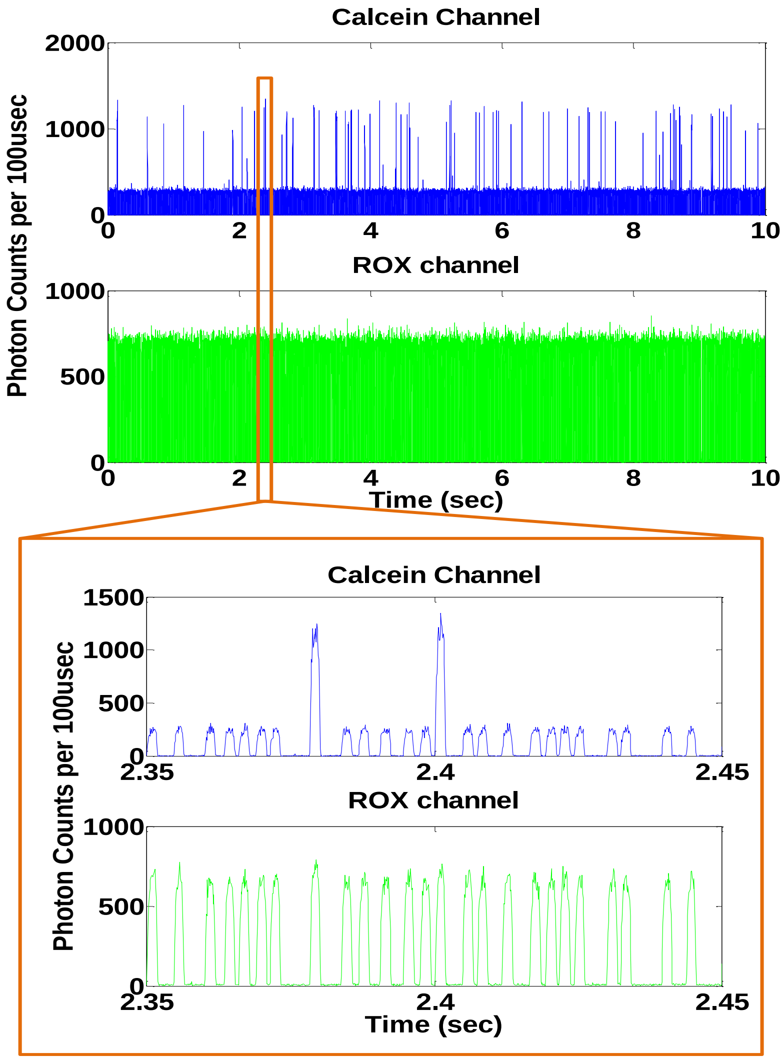
- 1176 chamber
- 6.25 nL each chamber

(J.R. Leadbetter, Science 2006)

Droplet Digital PCR: Picoliter-sized PCR arrays





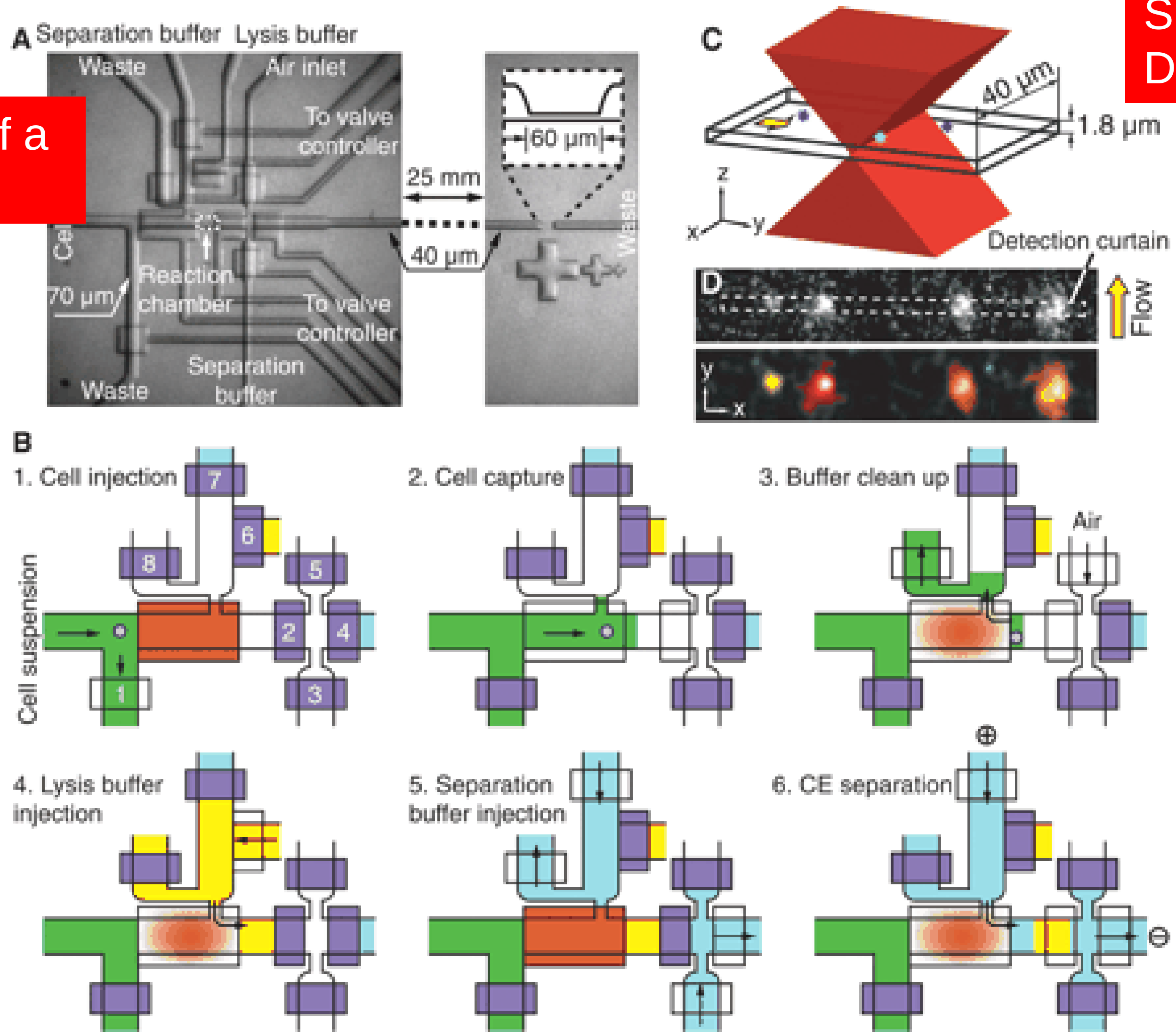


(T. Rane, Lab Chip, 2015)

Analysis of Single Cells

Single-Molecule Detection

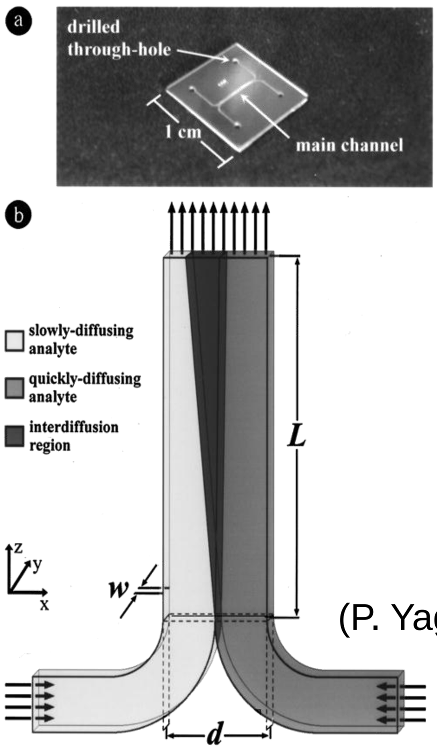
Preparation of a single cell



(R. Zare, Scinece 2006)

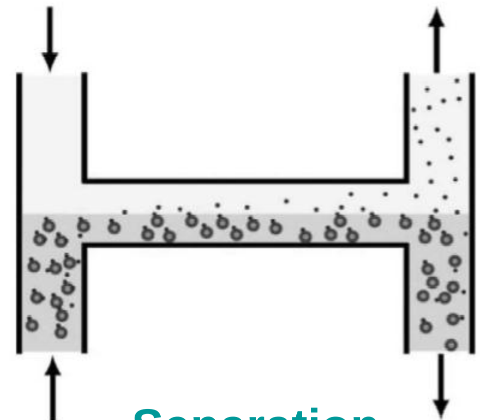
Laminar Flow-Based Assay

T-Sensor

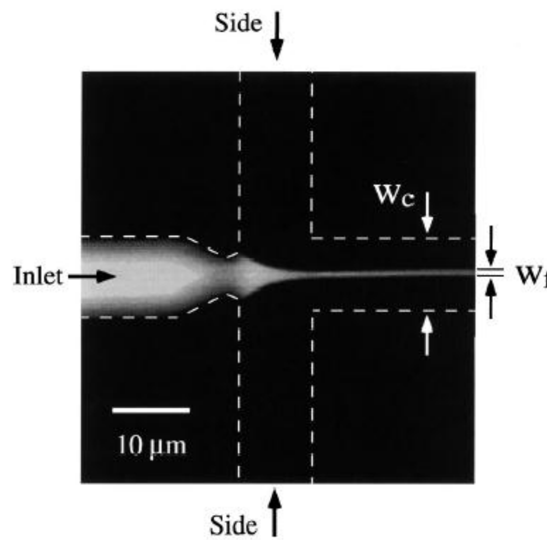


(P. Yager)

- Laminar flow – initiate reaction
- Diffusion-based analysis

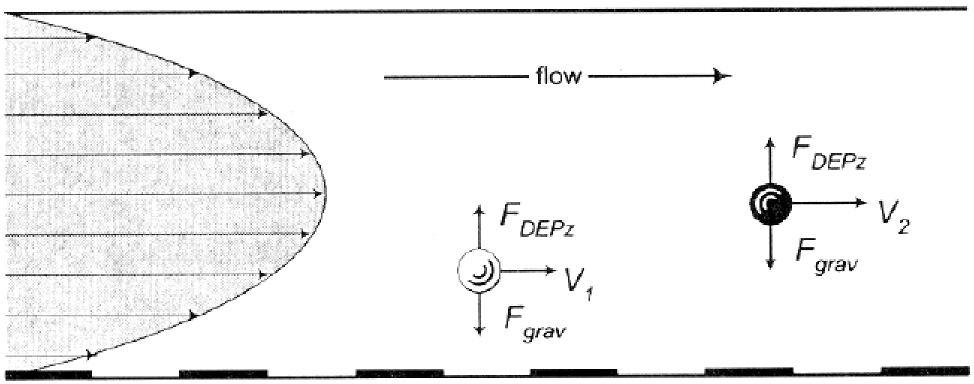


Separation

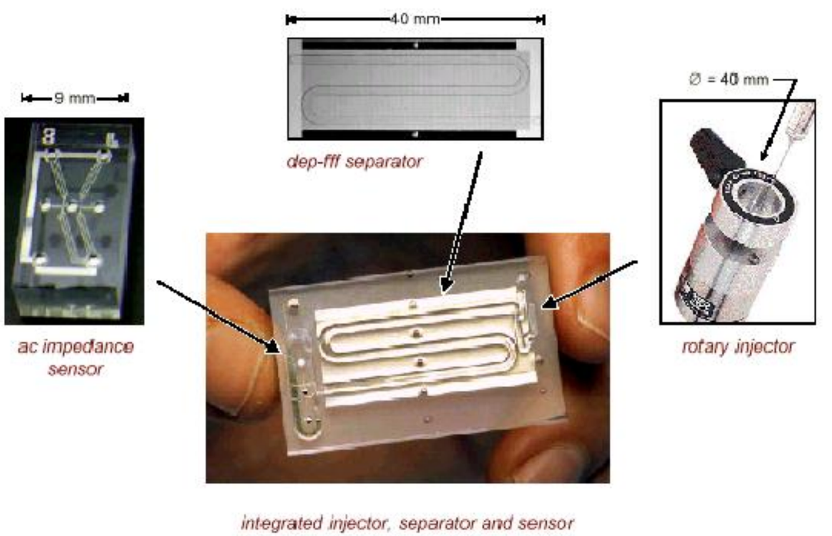


Rapid Mixing

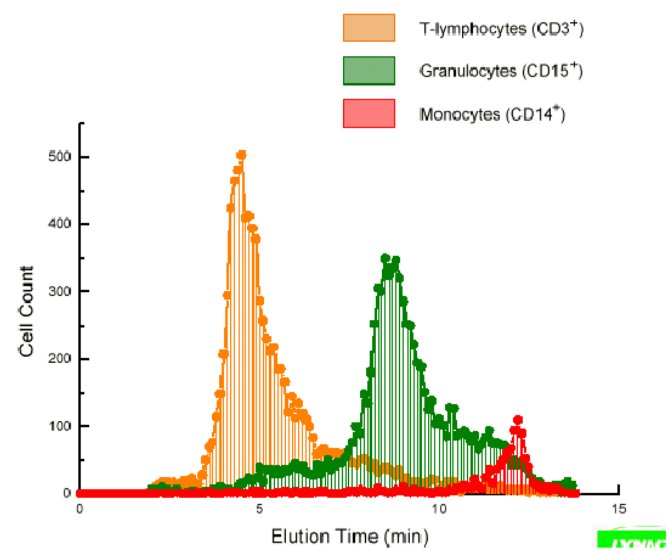
Flied Flow Fraction-DEP cell sorter



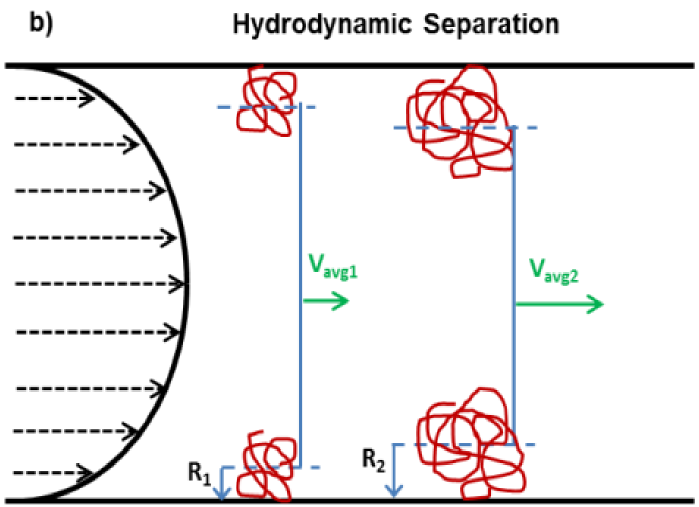
- Field flow fraction using DEP force

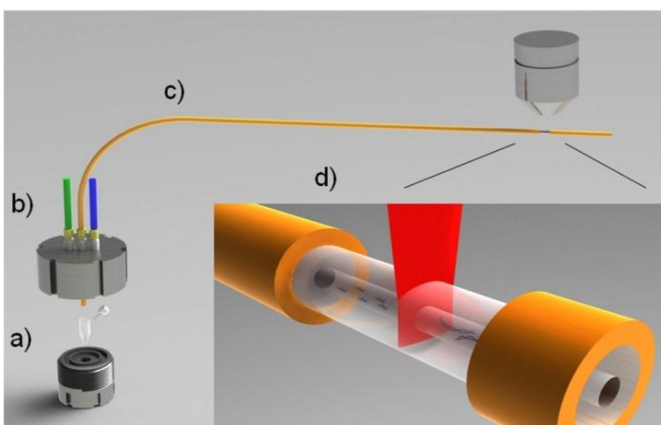


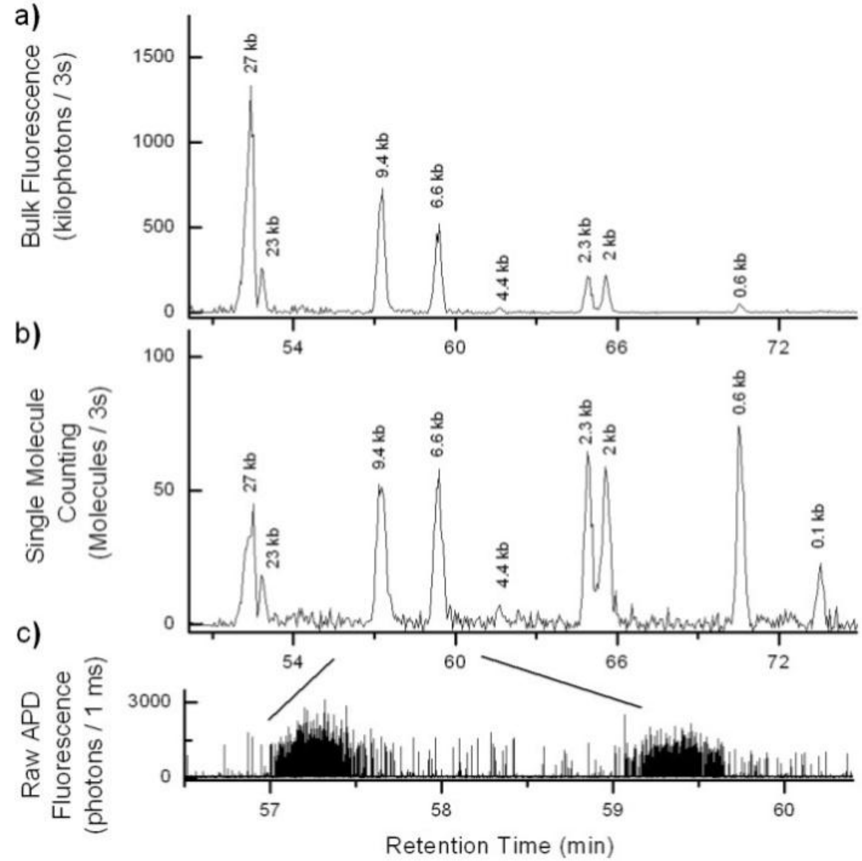
(U. Texas, Houston)



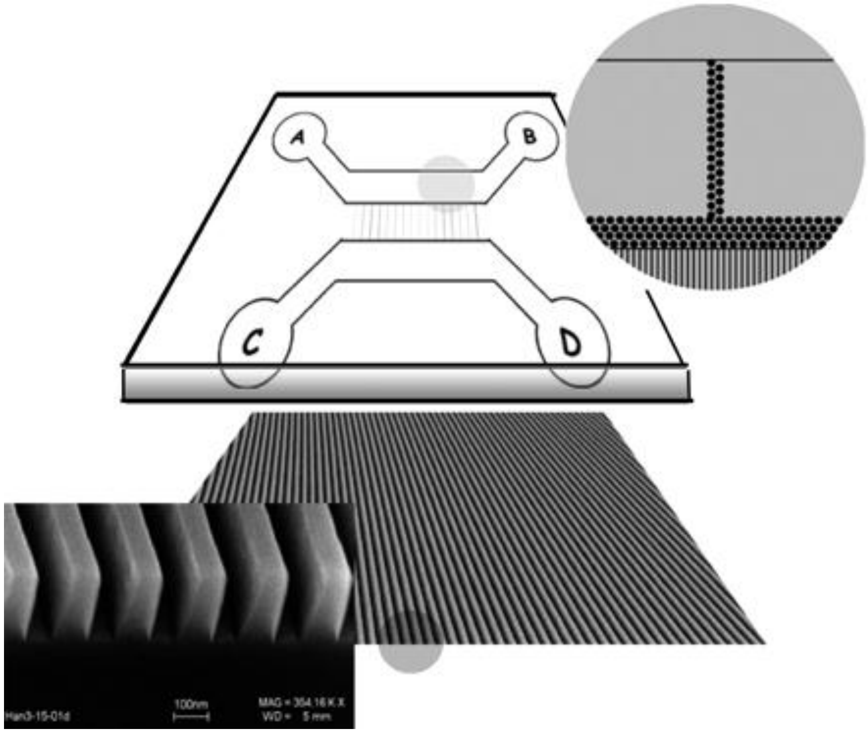
Free Solution Hydrodynamic Separation



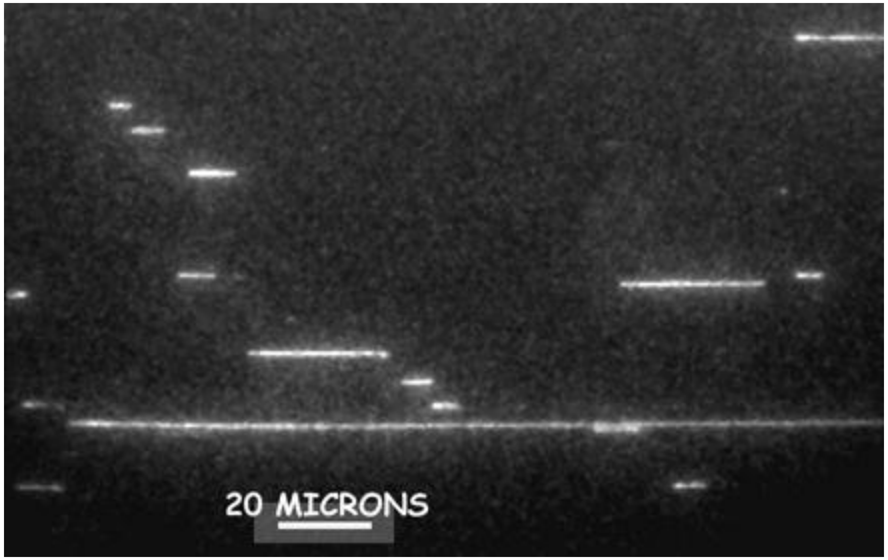




Nano Fluidics



100-nm-wide nanochannel array

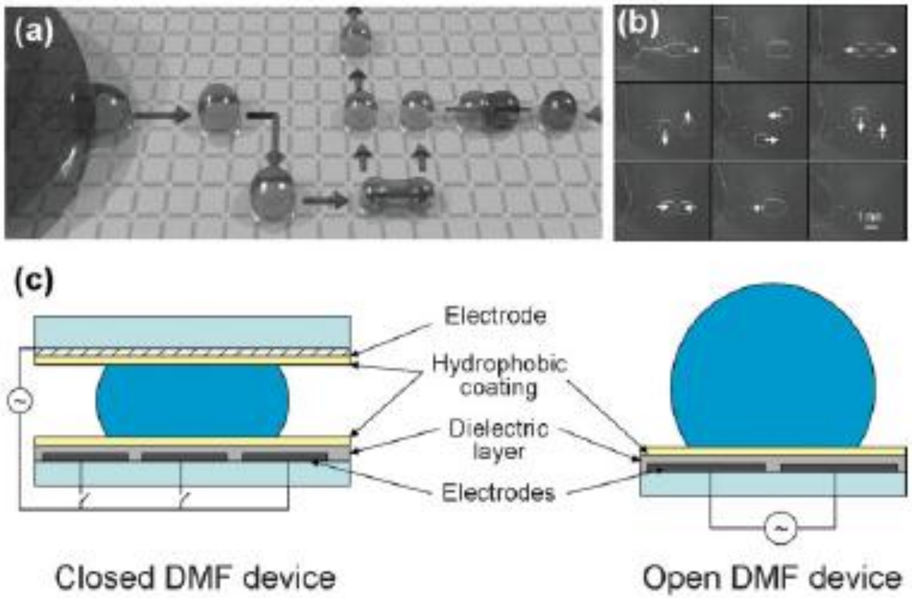


Stretch of λ DNA (48.6 kbp)fragment

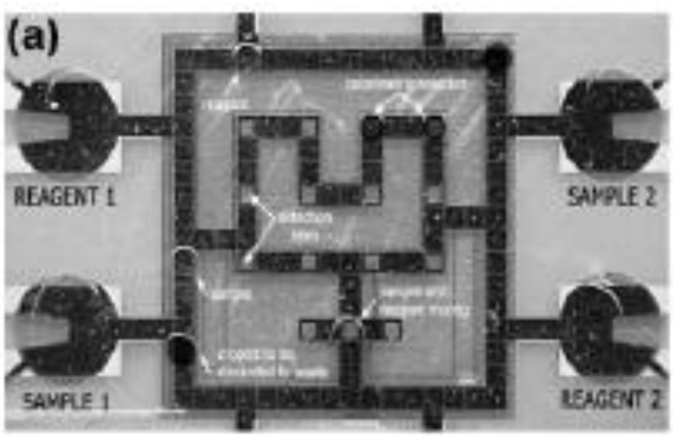
DNA is driven by E-field

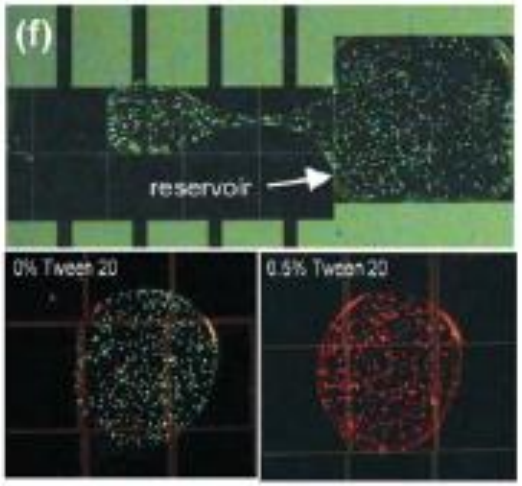
(R. Austin)

Digital Microfluidics

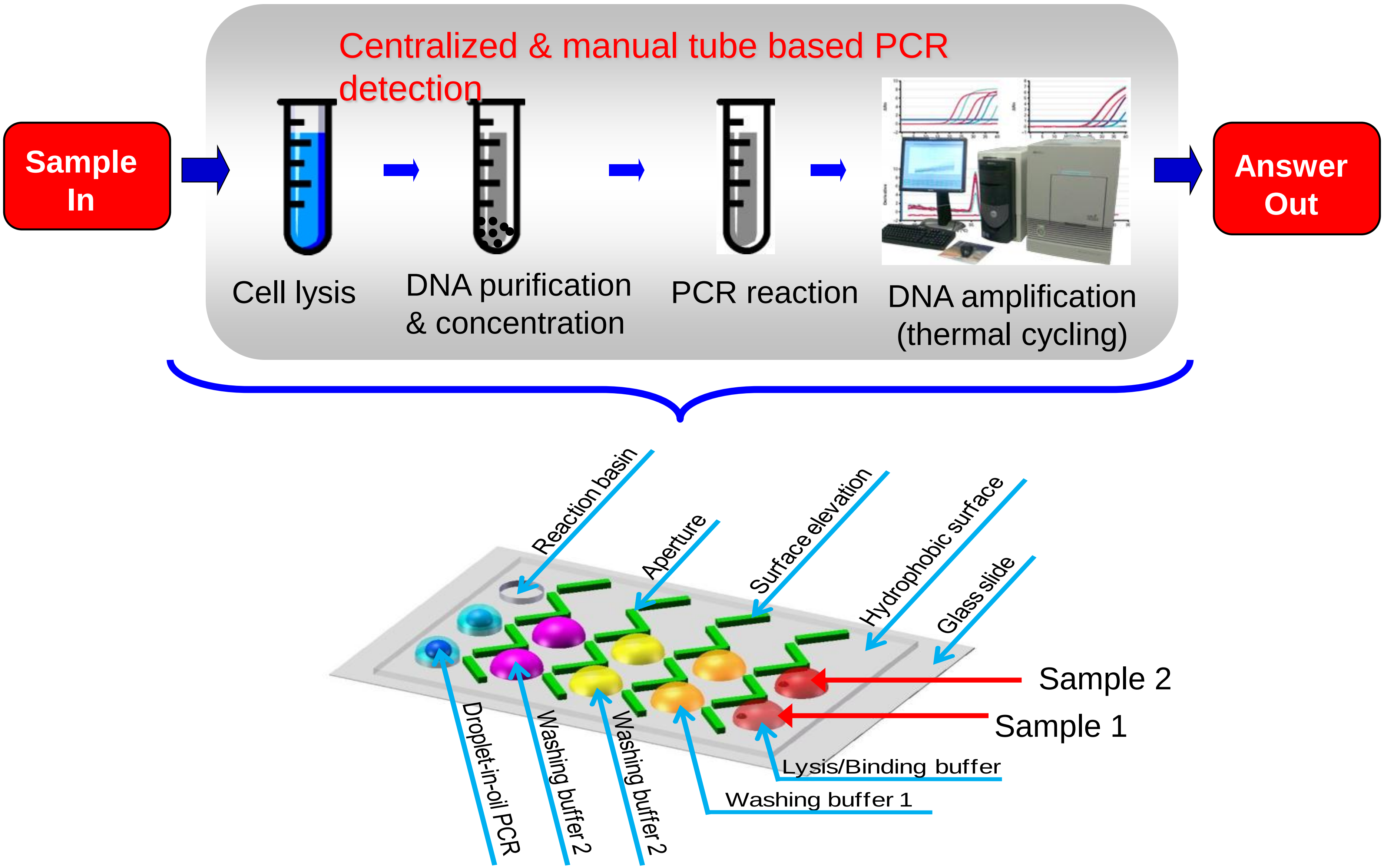


- Pump-free and valve-free
- Each sample and reagent is individually addressable
- Array-based analysis





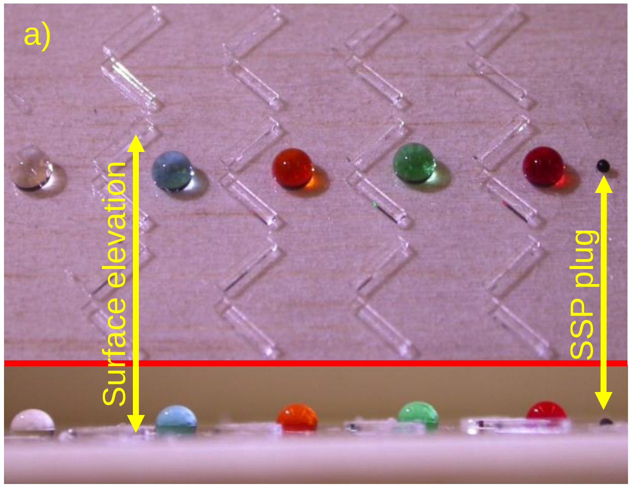
Integrated DNA Preparation and PCR Detection

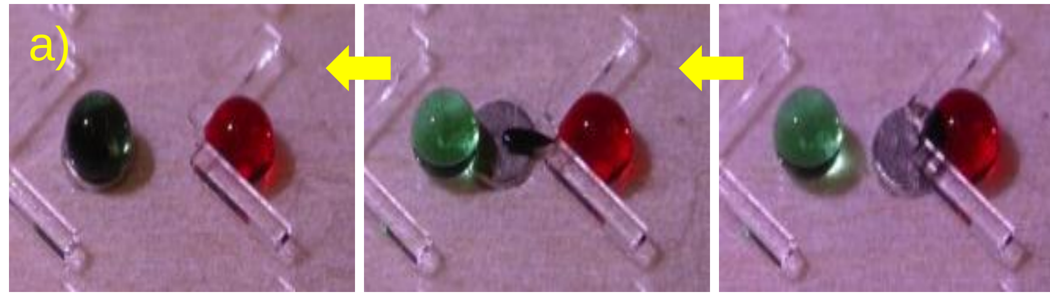


Using ***Silica Superparamagnetic Particles (SSP)*** as a solid phase within droplets

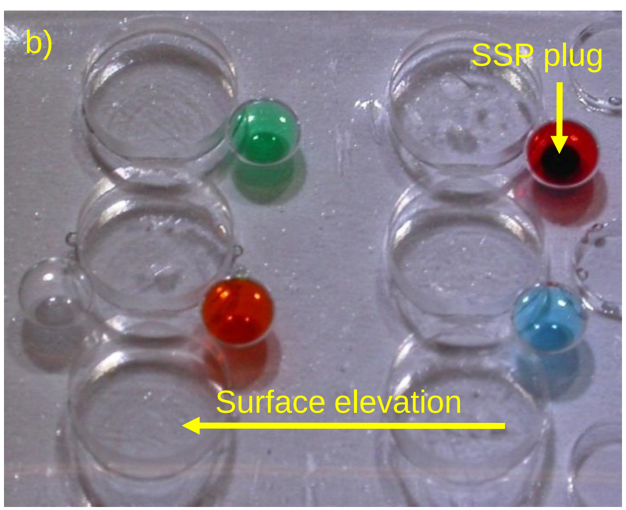
Surface topology assisted SSP and droplet manipulation

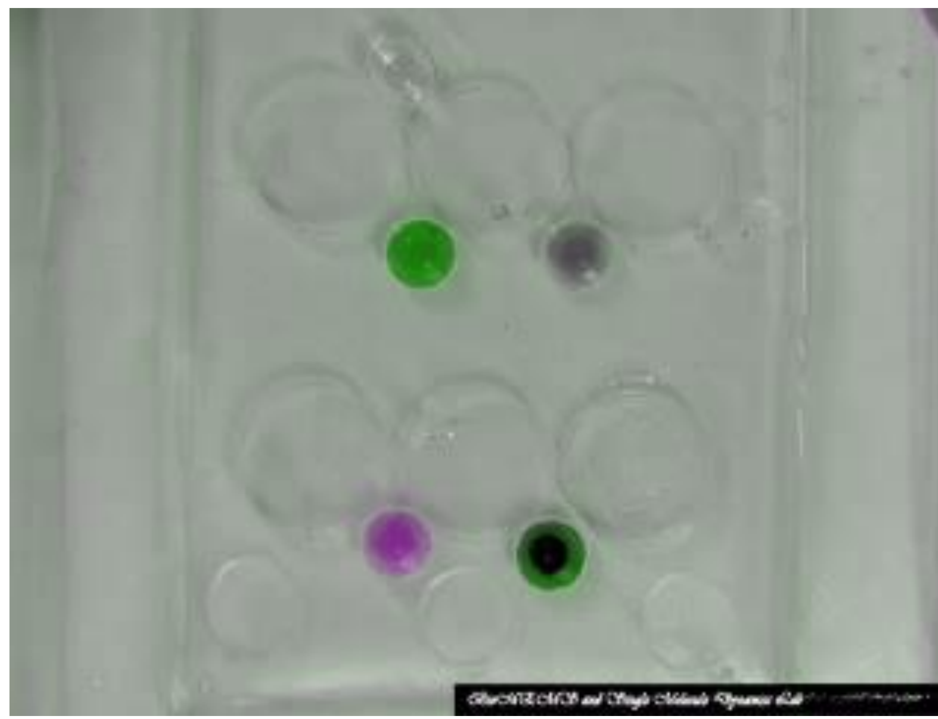
- ❑ **Drops in Air**





- ❑ **Drops in Oil**

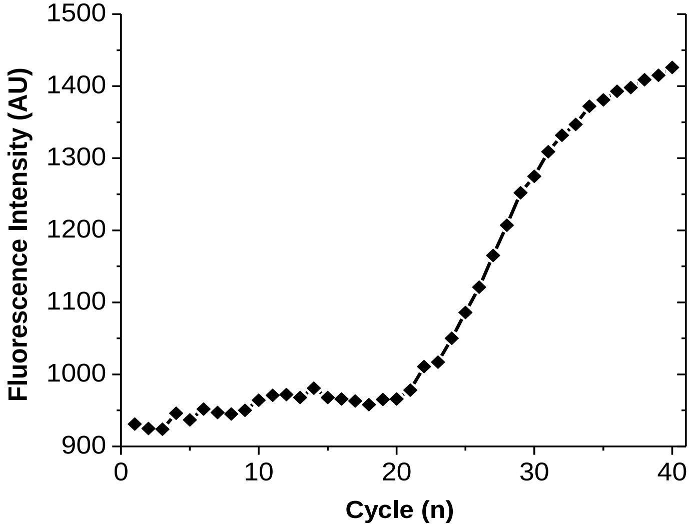


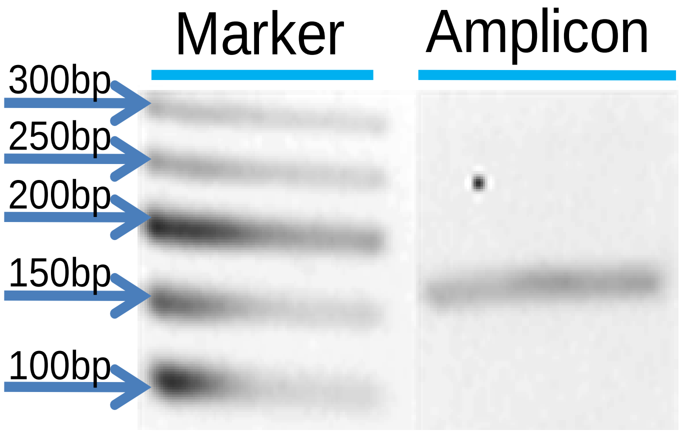


(Y Zhang, Lab Chip 2011)

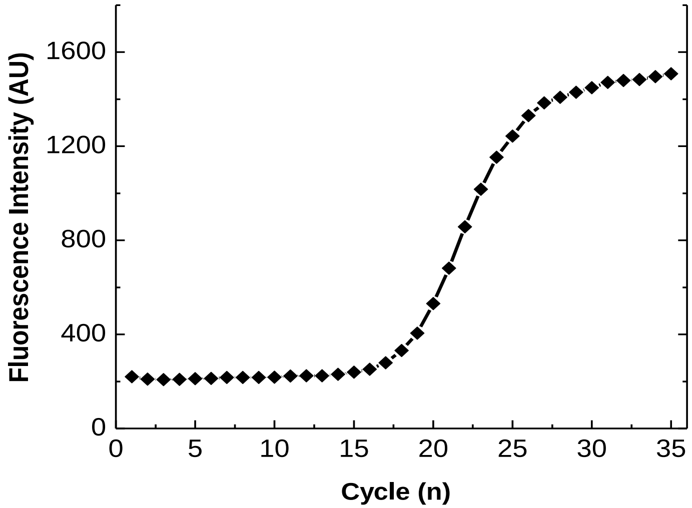
On-Chip Real-Time PCR Detection

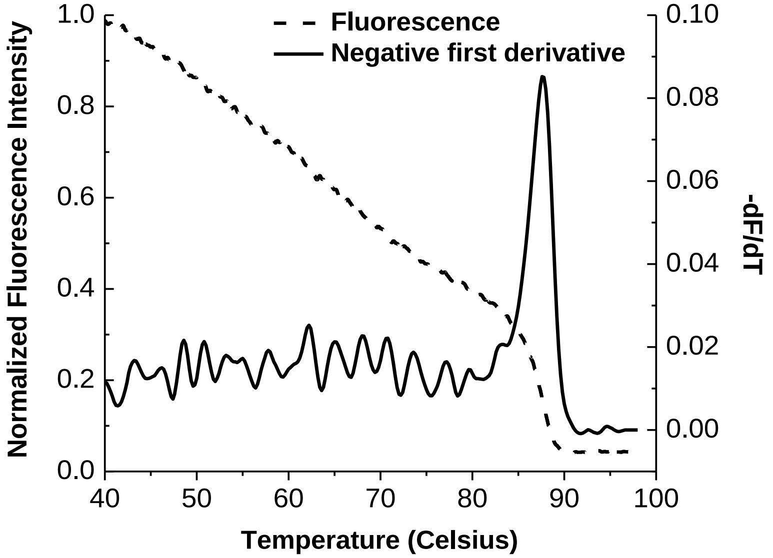
- **Detection of *E coli* 16S *gene from cell culture***



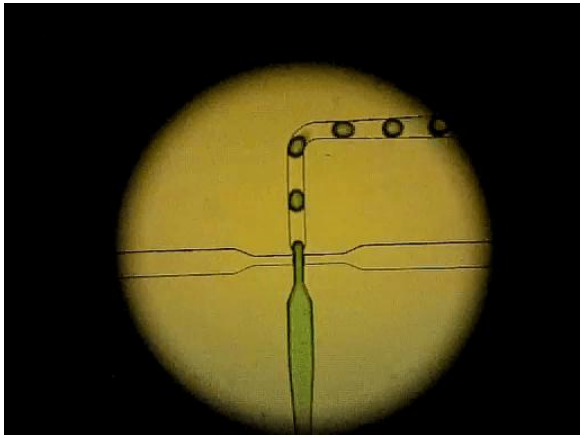


- **Detection of *Rsf-1 marker from whole blood***



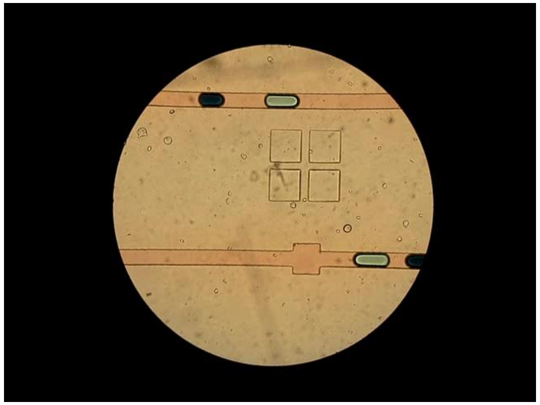


Microfluidic Droplet Technology for High-Throughput Analysis



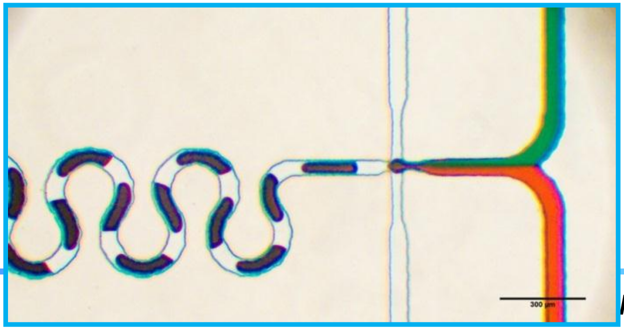
❑ Features

- Monodisperse droplets of sizes ranging from nL-pL
- High speed droplet generation of > kHz

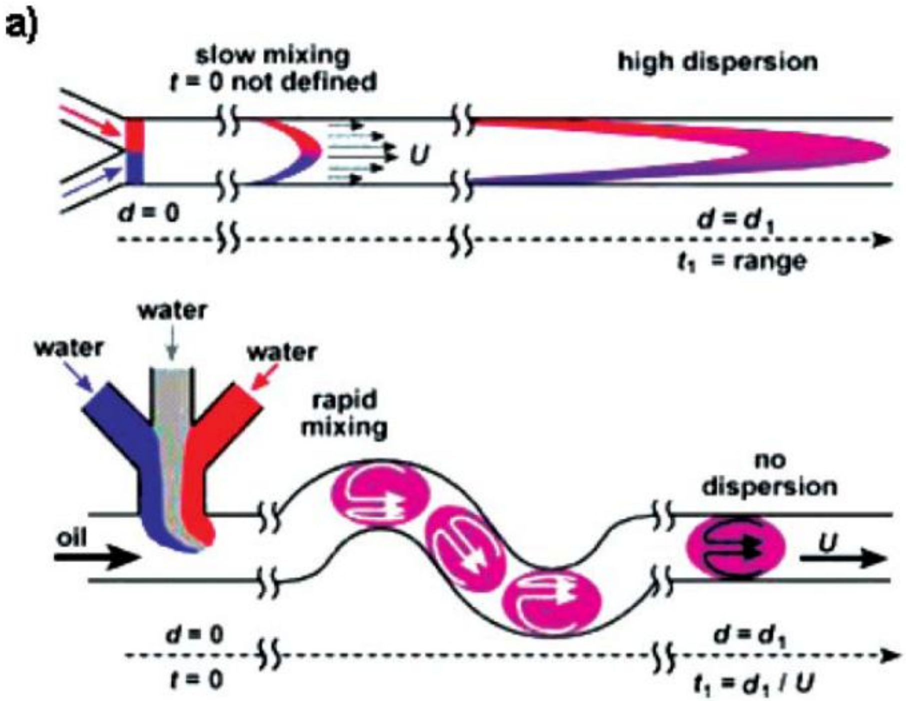


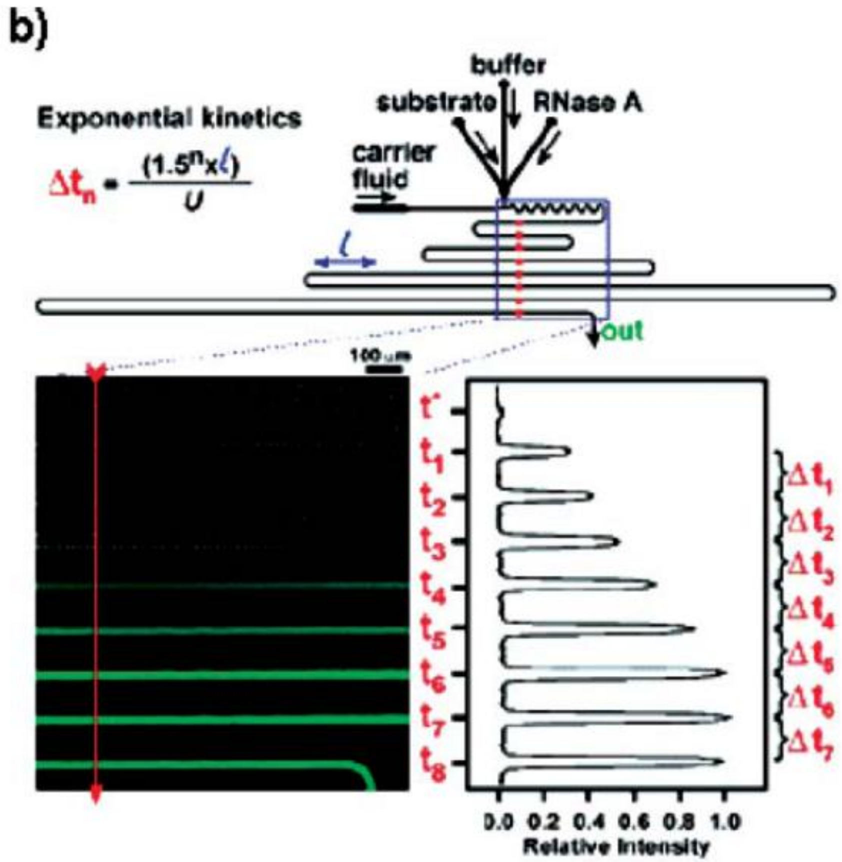
❑ Potential applications

- Low-cost & High throughput screening
- Biochemical synthesis
- Digital PCR
- Single-cell analysis



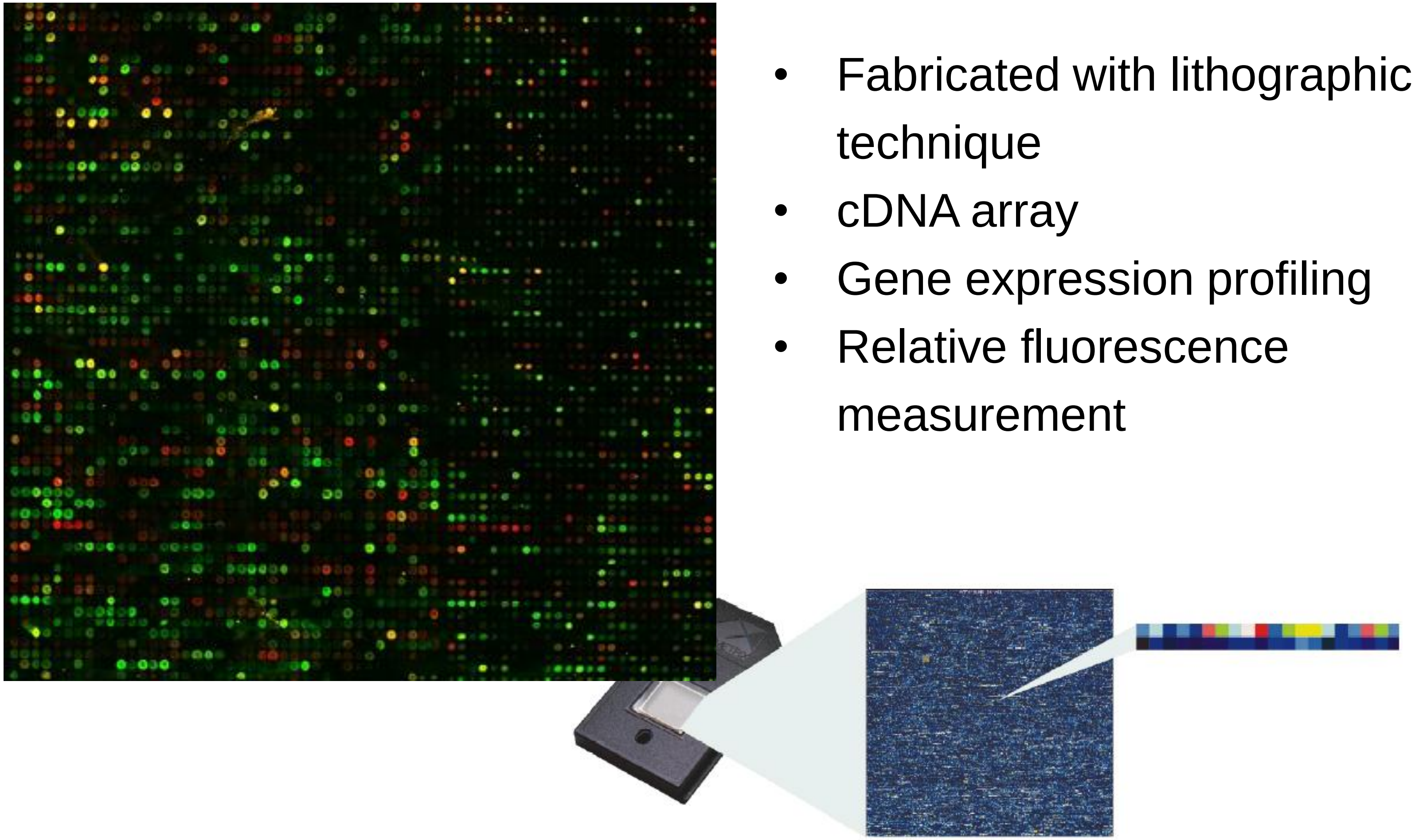
Droplet Microfluidics for Monitoring of Kinetics





DNA Microarrays

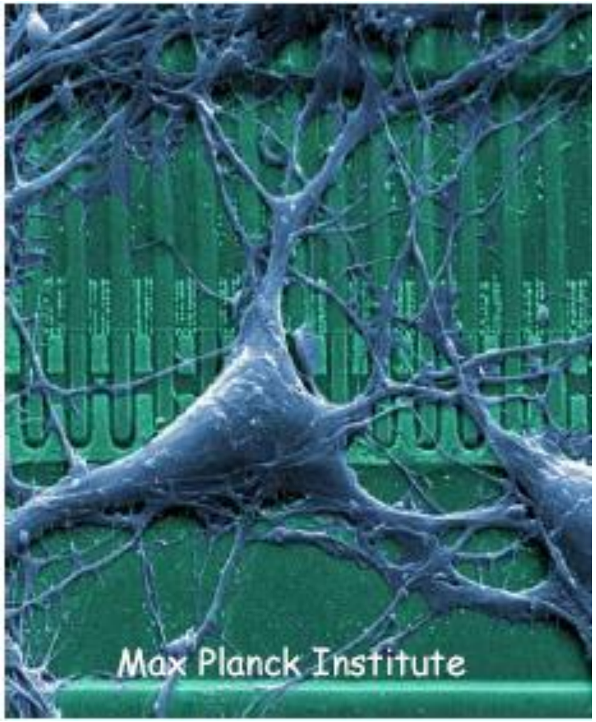
Affymetrix

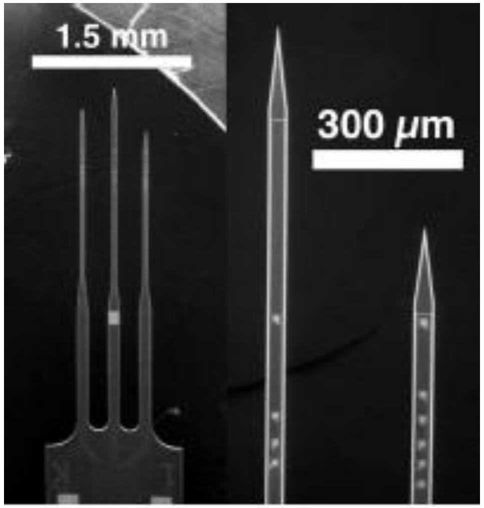


- Fabricated with lithographic technique
- cDNA array
- Gene expression profiling
- Relative fluorescence measurement

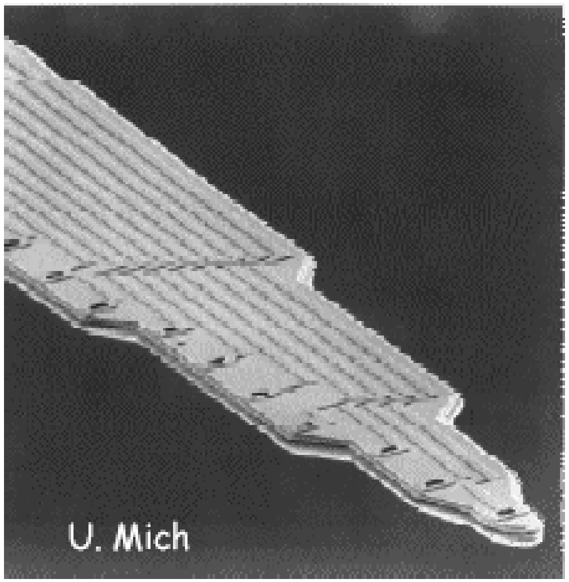
Neural Probe/ Neuro Implant

- Neuro-circuit interaction – neuro-recoding
- Prosthesis research
- Chemical delivery
- Issues with long term implant – bio compatibility



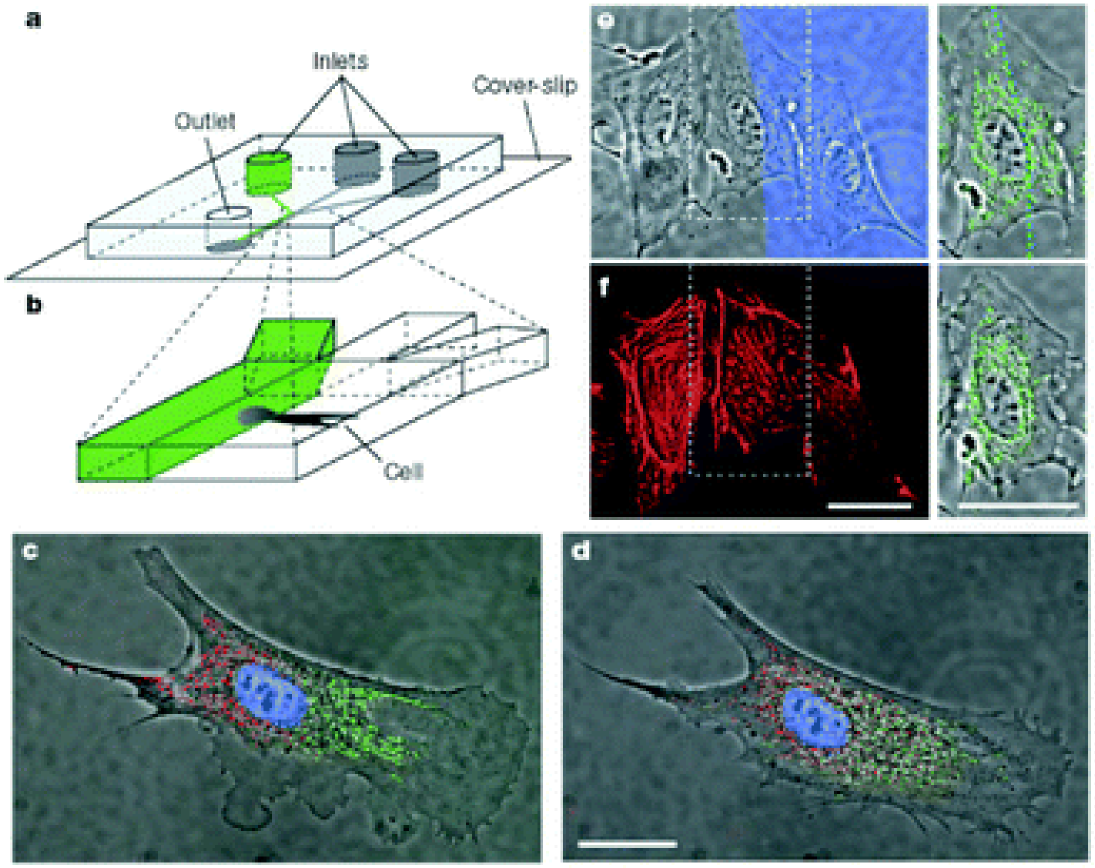


Stanford Neuro Probe



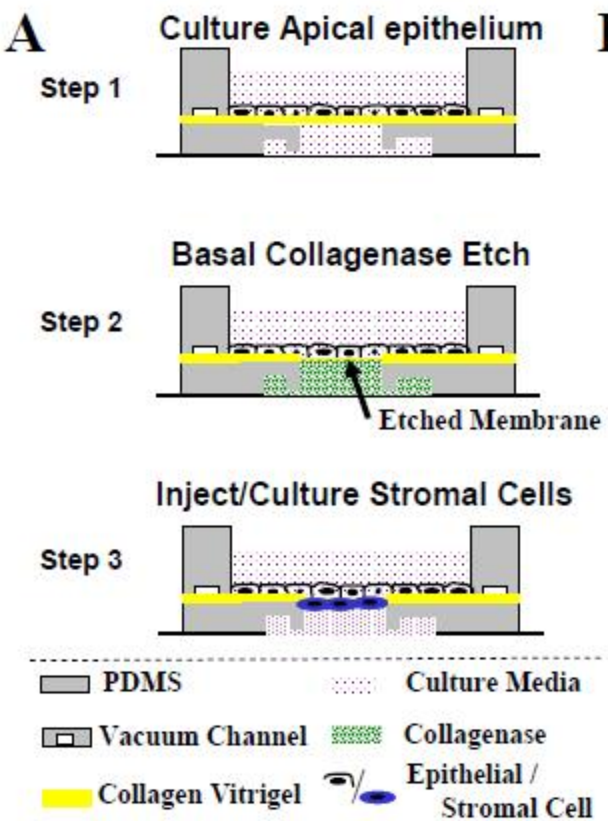
Tissue Engineering / Cell Patterning

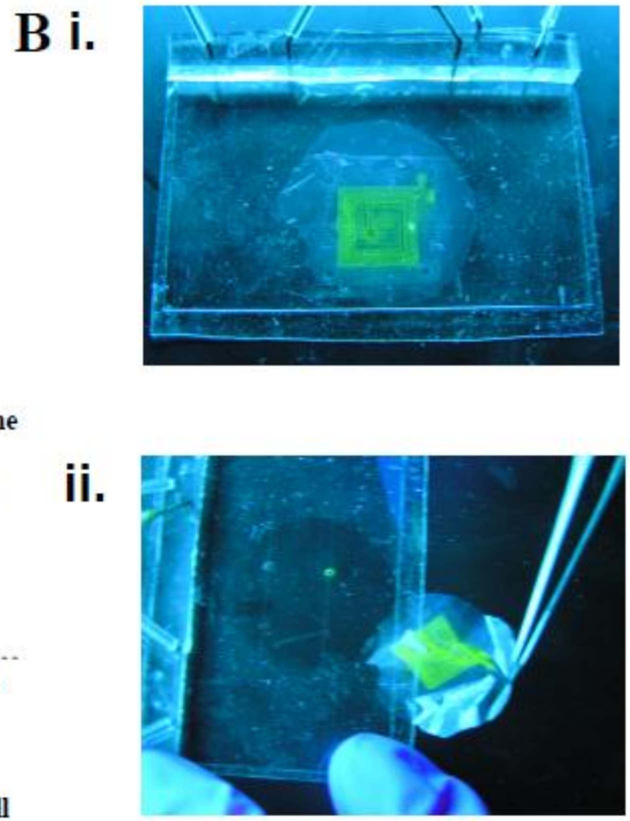
- Patterning cells using microfluidics
- Control of microenvironments using microfluidics
- Single-cell (controlled small number of cells) patterning
- High-throughput search for right cell conditions for controlling cell growth, differentiation, apoptosis)

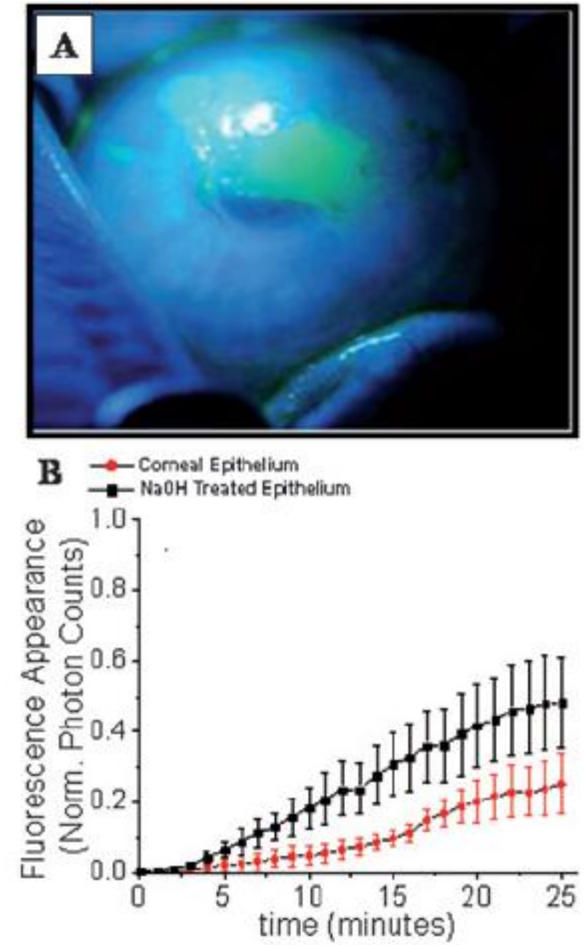


(Whitesides)

Corneal Microtissue Culture







(C. Puleo, Lab Chip. 2009)