Lab on a Chip and Microfluidics

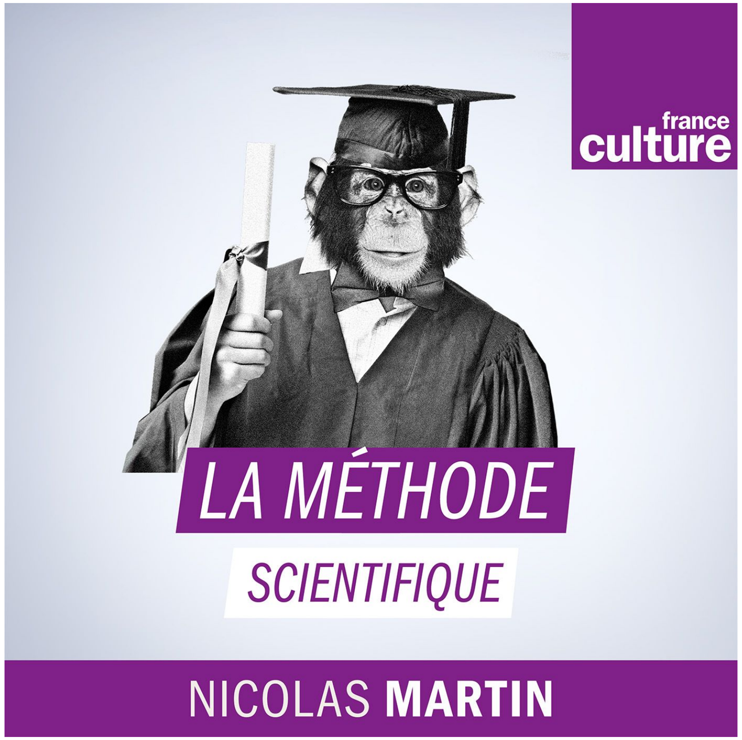
Benoît CHARLOT

http://www.ies.univ-montp2.fr/~charlot/

l'institut d'électronique

Préambule

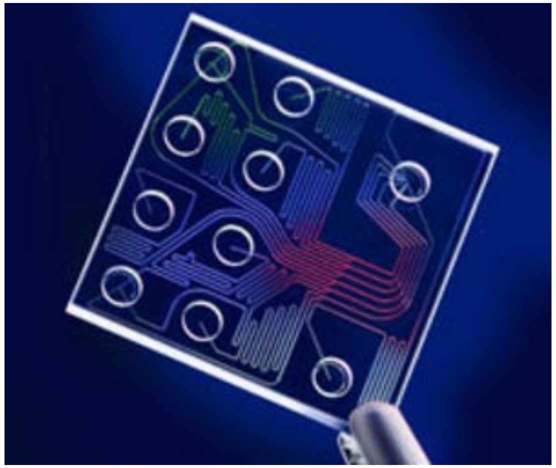
Pour des étudiants en Master 2 : deux podcasts indispensables



Outcome

0 Introduction
I Microfabrication technologies
II Lab On Chip Technologies
III Fluid transport
IV Electrokinetics
V Mixing, separation, Diffusion
VI Diphasic microfluidics
VII DNA microfluidics
VIII Detection
IX Cells on Chips
X Capillarity and wetting
XI Blood in microfluidics

Introduction : Lab On a Chip



Lab On a Chip (laboratories on chip) LOC
µTAS (micro Total Analysis System)
Point of Care

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 to achieve automation and high-throughput screening

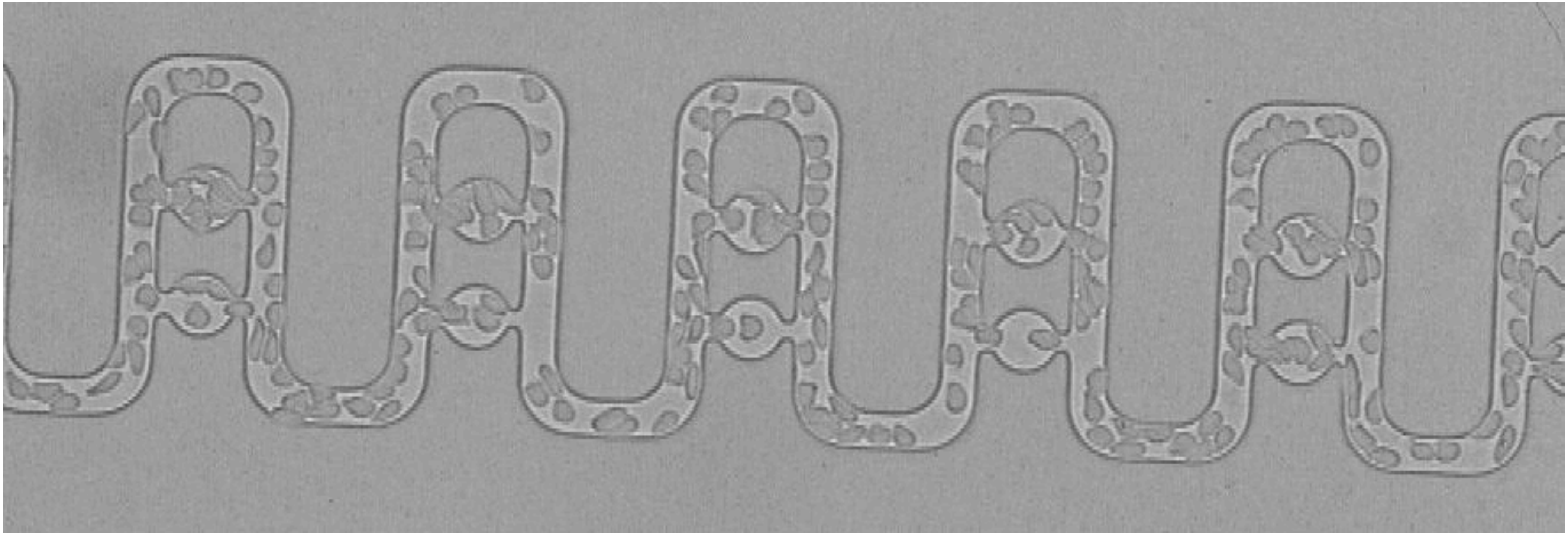
Functions operated on a Lab On Chip

- **Fluid transport** (Electro-osmosis, Electro-phoresis, Hydrostatic pressure)
- **Preparation** (Heating, Filtration, Extraction)
- **Separation** (diffusion, electrophoresis, isoelectric focusing)
- **Mixing** (diffusion, forced mixing)
- **Reaction** (culture chambers, markers)
- **Detection** (Chemiluminescence, electrochemiluminescence, fluorescence, Electrochemical detection, mass spectroscopy, Surface Plasmon Resonance)

Lab On Chips are based on **microfluidics**

Microfluidics

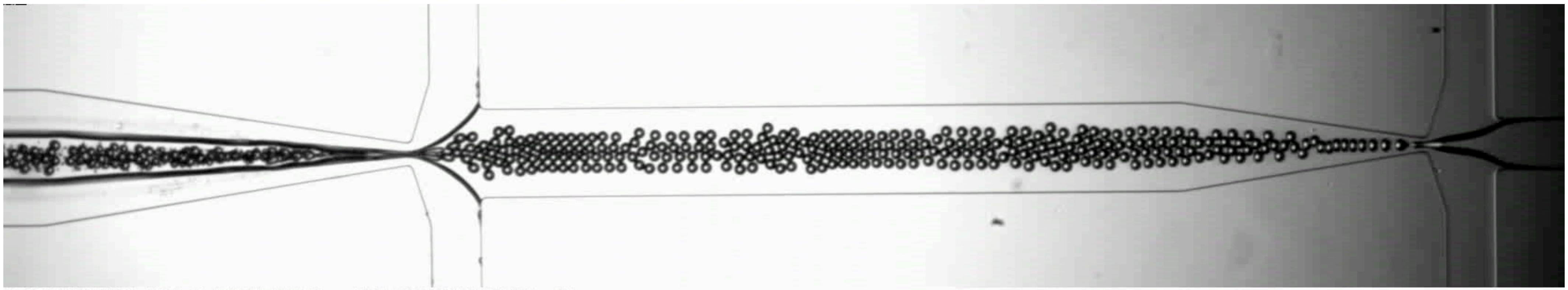
Microfluidics is the science that deals with the study and design flows at the micron scale



Microfluidics

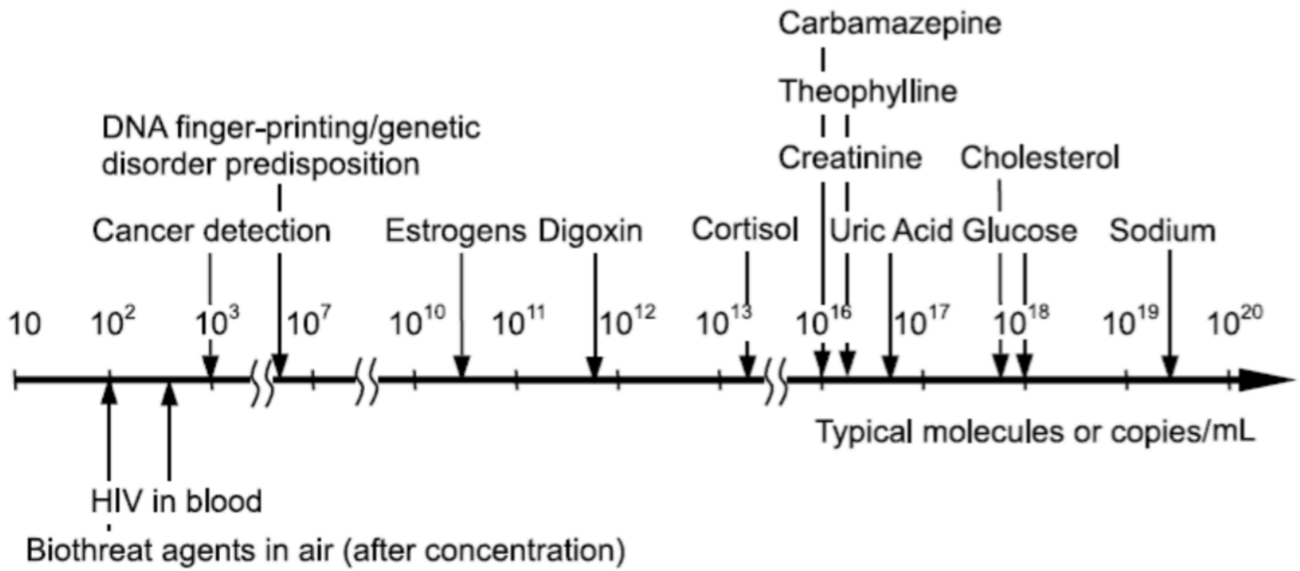
Why **MICRO** fluidics?

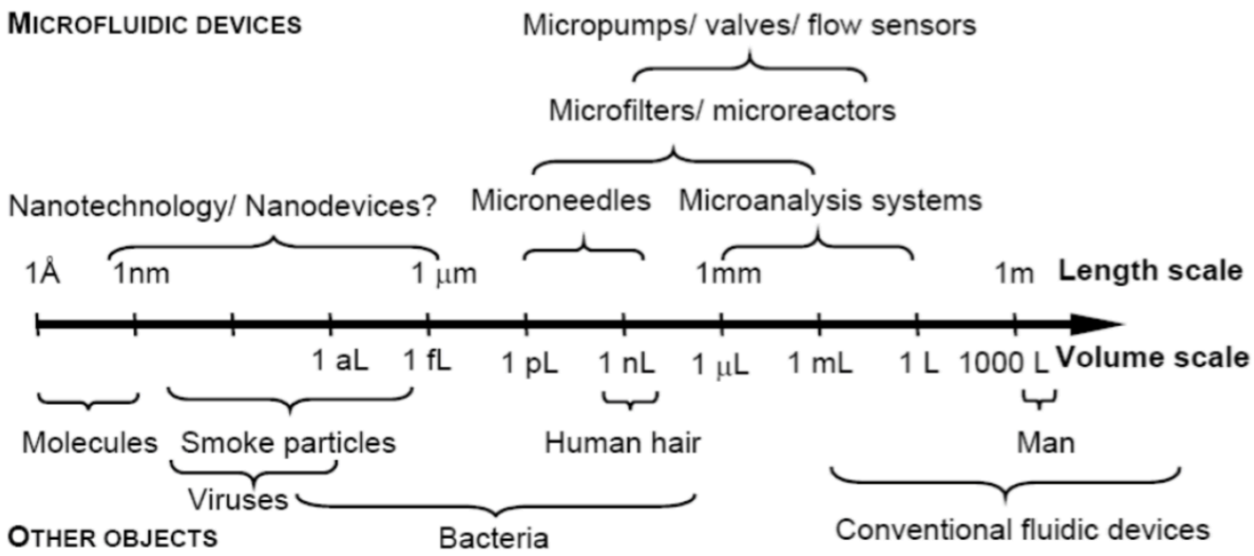
- Sample volume reduction
- Better sensitivity
- Reactives quantity reduction
- Shorter analysis time
- Parallel analysis
- High throughput analysis
- Integration
- Automation
- Batch fabrication
- Miniaturization
- Small energy consumption



4/4/2013 3:17:33 PM -00:00:04:073.85[HH:MM:SS:mm] 000002879 1680x305 1593fps 15µs

Concentration, size and volume





Introduction

Grandeur	Loi d'échelle
Force de Van der Waals intermoléculaire	l^{-7}
Densité de force de Van der Waals entre interfaces	l^{-3}
Temps	l^{0}
Force capillaire	l^{1}
Distance	l^{1}
Vitesse d'écoulement	l^{1}
Puissance thermique transférée par conduction	l^{1}
Force électrostatique	l^{2}
Temps de diffusion	l^{2}
Volume	l^{3}
Masse	l^{3}
Force de gravité	l^{3}
Force magnétique sous champ extérieur	l^{3}
Force magnétique sans champ extérieur	l^{4}
Puissance électrique motrice	l^{3}
Force centrifuge	l^{4}

Introduction Units

Kinematic properties :

linear and angular velocity   u ($m.s^{-1}$)

vorticity, curl (rotational) of the flow velocity u

acceleration, ($m.s^{-2}$)

shear rate (s^{-1})

Transport properties

viscosity, (Pa.s)

thermal conductivity, ($W.m^{-1}.K^{-1}$)

diffusivity ($m^2.s^{-1}$)

Thermodynamic properties

pressure (Pa)

temperature, (K)

density ($kg.m^{-3}$)

+

surface tension ($J.m^{-2}$)

vapor pressure (Pa)

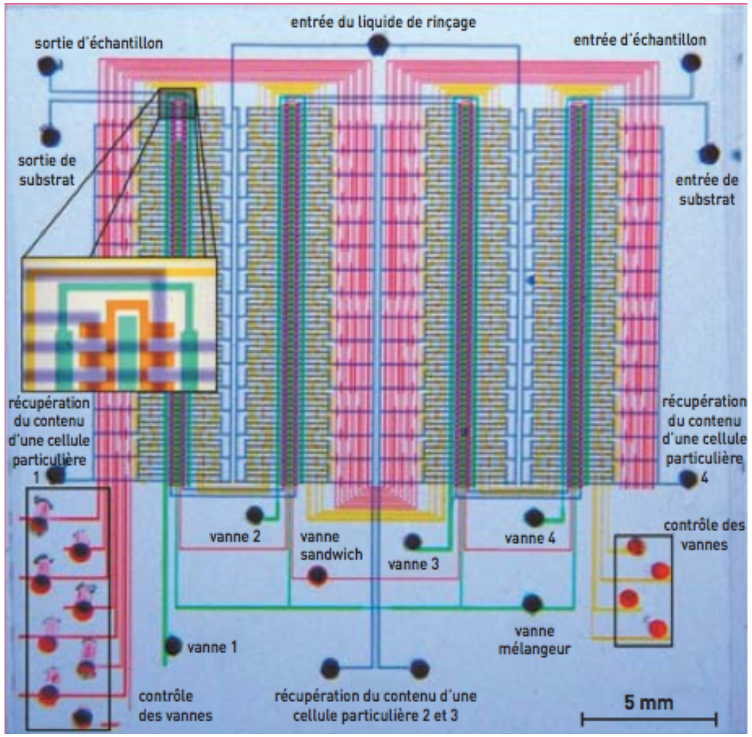
Part I. Microfabrication technologies

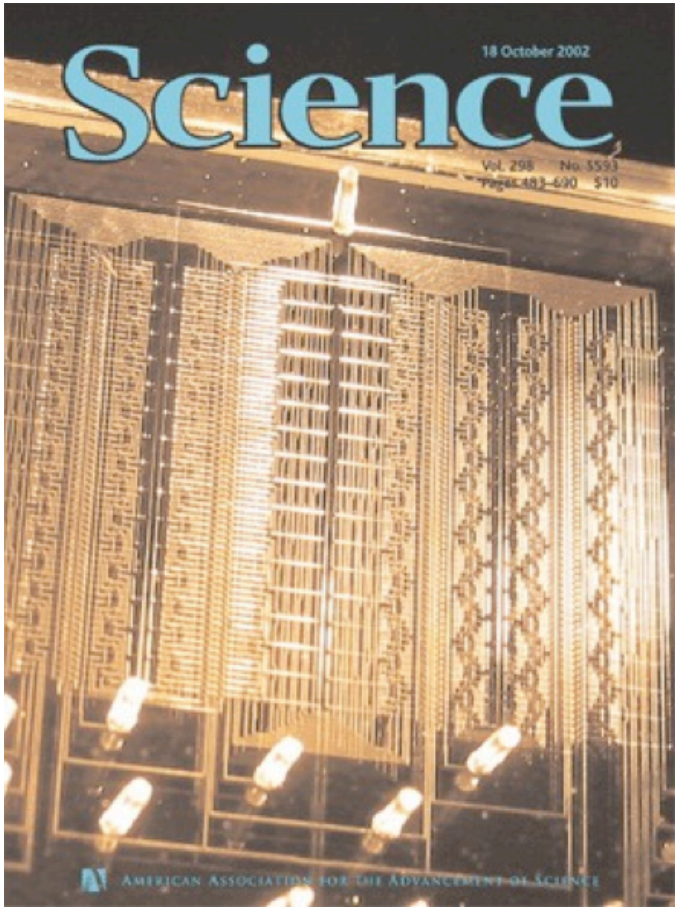
Lab On Chip

BioMEMS and microfluidics have started in 2000's

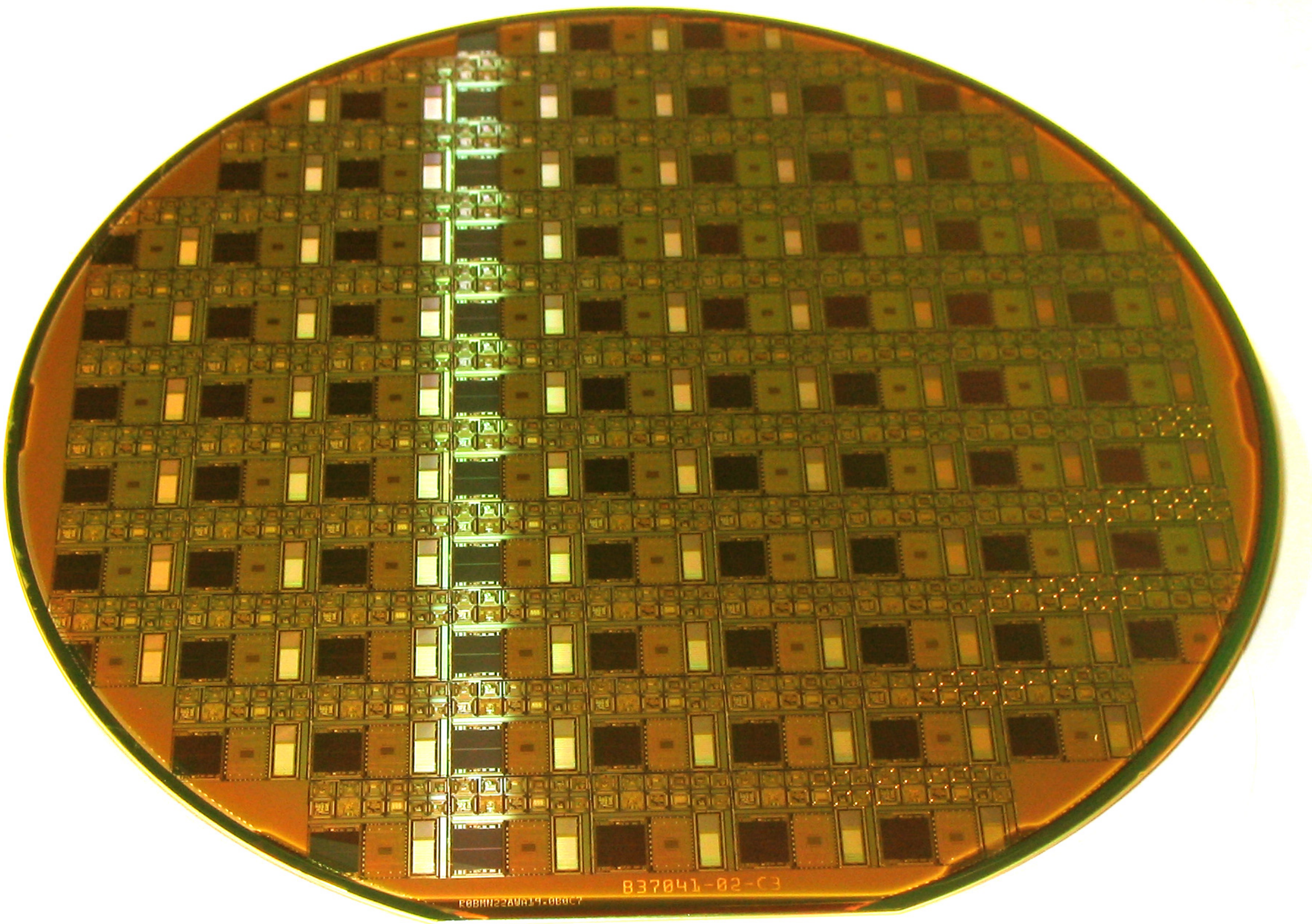
The idea is to use what has mad the success of microelectronics and MEMS to biochemical engineering and cellular biology.

Miniaturisation
Integration
Parallelism
Batch Fabrication





Microelectronics



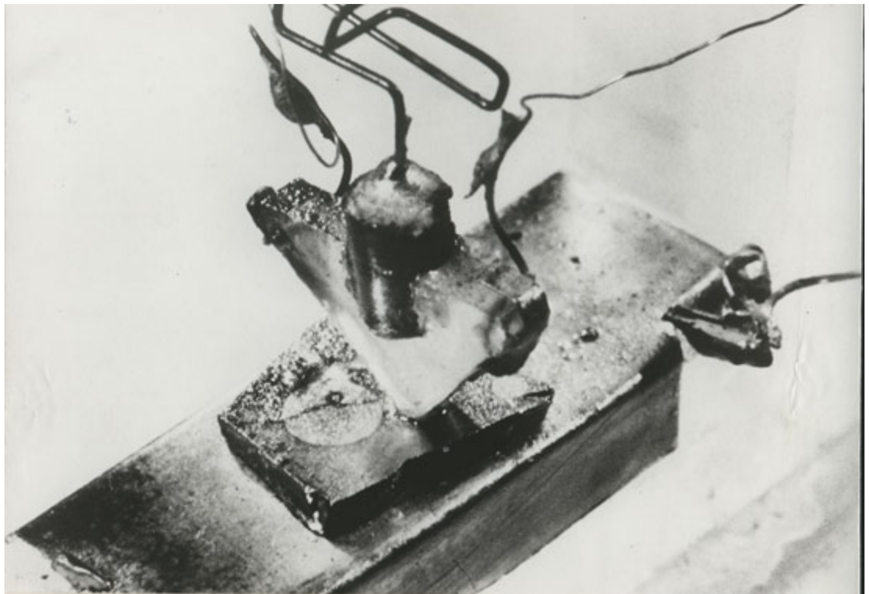
UNIVERSITÉ MONTPELLIER 2
SCIENCES ET TECHNIQUES

Miniaturisation
Integration
Parallelism
Batch Fabrication

Transistor

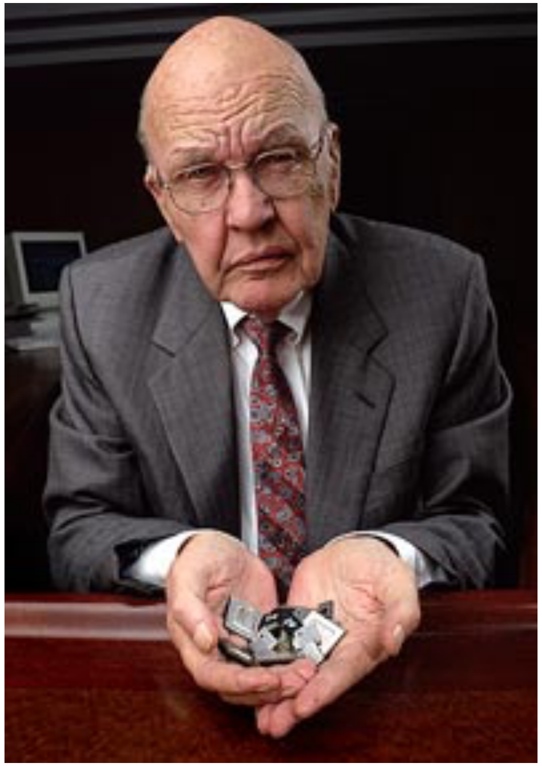
The first transistor : **1947** (BELL Labs)
Developed by John **Bardeen**, Walter **Brattain** and William **Shockley**
Nobel price in 1956

Solid state device that replace mechanical switches and tube amplifiers



THE FIRST TRANSISTOR AS IT WAS PATENTED BY THREE NOBEL PRIZE-WINNING BELL LABORATORIES SCIENTISTS

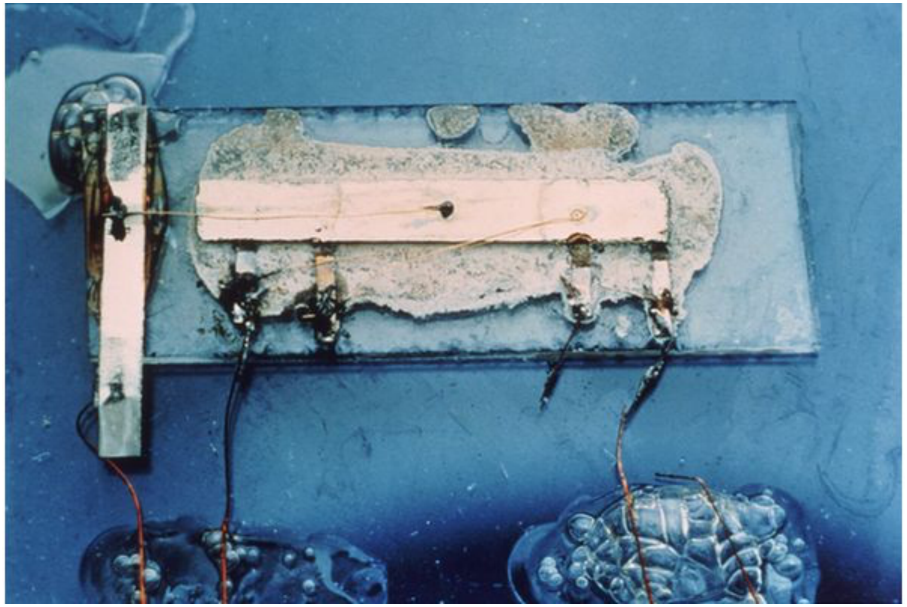
Integrated Circuit

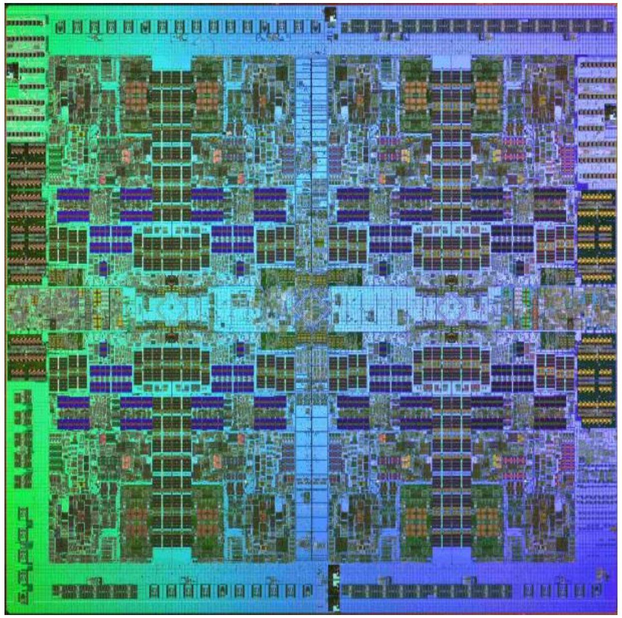


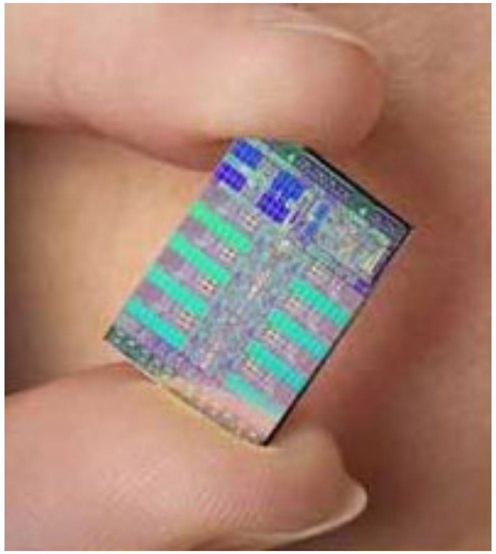
IC : Integrated circuit : a set of electronic circuits on one small plate ("chip") of semiconductor material

First IC : **1958** (Texas Instruments)
Developed by **Jack Kilby**
Nobel price in 2000

Also inventor of the handheld calculator and the thermal printer,





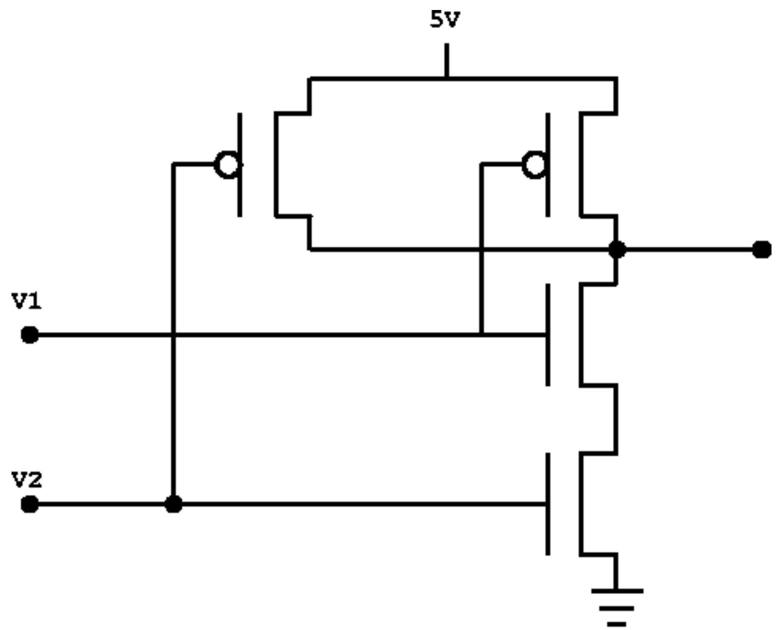


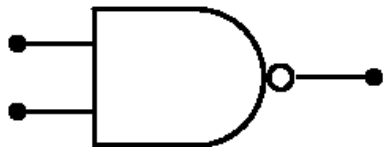
Nowadays : IBM Cell processor

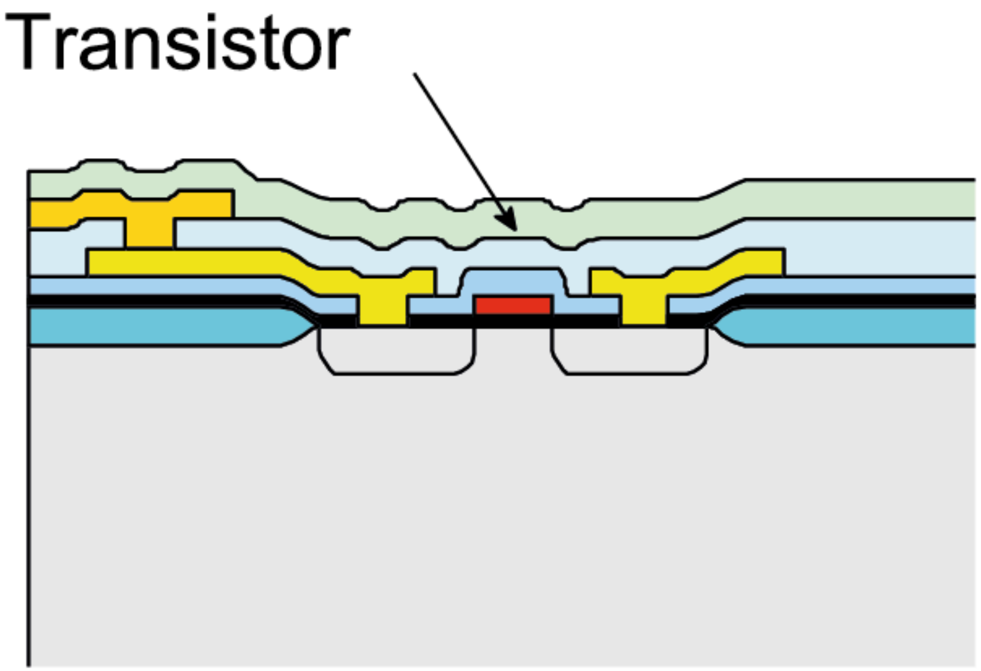
CMOS

Complementary Metal Oxide Semiconductor
Main Microelectronic technology
Based on complementary transistors: NMOS andPMOS
Bricks of the logic gates (NAND, XOR..)

(mainly) all microprocesors are made with CMOS
But also : memories, camera sensors (active pixel sensors)



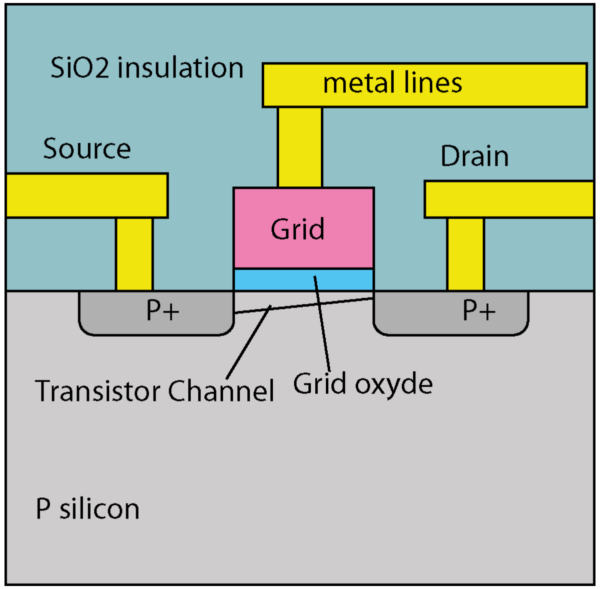




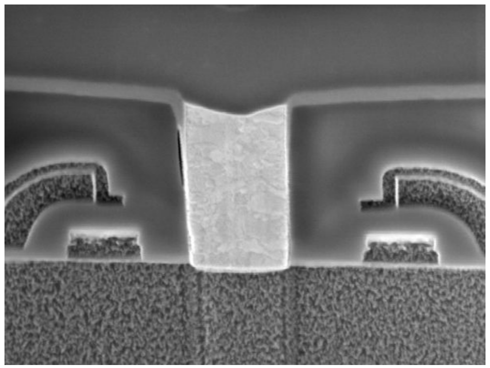
CMOS

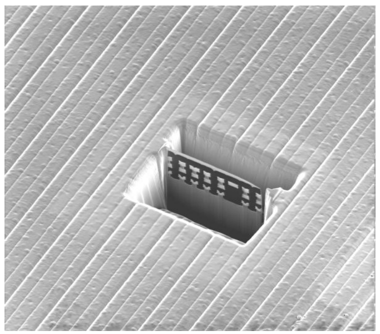
Silicon is a semiconductor material used for Field Effect Transistors

MOSFET: Metal Oxide Semiconductor Field Effect Transistor

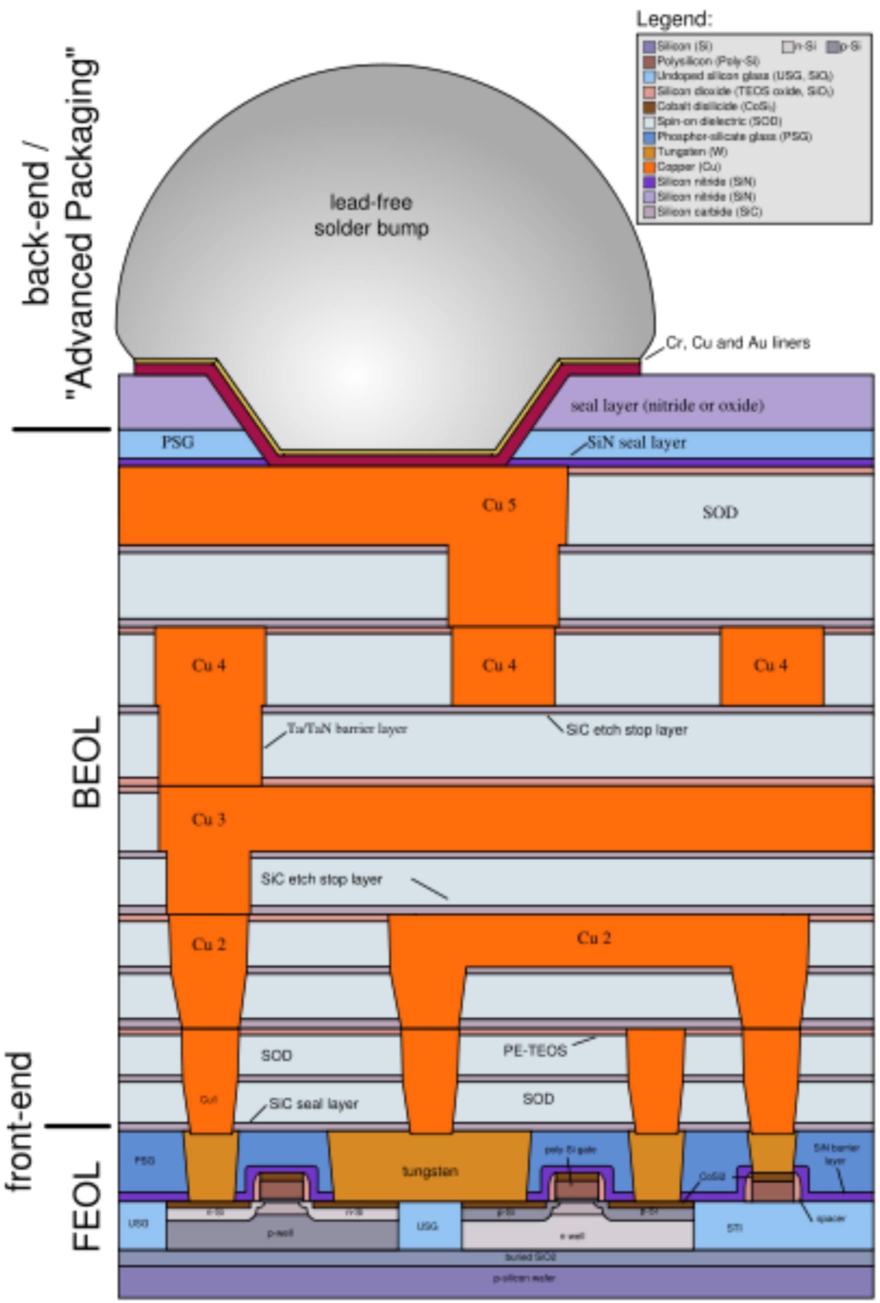


TEM view





FIB cross section



CMOS

In order to build transistors from a silicon wafers, once need :

Oxidation (Silicon dioxide growth from the silicon of the wafer)
Dopant implantation and diffusion (n and p junctions)
Lithography
Metals and dielectric thin film deposition (polysilicon, oxide and cilicon nitride, aluminium, copper, gold, tungsten,...)
Etching, wet and dry

SEM of desoxydized CMOS 6 level metal lines

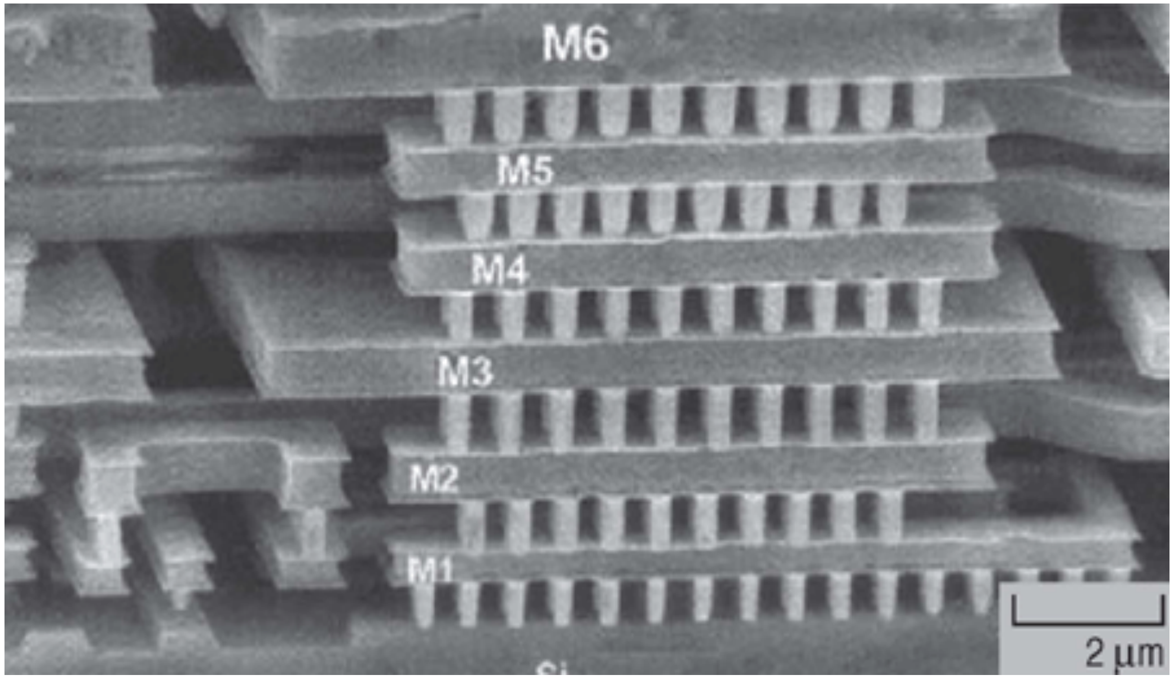
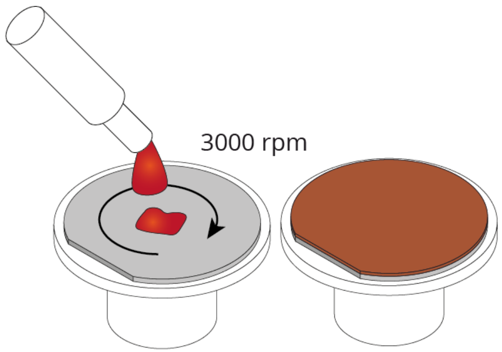


Image: L.J. CHEN, "Metal Silicides: An Integral Part of Microelectronics", JOM journal of the Mineral, Metals and materials society, Vol. 57, No.9, pp. 24-31

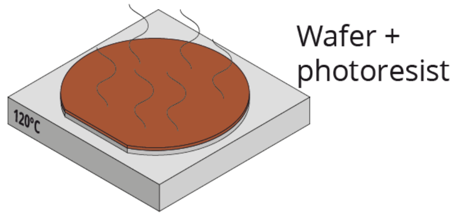
Lithography

Transfer of a pattern from a mask to a silicon wafer

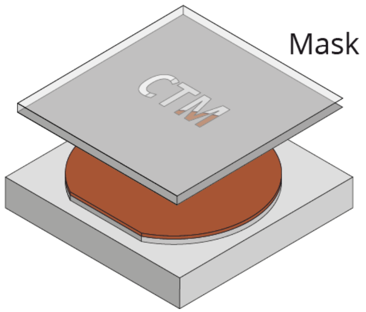
➡ *Spincoating*



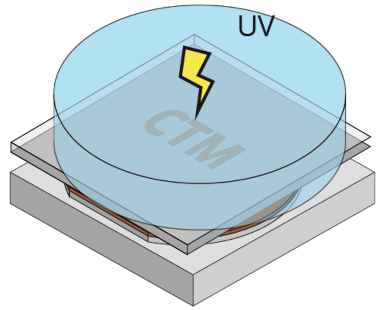
➡ *Baking*



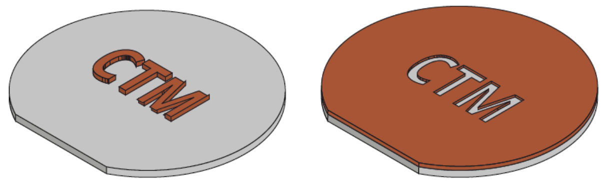
➡ *Mask alignment*



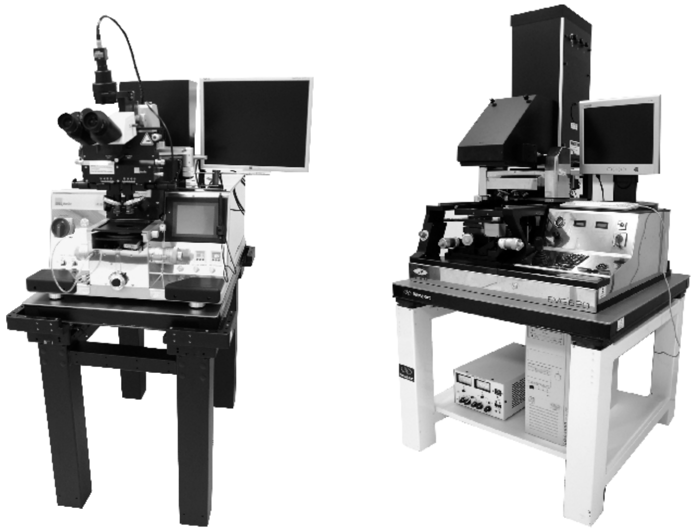
➡ *UV exposure*



➡ *Development*



negative photoresist   Positive photoresist



Small patterns -> problems with dust : work in cleanroom

Lithography

Transistors are small, and their size is decreasing

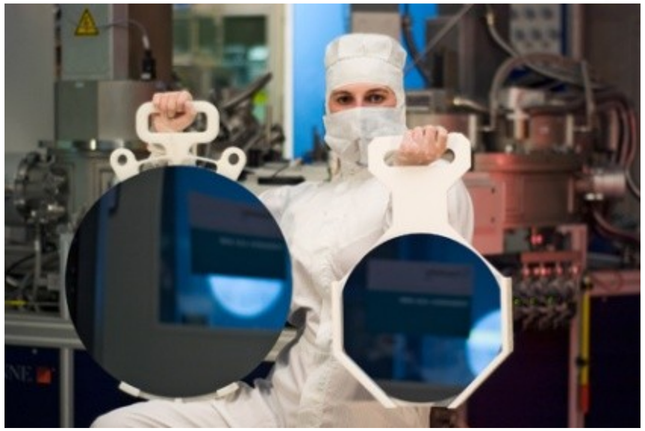
20µm (1975)

1µm (1985)

20nm (2010)

On the contrary, silicon wafers size is increasing

2inches and now 450mm (Pizza)



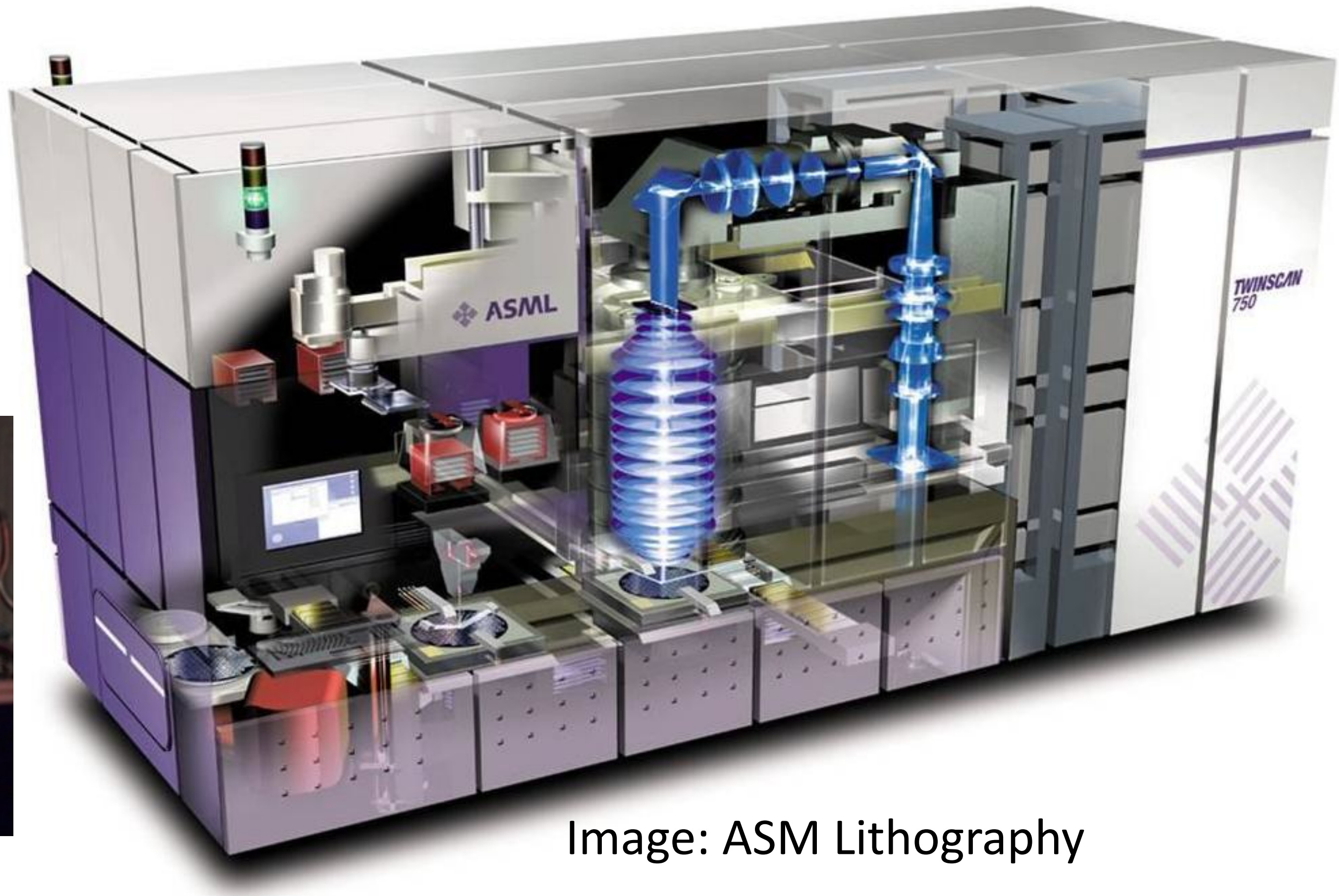
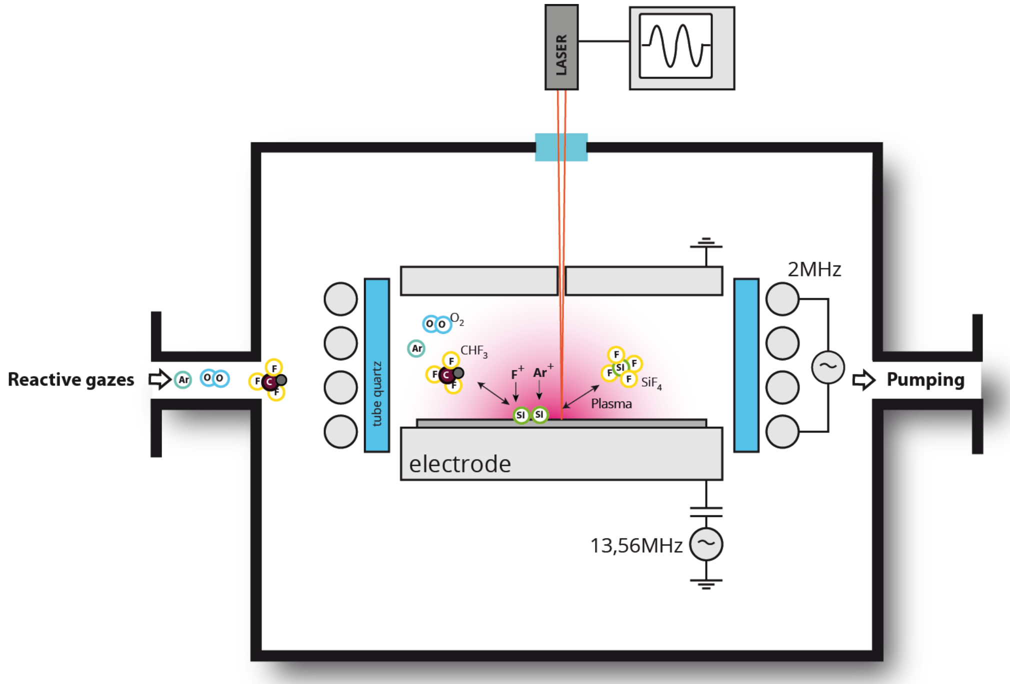


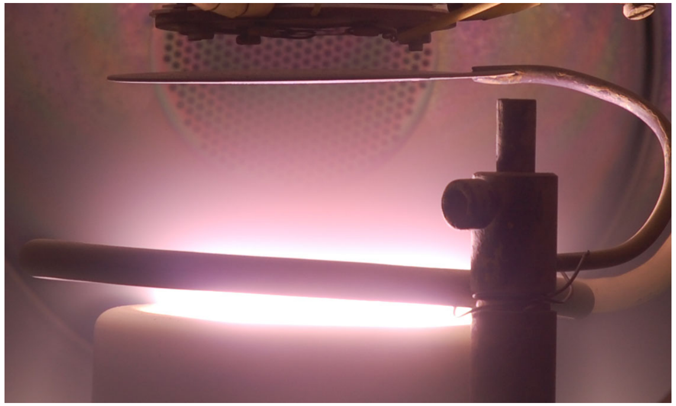
Image: ASM Lithography

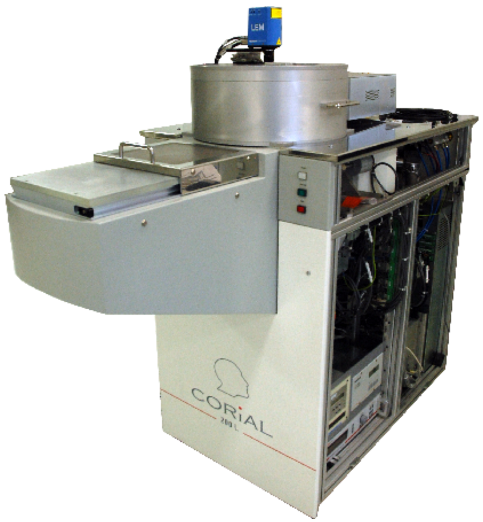
Etching

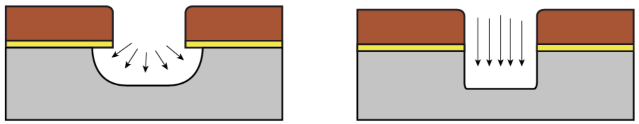
Wet etching : in liquid, acids and bases

Dry etching : plasma etching



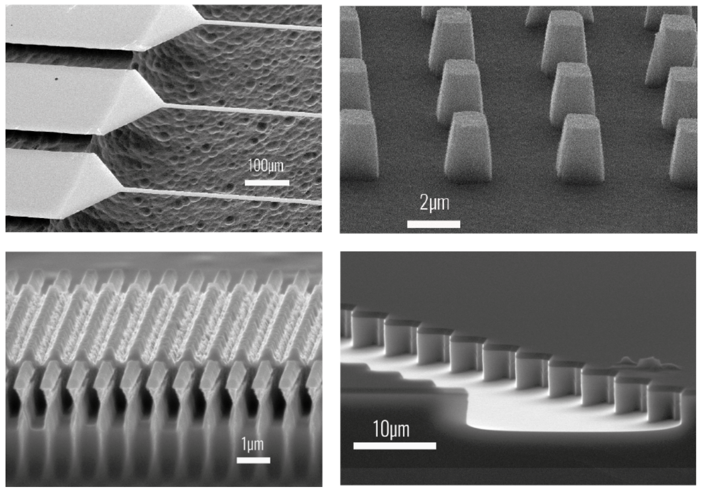




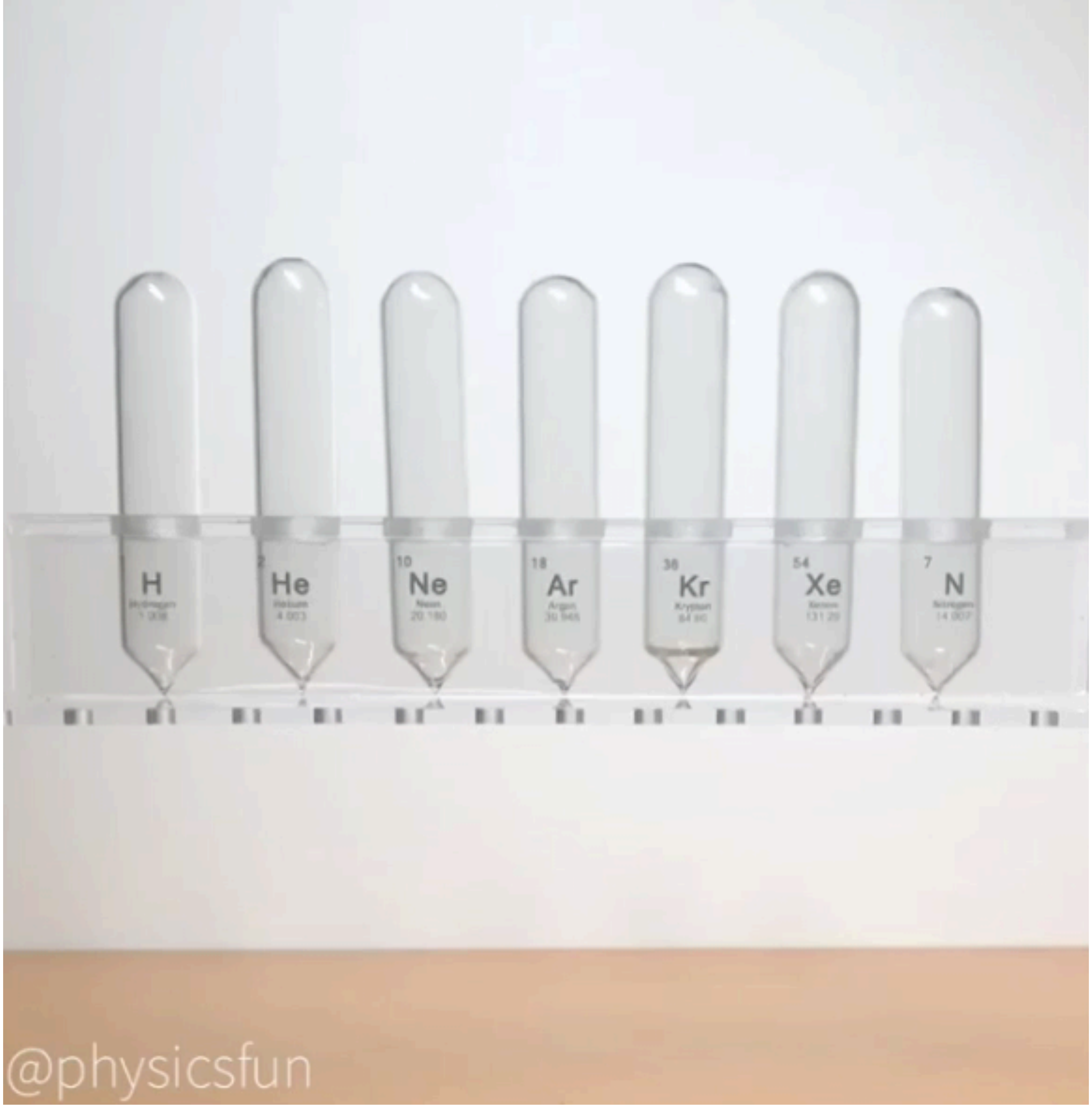


isotropic

anisotropic

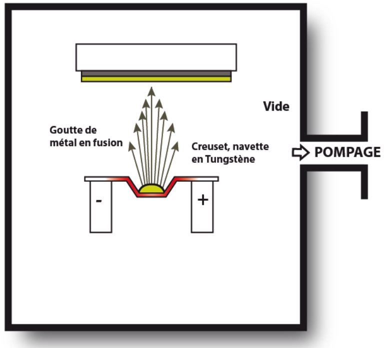


Plasma



Thin film deposition

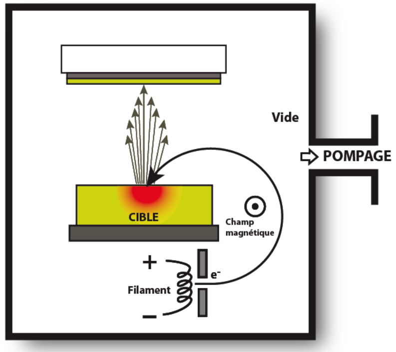
Evaporation



Aluminium, Gold, Chromium

Electron gun evaporator

Univex 350

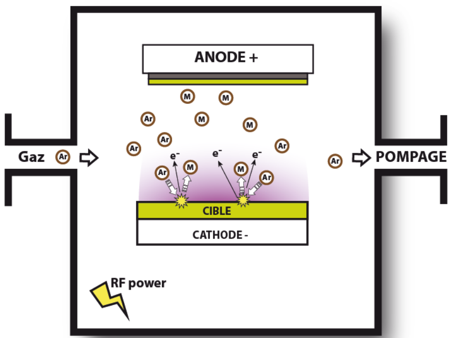


Gold, Platinum, Palladium
Titanium, Chromium

Sputtering

Univex 450

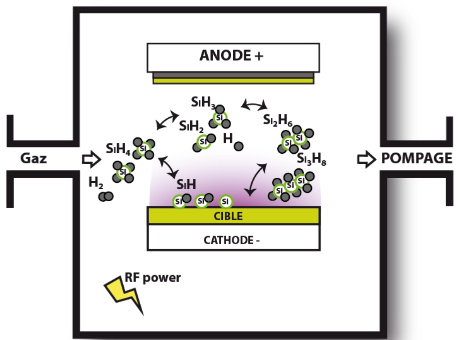
Alcatel SCM 600



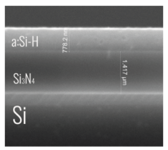
Or,Titanium, Chromium
Platinum, Al_2O_3, SiO_2,
Au/ge/Ni, Au/Zn, Au/Sn

Plasma enhanced chemical vapour deposition

Corial D250

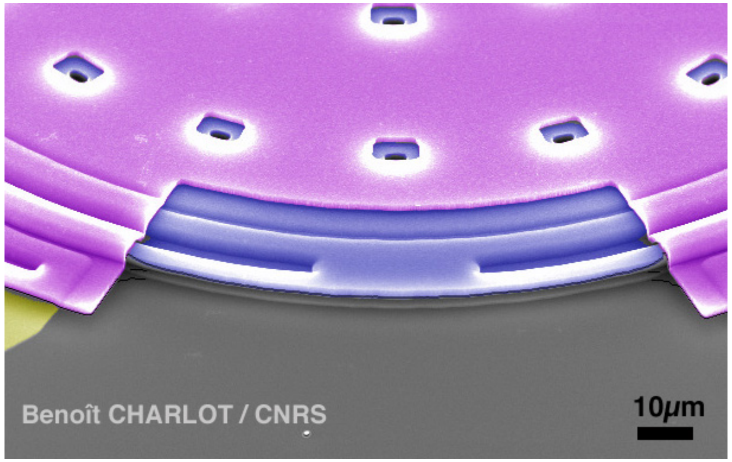


Si_3N_4, SiO_2, a:SiH

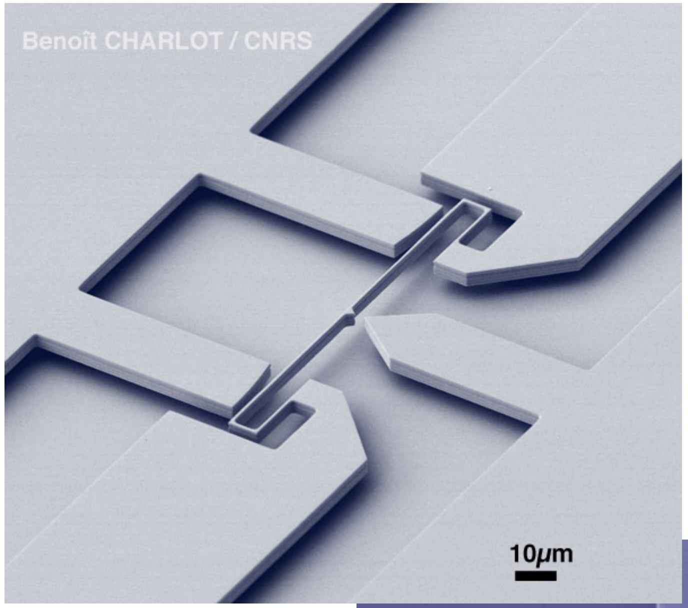


MEMS

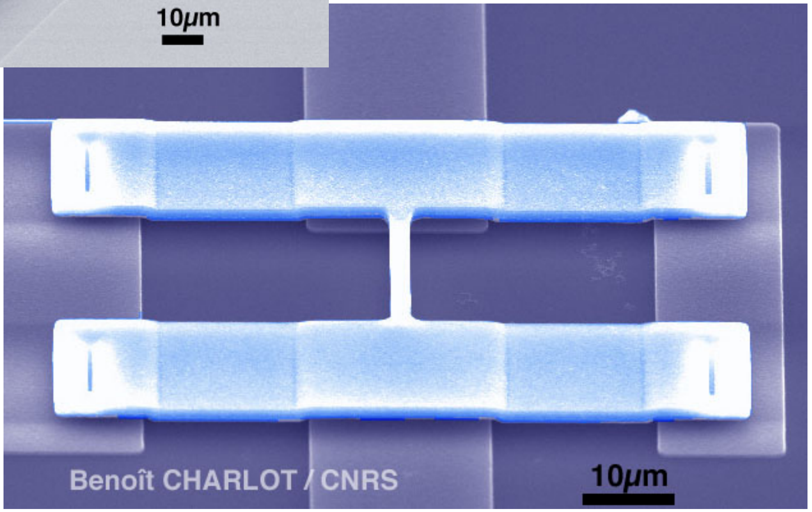
Micro
Electro
Mechanical
Systems



Micromechanics build from Microelectronic technologies



- Silicon substrate (Semiconductor, flat, pure)
- Thin film deposition (Metals, oxides, Nitrides, polysilicons, doping..)
- Lithography
- Etching (chemical, plasma)

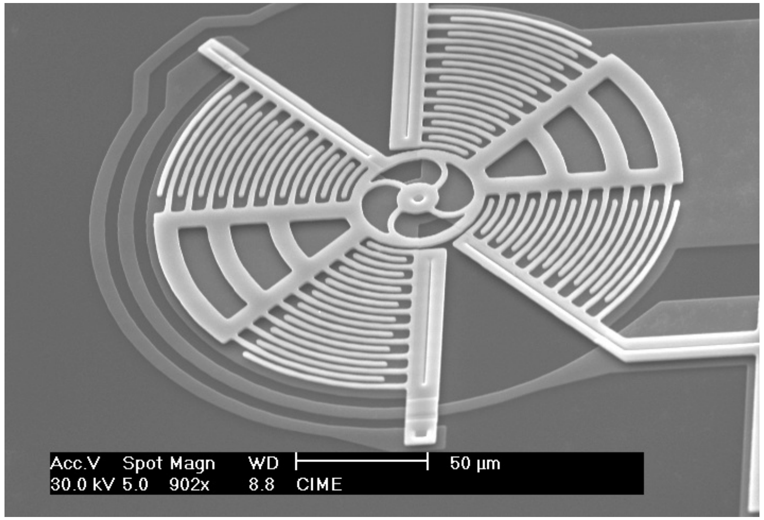


Sensors and actuators
Everywhere around us...

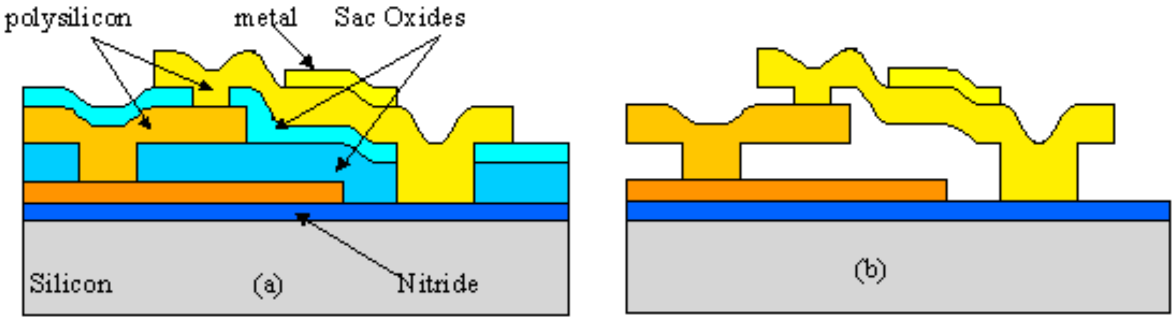
MEMS history

60's	Transistor Integrated Circuit Resonant gate transistor (1st MEMS)
70's	Pressure Sensor, magnetometers,
80's	Accelerometers, inkjet printers, surface micromachining
90's	Integrated Accelerometers, Gyrometers DMD DLP, RF MEMS, Microphones, oscillators, bolometers
2000	IMU, Autofocus, µspeakers, Energy Harvesting, joysticks BioMEMS, Nanotech, Lab On Chips

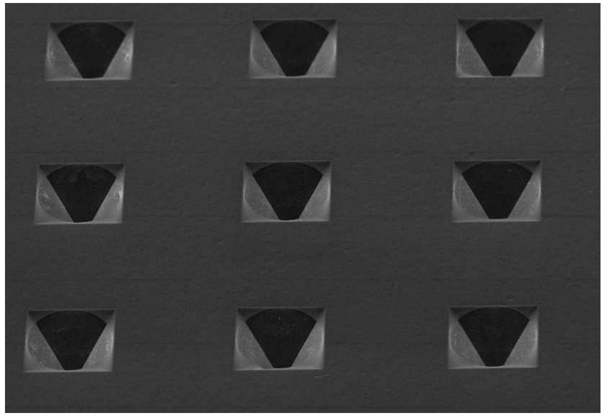
MEMS Microfabrication

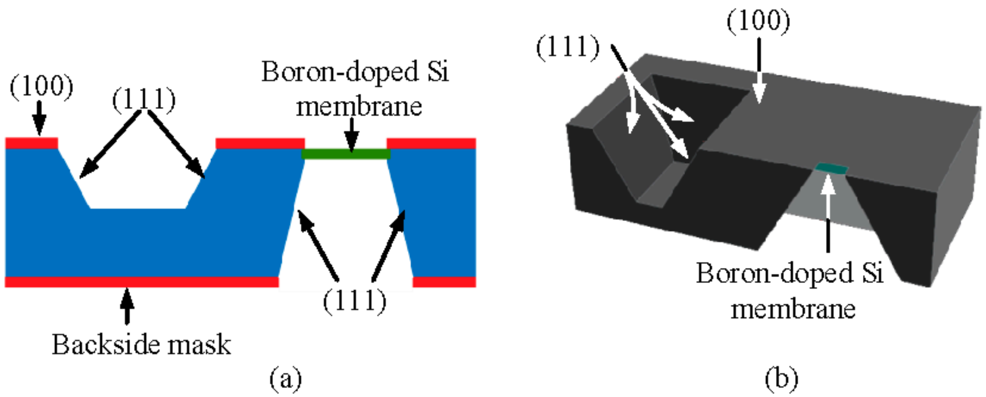


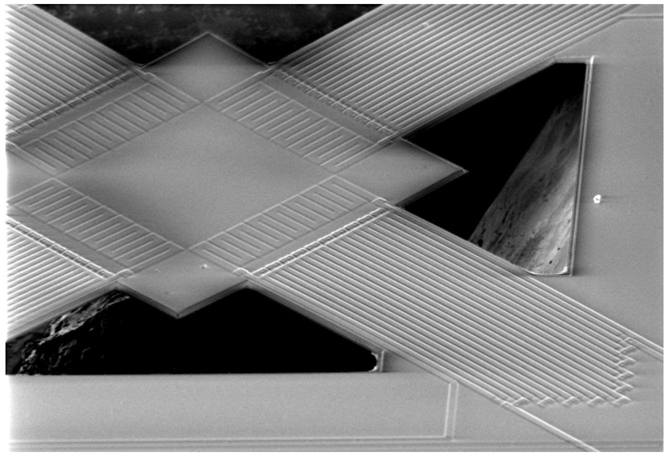
Surface micromachining : ex MEMSCAP MUMPS



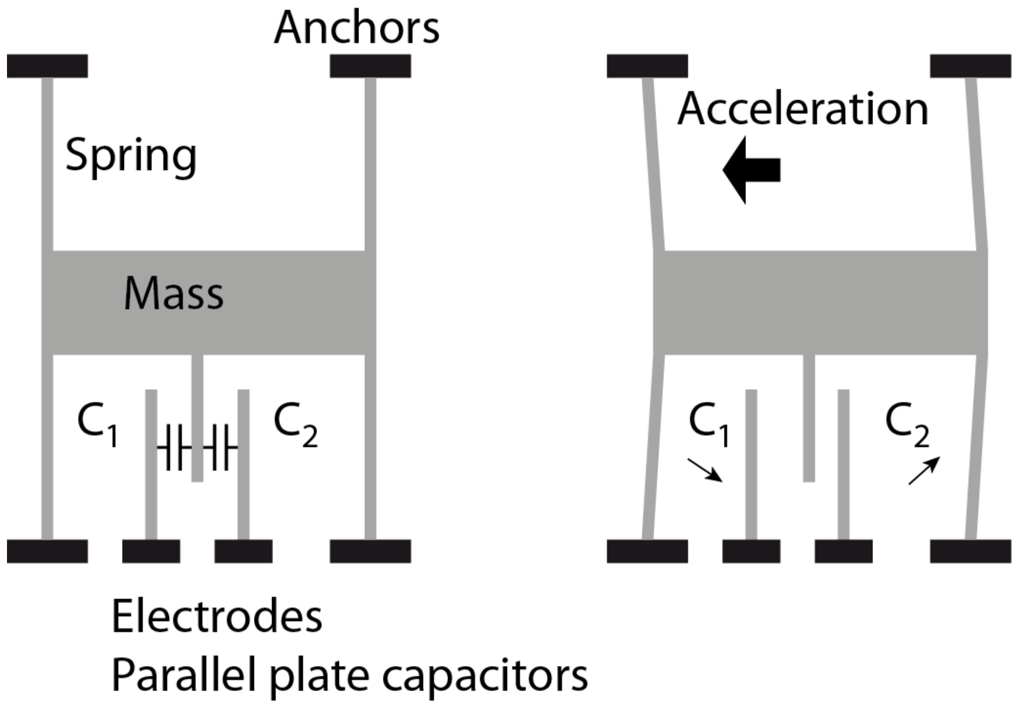
Bulk micromachining

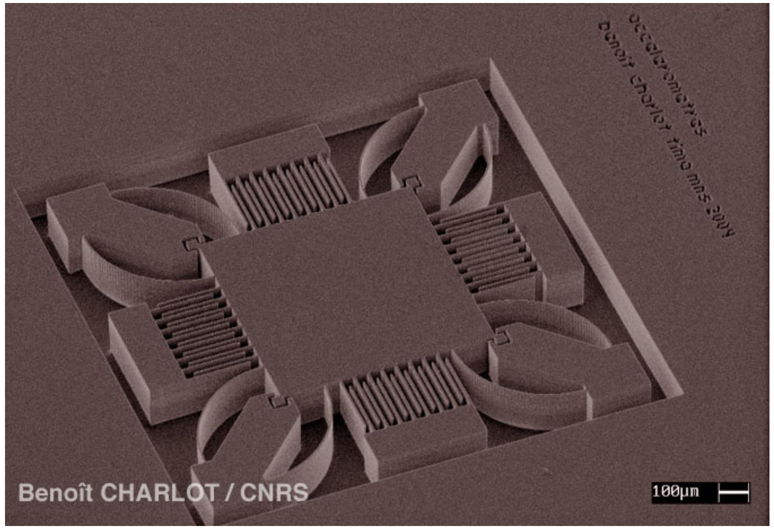






MEMS accelerometers





Analog Devices ADXL accelerometers

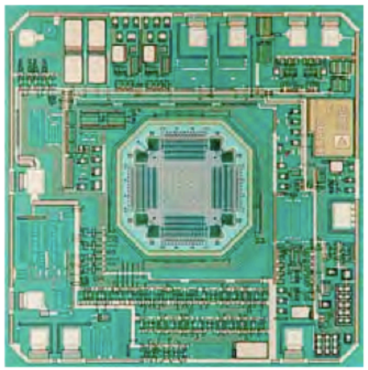
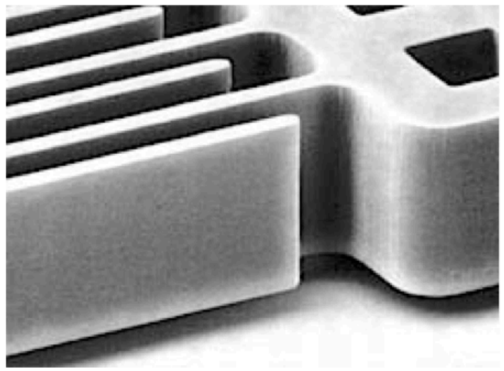
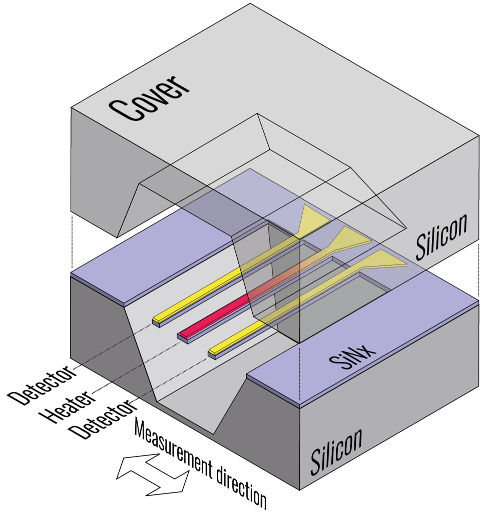




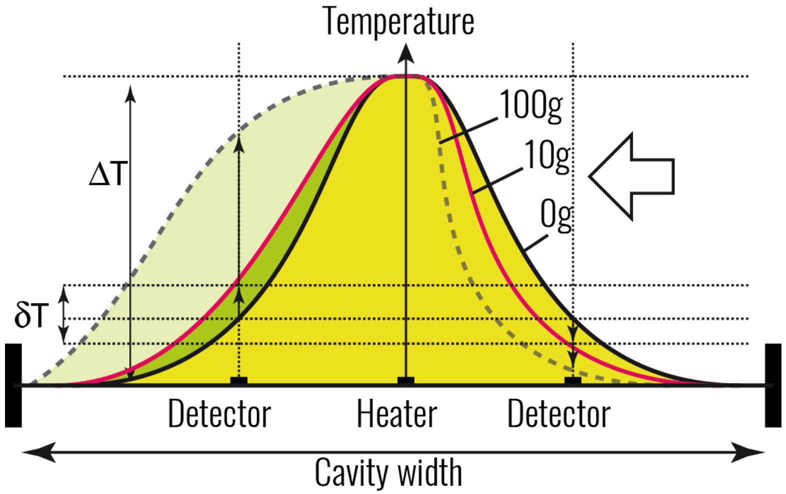
Image: Analog Devices

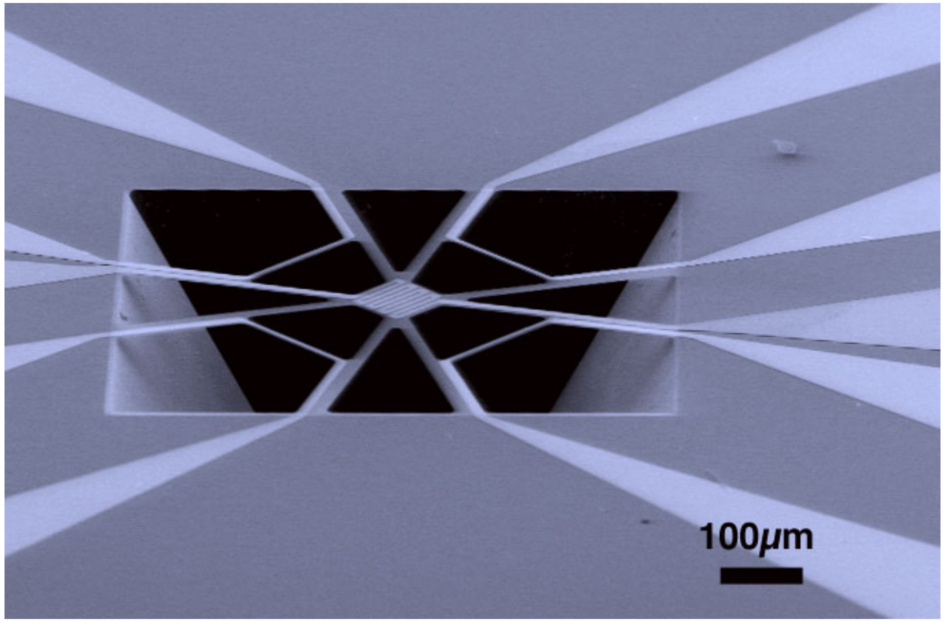
MEMS thermal accelerometers

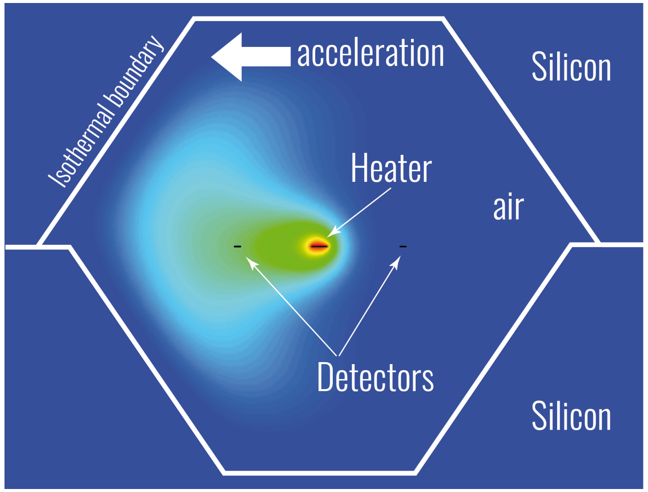
Seismic mass is a « bubble » of hot air
That has a different density than cold air

Movements of the hot air is sensed by
two thermometers





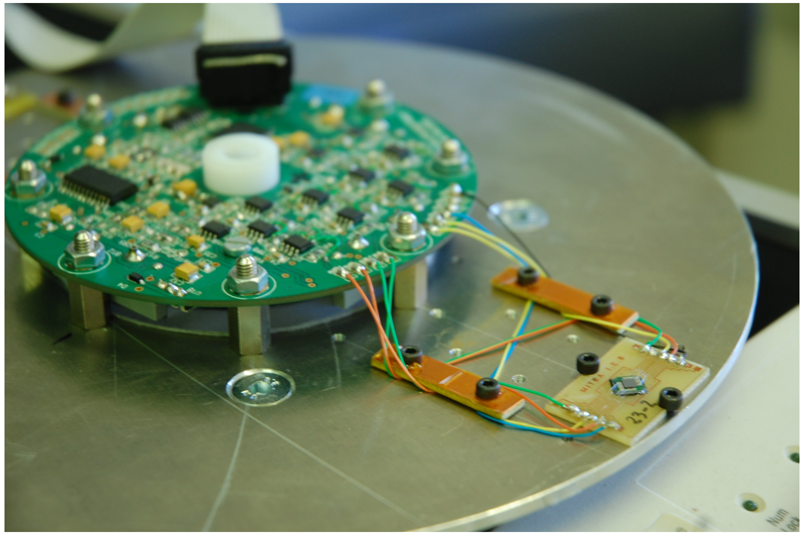


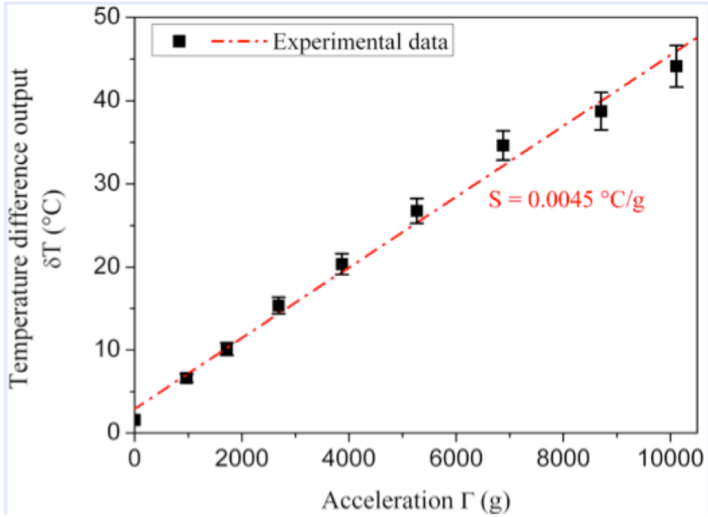


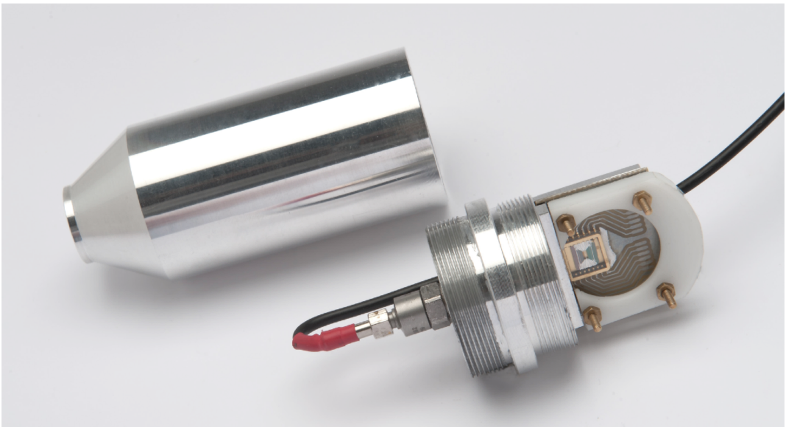
MEMS thermal accelerometers

Centrifuge testing

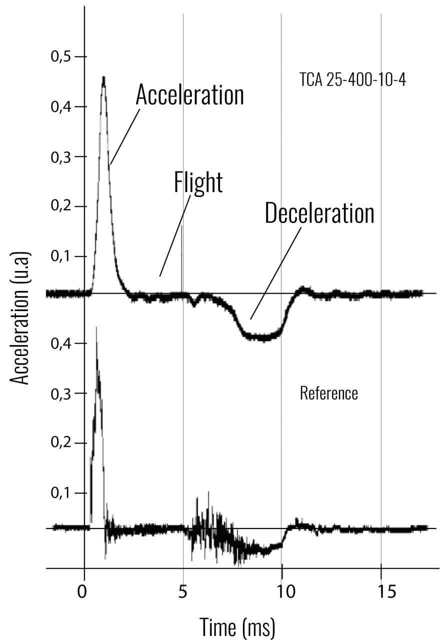
Up to 10000g measured





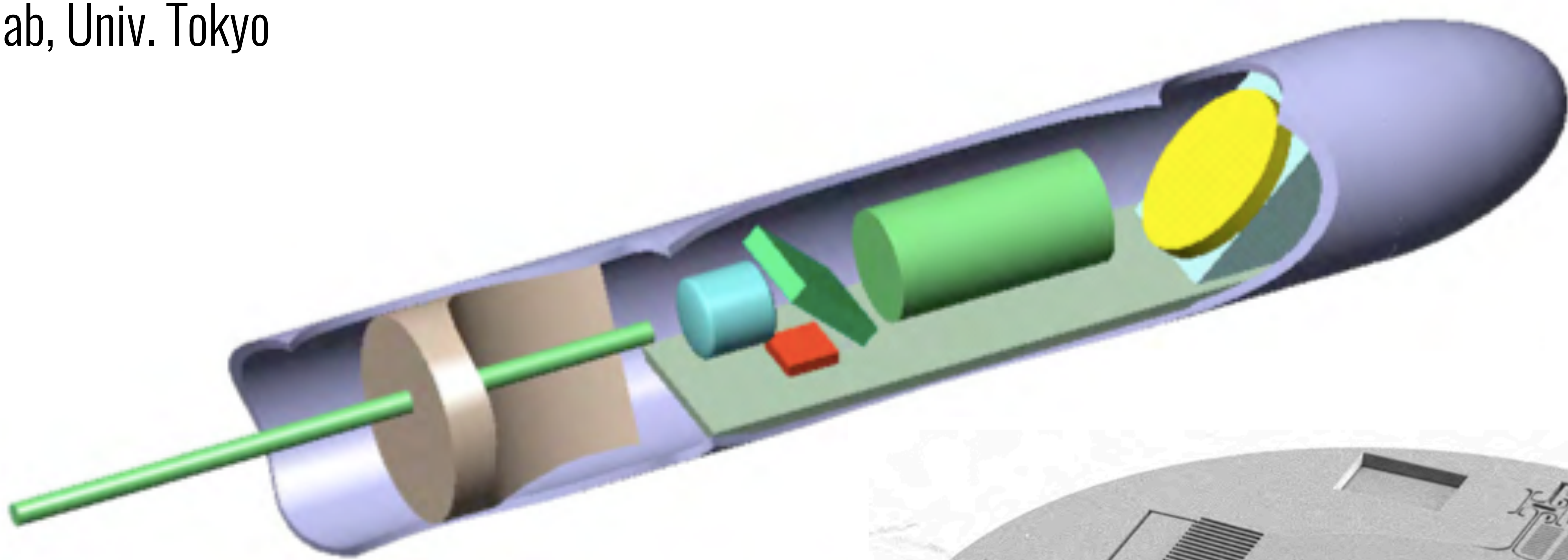


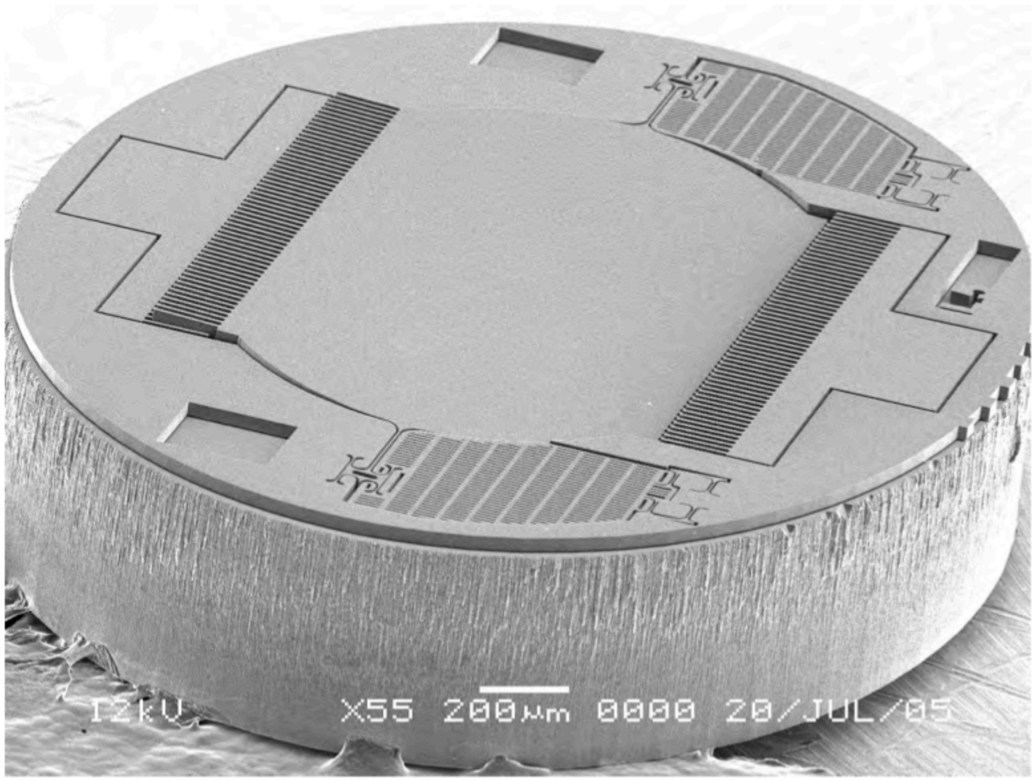
Missile launch



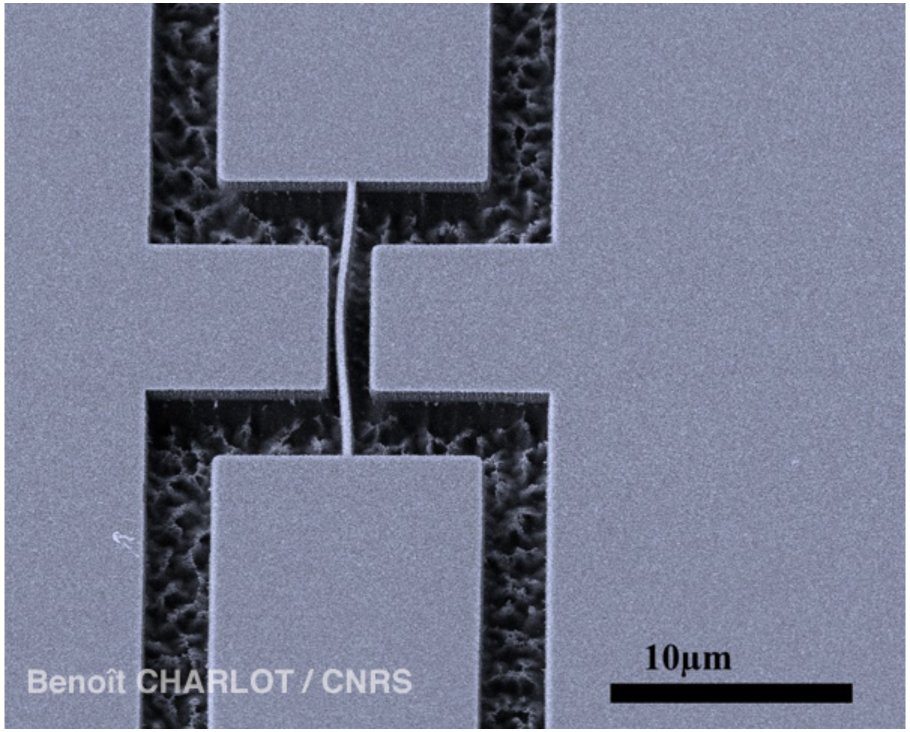
MEMS Endoscope

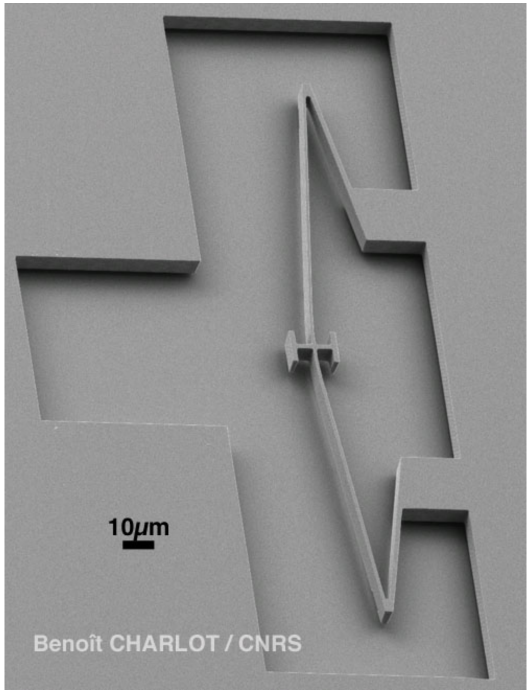
Toshilab, Univ. Tokyo

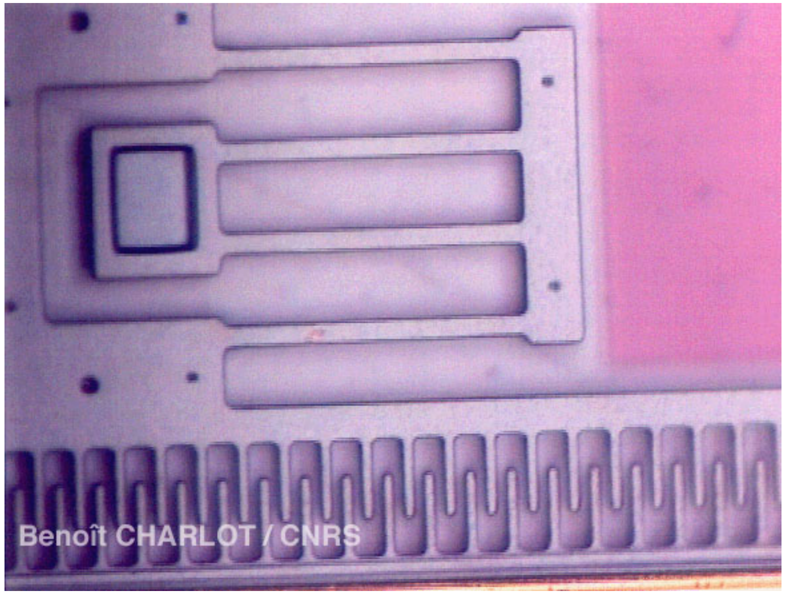


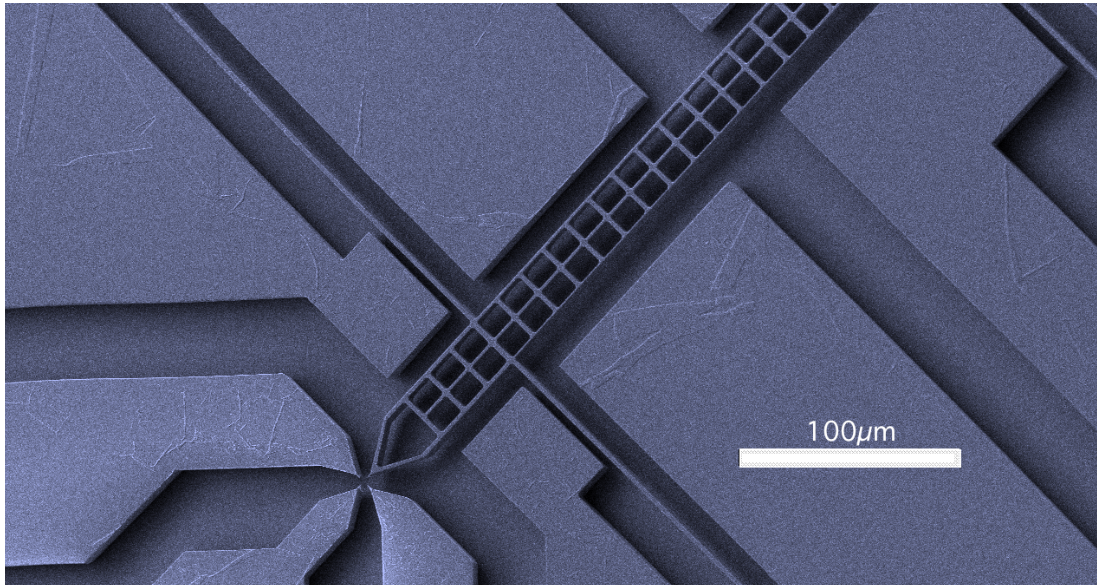


MEMS Resonators

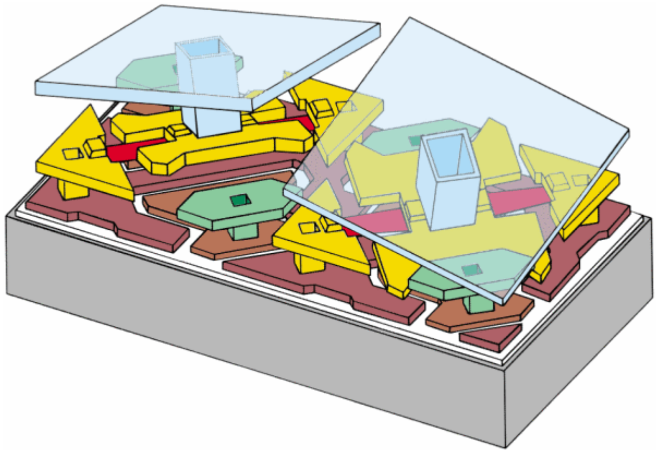


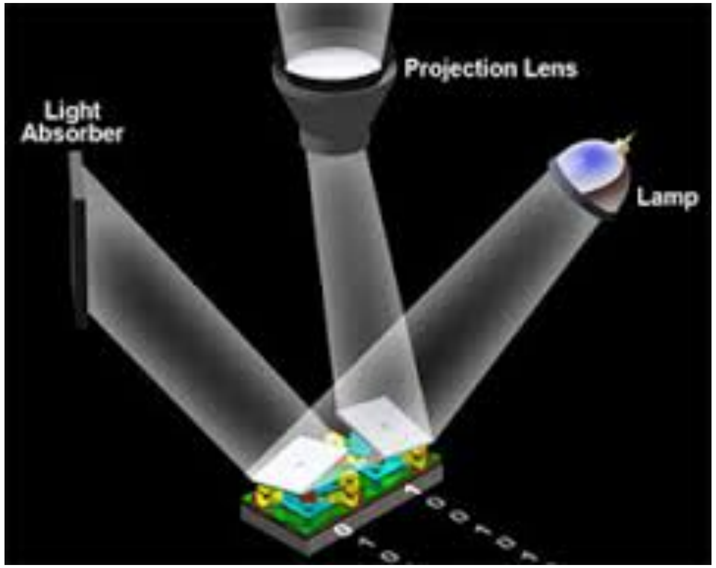


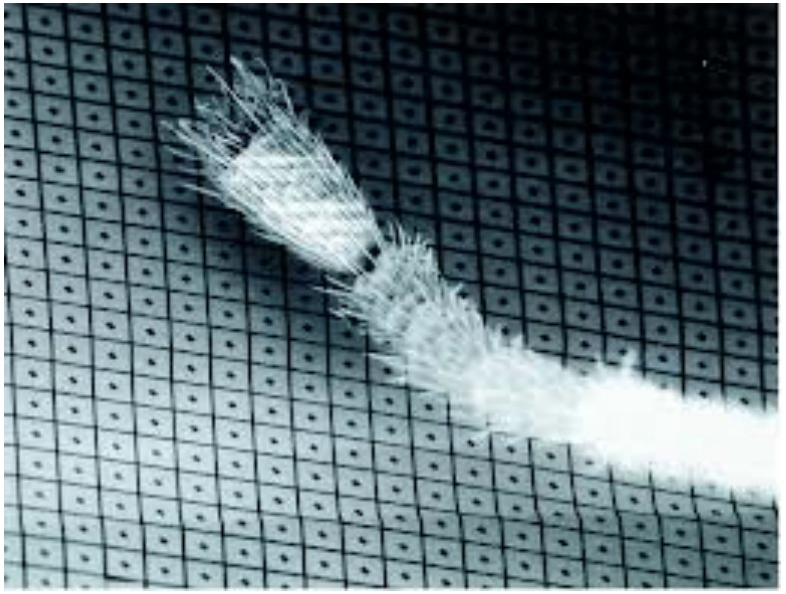


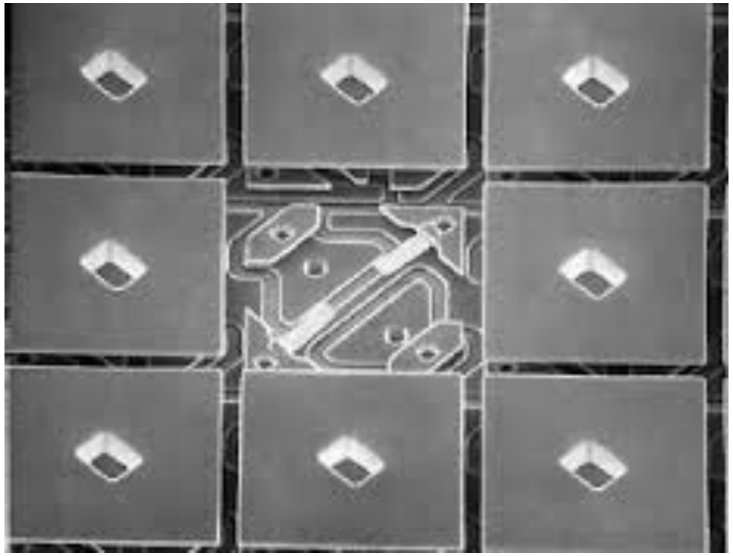


MEMS Micro Mirrors



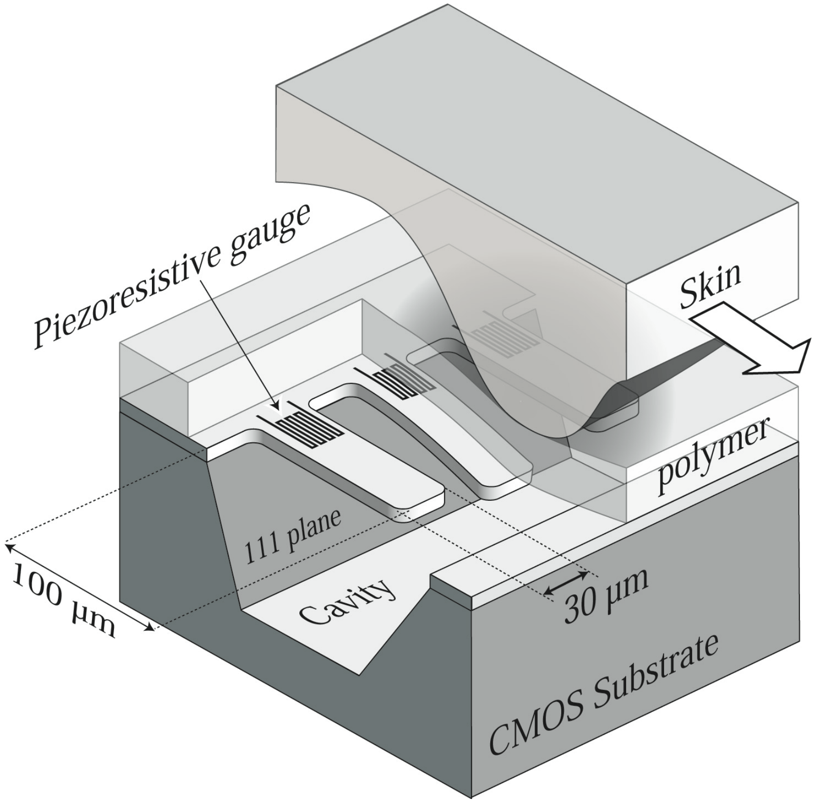


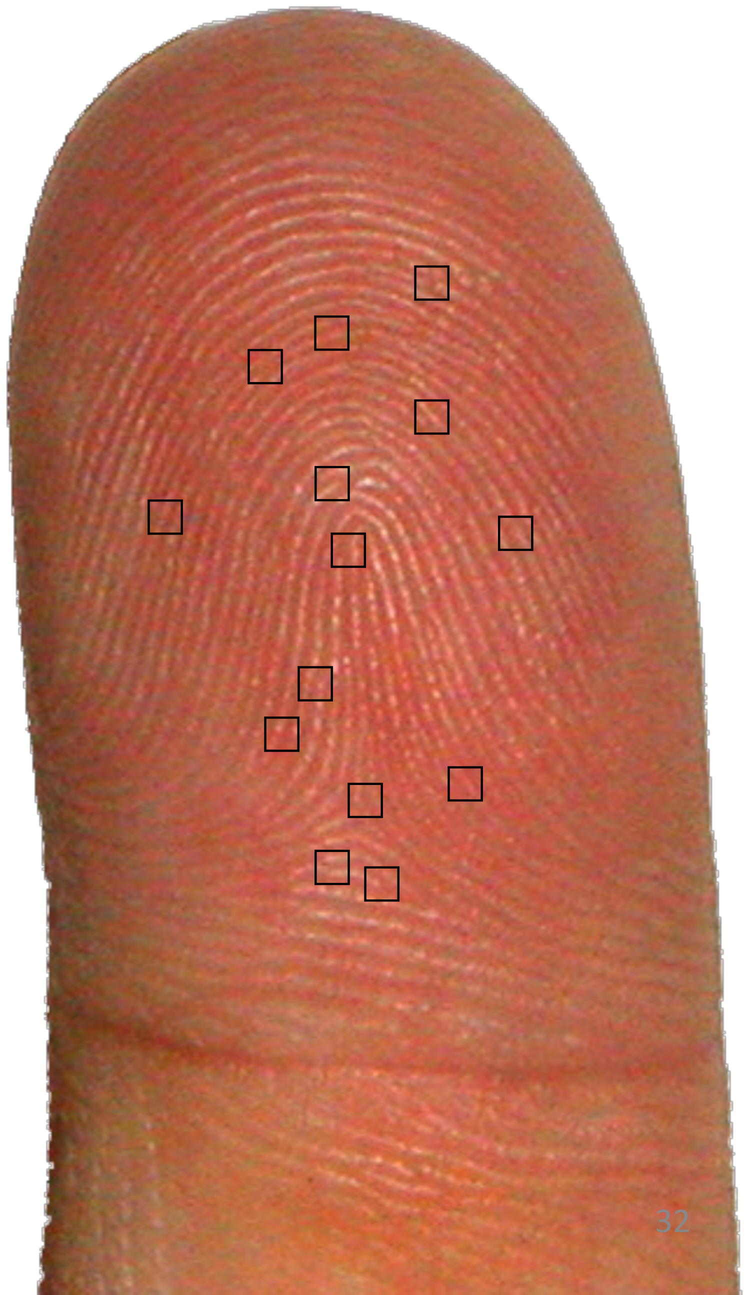


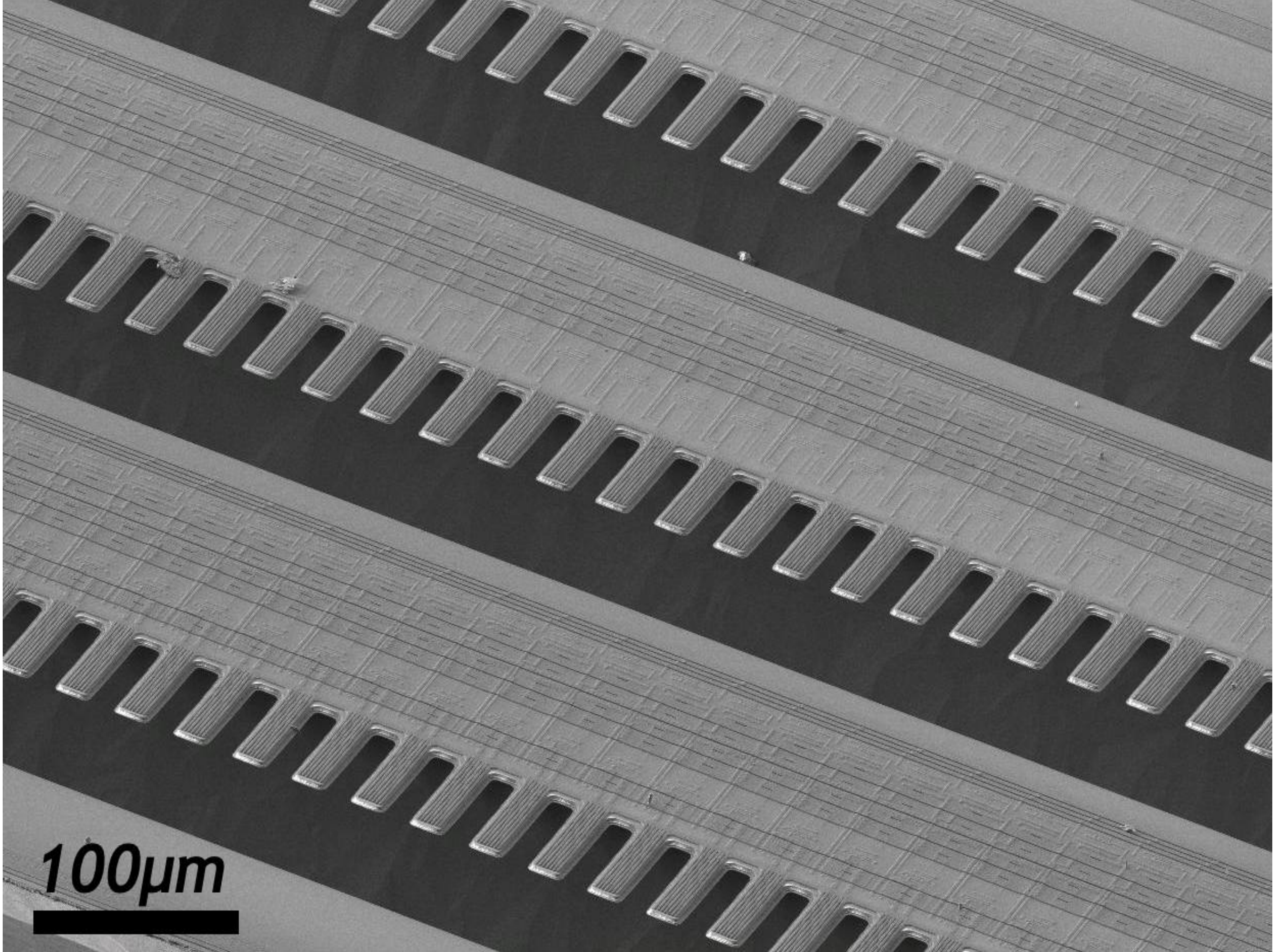


MEMS Fingerprint sensor

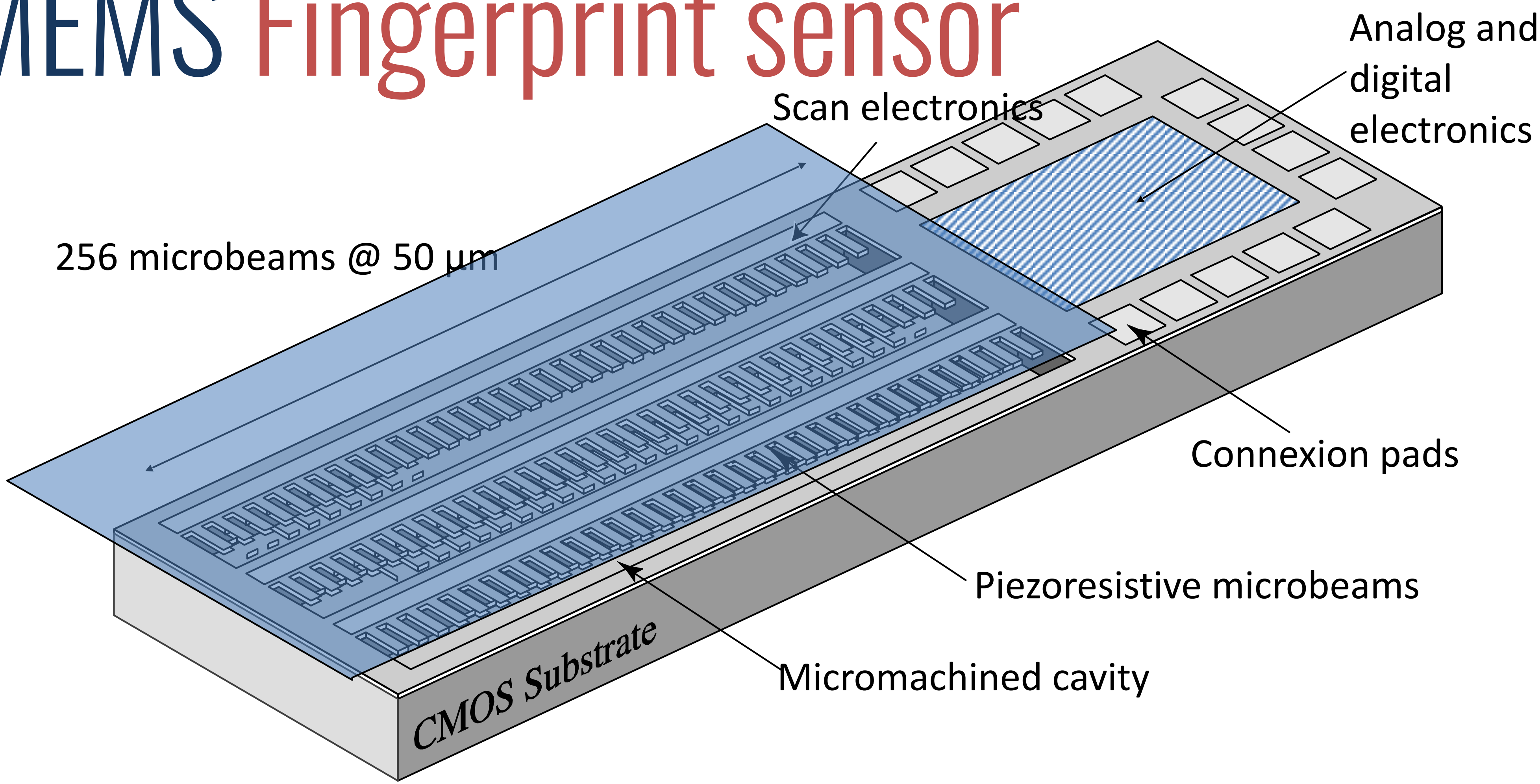
Integrated fingerprint sensor
Sweep mode

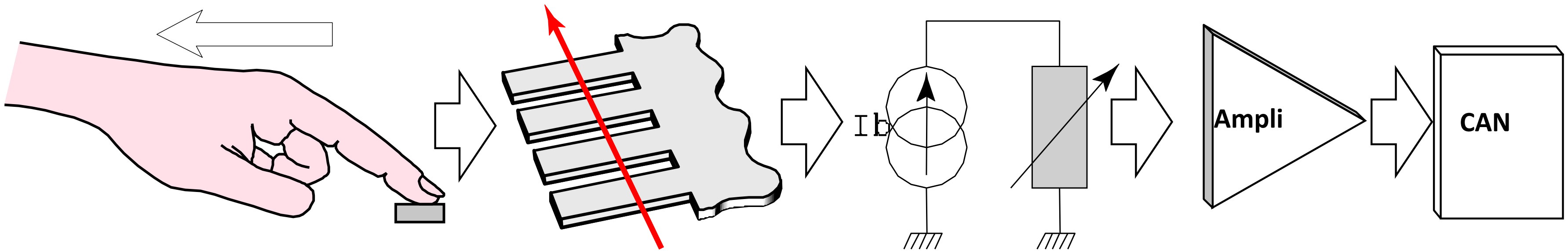





100μm

MEMS Fingerprint sensor





The user has to sweep his finger above the sensor

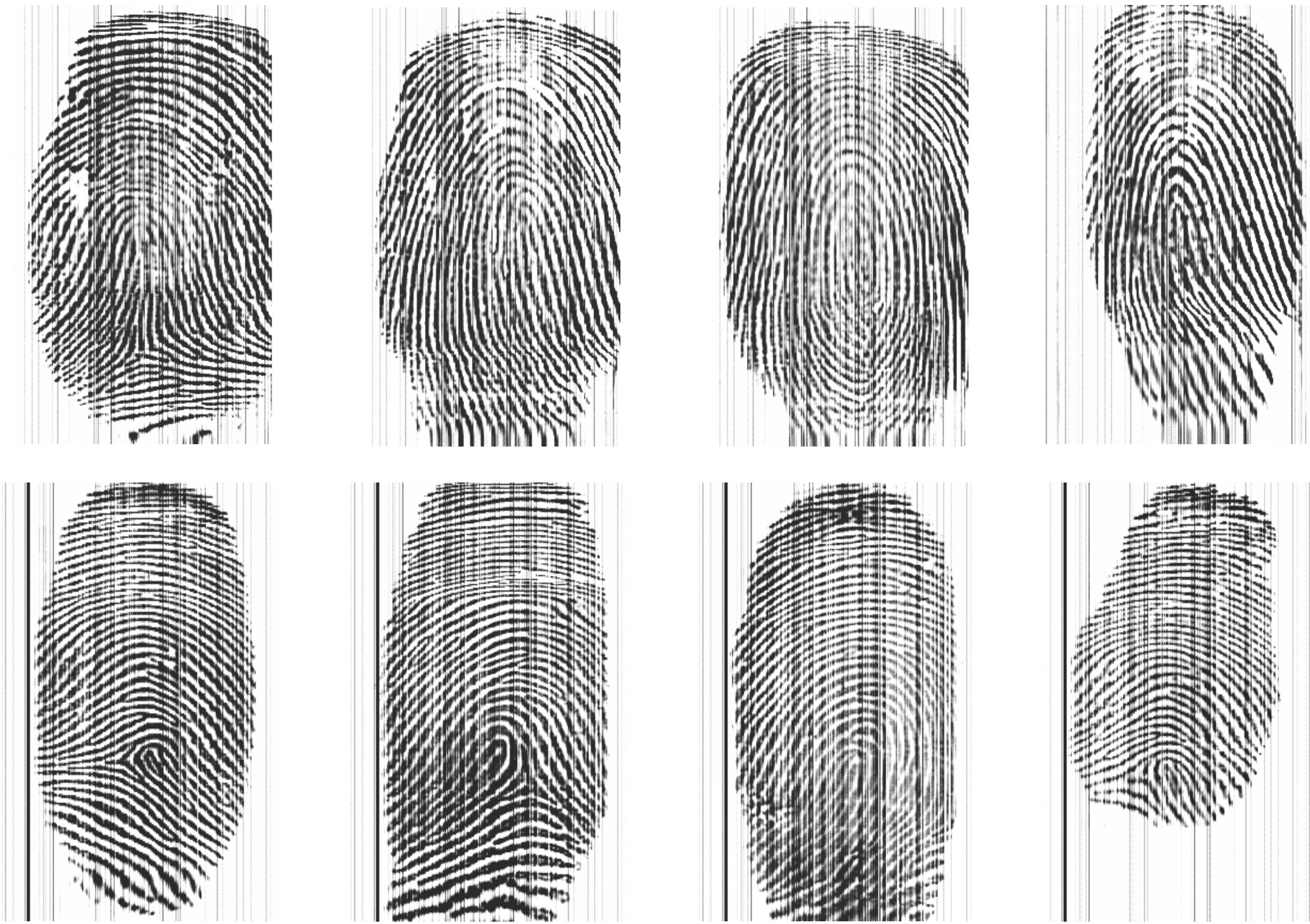
Scanning of the pixel line

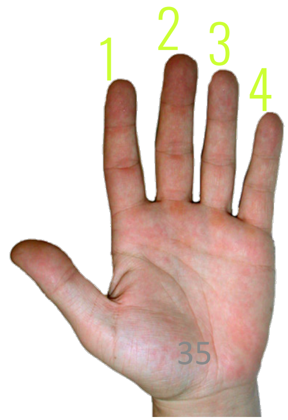
Transduction

Amplification

Conversion 8-bit ADC

MEMS Fingerprint sensor





Clean room

Clean room

Lab on a Chip and Microfluidics

Benoît CHARLOT

http://www.ies.univ-montp2.fr/~charlot/

l'institut d'électronique