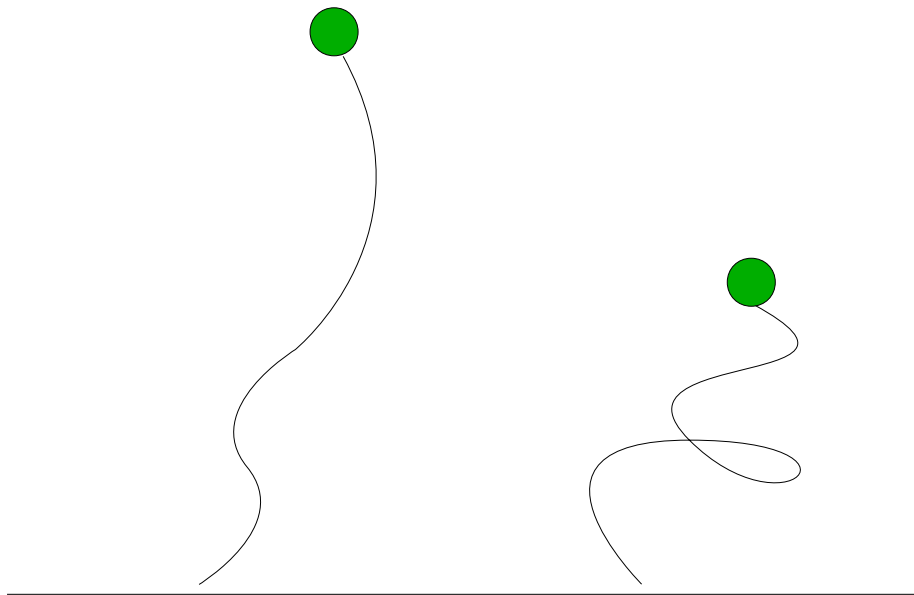


Presentation Phys 730 - Katia GASPERI

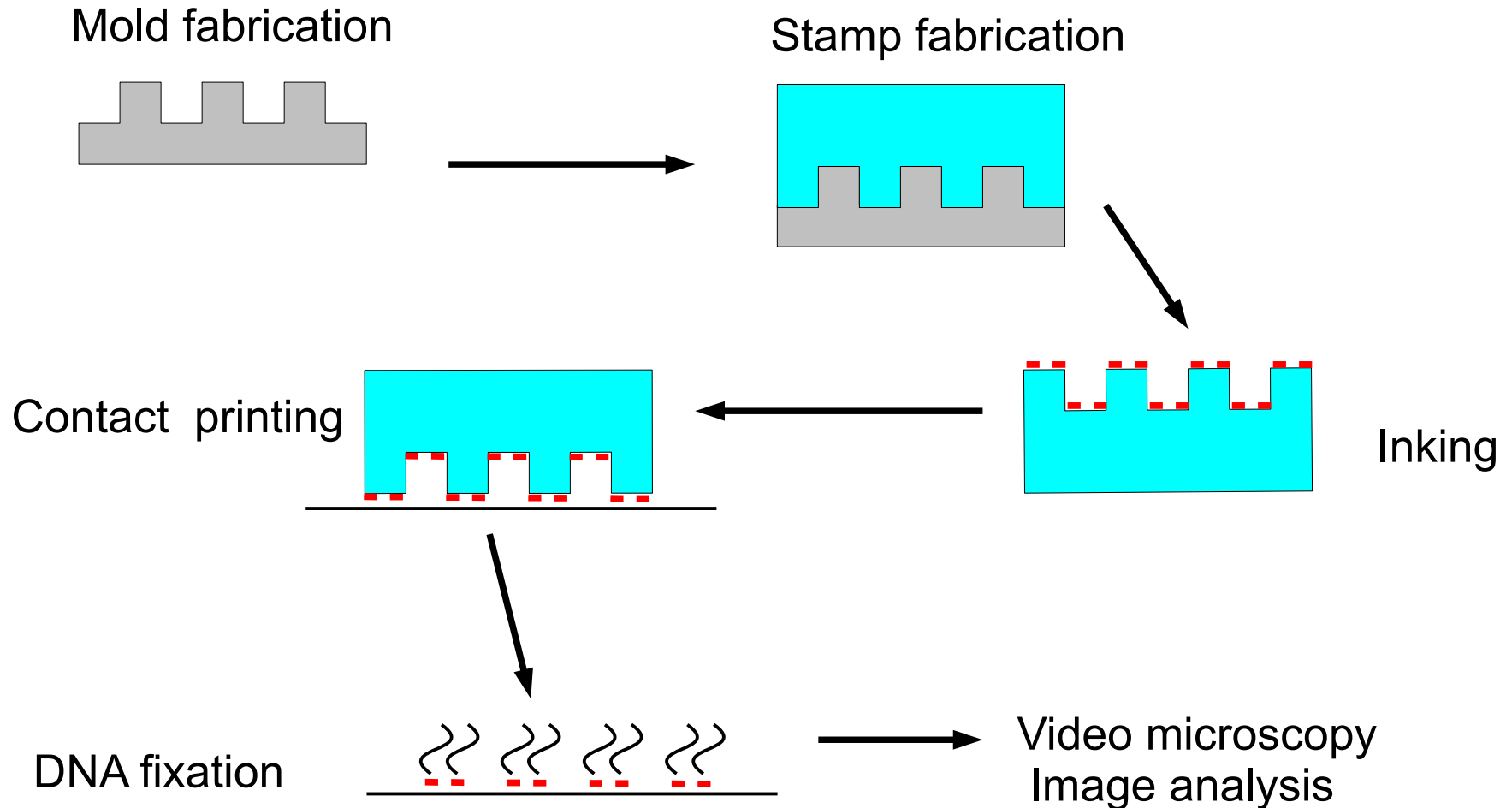
# Statistical study of single DNA molecules into dynamic array



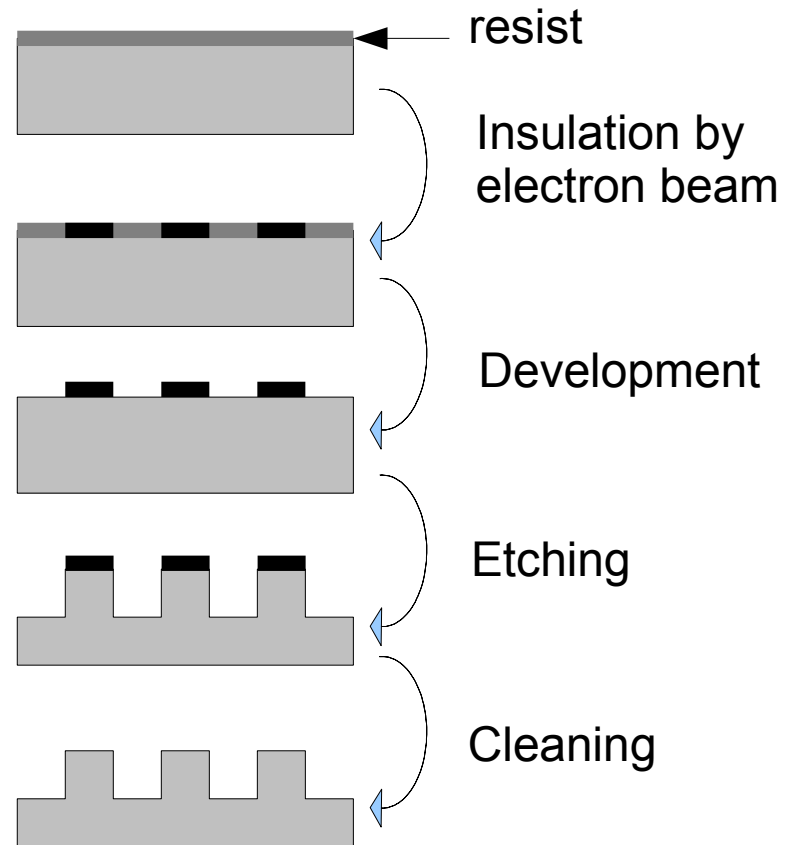
# Statistical study of single DNA molecules into dynamic array

- *Research project lead by Laurence SALOME and  
Christophe VIEU (collaboration IPBS / Laas-  
CNRS, Toulouse, France)*
- *The project initially was expected to involved 4/5  
teams.*

# The project step by step

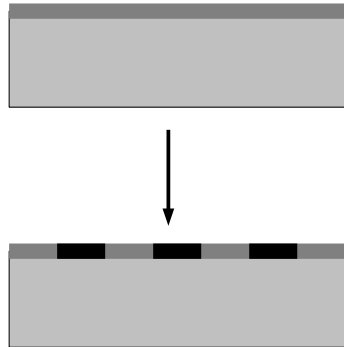


# Mold fabrication



# Mold fabrication : EBL

- EBL = Electron Beam Lithography



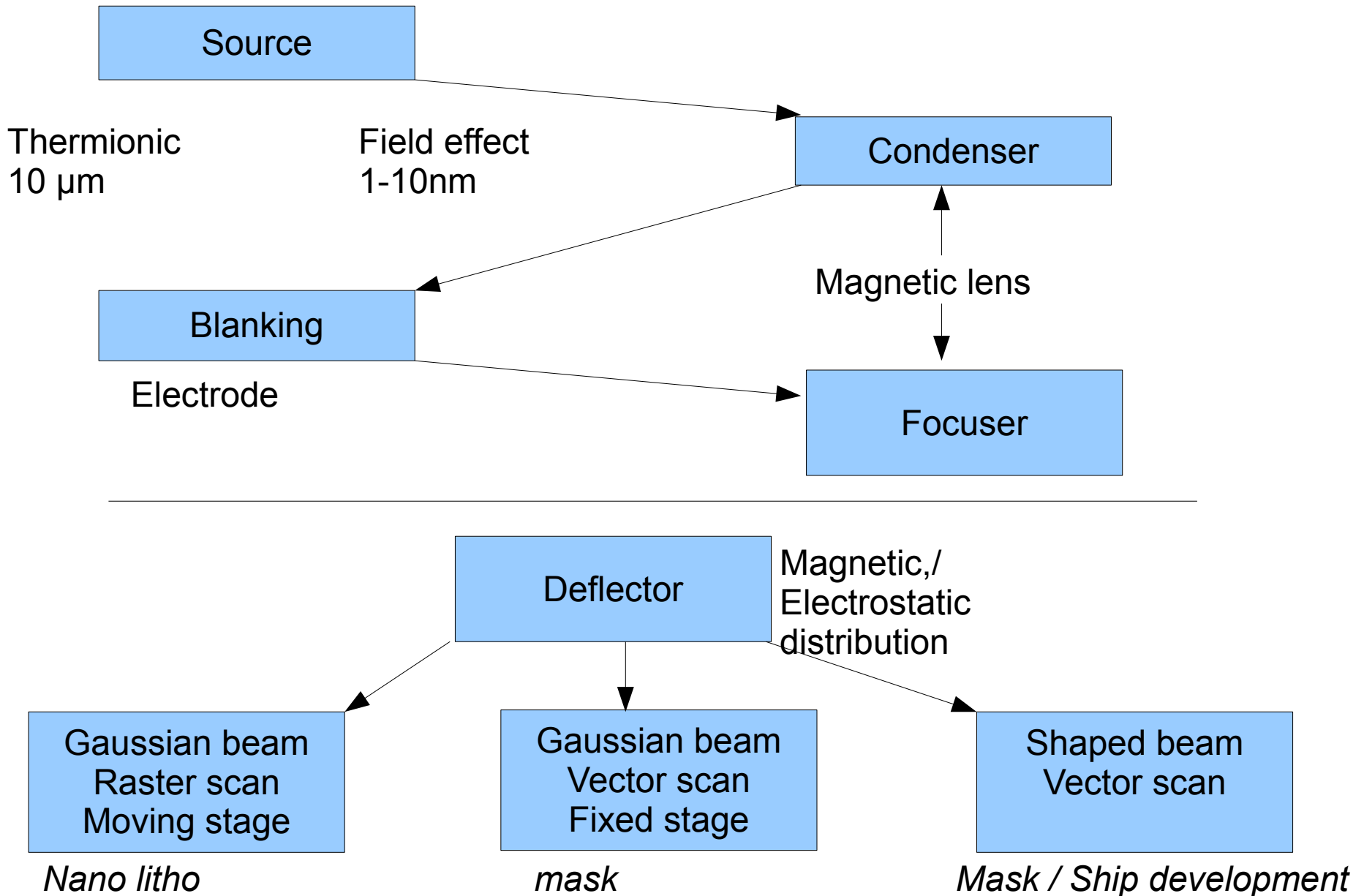
- Slow and expensive process
- High resolution



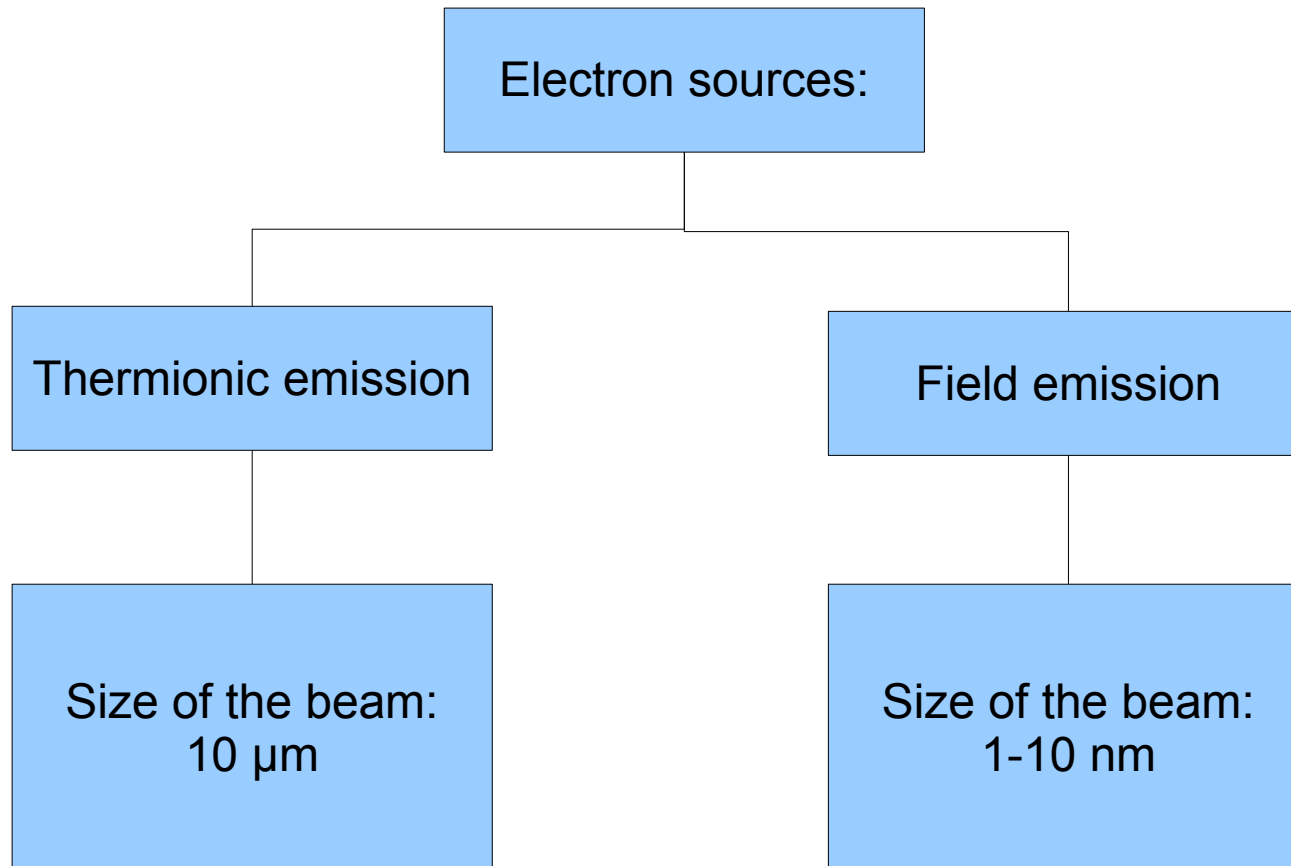
CM20

[www.stevens.edu/lmsi/Instrument/Instrument.htm](http://www.stevens.edu/lmsi/Instrument/Instrument.htm)

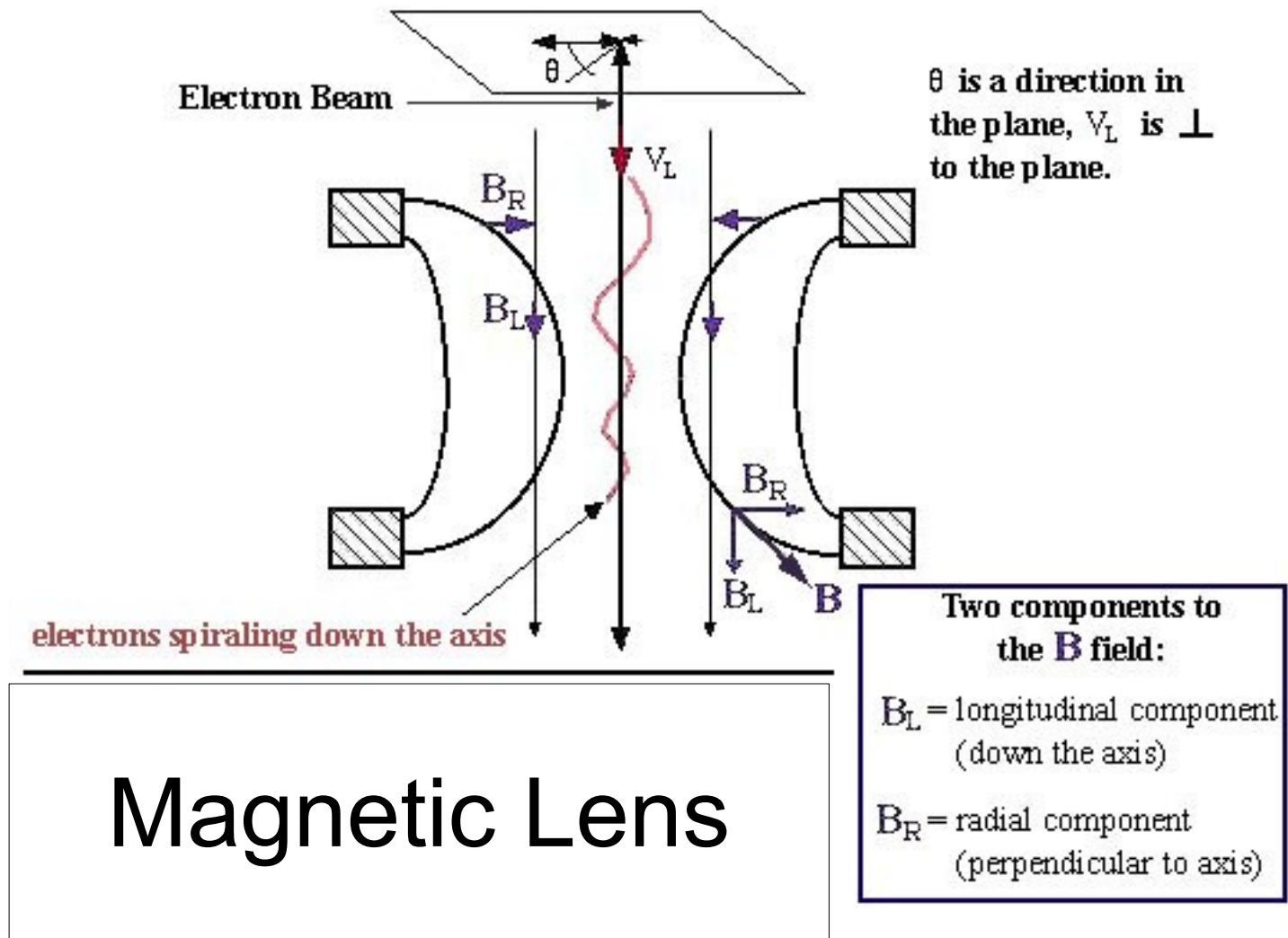
# Mold fabrication : EBL



# Mold fabrication : EBL Source



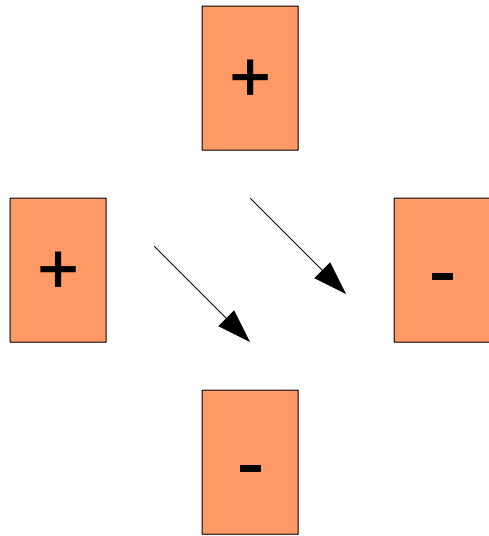
# Mold fabrication : EBL



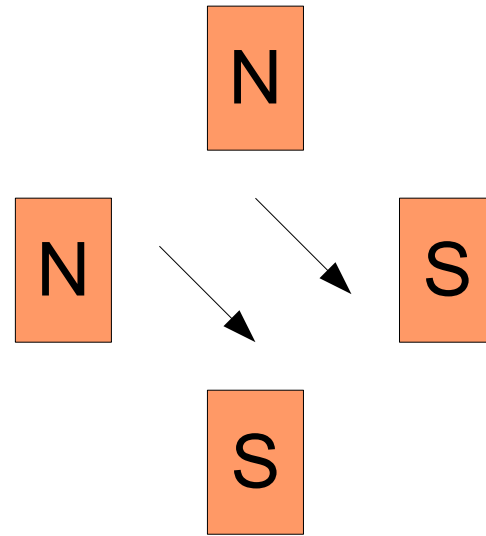


# Mold fabrication : EBL Deflector

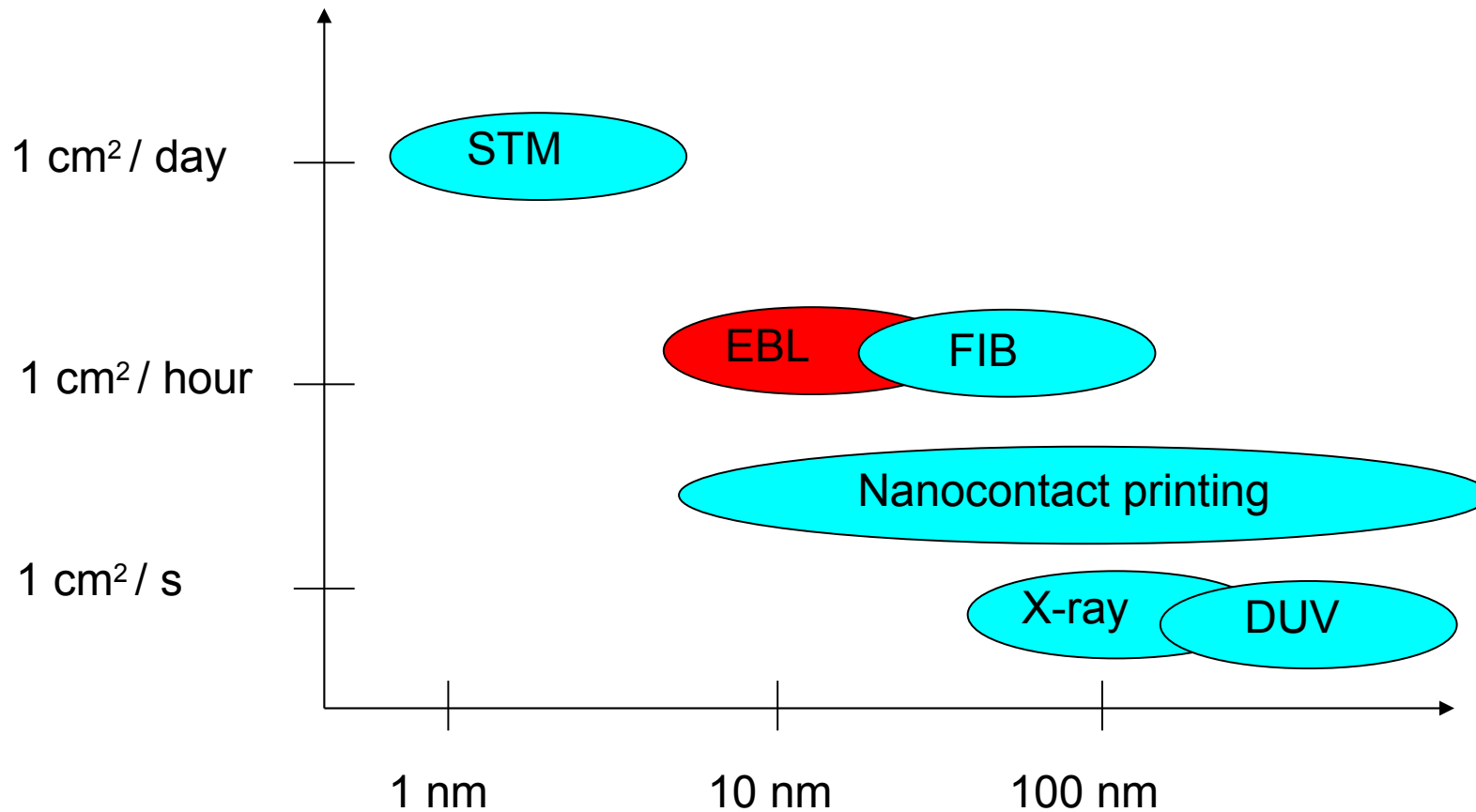
Electrostatic field



Magnetic field



# Mold fabrication : EBL



**STM = Scanning Tunneling Microscope**

**EBL = Electron Beam Lithography**

**FIB = Focused Ion Beam**

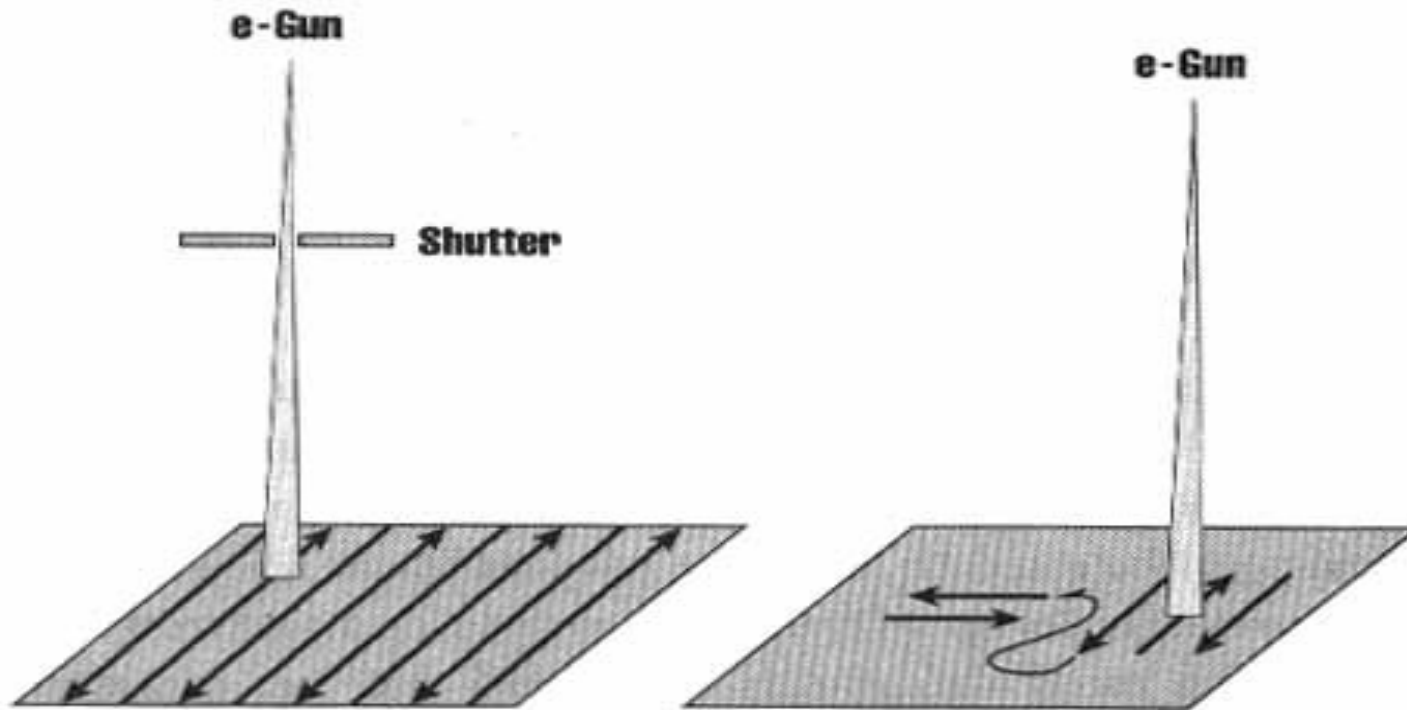
# Mold fabrication : EBL Blanker

Role: turning the beam on and off

- pair of plates set up as a simple electrostatic deflector
- fast response time

To turn the beam off, a voltage is applied across the plates which sweeps the beam off axis until it is intercepted by a downstream aperture.

# Mold fabrication : EBL Scanning methodologies



Raster scan

Vector scan

# Mold fabrication : EBL Aberrations

$$d = \sqrt{d_g^2 + d_s^2 + d_c^2 + d_d^2}$$

$d_g$  : size of the source / demagnification

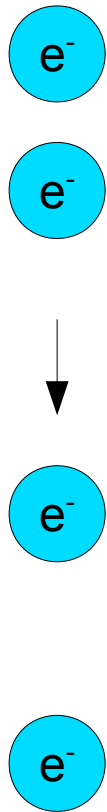
$d_s$  : spherical aberration

$d_c$  : chromatic aberration

$d_d$  : diffraction limit

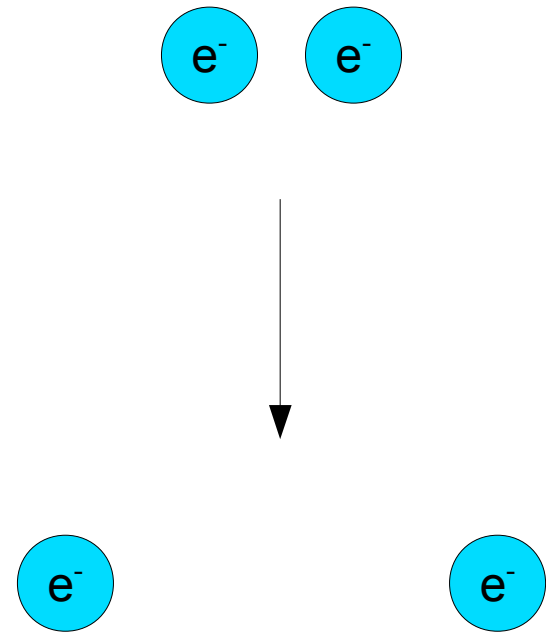
# Mold fabrication :EBL and more aberrations...

Boersh effect:



Energetic dispersion  
Chromatic aberration

Loeffler effect



Modification of the path  
Spherical aberration

# Mold fabrication : EBL Time

$$\text{Dose} = it/S$$

## Example:

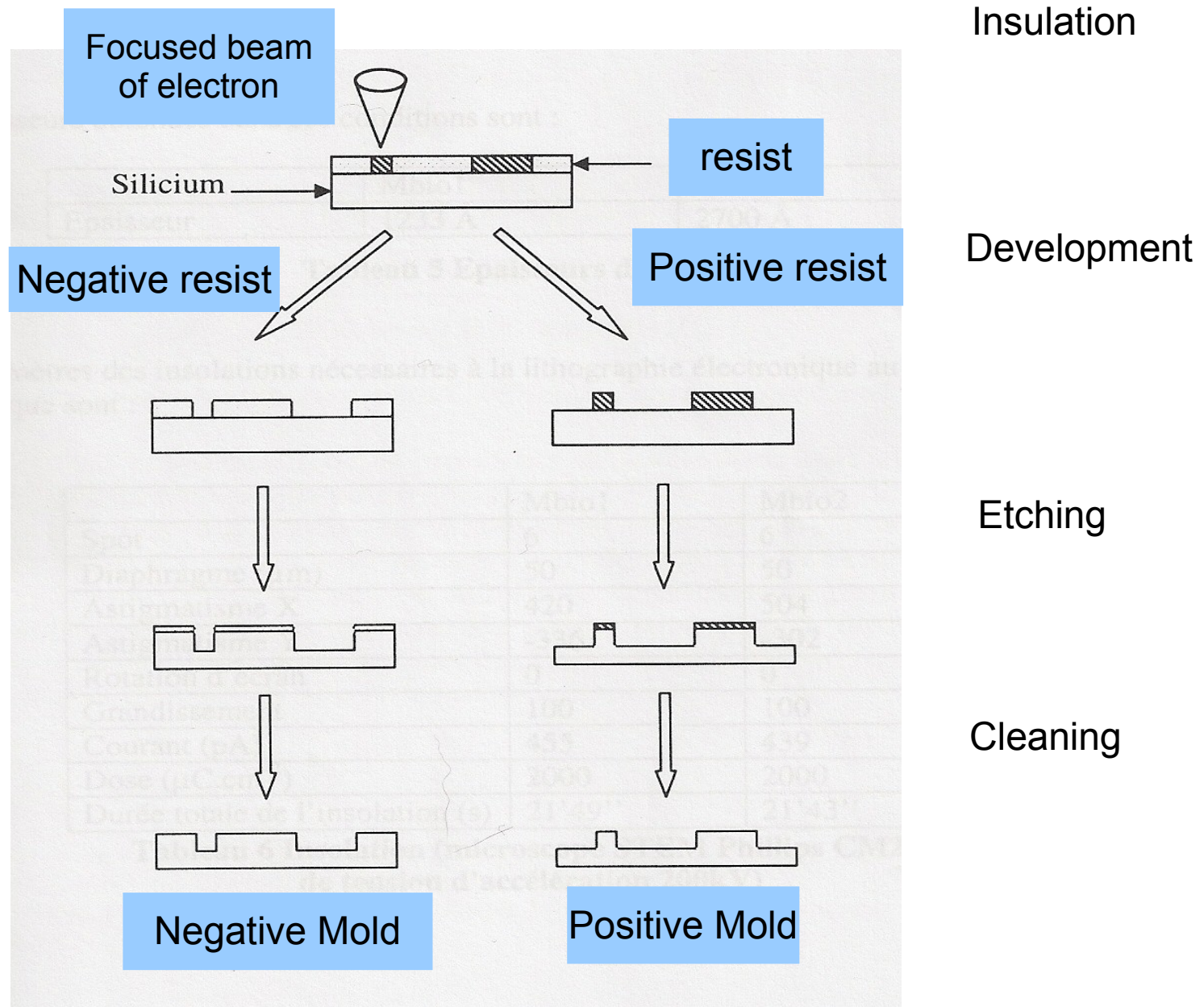
Current  $i = 450 \text{ pA}$

Dose =  $2000 \text{ } \mu\text{C} \cdot \text{cm}^{-2}$

Surface  $S = 2.8 \cdot 10^{-4} \text{ cm}^2$

→  $t = 23 \text{ minutes}$

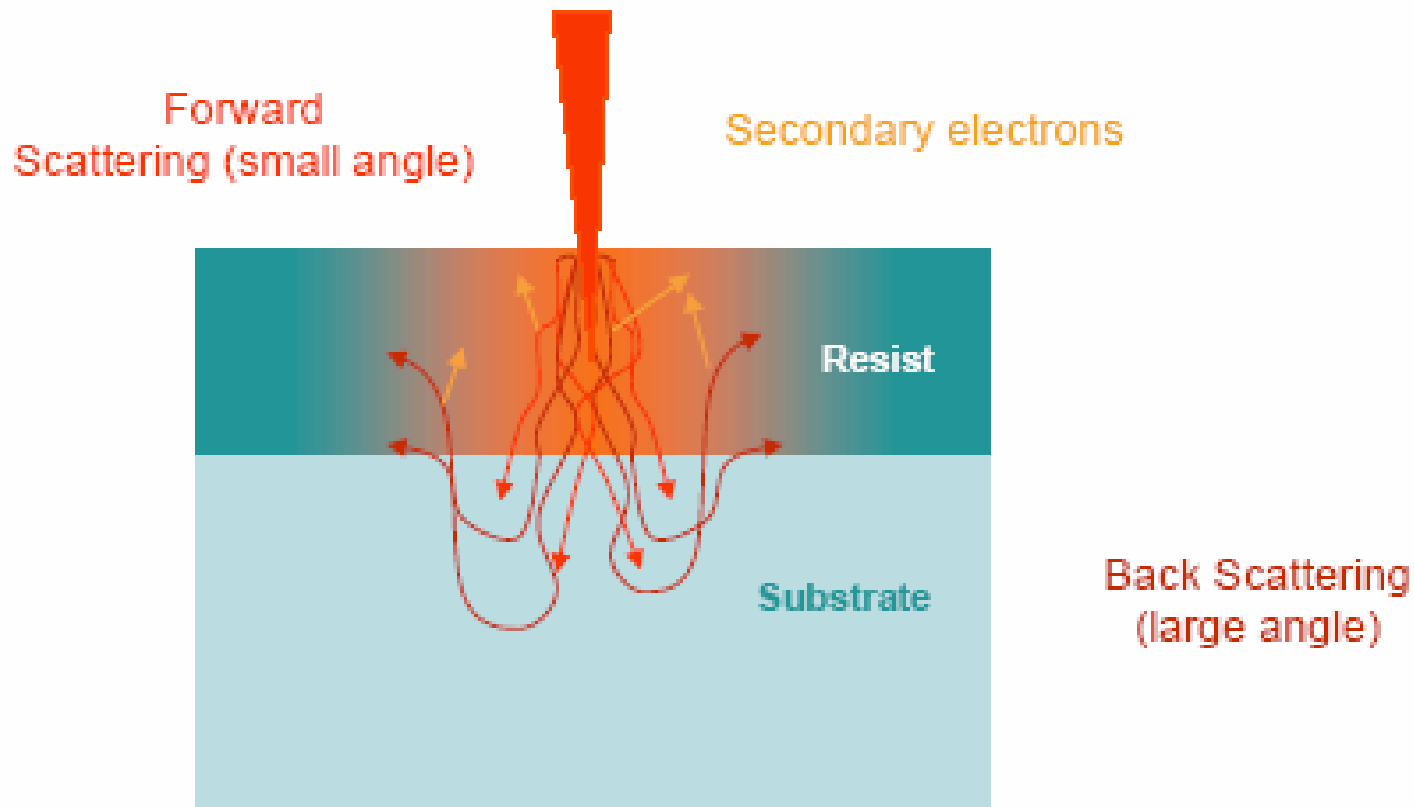
# Mold fabrication: positive/negative resist





# Mold fabrication : Resist

## Electron Scattering in Resist and Substrate

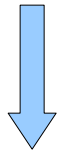


The scattered electrons also expose the resist!

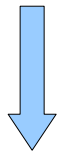
# Mold fabrication : Resist

**Positive resist:**

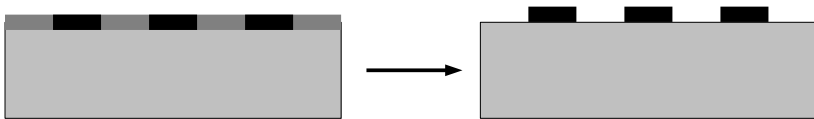
Bonds breaking



Molecular Weight ↘



Solubility ↗ in the developer

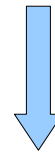


**Negative resist:**

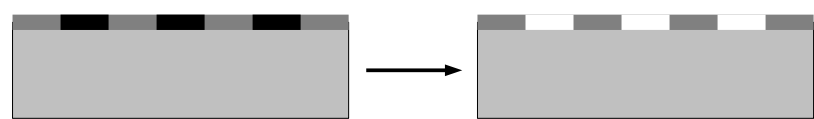
Cross linking



Molecular Weight ↗



Solubility ↘ in the developer

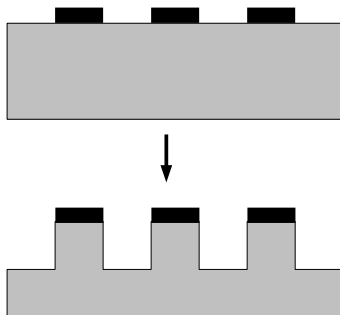


# Mold fabrication : RIE

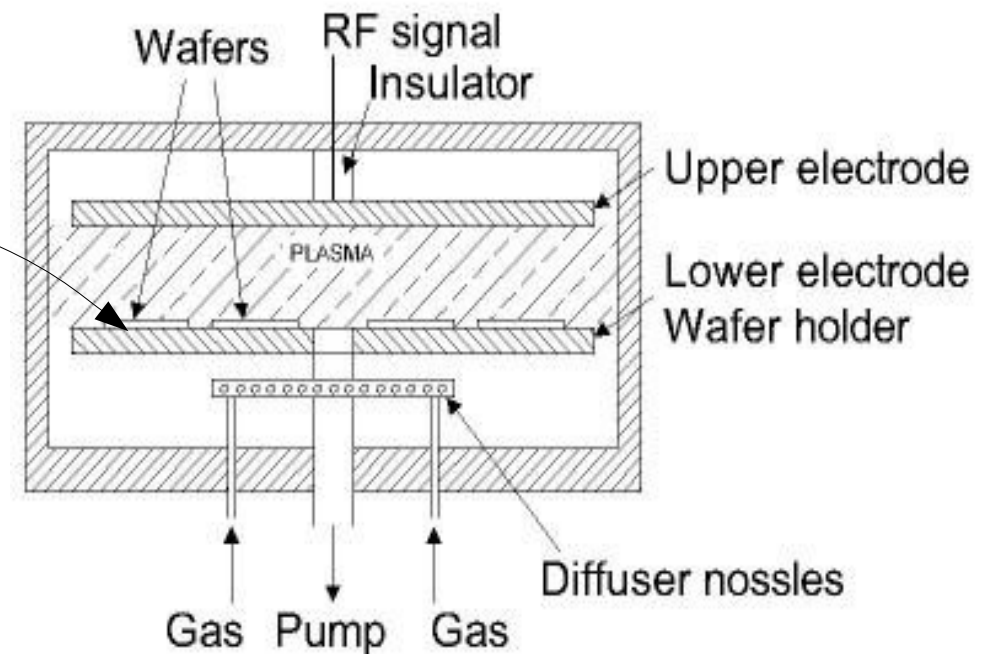
RIE = Reactive Ion Etching

- $U_0$  = bond energy of surface's atoms
- The neutral molecules of the plasma make  $U_0$  decrease
- The ions accelerates when they are closed to the surface
- substrate = cathode

Interest: very anisotropic.



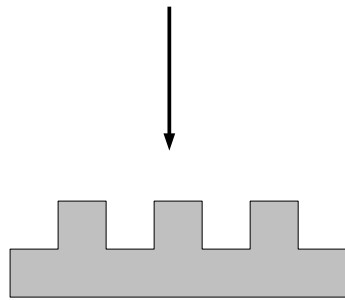
**Ion bombardement +  
chemical reaction**



Source: [www.memsnets.org](http://www.memsnets.org)

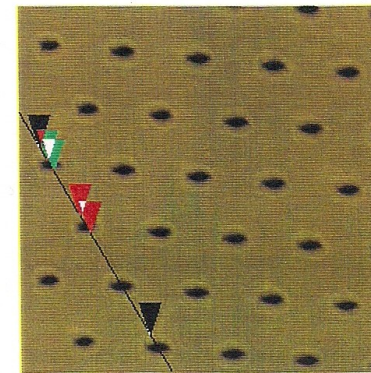
# Mold fabrication: cleaning + SAM

- Ultrasonic cleaning in acetone (remove the residues)
- Treatment anti-adherence  
(Self auto-assembled molecule)



The mold is ready !

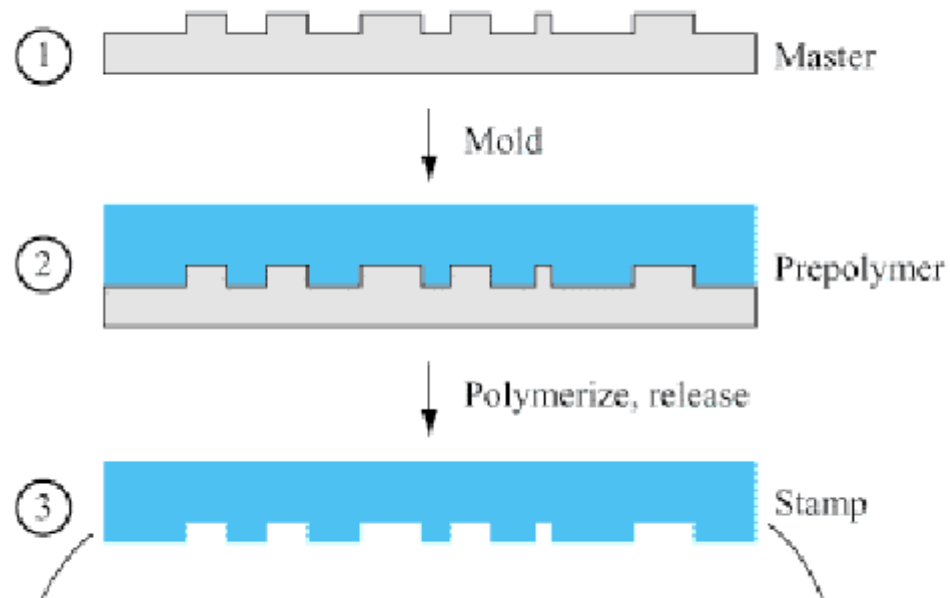
example:



*AFM picture of a mold  
Diameter of the holes : 200 nm  
Period of the array: 500  $\mu$ m*

*Resist: PMMA (Poly Methyl MethAcrylate)  
Developer: MIBK / IPA (1:3) and IPA  
(Methyl IsoButyl Ketone / IsoPropyl Alcool )*

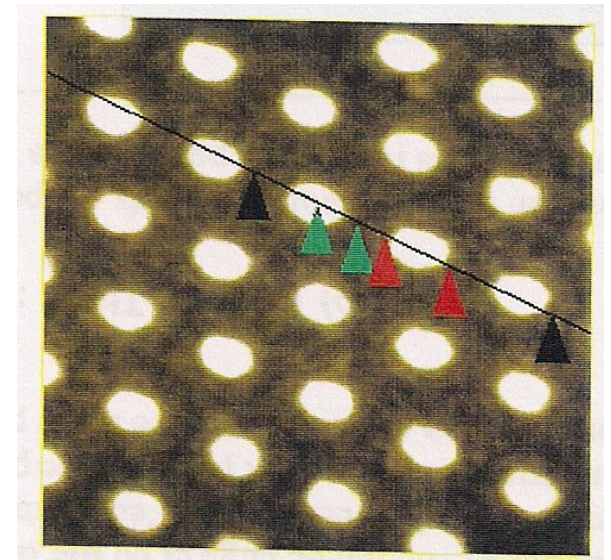
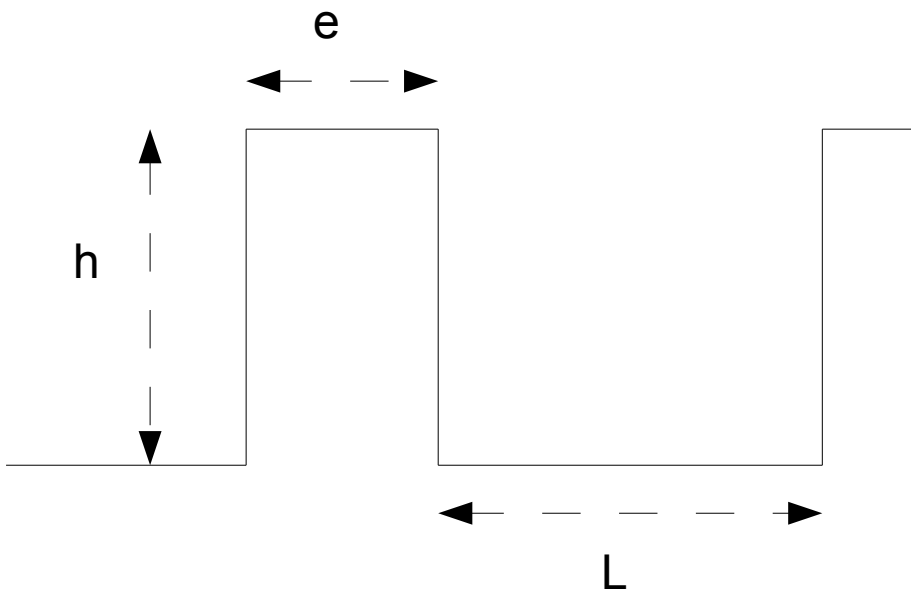
# Stamp fabrication



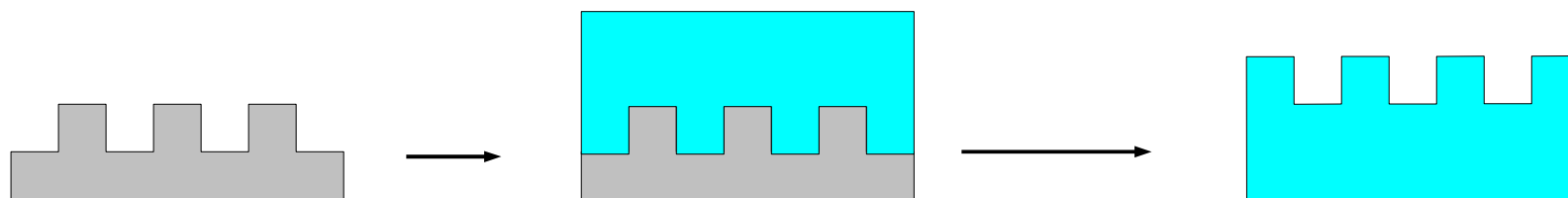
PDMS,  
e.g Sylgard 184,  
DOW Corning

# Stamp fabrication

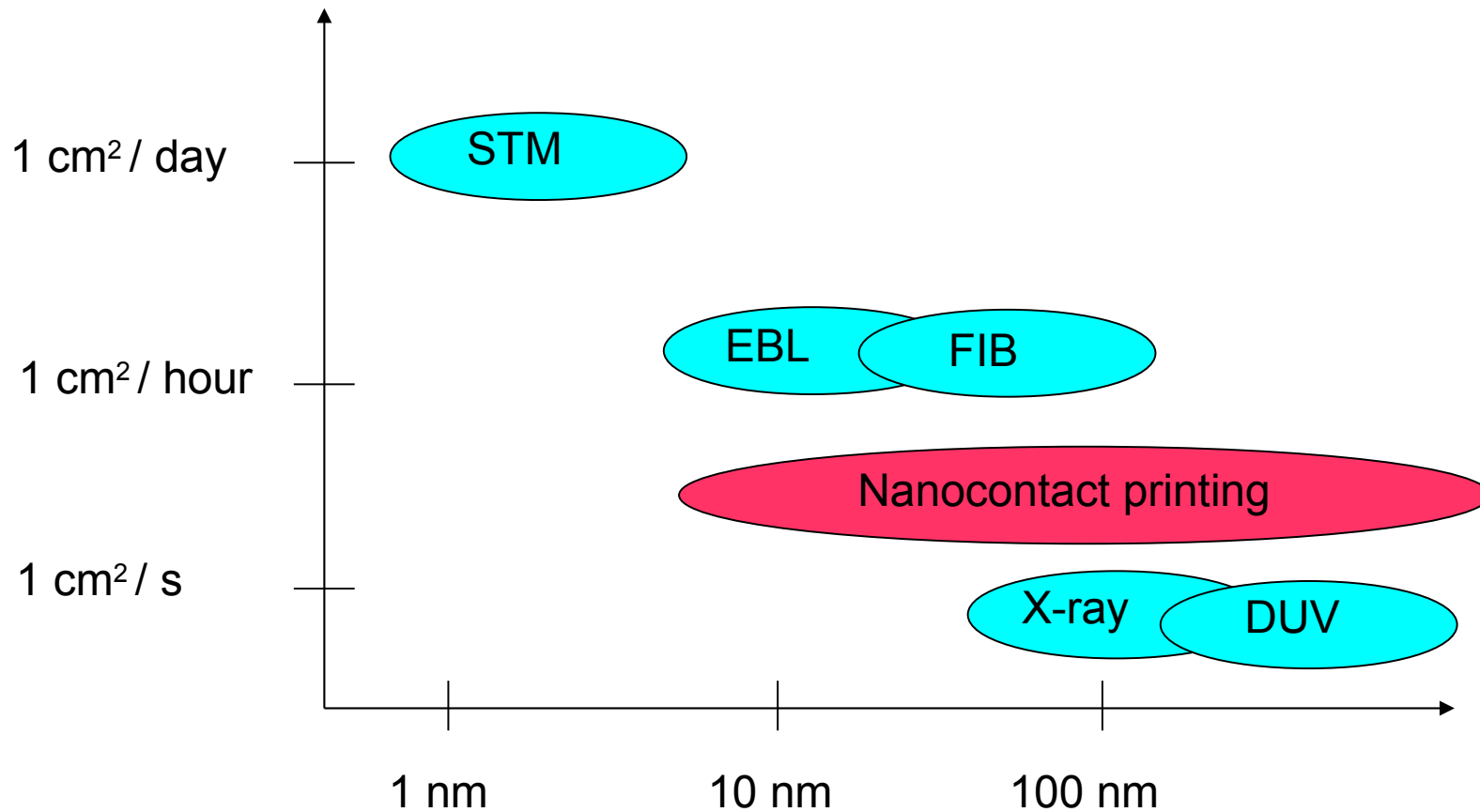
Dimensions constraints:  
 $L < 20h$        $h < 2e$



AFM picture of the stamp



# Nano contact printing



**STM = Scanning Tunneling Microscope**

**EBL = Electron Beam Lithography**

**FIB = Focused Ion Beam**

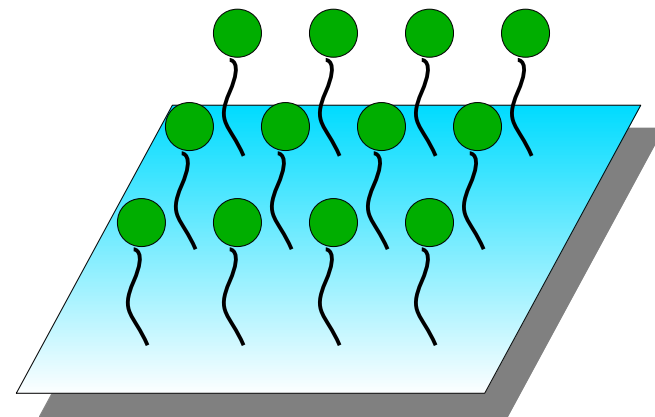
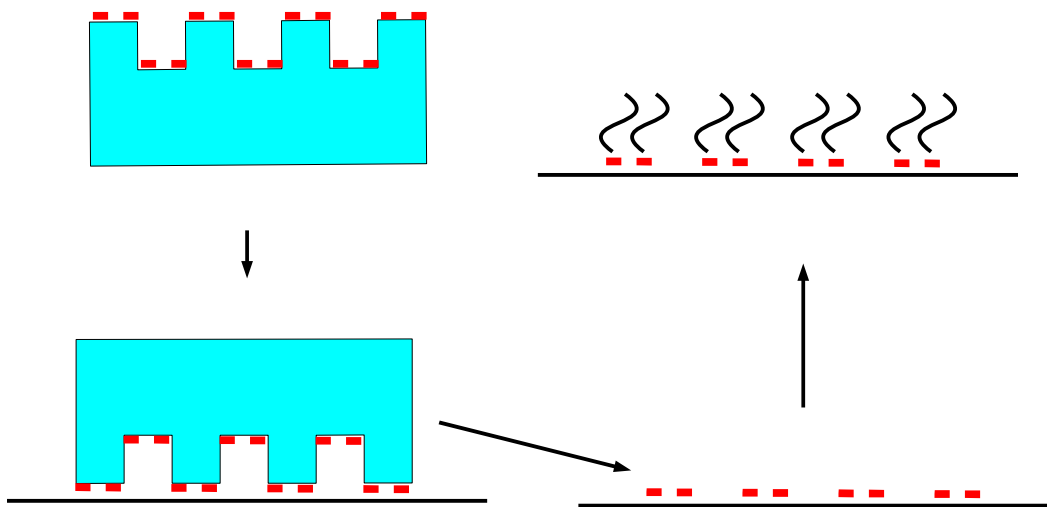
# Nano contact printing / DNA fixation

## Printing of biological molecules:

- The **dilution** well selected lead to the possibility to make arrays of single molecules.
- Important works: J.P. Renaud, A. Bernard, A. Bietsch, B. Michel, H.R. Bosshard, E. Delamarche, IBM Zurich.

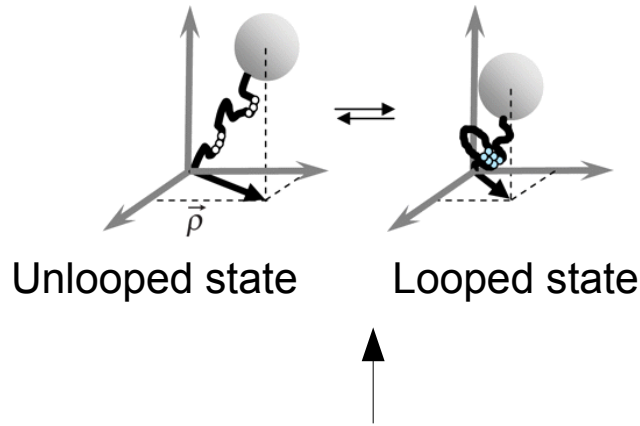
Example of application:  
DNA

1. Functionalization of the surface = stamping of oligomers
2. Hybridization of DNA
3. Addition of biotine molecules



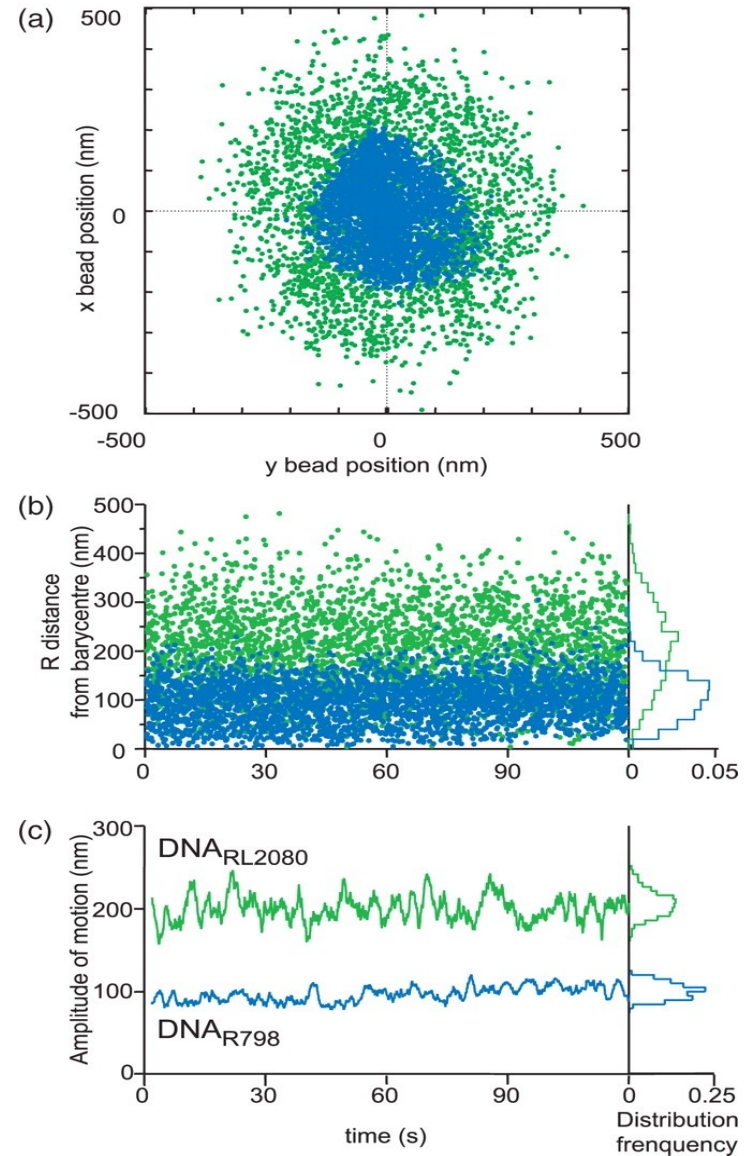


# Video microscopy / Image analysis



Physics Department, Cell  
Biology Department, Emory  
University, Atlanta, GA.

CNRS, Toulouse, France



# To conclude...

- Through this example, we can see that the nanotechnologies are a door open to multidisciplinary project
- Each technique improvement linked to this example is a step “forward” for other applications in various fields

# References

“Nanostructuration microsensor” , lecture, Christophe VIEU

SPIE Handbook of Microlithography, Micromachining and Microfabrication, Volume 1: Microlithography

Pouget, N., Dennis, C., Turlan, C., Grigoriev, M., Chandler, M. & Salomé, L. (2004, April 28). **Single-particle tracking for DNA tether length monitoring.** *Oxford Journal, Life Sciences, Nucleic Acids Research, Vol. 32, No. 9, e73.* Retrieved from <http://nar.oxfordjournals.org/content/32/9/e73.full.pdf+html>

Pouget, N., Turlan, C., Destainville, N., Salomé, L. & Chandler, M. (2006, August 21) **IS911 transpososome assembly as analyzed by tethered particle motion.** *Oxford Journal, Life Sciences, Nucleic Acids Research, Vol. 34, No. 16, 4313-4323.* Retrieved from <http://nar.oxfordjournals.org/content/34/16/4313.full.pdf+html>

Zurla, C., Manzo, C., Dunlap, D., Lewis, D. E. A., Adhya, S. & Finzi, L. (2009, March 10). **Direct demonstration and quantification of long-range DNA looping by the  $\lambda$  bacteriophage repressor.** *Oxford Journal, Life Sciences, Nucleic Acids Research, Vol. 37, No. 9, 2789-2795.* Retrieved from <http://nar.oxfordjournals.org/content/37/9/2789.full.pdf+html>

Renaud, J.P., Bernard, A., Bietsch, A., Michel, B., Bosshard, H.R., Delamarche, E., Kreiter, M., Hecht, B., Wild, U.P. (2002, October 14). **Fabricating Arrays of Single Protein Molecules on Glass Using Microcontact Printing.** *Journal of Physical Chemistry B.*

Saiz, L., Vilar, Jose MG. (2006, May 22). **DNA looping: the consequences and its control.** *Current opinion in Structural Biology 2006, 16:344–350.*  
Retrieved from [http://www.ehu.es/biologiacomputacional/reprints/cosb\\_2006\\_344.pdf](http://www.ehu.es/biologiacomputacional/reprints/cosb_2006_344.pdf)