Statistical study of single DNA molecules into dynamic array
Statistical study of single DNA molecules into dynamic array

- Research project lead by Laurence SALOMÉ 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

DNA fixation

Contact printing

Stamp fabrication

Inking

Video microscopy

Image analysis
Mold fabrication

- Resist
- Insulation by electron beam
- Development
- Etching
- Cleaning
Mold fabrication : EBL

- EBL = Electron Beam Lithography
- Slow and expensive process
- High resolution

EBL = Electron Beam Lithography

CM20
www.stevens.edu/lmsi/instrument/instrument.htm
Mold fabrication: EBL

- **Source**
  - Thermionic: 10 µm
  - Field effect: 1-10 nm

- **Blanking**
- **Electrode**

- **Condenser**
- **Magnetic lens**

- **Focuser**

- **Deflector**
  - Magnetic, Electrostatic distribution

- **Gaussian beam**
  - Raster scan: Moving stage
  - Vector scan: Fixed stage

- **Shaped beam**
  - Vector scan

- **Nano litho**
- **Mask**
- **Mask / Ship development**
Mold fabrication : EBL
Source

Electron sources:

Thermionic emission
Size of the beam: 10 µm

Field emission
Size of the beam: 1-10 nm
Mold fabrication: EBL

Electron Beam

$\theta$ is a direction in the plane, $V_L$ is perpendicular to the plane.

Electrons spiraling down the axis

Magnetic Lens

Two components to the $B$ field:

- $B_L =$ longitudinal component (down the axis)
- $B_R =$ radial component (perpendicular to axis)
Mold fabrication : EBL
Deflector

Electrostatic field

Magnetic field
Mold fabrication: EBL

STM = Scanning Tunneling Microscope

EBL = Electron Beam Lithography

FIB = Focused Ion Beam

Nanocontact printing

1 cm²/day

1 cm²/hour

1 cm²/s
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

Dose = \frac{it}{S}

Example:

Current \, i = 450 \, pA
Dose = 2000 \, \mu C.cm^{-2}
Surface \, S = 2.8.10^{-4} \, cm
\quad \rightarrow \, t = 23 \, minutes
Mold fabrication: positive/negative resist

Focused beam of electron

Silicium \rightarrow resist

Negative resist \rightarrow Positive resist

Insulation

Development

Etching

Cleaning

Negative Mold

Positive Mold
Mold fabrication: Resist

**Electron Scattering in Resist and Substrate**

- **Forward Scattering (small angle)**
- **Secondary electrons**
- **Back Scattering (large angle)**

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.

Source: www.memsnet.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 µm

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

1. Master
2. Mold
3. Prepolymer
4. Polymerize, release
5. Stamp

PDMS, e.g. Sylgard 184, DOW Corning
Stamp fabrication

Dimensions constraints:
\[ L < 20h \quad \text{and} \quad h < 2e \]
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


