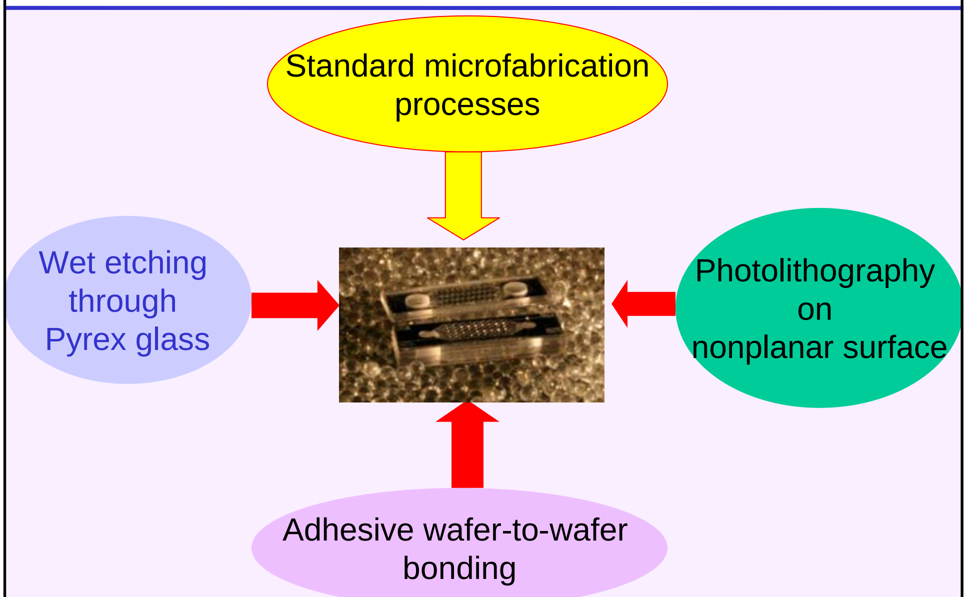
Dielectrophoresis
from 2D to 3D, from micro to nano….

Ciprian Iliescu

Working with platform technologies !



Dielectrophoresis from 2D to 3D
- outline -

1. **Introduction:**
   a. **Dielectrophoresis?**
   b. **DEP force**
   c. **Polarization factor**
   d. **Positive and negative DEP**
   e. **Classification of the DEP devices**
   f. **Problems associated with DEP**
2. **Structures of DEP with 3D electrodes and asymmetric electrodes**
3. **Simulation of the electric field in DEP structures**
4. **Consideration about Joule effect**
5. **Consideration about fabrication process**
6. **Application 1: cell trapping**
7. **Application 2: cell sorting**
8. ***DEP for nanoparticles***
9. **DEP filter**
10. ***DEP chip for liver cells assembly and culture***

Dielectrophoresis ?

Motivations…

Applications → Particle trapping; Particle separation

Definition:

Dielectrophoresis (DEP) = the movement of the neutral (but polarisable) particles in an electric field that is spatially inhomogeneous.

particles → Micro-size; Nano-size

DEP Force

The DEP force acting on a spherical particle:

$$F = 2\pi r^3 \varepsilon_m \mathrm{Re}[K]\ \nabla E^2$$

Polarization factor (!):

$$K = \left(\varepsilon_p^* - \varepsilon_m^*\right) / \left(\varepsilon_p^* + 2\varepsilon_m^*\right)$$

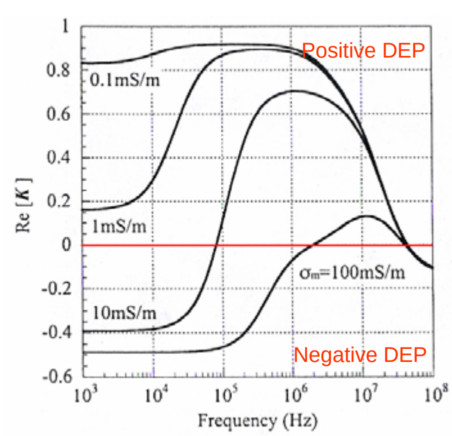
Complex permittivity

$$\varepsilon^* = \varepsilon - j(\sigma / \omega)$$

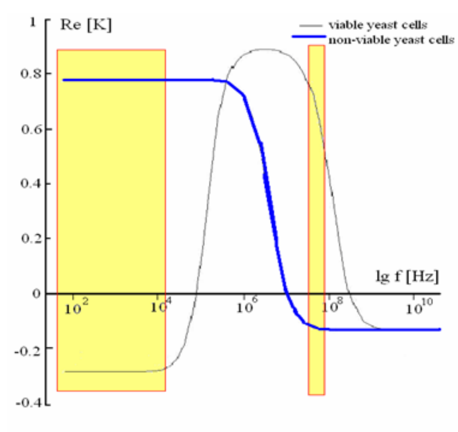
Polarization factor

Re [*K*] versus frequency

for viable yeast cells



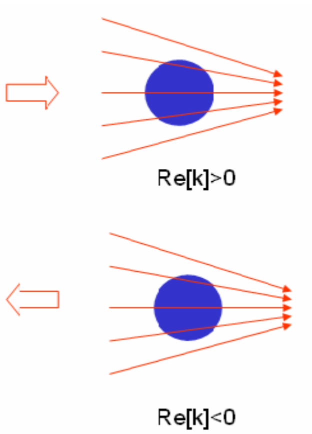
Yang, J., Y. Huang, X. Wang, X-B, Wang, F.F. Becker and P. R. C. Gascoyne. 1999. *Biophysical J.* 76: 3307-3314.

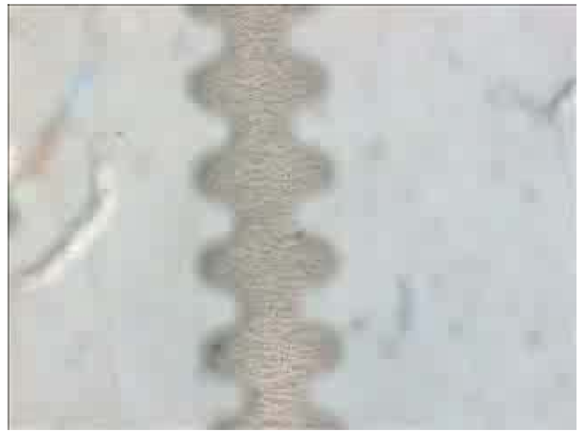


L. Yu, C. Iliescu, G. Xu and F.E.H. Tay, *JMEMS*, **vol. 16, issue 5**, October 2007, pp 1120-1129.

Positive and negative DEP

Positive DEP



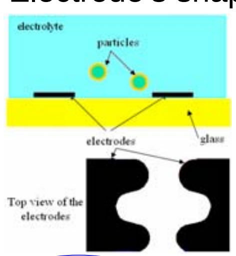


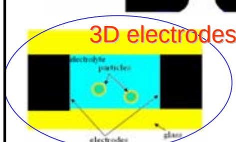
Negative DEP

Classification of DEP devices

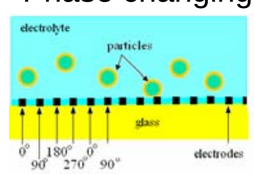
Key point: generation of a gradient of the electric field

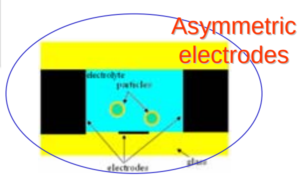
Electrode's shape



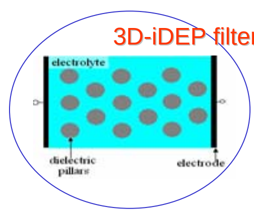


Phase changing





Modification of dielectric media



C. Iliescu, G.L. Xu, F.C. Loe, P.L. Ong and F.E.H. Tay, *"A 3 dimensional dielectrophoretic filter chip", **Electrophoresis, vol. 28, issue 7,** 2007, pp. 1107-1114*

C. Iliescu, L.M. Yu, G.L. Xu and F.E.H. Tay, ***JMEMS, vol. 15, no. 6**, 2006, pp. 1506-1513,*

C. Iliescu, G.L. Xu, V. Samper and F.E.H. Tay, ***Journal of Micromechanics and Microengineering*, vol. 15, no. 3**, 2005,494-500

Problems related DEP

1. Joule effect in DEP device (especially for application on biological samples !)

2. Possible modification induce by the electric field on biological samples

1. **Introduction**
2. **Structures of DEP with 3D electrodes and asymmetric electrodes**
   a. DEP with 3D electrodes
   b. DEP with asymmetric electrodes (3D electric field gradient)
3. **Simulation of the electric field in DEP structures**
4. **Consideration about Joule effect**
5. **Consideration about fabrication process**
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7. **Application 2: cell sorting**
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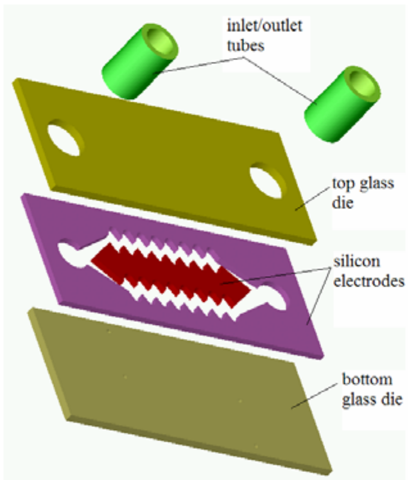
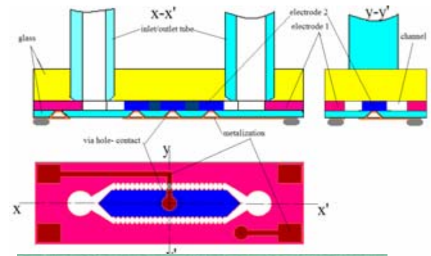
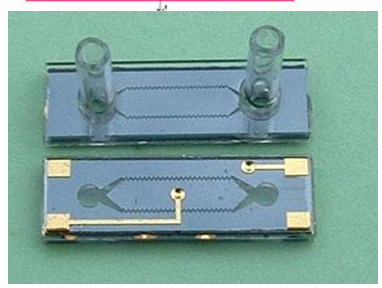
10. ***DEP chip for liver cells assembly and culture***

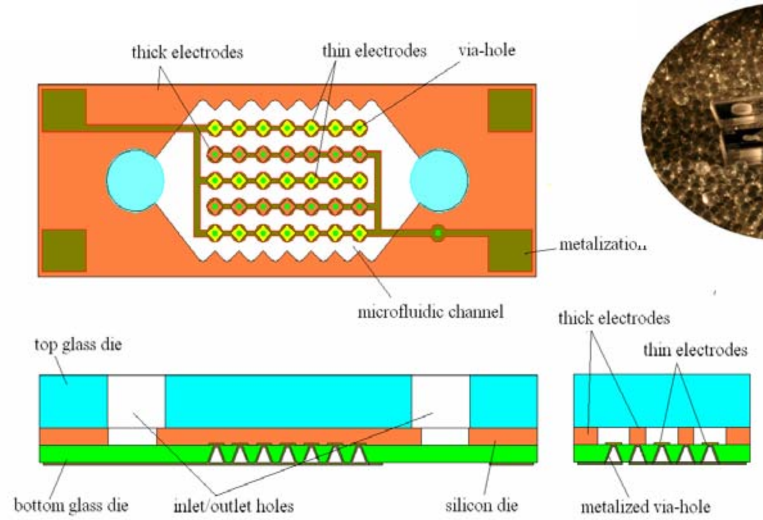
Structure of DEP chip – 3D electrodes

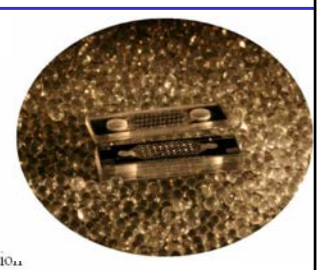






Structure of DEP chip - asymmetric electrodes





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Electric field gradient & DEP force

Co-workers: L. Yu, G.L Xu

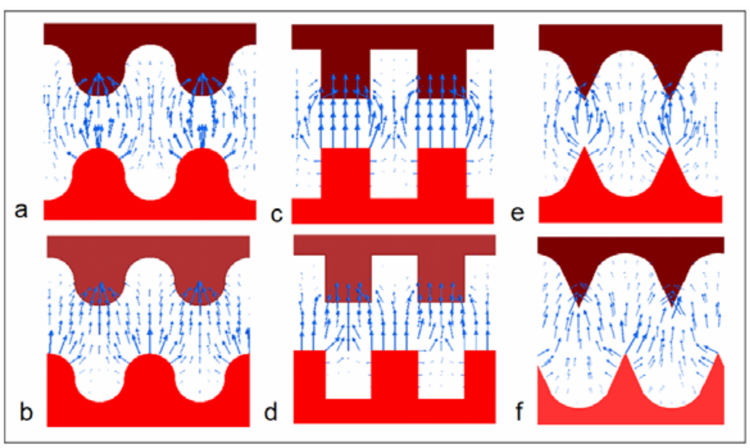
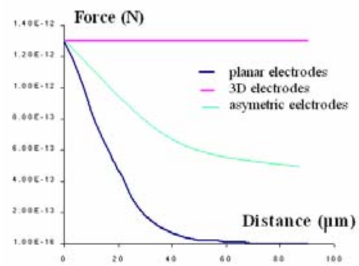


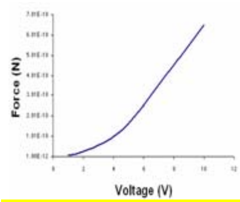
Table 1: Electric field strength and gradient for different electrode configurations with $10V_{pp}$ actuation voltage

Design	a	b	c	d	e	f
E [x 10^4V/m]	4.22	4.07	3.68	3.75	8.87	3.61
∇E^2 [X10^5 V^2/m^3]	2.91	1.76	2.29	2.38	12.8	5.53

Electric field gradient & DEP force

Planar electrodes 3D electrodes Asymmetric electrodes





Need more force?

Increase the voltage !

$$\Delta T \approx \frac{\sigma V^2}{k}$$

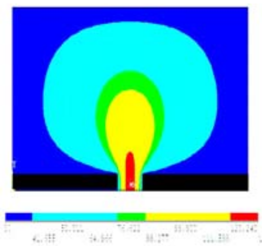
Increase the voltage !

Increase the temperature!

Joule effect

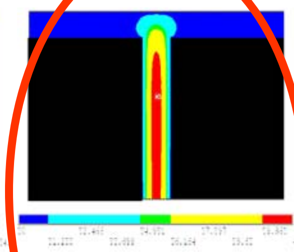
Co-workers: A.J. Pang

Planar electrodes | 3D electrodes | Asymmetric electrodes



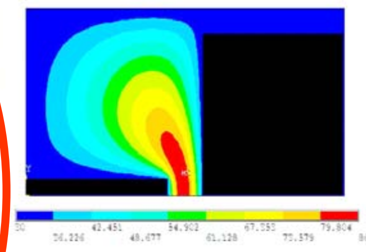
T=134 C

$$\Delta T \approx \frac{\sigma V^2}{k}$$



T=40 C

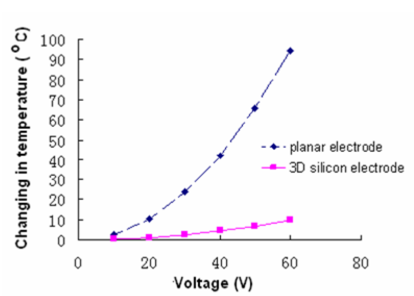
$$\Delta T \approx \frac{\sigma V^2}{8k}$$



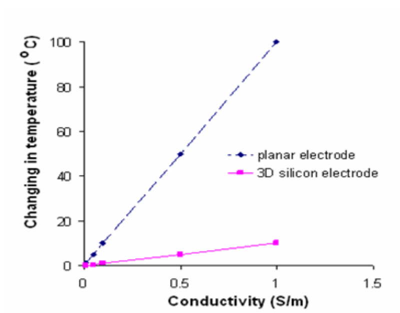
T=86 C

The structure is suitable for trapping nanoparticles (or even viruses) !

Joule effect



The relationship between change in temperature and applied voltage



The relationship between change in temperature and electric conductivity of medium

F.E.H. Tay, L. Yu, A.J. Pang and C. Iliescu, "Electrical and thermal characterization of a dielectrophoretic chip with 3D electrodes for cells manipulation," *Electrochimica Acta,* **vol. 52**, **issue 8,** 2007, 2862-2868

1. Introduction
2. Structures of DEP with 3D electrodes and asymmetric electrodes
3. Simulation of the electric field in DEP structures
4. Consideration about Joule effect
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9. DEP filter
10. *DEP chip for liver cells assembly and culture*

Fabrication process

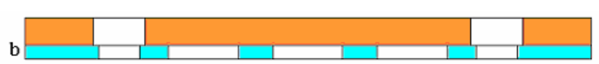
Anodic bonding of 100 um silicon wafer on glass

- Glass wafer- Corning 7740 with drilled holes

- Silicon wafer- heavy doped, 100um-thick

- Bonding conditions: T=305 C, F=500N, U=1000V (I reached 40% from the initial value)

DRIE of silicon wafer (thick electrode+ microfluidic channel)



-PECVD SiO2 mask (1um-thick)

-Alignment from the back side using ring feature

-Etching in a ICP DRIE/ Bosch process (SF6/C4F8) – after bonding with wax on a dummy Si wafer

Fabrication process

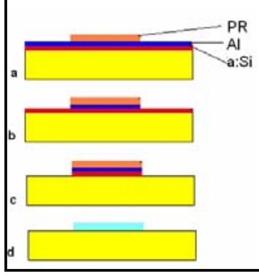
Fabrication of the thin electrode (doped a:Si on glass)

-Main disadvantage of a:Si – high compressive stress (500-600 MPa)

- a:Si - difficult to be doped

- Solution : annealing* doping with Al (solid source), followed by annealing at 500C/3h in vacuum. Resistivity 100ohm/sq, stress 150MPa compressive.

* **C. Iliescu**, J. Miao and F.E.H. Tay, "Optimization of PECVD amorphous silicon process for deep wet etching of Pyrex glass," *Surface and Coatings Technology*, **vol. 192/1**, 2005, 43-47



a) PR mask over a sandwich structure a:Si(2.5um)+Al(0.5um)

b) Al etch (RIE etch using SiCl4)

c) a:Si etch (Bosch process)

d) PR removing and annealing

Fabrication process

Anodic bonding +aligning of the wafers

- Bonding conditions: T= 450 C, U=1500V, F=1000N

Thinning of the bottom wafer to 100 um (wet etching process)

-A thinning process up to 100um is required

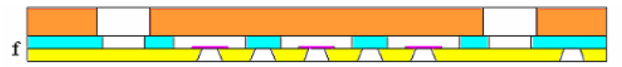
-Wet etching process in an optimized HF/HCl (10/1)**

-The roughness of the generated surface was 10nm

** C. Iliescu, J. Jing, F.E.H. Tay, J. Miao and T.T. Sun, "Characterization of masking layers for deep wet etching of glass in an improved HF/HCl solution," *Surface and Coatings Technology,* **vol. 198/ 1-3**, 2005, 314-318

Fabrication process

Via –holes fabrication



-The initial diameter of via-holes was 50um

-Wet etch process in the same HF/HCl solution using Cr/Au mask (optimized in ***)

-Process with “etch-stop” on a:Si membrane

Metallization

- Cr/Au & Al deposition were used for metallization
- Critical aspect patterning of the metal layer ****)

*** C. Iliescu, F.E.H. Tay and J. Miao, “Strategies in deep wet etching of Pyrex glass,” *Sensors and Actuators A,* **vol. 133/2,** 2007, 395-400

**** L. Yu, Y.Y. Lee, F.E.H. Tay, C. Iliescu, “Spray coating of photoresist for 3D microstructures with different geometries,” *J. Phys.: Conf. Ser.*, **vol. 34**, 2006, 937-942

Fabrication process

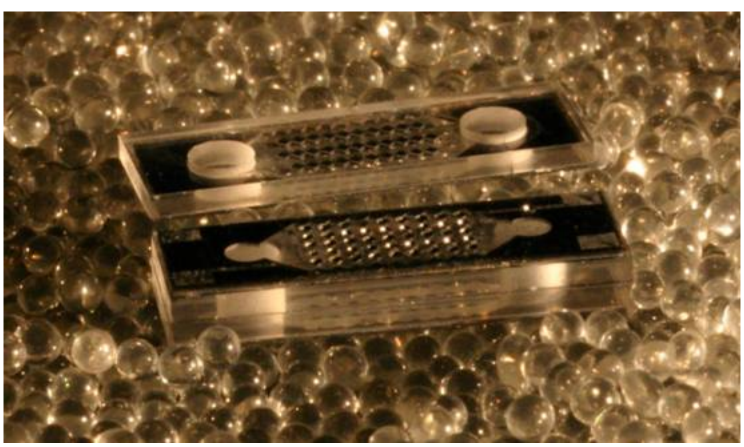


Photo of the fabricated DEP with 3D electric field gradient (asymmetric electrodes)

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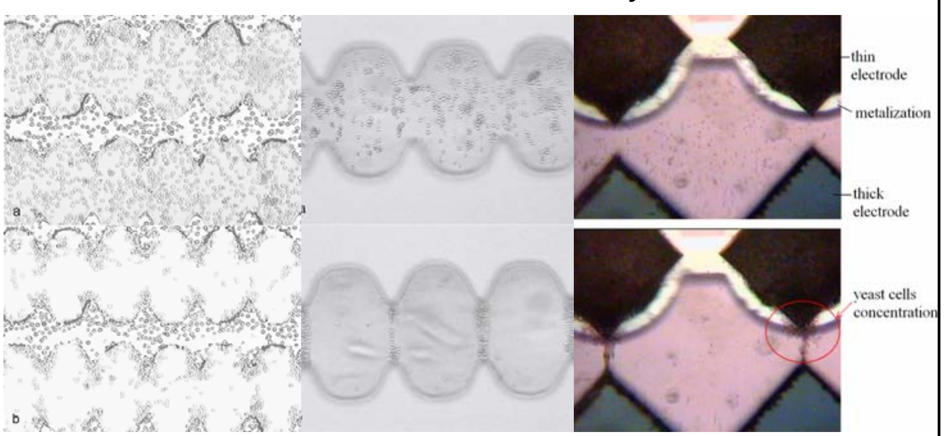
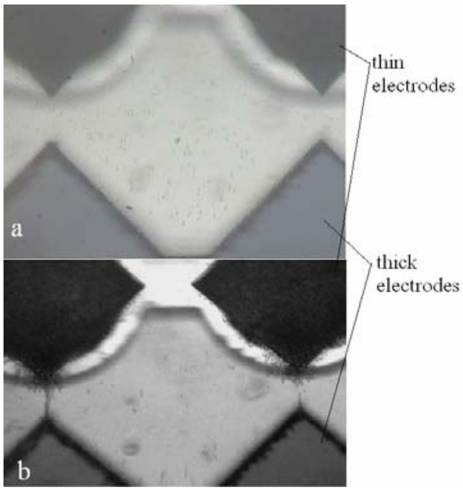
Cells trapping (positive DEP)

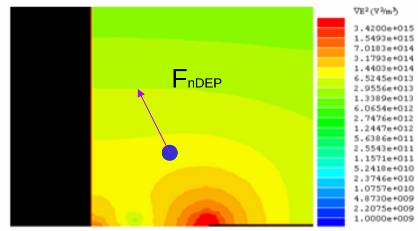
Planar electrodes   3D electrodes   Asymmetric electrodes



Cells trapping (negative DEP)

Asymmetric electrodes





For nDEP the cells are levitated at 30-35um !

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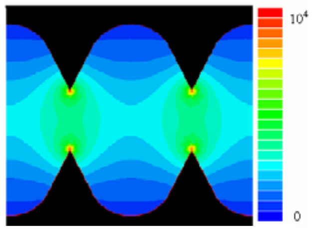
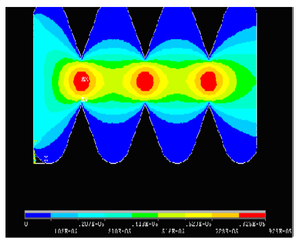
6. **Application 1: cells trapping**
7. **Application 2: cells sorting**
   a. Sequential cells sorting in DEP with 3D electrodes
   b. Separation under the continuous flow
   c. Bidirectional separator
8. ***DEP for nanoparticles***
9. **DEP filter**
10. ***DEP chip for liver cells assembly and culture***

Cells separation –DEP with 3D electrodes

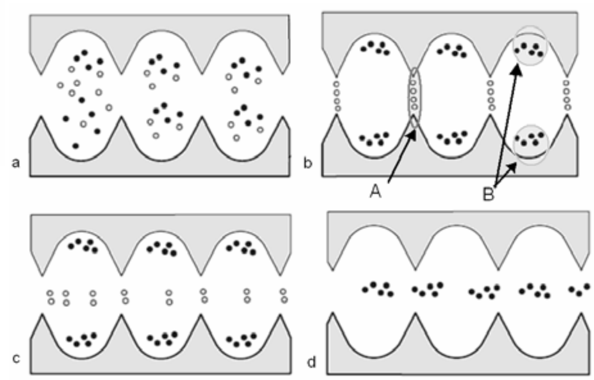


Electric field



Flow gradient

Sequential flow separation in a DEP device with 3D electrodes

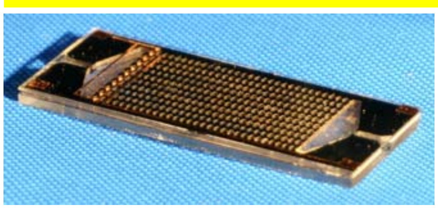


Separation principle

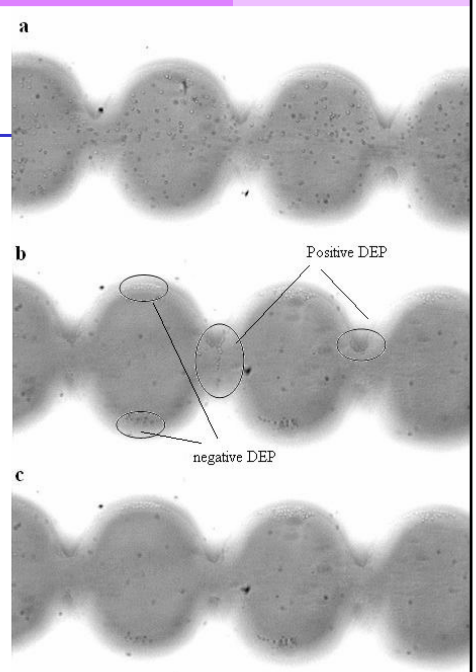
L. Yu, C. Iliescu, G. Xu and F.E.H. Tay, *JMEMS*, **vol. 16, issue 5**, October 2007, pp 1120-1129.

Cells separation–DEP with 3D electrodes

Viable and non-viable yeast cell separation using sequential field-flow separation method in a DEP chip with 3D silicon electrode

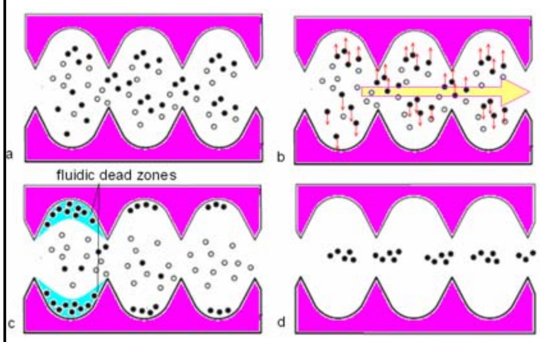


Optical view with the DEP device with lateral inlet/outlet

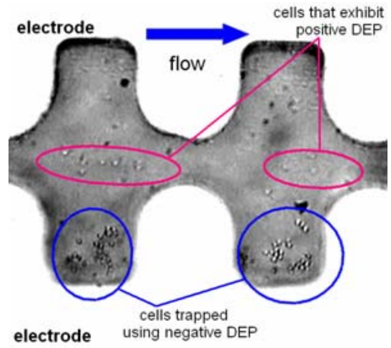


Cells separation –DEP with 3D electrodes

Continue flow separation in a DEP device with 3D electrodes



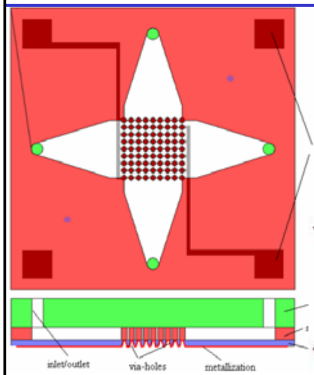
Separation principle



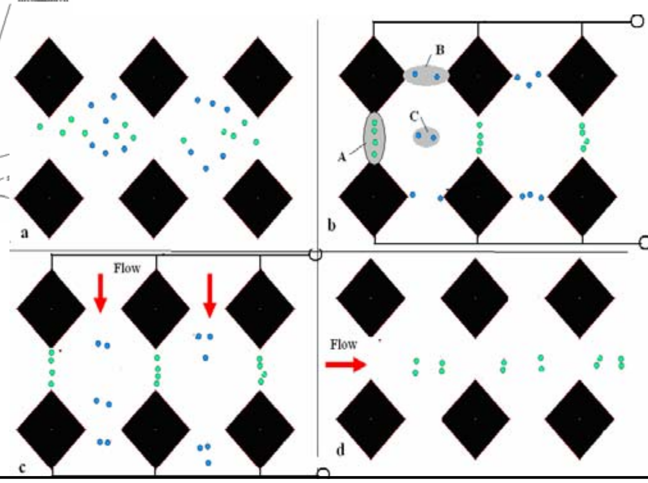
Optical view taken during the separation process

C. Iliescu, G. Tresset and G.L. Xu, *Applied Physics Letters,* **vol. 90, issue 23**, June 2007, pp. 234104/1-3

Bidirectional separation

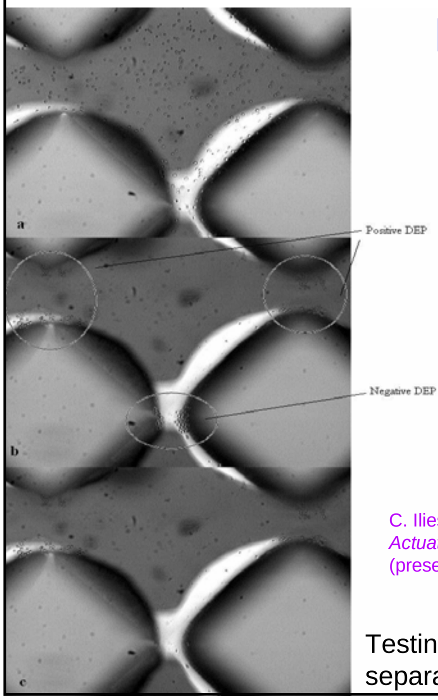


Schematic view of the DEP device



Separation principle

Bidirectional separation



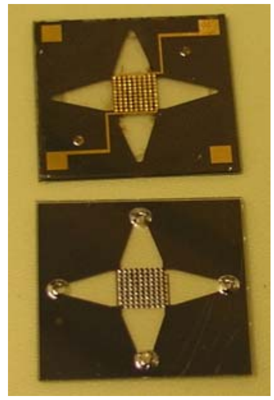


Photo with the DEP device

C. Iliescu, L.M. Yu, F.E.H. Tay and B.T. Chen, *Sensors and Actuators B,* **vol. 129, issue 1**, January 2008, pp. 491-496 (presented at "Transducers an Eurosensors" July 2007)

Testing of the bidirectional DEP separator

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6. **Application 1: cells trapping**
7. **Application 2: cells sorting**
8. ***DEP for nanoparticles (in testing)***
9. **DEP filter**
10. ***DEP chip for liver cells assembly and culture***

DEP chip for nanoparticles trapping

- Motivation: viruses purification

- Challenges:

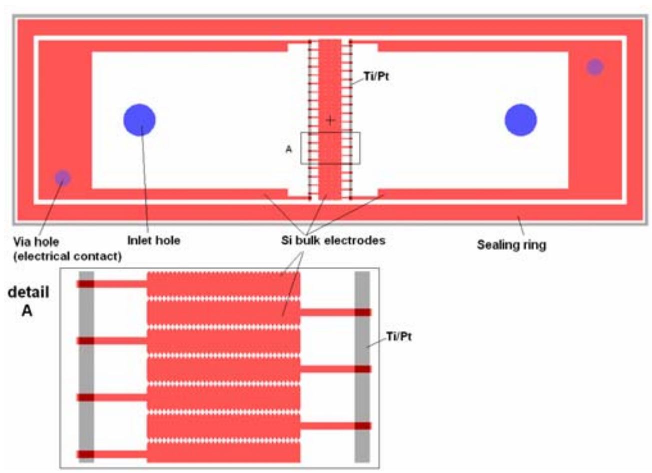
  DEP force acting on a spherical particle:

- $$F = 2\pi r^3 \varepsilon_m \mathrm{Re}[K] \nabla E^2$$

F ~ volume of the particle ! ⟷ ***Joule effect***

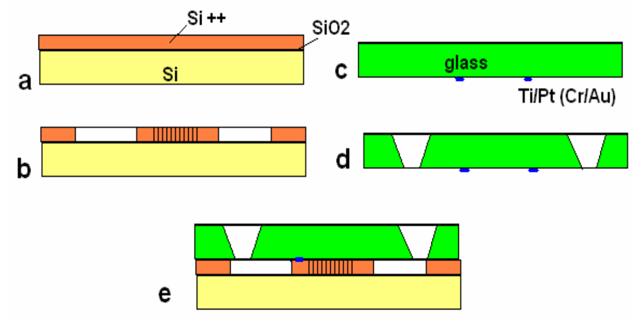
DEP chip for nanoparticles trapping

- Schematic view:



DEP chip for nanoparticles trapping

- Fabrication process:



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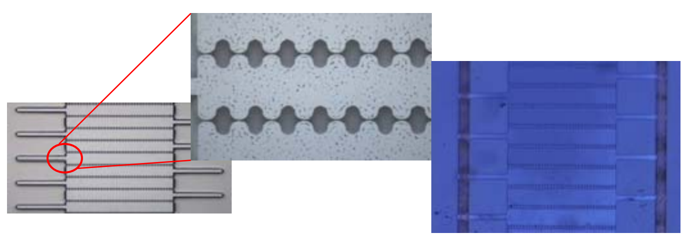
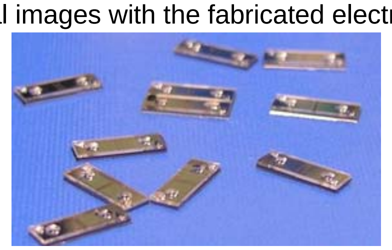
a) SOI silicon wafer
b) Etching of Si electrodes
c) Ti/Pt electrodes on glass
d) Etch through holes for inlet/outlet and electrical contact
e) Anodic bonding Si/glass

DEP chip for nanoparticles trapping



SEM and optical images with the fabricated electrodes

Fabricated DEP chips



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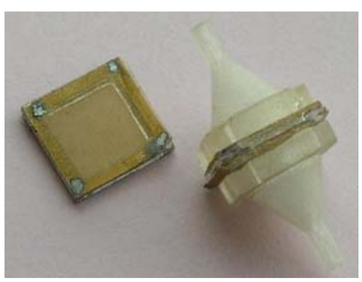
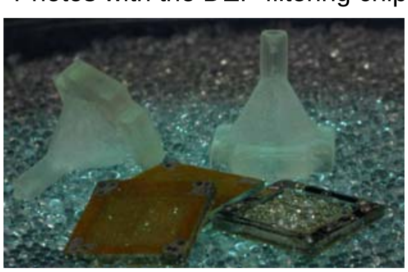
    a. Structure
    b. Simulations
    c. Fabrication
    d. Results
    e. Cells sorting in 3D iDEP filter
10. *DEP chip for liver cells assembly and culture*

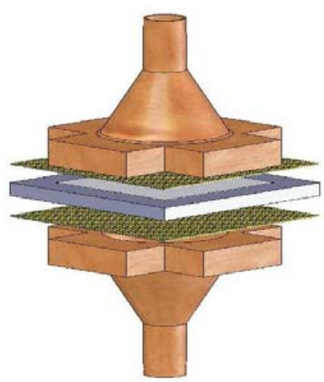
3D iDEP chip – cells trapping

Co-workers: Felicia Loe (GPBE_NUS)
Poh Lam Ong



Photos with the DEP filtering chip

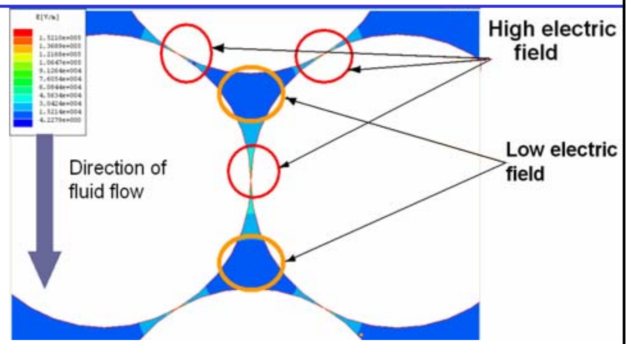


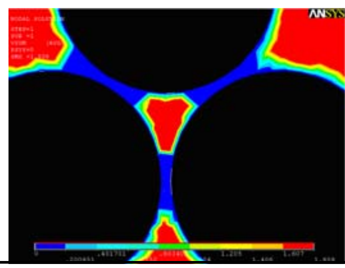


Schematic view of the DEP filtering chip

Simulation of the electric field and flow

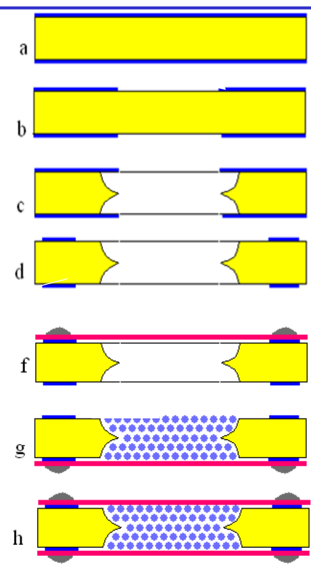
Electric field simulation using Maxwell software





Simulation of the flow velocity between the beads using ANSYS

Fabrication process



a) Cr/Au deposition on both sides of a 1mm glass wafer

b) Cr/Au patterned with 1st mask and etched in clasical Cr/Au echants.

c) Central hole created via simultaneous etching of glass wafer from both sides in conc.HF (49%).

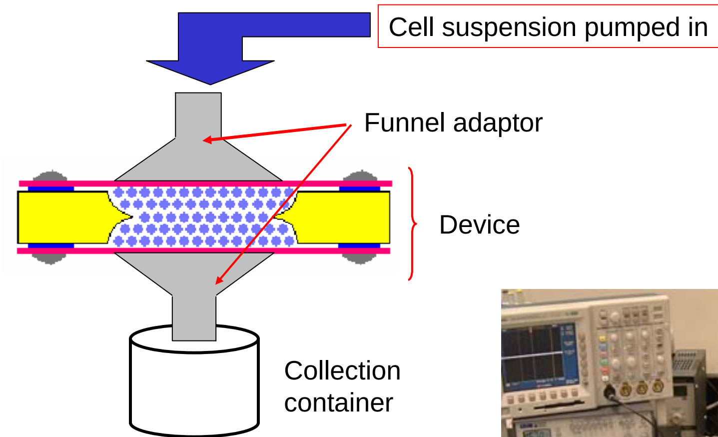
d) Cr/Au layer patterned with 2nd mask to create a bonding ring.

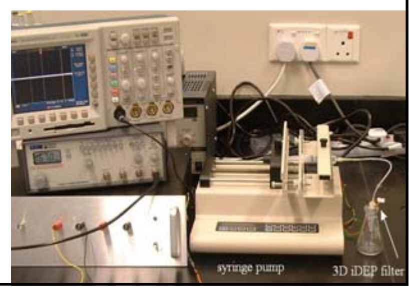
f) Wire mesh solder bump to Cr/Au bonding ring on one side of wafer.

g) Silica beads packed into central hole.

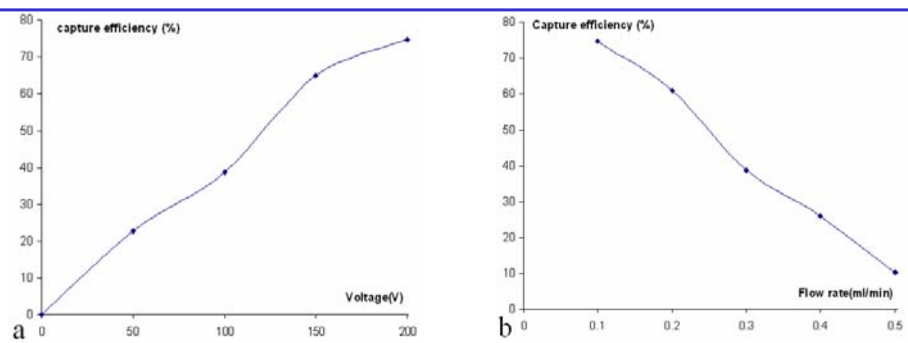
h) Wire mesh is solder bump to Cr/Au ring on other side of wafer. Enclosing the silica beads.

Testing setup





Results

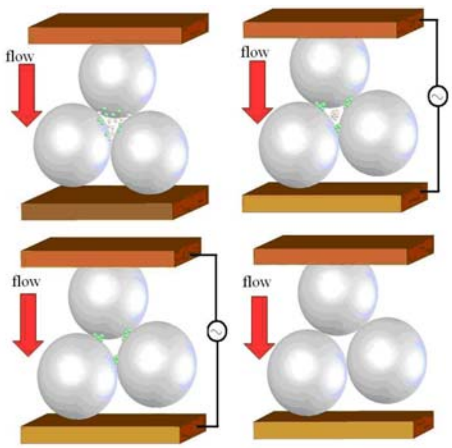


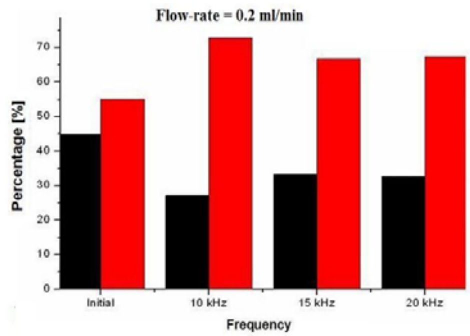
Influence of the applied voltage and the flowing rate on capture efficiency

The device was tested also in DC !

<u>**C. Iliescu**</u>, G.L. Xu, F.C. Loe, P.L. Ong and F.E.H. Tay, *Electrophoresis*, **vol. 28, issue 7,** April 2007, pp. 1107-1114

3D iDEP Chip – Cells separation

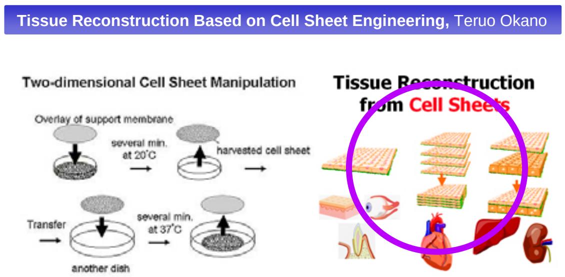


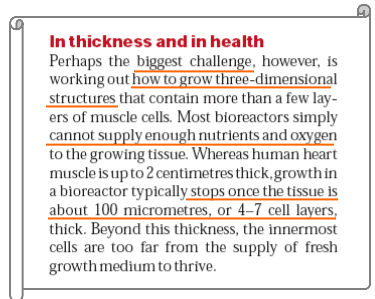


Working principle of cells separation in a 3D iDEP chip

C. Iliescu, G.L. Xu, P.L. Ong and K.J. Leck, *Journal of Micromechanics and Microengineering*, **vol. 17/ 7,** 2007, S128-S136.

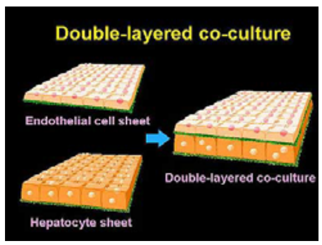
Tissue reconstruction: state-of-the-art

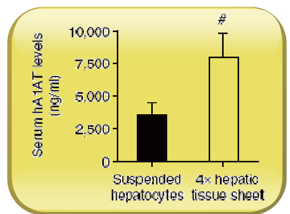




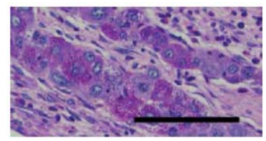
In thickness and in health
Perhaps the biggest challenge, however, is working out how to grow three-dimensional structures that contain more than a few layers of muscle cells. Most bioreactors simply cannot supply enough nutrients and oxygen to the growing tissue. Whereas human heart muscle is up to 2 centimetres thick, growth in a bioreactor typically stops once the tissue is about 100 micrometres, or 4–7 cell layers, thick. Beyond this thickness, the innermost cells are too far from the supply of fresh growth medium to thrive.

Nature **421, 884-886 (2003)**





Nature Medicine **13, 880-885 (2007)**

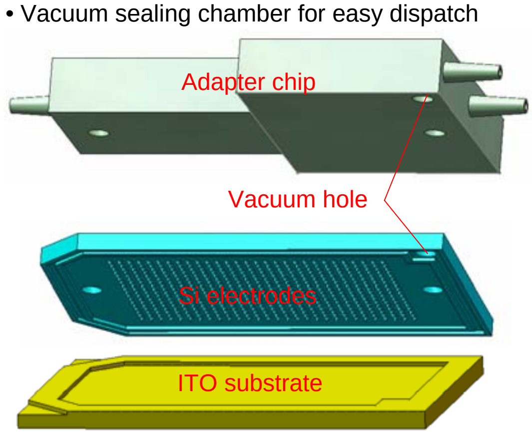


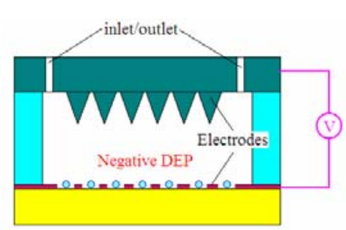
Courtesy of J. Hsieh- IBN

DEP chip for liver cells assembling & culture

Co-workers: B. Chen & H. Yu

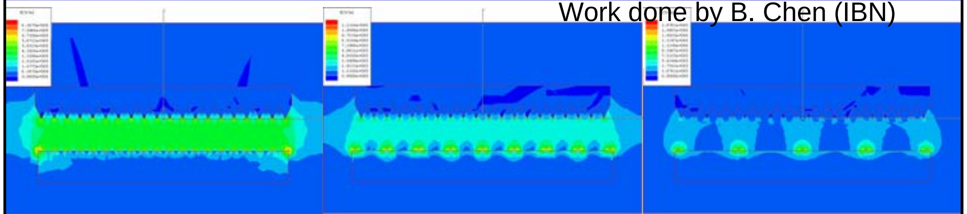
- DEP chip with vertical-electrode configuration, top inlet/outlet
- Silicon tips as top electrodes, planar bottom electrodes
- Vacuum sealing chamber for easy dispatch



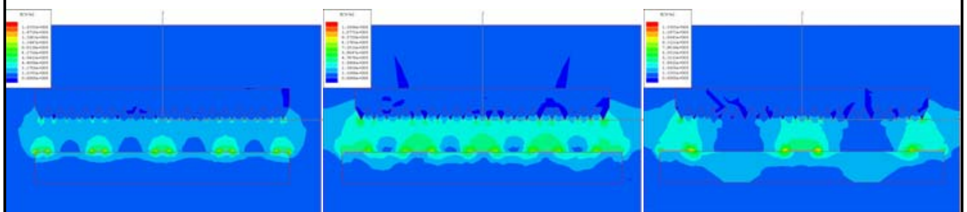


Design and simulation of bottom electrodes

Work done by B. Chen (IBN)



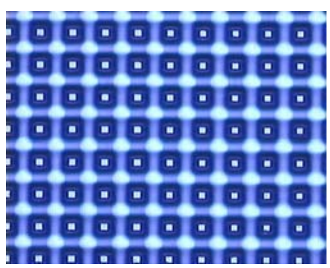
P=20µm, W_e=10µm | P=50µm, W_e=10µm | P=100µm, W_e=10µm

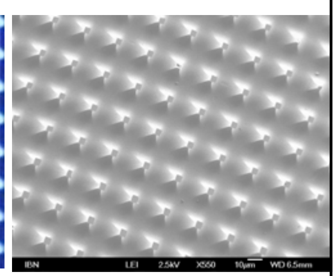


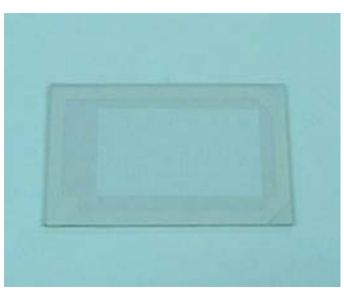
P=100µm, W_e=20µm | P=100µm, W_e=40µm | P=200µm, W_e=50µm

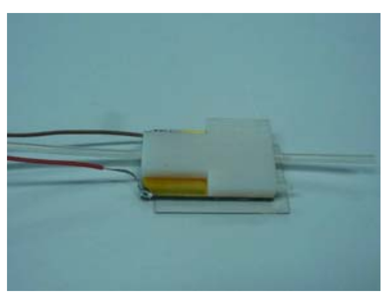
- Pitch of the bottom electrode will be 50-200 µm.
- Width of the electrode will probably be smaller than the pitch.

Fabrication result of the DEP chip

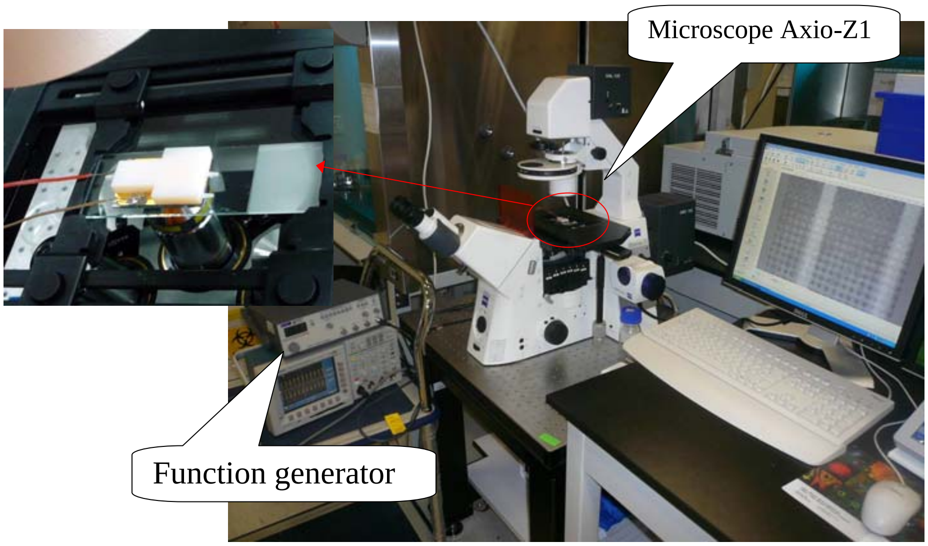




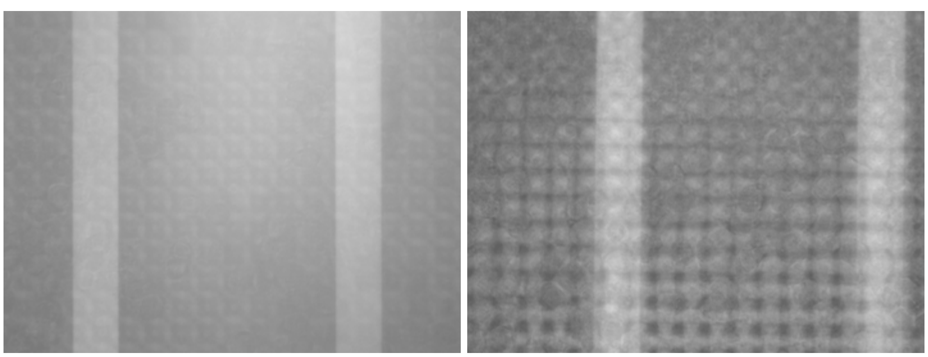




Experimental setup



Preliminary cell trapping results



HEPG2 cell trapping by vertical-electrode DEP


Thank you for your attention!