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# Lab-on-a-Chip: nanofluidic research and microfluidic applications


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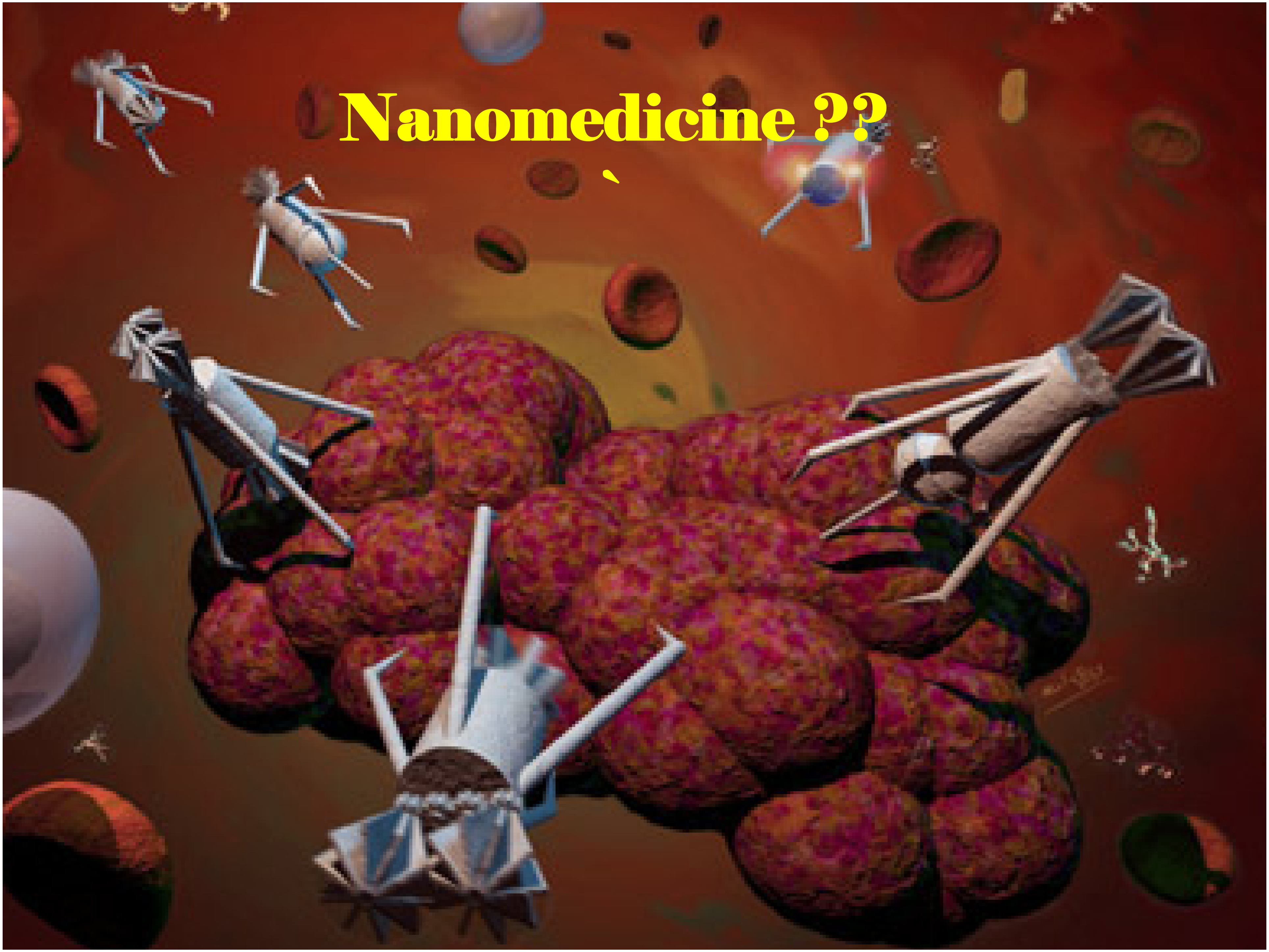
University of Twente, The Netherlands


*Nanospain, March 9th, 2009*


Aljaferia

# Outline

- Nanomedicine
- Capillary force based nanofluidics
  - Flow independent droplet generation/liquid crystallography
- Electrokinetic nanofluidics
  - DNA transport through nanochannels
- Biomedical applications using microfluidics
  - Fertility chip
  - Cancer chip


Nanomedicine ??

# Nanomedicine

- Nanoparticles/CNT's:
  - (bio)medical imaging
  - localized therapy (nanoparticle heating)
  - targeted drug delivery
  - regenerative medicine (neurons, scaffolds)

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# Nanomedicine

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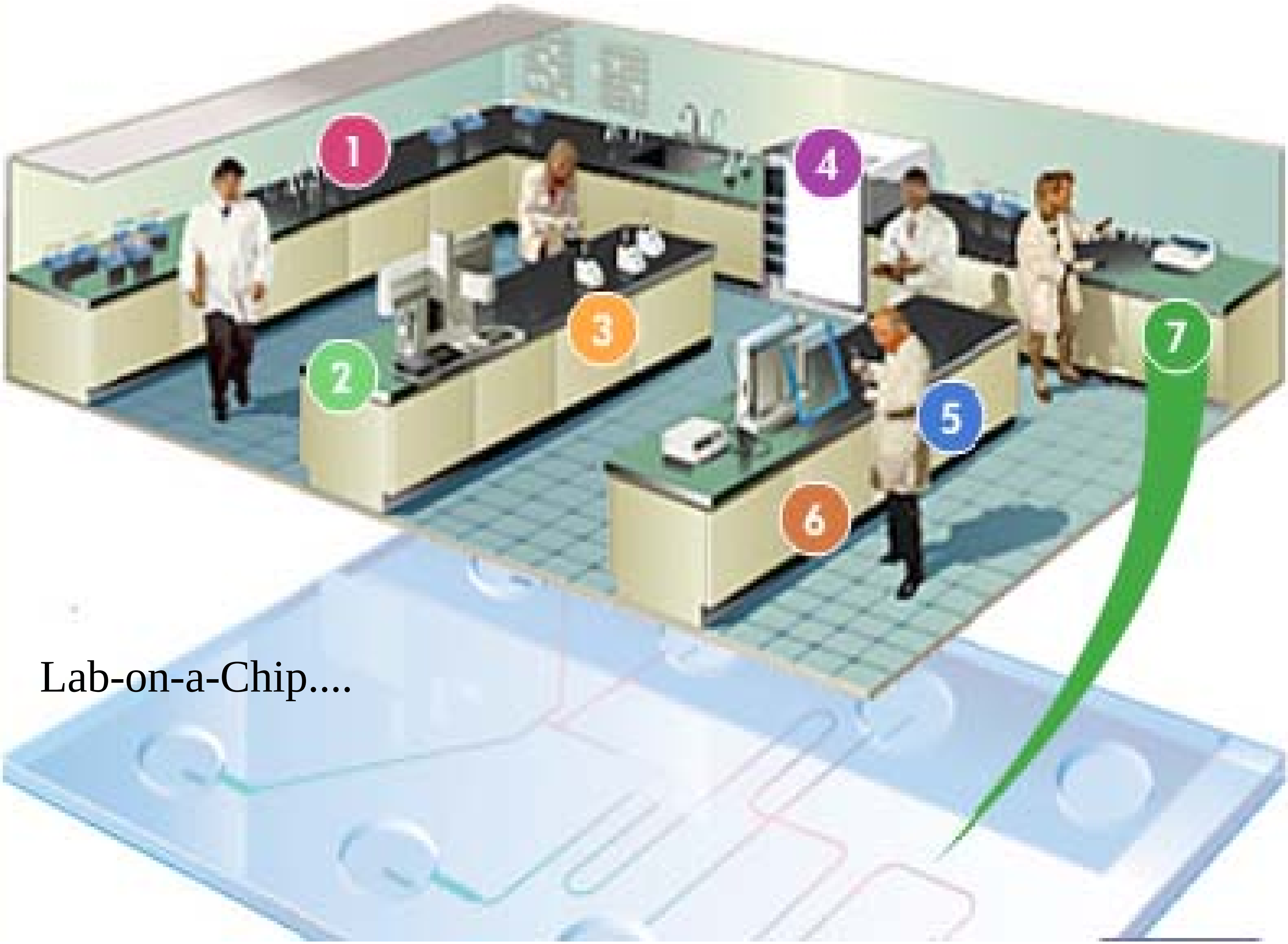
# Nanomedicine

- Nanoparticles/CNT's:
  - (bio)medical imaging
  - local treatment (nanoparticle heating)
  - targeted drug delivery
  - regenerative medicine (neurons, scaffolds)
- Nanofluidics and nanosensing: diagnostics
  - control of drug dosing
  - DNA analysis
  - biomarker detection (nanosensors)
  - cell analysis

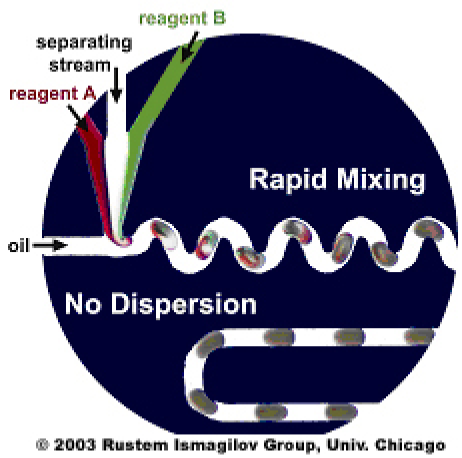



Lab-on-a-Chip....


A. van den Berg and P. Bergveld, *Lab Chip*, **6**, (2006), 1266-1273.

# Two-phase flow microfluidics

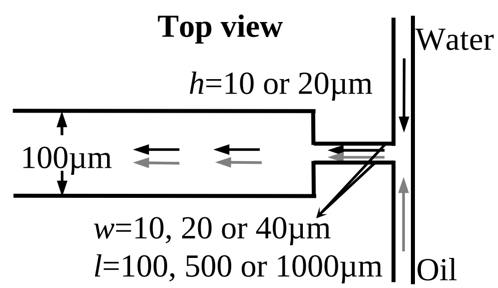
## Shear flow determined droplets

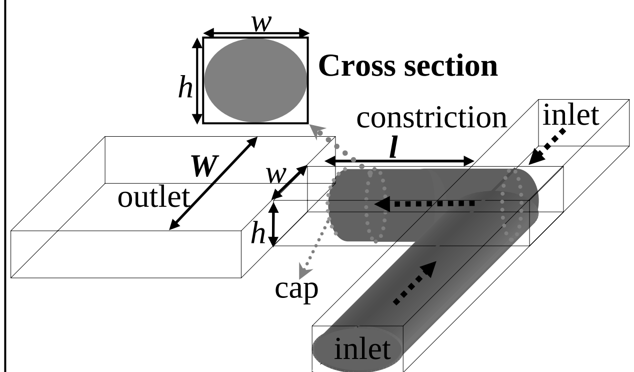


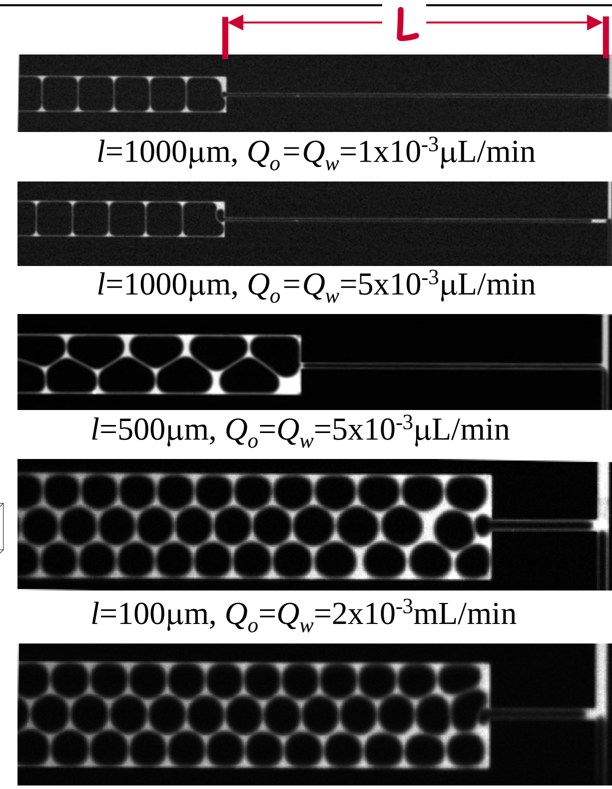

(Ismagilov)

## Geometry determine droplets

→ inlet-length L determined droplets




$l$=1000μm, $Q_o=Q_w$=1x10$^{-3}$μL/min

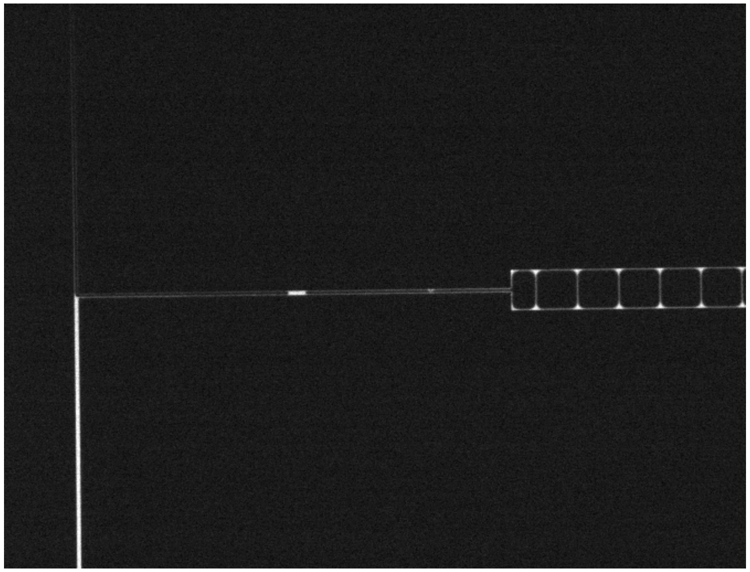
$l$=1000μm, $Q_o=Q_w$=5x10$^{-3}$μL/min

$l$=500μm, $Q_o=Q_w$=5x10$^{-3}$μL/min

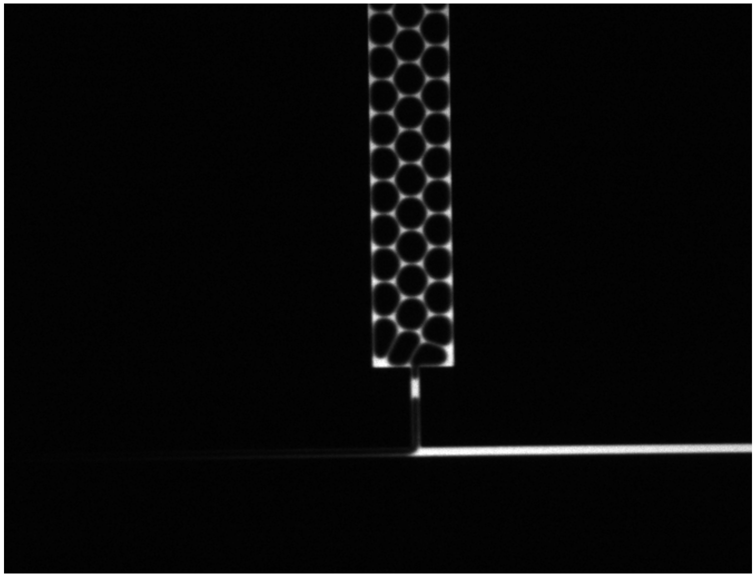
$l$=100μm, $Q_o=Q_w$=2x10$^{-3}$mL/min

$l$=100μm, $Q_o$=2.5$Q_w$=5x10$^{-3}$mL/min

# Geometry determined droplet generation

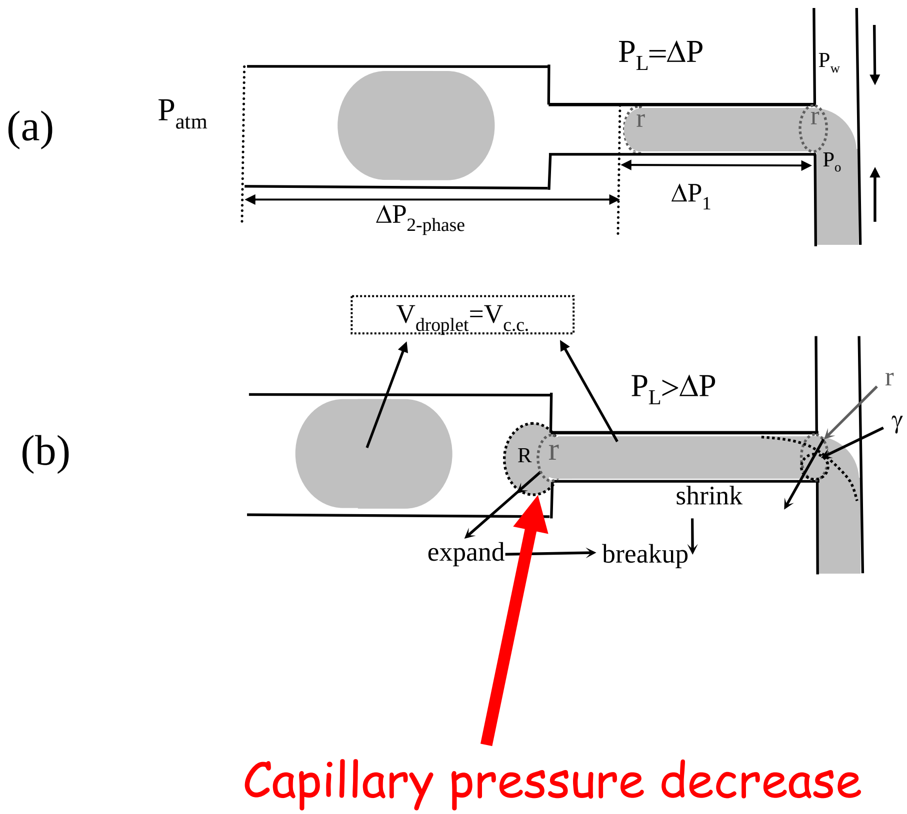


$L$=1000µm, $h$=$w$=10 µm



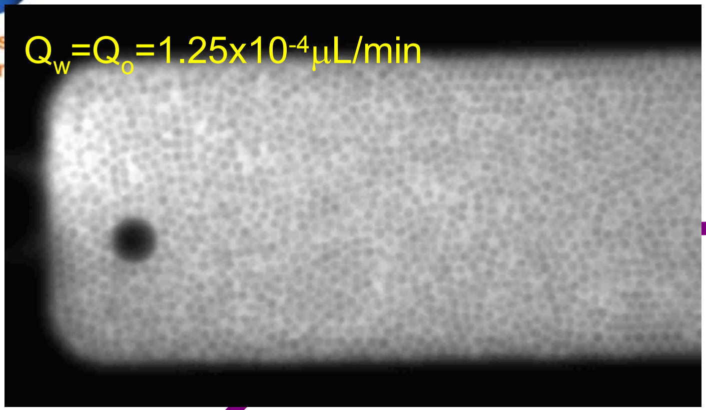
$L$=100µm, $h$=$w$=10 µm

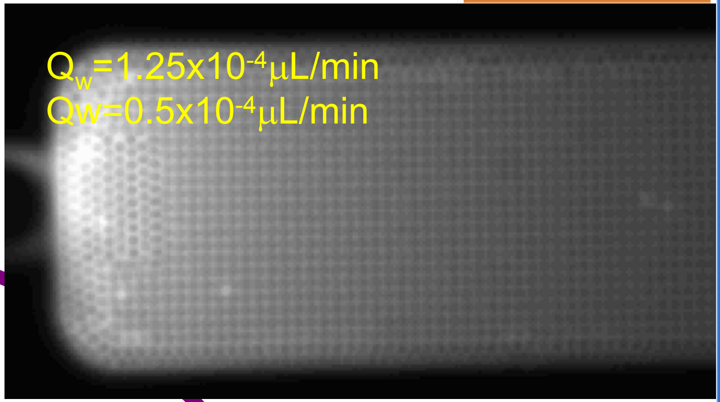
# Droplet formation mechanism

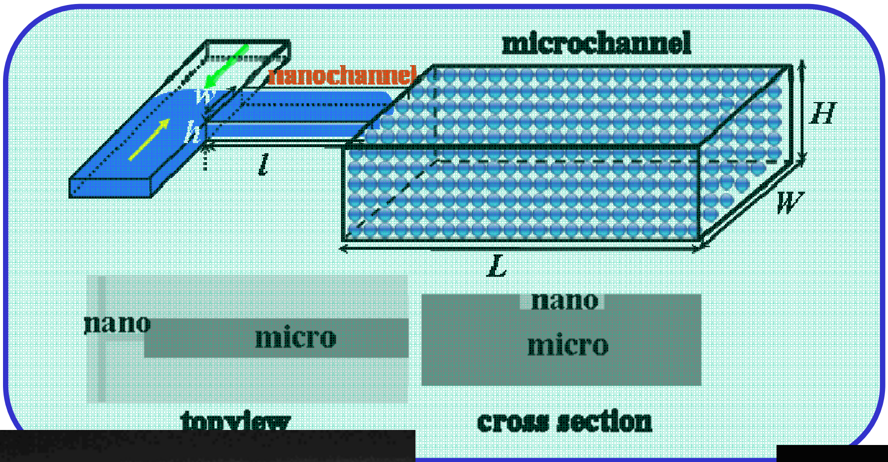


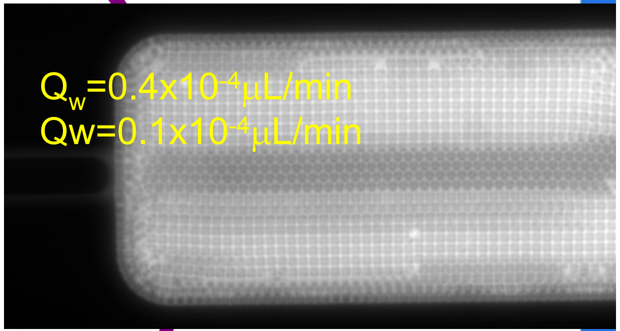

L.L. Shui, F. Mugele, A. van den Berg, J.C.T. Eijkel, *Applied Physics Letters*, **93(15),** 153113, (2008)

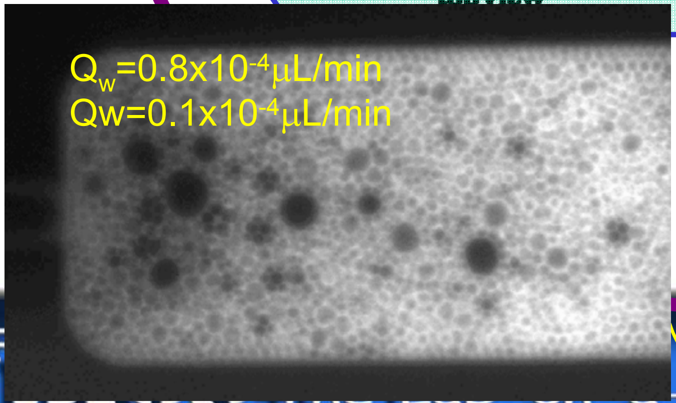
# Liquid Crystallography in Nano/Microfluidic Channels

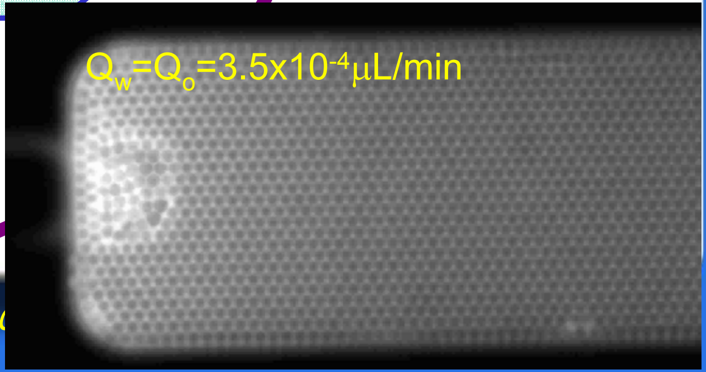


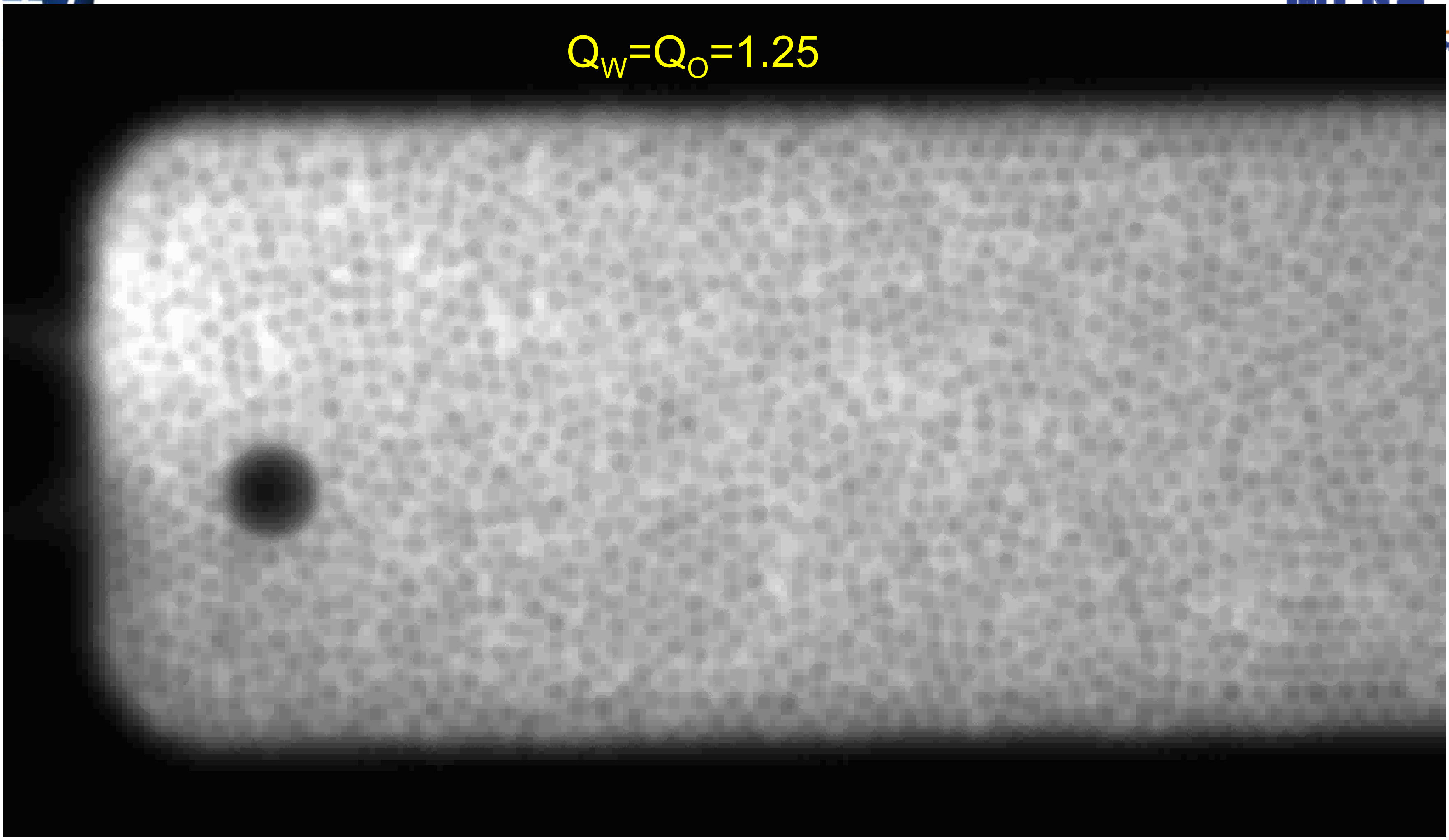



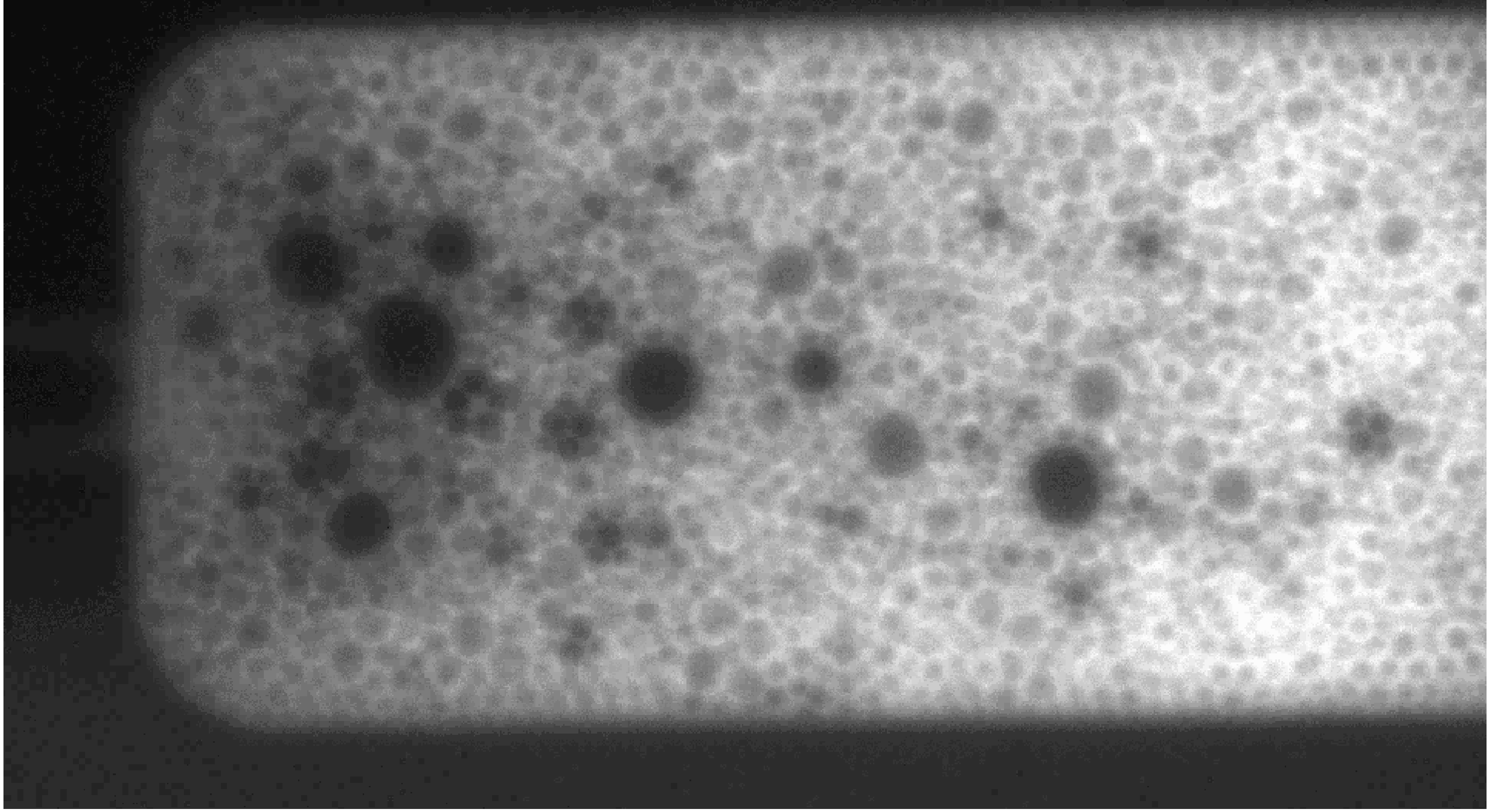



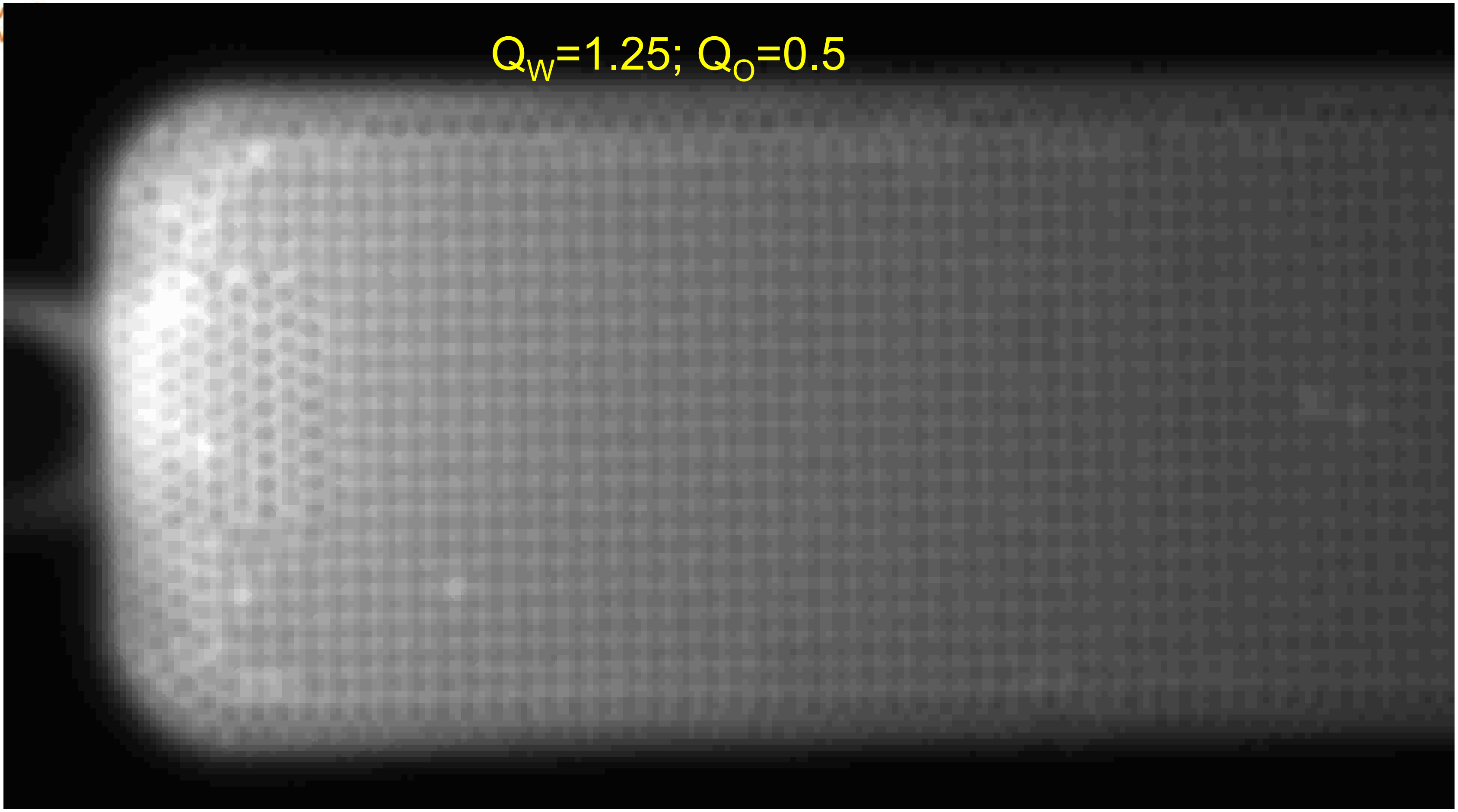



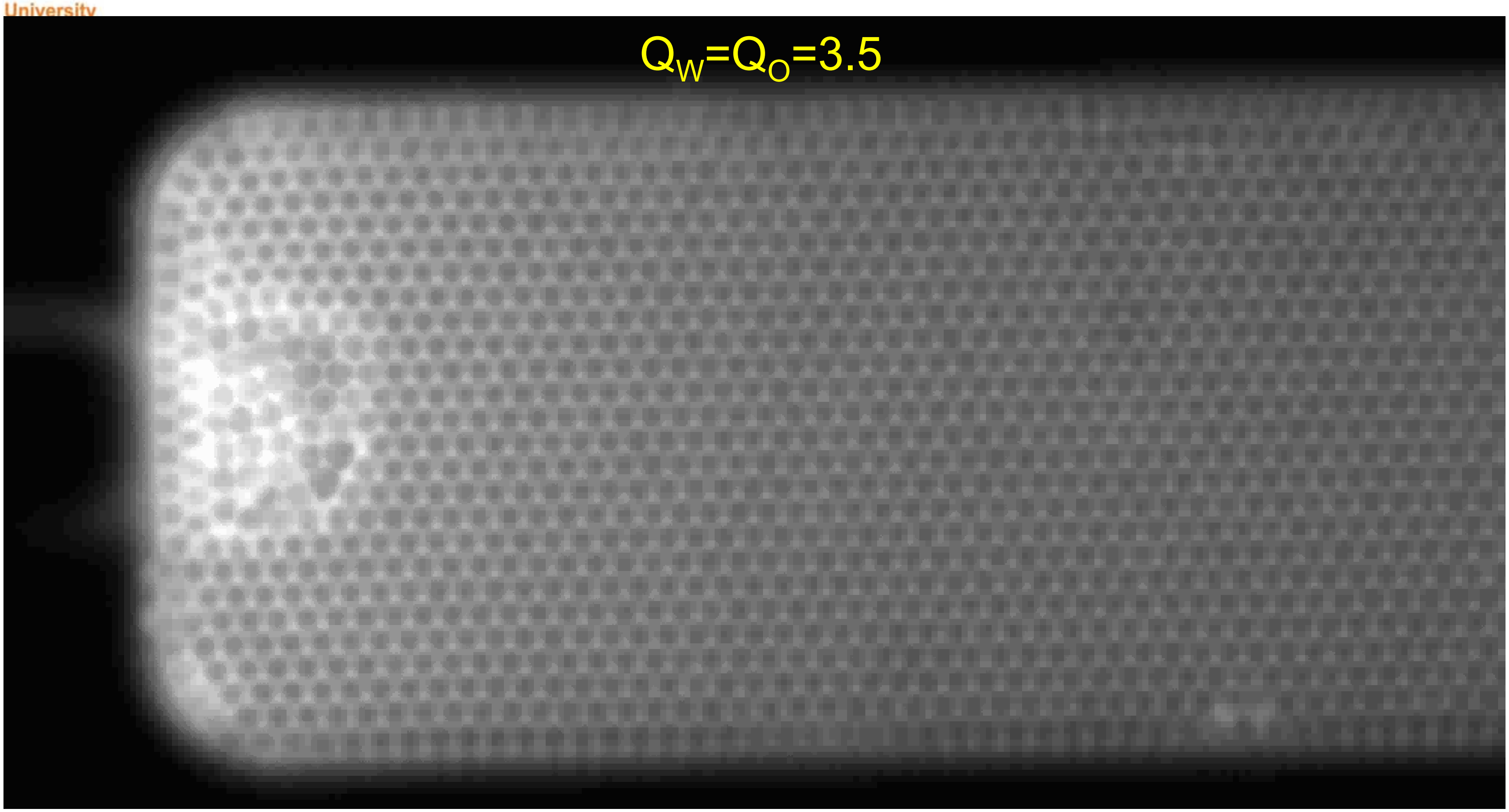


$Q_W=Q_O=1.25$

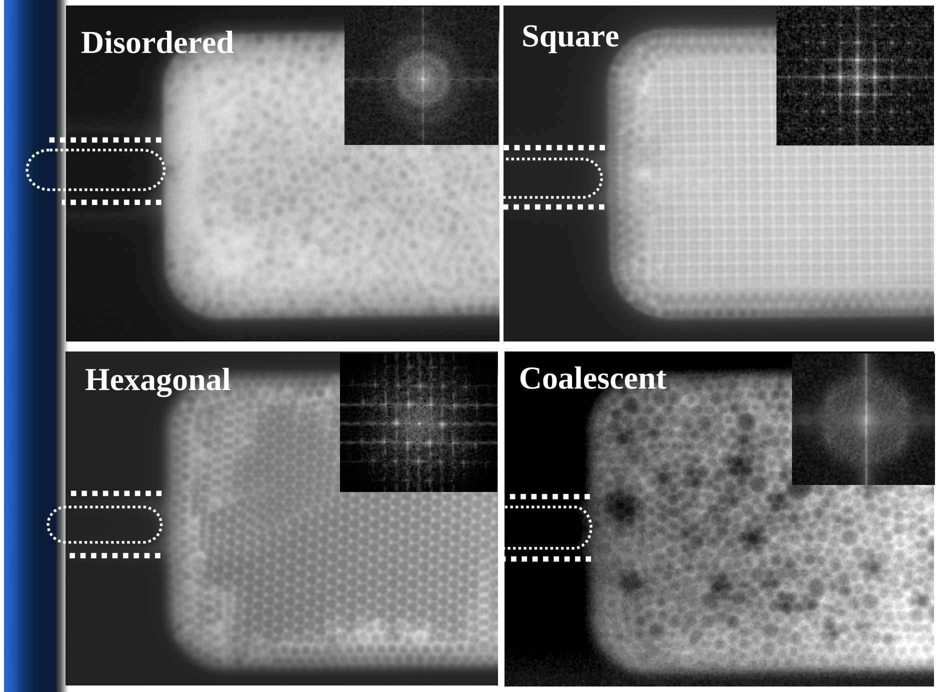
$Q_W$=0.8; $Q_O$=0.1



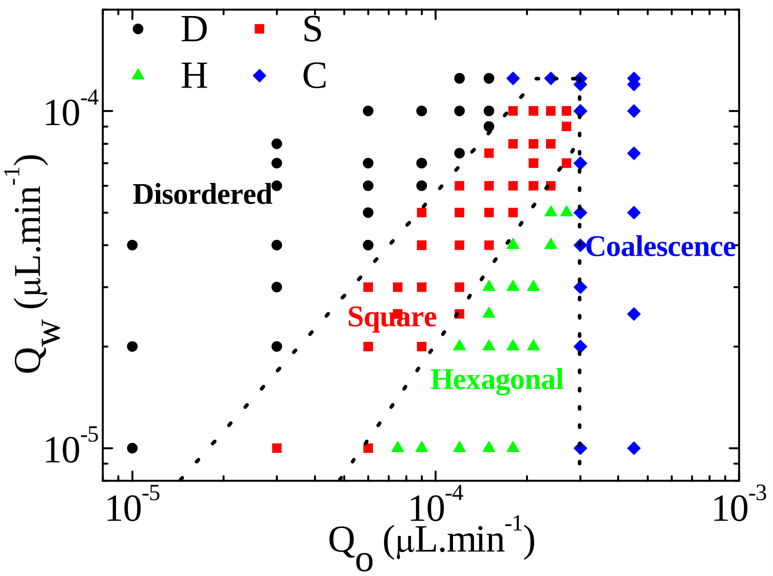

$Q_W$=1.25; $Q_O$=0.5


$Q_W=Q_O=3.5$

# Droplet arrangement

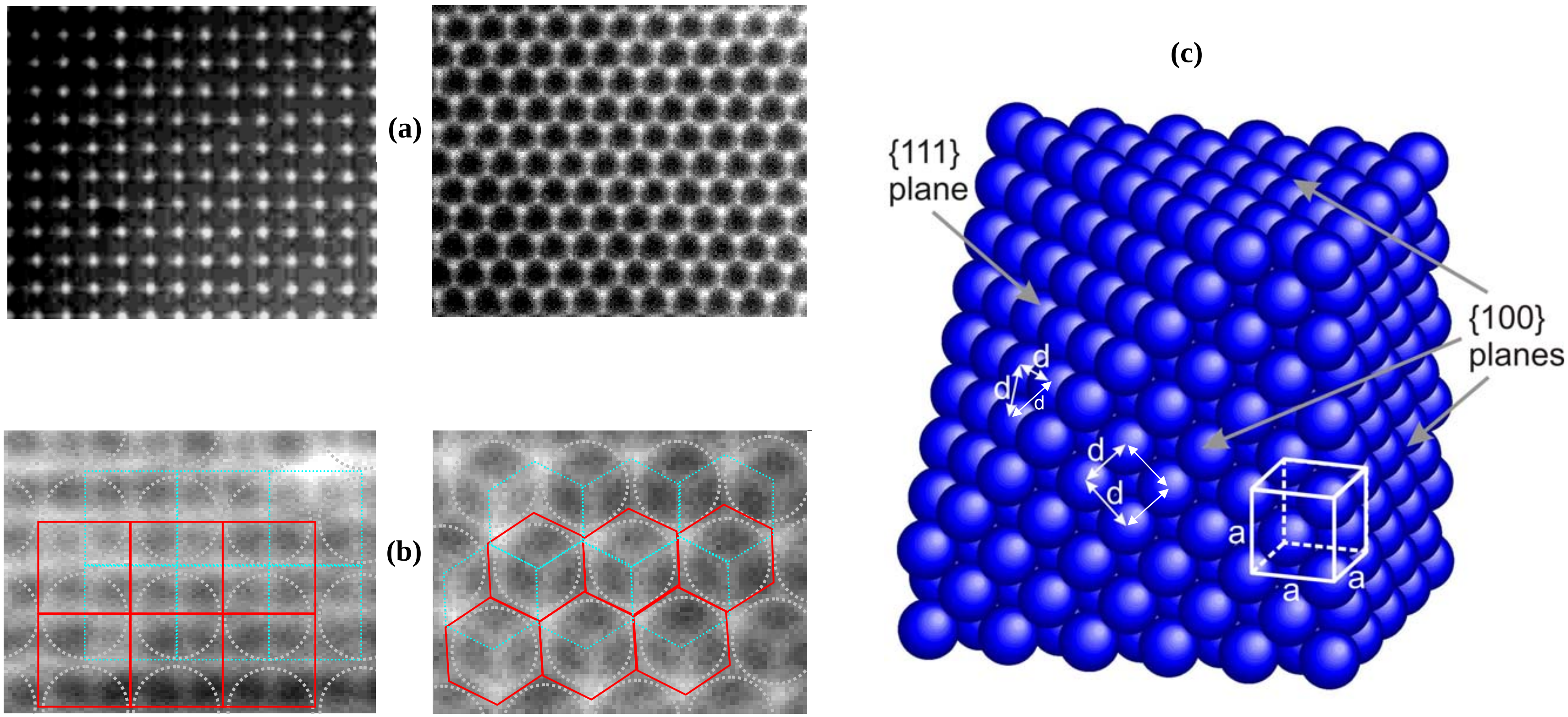



Flow Map

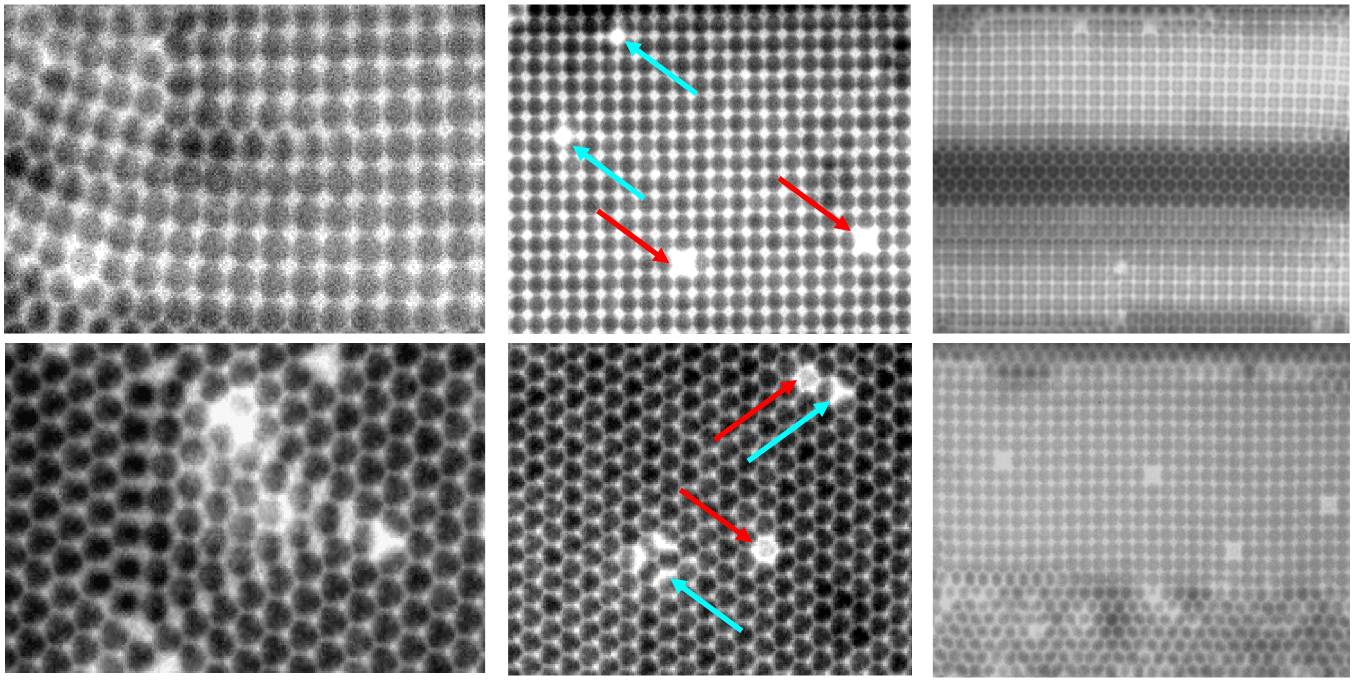



L.L. Shui, S. Kooy, J.C.T. Eijkel, A. van den Berg, in preparation.

# 3D Liquid Crystallography



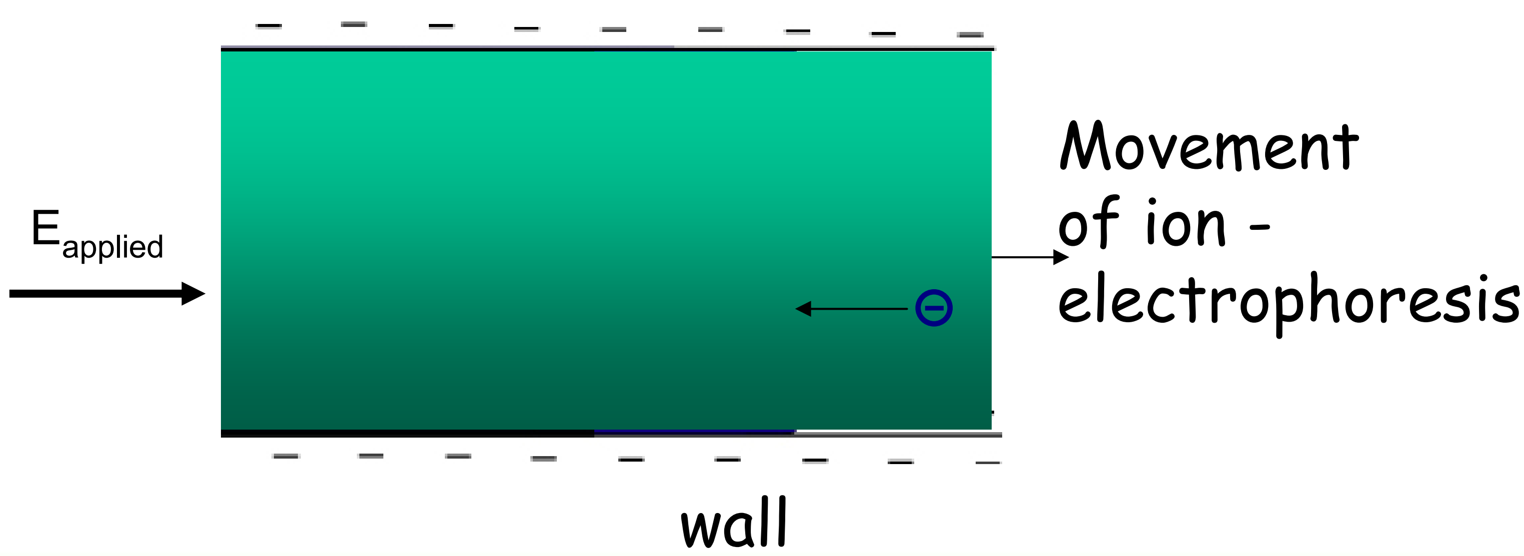
# Dynamic Organizations



# General Electrokinetics

- Electrophoresis – individual movement of ions and colloids with respect to fluid
- Electro-osmosis – bulk movement of liquid induced by localized charge of the wall

$SiOH \leftrightarrow SiO^- + H^+$

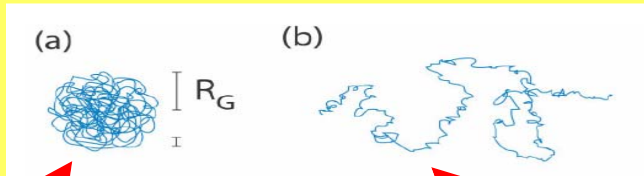


# Separation of DNA in open nanochannels


N. Kaji et al, *Anal Chem.*, (2004), **76(1),** 15-22.

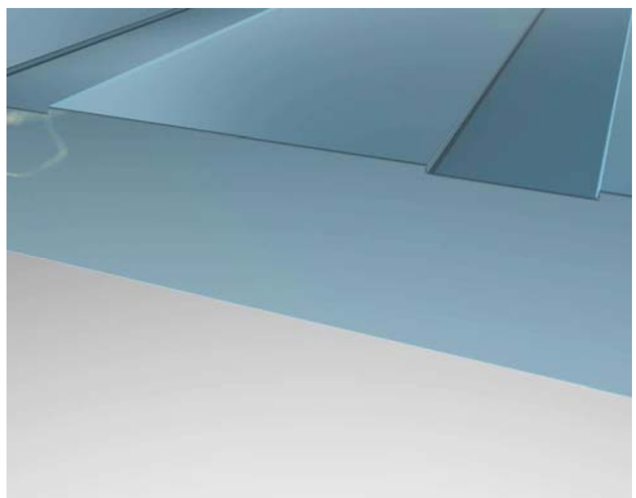
# Separation of DNA in open nanochannels






3d DNA blob

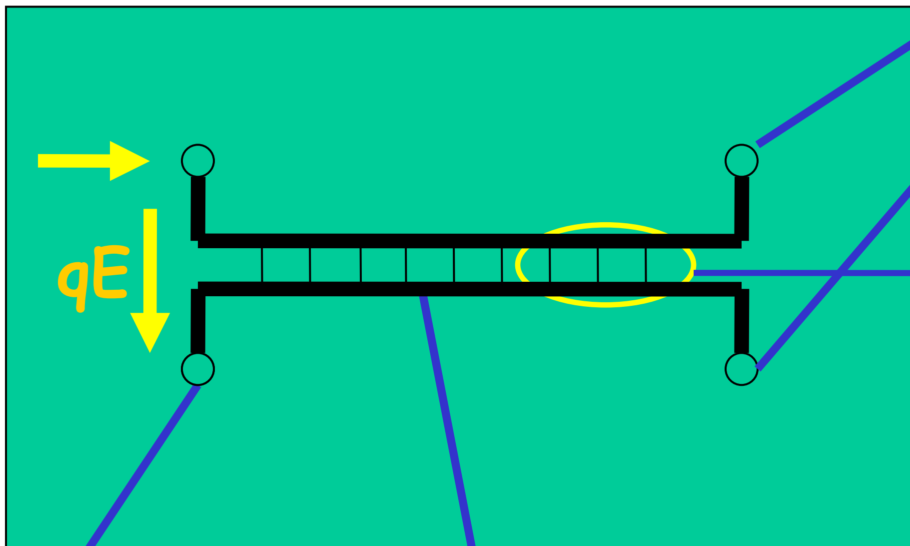
In slit: 2d DNA pancake

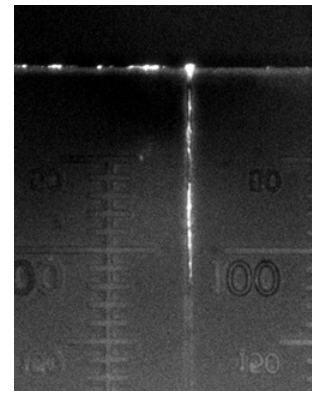


qE

# Nanoslit device

DNA
and buffer inlet




Nanoslit array

( between microchannels)

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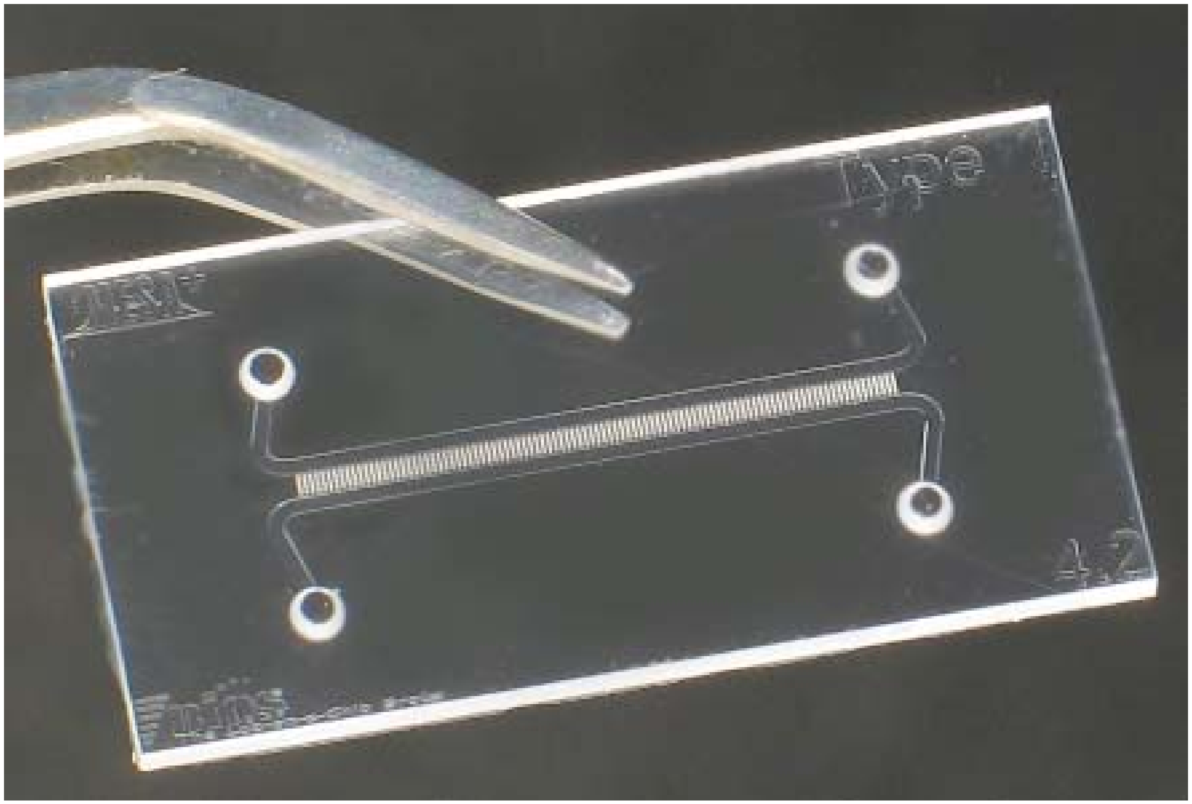
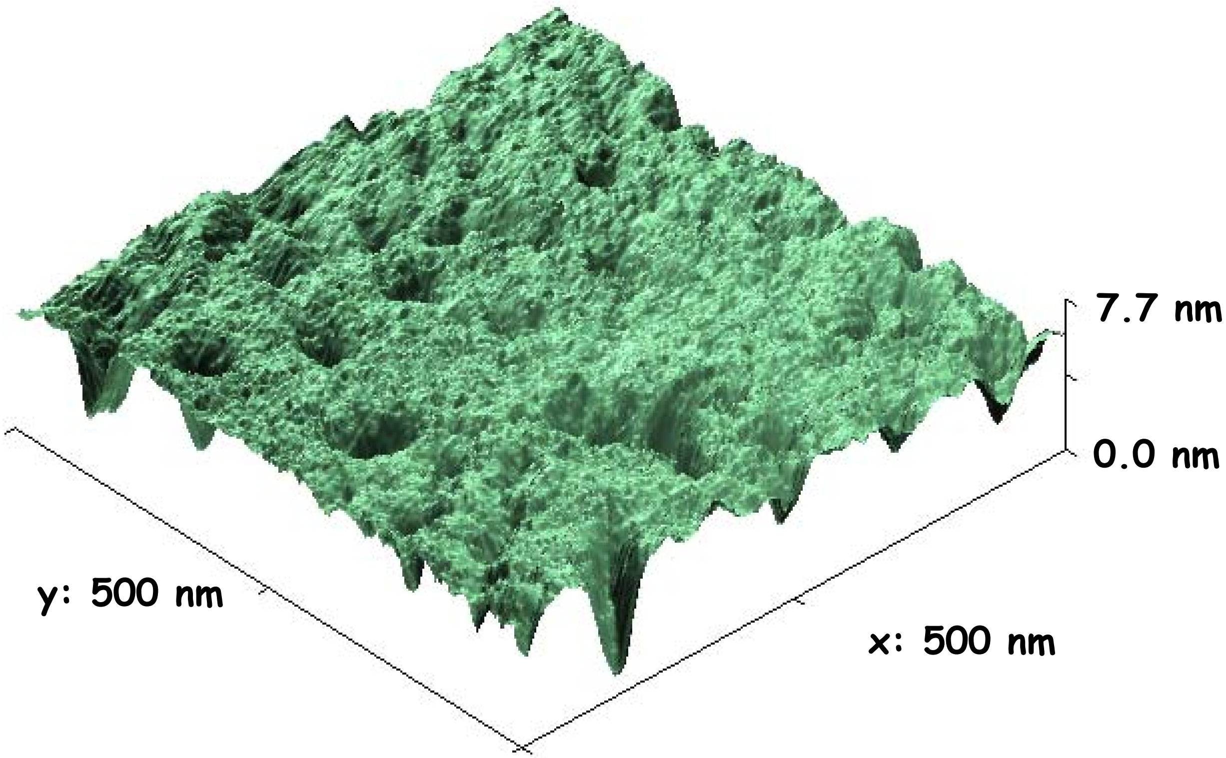
# Nanoslit device



Fused Silica sandwich

# Surface roughness nanoslit




Etched surface AFM scan; tip-radius 2 nm; 1 nm rms

# Experimental conditions

- YOYO-1 - λ -DNA (1/5 bp), length 20 μm
- Tris-Borate-Na-EDTA buffer, pH = 8.3
- β-MercaptoEthanol 3% against photobleaching and photoknicking
- Polyvinylpyrrolidone MW 10.000, 2.5% against electroosmotic flow

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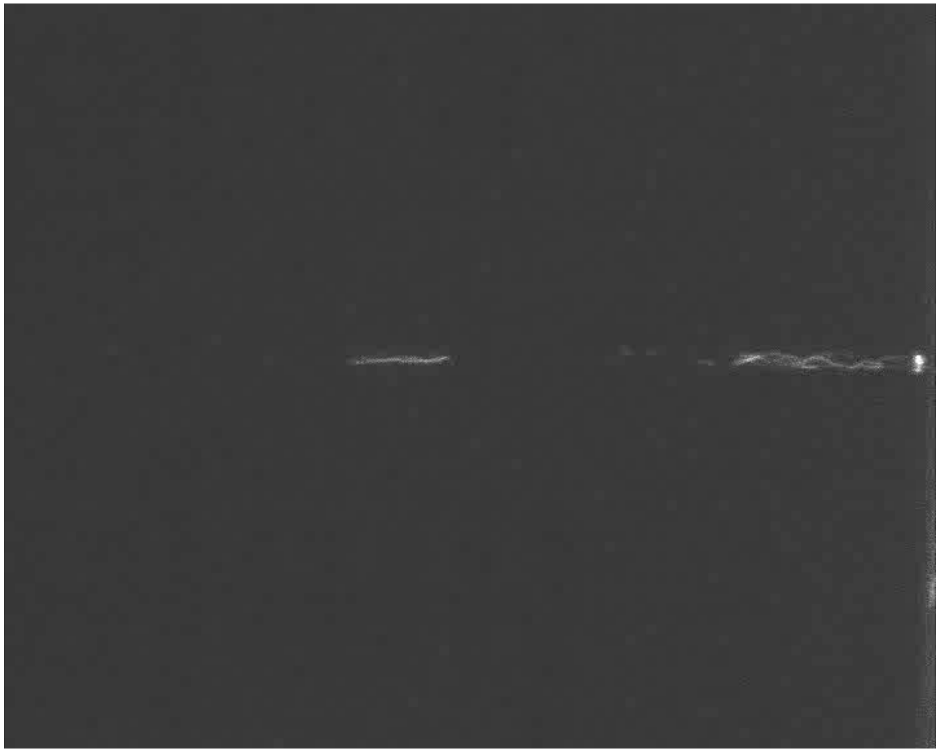
# YOYO-1 λ-DNA in a 20 nm nanoslit – high field

Electrical field
200 kV/m



qE

50 μm

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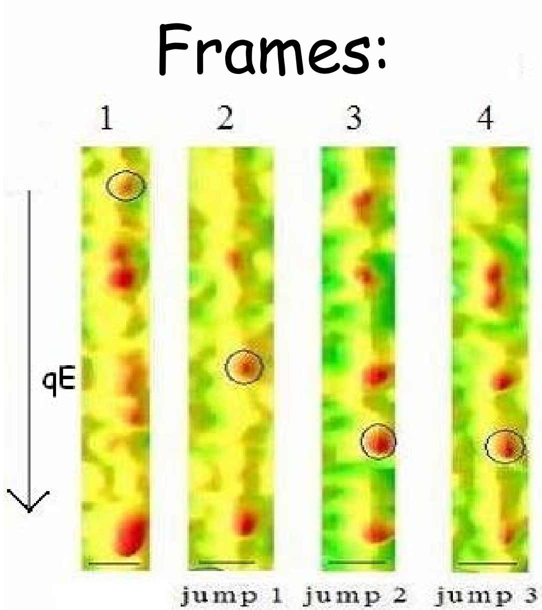
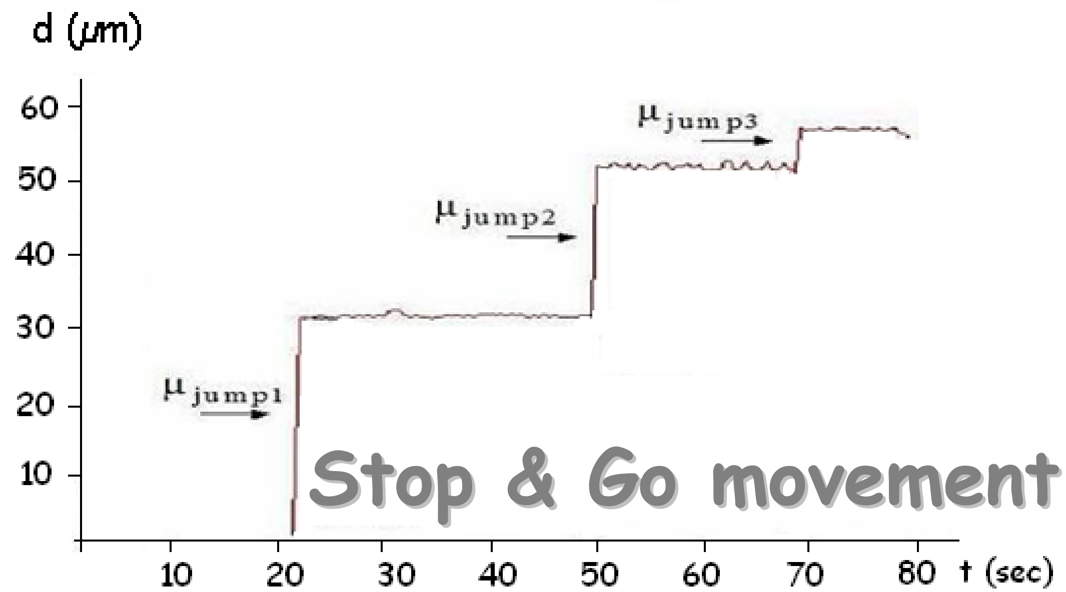
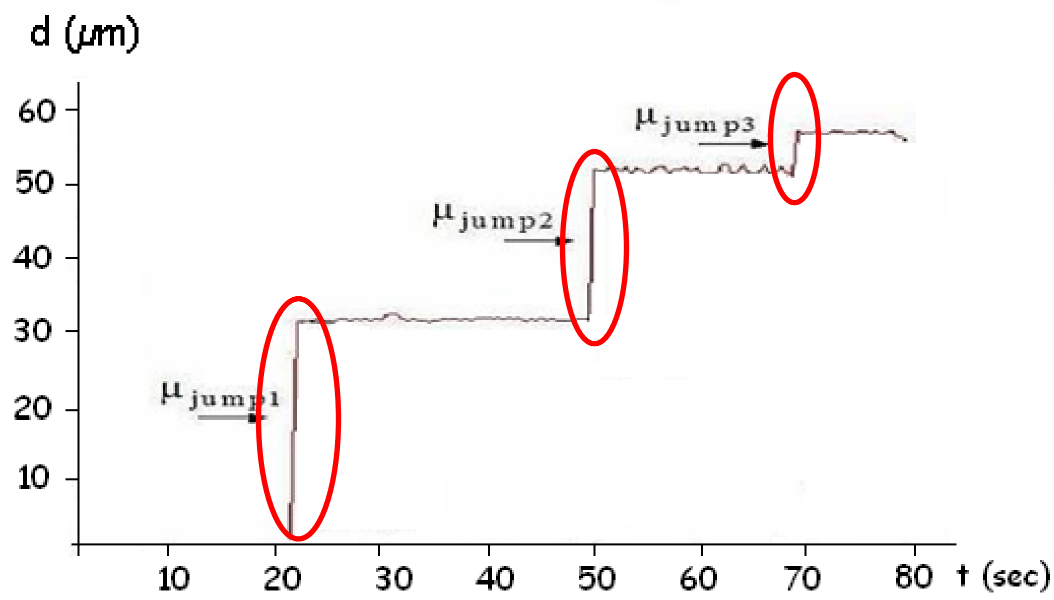
# High field λ-DNA movement



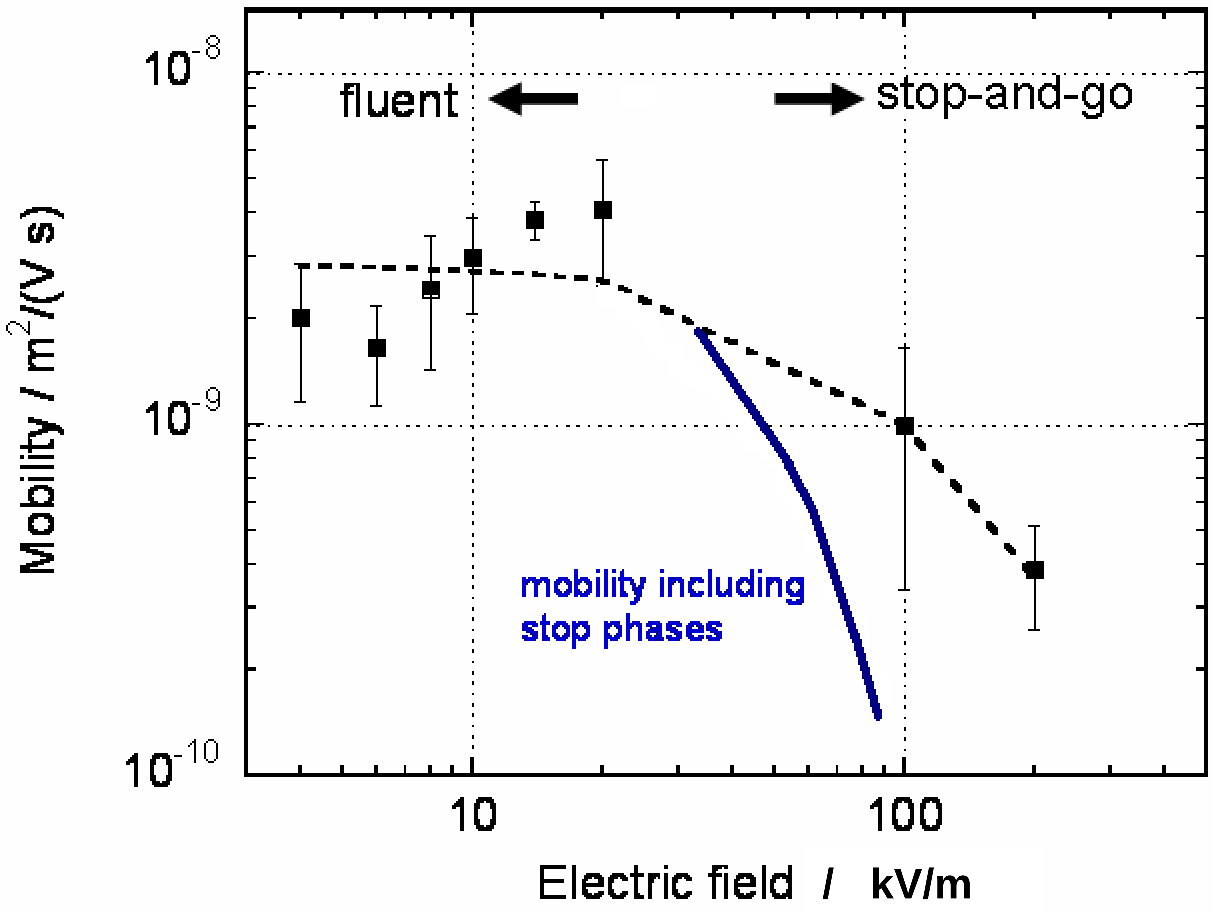

Electrical field 200 kV/m

# High field λ -DNA movement

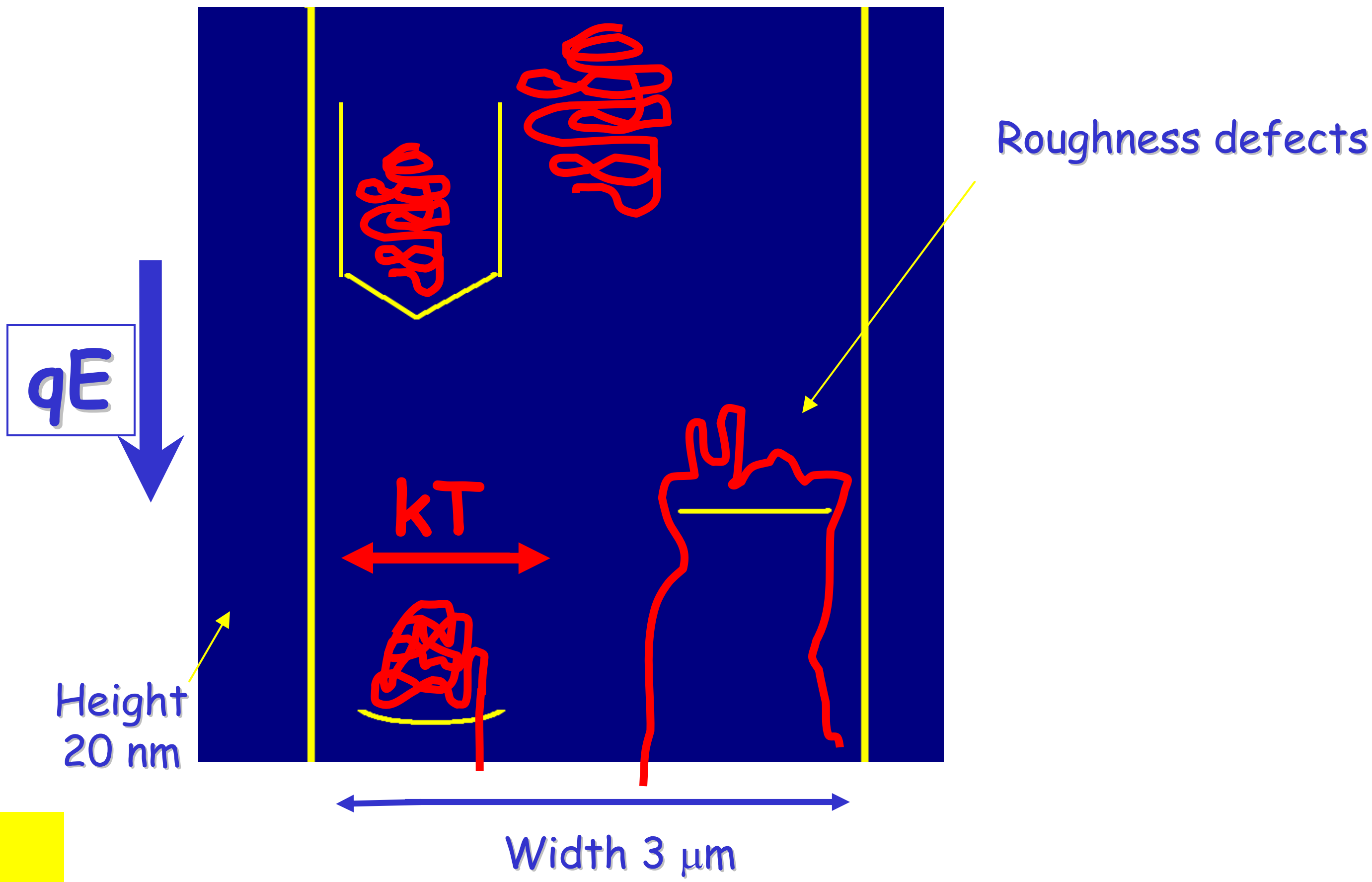



- Mobility in go phase 1% of bulk mobility!
- On average: 10% of time “go”, 90% “stop”
- Overall mobility: ~ 0.1% of bulk

# Field-strength dependent mobility



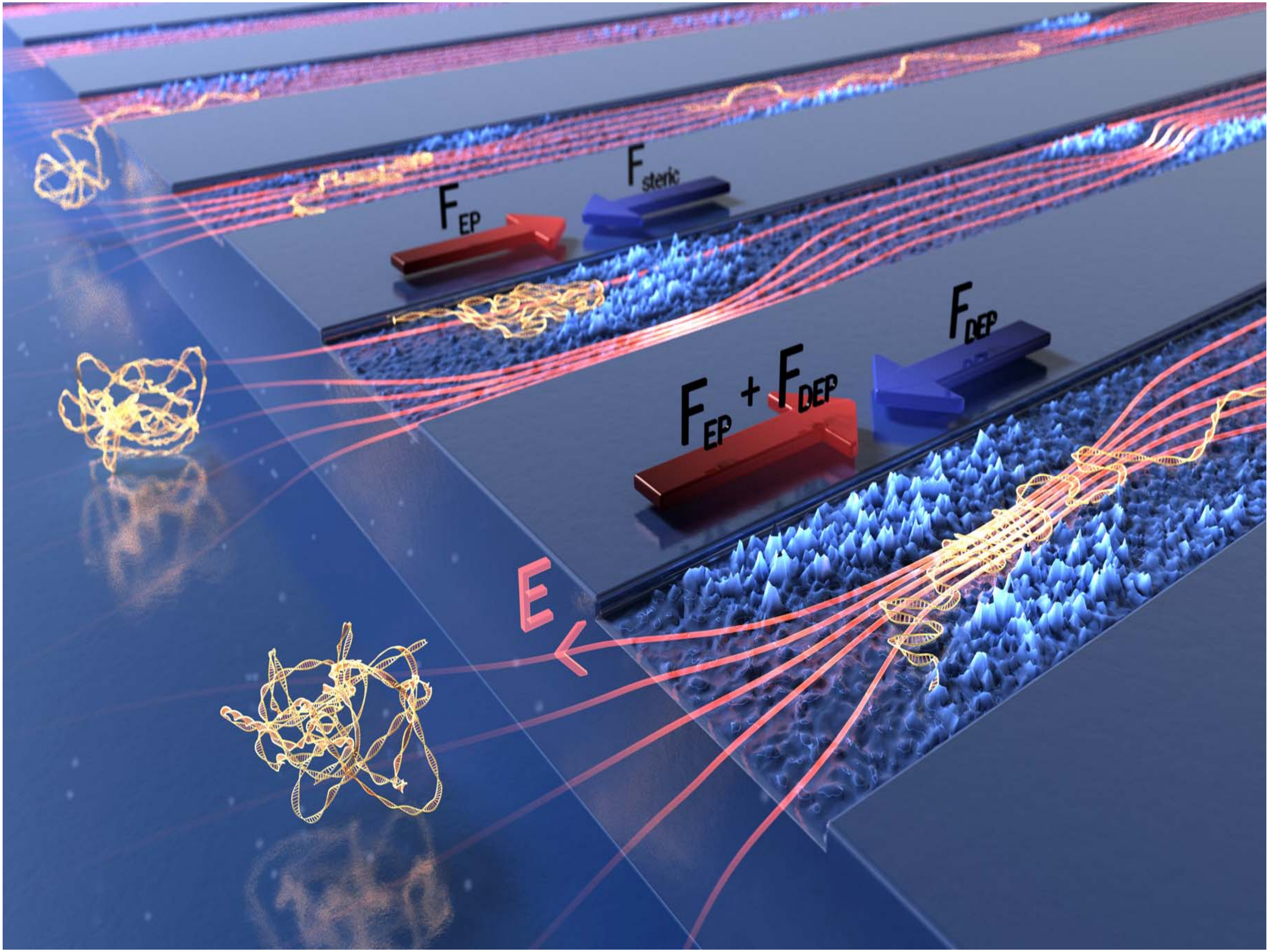
# Steric trapping




$$\mu = \frac{\mu_0}{\exp\left[cE\right]}$$

**Retardation by a series of trapping events**

e.g. Gauthier and Slater, J.Chem.Phys. 117 (2002) 6745



F_steric
F_EP
F_DEP
F_EP + F_DEP
E

# Previous studies:

## no mobility dependence on E-field

| | | |
|---|---|---|
| Tegenfeldt 2004 | 100x200 nm | 0.5 kV/m |
| Mannion 2006 | 100 nm cylinders | 2.1 kV/m |
| Cross 2007 | 19 and 70 nm slits | 3.3 kV/m |
| we | 12 and 20 nm slits | 2-200 kV/m |

# DNA separation

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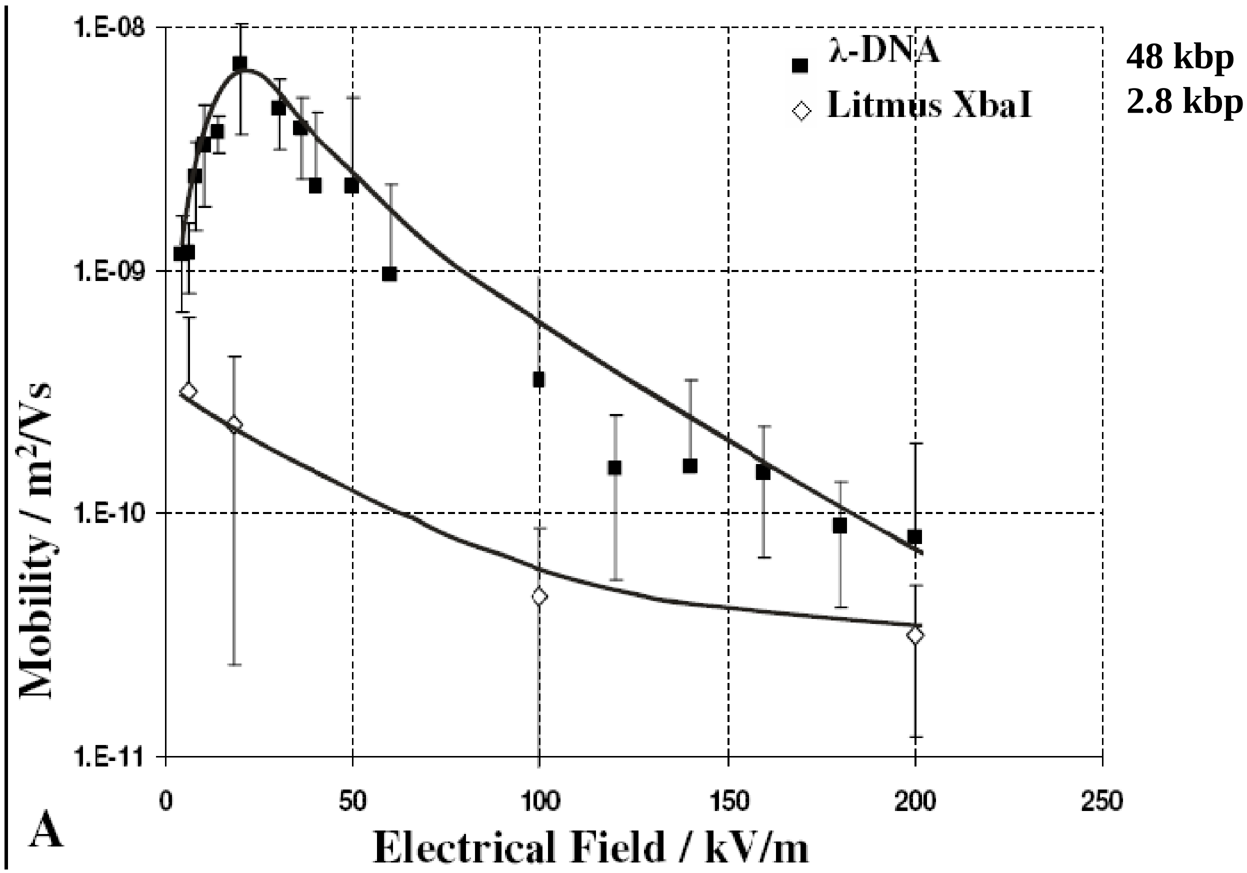


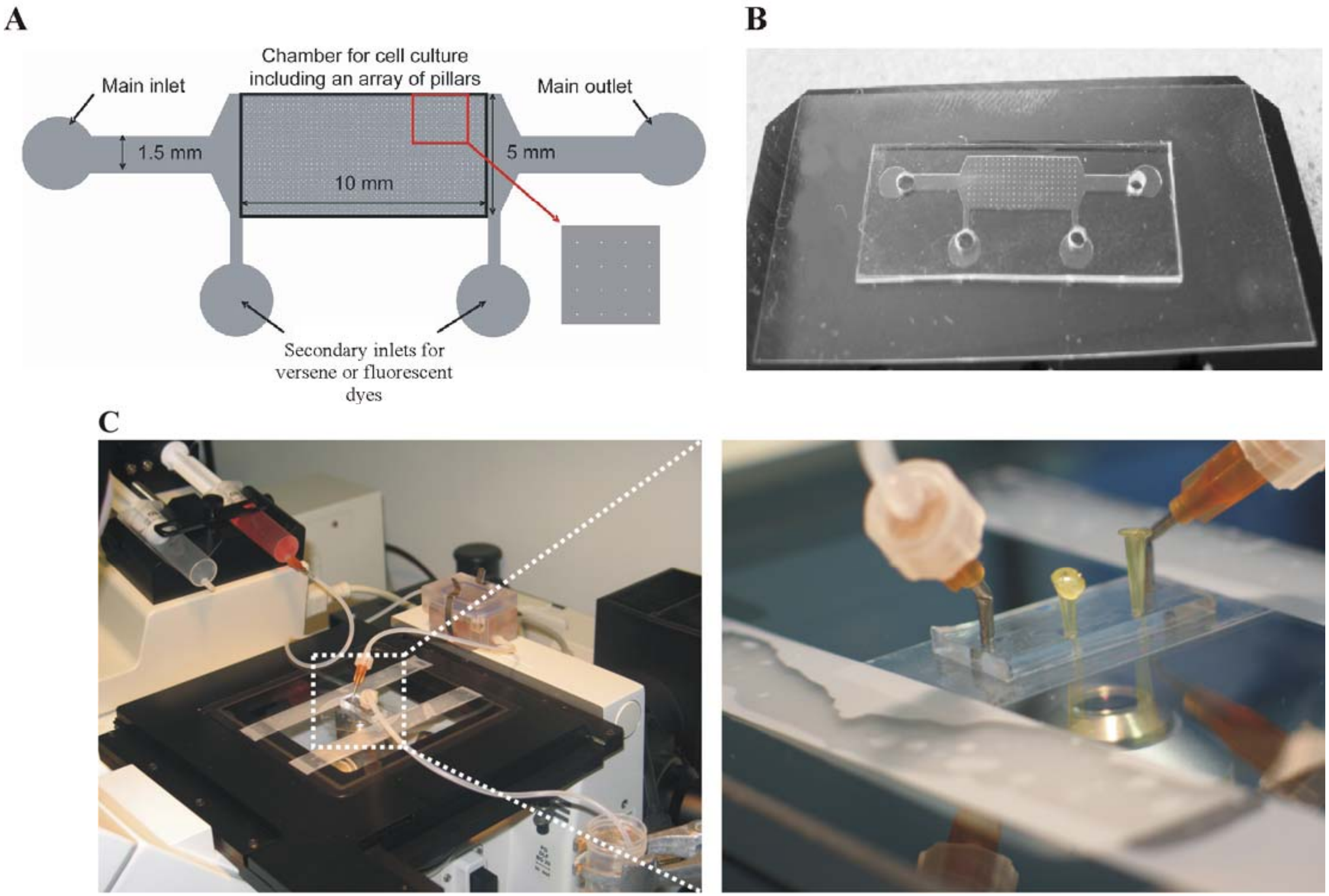

G.B. Salieb-Beugelaar et al., *Nano Letters*, (2008), **8(7)**, 1785-1790.

# Breastcancer chip

- 1/9 women affected
- Treatment depends on age, genetic factors, tumor type, etc.
- Lab-on-Chip technology for optimal choice of drugs
- First tests with cancer cell lines, later microbiopsy's

# Cancer chip

# Chip under microscope



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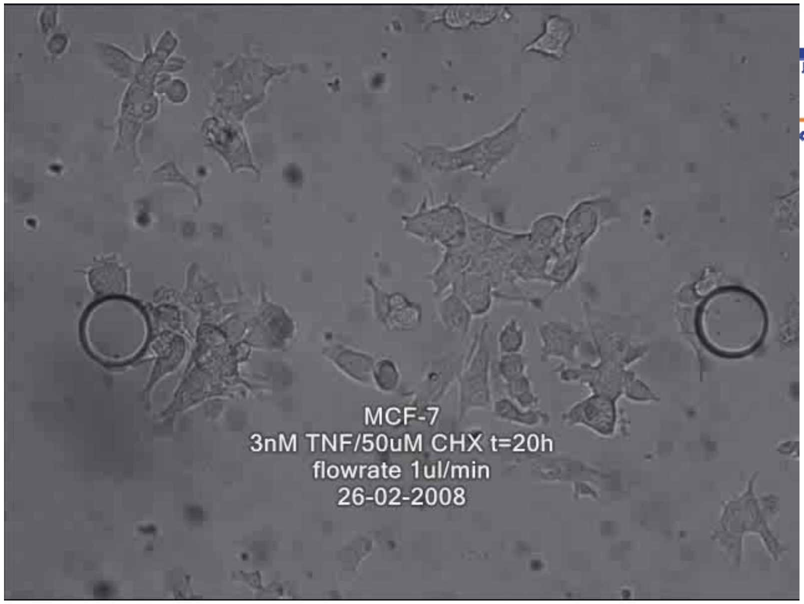
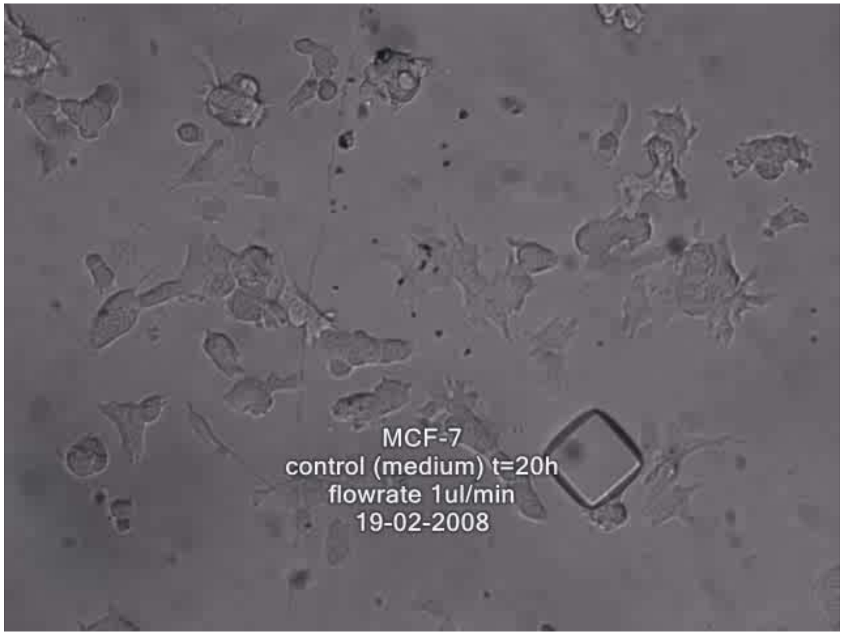
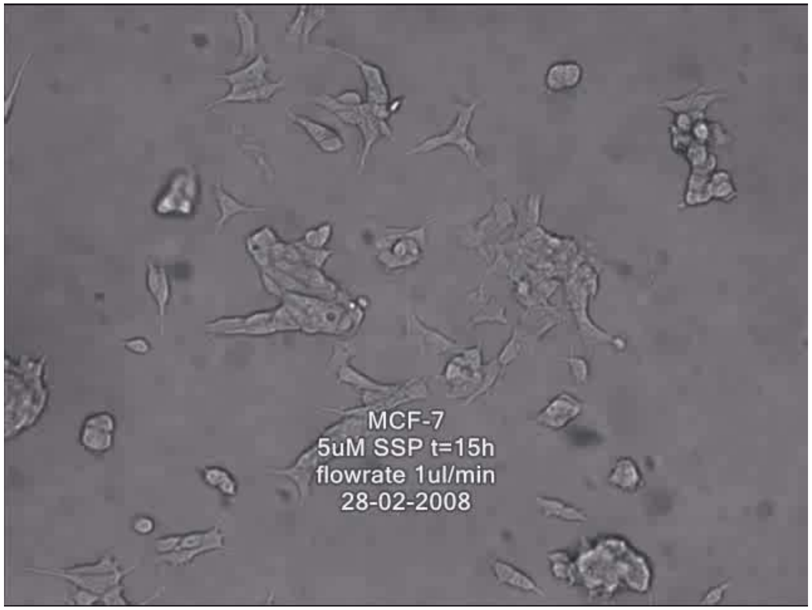
# TNF-α




control

SSP



# Cell-covered area measure for drug-efficiency

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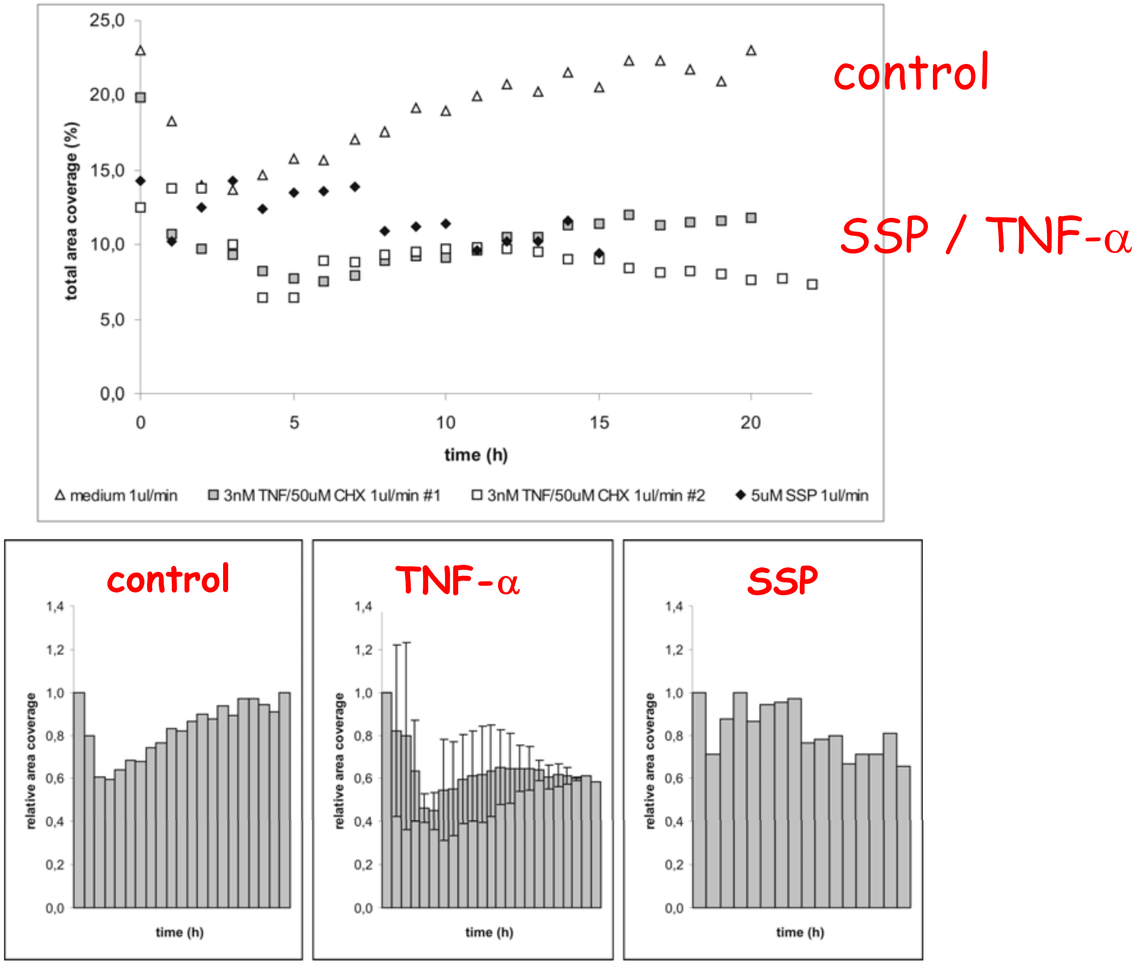
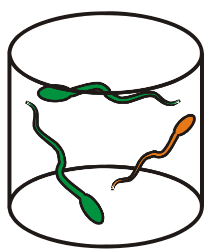


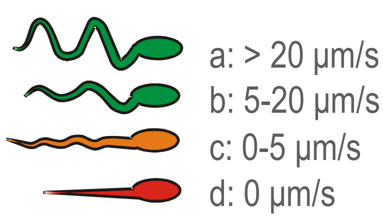
# Fertility chip

- 10% of couples
- Semen analysis:
  - Concentration, motility en morphology
  - Con's: patient unfriendly, labor intensive, unreliable

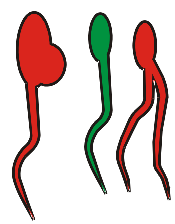
→ fertility chip



Concentratie > 20 miljoen cellen per mL




Motiliteit a>25% of a+b>50%



Morfologie > 15% normaal

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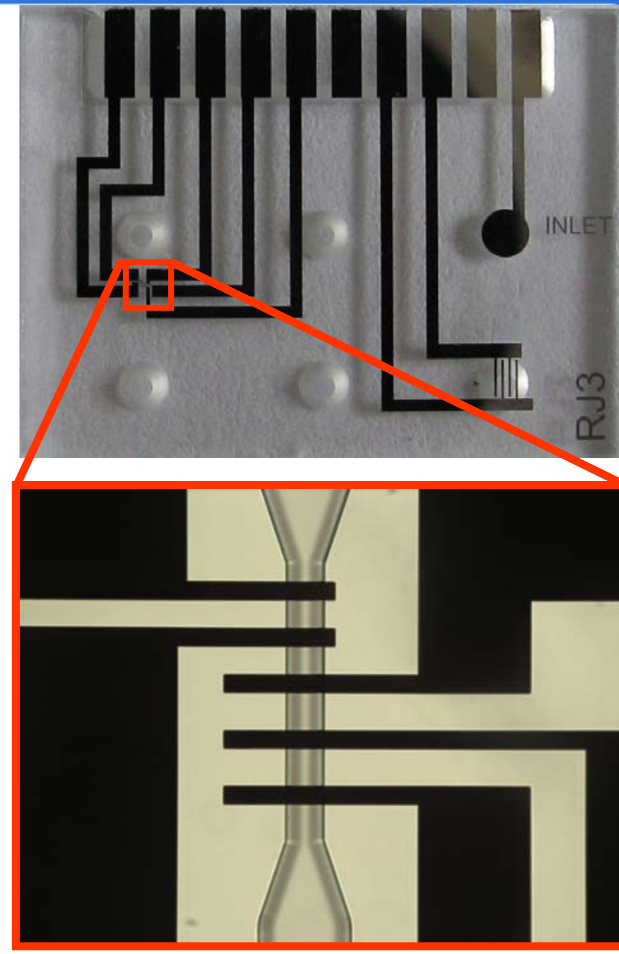
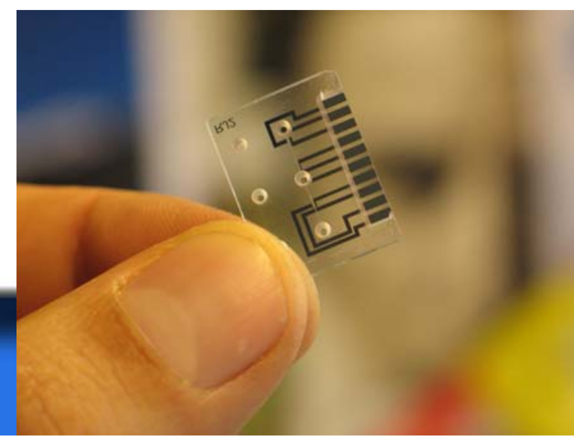
# Semen-on-chip

- Semen cells
  - Head: 3 µm wide, 5 µm long
  - Tail: 45-50 µm long
- Concentration:
  - Counting cells in fixed volume
- Chip
  - Channel: 20 µm deep en 42 µm wide



# Can we count semen cells?

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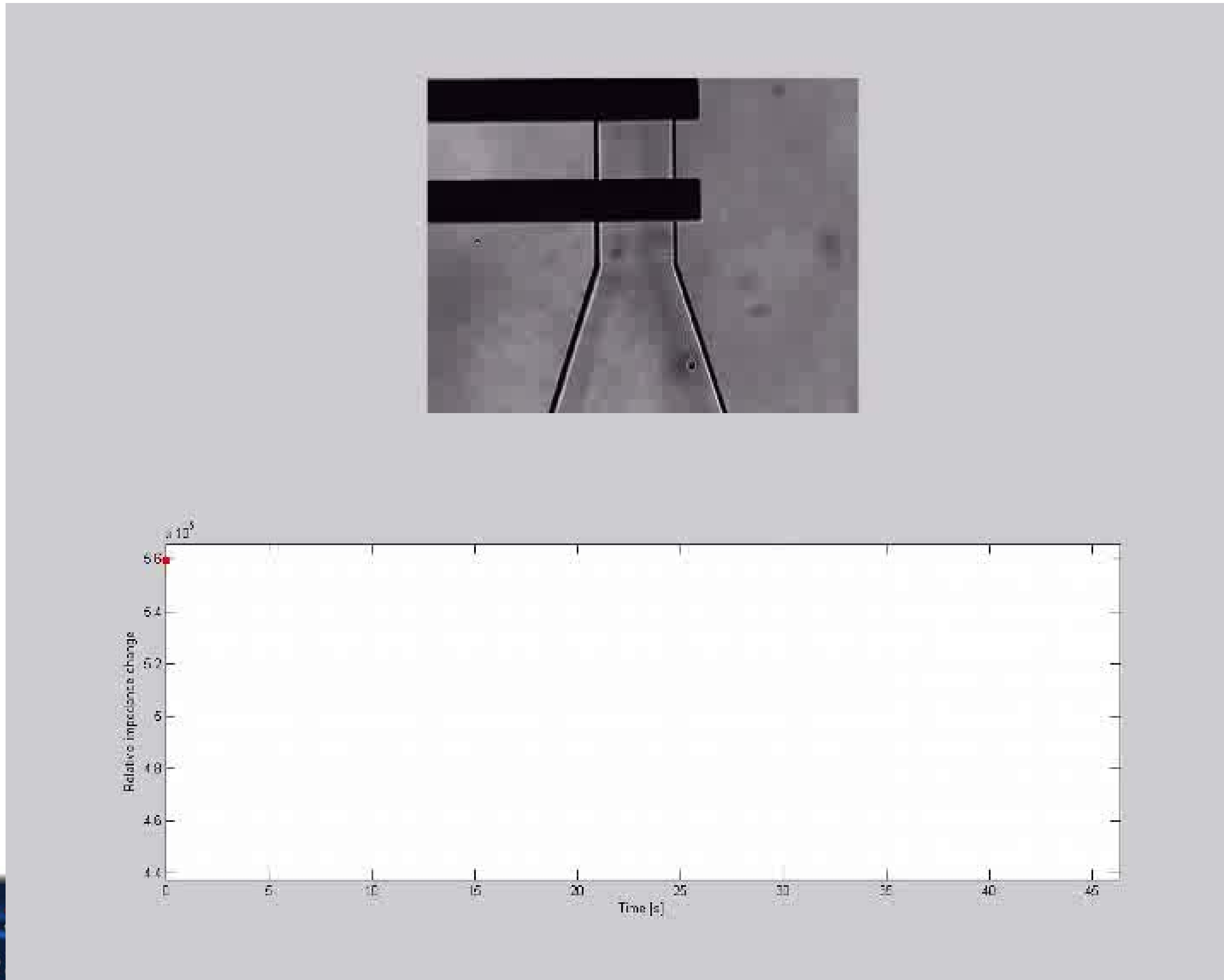
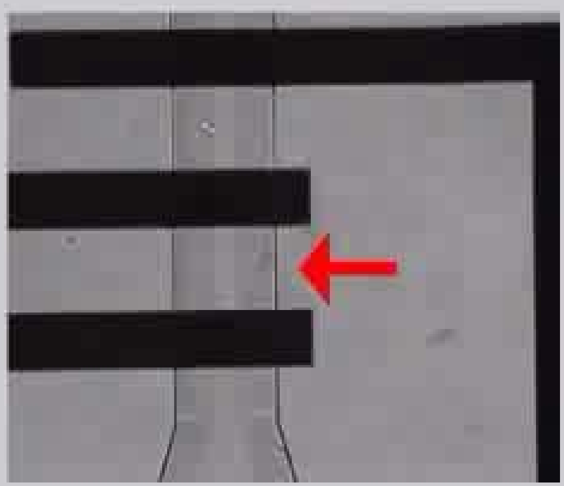
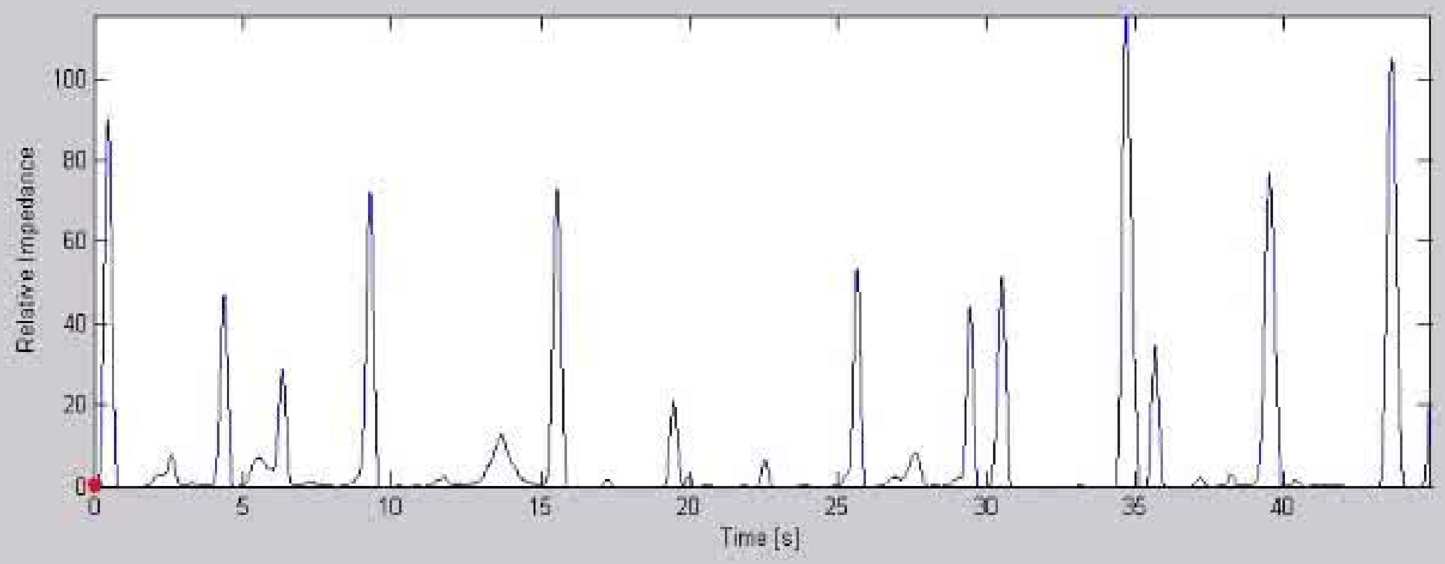
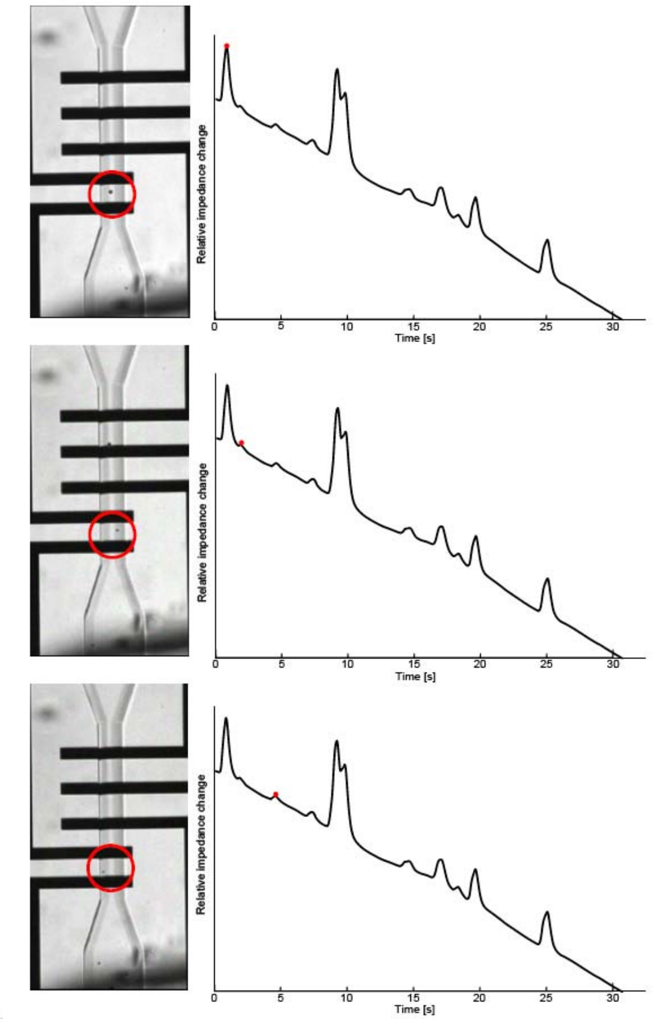


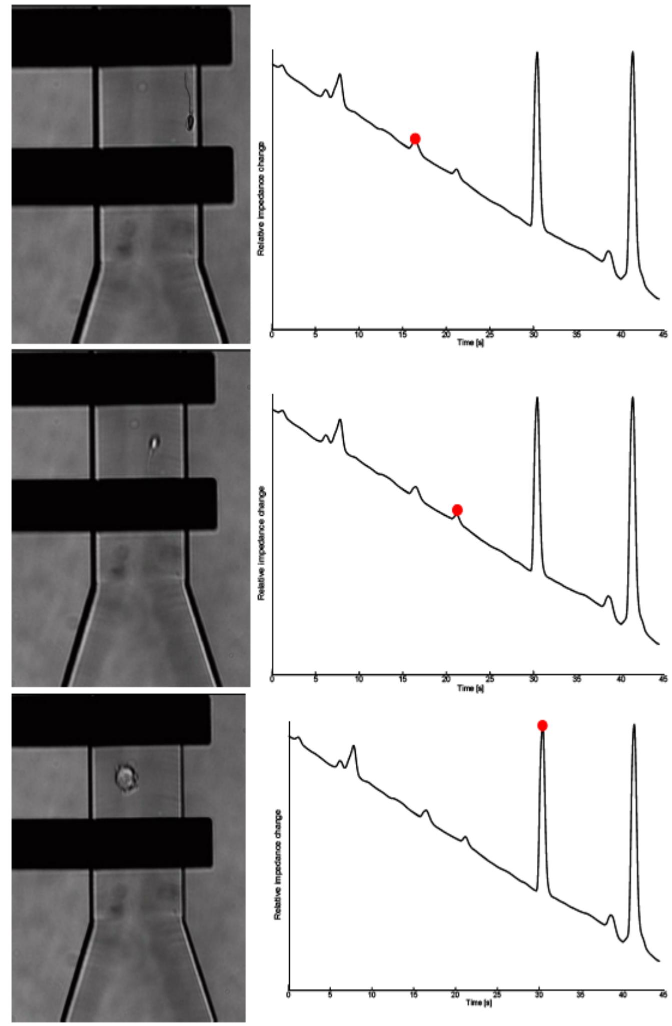



Relative Impedance
0
20
40
60
80
100
0
5
10
15
20
25
30
35
40
Time [s]

## 3,4,5 μm beads




## semen cells



# Conclusions

- Electrokinetics and capillary forces important for micro/nanofluidics
- Microfluidics enable LOC systems (lithium)
- Opportunities in biomedical applications

# Thank you for your attention !