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

Albert van den Berg

BIOS/Lab-on-a-Chip group
MESA+ Institute for Nanotechnology
University of Twente, The Netherlands
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)
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
Nanospain, March 9th, 2009

Development of µTAS/LOC concept

1970

1980

1990

2000

2010

Lab-on-a-Chip....
Two-phase flow microfluidics

Shear flow determined droplets

Geometry determine droplets
→ inlet-length L determined droplets

Ismagilov

Top view

Cross section

Water

Oil

h=10 or 20 µm

w=10, 20 or 40 µm

l=100, 500 or 1000 µm

l=1000 µm, \(Q_o=Q_w=1\times10^{-3}\) µL/min

l=1000 µm, \(Q_o=Q_w=5\times10^{-3}\) µL/min

l=500 µm, \(Q_o=Q_w=5\times10^{-3}\) µL/min

l=100 µm, \(Q_o=Q_w=2\times10^{-3}\) mL/min

l=100 µm, \(Q_o=2.5Q_w=5\times10^{-3}\) mL/min
Geometry determined droplet generation

$L = 1000 \mu m, h = w = 10 \mu m$

$L = 100 \mu m, h = w = 10 \mu m$
Droplet formation mechanism

(a) \[ P_{\text{atm}} - \Delta P_{\text{2-phase}} - P_L = \Delta P \]

(b) \[ V_{\text{droplet}} = V_{\text{c.c.}} \]

Capillary pressure decrease

Liquid Crystallography in Nano/Microfluidic Channels

\[ Q_w = Q_o = 1.25 \times 10^{-4} \mu L/min \]

\[ Q_w = 0.5 \times 10^{-4} \mu L/min \]

\[ Q_w = 0.8 \times 10^{-4} \mu L/min \]

\[ Q_w = 0.1 \times 10^{-4} \mu L/min \]

\[ Q_w = Q_o = 3.5 \times 10^{-4} \mu L/min \]

\[ Q_w = 0.4 \times 10^{-4} \mu L/min \]

\[ Q_w = 0.1 \times 10^{-4} \mu L/min \]
$Q_W = Q_o = 1.25$
$Q_W = 0.8; Q_O = 0.1$
$Q_w = 1.25; Q_o = 0.5$
$Q_W = Q_O = 3.5$
Droplet arrangement

3D Liquid Crystallography
Dynamic Organizations

- distortion
- defects
- coexistence
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

\[ \text{SiOH} \leftrightarrow \text{SiO}^- + \text{H}^+ \]

Movement of ion - electrophoresis
Separation of DNA in open nanochannels


*Nanospain, March 9th, 2009*
Separation of DNA in open nanochannels

3d DNA blob

In slit: 2d DNA pancake

qE
Nanoslit device

DNA and buffer inlet

Buffer inlet

Microchannels

Nanoslit array (between microchannels)

Outlets

Nanospain, March 9th, 2009
Nanoslit device

Fused Silica sandwich

Nanospain, March 9th, 2009
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**
YOYO-1 λ-DNA in a 20 nm nanoslit - high field

Electrical field
200 kV/m

50 µm
High field λ-DNA movement

Frames:

1. Stop & Go movement
2. High field
3. λ-DNA movement
4. Electrical field 200 kV/m

\[ qE \]

\[ \text{Jump 1, Jump 2, Jump 3} \]

\[ d (\mu m) \]

\[ \mu_{jump1}, \mu_{jump2}, \mu_{jump3} \]

Stop & Go movement

Electrical field 200 kV/m

Nanospain, March 9th, 2009
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

Mobility / m²/(V·s)

Electric field / kV/m

10⁻⁸
10⁻⁹
10⁻¹⁰

fluent → stop-and-go

mobility including stop phases

Nanospain, March 9th, 2009
Steric trapping

\[ \mu = \frac{\mu_0}{\exp(CE)} \]

Retardation by a series of trapping events

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

Nanospain, March 9th, 2009
Dielectrophoretic trapping

\[ \mu = \mu_0 \exp(2\kappa E) \]

*For example, Ajdari and Prost, PNAS 88 (1991) 4468*
## Previous studies:

### no mobility dependence on E-field

<table>
<thead>
<tr>
<th>Study</th>
<th>Feature</th>
<th>Voltage (kV/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tegenfeldt 2004</td>
<td>100x200 nm</td>
<td>0.5</td>
</tr>
<tr>
<td>Mannion 2006</td>
<td>100 nm cylinders</td>
<td>2.1</td>
</tr>
<tr>
<td>Cross 2007</td>
<td>19 and 70 nm slits</td>
<td>3.3</td>
</tr>
<tr>
<td>We</td>
<td>12 and 20 nm slits</td>
<td>2-200</td>
</tr>
</tbody>
</table>
DNA separation

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
Chip under microscope
Cell-covered area measure for drug-efficiency

control

SSP / TNF-α
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
Motilitéit a>25% of a+b>50%
Morfologie > 15% normaal
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?
3,4,5 μm beads

Nanospain, March 9th, 2009

The Lab-on-a-Chip Group
Conclusions

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

• Floor Wolbers, Job Komen and prof. Istvan Vermes (MST) (apoptosis studies)
• Colin Ingham, Ad Sprenkels, Johan Bomer (million well Petri Dish)
• Elwin Vrouwe, Regina Luttge and Han Gardeniers, Pieternel Kolling (microneedles and lithium chip)
• Ana Valero, Janine Post and prof. Wiebe Kruijer (single cell electroporation)
• Loes Segerink, Robert-Jan Raterink (Vruchtbaarheidschip)

Thank you for your attention!