

Applied Microfluidics

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Why downscaling?



Volume V ~
$$d^3$$

Area A ~ d^2

Length L ~ d



Why downscaling?



Volume V ~ d^3 \Rightarrow 1. Individual handling and
manipulation of microscale
objects in a liquid environment
requires systems of the same
magnitude order

Length $L \sim d$



Smal	l scal	le o	bj	ects
	<u> </u>			





Why downscaling?



Volume V ~ d^3 \rightleftharpoons 2. Handling and manipulation
of very small sample volumes
(<10 µl) requires system
features of the same
magnitude order

Length L ~ d



gas liquid			Volume		/olumes
		1	Volume	size	
			1 ml=10 ⁻⁶ m ³	1 cm	
Conti mo	dels		1 μl =10 ⁻⁹ m ³	1 mm	Smallest pipettes dispense ~0.5µL
		uidics	1 nl=10 ⁻¹² m ³	0.1 mm	Inkiet print droplets ~50 pl
		Aicrofl	1 pl=10 ⁻¹⁵ m ³	10 µm	
		dics	• 1 fl =10 ⁻¹⁸ m ³	1 µm	
		ofluic	1 al =10 ⁻²¹ m ³	0.1 µm	
Mole	ecular	n Nar	1 zl =10 ⁻²⁴ m ³	10 nm	
Qua	ntum	kdow	1 yl=10 ⁻²⁷ m ³	1 nm	
ppy	/SISS	Cont brea	1 xI=10 ⁻³⁰ m ³	1 Å	



Why downscaling?



Volume V ~
$$d^3$$

Downscaling leads to an increased area per volume: A/V ~ 1/d

Area A ~ d^2

Length L ~ d

Surface related physical effects become dominant in the microscale



Examples of surface related effects in fluidics

- Friction at the liquid-solid boundary:
 - Zero slip at the wall results in laminar flow
- Electro-fluidic interaction:
 - Electric double layer related phenomena:
 - Electro-osmotic flow
 - Electro-viscous effect

. . .



Why downscaling?



Volume V
$$\sim$$
 d³

Diffusion becomes a transport phenomenon of importance

Area A ~ d^2

Length L ~ d



Diffusion as a transport mechanism

Diffusion is described by Fick's first and second law (see Wikipedia for more information).



Molecule in H ₂ O	Typical D	L _D for 1 s	L _D for 100 s
N_2	1e-6	2 mm	20 mm
Protein (100 kDa; 5 nm diameter)	1e-10	20 µm	200 µm

Why downscaling (fluidic) components?





Lecture outline

- Classification of microfluidic components and systems
- Gas microvalves
- Inkjet printheads
- Micropumps
- Power-MEMS
 - ♦ Fuel cells
 - Microcombustion systems
- Examples of commercially available multifunctional microfluidic platforms
 - PDMS based fluidic microfluidic platforms
 - CD-based microfluidic platforms
- Microfluidic solutions for diagnostic devices
- Micro-macro fluidic interfaces
 - Nebulisers
 - ESI tips

Bubblejet printhead principle





Some typical figures:

- heater temp: 400°C
- drop velocity: 10 m/s
- drop volume: 100 pl
- pressure range:
 - bubble growth: 10 40 atm
 - bubble collapse: 100 atm
- cycle frequency: 1 10 kHz



Inkjet printheads - Examples



Figure 1. Bubble-jet principles (left Edgeshooter, right Sideshooter)



Fig. 4: Close-up of the nozzle array. At the rear of each microchannel is the integrated polysilicon heater.



Figure 6. Cross sectional SEM-images of Backshooter microsystems.



Inkjet Printers – Monolythic system integration

Need for large data handling requires high level of integration !



Figure 4. Structure of the Backshooter microsystem inkjet printhead (not true to scale) Layers: (1) Substrate (<110>silicon); (11) etch stop layer (LPCVD-Si₃N₄); (12)PECVD-SiO₂; (13)BPSG; (14) 1. metal layer(Al); (15) undoped silicate glass (USG); (16) heater layer (HfB₂); (17) 2. metal layer (Al); (18) thermal throttle layer (PECVD-Si₃N₄); (19) galvanic adhesive layers (Ti / Cu); (20) carrier layer (Ni / Au); (21) thermal SiO₂. Elements: (a) bond pad (Al); (b) heating element (HfB₂); (c) nozzle; (d) PMOS transistor; (e) NMOS transistor; (f) ink chamber / ink; (g) vapour bubble



Figure 3. Material and signal flow in the Backshooter microsystem inkjet printhead



Figure 2. Schematic Backshooter printhead (filled half with ink)



Group discussion

What limits the amount of pages/minute that a bubble jet printer can produce?





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Micropumps – a classification











Micropump applications

The following is a non-exhaustive list of used and suggested applications:





Bubble valve pump



Top to bottom net flow



Freely adapted from [A planar laminar mixer, Evans et al, Berkeley]

Hydrolysis as actuator

- positive current dissociates the water
 - \rightarrow gas bubbles push out the liquid
- Negative current reduces the gas
 → liquid is sucked back
- 3 electrodes:
 - 2 used for actuation (red, green)
 - 2 used for conductivity measurement (green, blue)



Figure 6: Drawing dispensed liquid back into the meander by current reversal. In the first phase (t<70 s) 50 nl is dispensed and drawn back in the second phase.







Expandable bead actuators



Expandable microspheres in PDMS

- Mixing PDMS and Expancel® microspheres: XB-PDMS
 - \rightarrow A thermally responsive PDMS composite
 - ◆ Large expansion (> 100%)
 - Highly elastomeric
 - Non-toxic and chemically inert
 - Allows for e.g. soft lithography, casting, spinning...
 - Highly integratable actuator







Expandable bead pumps





Peristaltic pump principle



Other examples of peristaltic movements in nature:

- Movement of worms and larves
- Intestines pressing through food



A peristaltic micropump example



J. G. Smits, "Piezoelectric Micropump with Three Valves Working Peristaltically," *Sensors and Actuators*, vol. A21-A23 (1990) 203-206.



Reciprocating Pumps

A pump consisting of:

- One pressure chamber enabling volume displacement (with at 1. one side most often a diaphragm actuator);
- Flow directing elements at the inlet and outlet: 2.





Passive mechanical microvalves



[Shoji et al., Microflow devices and systems, JMM 4 (1994), pp. 157-171]

Reciprocating passive valve micropump

Piezoelectrically actuated flap valve micropump



[R. Linneman et al., MEMS'98, Heidelberg]



Electrostatically actuated flap valve micropump actuation chamber pump diaphragm / counterelectrode pump chamber isolation layer actuation unit valve uni

[R. Zengerle et al., MEMS'95, Amsterdam]

Thermopneumatically actuated diaphragm valve micropump [van de Pol et al., Sensors & Actuators, 1990]



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PDMS based microfluidic microfluidic platform





PDMS based microfluidic microfluidic platform

100 1000

Interfacing requirements:

• Input:

Sample Reagents

• Output:

Reaction products Waste

• Pneumatic control lines:

Integrated fluidic multiplexer:

2n+1 control lines steer n² single valve units

More information: Stanford online lecture on http://www.youtube.com/watch?v=n0gmTc2wA3k

KTH-EE-MST – Microfluid



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- Fabrication:
 - 2-layer plastic CD
 - molded microfluidic channels
- Liquid manipulation forces
 - ♦ Capillary force
 - Spinning
 - Coriolis forces
 - Integrated fluidic functionality:
 - Valving, Dosing, Pumping, Mixing
 - Applications:
 - MALDI preparation
 - Cell incubation

[Photographs: Gyros Microlabs, Upsala]

Dosing in a rotational fluidic microfluidic platform

Capillary force draws liquids into a distribution channel, filling a volume definition chamber.

A hydrophobic break (in red) prevents liquid moving further into the

microstructure.

As the CD spins, the distribution channel empties, leaving behind a precisely defined liquid volume.



A second spin, at higher speed, creates a g-force sufficient to drive the liquid over the hydrophobic break.

> [illustrations: Gyros Microlabs, Upsala]

Gyros Lab-CD technology

Towards disc centre



1. Liquid drawn in by capillary action.

2. Overflow channel activated at a low spin speed, removing excess liquid.

3. Volume (60 nl) defined within the chamber.

4. Defined volume moves through packed column by increasing spin speed.



Towards disc edge

[www.gyros.se]
Gyros Lab-CD technology

Towards disc centre



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KTH-EE-MST – Microfluidic devices – Wouter van der Wijngaart – Spring 2009

[www.gyros.se]



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EWOD: ElectroWetting On Dielectric



- The water and solid electrode form the electrodes of a capacitor.
- When charging the capacitor, the capacitor will try to minimise its energy by bringing charges close to eachother.
- It does this by spreading the water on the surface



EWOD as transport mechanism

U = V U = 0 U = V

[CJ Kim, UCLA]



- When a droplet is in contact with several electrodes, it will move to the region with lowest contact angle.
- This can be used to move, split and merge droplets.

VIDEO: http://www.youtube.com/watch?v=_OJ_lorXUg4&NR=1

Some examples of EWOD platforms:

Digital microfluidic DNA analysis

http://www.youtube.com/watch?v=JvDZh8hmR84&feature=related

Digital microfluidics for point-of-care





Duke Uni Digital Microfluidics.mp4



[Advanced Liquid Logic Inc]



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Droplet based microfluidics



[www.raindancetechnologies.com]



Droplet based microfluidics

Basic microfluidic operations:



Video: http://raindancetechnologies.com/technology/pcr-genomics-research.asp



Some examples of the use opf droplet based microfluidics

- Major application: high throughput drug screening
- Screening for directed protein evolution [Agresti et al., PNAS, vol 107, no 9, 2010, 4004-4009]
- Culture mamalian cells and entire animals (C. Elegans) on chip. [Clausell-Tormos et al., Chemistry & Biology 15, 427–437, 2008]



C. Elegans: egg

larvae



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Microfluidic solutions for label-free diagnostic sensors



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Collaborators:

- Work on narcotics detection platform:
 - Thomas Frisk, Wouter van der Wijngaart, Göran Stemme (KTH – the Royal Institute of Technology)
 - David Rönnholm, Per Månsson, Lars Eng (Biosensor Applications, Stockholm, Sweden)
- Work on virus detection platform:
 - Niklas Sandström, Thomas Frisk, Göran Stemme Wouter van der Wijngaart, (KTH – the Royal Institute of Technology)
 - Hans Wigzell (Karolinska Institutet)
 - Lennart Svensson (Linköping University)
- Work on integrated microfluidic actuators platform:
 - Björn Samel, Niklas Roxhed, Patrick Griss, Göran Stemme (KTH – the Royal Institute of Technology)









Potential drivers for miniaturization in IVD



Increased performance

- Novel functionality
- Faster system
- Low sample dispersion
- Sensor sensitivity

Decreased cost

- Manufacturing cost
- Materials cost
- Consumables reduction
- Enabling disposables



Increased performance

- Novel functionality
- Faster system
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- Materials cost
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Generic microfluidic solutions for improved analyte transport





Example: Miniaturisation of a narcotics detection instrument





Example: mass transport in a narcotics detection instrument



[www.biosensor.se]



Example: narcotics detection immunoassay



[www.biosensor.se]



Example: Miniaturisation of a narcotics detection instrument





- Reduce tubing \rightarrow Reduce sample transport time
- Reduce tubing \rightarrow reduce dispersion
- Reduce costs of valves and pumps







[Frisk et al., Lab Chip 6, 2006]





[Frisk et al., Lab Chip 6, 2006]





Microstructured interface design

 $P_{air} - P_{liquid} \propto \frac{\gamma}{d}$ Surface tension provides a robust interface



[Frisk et al., Lab Chip 6, 2006]



Microstructured interface design

 $P_{air} - P_{liquid} \propto \frac{\gamma}{d}$ Surface tension provides a robust interface



[Frisk et al., proc. Transducers, 2005]

in a

Driving, sensing, control and interface electronics

Interface

QCM sensor array

Cocaine

Heroin

Cocaine

Heroin

Reference







→ Cell 1 Cocaine → Cell 2 Heroin → Cell 3 Cocaine → Cell 4 Heroin

QCM sensor array

Cocaine

Interface

Heroin

[Frisk et al., proc. Transducers, 2005]

Cocaine

Heroin

Reference



Phase 1 enablers





Part 1 Device improvements

- Sample introduction without introducing air bubbles
- Transport time interface \rightarrow transducer: 60s \rightarrow 30s
- Sample dispersion during transport strongly reduced
- System cost is strongly reduced

[Frisk et al., proc. IEEE MEMS, 2007]





[Frisk et al., proc. IEEE MEMS, 2007]

Sample interface

Fluid

channel

Put the interface on top of the QCM













Cocaine detection




Norovirus detection





Phase 2 additional enablers





Part 2 Device improvements

- Transport time interface \rightarrow transducer is minimised
- Sample dispersion eliminated
- Buffer flow: 100μ L/min \rightarrow 2,5 μ L/min
- Cost system assembly is further reduced

[Frisk et al., proc. IEEE MEMS, 2007]



Phase 3 of integration



[Sandström et al., proc. MicroTAS, 2007]



ElectroHydroDynamic (EHD) airborne sample acquisition





EHD airborne particle collection





Phase 4 of miniaturisation



[Roxhed et al., J. Micromech. Microeng, (dec) 2006]

Integrated pumps and valves: Expandable Microspheres

- Consist of polymer shells encapsulating liquid hydrocarbons
- Expancel® Microspheres expand upon heat
 - Shell softens,
 - Hydrocarbon changes phase,
 - Volume increases
- Properties:
 - Expansion up to 60 times
 - Expansion starts at 70°C
 - Chemically inert
 - ♦ Irreversible expansion





Continuous liquid dispensing



[Roxhed et al., J. Micromech. Microeng, (dec) 2006]

Continuous liquid dispensing



[Roxhed et al., J. Micromech. Microeng, (dec) 2006]



Phase 5 of miniaturisation



[Samel et al., Biomedical Microdevices, 9 (1), 2007]

Expandable microspheres in PDMS

- Mixing PDMS and Expancel® microspheres: XB-PDMS
 - \rightarrow A thermally responsive PDMS composite
 - ◆ Large expansion (> 100%)
 - Highly elastomeric
 - Non-toxic and chemically inert
 - Allows for e.g. soft lithography, casting, spinning...
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Single-use pumps and valves

• Pump



• Valve



 Picture sequence of the valve in its open (a) and closed (b) state.

[Samel et al., Biomedical Microdevices, 9 (1), 2007]

Picture sequence showing the release
of 25nl of liquid from a reservoir



Dosing, transportation and merging of nanoliter volumes







XB microfluidic dispensers





Phase 2 additional enablers





Microfluidic solutions for label-free diagnostic sensors

