# Microfluidics and BioMEMS

## Introduction
## 13.1.2020

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Aalto University
School of Chemical Technology

# Microfluidics and BioMEMS
# CHEM-E8135 (5 cr)

Teachers: University Lecturer Ville Jokinen, Professor Sami Franssila

Microfluidics is a multidisciplinary field combining physics, chemistry, materials science and biology. It is used for handling miniature liquid samples on chips for example for:

-Chemical analysis (separation, detection) on chip
-Handling and manipulating single cells or populations
-Medical diagnostics devices

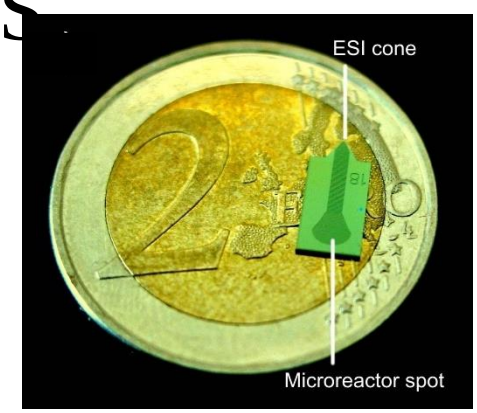
**Learn to analyze fluid flow and forces in the microscale**.
Keywords: diffusion, adsorption, superhydrophobicity, surface tension, laminar flow, Reynolds number

**Learn to design microfluidic chips**: channels, mixers, reactors, droplet generators, gradient devices. On this course you will design one chip!

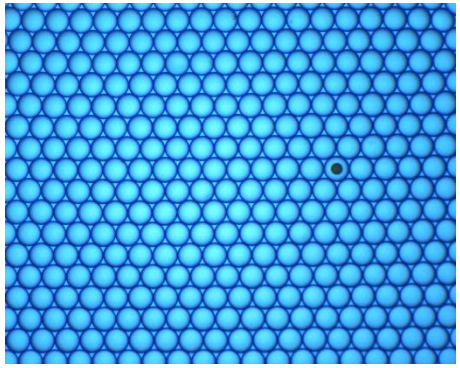
**Learn about the lab-on-a-chip** and the **organ-on-a-chip concepts.**

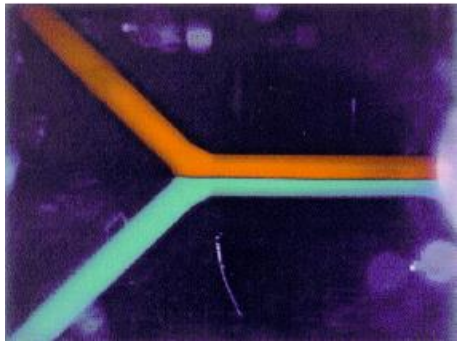
Spring 2021 the course **is fully digital in Zoom**

***Wednesdays 10:15 – 12:00 from 13.1.2021 to 7.4.2021*** *(periods 3-4)*



Analytical microchip


Microdroplets


Parallel laminar flows

# On this course:

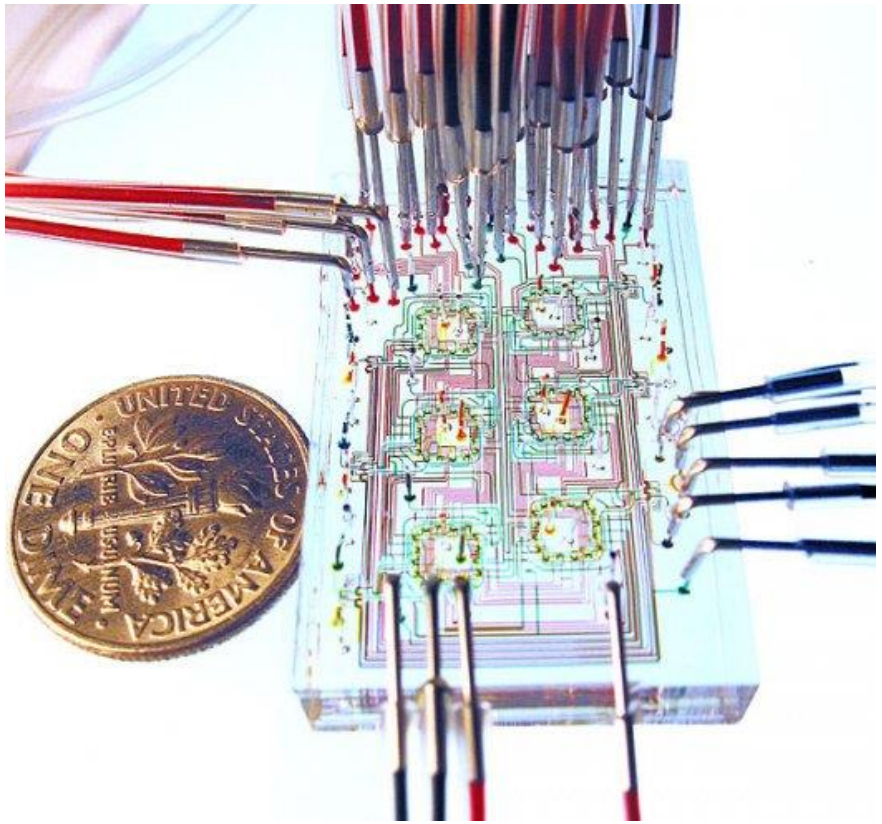
Microfluidics basic physics, how is it different from macro?

Microfluidic chips, design (and fabrication.)

Applications in analytical chemistry, biology and medicine.

Terms used for the field:

- Microfluidics
- Bio-MicroElectroMechanical Systems (BioMEMS)
- Lab-on-a-chip
- Micro total analysis system (µTAS)



# Intended learning outcomes

ILO1: The student understands fluid flow at the microscale, scaling laws and can analyse microfluidic circuits. Laminar flow, diffusion, Reynolds number.

ILO2: The student is familiar with liquid and solute interactions with surfaces. The student understands wetting and capillary filling in microfluidic systems. The student is familiar with mechanisms for biomolecular adsorption on surfaces.

ILO 3: The student understands the basics of advantages and disadvantages of polymers, glass, silicon and paper as materials for microfluidic chips.

ILO 4: The student can design microfluidic components: channels, mixer, reactors, droplet generators. The student recognizes many different types of microfluidics (channels, droplets, paper etc.).

ILO 5: The student can describe the advantages of miniaturization for analytical chemistry, and is familiar and is familiar with the lab-on-a-chip concept.

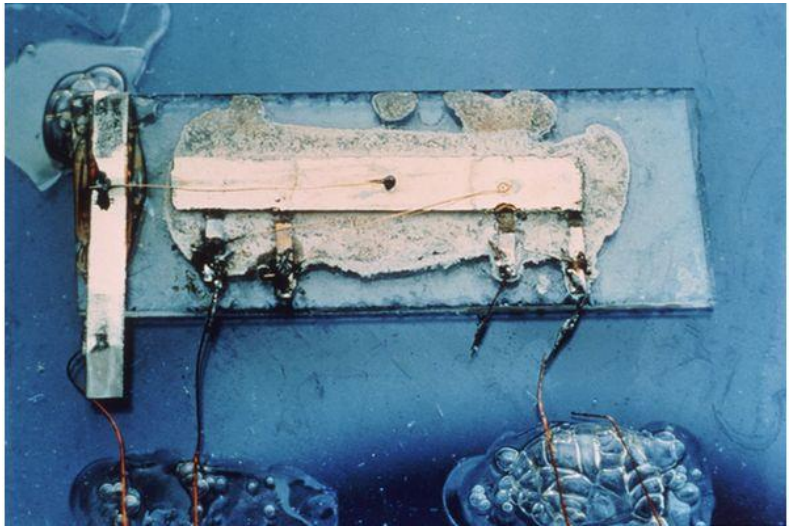
ILO 6: The student understands interactions between cells and microfluidic chips. The student can give several examples of applications where chips are used in cell biology. The student knows the organ-on-chip concept.

# Microelectronics

- Integrated circuit invented in the 1950:s, nowadays omnipresent.

Key advantages of microelectronics:

- cheap per unit materials and fabrication costs
- possibility to integrate components
- new possibilities arising at micro- and nanoscale



The original integrated circuit of Jack Kilby from 1950s. Single transistor


XBOX One main processor. Contains 5 billion transistors.

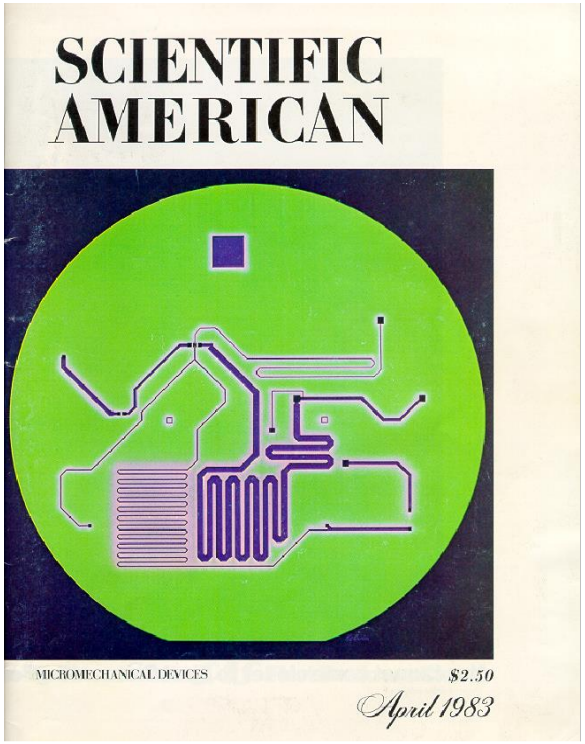
# Microfluidics

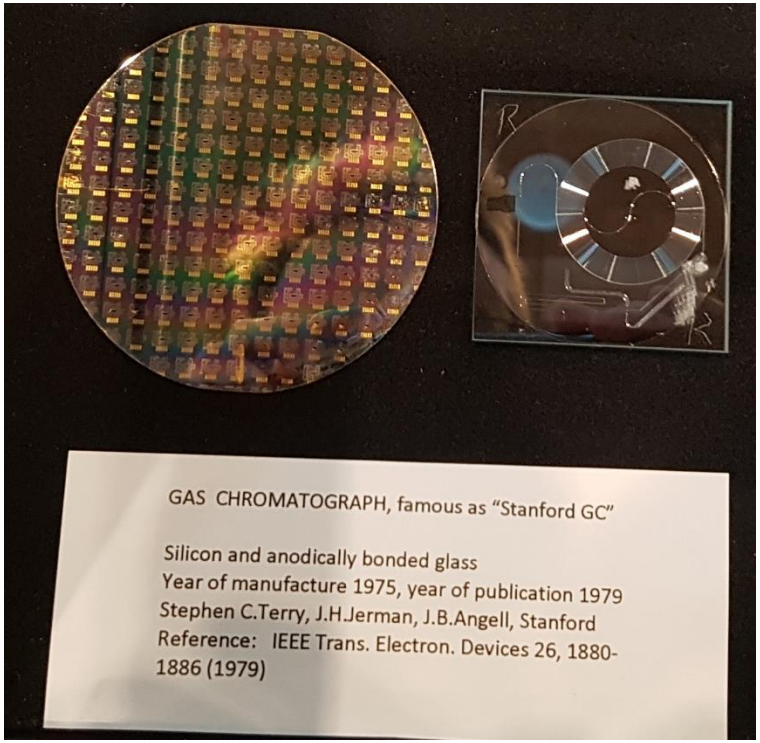
- Start of an era: Gas chromatograph on silicon (1979): injector, separation channel, thermal conductivity detector

- Gas fluidics is today a minor activity compared to liquid fluidics (which started in 1990s)

- Parallels between microelectronics and microfluidics? That's the dream!

- Microfluidics increasing in prominence year by year in labs and commercially. Current market is in the billions, rising double digit percentages yearly.



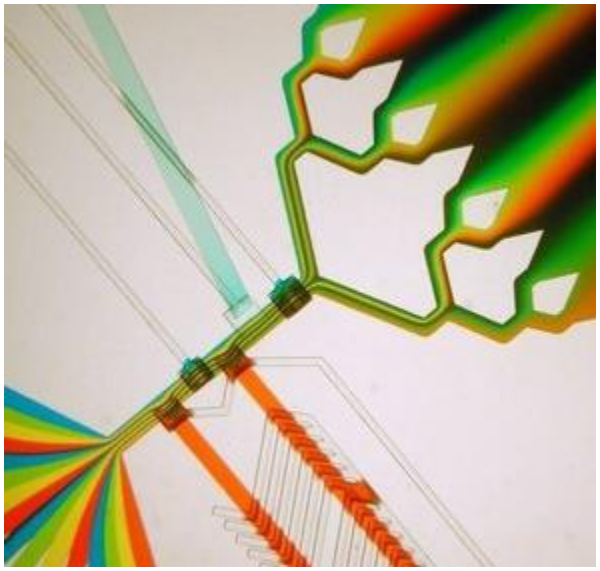
| | Microelectronics | Microfluidics |
|---|---|---|
| **Processes** | Standard processes around the world | Each lab has their own processes. Etching, milling, additive manufacturing, embossing, printing, each with variations. |
| **Materials** | Standard materials (silicon, thin films) | Many materials, new ones being developed all the time. Prototyping and mass production use different materials. |
| **Components** | Standard components | A vast array of components, for example there are 100s of different valves for microfluidics. |
| **Fluid** | Transport of electrons, ”standardized fluid” | Different fluids (viscosity, surface tension), different solutes (small molecules, polymers, biomolecules), cells, tissue pieces, organisms. |

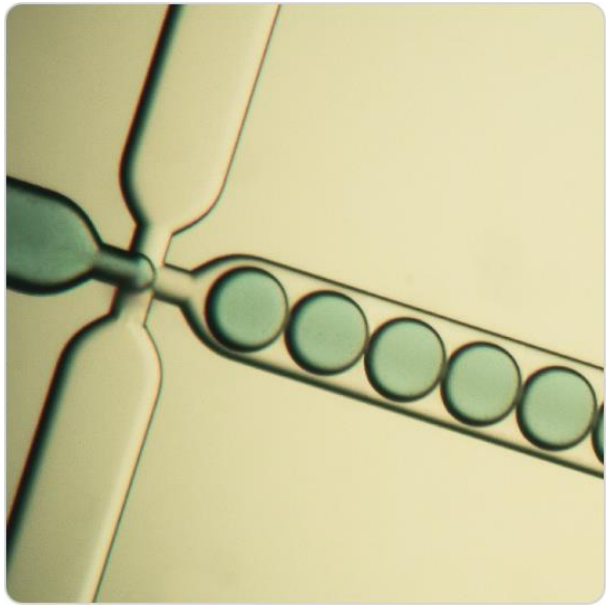
Microfluidics is less mature than microelectronics partly because of the relative ages of the disciplines.

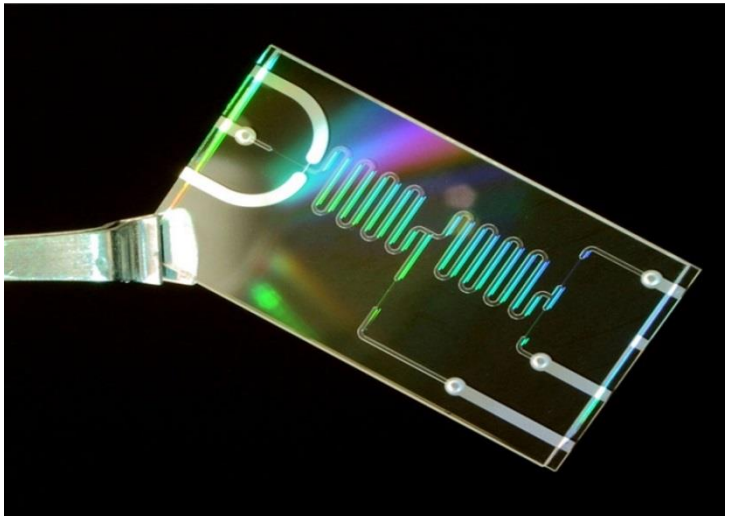
But mostly the difference comes down to the wider variety of application areas and degrees of freedom (liquids, materials, cells, analytes etc.) in microfluidics.

# Why miniaturize ?

- because it is possible?
- because it is improves performance?
- because it opens up new possibilities?







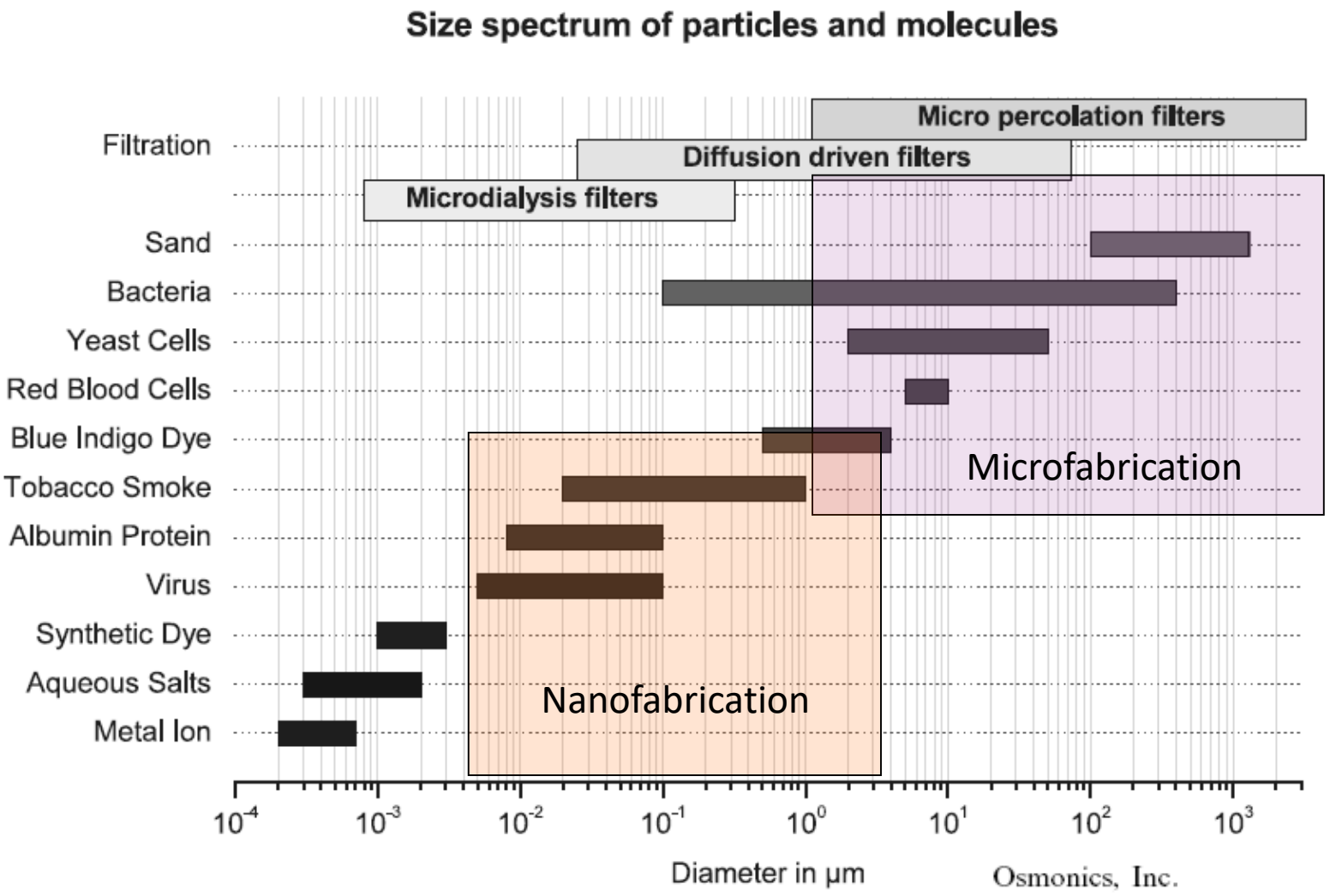
# Some initial answers:

1. **Small size scales**
- Size scale matching (micro-organisms, cells, organelles, viruses)
- Low sample consumption (expensive reagent, blood sample)

2. **Scaling effects**
- Rapid reactions
- Laminar flow
- Surface effect utilization

3. **Parallelization and integration**
- Many experiments at once
- Many steps on the same device

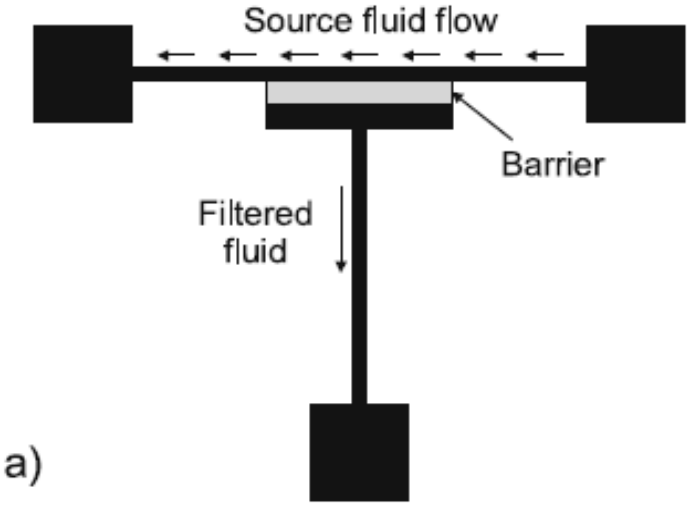
# 1. Small size scales

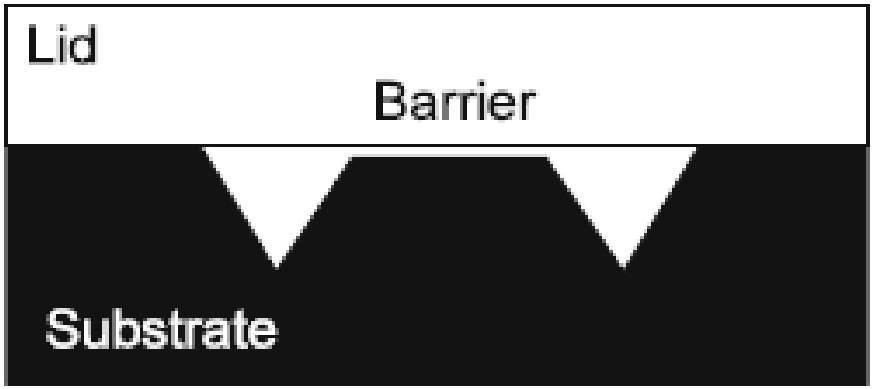



- Matching size scales of microfabrication and biology

# 1.1 Typical sizes in microfluidics

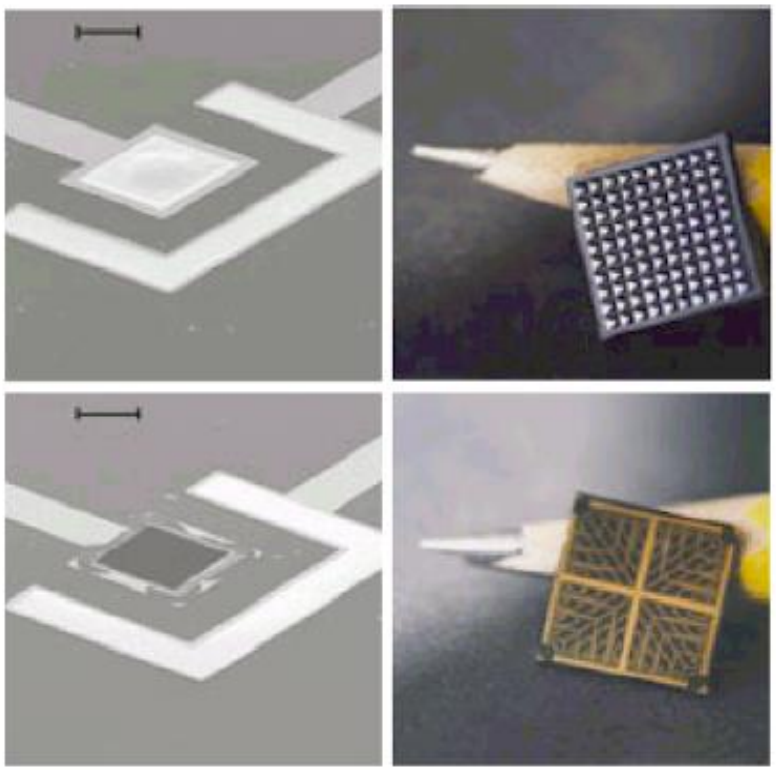
- Microfluidic channels: width and height 10 – 100 µm, length 1 mm – 1 cm
- Pores and gaps, > 10 nm
- Volumes: a microfluidic chip 1 µl, ink jet droplets 1-10 pl
- Size of a microfluidic chip, 5mm – 5 cm.

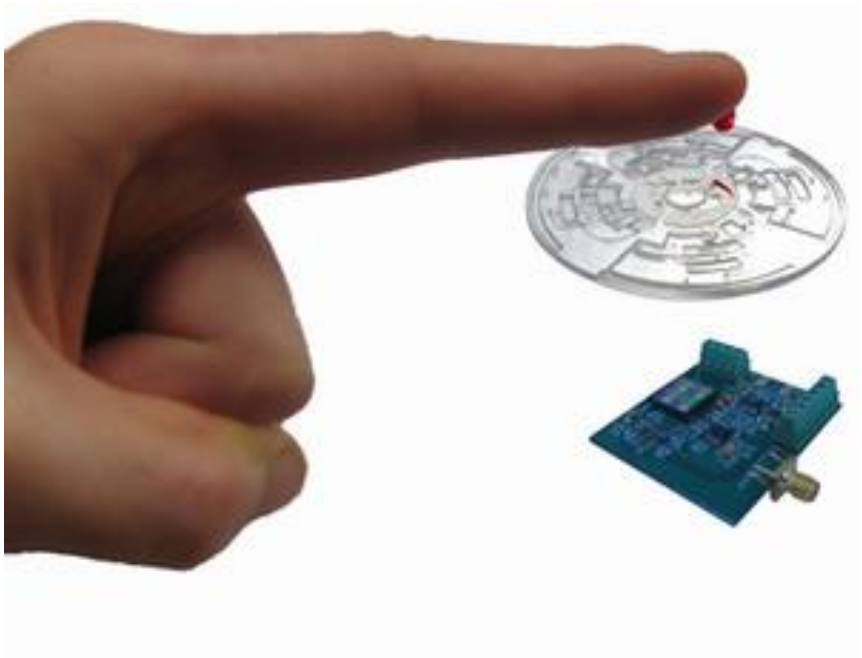



J.P. Brody, T.D. Osborn, F.K. Foster, P. Yager, Sens. Actuators A 54 (1996) 704–708.

# 1.2 Drug release and blood samples





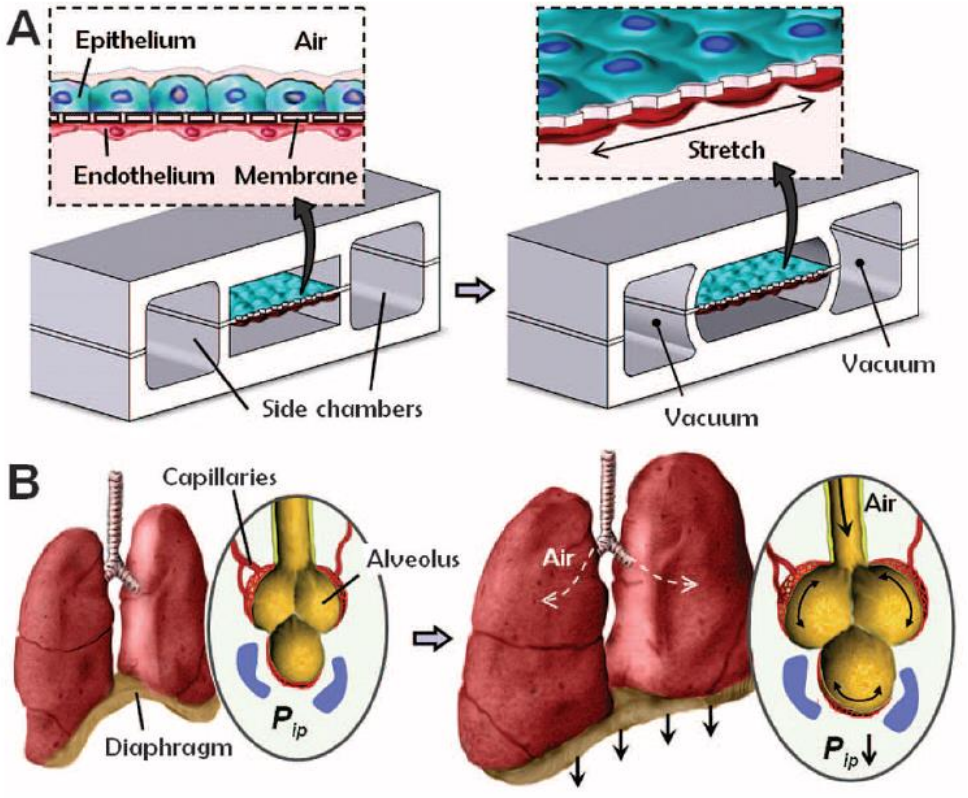
100 identical drug chambers

Drug release by electrical puncturing of a gold membrane

Many analyses from a droplet of blood

Or, microneedle for even smaller droplet

# 1.3 Lung model (organ-on-a-chip)




Ingber et al. Wyss Institute

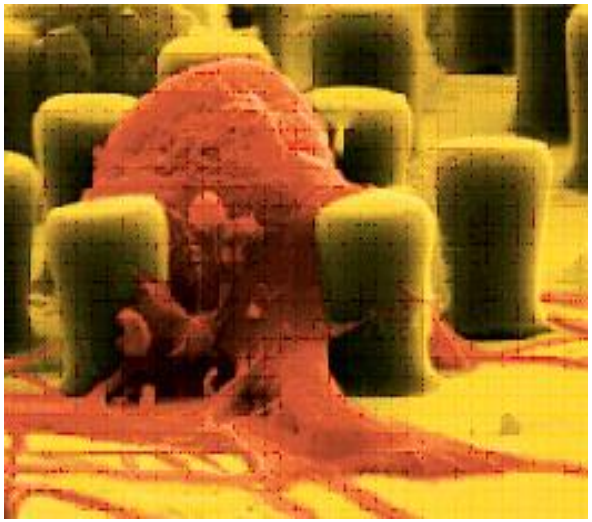
Chip for mimicking lungs.

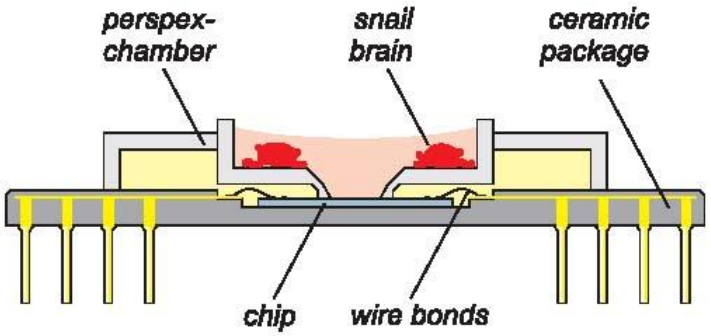
2 types of cells cultured on opposite sides of a stretchable membrane.

Stretching simulates breathing-induced mechanical movements.

# 1.4 BioMEMS

- Microdevices for handling biomolecules, cells, bacteria, viruses, tissue, model-organs
- Division between microfluidics and BioMEMS is diffuse because biology takes place in water.






**Bio-MEMS Devices to Monitor Neural Electrical Circuitry**
Andres Huertas, Michele Panico, Shuming Zhang

# 2. Scaling effects

**Volume scales as $d^3$**
**Surface area scales as $d^2$**
→ Body forces to surface forces scale as d.
→ Micro and nanoscale is dominated by surface effects.

*Example: A small glass capillary will fill spontaneously by capillary action (surface force) even against gravity (body/volume force) while a garden hose will not.*

**Diffusion time scales as $d^2$**
→ Micro and nanoscale diffusion is fast and can even be used for mixing.

**Amount of analyte scales as $d^3$**
→ Amount of analyte can be low, detection methods need to be sensitive.

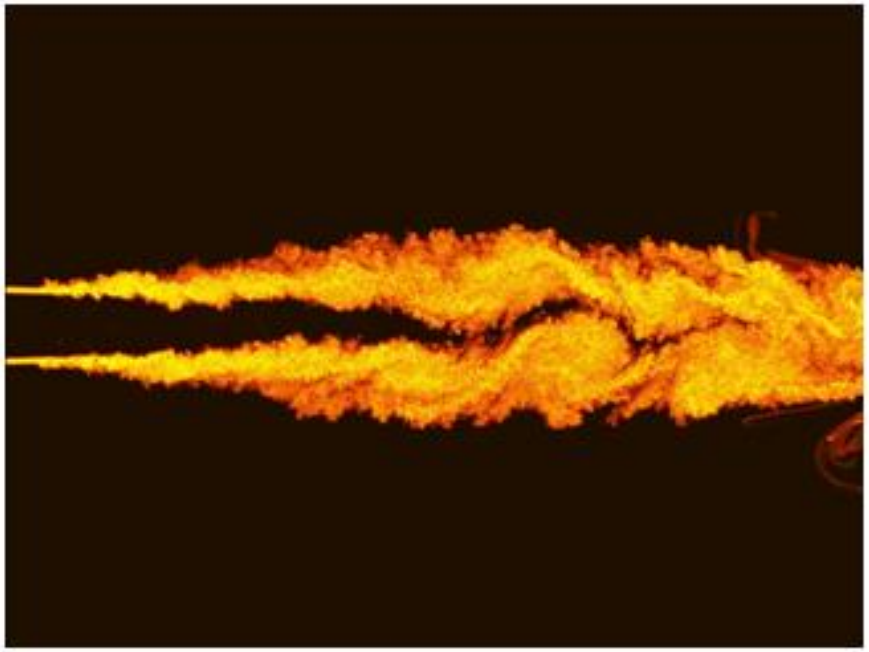
# 2.1 Scaling: surface tension

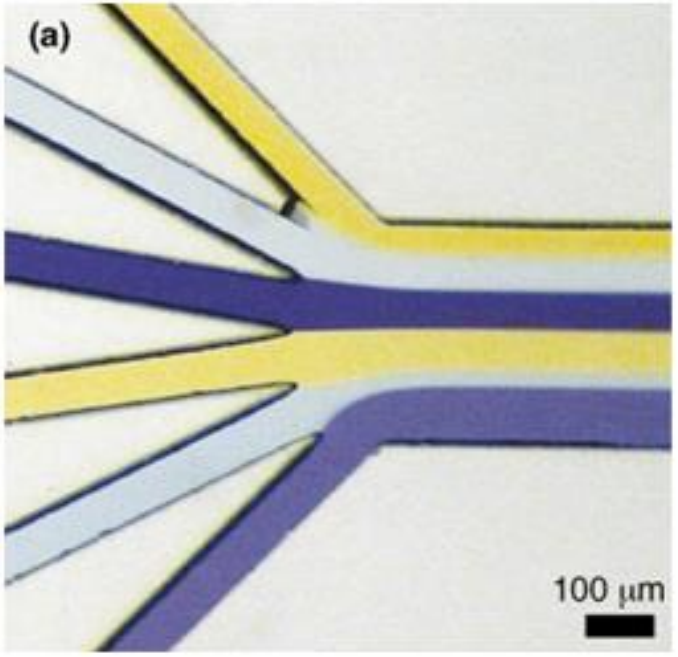
- Water droplet beads up on a superhydrophobic surface, (surface tension vs gravity)

# 2.2 Scaling: diffusion & detection

| | | | | |
|---|---|---|---|---|
| Cube edge | 1 mm | 100 µm | 10 µm | 1 µm |
| Cube volume | 1 µL | 1 nL | 1 pL | 1 fL |
| Diffusion time (small protein) | $\approx 3$ hours | 100 s | 1 s | 10 ms |
| #molecules (1 µM) | $6*10^{11}$ | $6*10^{8}$ | $6*10^{5}$ | 600 |

# 2.3 Turbulent vs. laminar flow






Turbulent = efficient mixing

Laminar: slow mixing by diffusion

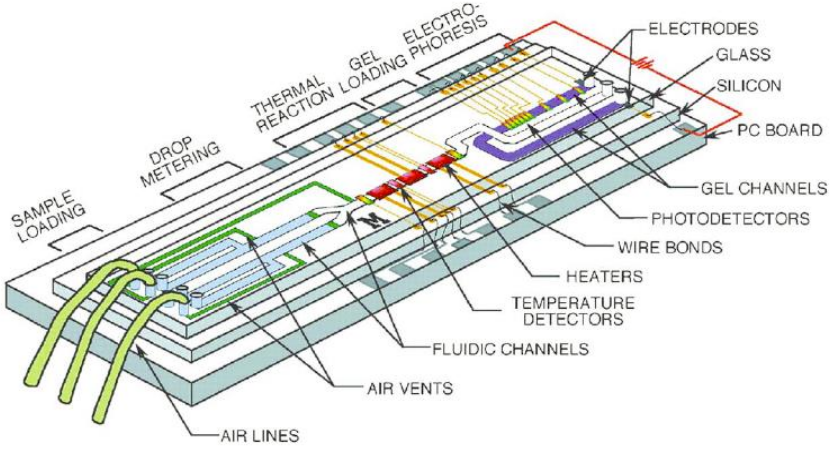
- Microfluidic flows are laminar

# 3. Parallelization and integration

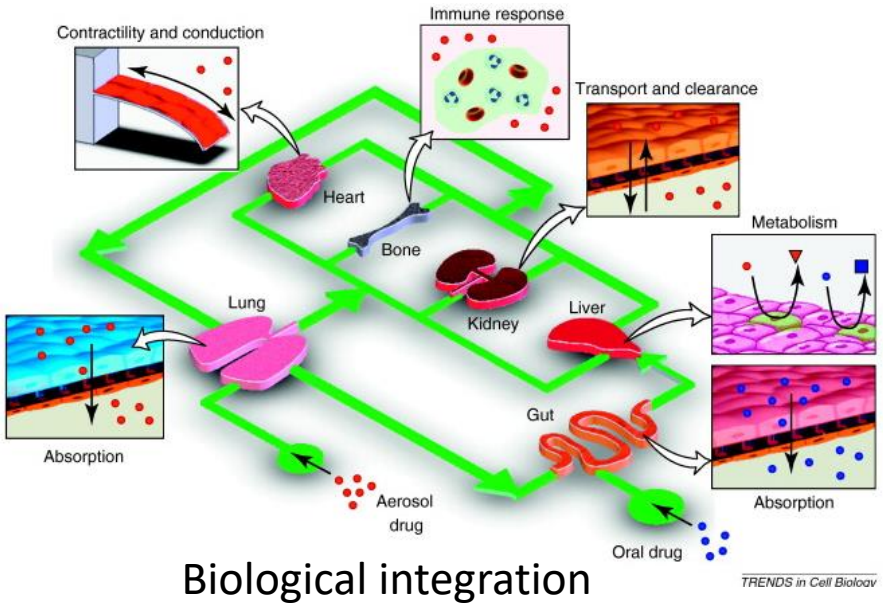
• Microfluidic devices lend themselves well to parallelization due to the small size and the parallel nature of many microfabrication processes. ("*There's plenty of room at the bottom*", -Richard Feynman).

• Lab-on-a-chip concept: everything necessary for the application is provided on chip. (also called µTAS, micro total analysis system)

• Organ-on-chips integrated into body-on-chip?



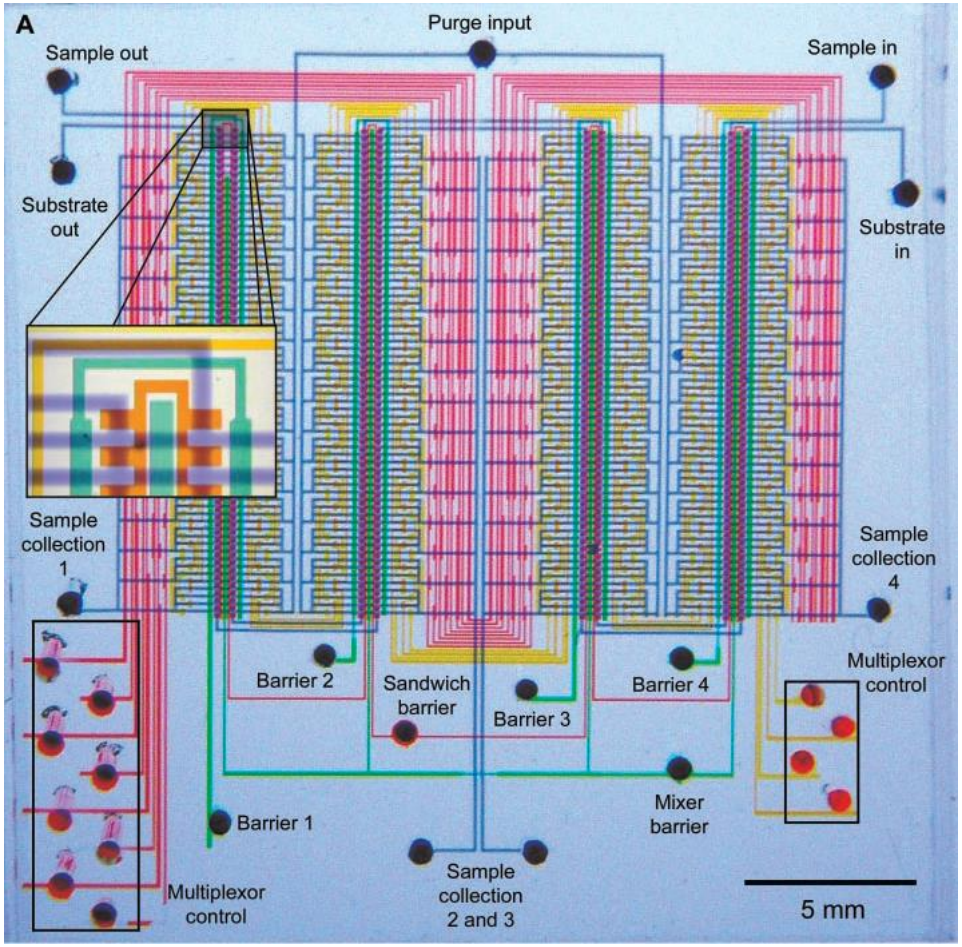

Chemical integration



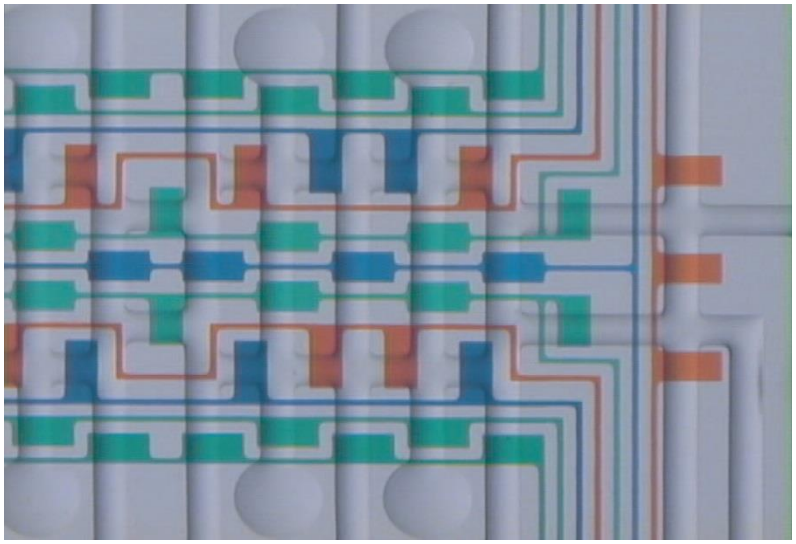

Biological integration

Trends in Cell Biology (2011) 21, 12, p. 745-754

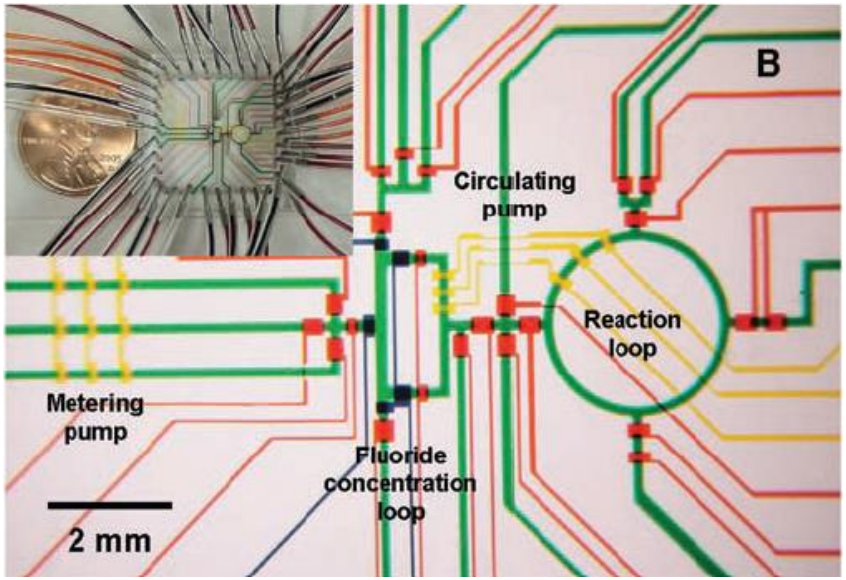
# 3.1 Large scale fluidic integration




256-mixer S. Quake



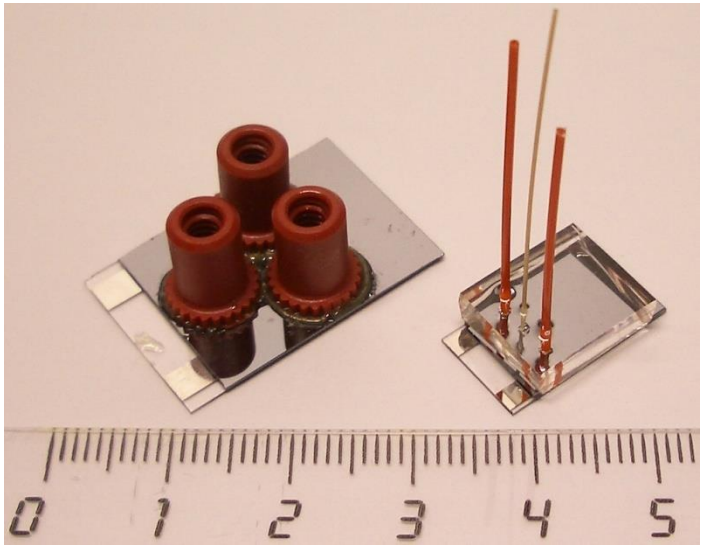
Protein interaction chip

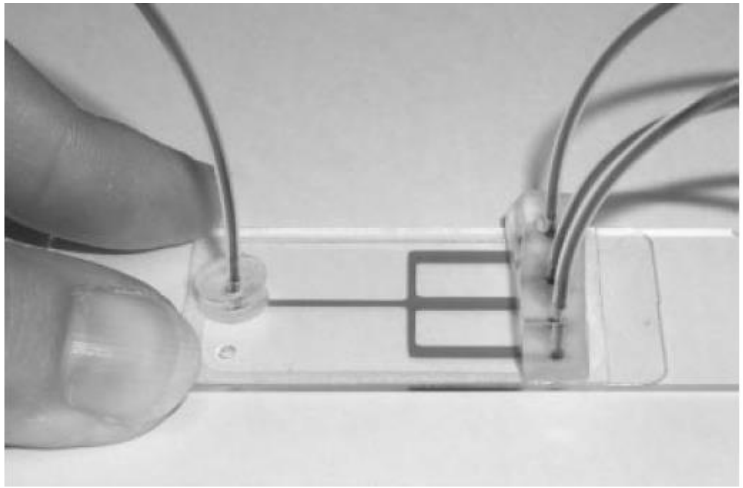



Radiolabeling synthesis reactor for PET

# 3.2 Fluidic connectors

-Often the limiting factor of integration and parallelization



# Course structure

**Lectures and exam, 40 points**

-40 points for exam, must get 50% of exam points to pass the course

**Exercises, 30 points (1st half of course)**

-The goal of the exercises is for the students to utilize the concepts they learned in the lectures.

-There are 4 x 1h in class exercise sessions, participation is **4x2** points.

-three short one week home design tasks, **3x4** points

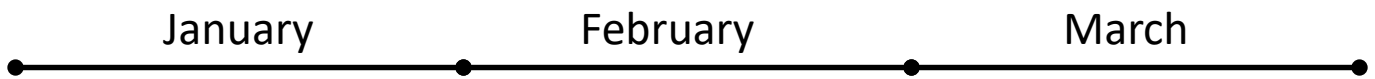
-one two week design task, **10** points.

**A poster work and presentation, 30 points (2nd half of course)**

-A research project on a personalized topic, done in pairs (or individually)

-Presentation in poster format, 7.4.2021

# Course timetable and workload




Lectures 55h

Exam: 12.4

Exercises 40h

Exercise sessions 20.1, 27.1, 3.2, 10.2, **these give 4x2 points.**
After the first 3 of these, 1 week time for **homework worth 3x4 points.**

Last homework, kickoff 10.2, is a longer design task, **worth 10 points.**
Possibility to get personal tutoring for this task will be arranged
The DL for design task return is Sunday 7.3, 23:59

Poster work 40h

3.3 Poster project kickoff lecture
Mandatory mid project tutoring on 17.3
Onlne poster session, 7.4

# Topics and Teachers

| | |
|---|---|
| Prof. Sami Franssila, Aalto | Microfabrication and components |
| Dr. Ville Jokinen, Aalto | Microfluidic basics, organs-on-chip |
| Prof. Tiina Sikanen, UH | Microfluidics for chemical analysis |
| Dr. Tarja Nevanen, VTT | Biomolecules and microfluidics |
| Dr. Emilia Peltola, Aalto | Cells on chips |
| Dr. Päivi Saavalainen, UH | Microfluidics for biological applications |

# Schedule

Part 1 of course:
Topic: Fundamentals
-Exercises and chip design task

Part 2 of course:
Topic: Applications
-Personalized poster project

| Date | Topic | Teacher | Student will do: |
|---|---|---|---|
| 13.1. | Introduction | VJ SF | |
| | Microfluidics 1 | VJ | |
| 20.1. | Exercise 1 | VJ | |
| | Microfluidics 2 | VJ | HOME 1 |
| 27.1. | Exercise 2 | VJ | DL HOME 1 |
| | Microfluidics 3 | VJ | HOME 2 |
| 3.2. | Exercise 3 | VJ | DL HOME 2 |
| | Fabrication Basics | SF | HOME 3 |
| 10.2. | Exercise 4 | VJ | DL HOME 3 |
| | Components | SF | DESIGN TASK START |
| 17.2. | Types of Microfluidics | VJ | |
| | BioMEMS devices | VJ | |
| 24.2. | Exam week, no teaching | | |
| 3.3. | Microfluidics in biomedicine (single cell trapping) | PS | DESIGN TASK DL |
| | Scientific Posters | VJ, SF | POSTER KICKOFF |
| 10.3. | Microfluidics for Analytical Chemistry | TS | |
| | Microfluidics for Analytical Chemistry | TS | |
| 17.3. | Microfluidic Business | SF | |
| | Poster tutoring | VJ, SF | POSTER TUTORING |
| 24.3. | Biomolecules on chip | TN | |
| | Biomolecules on chip | TN | |
| 31.3. | Cells on chips | EP | |
| | Organs on chips | VJ | |
| 7.4. | Poster session | VJ, SF | POSTER SESSION |
| | Poster session | | |
| 12.4. | Exam 1. 13:00-16:00. Online exam in MyCourses | | |
| 27.5. | Exam 2. 9:00-12:00. Online exam in MyCourses | | |

# Course practical issues

Course webpage is in MyCourses :
https://mycourses.aalto.fi/course/view.php?id=20499

Or search for CHEM-E8135 – Microfluidics and BioMEMS in mycourses.

In mycourses page you will find:

1. Schedule
2. Lecture slides
3. Additional material (articles, book chapters etc.)
4. Homework design tasks under *design tasks*
5. In class exercises, model solutions and attendances under *exercises*
6. News

(Students from University of Helsinki need to visit the page once and then I can manually add the rights to them for the page.)

There is no book for the course. The material is lecture slides plus supplementary reading materials given. We will try to make the material available some days before the lecture

# Feedback

At the end of the course please give feedback through the Webropol system. (the threshold for getting the Webropol feedback is 5 students, we have always cleared that bar which is essential)

In 2020, the average grade for the course was 4.3 (typically it fluctuates between 3.5-4.5)

"The course was interesting and structured quite well. The lectures and exercise sessions were well balanced and supported the learning well. I would have preferred scheduling the last big design task to week after exam week or week before." **–Design task timing moved after exam week.**

"I found the first half of the course better. I liked that exercises we had, it kept me more active during the lecture. The poster and larger homework was good." **–No changes made this year, if we get more of this feedback then we consider adding some extra activation to period IV as well.**

*"Remove either the group project or the poster project. (from 2019)"* ***–Done, design tasks replaced another group work. Design tasks were well liked in 2020.***

*"To be honest I only joined the course because my friend was on the course. But I am extremely happy that Idid! This was one of the best master courses I've taken. It was a subject completely unknown to me from before, but now I feel that I gained the right amount of knowledge about microfluidics and biomems so that if I would like to, I could study in the field further, which I most likely will do."* **–If we manage to achieve this in at least some students also this year then the course has succeeded!**