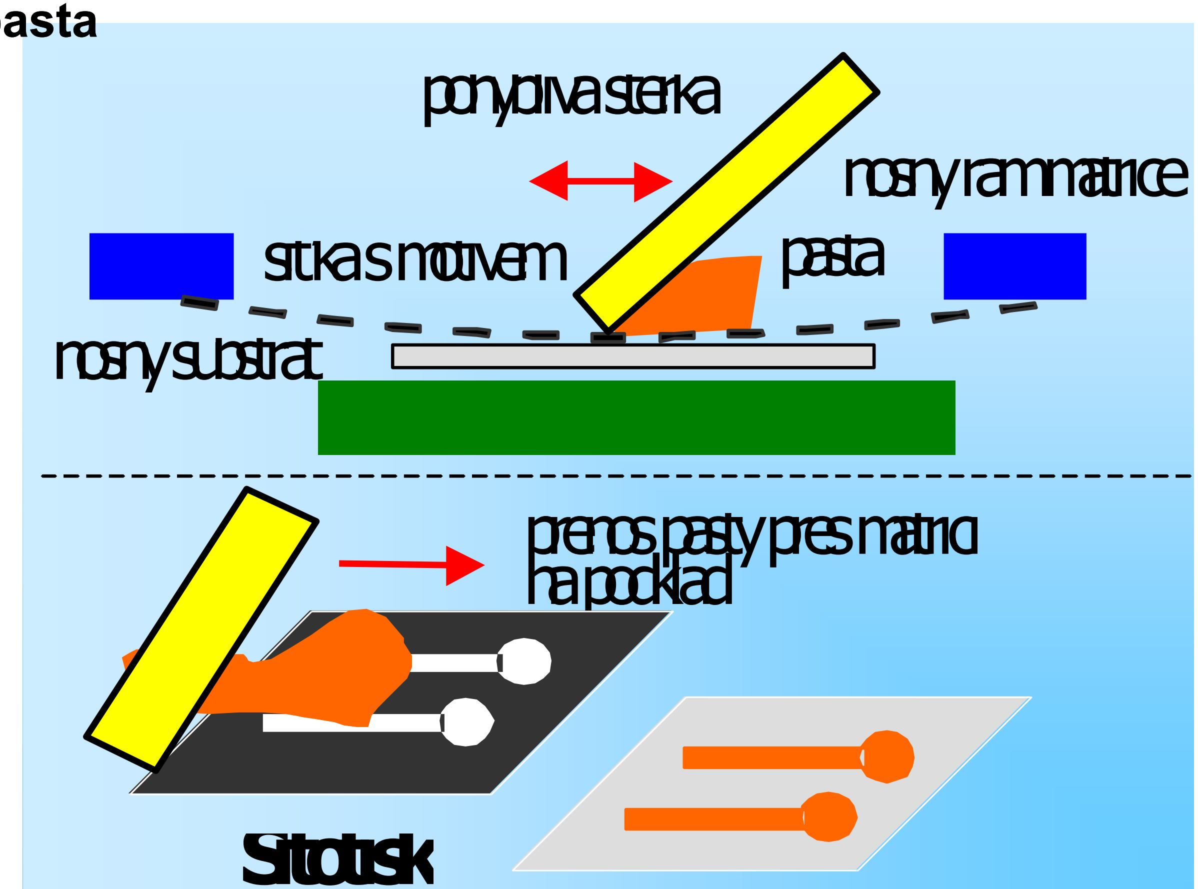
Technologické aspekty biosensorů

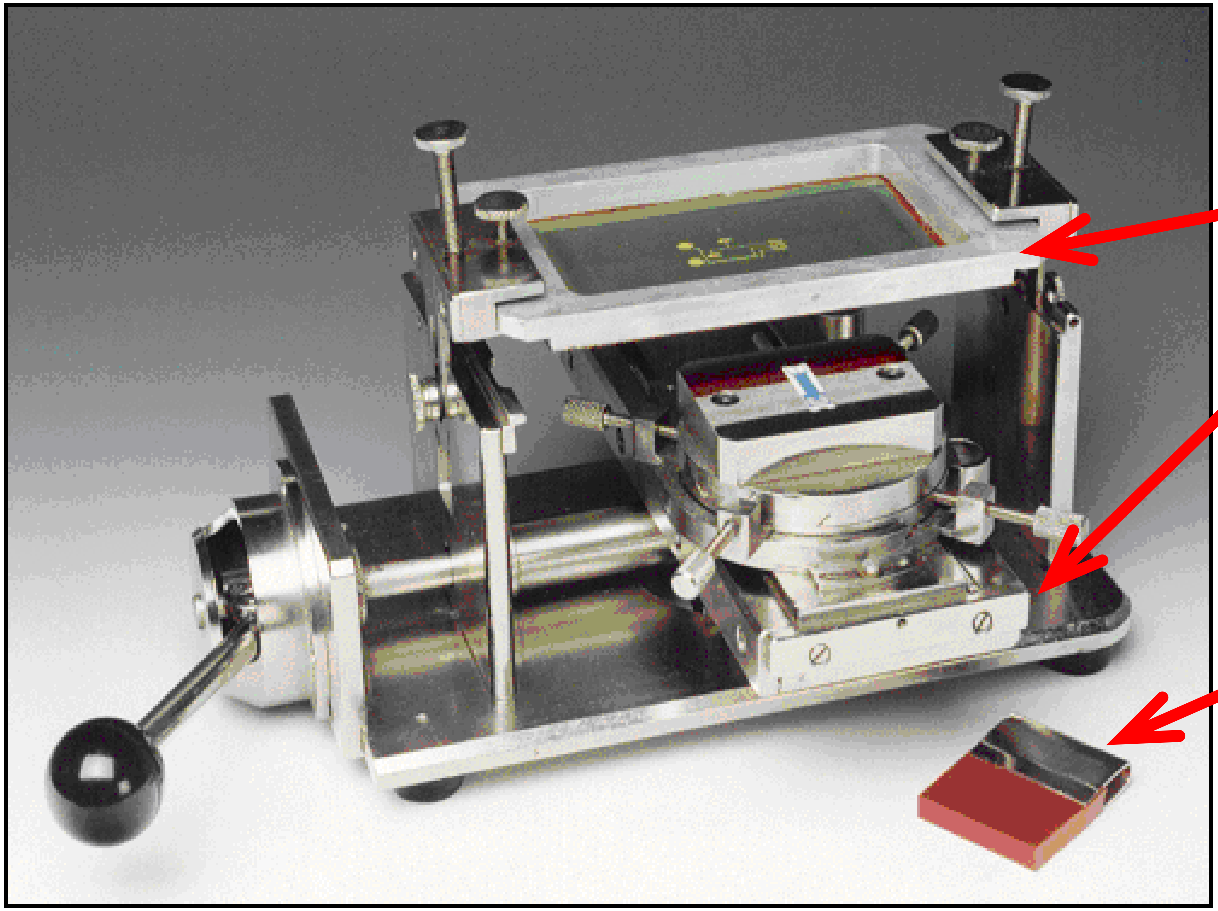
- <u>techniky pro masovou produkci (bio)sensorů</u>

Sítotisk

- sítotisk (screen printing) vychází z elektronické technologie tlusté vrstvy
- vlastní postup je obdobný jako při tisku grafických listů; na nosnou podložku se tiskem přes matrici postupně nanáší různé pastovité vrstvy, které po vytvrzení vytváří jednotlivé elementy biosensoru
- pasty jsou směsí práškovitého materiálu konečné vrstvy (např. směs prášku z grafitu a pojiva) a rozpouštědla, aby se získala viskózní tekutá pasta

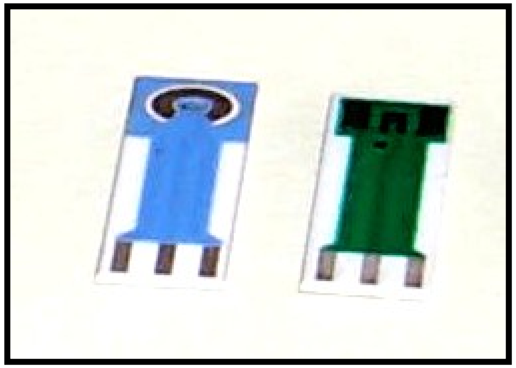


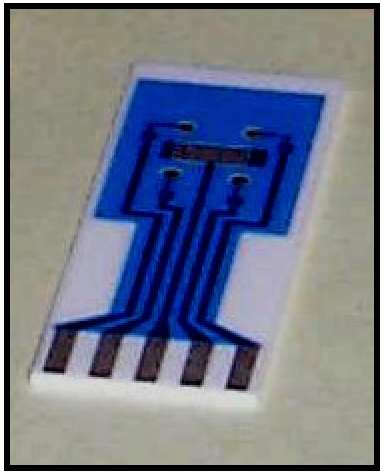
Sítotiskový stroj
(manuální)

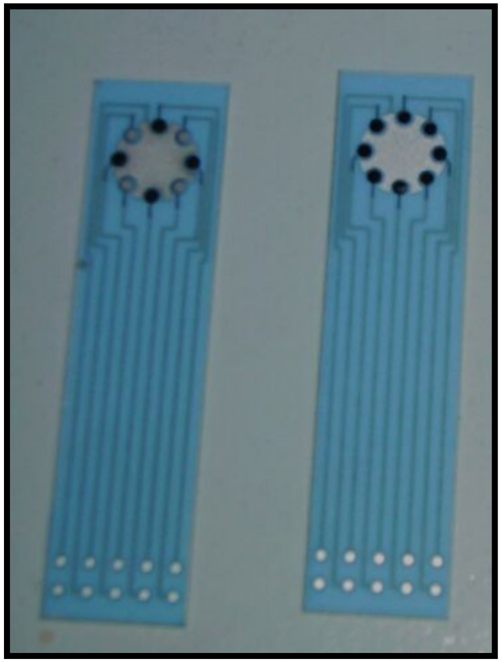


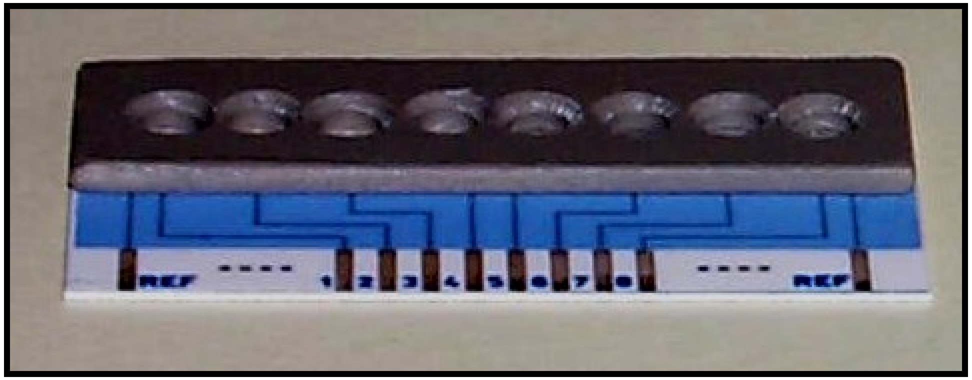
- matrice
- posuvný stolek
- stěrka

Sítotiskové sensory
(keramický podklad)



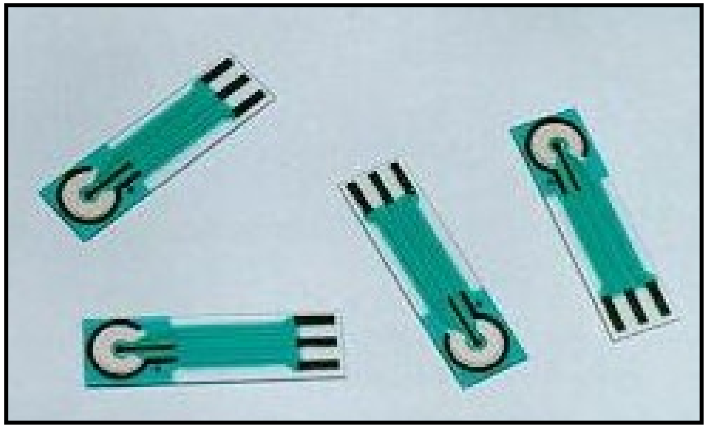






- produkty firmy BVT Technologies (Brno)

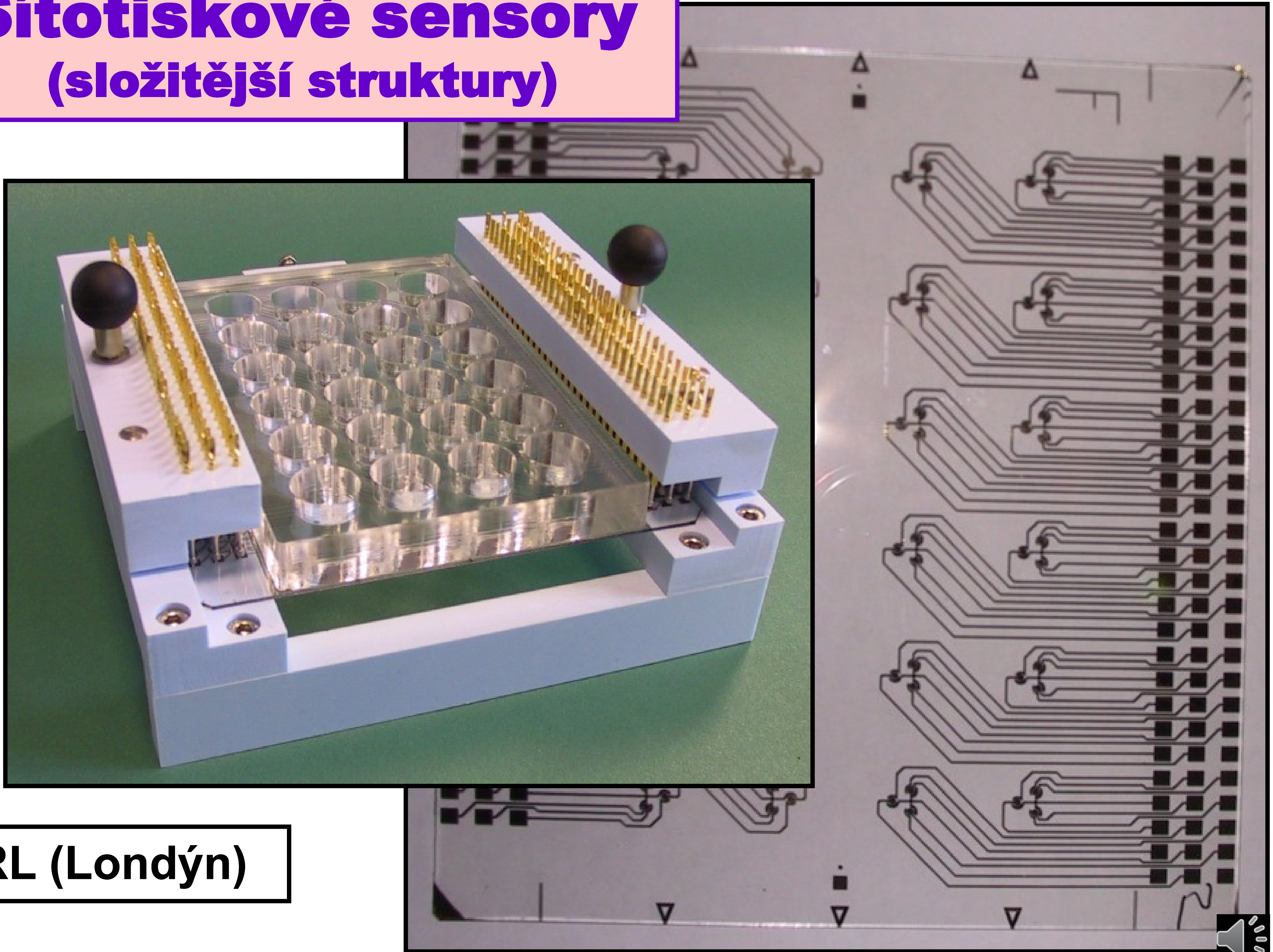
Sítotiskové sensory (plastový podklad)



BVT Technologies

Univ. Florencie

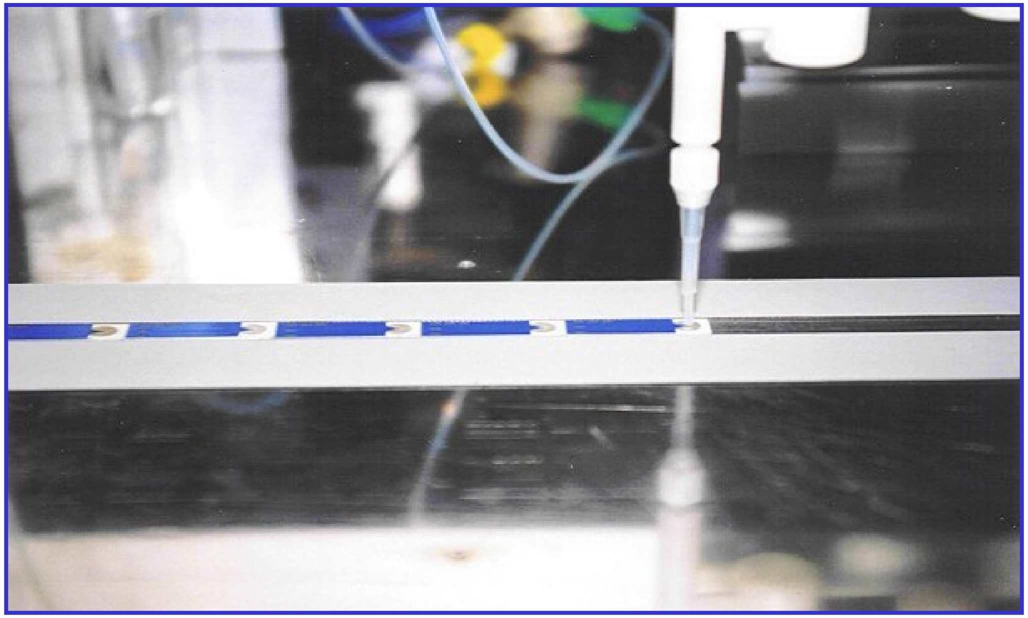
Sítotiskové sensory
(složitější struktury)



CRL (Londýn)

Sítotisk

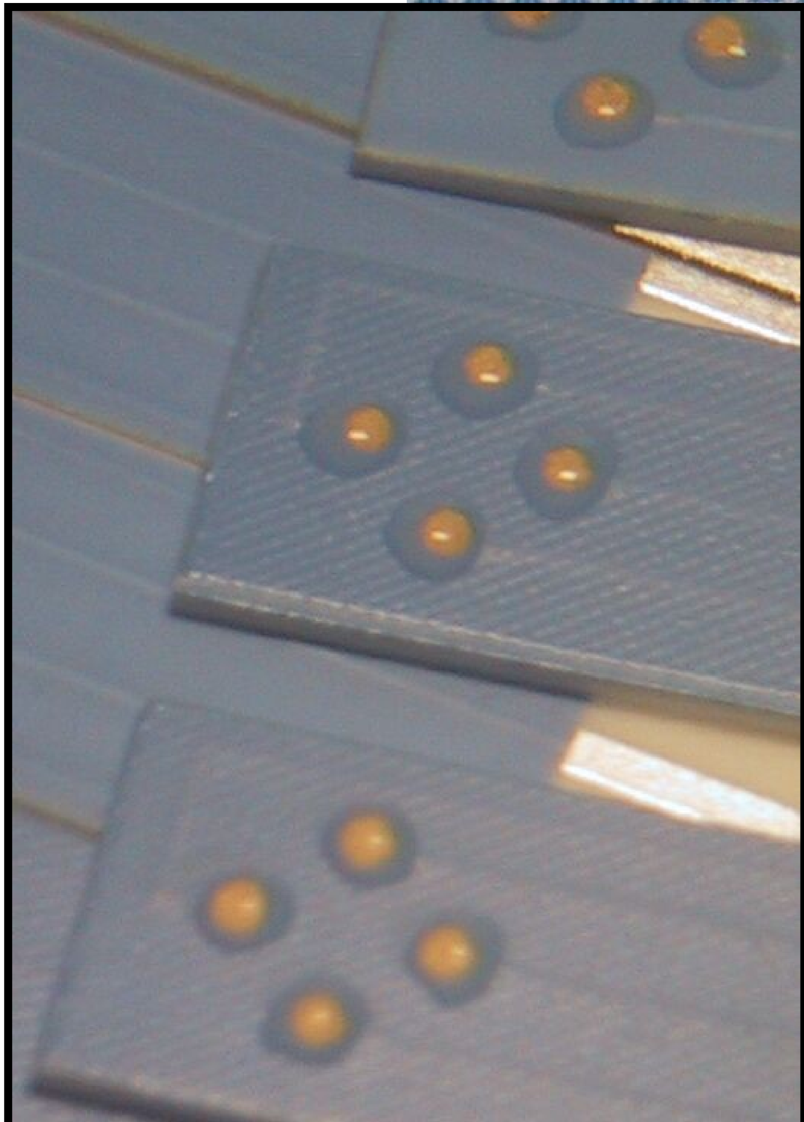
- relativně jednoduchá a levná technologie, použitelná i v laboratorním měřítku (pozor na přílišný optimismus – důležité je i know-how)
- široká dostupnost tiskových past, vhodných i pro nanášení enzymů (pasty na vodné bázi, event. UV polymerizovatelné)
- „rozlišení“ cca 1 μm
- využíván i pro komerční výrobu biosensorů pro měření glukosy



BST Biosensors (Berlin)

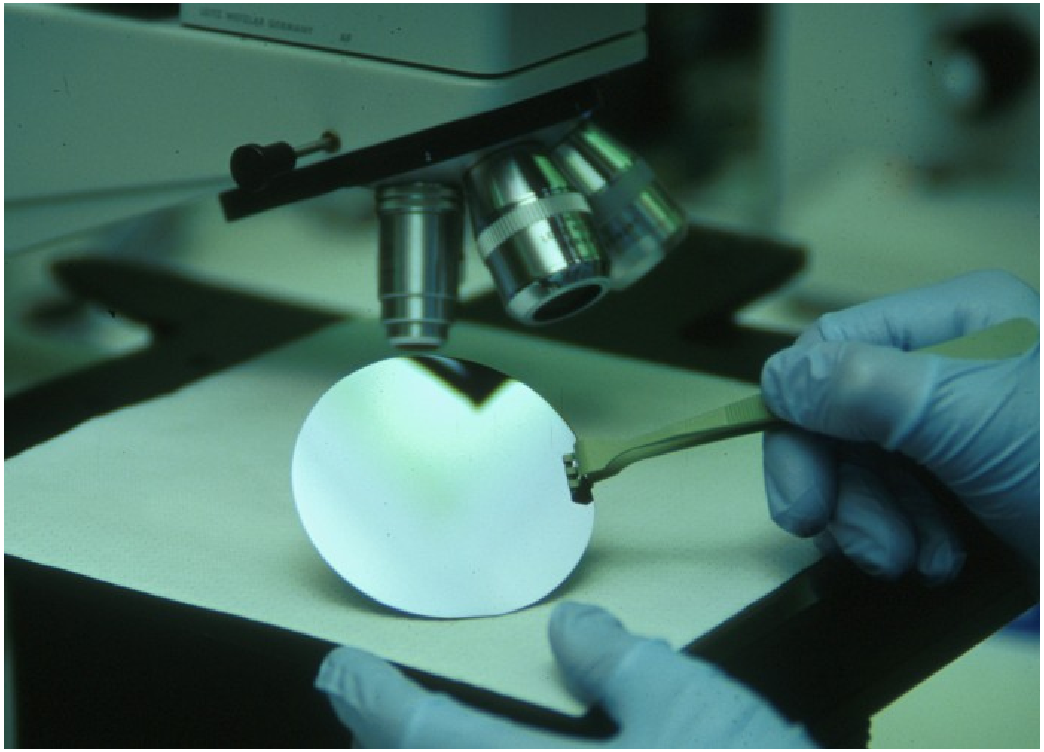
automatické nanášení enzymu

Ruční nanášení biovrstev



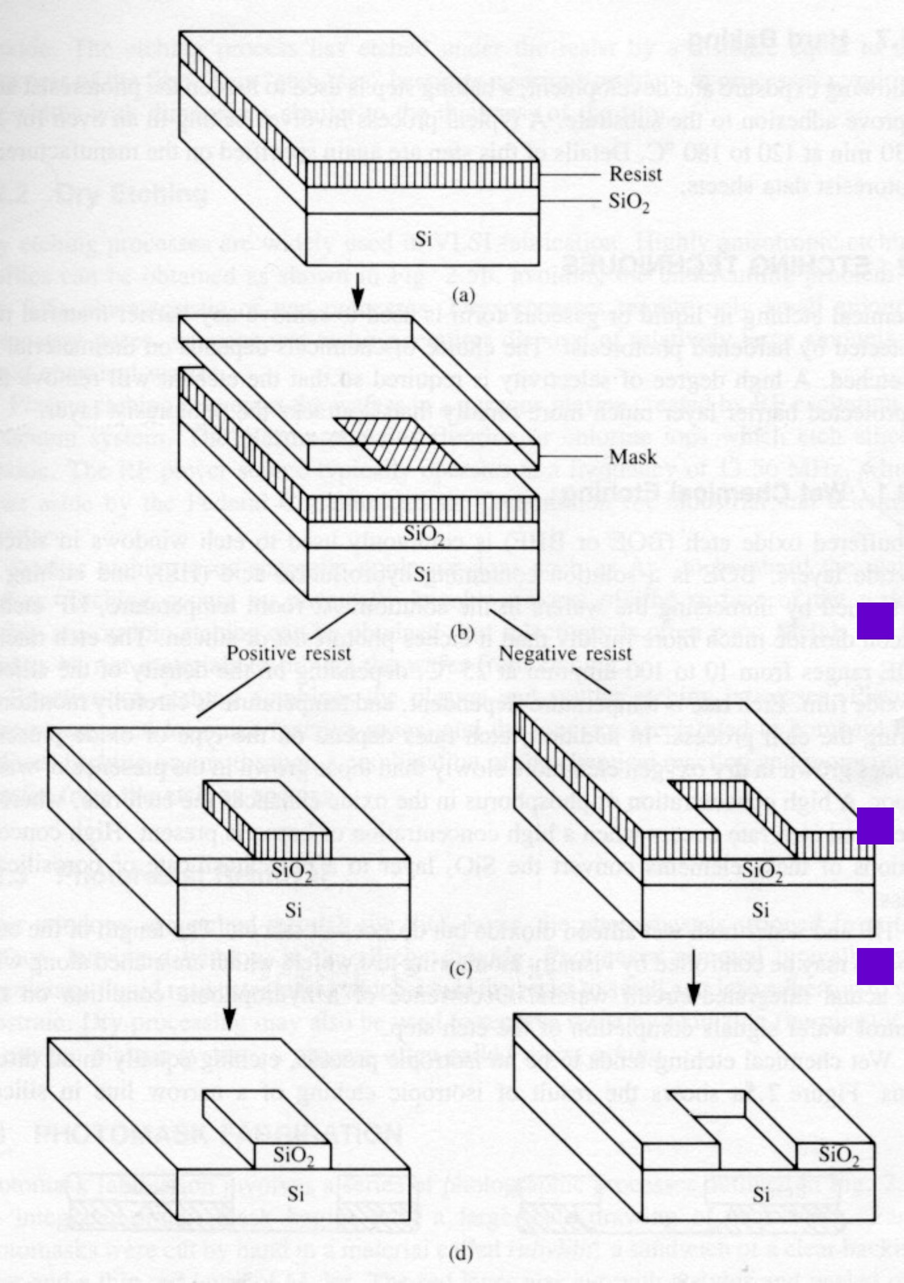
- cca 1 µl kapka na elektrodu o průměru 1 mm

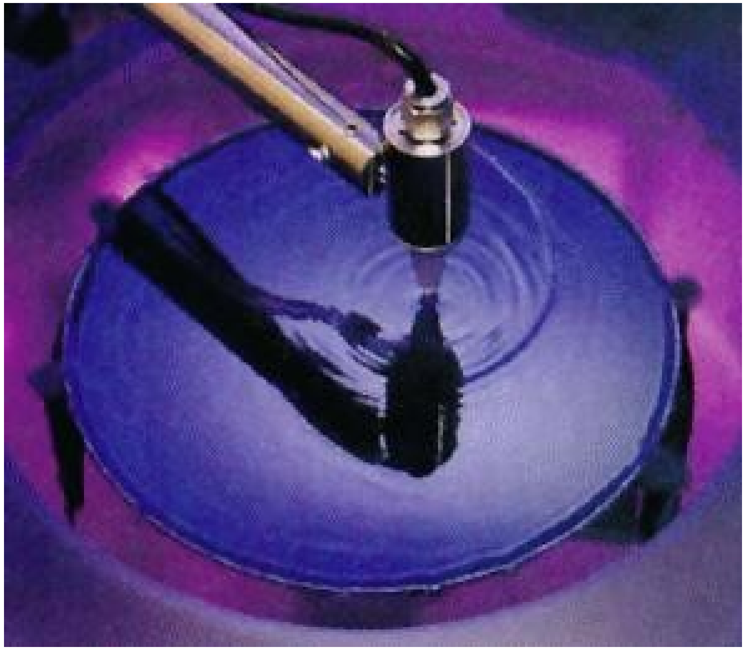
Litografie



- techniky přenosu kopie výchozího motivu („master pattern“) na povrch pevného materiálu
- tenkovrstvá technologie nejen pro výrobu základního chemického sensoru, ale i mikroanalytických systémů, jakési miniaturní laboratoře na povrchu čipu
- základním materiálem je křemík („silicon wafer“)

Fotorezist

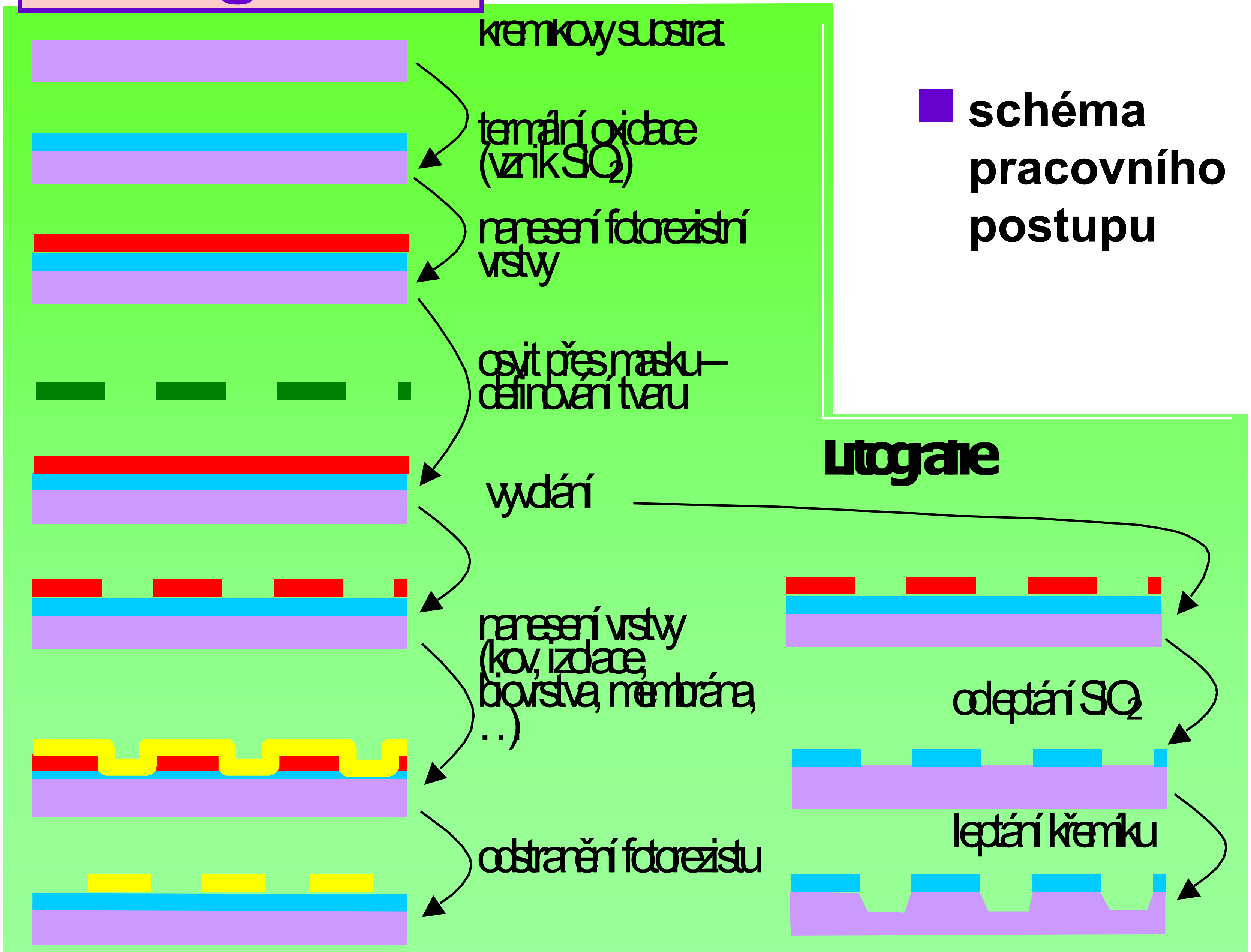




- modifikovaný materiál se pokryje tenkou vrstvou fotocitlivého materiálu - fotorezist (spin-coating)
- ten se pak osvětlí přes masku nesoucí žádaný motiv
- fotorezist – pozitivní nebo negativní

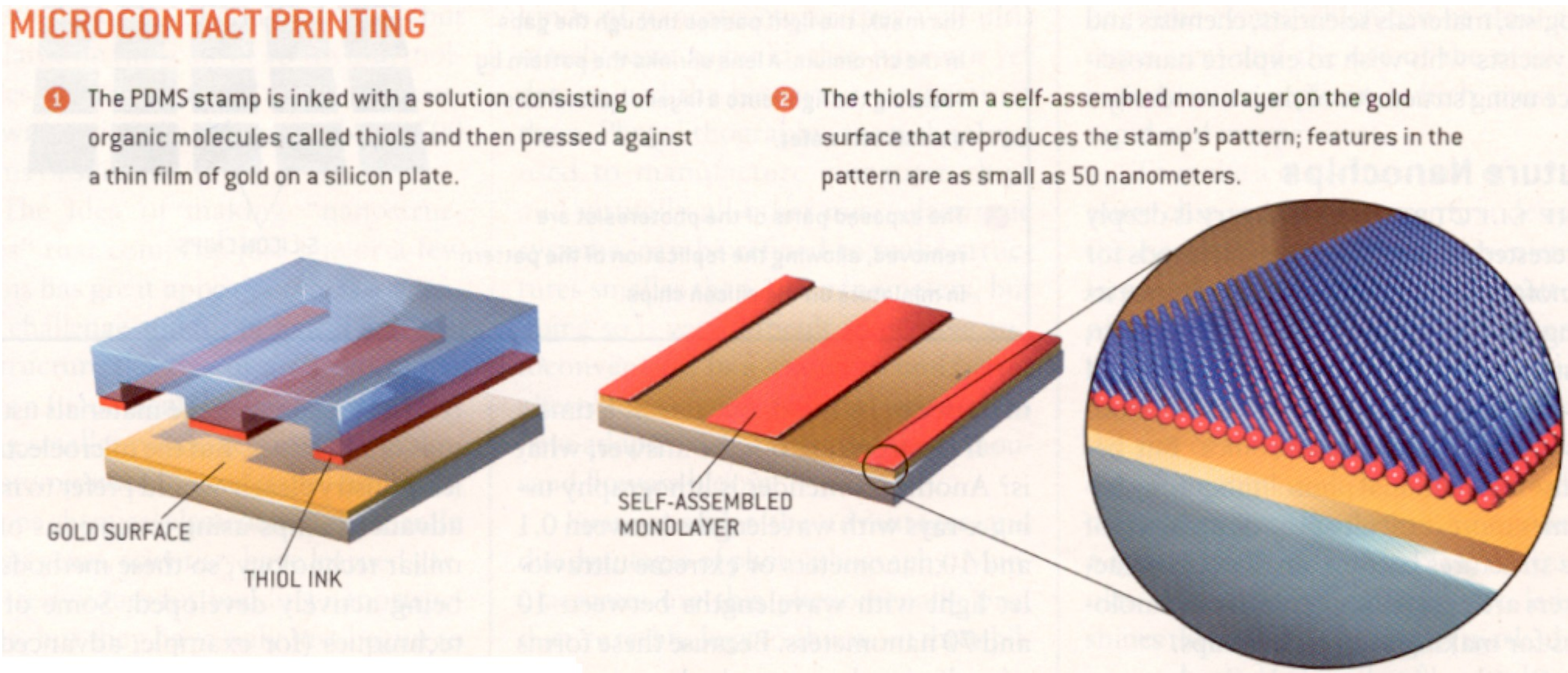
Litografie

- **schéma pracovního postupu**

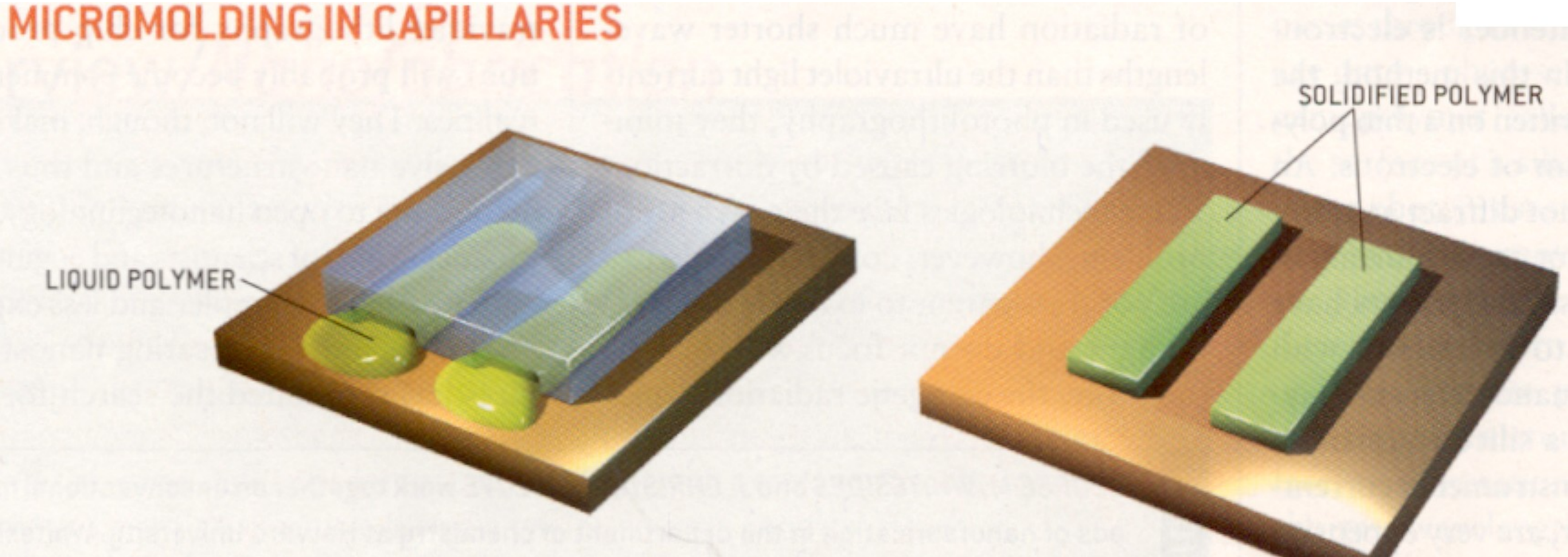


Emerging: soft litography

Soft lithography: microcontact printing

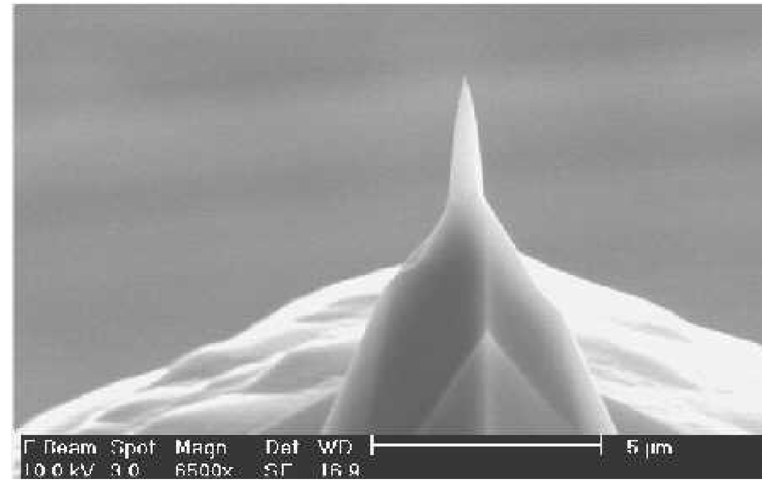


Soft lithography: micromolding



1. The PDMS stamp is placed on a hard surface, and a liquid polymer flows into the recesses between the surface and the stamp.
2. The polymer solidifies into the desired pattern, which may contain features smaller than 10 nanometers.

Subtractive techniques



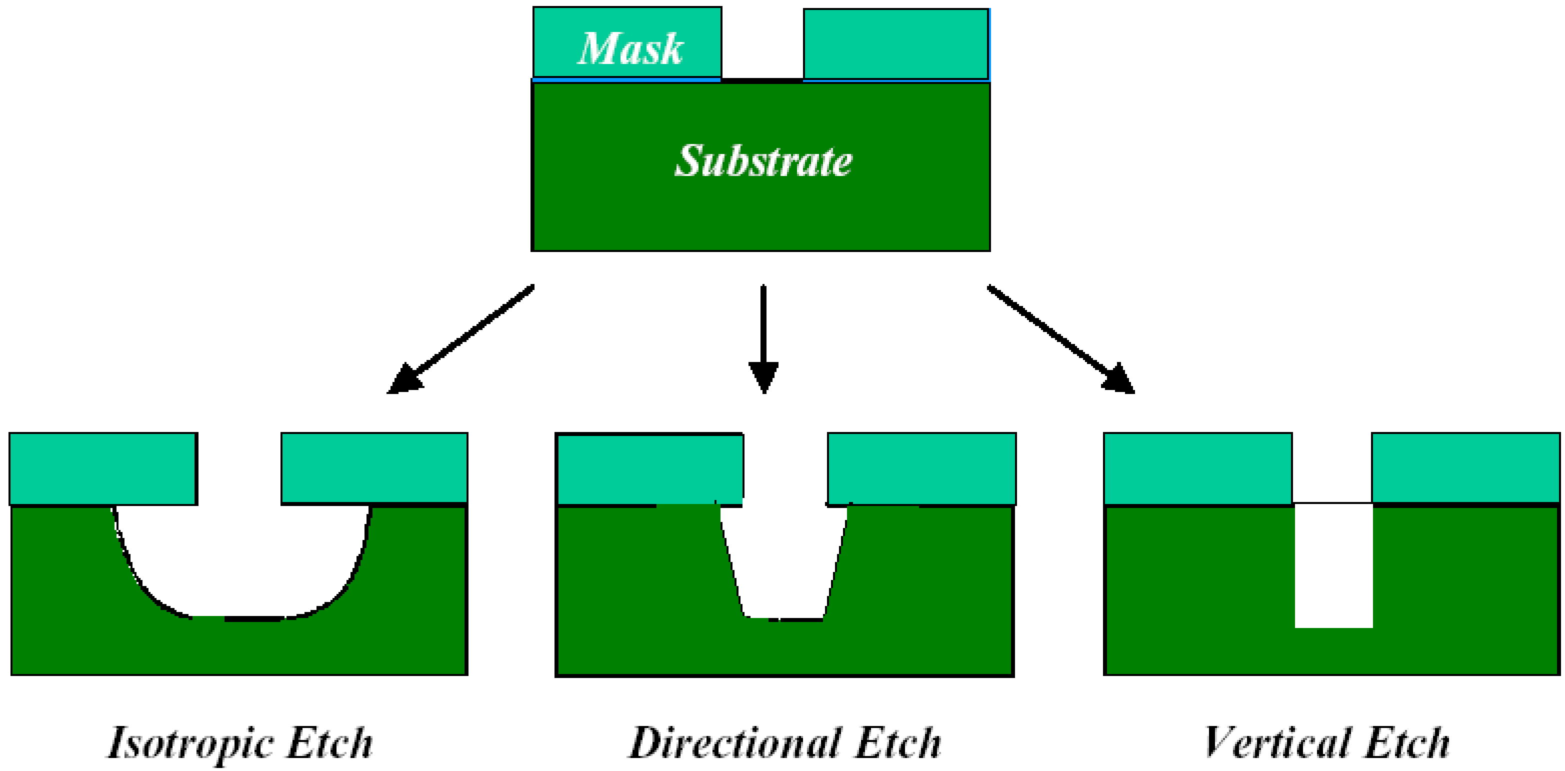
- **Etching**
- **Focused Ion Beam (FIB) milling** **(metal ions, e.g. Ga)**
- **Laser machining**
  (short, ultrashort, long pulses)
- **Ultrasonic drilling**
  (25 µm amplitude at 20-100 kHz, stress free in brittle materials)
- **Traditional precision machining**

Etching

wet etching
(attacco chimico)

dry etching

Chemical/physical removal of a material from a substrate



Srovnání technologií

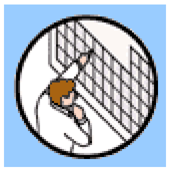
TABLE 3.13 Comparison of Different Sensor Technologies: Economic and Technical Aspects

	Classic construction	Thick film technology	Thin film technology	IC technology
Technology substrate	Wires and tubes	Screen-printing Al_2O_3, plastic	Evaporation-sputtering Al_2O_3, glass, quartz	IC techniques silicon, GaAs
Initial investment	Very low	Moderate	High	High
Production line cost	>$10k	>$100k	>$400k	>$800k
Production	Manual production	Mass production	Mass production	Mass production
Units per year	1 to 1000	1000 to 1,000,000	10,000 to 10,000,000	100,000 to ?
Prototype	Cheap	Cheap	Moderate	Expensive
Sensor price	Expensive sensor	Low cost per sensor	Low cost per sensor	Low cost per sensor
Use	Multiple use, *in vitro–in vivo*	Disposable, *in vitro*	Disposable, *in vivo*	Disposable, *in vivo*
Markets	Research, aerospace	Automotive, industrial	Industrial, medical	Medical, consumer
Dimension	Large	Moderate	Small	Extreme miniaturization
Solidity	Fragile	Robust	Robust	Robust
Reproducibility	Low	Moderate	High	High
Maximum temperature	800°C	800°C	1000°C	150°C (Si)
Interfacing	External discrete devices	Smart sensors, surface mount	Smart sensors, surface mount	Smart sensors, CMOS, bipolar

Source: M. Lambrechts and W. Sansen, *Biosensors: Microelectrochemical Devices*, The Institute of Physics Publishing, Philadelphia, 1992.[68] Reprinted with

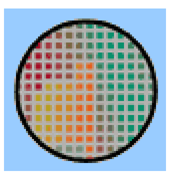
Material science - combinatorial approach

Imagine and Define
A new material with desired characteristics and qualities is defined.

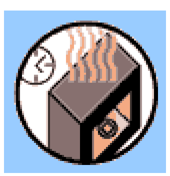


Select Likely Elements
From the whole Periodic Table, a chemist selects the combination of elements most likely to yield the desired material.

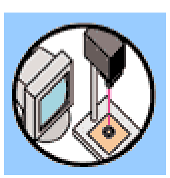
Create a library
Using robots and other automated devices, a library composed of thousands of different chemical combinations is rapidly created.



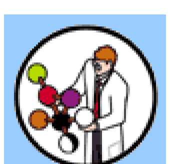
Process in Parallel
The library is an example of parallel processing, allowing up to 25,000 variations of material to be tested at one time.



Process
Processing can include any number of variables, including heat, high or low pressure, and time.



High Throughput Analysis
The library is screened by detectors that quickly scan various optical, magnetic, electrical, or other chemical/physical properties of a material, and the results are entered into a massive database.



Discovery and Information
Our scientists apply this analysis to identify the most successful new materials and the process used to produce them.

MEMS = Micro Electro Mechanical Systems

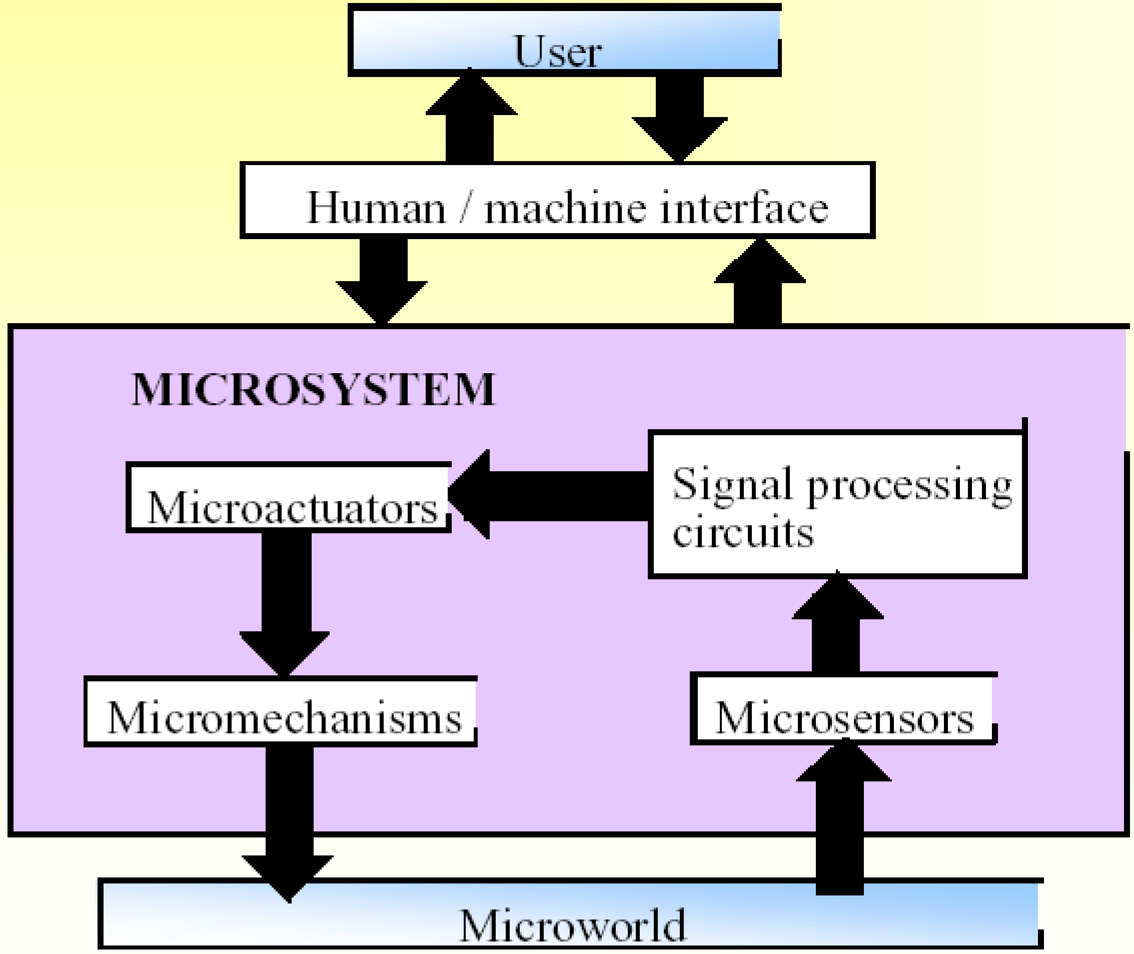
MST = Micro System Technology

Micro Machines

- MEMS
  - Used mainly in the USA
  - Background in IC technology => mass-production
- MST
  - Used mainly in Europe
  - System approach, covers both MEMS and micro machines
- Micro machine
  - Used mainly in Japan
  - Background in precision engineering

AUTOMATION AND

MEMS



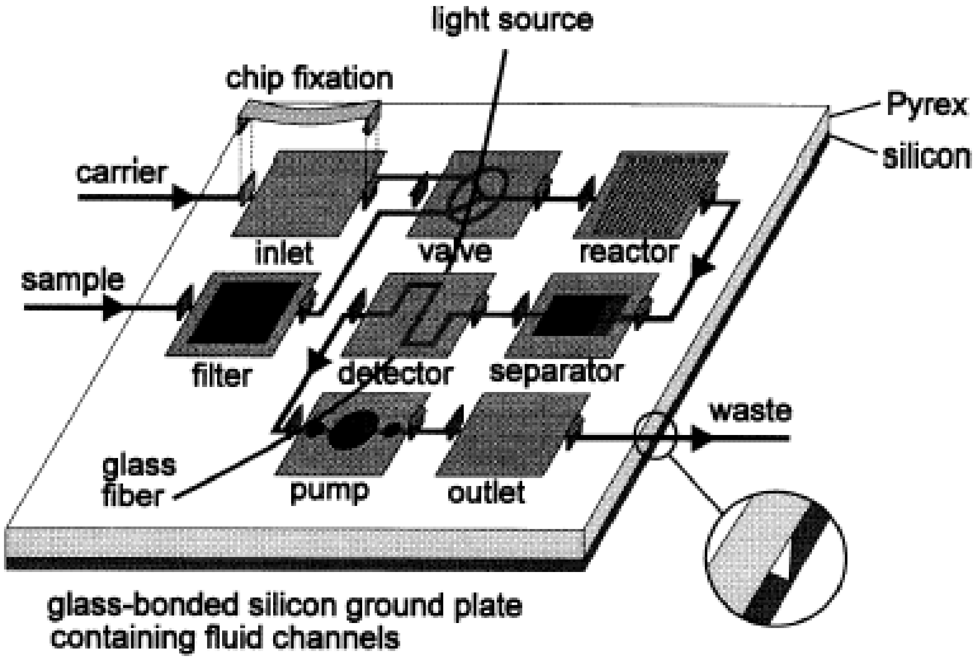
- No general agreement concerning the dimensions of a microsystem (cm…µm)
- One compromise is to refer microsystems as systems realized within a very small space and having at least one microfabricated component (Fatikow)

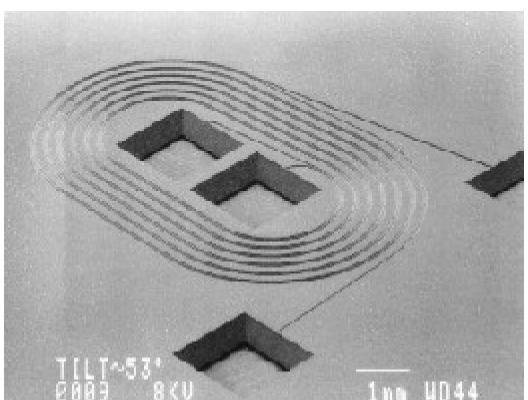
LAB on a chip / μTAS

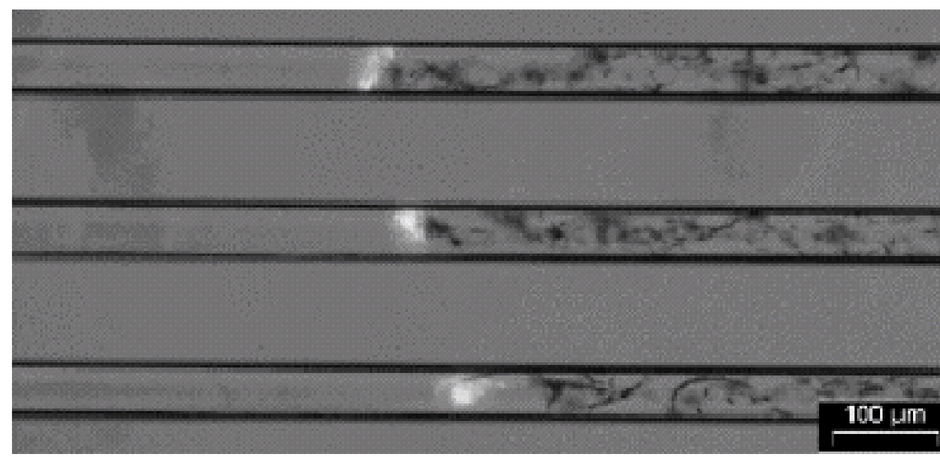
- Micro Total Analysis System (uTAS)
- What: miniaturization of chemical analysis systems
- Where: laboratory, factory or field.
- How:
  - Planar device/stack facilitating microcomponents
  - Number of chemical processes are being performed
  - From reactants to products or from sample to analysis
- It might be considered also as a total analysis system transforming chemical information into an electronic or optical signal.

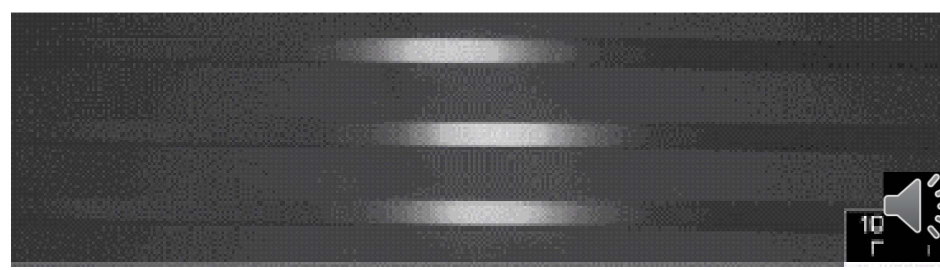
Lab-on-a-Chip

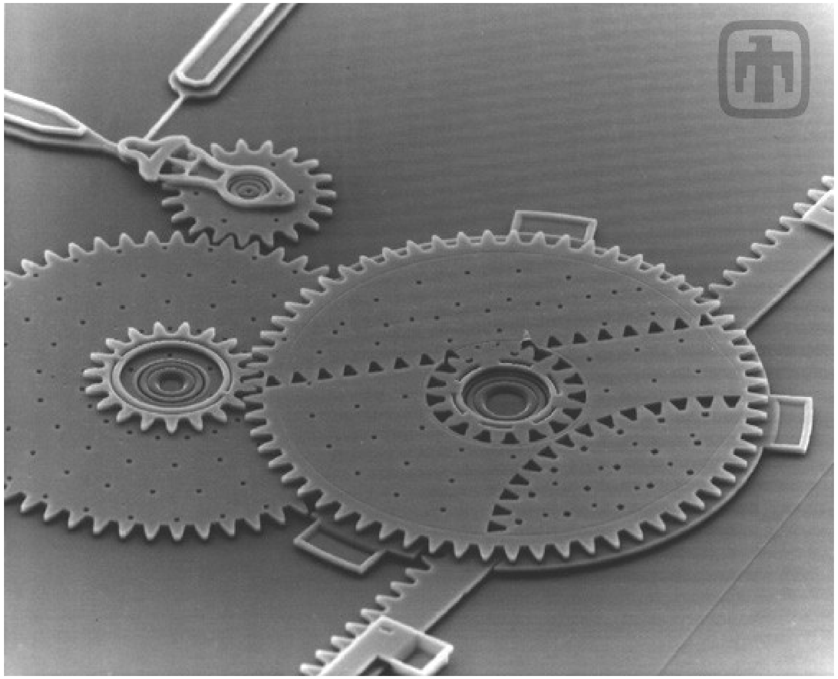
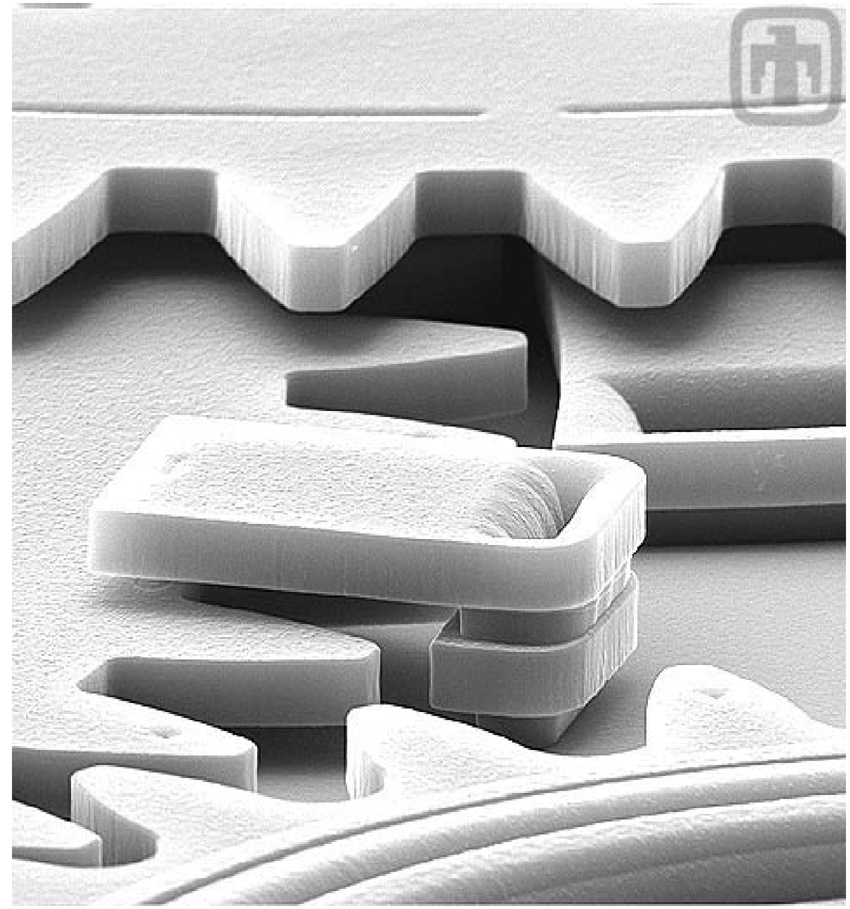
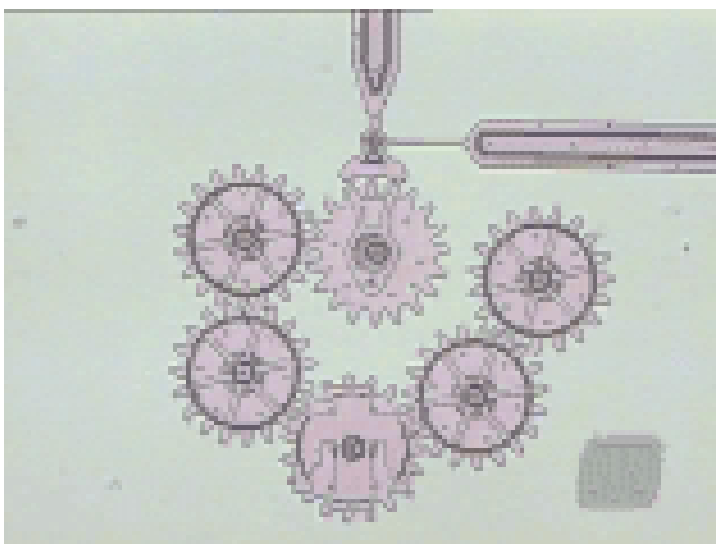
- **stejné či podobné procesy jako v makro-měřítku, ale odlišná technologie**
- **aktivní komponenty**
  - mikropumpy
  - mikroventily
  - mikro(bio)sensory
  - mikromíchače
  - mikroreaktory



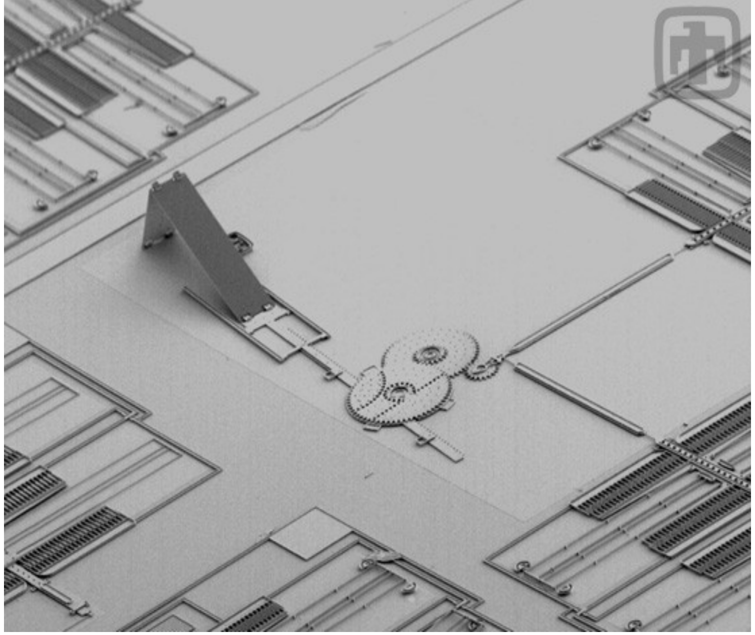


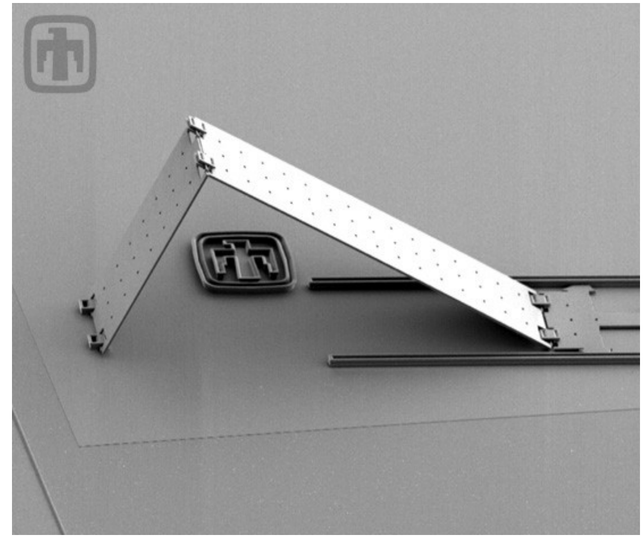


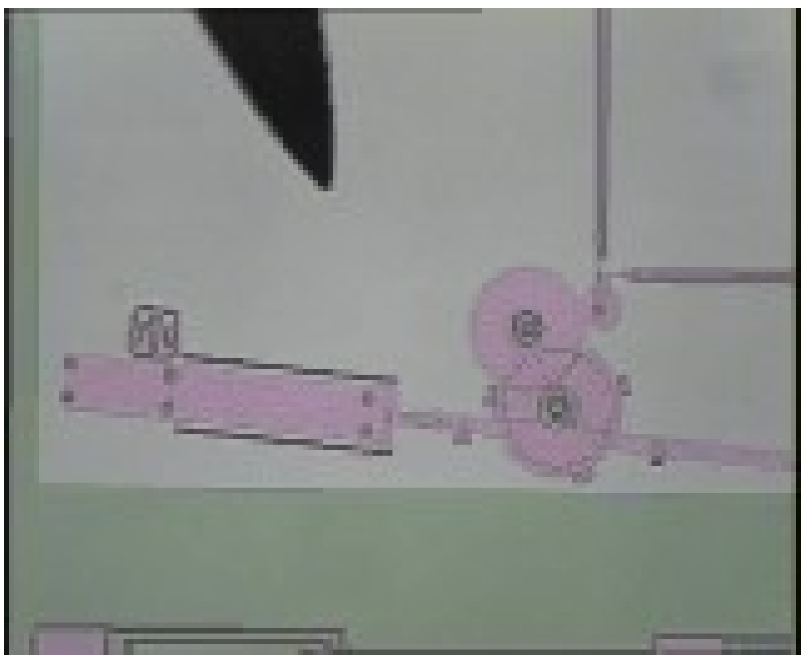


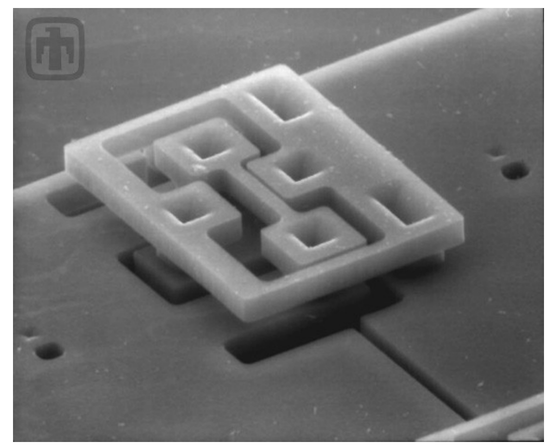




Silicon Mirror and Drive System
mirror design, driven by a three gear torque increasing system.









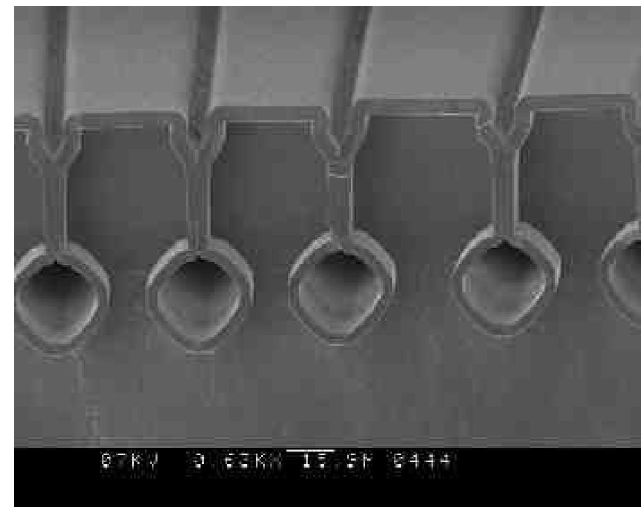
Pop-up Silicon Mirror
Comb drive forces propel a linear rack, which pushes and pulls on a hinged sheet of silicon. A HeNe optical-band (red) laser i
focused at an angle such that at full extension, the coherent light is reflected onto the microscope camera.

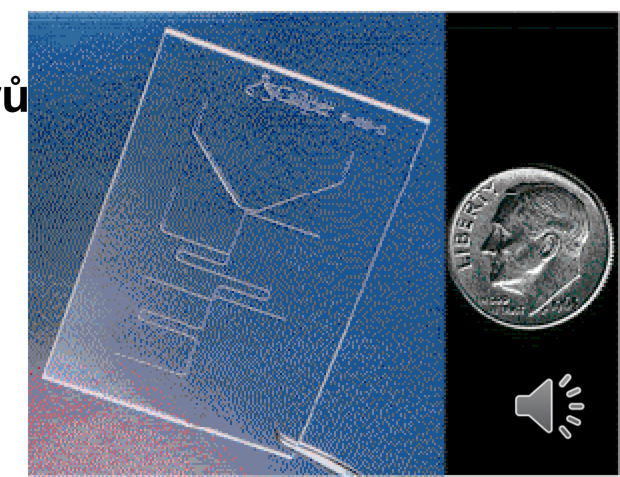
Microfluidics

- popisuje průtočný systém s rozměry v oblasti mikrometrů; zahrnuje miniaturní zařízení zajišťující pohyb, míchání, filtrování, zahřívání/chlazení a reakce roztoků činidel, případně včetně suspendovaných částic

Výhody

- **úspora činidel, vzorků, rozpouštědel, méně odpadu**
- **zvýšená prostupnost - řada reakcí běží rychleji, paralelní zpracování**
- **přesná geometrie pracovního prostoru - dávkování, uzavřeno - lze používat labilní reagencie, pracovat s nebezpečnými látkami za normálních podmínek**
- **lepší kontrola reakcí - čistší produkty**
- **rychlé ustavení požadované teploty kapalin a reaktorů**
- **malá velikost - úspora pracovního prostoru**
- **robustnost**





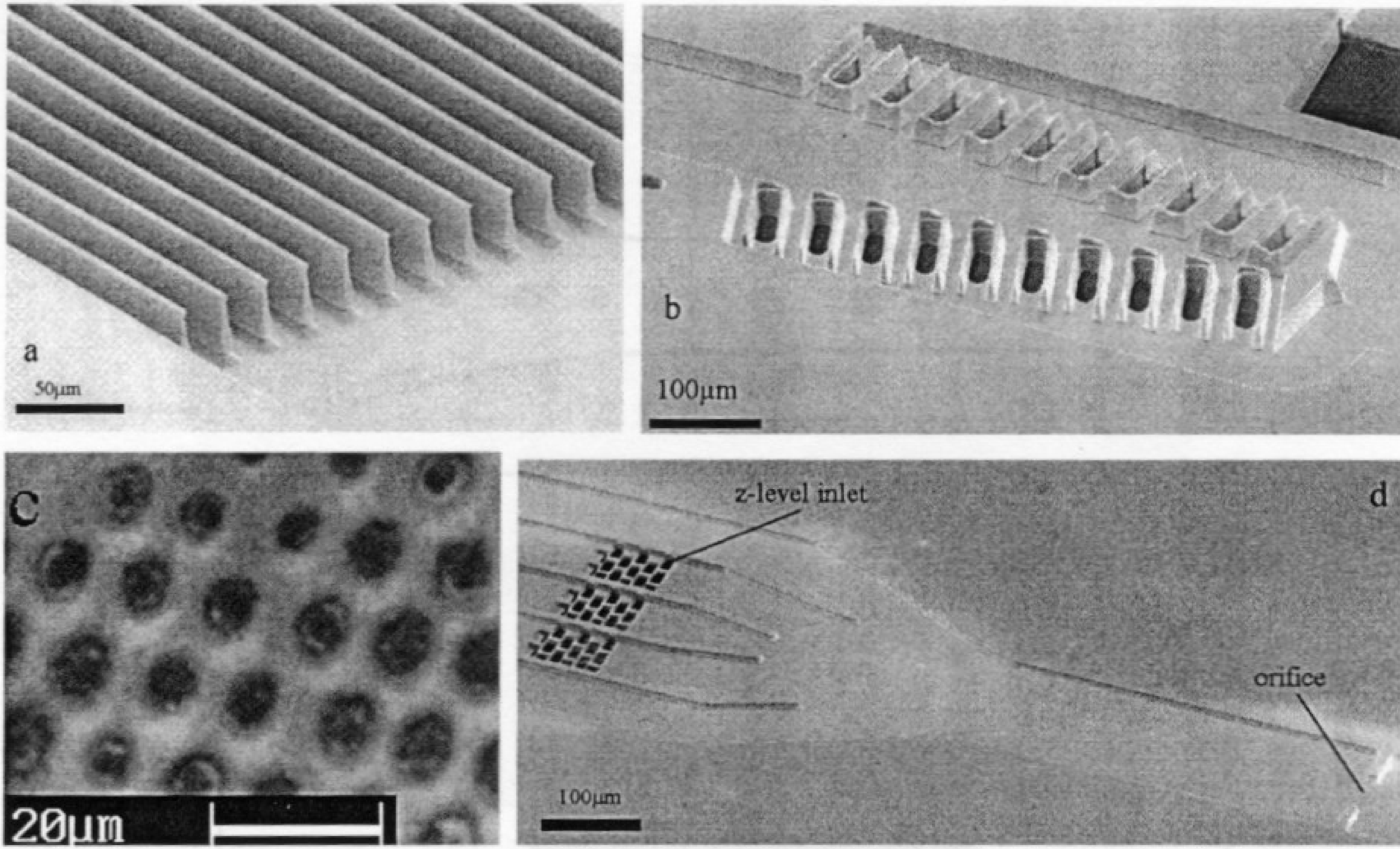


Fig. 6. Scanning electron microphotographs of some microfabricated devices. a) Immobilization reactor with 5 μm wide lamellas in a 50 μm deep channel. b) A mixer structure in a 50 μm deep channel. c) Inlet filter: Silicon membrane (15 μm) with laser micromachined pores. d) Coulter sizer setup with 5 planar inlets and a z-level inlet.