The Abdus Salam
International Centre for Theoretical Physics

United Nations
Educational, Scientific
and Cultural Organization

International Atomic
Energy Agency

SMR.1670 - 10

INTRODUCTION TO MICROFLUIDICS

8 - 26 August 2005

Plastic Fabrication

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Topics in this lecture

Cheaper production capabilities
Many by many shots…short cycle times…shifting complexity from the fabrication to the design stage

Classical polymer processing goes micro/nano
Continuous development; if there is a mold, replication is possible…

First products
Addressing successful strategies leading to microfluidic products

1. Polymer fabrication: techniques and material diversity

- Introduction
- Strategic developments
  - Cheaper production
  - Dedicated choice of materials
- Tool box
  - Primary
  - Secondary
- Polymer integration
- Outlook: Future developments
- Summary

Topics in this section

Plastic

Its everywhere also in high tech applications.

Introduction

- From consumer goods to high tech plastics in 75 minutes
  - Development from standard plastic fabrication industry to advanced micromachining technique
  - Materials
  - Why is plastics so popular in microfluidics?

Do microchips need polymers?

Available:

- Current lab-on-a-chip devices adapt mainly processes from the microelectronics industry.
- Silicon and glass wafers (substrates) are commonly used.

Required:

- Parallel scale-out philosophy
- Biological applications require sterile and oxygen permeable devices.
- Devices used in toxicological and medical point-of-care studies must be disposed off.

Impact of polymers on microfabrication

- In the natural world, starch, cellulose, and rubber all possess polymeric properties. Man-made polymers have been studied since 1832. Today, the polymer industry has grown to be larger than the aluminum, copper and steel industries combined.
- Polymers already have a range of applications that far exceeds that of any other class of material available to man.
- Current applications extend from adhesives, coatings, foams, and packaging materials to textile and industrial fibers, composites, electronic devices, biomedical devices, optical devices, and precursors for many newly developed high-tech materials.

Polymer etymology

- Polymers are substances containing a large number of structural units joined by the same type of chemical linkage (macromolecule).
- The word comes from Greek: poly means `many' and mer comes from merous which roughly means `parts'. The word polymeric comes directly from the Greek polumeres which simply means `having many parts'.

Ubiquitous "MERS"

- Ethylene
- Styrene
- Acrylamide

- Polyethylene
- Polysterene
- Polyacrylamide

Thermoplastics

......are generally carbon containing polymers synthesized by addition or condensation polymerization.

Usually, the forces between molecule chains can be easily overcome by thermal energy, making thermoplastics moldable at elevated temperatures.

Thermoplastics will also retain their newly reformed shape after cooling.

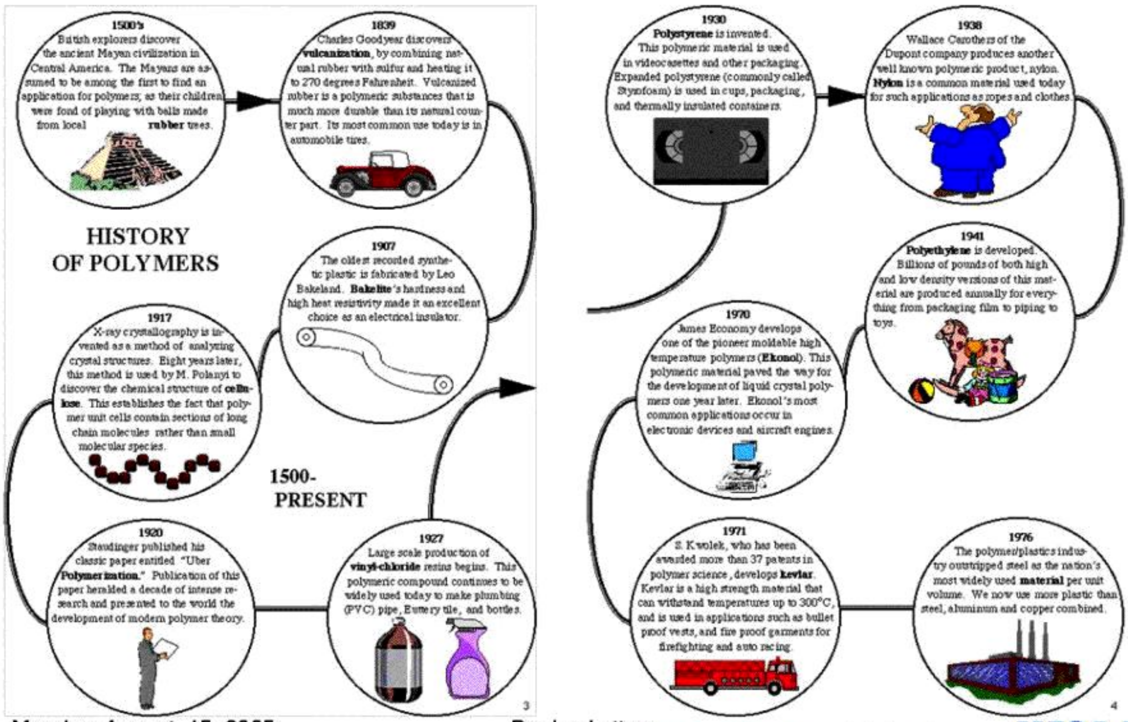
Thermosets

......are polymers that solidify or "set" irreversibly when heated. They also have a stronger linkage to other chains.

Strong covalent bonds chemically hold different chains together in a thermoset material.

Phenolics, alkyds, amino resins, polyesters, epoxides and silicones are usually considered to be thermosetting but the term also applies to materials where additive-induced crosslinking is possible, e.g., natural rubber.

Historical development



 (www.google.com ⟹ *find picture*)

Summarized historical overview

1500's Discovered: ancient Mayas used rubber products
1839 Charles Goodyear discovers vulcanization
1907 Leo Bakeland fabricates Bakelite
1917 X-ray crystallography to analyze cellulose
1920 Staudinger publishes: *Über Polymerization*
1927 Large scale production of vinylchloride resins
1930 Polysterene is invented
1938 Wallace Carothers of Dupont Company produces Nylon
1941 Polyethylene is developed used from piping to toys!
1970 James Economy develops Ekonol that paved way for LC
1971 S. Kwolek develops Kevlar
1976 Polymer plastic industry outstrips steel in production
1990's Polymers get established in microfabrication

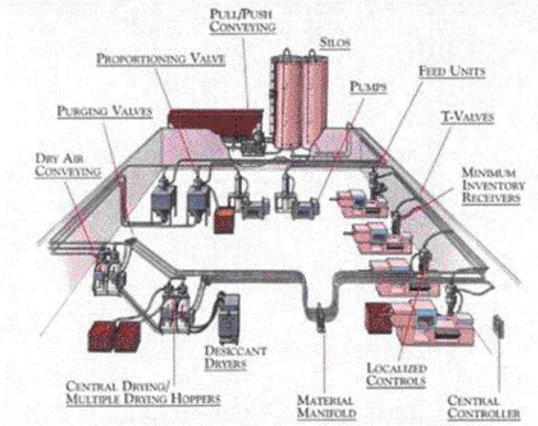
Chemical & engineering industry

- Raw material production

ABS
Acrylic
Bakelite
Celcon
Delrin®
Delrin® AF
Hydex 202
Hydex 301
Hydex 4101
Hylar
KEL-F
Kydex®
Kynar® (PVDF)
Lexan
Methylpentene
Micarta
Noryl
Nylatron® GS

Nylon
MD Nylon
PVC
Phenolics
Polycarbonate
Polyether
Polyethylene (high/low density)
Polymer
Polypropylene
Polystyrene
Polystyrene
Polysulfone
Rulon
Ryton
Sulfone

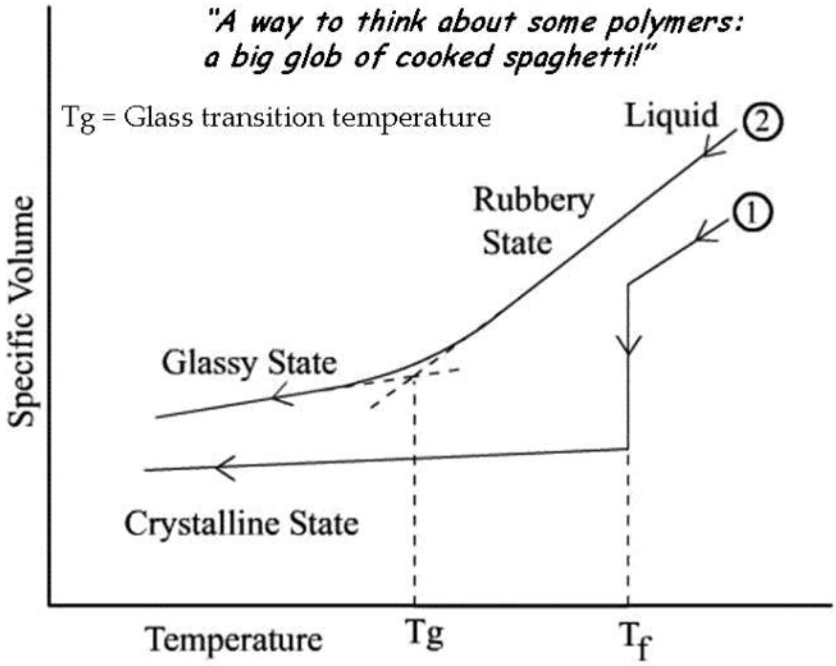
TPX
TPX (Methylpentene polymer)
Teflon
Torlon®
UHMW
Ultem
Vespel®
Victrex®
Victrex® VES
Zelux



http://www.matweb.com/search/SearchTradeName.asp

Molecular entanglement

"A way to think about some polymers: a big glob of cooked spaghetti!"

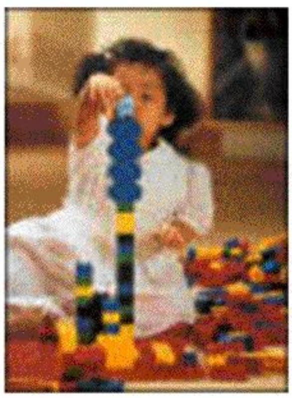


Properties & forces

- Long, chainlike molecules (polymers)
- Molecular weights
  - Tens of thousands and several million Daltons
- Distinct properties
  - Rooted in large molecular weight and structural properties
- Two fundamental forces govern properties
  - strong **covalent intramolecular bonds** constitute backbone
  - Individual chains electrostatically attracted by neighboring macromolecules
  - Rather weak **electrostatic coupling** between single molecular constituents accumulates along whole extension of chain molecules
  - Strong overall electrostatic forces
    - Plastics keep their shape after molding

Source: Jens Ducrée and Roland Zengerle

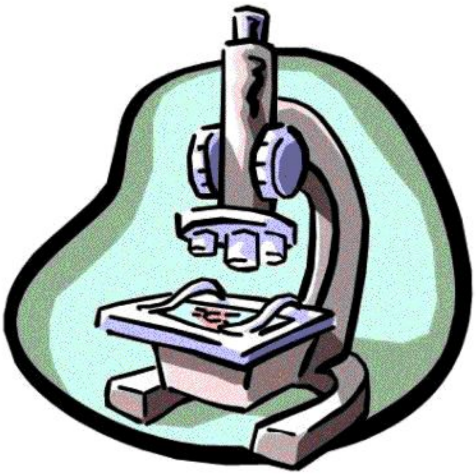
Plastic products



Why so popular in microfluidics?

Lab-on-a-Chip devices

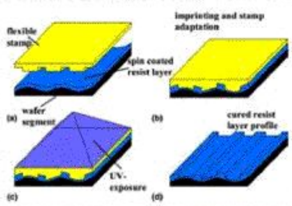
- Must be compatible to optical detection.
- Should be cheap and highly reproducible (statistical research = many Petri dishes!).
- Should be used as a consumable like a syringe.
- Must allow further integration: closed channels, electrodes, mixing, pumping of various reagents.



Topics in this section

Basic processing

Plastic micro- and nanofabrication



U. Plachetka et al., Microelect. Eng. 73–74 (2004) 167–171

Strategic developments

Small lot production

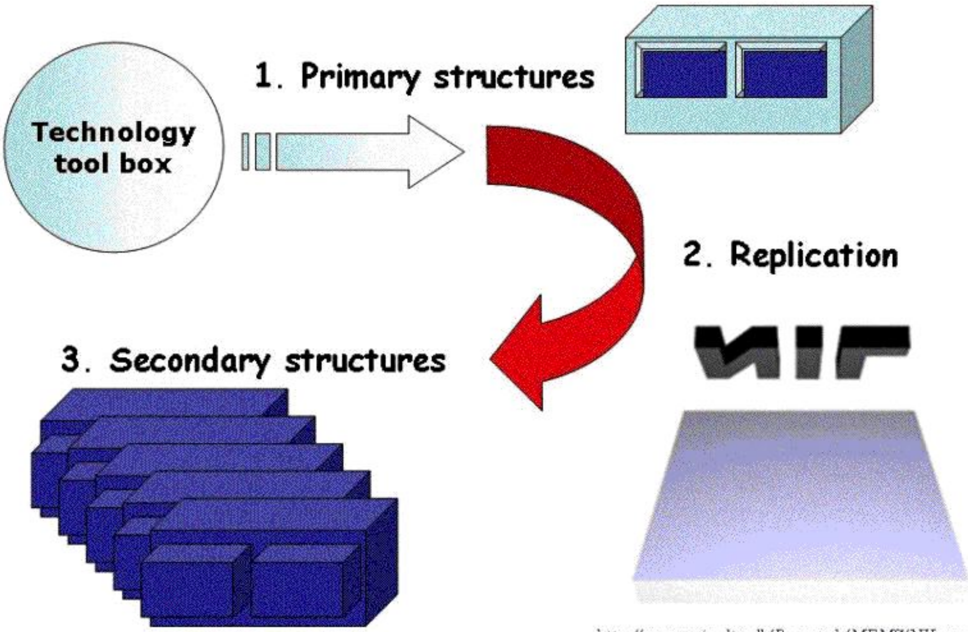
- Bulk micromachining
  - Mechanical micromachining
  - Laser ablation (e.g. excimer)
  - LIGA
  - etc.
- Additive technologies
  - Stereolithography, photoforming
  - Additive laser micromachining
  - etc.

Mass production

1. Master tool fabrication
   - Mechanical micromachining
   - Silicon micromachining
   - Galvanic forming (see LIGA)
   - Electrodischarge machining
   - etc.
2. Replication technology
   - Injection Molding
   - Hot embossing
   - Casting techniques
   - Lamination techniques
   - etc.

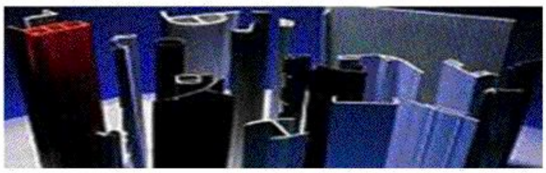
Source: Jens Ducrée and Roland Zengerle

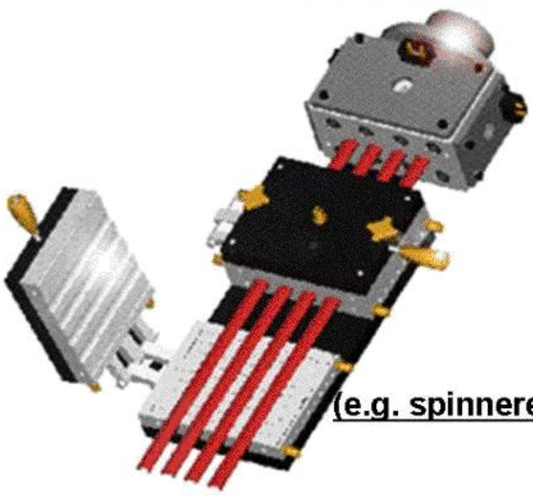
Process flow



http://www.mic.dtu.dk/Research/MEMS/NIL.aspx

Extrusion molding



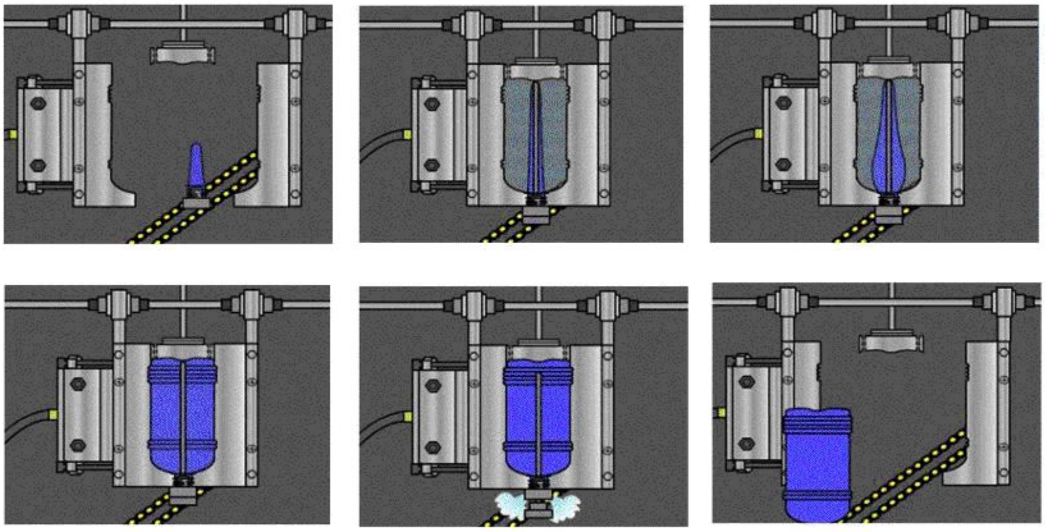


An extrusion line can produce plastic sheets or other "endless" plastic products depending on the mold insert.

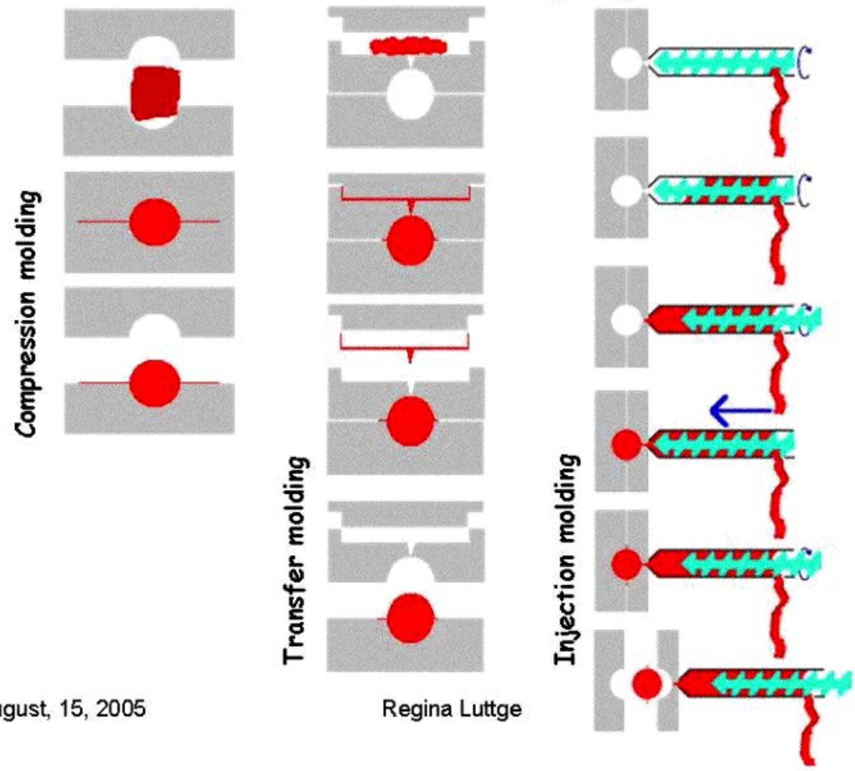
Extrusion master tool
(e.g. spinneret plate for synthetic fibres)

Blow molding

A plastic sheets (PP,PE,PS,PVC,ABS,etc.) can be used as raw materials for producing various kind of the thermoformed containers.



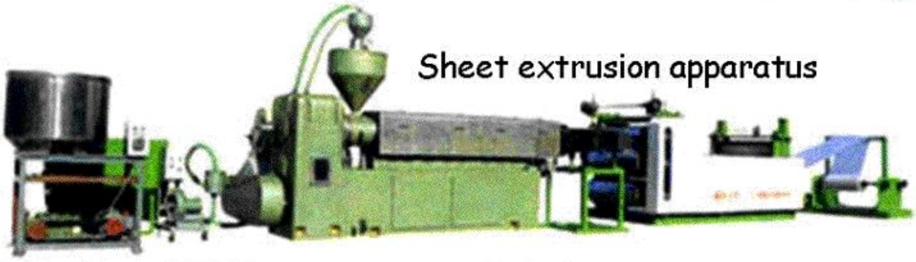
Molding by master filling



"Steam engines" for plastic production

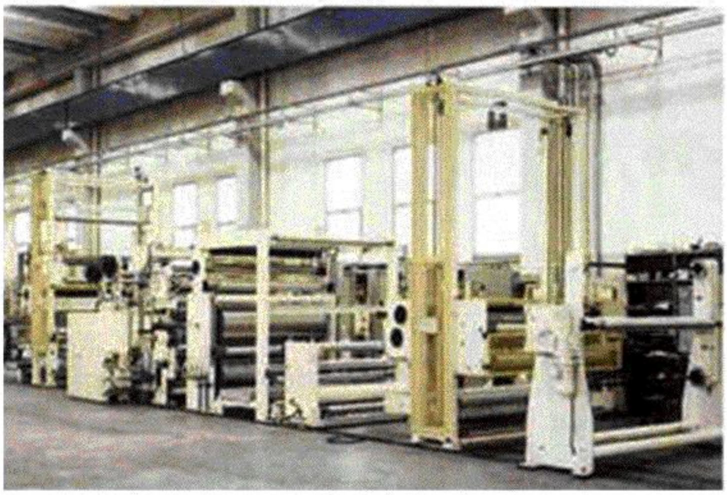
Injection molding apparatus

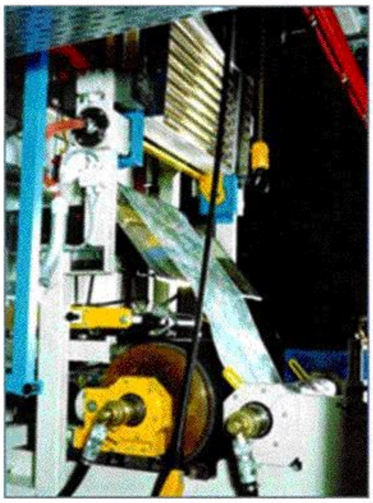
Sheet extrusion apparatus



High volume production

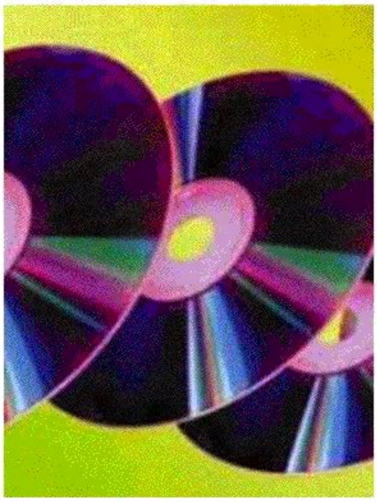
Embossing/printing machine for the hot embossing of vinyl wallpaper and vinyl flooring





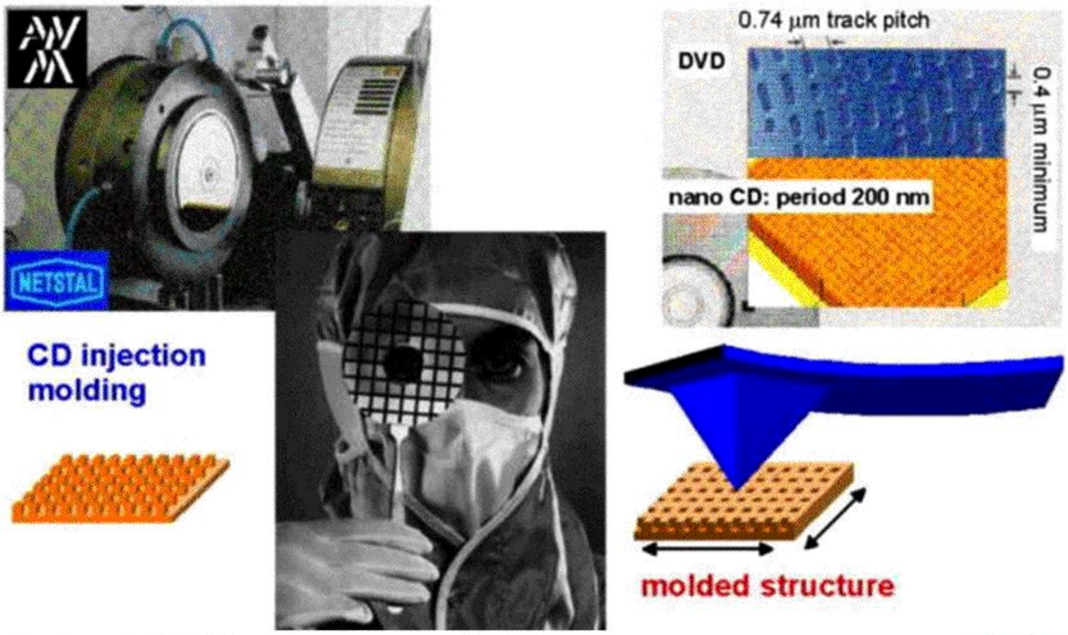
Cups and compact discs- just the same?

The new age (1990 and beyond): from macro to micromolding



1.2. Strategic developments

Success of "nano" injection molding

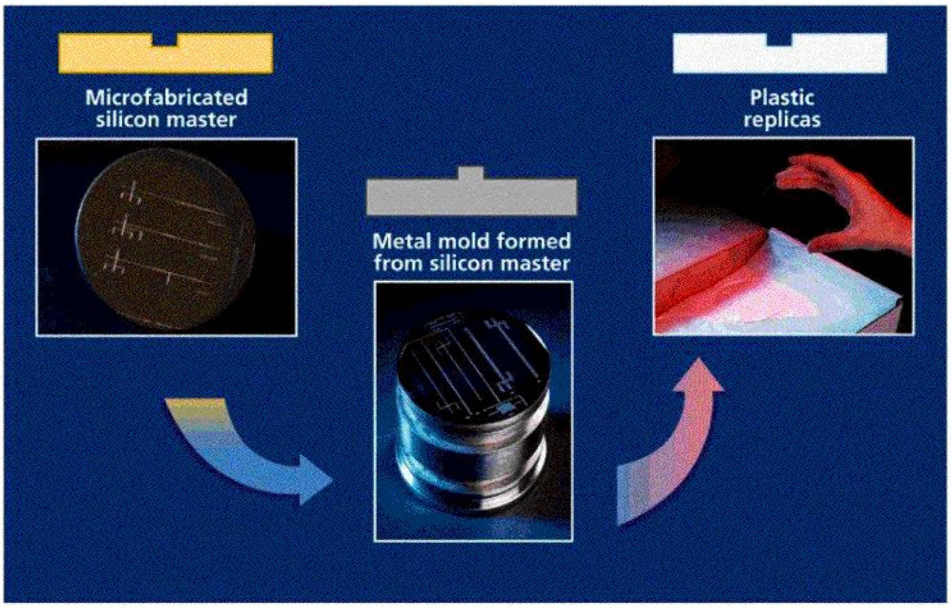


Monday, August, 15, 2005 Regina Luttge

1.2. Strategic developments

ALCLARA develops plastic biochips

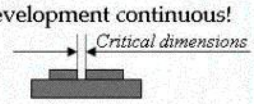
- Exploiting micromolding



Microfabrication tool box

Topics in this section

Master fabrication
Primary structuring process demanded > 30 years of microfabrication research attention…
development continuous!



Replication efforts
Automated injection molding.

(Source: Ferromatik Milacron)

Adapted from: http://hikwww1.fzk.de/mikro/arbeitsthemen/e_inhalt_fertigungstechnologien.html

"Single Source" supplier

PROTOTYPE • PRODUCTION • ASSEMBLY

Plastic & Metal Center, Inc
ENGINEERING • DESIGN • MANUFACTURING
ISO & GMP Compliant

Thermo Vacuum Forming
- Tool Design
- Any Thickness
- Complex Designs
- Trimming
- Packaging

Injection Molding
- Commodity Plastics
- Assembly
- Any Material
- Mold Making
- Finishing

CNC Machining
- Milling
- Turning
- Exotic Material
- CAD/CAM
- Tooling & Fixtures
- Custom Machinery
- EDM Sinker
- Grinding
- Assembly

Fabrication
- Plastic
- Sheet Metal
- Welding
- Bending
- CNC Routing
- All Materials
- POP Displays
- Fulfillment

Product Assembly
- Sub Assemblies
- Multiple Welding
- Screening
- Packaging

Product Design
- Conceptual Design
- Electronics
- Mechanical
- Engineering
- CAD/CAM 3D SolidWorks

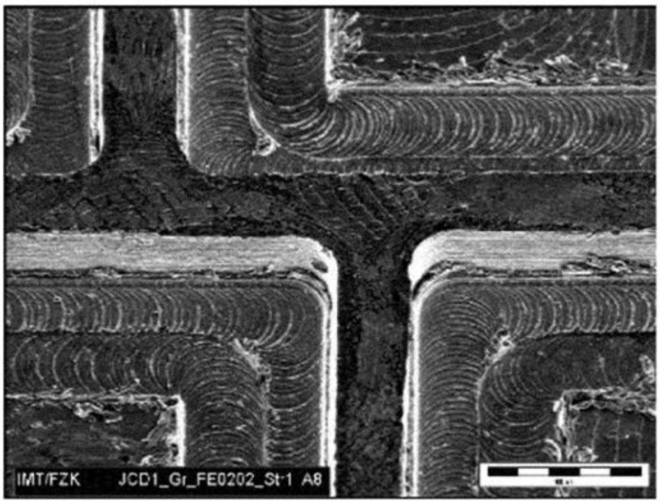
Primary structure pattering

Molding master and direct plastic patterning

- Machining
- UV Lithography
- Laser, x-rays…
- Electroforming (Galvanic) metal mold master for better thermal conductivity
- LIGA

Micromilling

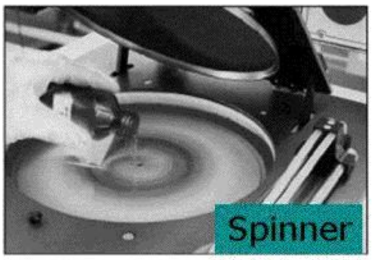
Mechanical micro machining



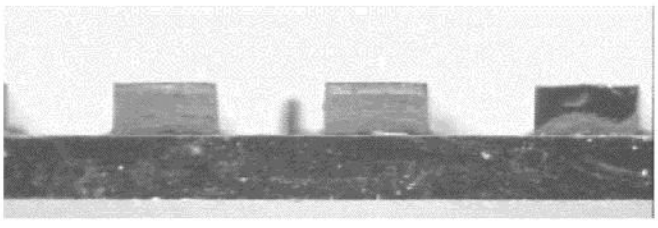
Metal mold insert
made of brass

A.E. Guber et al., Chemical Engineering Journal, (2004)

Optical lithography

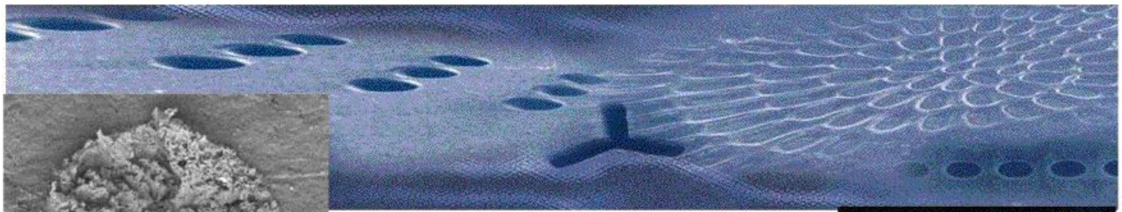


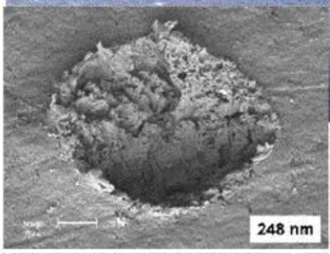
- Spinning and exposure of photoresist from a few 100 nm to 1000 μm
- Example of 250μm thick photoresist structure (SU-8) on a silicon substrate

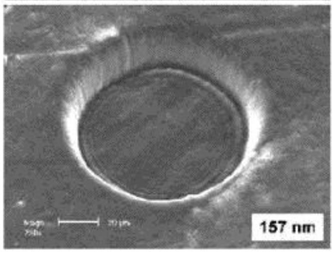


B.E.J. Aldermann et al., J. Micromech. Microeng. 10 (2000) 334–336.

Laser ablation





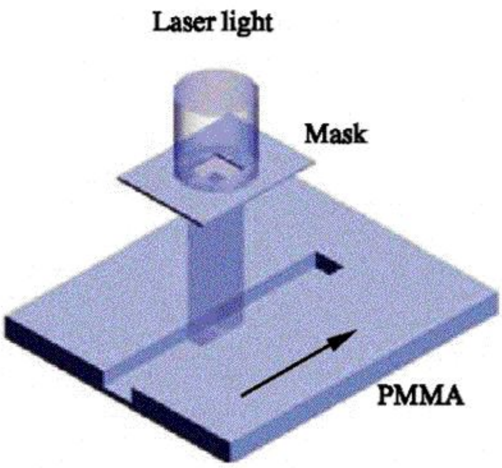


- Material: PTFE
  Laser: Excimer
  λ = 157nm
  Energy density 1 J/cm^2
- Low absorption coefficient @248nm (193) nm results in rough surface and edge quality
- 157nm wavelength gives smooth results

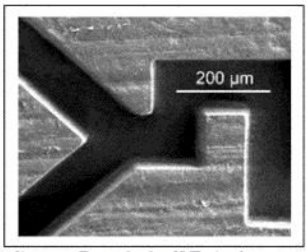
LAMBDA PHYSIK

Laser direct write and drilling

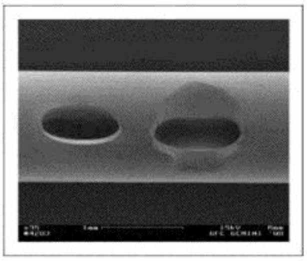
Biomedical devices



Lin et al., J. Micromech. Microeng. 11 (2001) 189–194



Source: Fraunhofer ILT, Aachen (Fluidic structure)



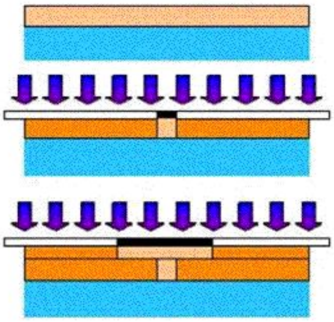
Source: Lambda Physics (Drilled catheter)

1.3. Microfabrication tool box

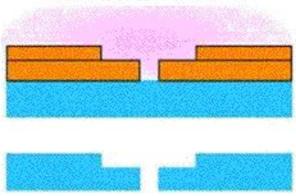
Plasma etching

Etching

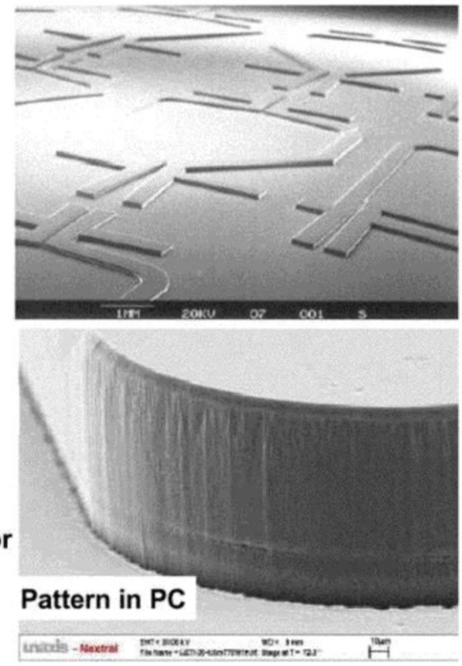
1- SU8 litho on polymer



2-Transfer pattern into the polymer



High density
Low temp
ICP plasma reactor



CEA LETI Annual Review June 2003

Plasma polymerization

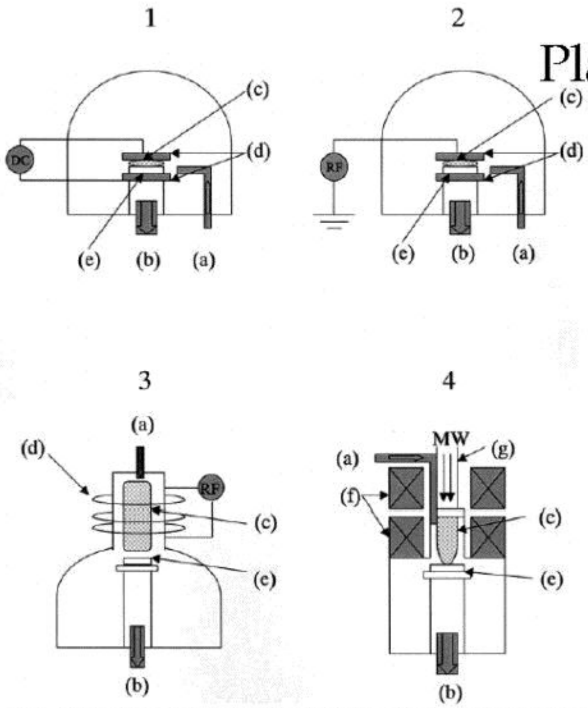
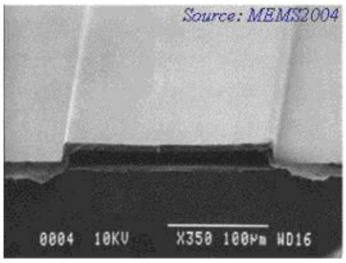


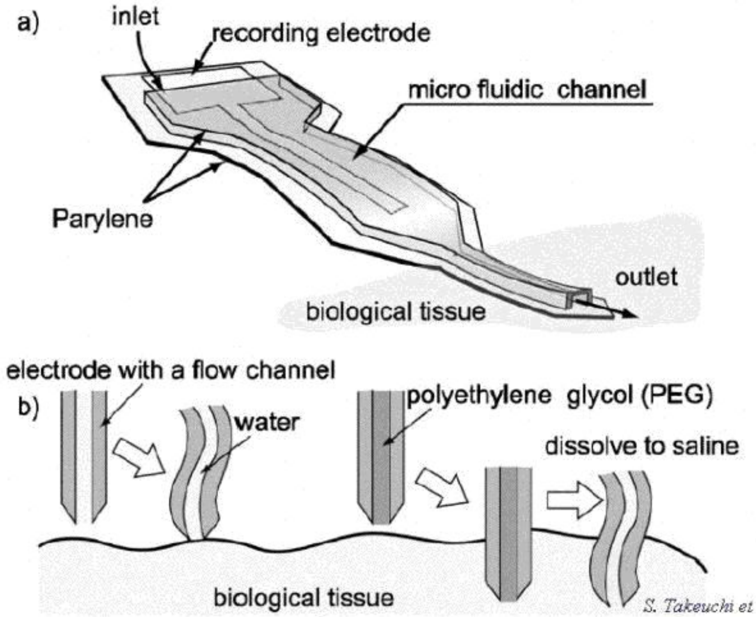
Fig. 2. Schematic representation of several reactor types for plasma polymerized films. 1) Internal electrode reactor with DC power supply, 2) internal electrode reactor with RF power supply, 3) external electrode reactor with RF power supply, 4) electrodeless microwave (2.45 GHz) reactor. a) Monomer gas inlet, b) to vacuum pump, c) plasma, d) electrodes, e) sample, f) magnet coil, g) wave guide.

A. Hiratsuka and I. Karube, Electroanalysis 2000, 12, no.9, 695-701

- Polymer layers can be deposited from the plasma or vapor phase of their precursors.
- Parylene-C

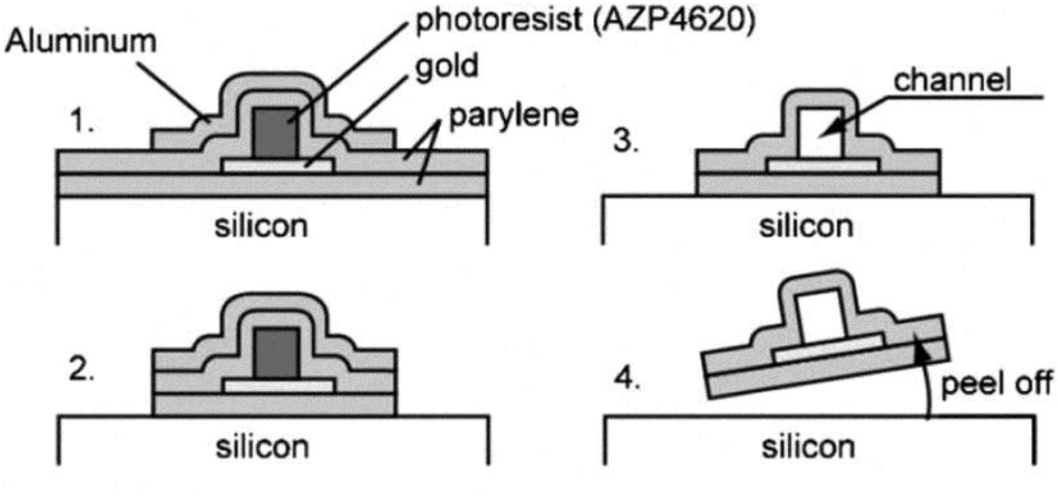


Flexible tissue probes



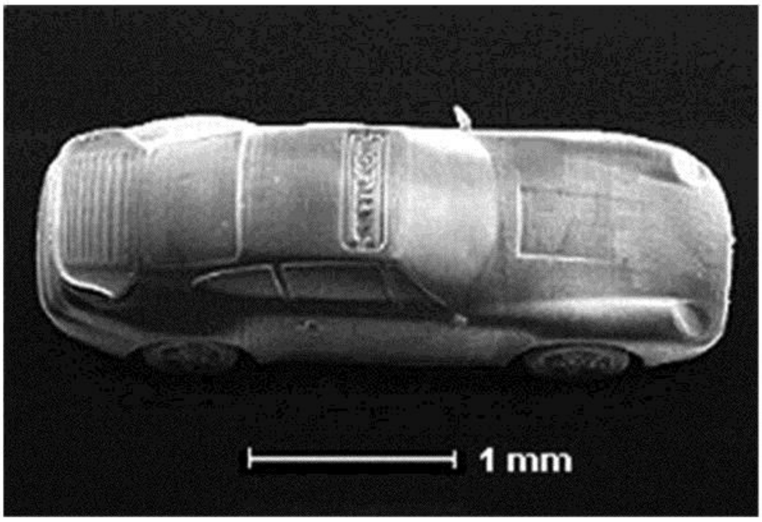
S. Takeuchi et al., Lab Chip, 2005, 5, 519–523

Probe fabrication process

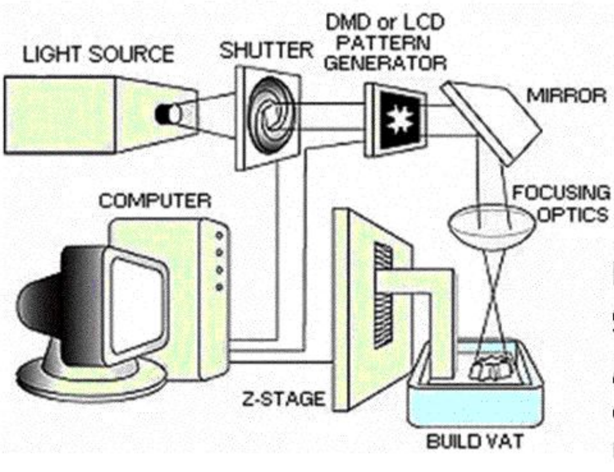


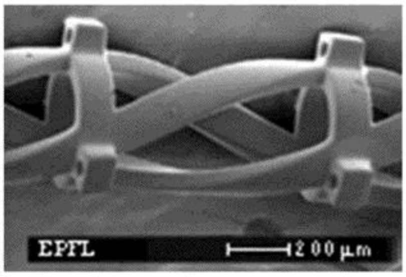
S. Takeuchi et al., Lab Chip, 2005, 5, 519–523

Micro-stereo lithography



Micro-stereo lithography

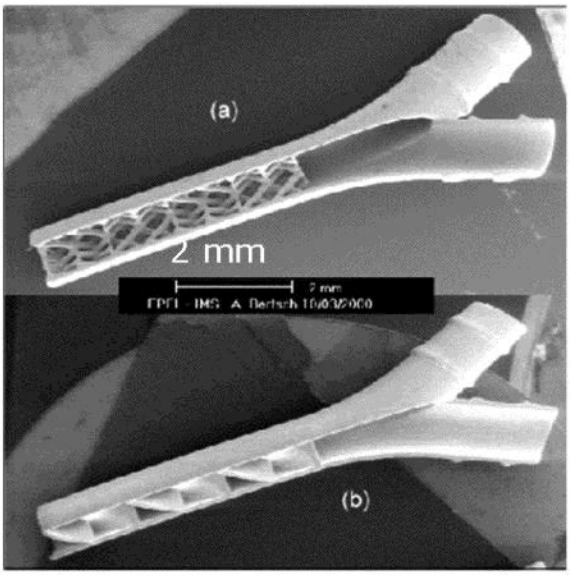


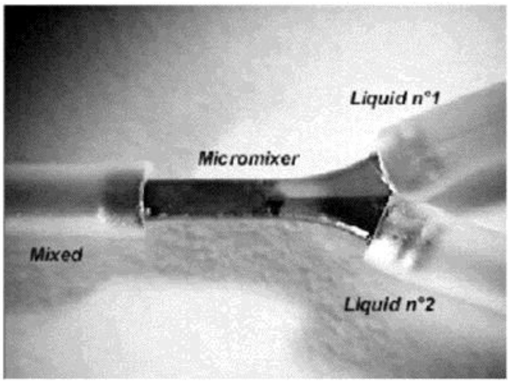


Fully three-dimensional geometry.

Micro-components that are complex in shape can be manufactured with a 5 µm resolution.

Assembled micromachined mixer

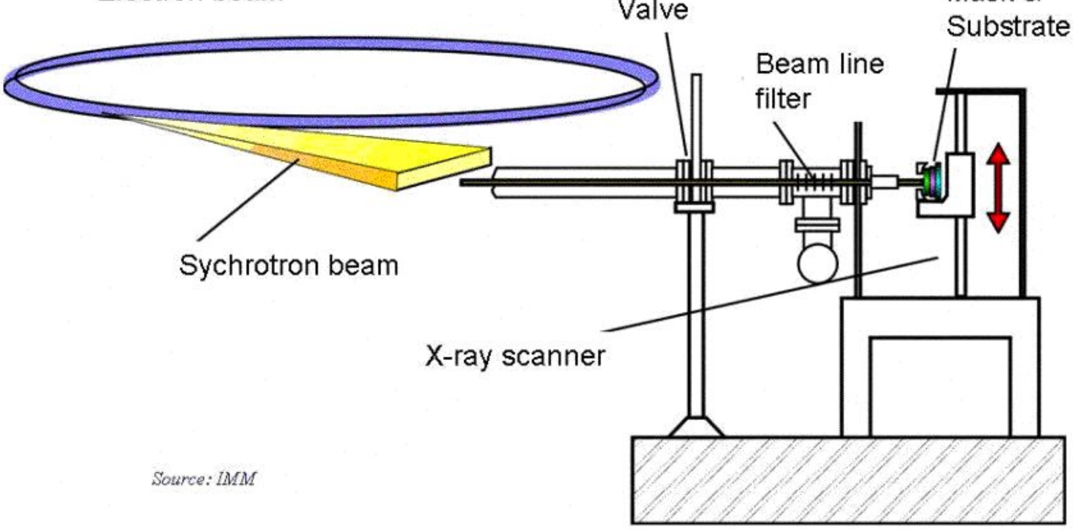




Layer-by-layer polymerization of liquid resin (stereolithography)

Arnaud Bertsch, Lab on a Chip, 2001, 1, 56–60

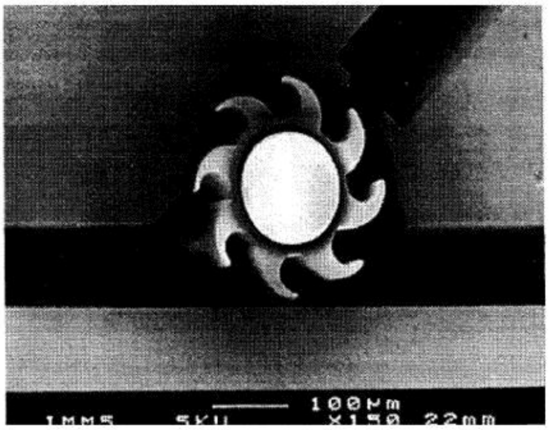
X-ray lithography



Source: IMM

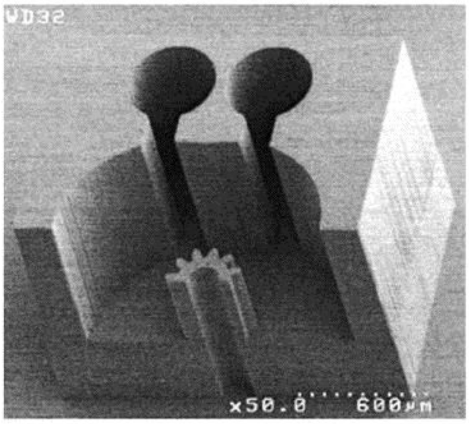
Thick PMMA, SU-8

Assembled and multilayer structures



Microturbine developed at FZK, 1990

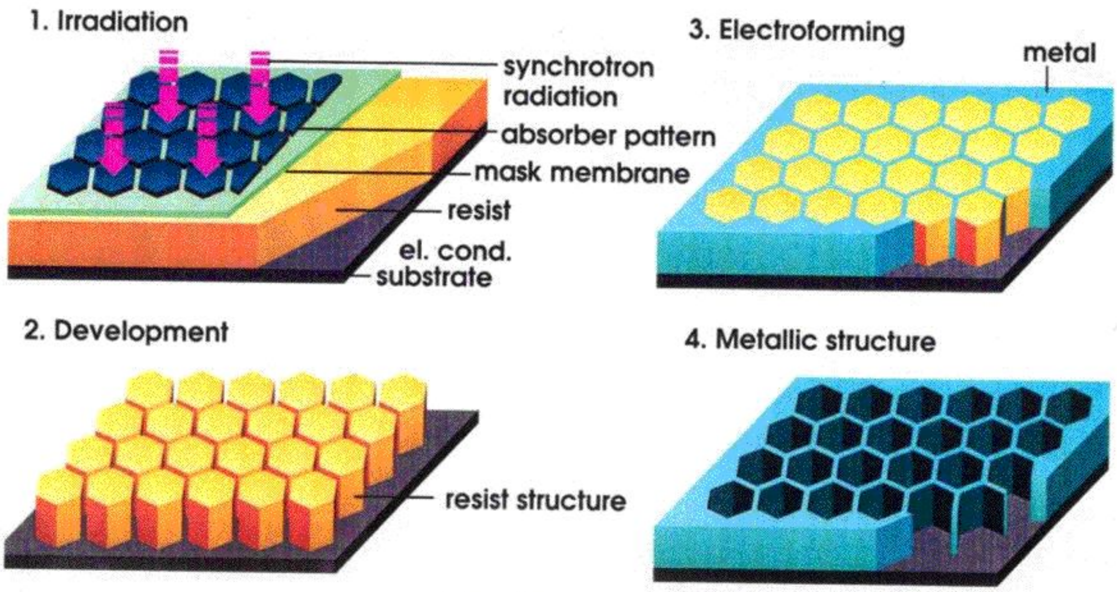
Mohr et al.



3-D SU-8 with step heights of 300,600 and 900 µm

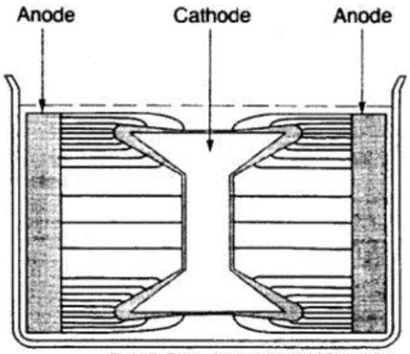
J.Hormes et al.

LIGA technology

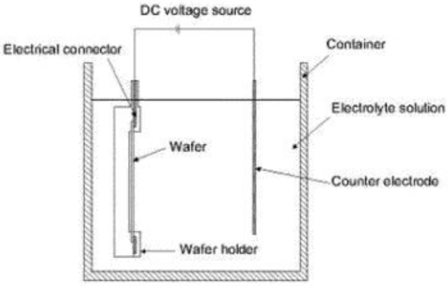


Source: IMM

Electroforming



G.A. DiBAri, International Nickel Inc.



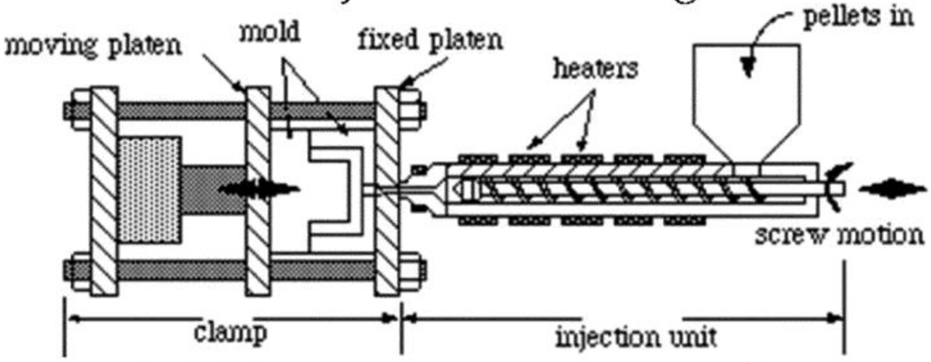
http://www.memsnet.org/mems/beginner/

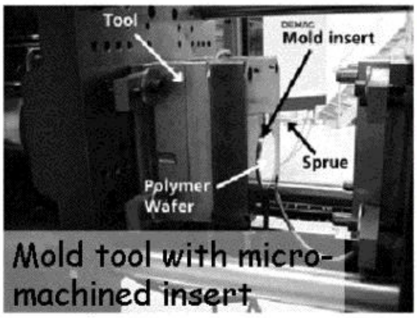
www.ca.sandia.gov

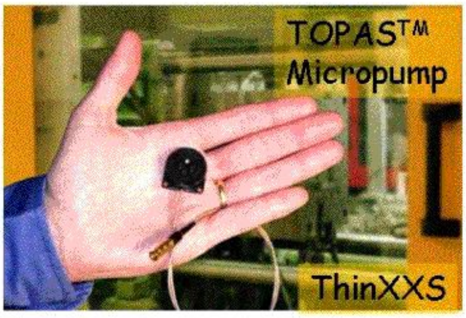
Secondary structuring by replication

- Injection micromolding
- Hot embossing
  - Micromolding
  - Soft lithography, nanoimprinting,
- Quality

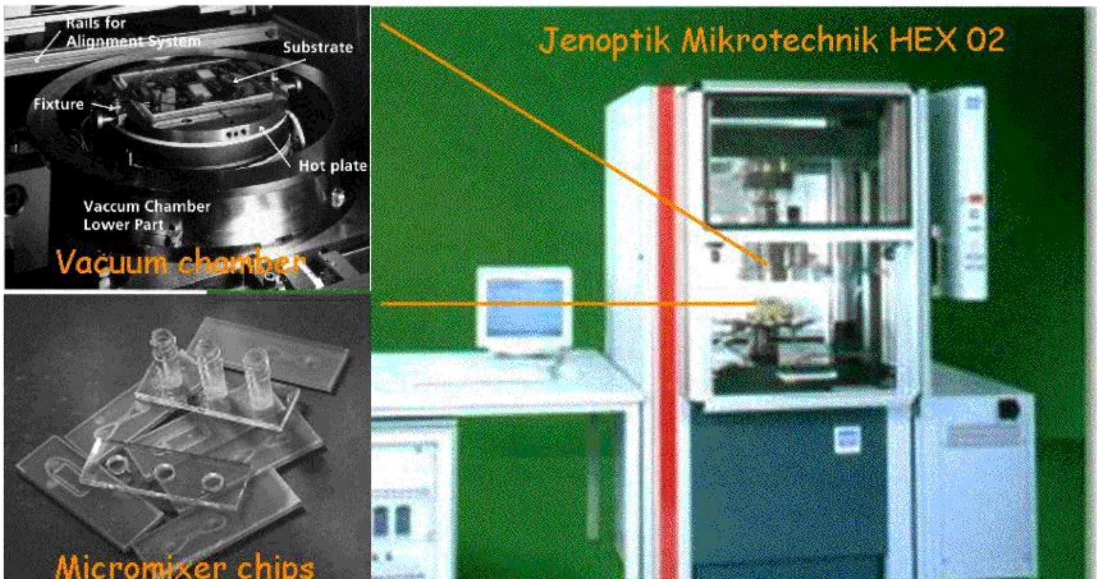
Injection molding machine







Hot embossing



H. Becker, C. Gärtner Reviews in Molecular Biotechnology 82 (2001) 89-99

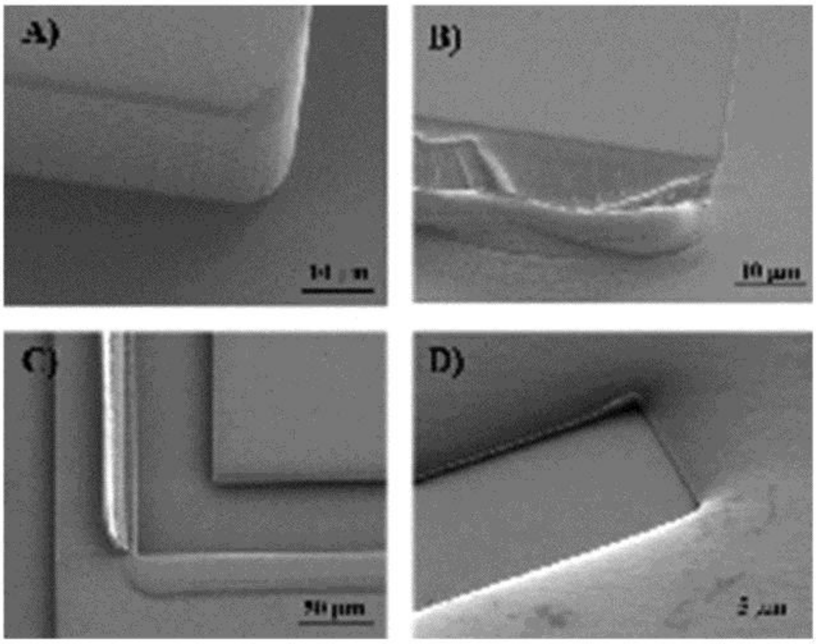
Embossing with a silicon die

A: optimized

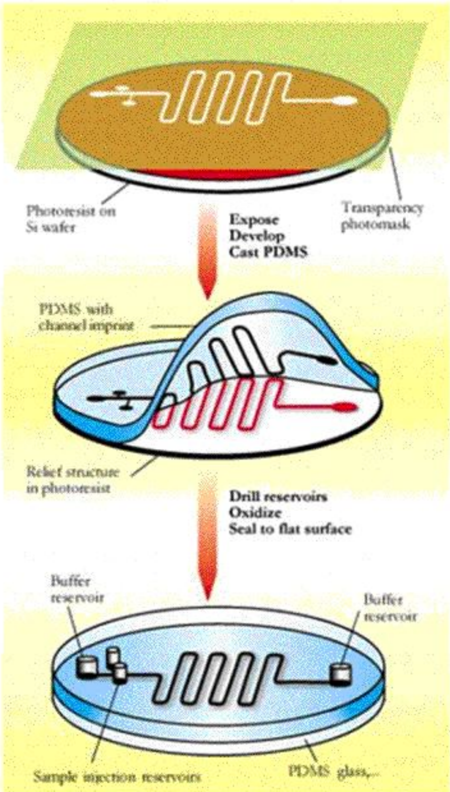
B: temperature sub-optimal (too low)

C: de-emboss temperature sub-optimal (too high)

D: embossing pressure sub-optimal (too low)



Esch et al. , Lab Chip, 2003, 3, 121–127

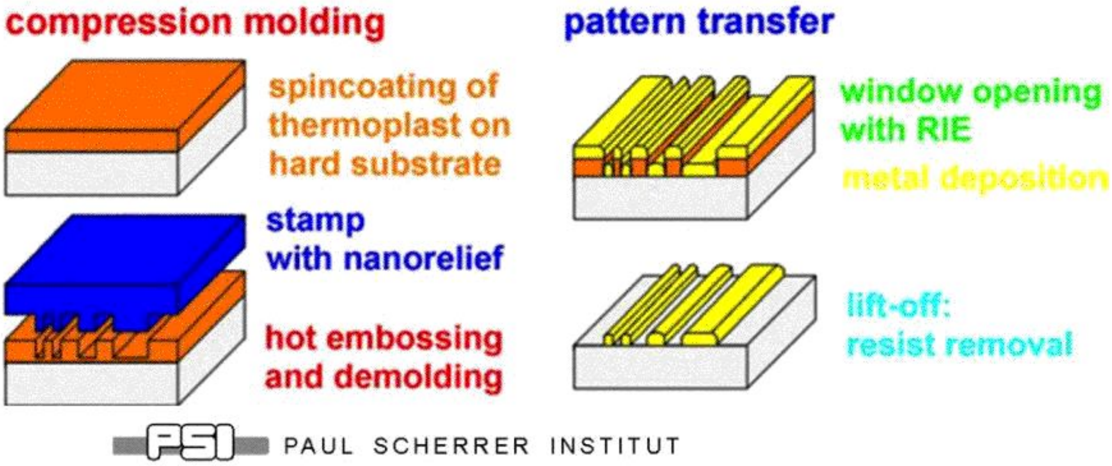


Soft-lithography

- **George M. Whitesides' group, Harvard University**
  - Conventional primary structure
  - Casting a thermosetting polymer on the mold
- **Lab-on-a-Chip: killer application**

http://www.physicstoday.com/pt/vol-54/iss-6/p42.html

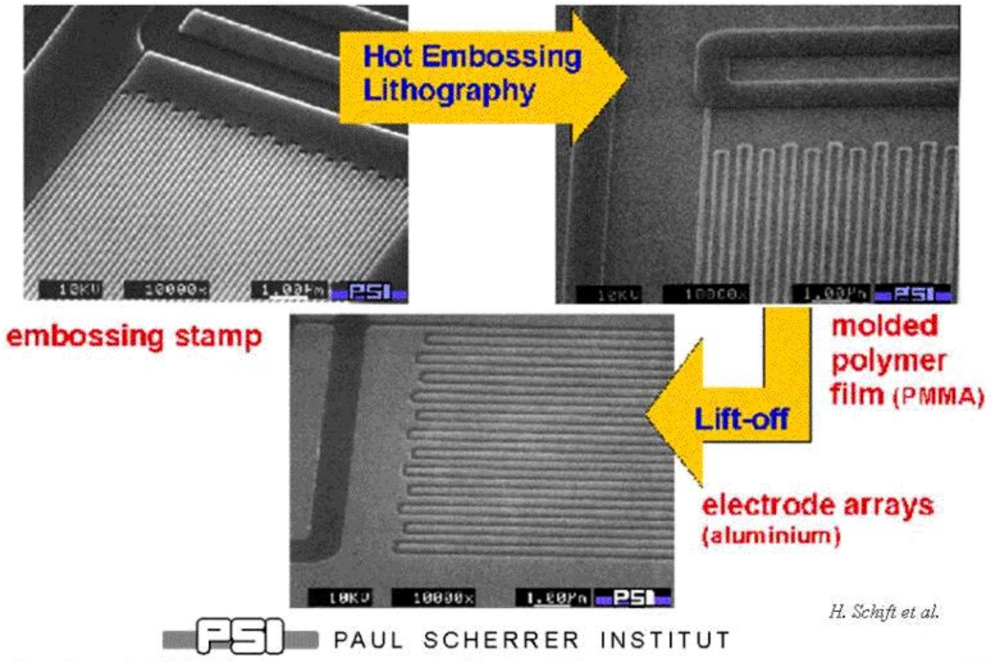
Nano imprint lithography



H. Schift et al.

1.3. Microfabrication tool box

Replication results



H. Schift et al.

Hot embossing apparatus

Equipment

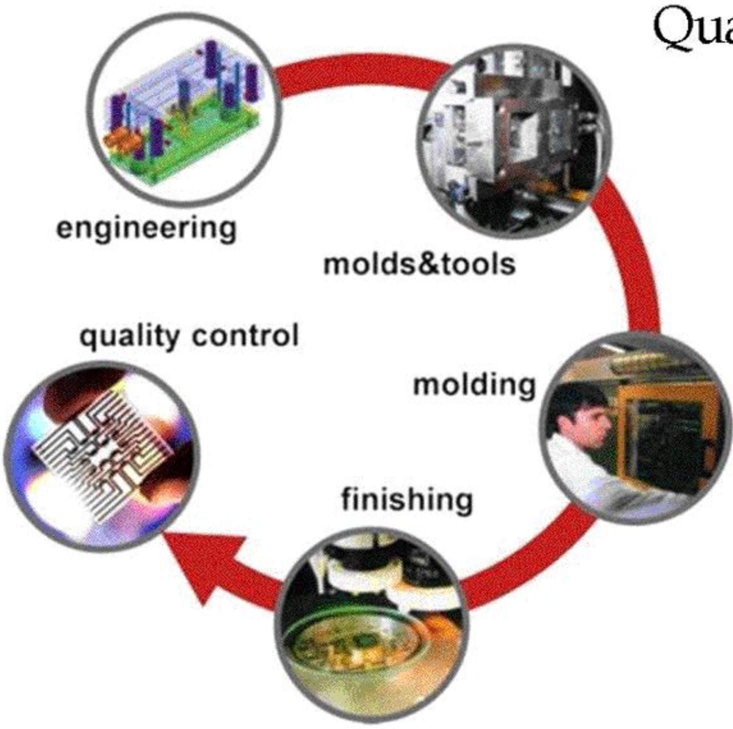
- EVG 520 Hot Embosser

Capability

- Embossing and de-embossing of polymers with Si or Ni masters
- Emboss with ± 1 μm alignment using EV620
- Nano-imprint lithography
- Process: max 550 °C and 40 kN force

(http://www.evgroup.com/applications.asp)

Quality control



1.3. Microfabrication tool box

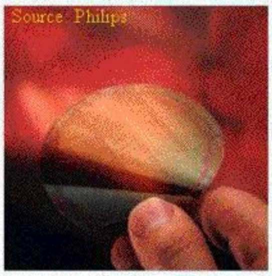
Overview fabrication techniqes

Technology	Choice of Geometry	Minimum Feature Size	Height	Total Surface Area	Aspect Ratio	Lifetime	Cost	Availability
Wet Silicon Etching	--	+	0	++	-	+	+	++
Dry Silicon Etching	+	++	+	++	+	-	0	+
Optical Lithography & Electroforming	+	++	+	++	0	+	0	0
Laser Ablation & Electroforming	++	+	+	-	+	+	-	-
LIGA	+	++	++	-	++	+	--	--
Mechanical Micromachining	+	0	+	+	0	++	-	-
µ-EDM	-	0	+	-	+	++	-	-

H. Becker & L. E. Locascio, Review, Talanta 56 (2002) 267–287

Topics in this section

From microelectronics



Phys. Rev. Focus 6, story 18, 24 Oct. 2000

To integrated plastic

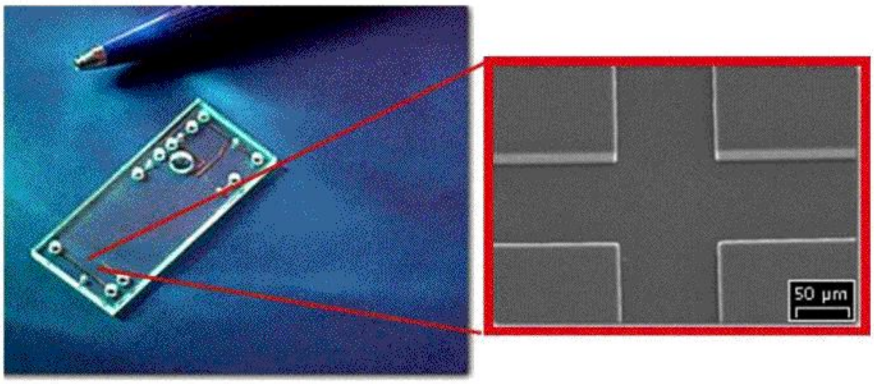
www.gyrosmicro.com

Polymer integration

- Customized polymer fabrication
- Large scale integration
- Functional integration
  - Multi-layer processing
  - Surface modifications
  - Special materials

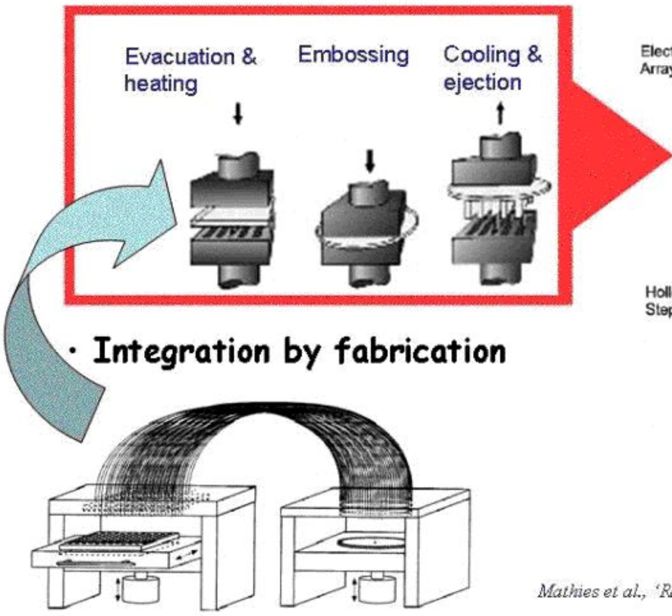
Customized polymer µ-fluidics

Capillary Electrophoresis Chip with electrodes

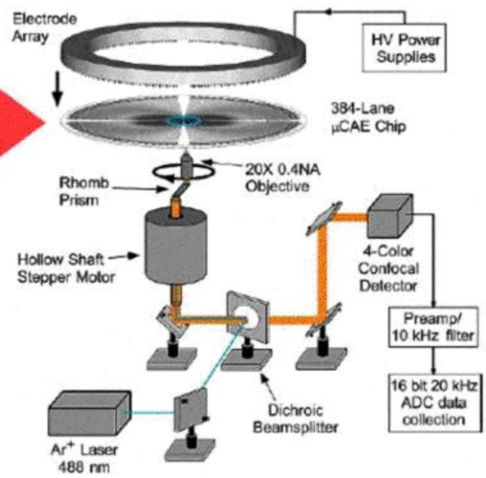


www.microfluidic-chipshop.de

The Lab-on-a-Chip disc



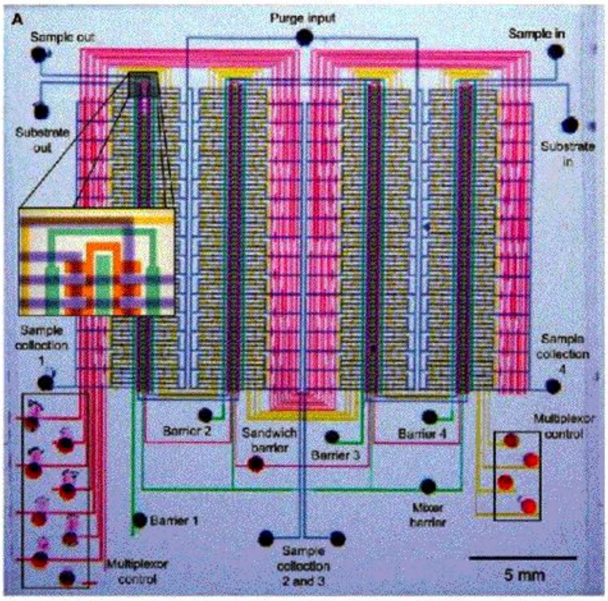
- **Integration by fabrication**

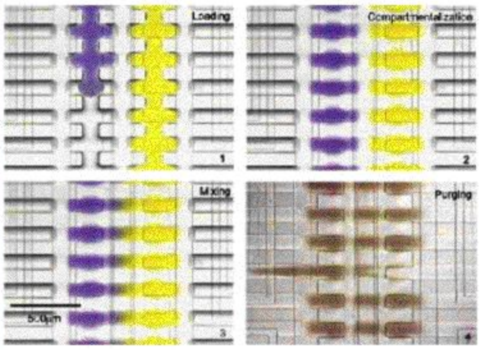


Mathies et al., 'Radial capillary microplate with up to 384-lanes'

Large-scale integration

- **Steve Quake's group, Caltech**





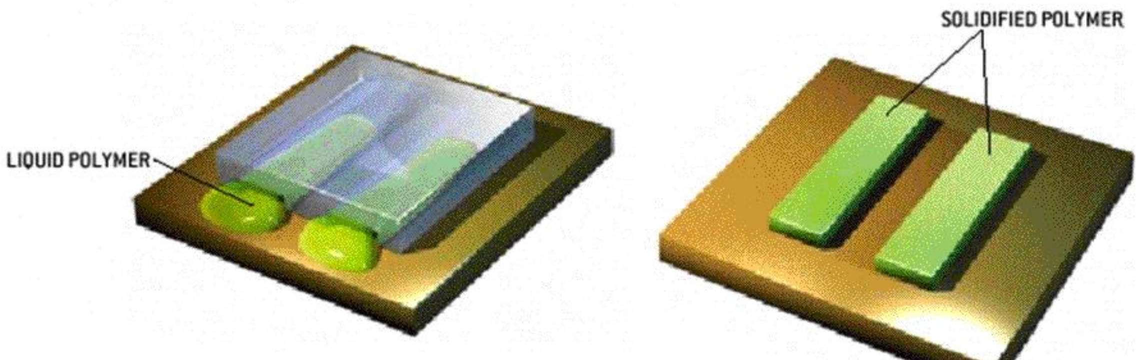
Soft-lithography and leakage test using food dyes

Todd Thorsen et al., 18 Oct. 2002 Vol 298 SCIENCE

Soft-lithography-assisted processing

Combined techniques

- Molding from primary structure
- Micro/Nanofluidic-assisted replication, e.g., to modify polymer properties, poros column, etc.

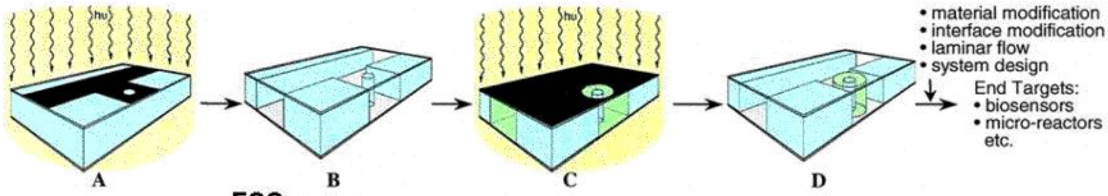


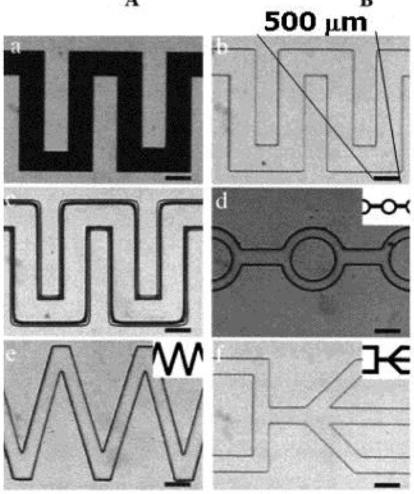
1. The PDMS stamp is placed on a hard surface, and a liquid polymer flows into the recesses between the surface and the stamp.
2. The polymer solidifies into the desired pattern, which may contain features smaller than 10 nanometers.

Whitesides' group, punblished in Scientific American, 2001

µ-fluidics TECTONICS

- **David Beebe's group, University of Wisconsin**





A comprehensive construction platform for microfluidic systems

Monomer mixture: isobornyl acrylate (IBA), tetra-ethyleneglycol dimethacrylate (TeEGDMA), and Irgacure 651 as photoinitiator.

(a) Photomask placed on top of the channel. (b) After photopolymerization. (c) After removing the un-polymerized monomer mixture with MeOH.

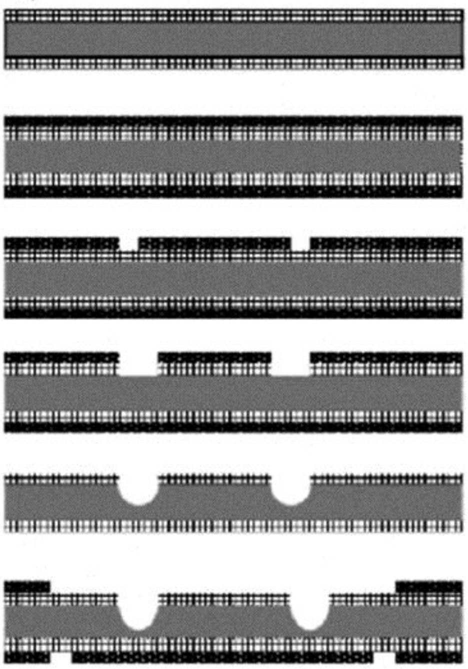
(d- f) A variety of possible channel geometries with the corresponding photomask.

13488–13493 | PNAS | December 5, 2000 | vol. 97 | no. 25

Regina Luttge

Metal-integrated polymer processing

A)



5 µm copper coated on both sides of a 50 µm polyimide foil

Foil coated with photoresist

Resist exposed and developed to pattern electrode holes on one side of the foil

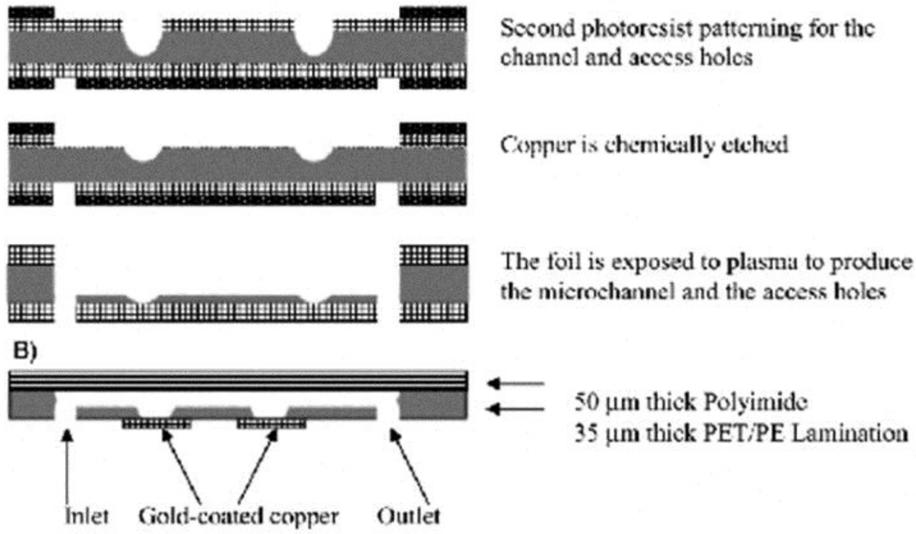
Copper is chemically etched

The foil is exposed to plasma to produce blind vias at the electrode places

Second photoresist patterning for the channel and access holes

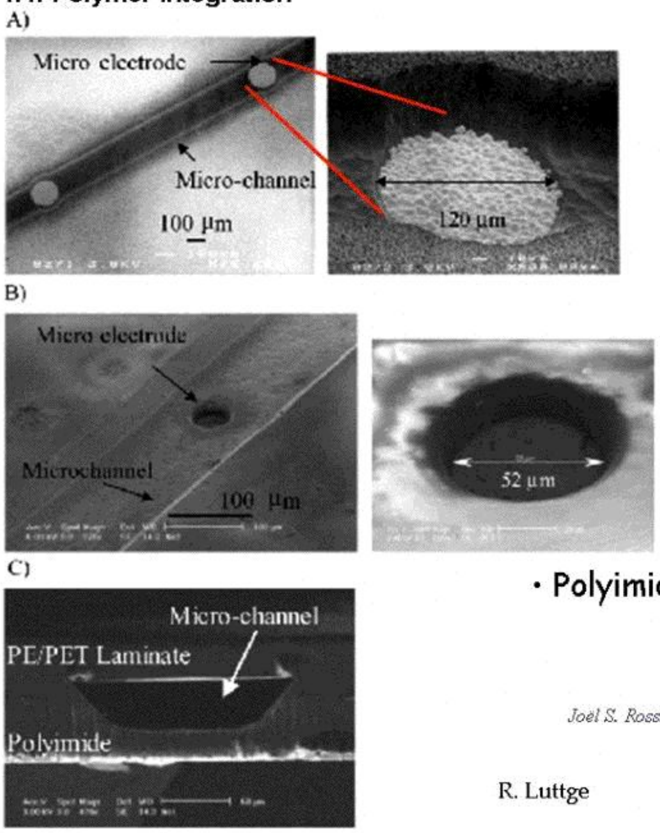
Joël S. Rossier et al, Lab Chip, 2002, 2, 145–150

Process continuous



Joël S. Rossier et al, Lab Chip, 2002, 2, 145–150

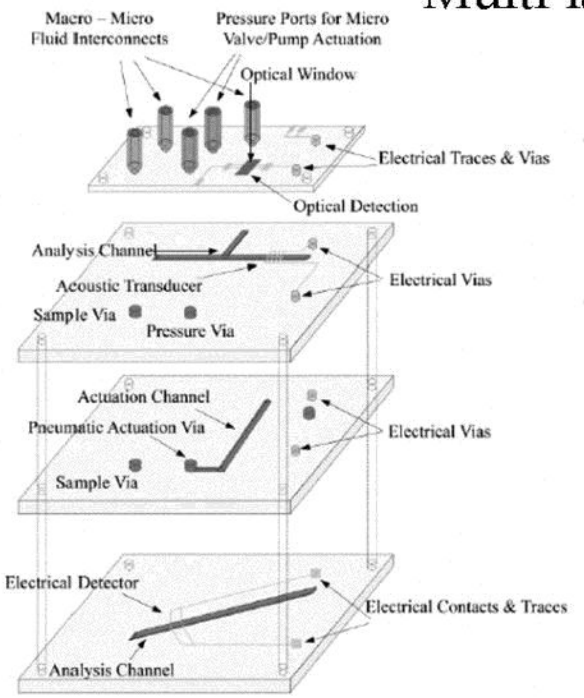
Process results



- Polyimide dry etching

Joël S. Rossier et al, Lab Chip, 2002, 2, 145–150

Multi-layer plastic devices

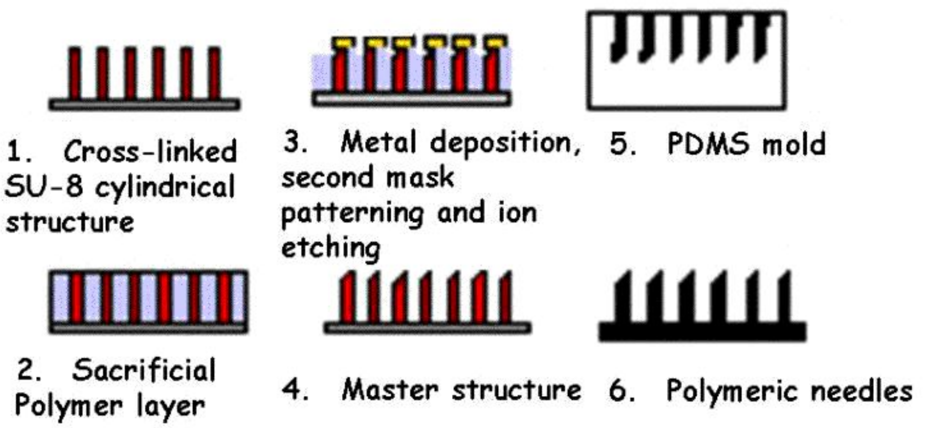


- Plastic/glass microfluidic systems containing electrical and mechanical functionality.
- Paper describes various combination of processes for plastic integrated devices including heat stacking (bonding).

A. Han et al., Lab Chip, 2003, 3, 150–157

Biodegradable plastic microstructures

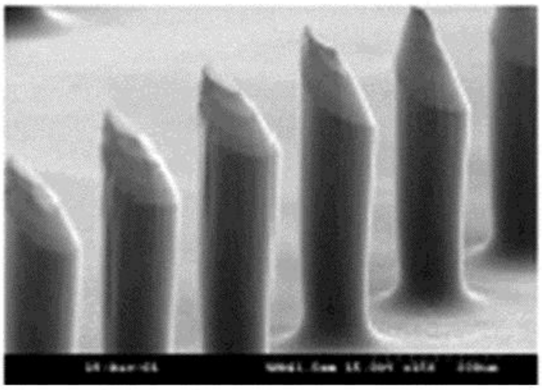
- **Prausnitz' group, Georgia Institute of Technolog**
- **Fabrication sequence of microneedles with beveled tips**



J.-H. Park et al.

Replicated PGA needles

- **Biodegradable material can be filled with drugs or food supplements**



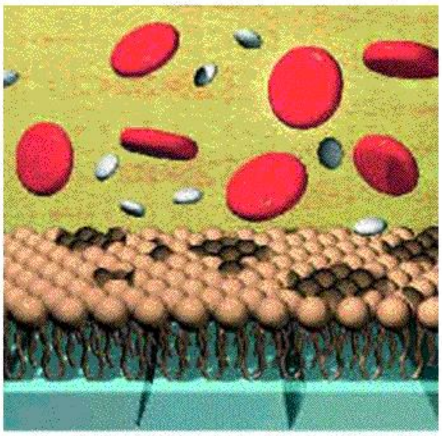
Micromolded PGA microneedles

Bio-membrane mimicry

- **Discovery of Phospholipids**

Synthesised PC molecule which can be attached to surfaces to form a coating on materials such as plastics and metals. This principle is already in use in contact lenses, drainage catheters and stents.

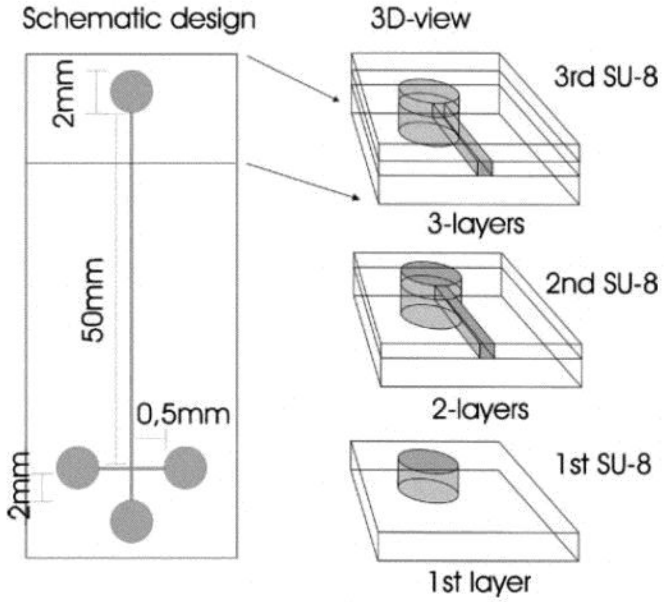
The coating of material surfaces with phosphorylcholine (PC) is an approach to modify the surfaces in such a way that they become biocompatible. PC does not actively influence the coagulation process, but basically "mimics" a biological surface rather than a synthetic material.



Case Study I:

SU-8 multilevel processes- classical photolithographic approach to plastic microfluidic devices

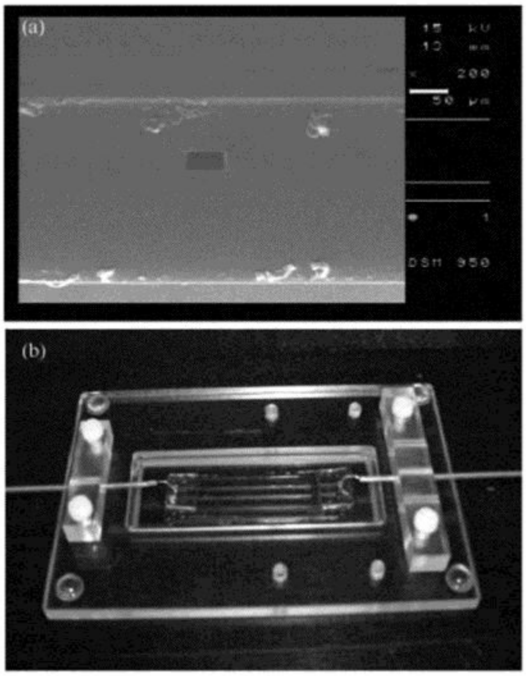
Process outline



- All SU-8 chip by photolithographic processing and adhesive bonding.

T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Processing results and assembly

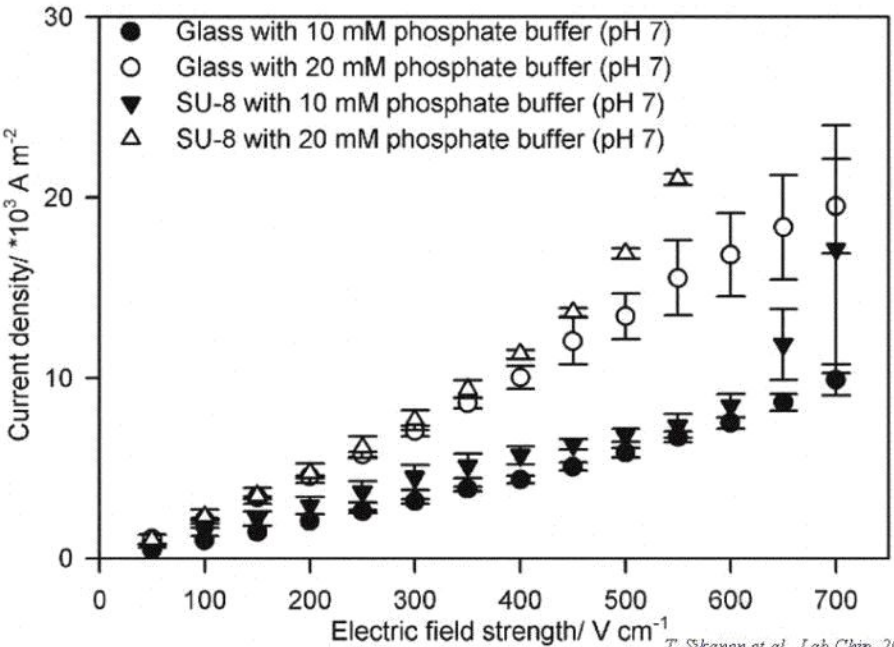


- SU-8 microchip cross section. (30 μm x 50 μm).
- Resulting microchannel array attached to a lab-built chip holder.
- Inlet and outlet of the microchannel are covered with PDMS sheets with equally sized inlet holes in order to increase the volumes of the sample inlet and outlet.

T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Characterization (1)

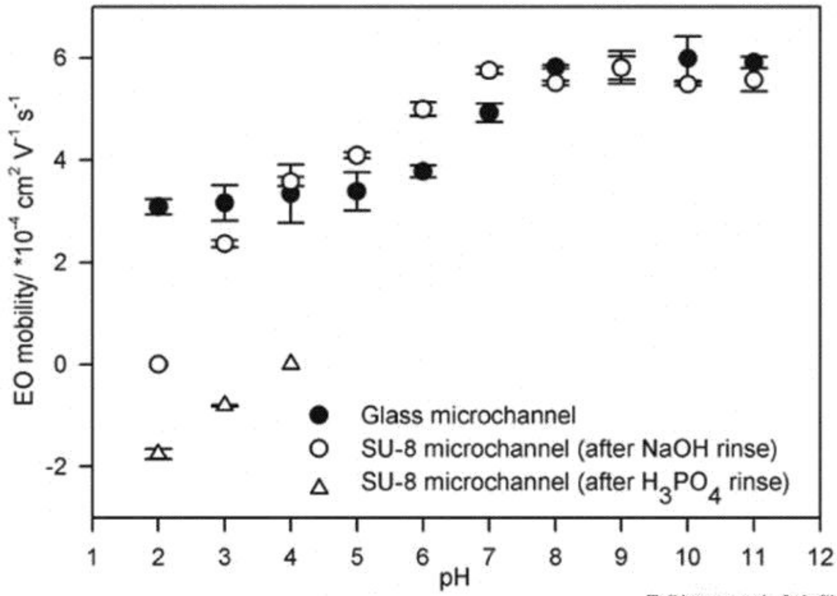
Heat dissipation



T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Characterization (2)

Cathodic electroosmotic (EO) mobility as a function of pH

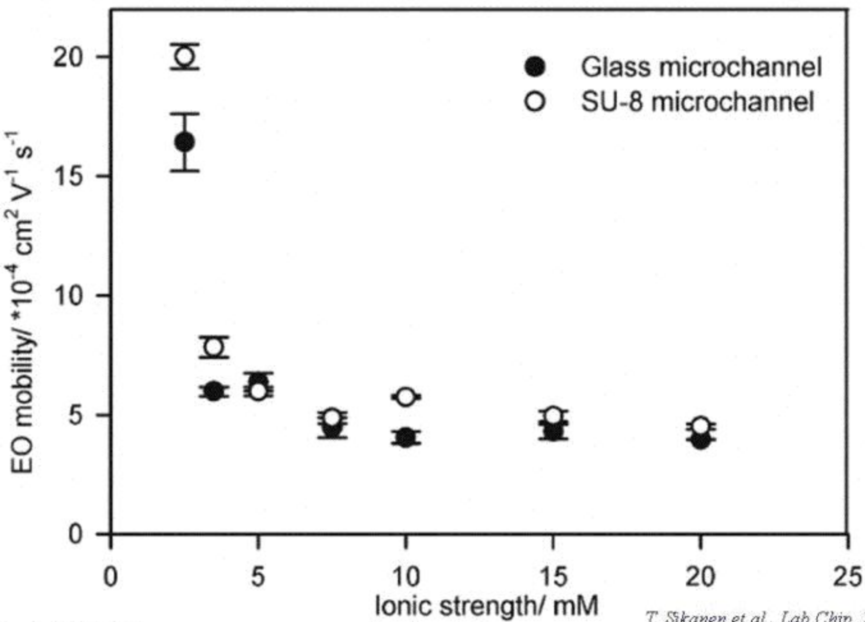


T. Sikanen et al., Lab Chip, 2005, 5, 888–896

1.4. Polymer integration

Characterization (3)

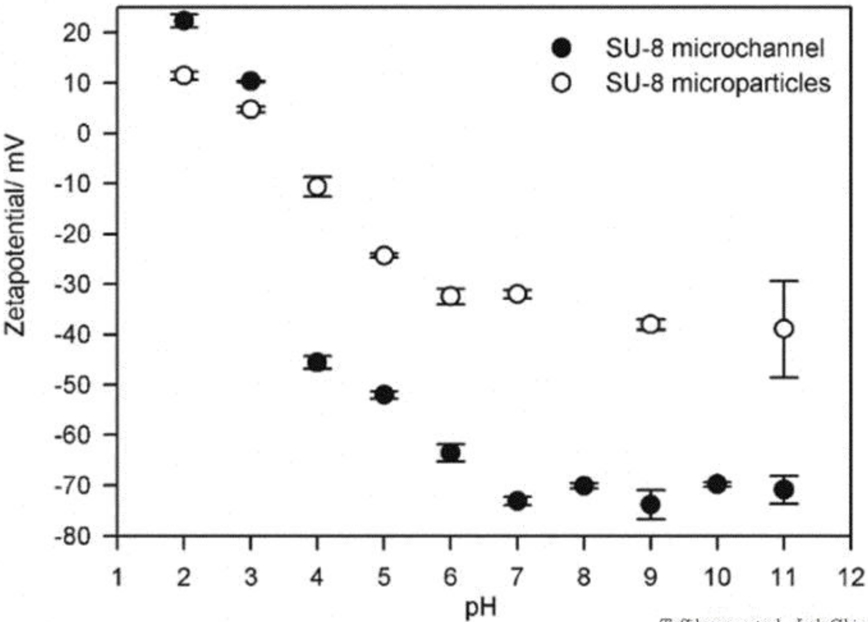
EO mobility as a function of ionic strength



T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Characterization (4)

Zeta-potential as a function of pH



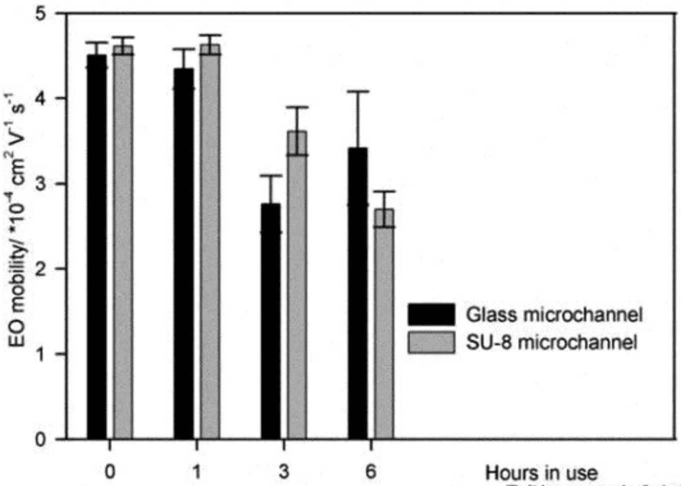
T. Sikanen et al., Lab Chip, 2005, 5, 888–896

1.4. Polymer integration

Characterization (5)

Electrokinetic stability in SU-8

- Microchannels after 1-6 h in continuous use in 20 mM phosphate buffer (pH 7). Applied electric field strength was 200 V cm^{-1} for SU-8 and 300 V cm^{-1} for glass microchannels.



T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Comparison of plastics

- Measured EO mobilities in SU-8 and glass microchannels in 20 mM phosphate buffer (pH 7) and respective values reported for various polymers and plastics used in microfluidic applications.

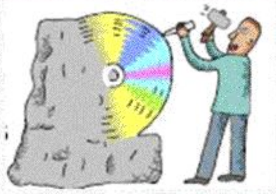
Material	EO mobility $/10^{-4}$ cm^2 V^{-1} s^{-1}	Buffer conditions	Reference
SU-8	4.5	20 mM phosphate (pH 7)	This work
Glass (Schott Borofloat®)	4.0	20 mM phosphate (pH 7)	This work
Silica (capillary)	~6–7	20 mM phosphate (pH 7)	6,8
Glass	7.7	borate buffer (pH 9.2)	51
PDMS (oxidized)	~1–3 (~4–6)	20 mM phosphate (pH 7/9)	6,8,10
Polystyrene, imprinted	1.8	20 mM phosphate (pH 7)	9
PMMA	~2.5	20 mM phosphate (pH 7)	50
Copolyester	4.3	20 mM phosphate (pH 7)	9
Zeonor	1.1	20 mM phosphate (pH 7)	4
Thermoset polyester (oxidized)	1.3 (2.6)	20 mM phosphate (pH 7)	8

T. Sikanen et al., Lab Chip, 2005, 5, 888–896

Future developments

- From niche to mass market: chemical sensors, biomedical devices, high-throughput screening.
- More and more characterization and verification instead of proof-of-concept research.
- Plastic microfluidics reaches engineering development phase for many different application areas.

Summary



- Today, plastic technology often first choice
  - Material costs negligible.
  - Medium large investment ($ 300,000).
  - Manufacturing by replication:
    - From molts
    - From semi-finished products.
  - Amenable to mass fabrication at modest costs.
  - Widely tunable material properties:
    - Very small scale pattering (nanoimprint) even guides to new properties deviating from the macroproperties of the plastic.
  - Rapid prototyping by laser ablation, (stereo)lithographic techniques and mechanical micromachining etc.

Adapted from: Jens Ducrée and Roland Zengerle