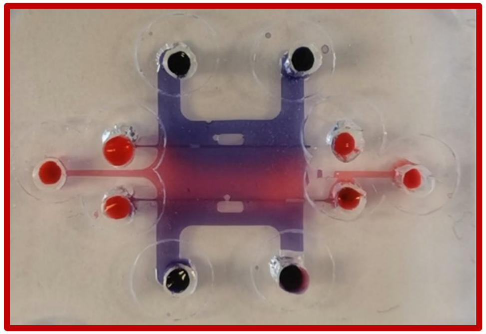
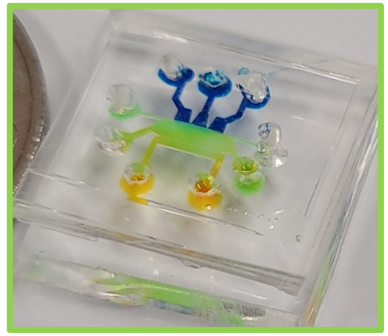
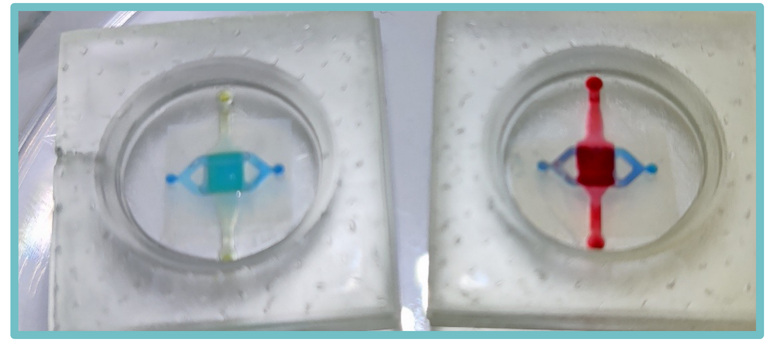
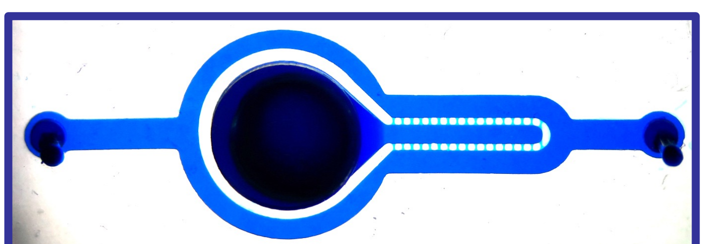






Microfabrication II
Polymer devices

Séverine Le Gac
Applied Microfluidics for BioEngineering Research,
University of Twente
s.legac@utwente.nl

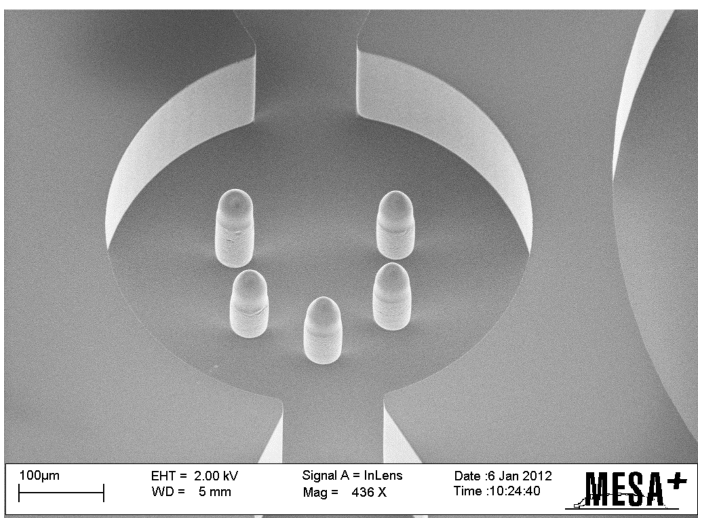


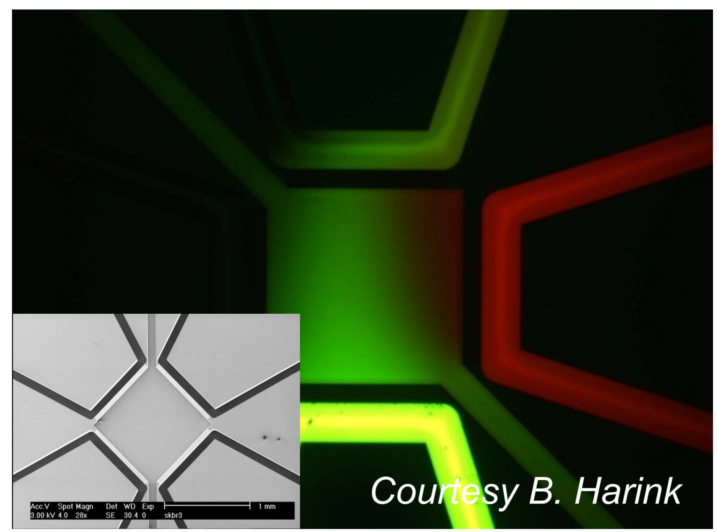
UNIVERSITY OF TWENTE.

Content and scope of the course

Outline

- What is a polymer?
- Which classes of polymer do exist?
- Various fabrication processes
  - Machining techniques
  - Replication techniques
  - 3D printing techniques
- Examples

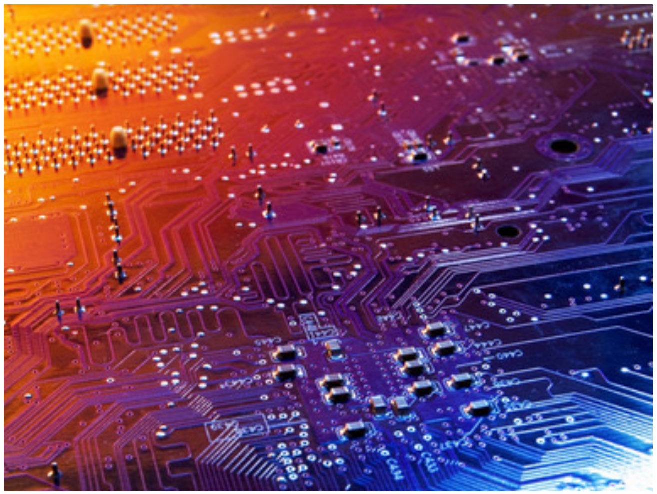




From Microelectronics…

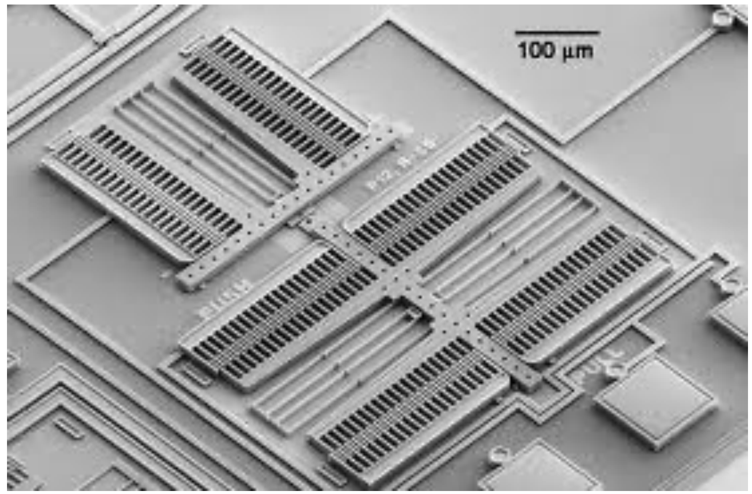
Historically: LOC technology derived from the industry of microelectronics

Microelectronics



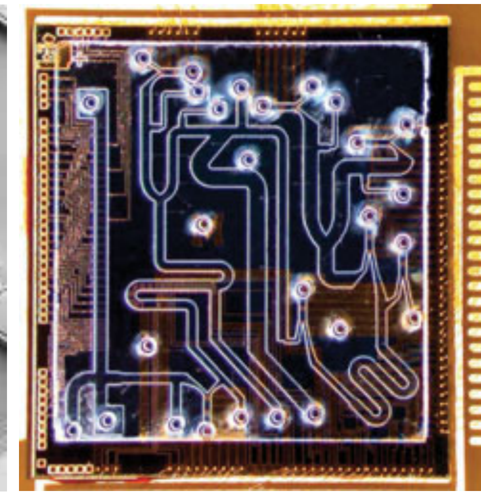
www.siliconrepublic.com

MEMS



http://theofficialstleblog.blogspot.nl

Microfluidics



http://www.dailykos.com

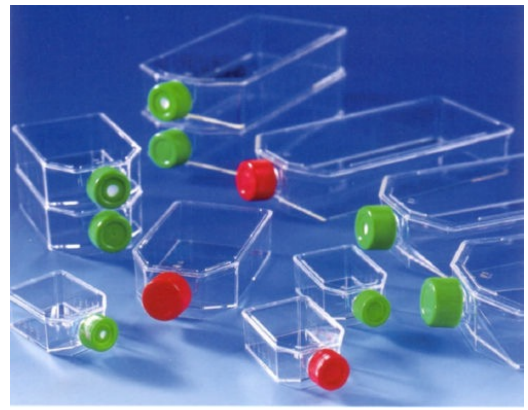
- Initially: mostly **silicon**-based materials
- Quickly: use of **glass/quartz** (transparent & insulating materials)

Why? 1. Fabrication processes available and mature
2. Well-known physical and chemical (bulk) properties
3. Well-characterized surface derivatization chemistries

Issues: fabrication costs, device price, need for a clean-room environment and the associate fabrication knowledge, conductivity of silicon, etc.

… to polymers…

- **Routine tools** in the lab based on plastics (or polymer)
  - Biocompatibility, single-use device (no risk of cross-contamination)



- **Mature fabrication processes** in the polymer industry

- Larger scale production (faster fabrication cycle); lower production costs

- Great variety and tuneable **properties** (surface, thermal, optical, mechanical, electrical, porosity, etc.)

- **Materials**: PC, PS, PMMA, PET, PE, OSTE, COC, Parylene, PDMS….

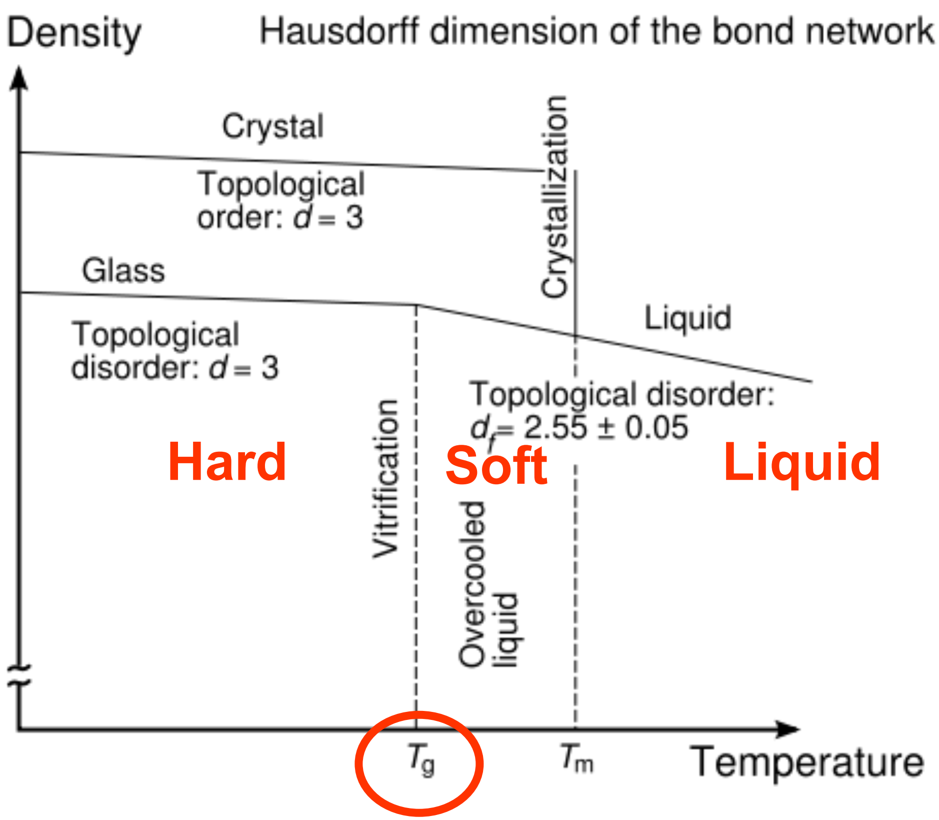
PC polycarbonate; PS polystyrene; PMMA polymethylmethacrylate; PET polyethylene terephtalate, PE polyethylene; OSTE off-stochiometry thiol-ene; COC cyclic olefin copolymer; PDMS polydimethylsiloxane

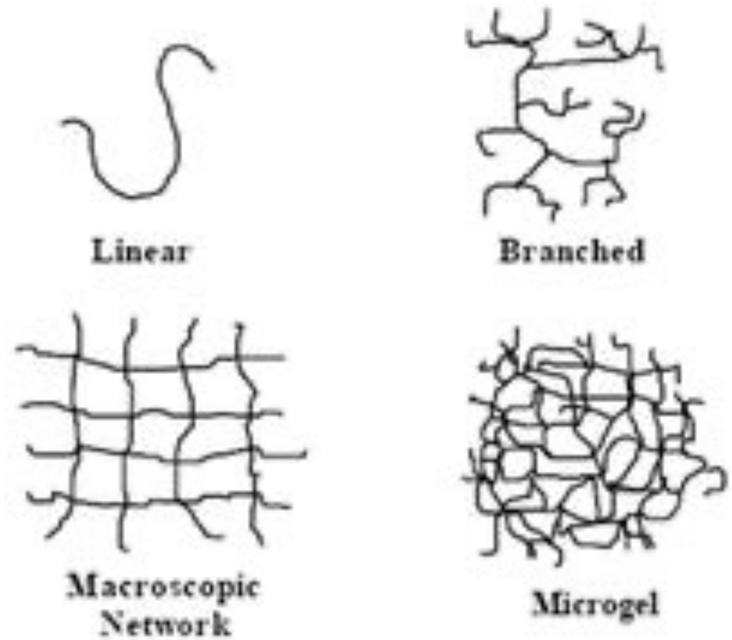
What is a polymer?

Definition:

- **Polymer** (from the Greek πολυ, polu, "many"; and μέρος, meros, "part“)
- Substance composed of molecules consisting of repeating structural units (**monomers)** connected by **covalent chemical bonds** and having a **large molecular mass** .

- A polymer can exist in **different forms.**





http://www.pharmainfo.net

Polymer processing:

1. Polymerization reaction
2. Temperature change

Focus on polymer materials

3 classes of polymers used for microfabrication

- **Thermosets** (photoresists): Normally crosslinked and rigid, intractable once formed, and degrade rather than melt upon the application of heat.
- **Thermoplastics**: Linear or branched polymers which can be melted repeatedly upon heating.
- **Elastomers**: Crosslinked rubbery polymers that can be stretched easily to high extensions and rapidly recover once the applied stress is released.

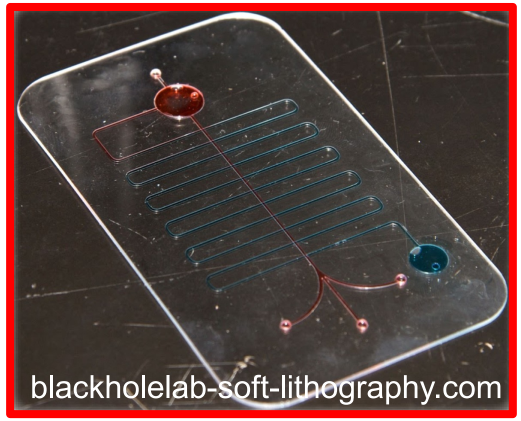
(Differences in macroproperties ⇔ differences in molecular arrangement at the microscale)

Fabrication techniques

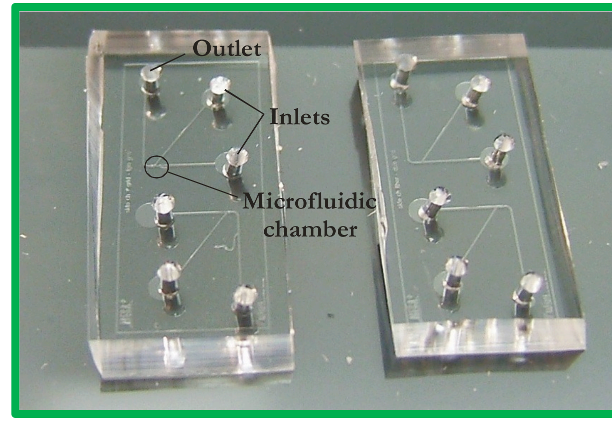
- Lithography ⇨ photoresists
- Ablation techniques: all classes
- Replication techniques: thermoplastics and elastomers
- 3D printing: different classes of polymers

Focus on polymer materials

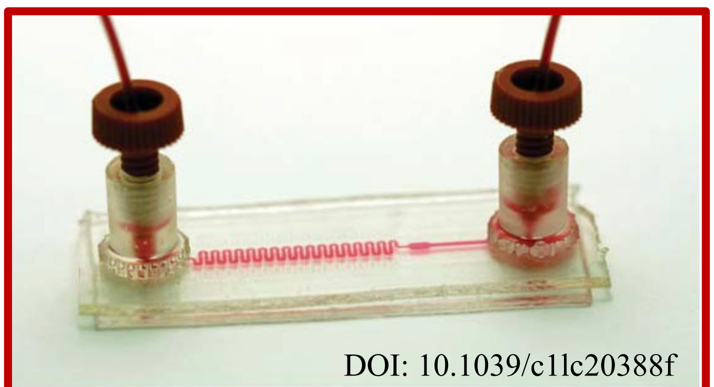
Cleanroom - photoresists



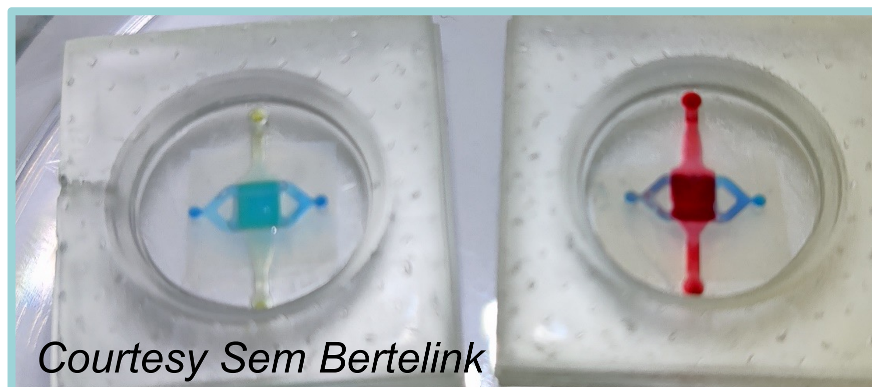
Thermoplastics material



Soft-lithography - PDMS



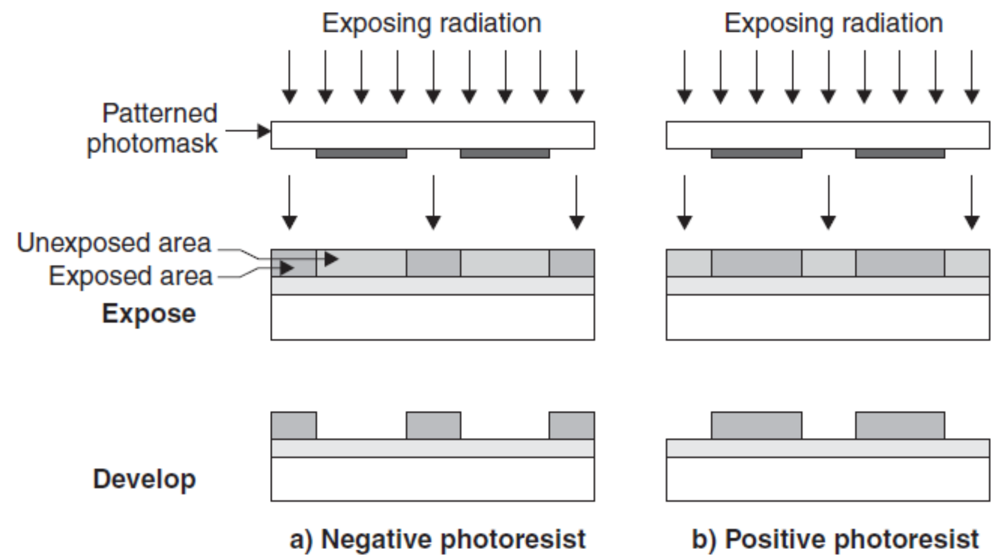
Thiol-ene material



3D printing technique

Photolithography

- Transfer of 2D structures from a mask in a thin layer of photoresist
- Layer of **resist** spin-coated
- Thickness: 1 µm or more
- Mask: Cr on glass



http://2009.igem.org

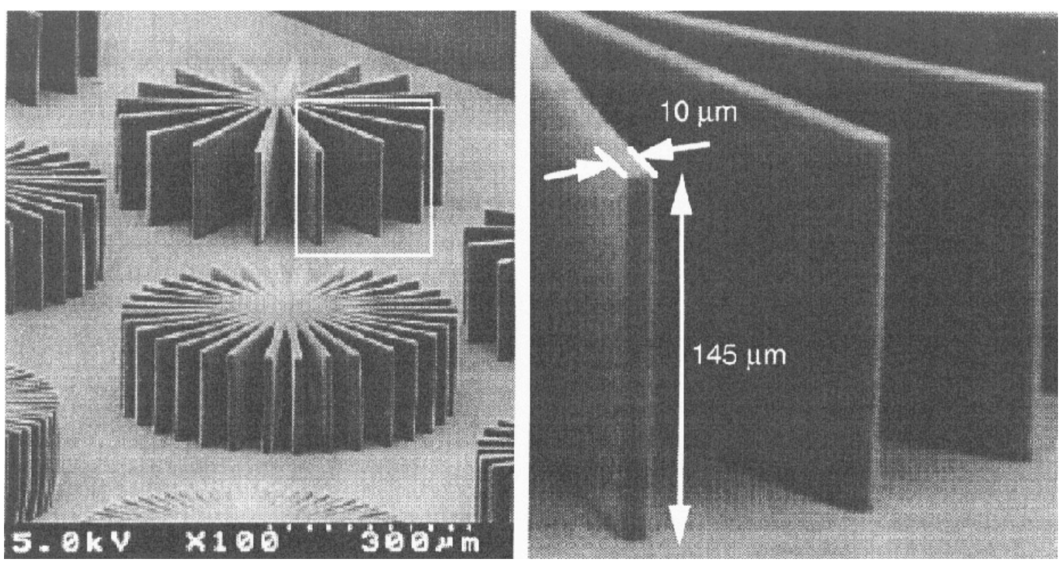
- **Limitations**:
  - Mostly **shallow structures** (low penetration depth of light)
  - **Low throughput**: 1 h total process time
  - **Resolution** limited by the optics (typically ~ 1 µm)

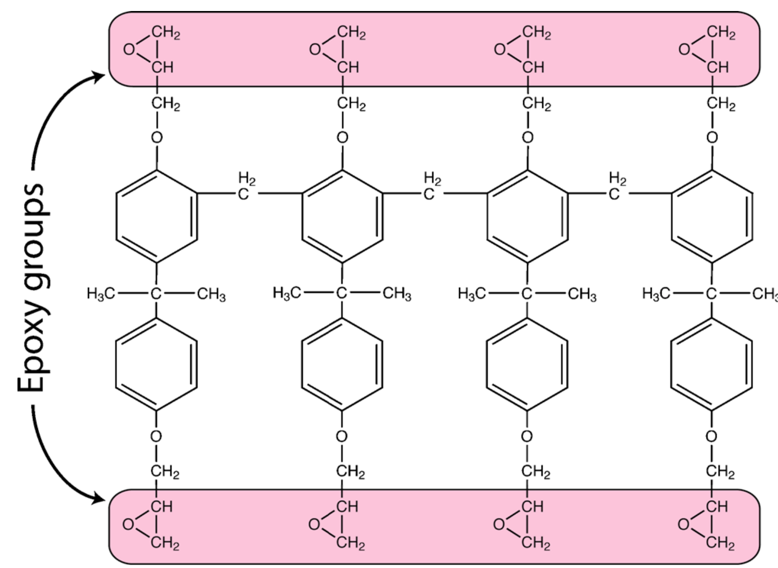
http://www.technoscene.co.za

UV Photolithography

☺ Negative Photoresist SU-8

- Material developed for higher structuration in up to **1 mm thick layers**
- Aspect ratio up to **1:20**;
- Resolution down to **1 µm** (limit of photolitography)
- Total proces time around **1 h** ⇨ limited throughput

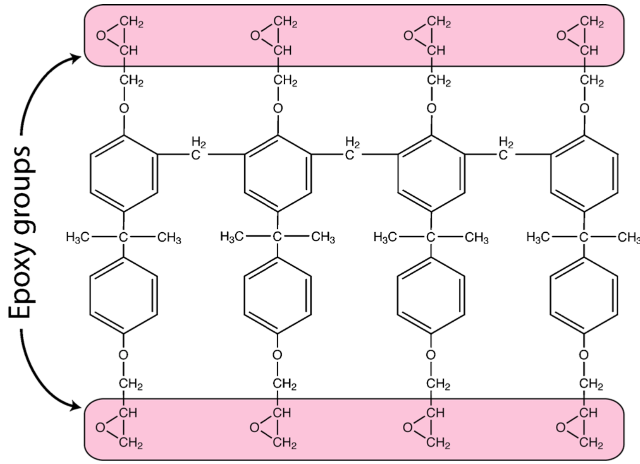




DOI:10.1063/1.3477192

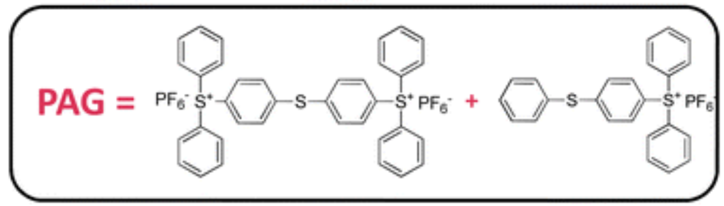
SEM views of star patterned lines, aspect ratio of 14.5.

UV Photolithography



DOI:10.1063/1.3477192

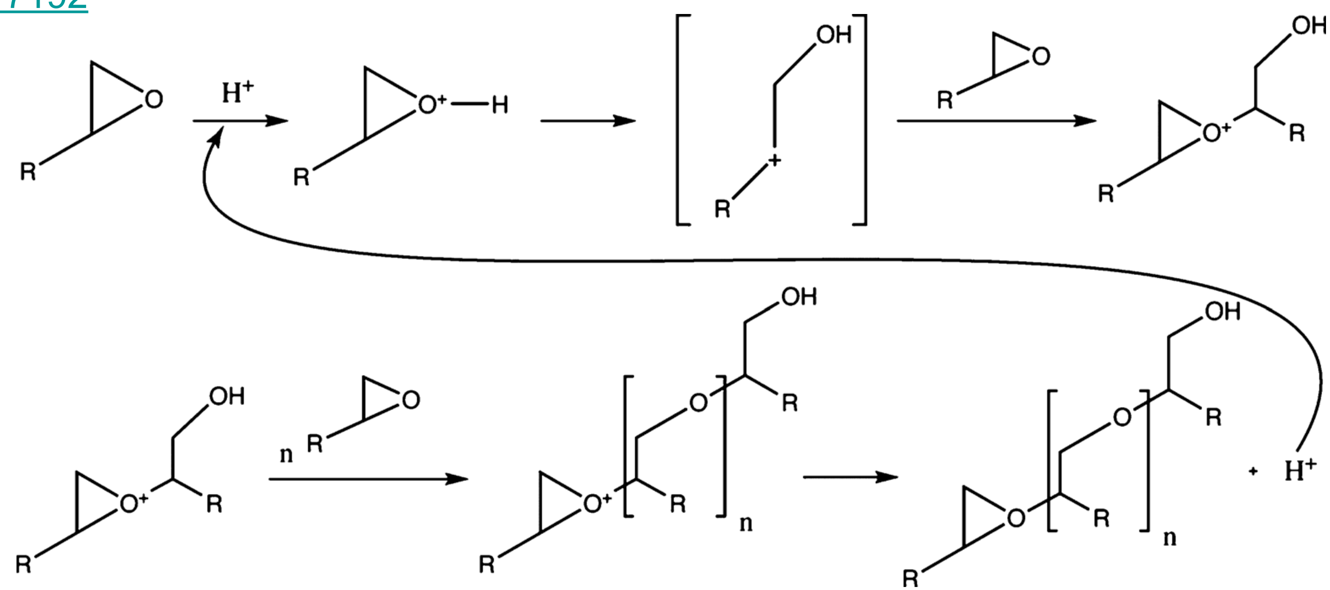
- UV irradiation (365 nm): activation of the photosensitizer (PAG – photoacid generator), releasing a strong acid



doi.org/10.1039/C2CC38114A

- Strong acid initiating the reaction (*cationic polymerization*)

- Polymerization promoted at high temperature (*post-exposure bake*)

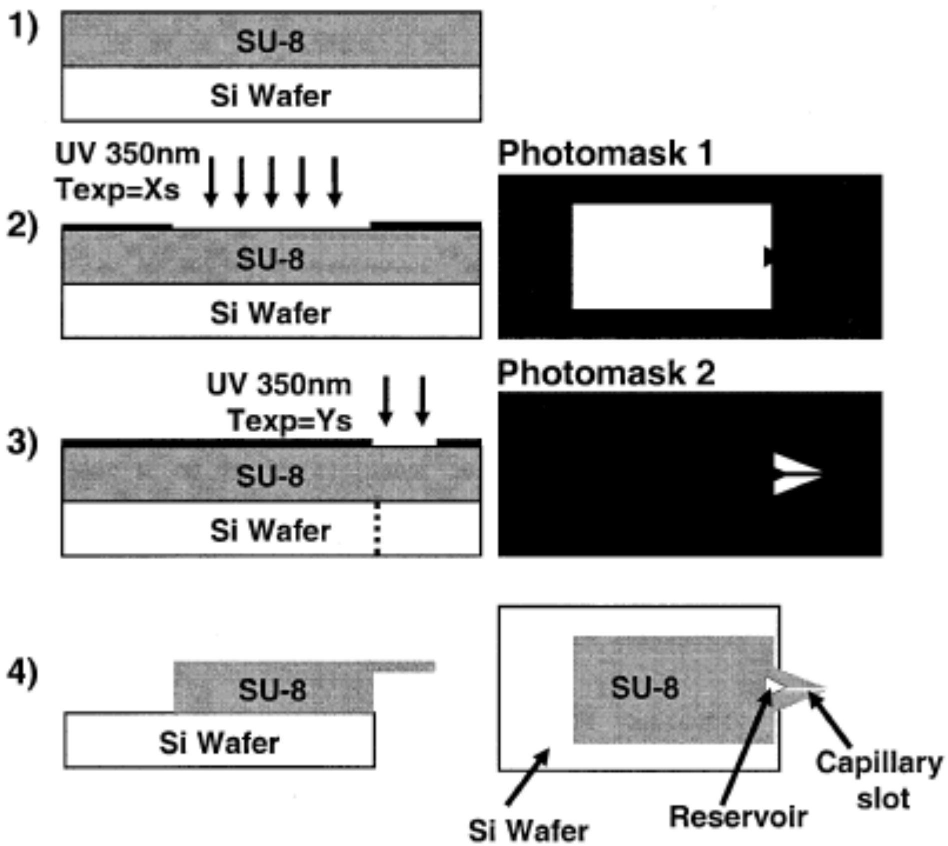


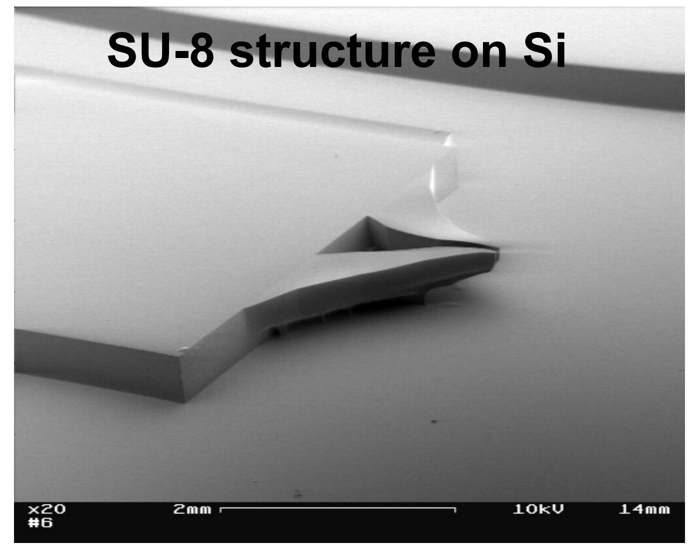
DOI:10.1063/1.3477192

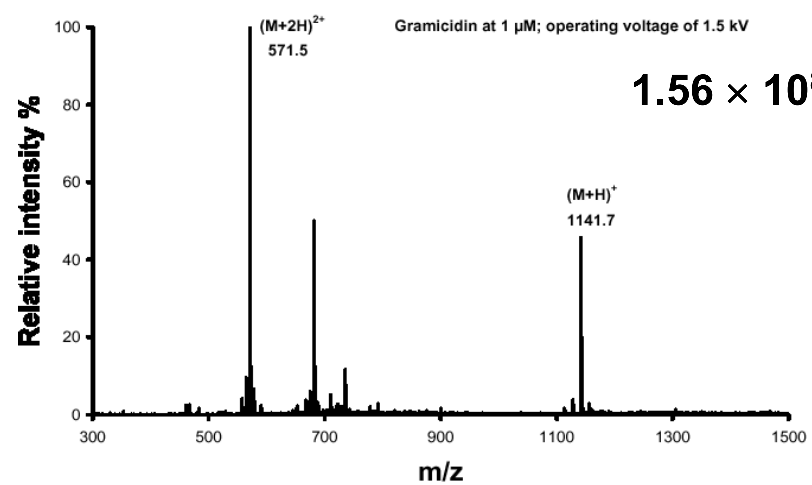
PAG = triaryl-sulfonium hexafluoroantimonate

Microfabricated ionization tips for ESI-MS

Fabrication of SU-8 nib structures using 2.5 D photolithography



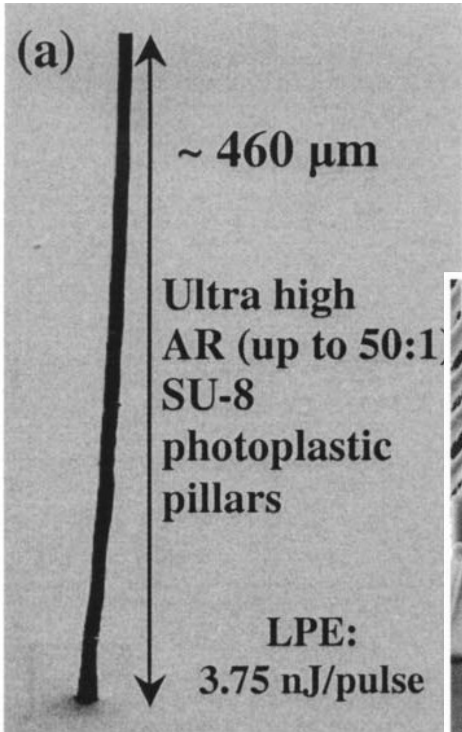


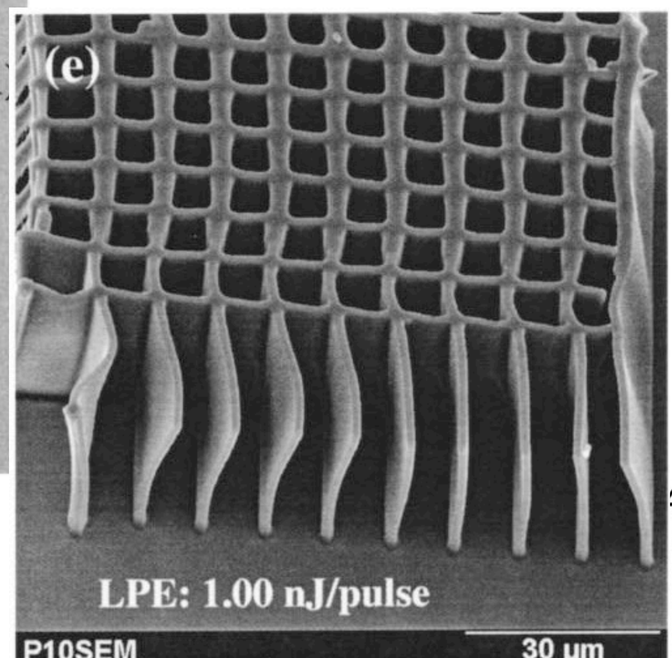


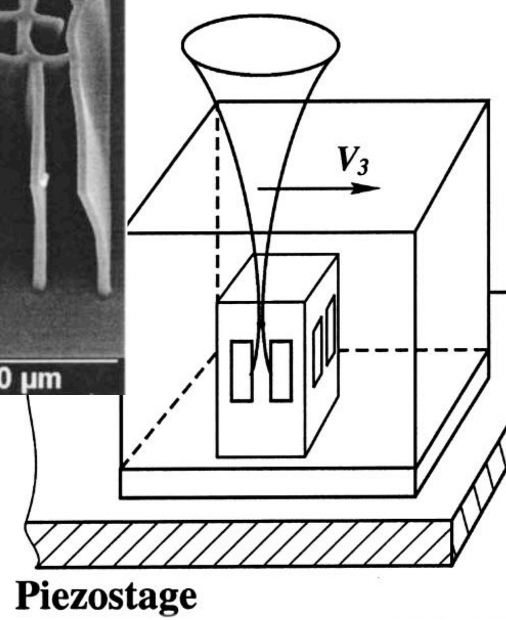
S. Arscott & S. Le Gac, JMM 2004, JASMS 2004

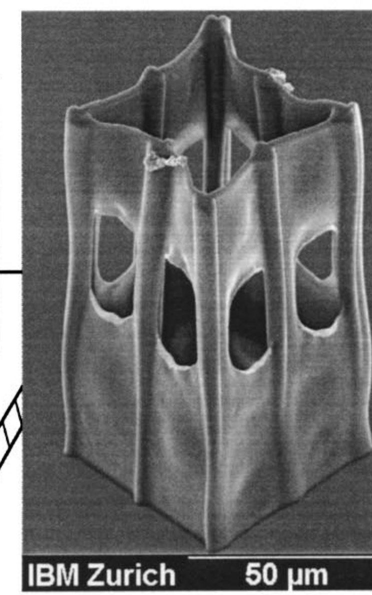
Stereolithography

- **Resolution**: optics-dependent down to sub-diffraction limit
- High **aspect ratio** structures: > 50:1









Structures made from SU-8

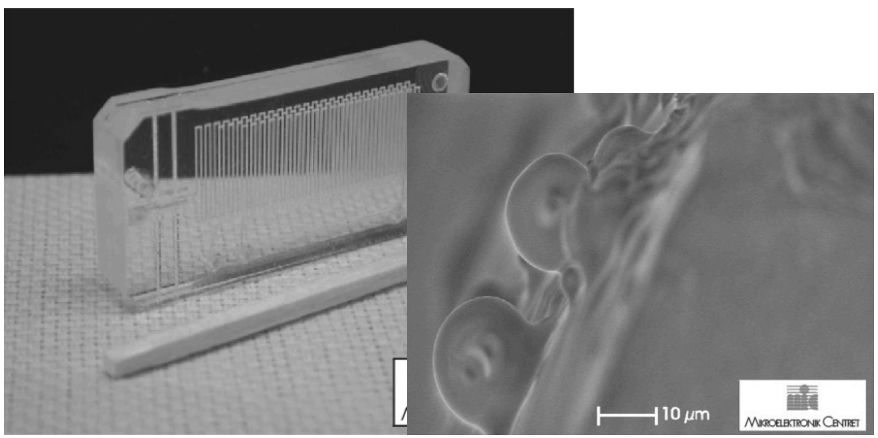
Material ablation techniques

Two approaches

- **Laser-based**: removal of material at the focal point of the laser beam (highest energy concentration)
- **Mechanical**: removal of material using a small revolving tool (milling).

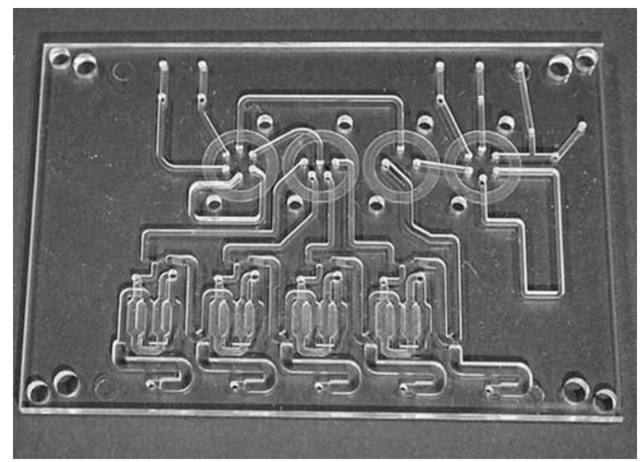
- Fabrication controlled with the help of 2D-CAD software

Optical approach



- Any material (laser-dependent)
- ***Resolution***: laser/optics-dependent
- High aspect-ratio structures
- Change of surface properties: hydrophilicity, roughness….

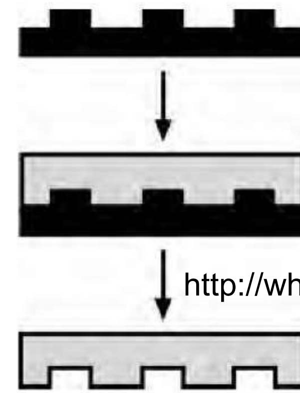
Mechanical approach



Becker et al., 2008

- Micromilling
- Method limited to thermoplastics
- ***Resolution*** limited to 100 μm
- High surface roughness

Replication methods – Polymer materials



Principle:
Replication of (negative) structures placed on the **master** (mold) in a polymer that adopts the features on the master

Techniques:

- Hot embossing; microthermoforming; injection molding; injection compression molding – thermal process (**thermoplastics**)
- Casting (or soft lithography) – polymerization (**elastomer** (PDMS); OSTE).

Advantages:

- Low cost production
- High volume fabrication process

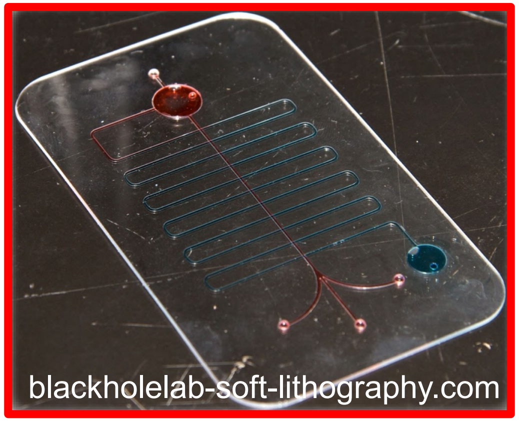
Key-aspect: quality of the mold!!!!

- Resolution of the mold ⇨ resolution of the features
- Low surface roughness
- Suitable surface properties
- No undercuts

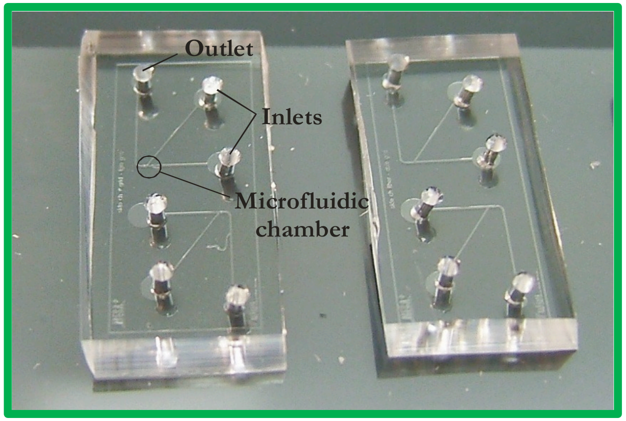
PDMS polydimethylsiloxane; OSTE off-stochiometry thiol-ene

Focus on polymer materials

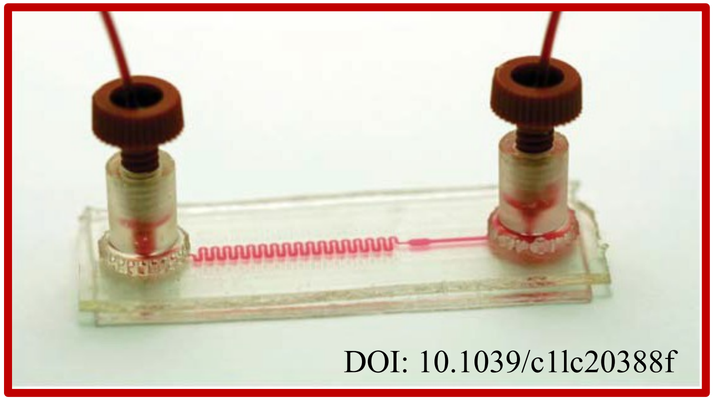
Cleanroom - photoresists



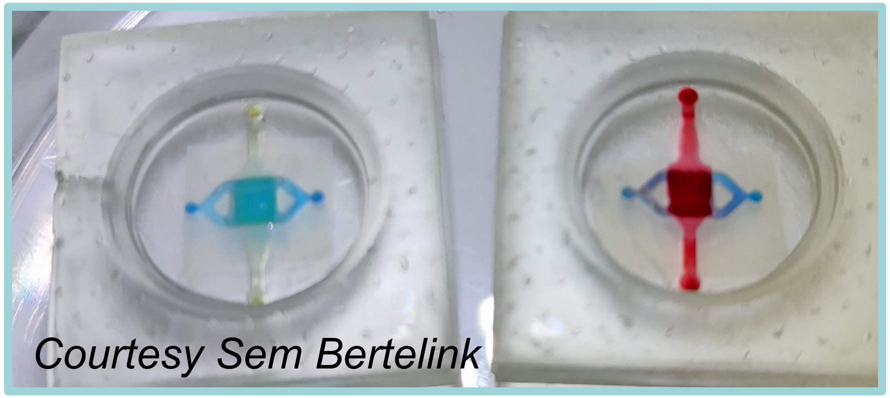
Thermoplastics material



Soft-lithography - PDMS



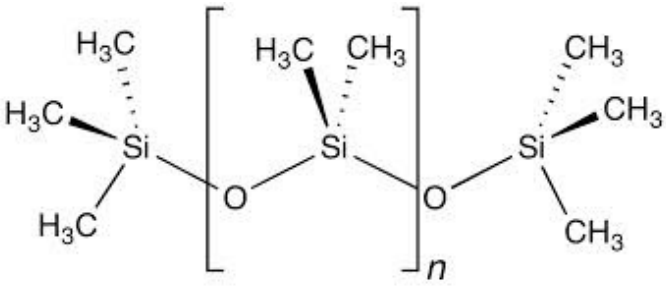
Thiol-ene material



3D printing technique

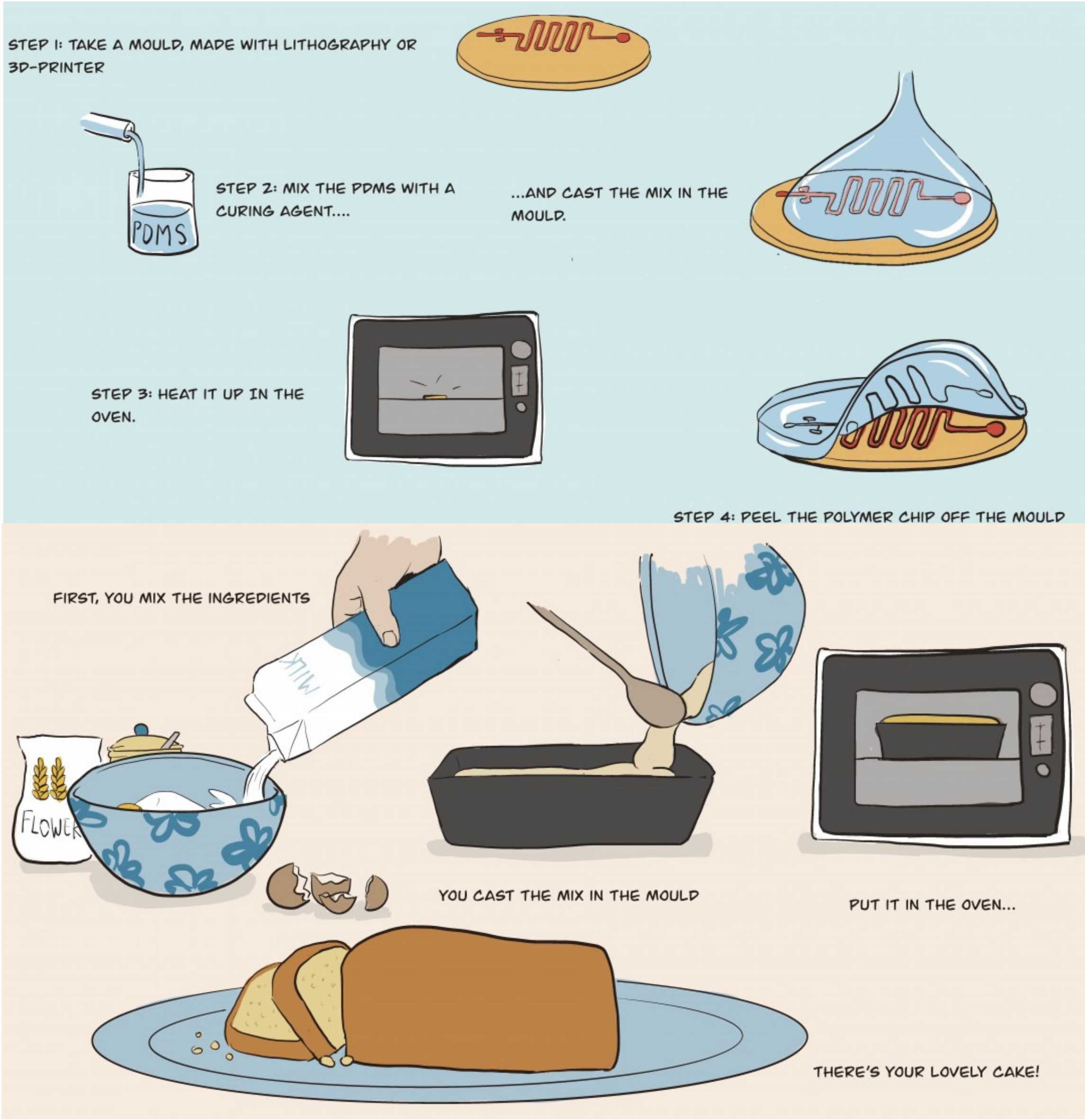
Soft lithography

Polydimethylsiloxane or PDMS
Elastomeric material



- *In situ* thermal **polymerization**
- **Reservoir** punching
- **Bonding** - plasma activation

- **#1 material in "academic microfluidics"**
- Easy, cheap
- "Biocompatible"
- Replication accuracy/ resolution: 100 μm (routine) - 10 nm (mold-dependent)



www.utoday.nl; cartoon by Enith Vlooswijk

Mold fabrication for soft lithography

1. Dry-etching of silicon

- Smaller features
- Shallow features
- Higher precision
- Longer mold lifetime

2. SU-8 patterns on a Si/glass wafer

- Poor adhesion of SU-8: reduced lifetime of the mold
- Thicker structures (up to the mm scale)

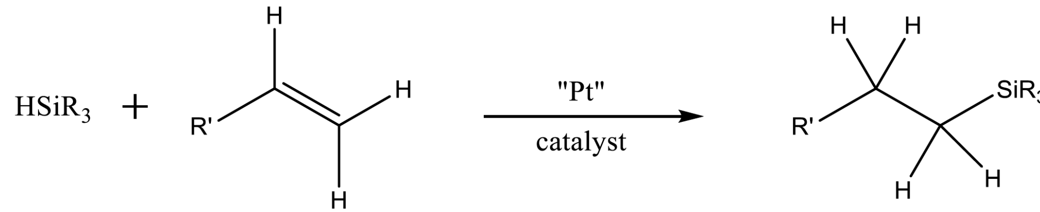
- **Post-processing step**: hydrophobic coating to facilitate the removal of cured PDMS

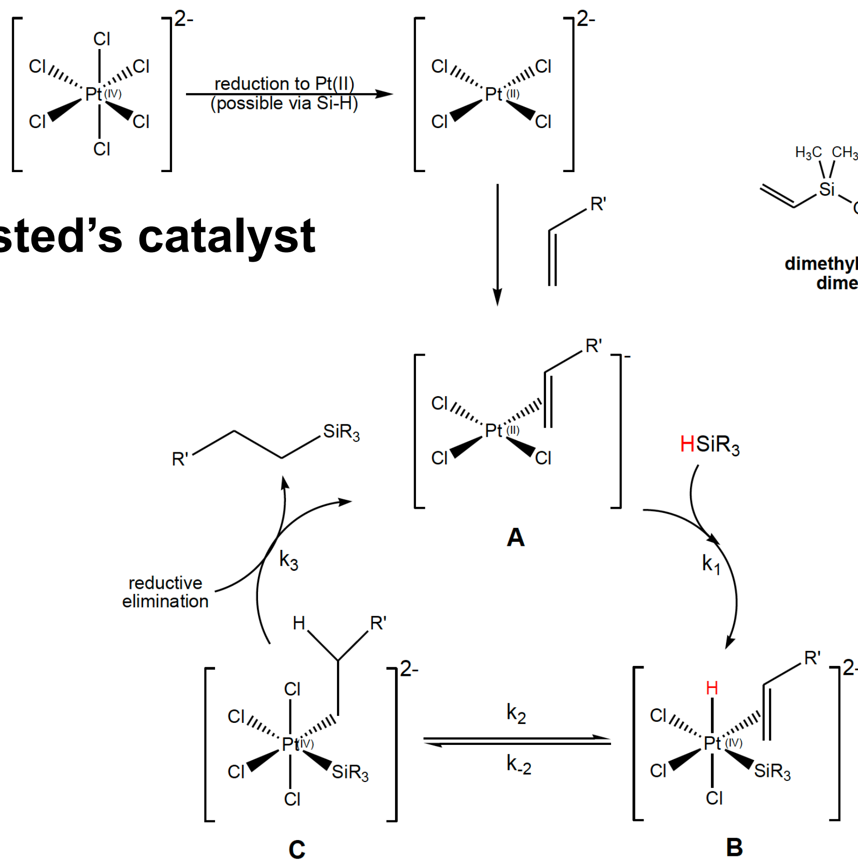
3. 3D printing….
(Later in the course)

- Much larger structures (printer-dependent)
- More flexibility on structure shape (3D!!!)
- Possibility to include reservoirs
- Surface roughness (---)
- PDMS curing inhibition (---)
- Biocompatibility (???)

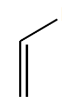
Soft lithography - PDMS

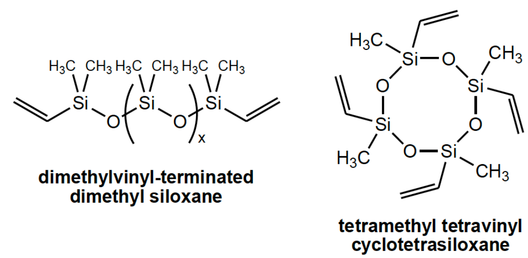
- General **hydrosilylation** reaction scheme



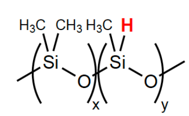


Karsted's catalyst





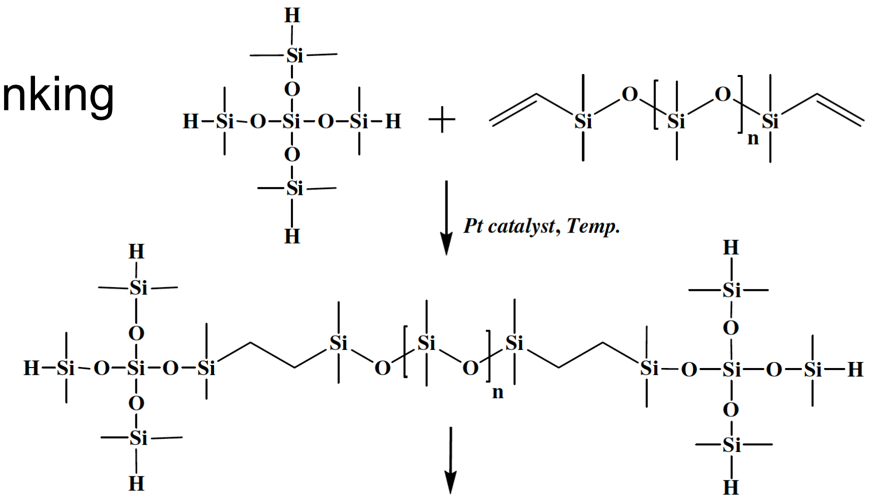
Where $HSiR_3$ is = to:



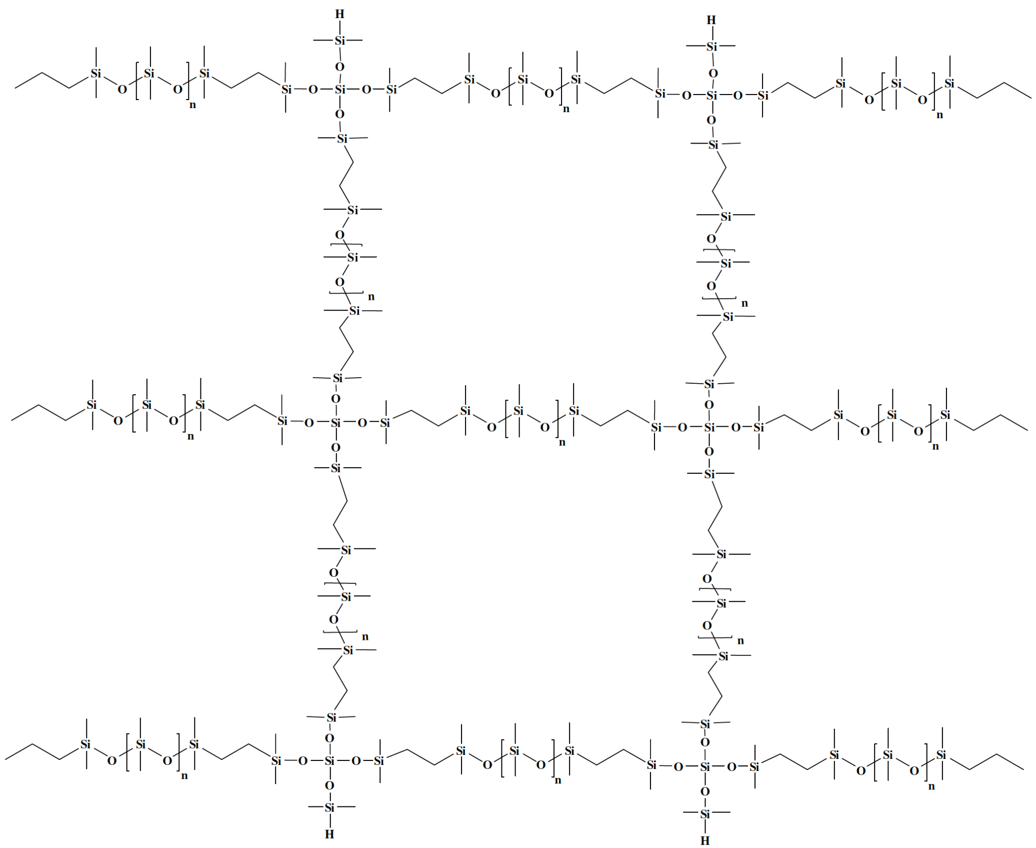
Sylgard® Cure Inhibition Characterization

Denisse Ortiz-Acosta and Crystal Densmore
Chemistry Division
Chemical Diagnostics and Engineering Group

Crosslinking agent



base



- “Standard” PDMS:
10:1 wt % base:curing agent

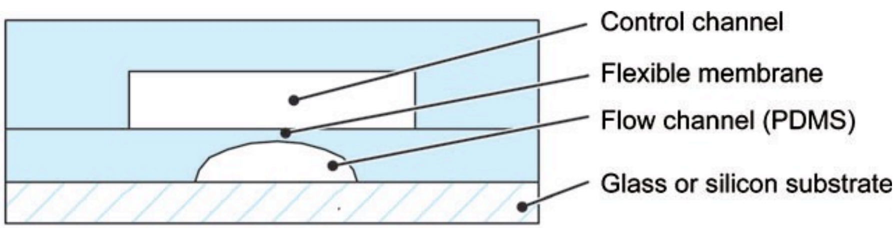
- % curing agent ⇔ material properties ⇔ material stiffness

- More curing agent: stiffer material
- Less curing agent: softer (more deformable) material

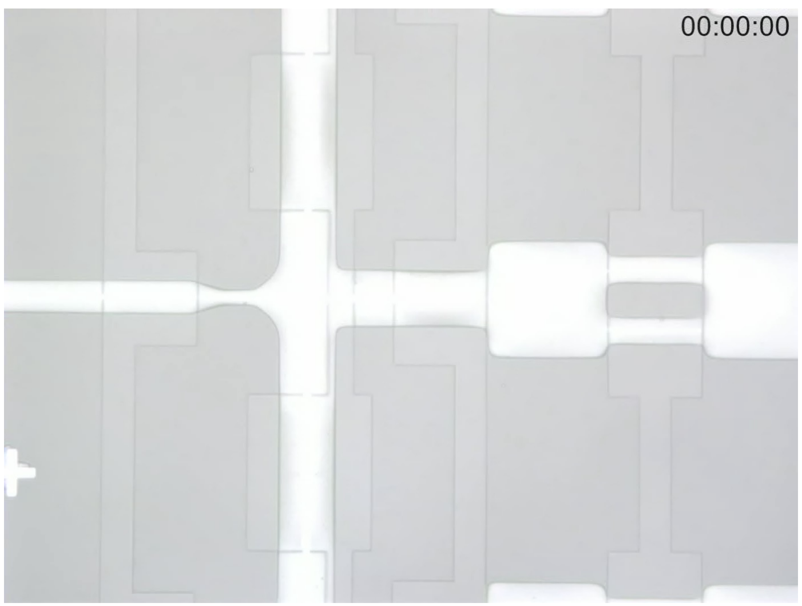
doi:10.1016/j.polymer.2009.06.022

PDMS: deformable material

- Realization of **valves and pumps** using **multi-layer structures**

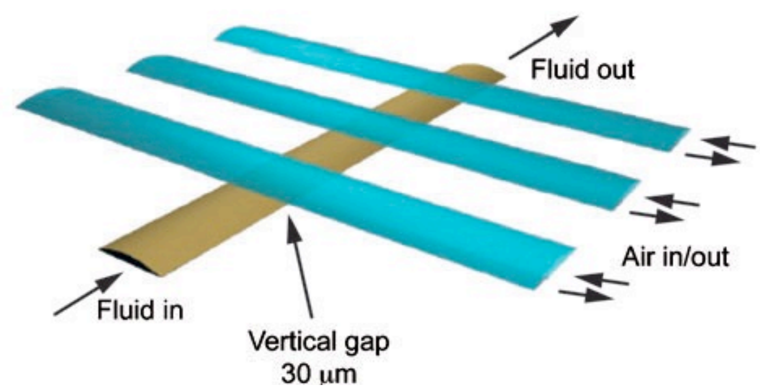


- Thin elastomer layer deflected upon application of a pressure from a control channel
  ⇨ Creation of a **valve**



Courtesy Yoon-Sun Yang

- Valves actuated sequentially
  ⇨ Creation of a **peristaltic pump**



Unger et al., Science, 2000; DOI: 10.1126/science.288.5463.113

What happens at the PDMS surface?

O_2 Plasma Treatment

Hydrophobic
Air bubbles!!

Silanol groups Si-O-H

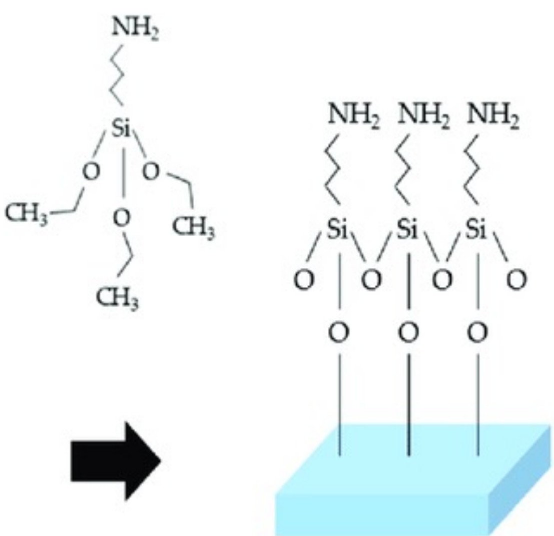
Hydrophilic
No air bubbles!!

Native surface

Oxidized surface

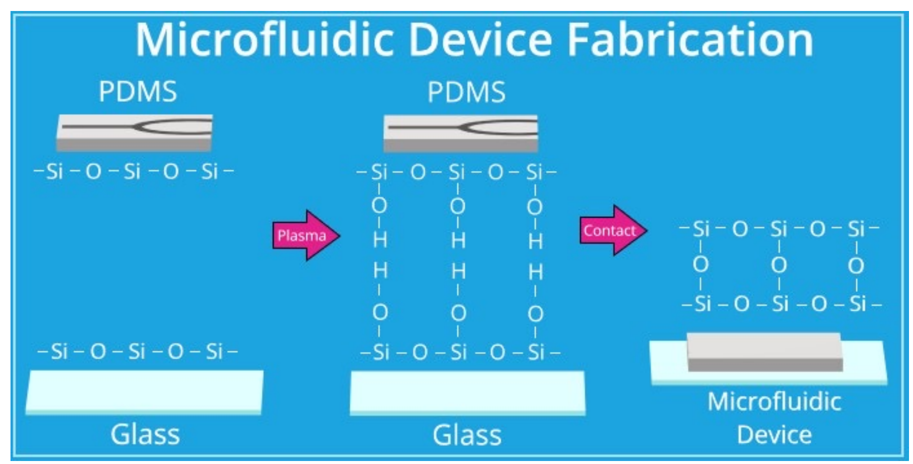
1. Well-established surface chemistry procedures

2. Covalent bonding to another substrate (glass, PDMS, silicon, etc.)



Silanization

DOI:10.3390/s22072741



harrickplasma.com

What happens at the PDMS surface?

Hydrophobic
Air bubbles!!

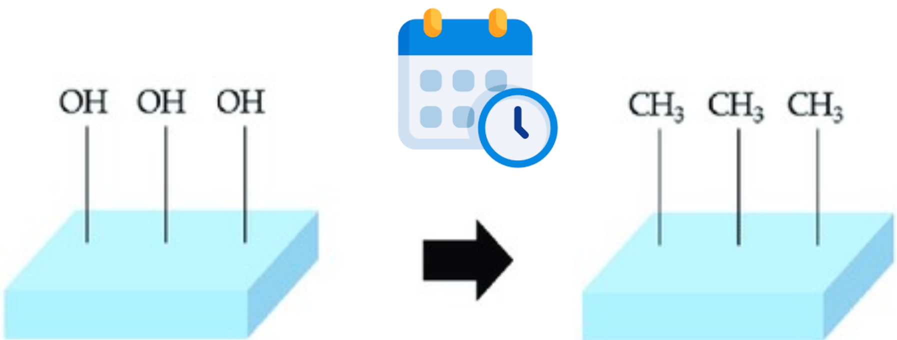
Native surface

Oxidized surface

Silanol groups
Si-O-H

Hydrophilic
No air bubbles!!

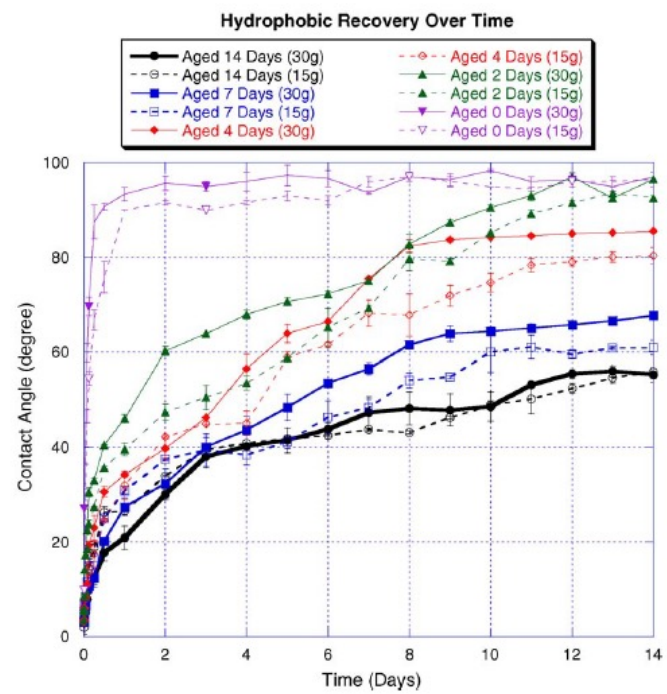
Hydrophobic recovery



Oxidized surface

Native surface

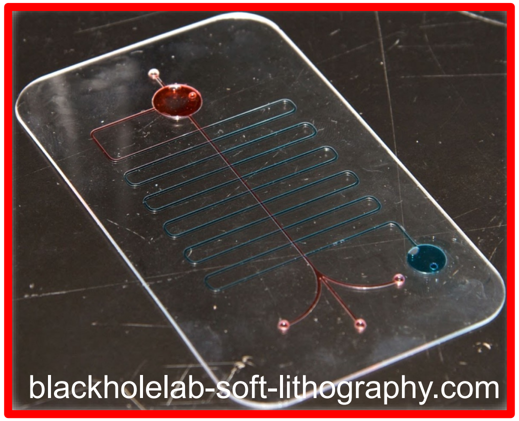
DOI:10.3390/s22072741



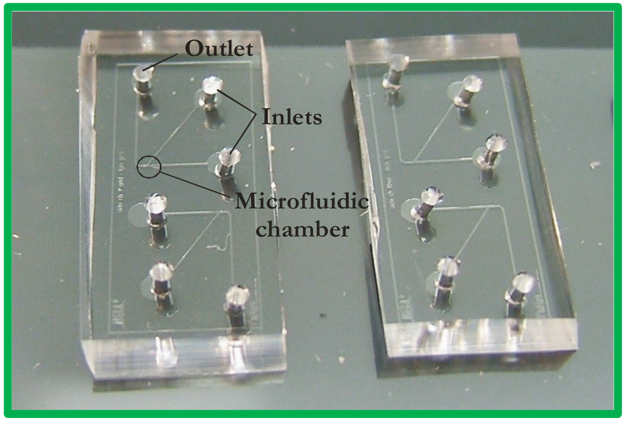
doi:10.1016/j.snb.2005.04.037

Focus on polymer materials

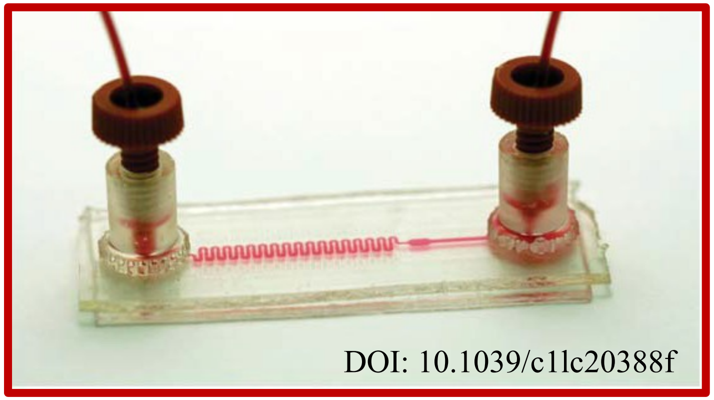
Cleanroom - photoresists



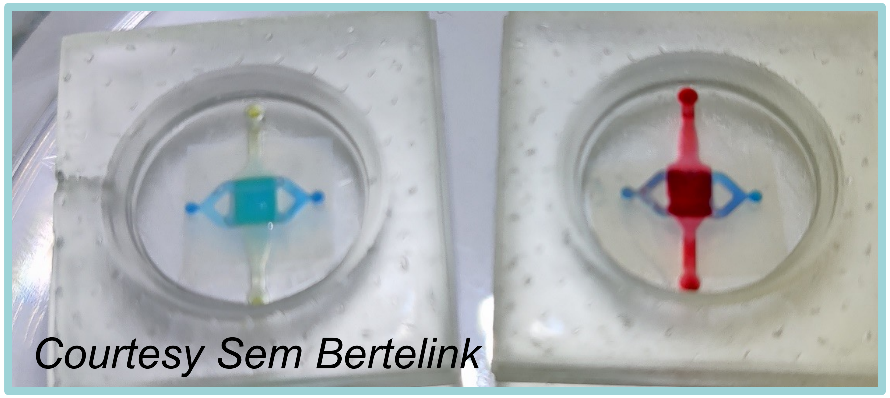
Thermoplastics material



Soft-lithography - PDMS



Thiol-ene material

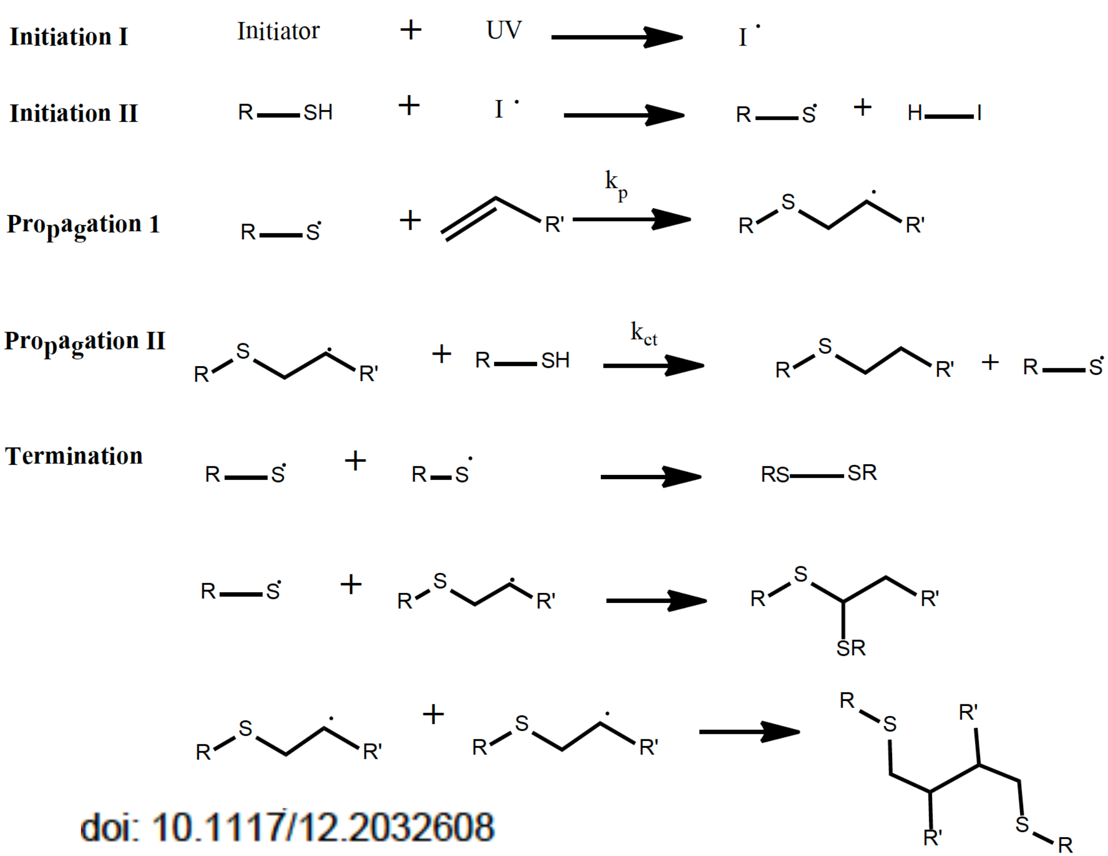


3D printing technique

Thiol-ene polymers - OSTE

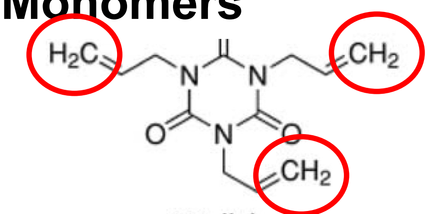
Motivations

- Low-technicality level in terms of fabrication (like PDMS)
- Better defined surface properties
- Better amenable to commercial applications

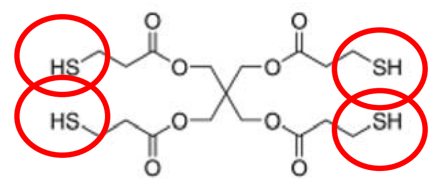


doi: 10.1117/12.2032608

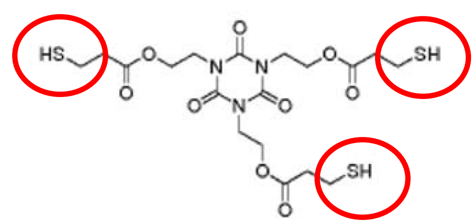
Monomers



Triallyl

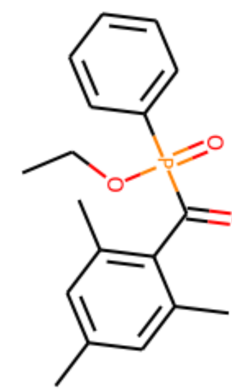


Tetrathiol



Trithiol

Photoinitiator



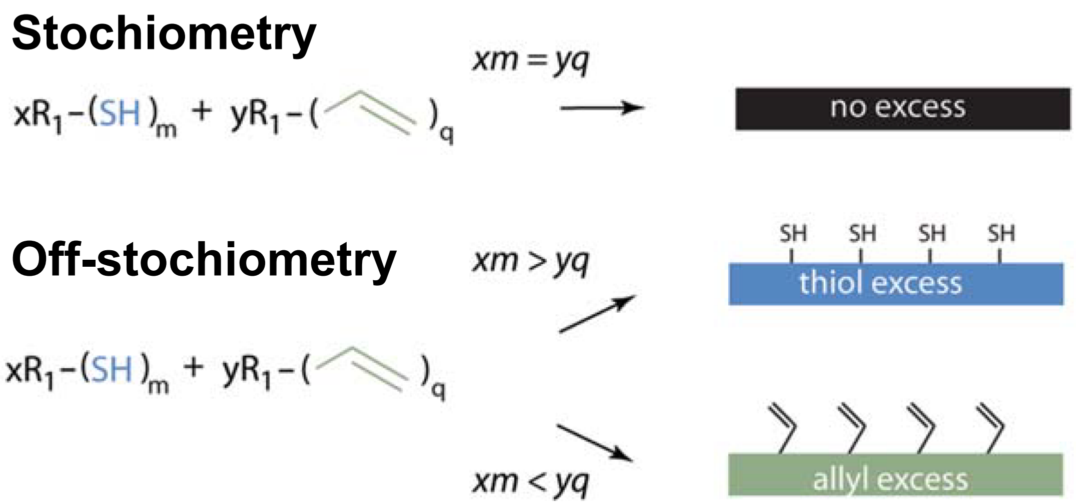
Lucirin TPO liquid

DOI: 10.1039/c1lc20388f

OSTE off-stochiometry thiol-ene

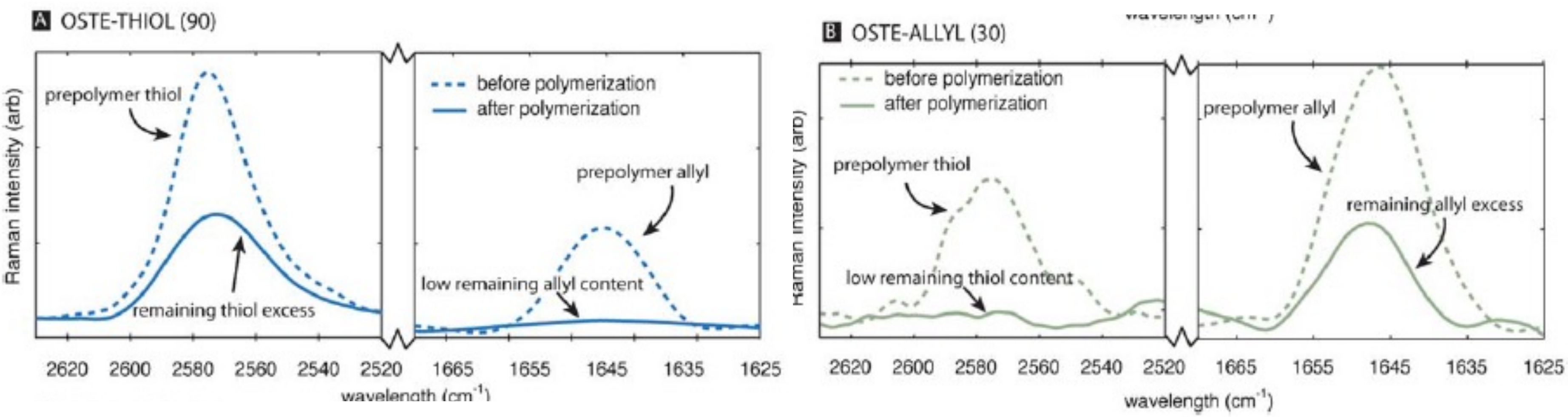
Ethyl-2, 4, 6 trimethylbenzoylphenyl phosphinate

Thiol-ene polymers - OSTE



- Inclusion of active groups at the surface for surface functionalization

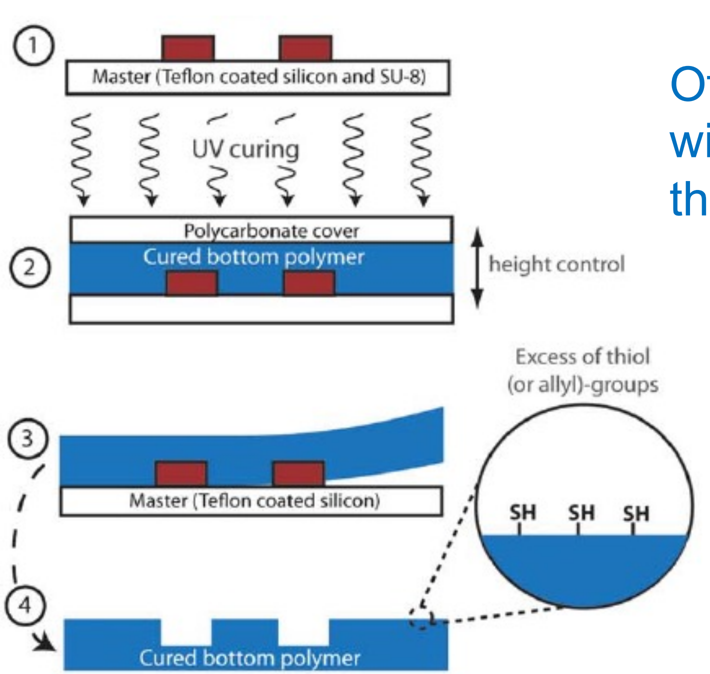
- **Monitoring by FT-IR the chemical composition of the OSTE materials**



DOI: 10.1039/c1lc20388f

OSTE off-stochiometry thiol-ene

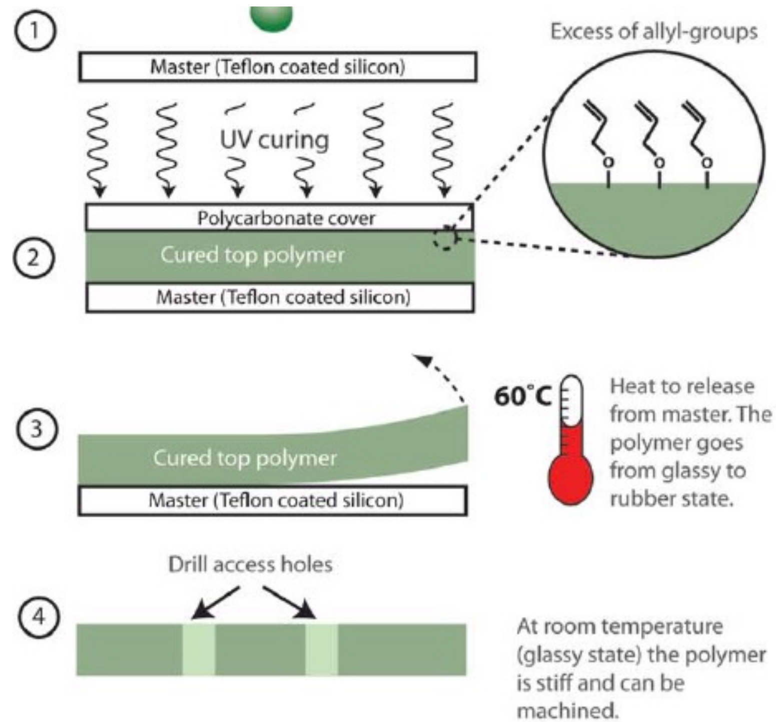
Thiol-ene polymers - OSTE

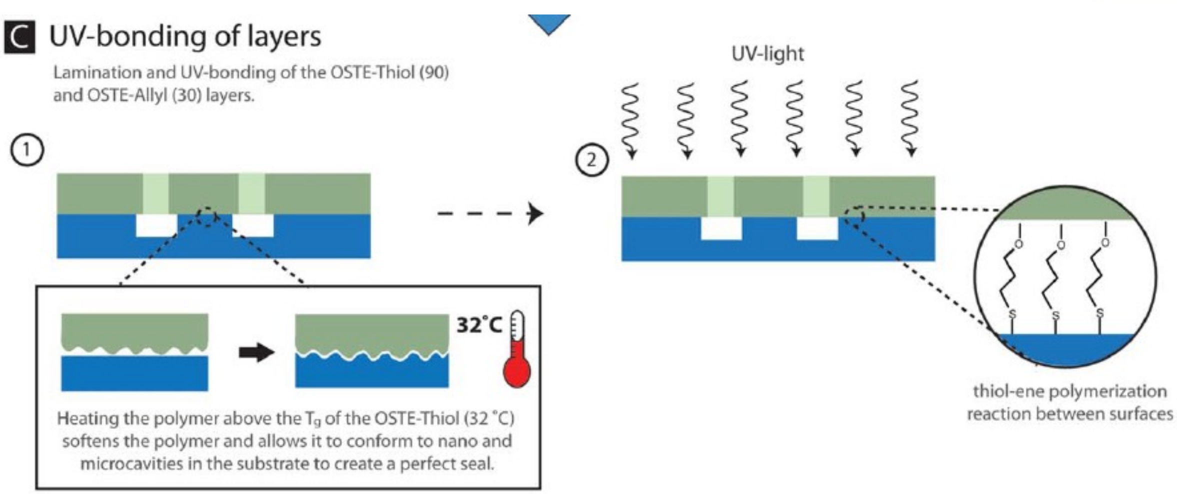


Off-stochoimetry with excess of thiols (90:10)

UV curing at 365 nm (photoinitiator)

Off-stochoimetry with excess of Allyl (30:70)



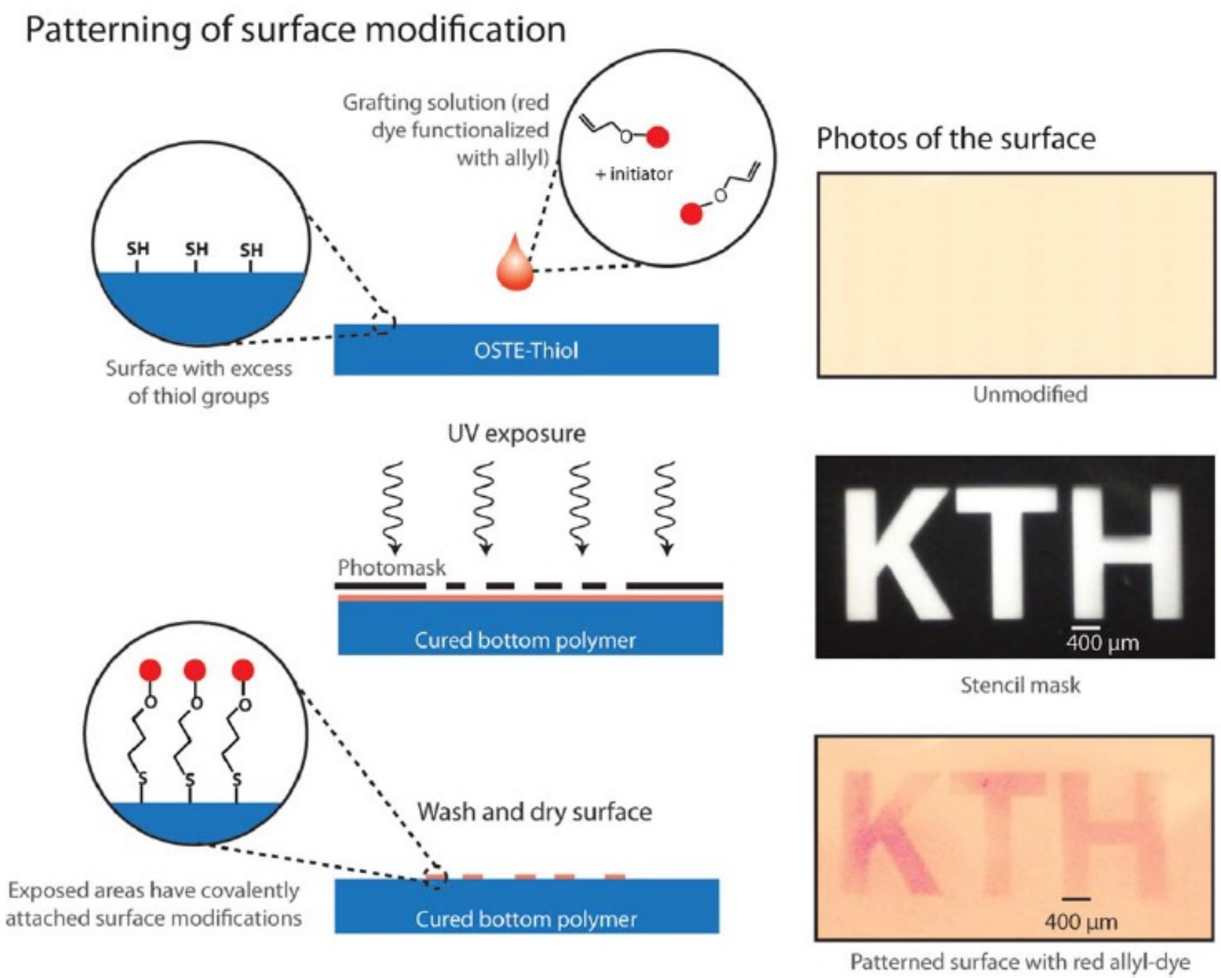


Device assembly:
UV light exposure
(254 nm; few minutes)

DOI: 10.1039/c1lc20388f

Thiol-ene polymers - OSTE

- **Exploiting the remaining active surface groups for functionalization**

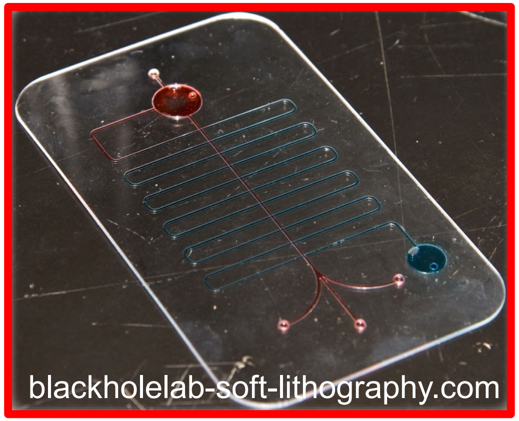


Applications:
- Patterning of molecules
- Control on surface properties (hydrophilic, hydrophobic)

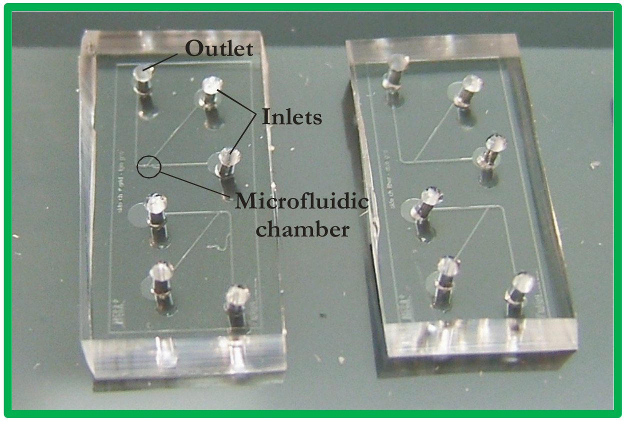
DOI: 10.1039/c1lc20388f

Focus on polymer materials

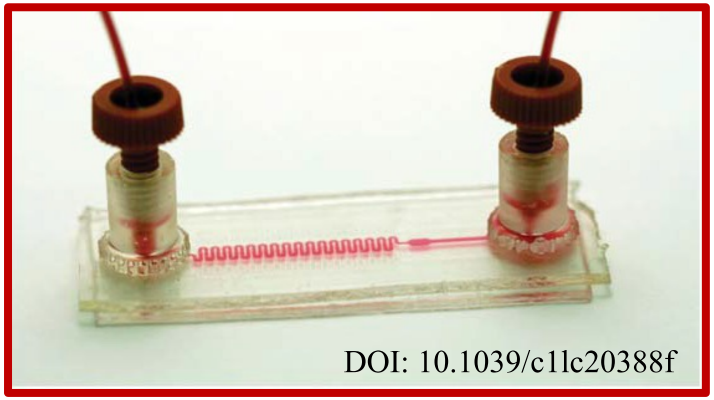
Cleanroom - photoresists



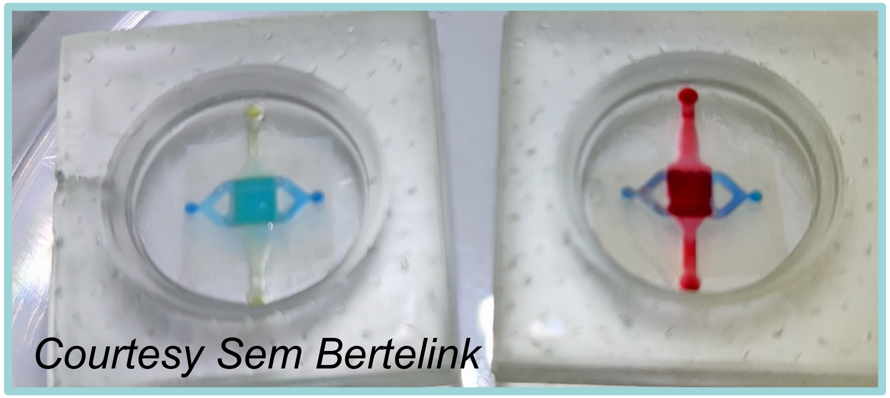
Thermoplastics material



Soft-lithography - PDMS



Thiol-ene material

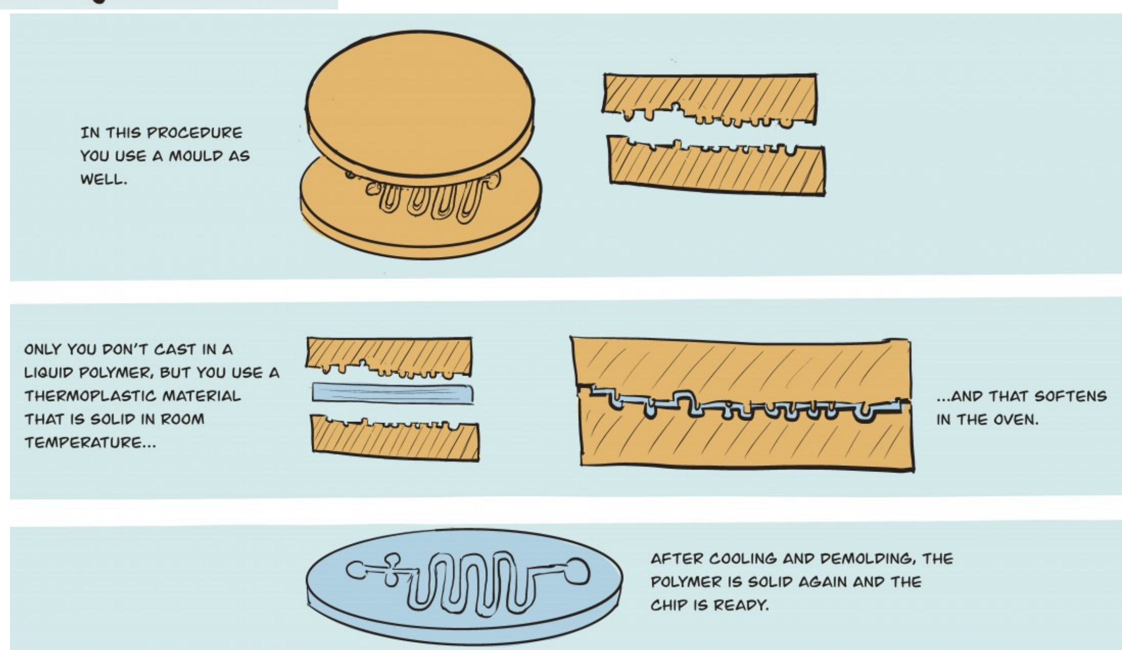


3D printing technique

Replication methods - Thermoplastics

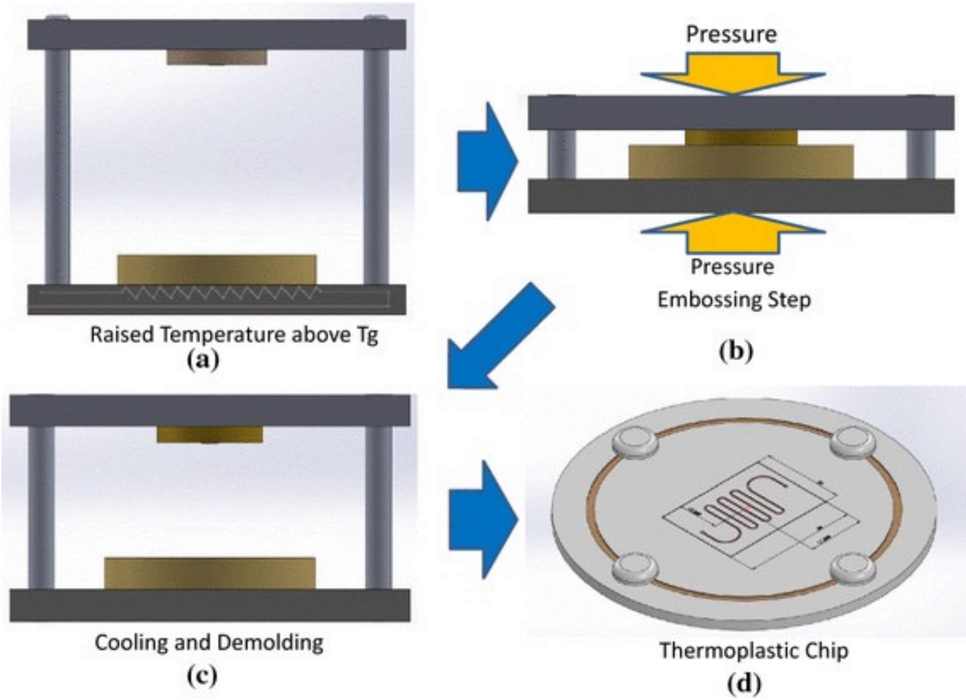
- Heating of the polymer material above the *Tg* or *Tm*
- Soft or liquid polymer that can be reshaped with the help of a mold (and pressure)
- No polymerization reaction!

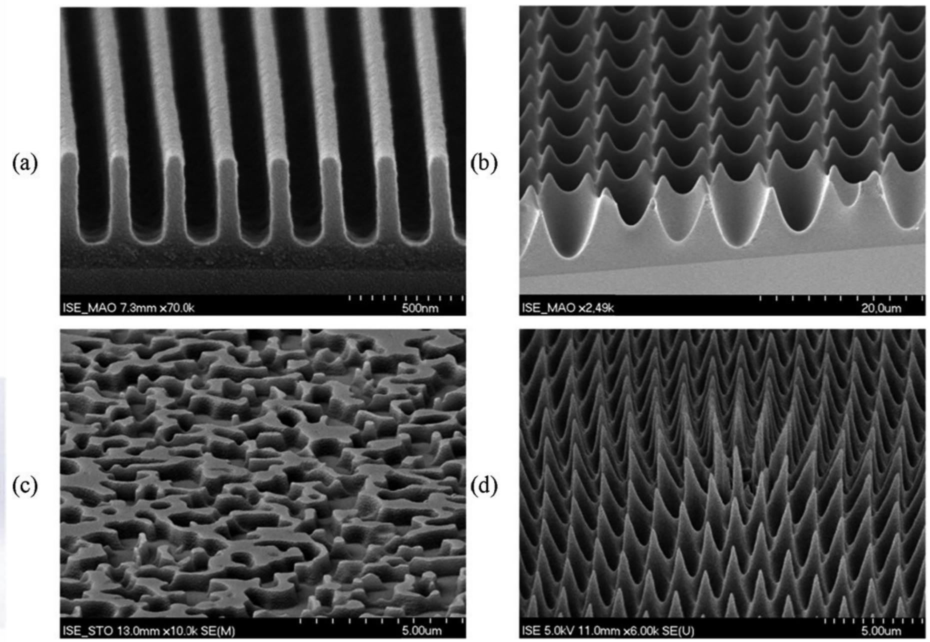
- <u>*Soft state*</u>: hot embossing
- <u>*Liquid state*</u>: injection molding



www.utoday.nl; cartoon by Enith Vlooswijk

Replication methods - Hot embossing





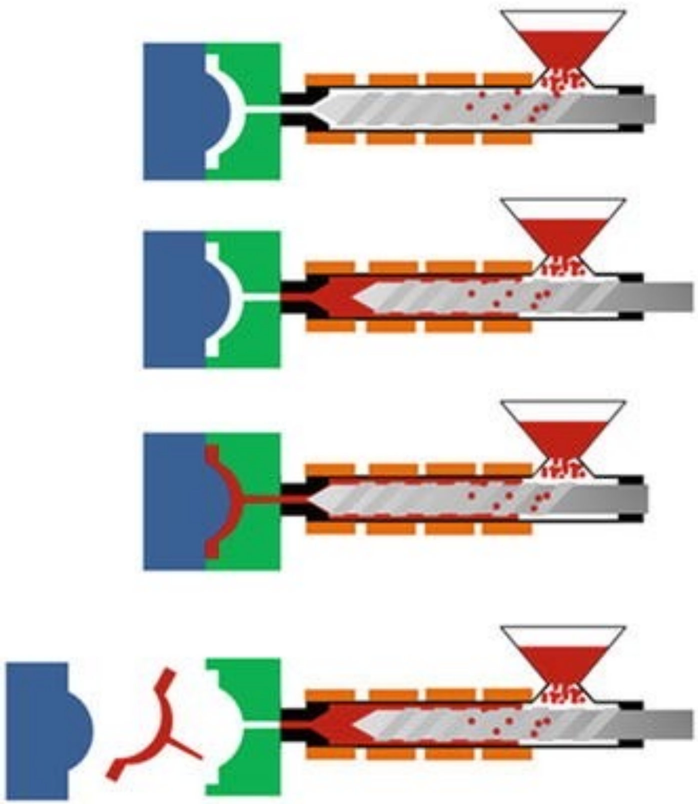
https://spie.org/news

DOI:10.1007/s00542-016-3035-8

Features down to a **few tens of nm** (nanoimprint lithography)

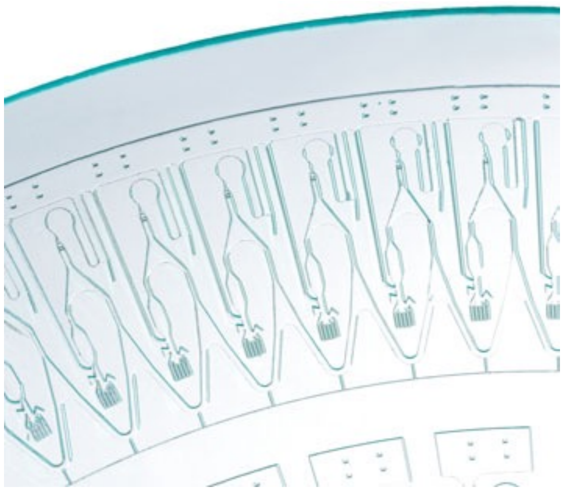
- **Number 2 technique** for polymer industry
- Large fabrication throughput

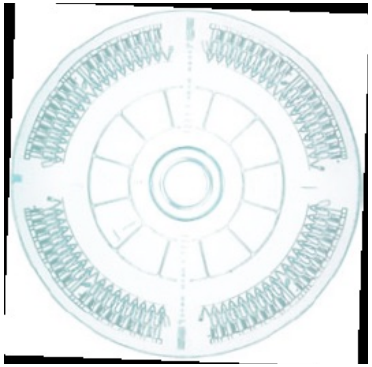
Replication methods - Injection molding



doi.org/10.1007/978-1-4614-5491-5_694

- Ability to create 3D structures
- CD industry: use of compression/injection molding technique





Gyros AB

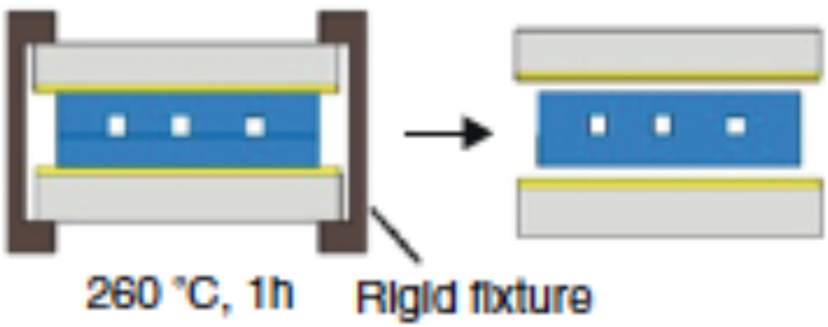
CD-shape device for biomolecule sample preparation

- **Number 1 technique** for polymer fabrication
- More for commercial products and industrial applications (cost of the equipment)

Bonding of thermoplastics

Direct bonding

- Thermal process while applying a pressure or solvent-assisted bonding



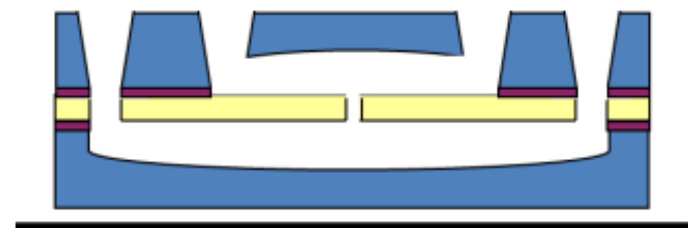
Temperature related to *Tg* of the material

Pro: Same set-up as for hot embossing
Con: Risk to deteriorate the microstructures

Ren et al., 2014

Indirect bonding

- Use of an intermediate layer of adhesive



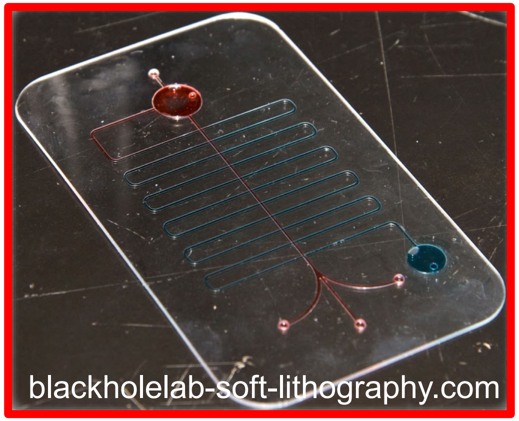
Curing of glue using UV/T˚C

Pro: Room temperature process (UV curable glue)
Con: Optimization of the process depending on the glue and materials: risk of glue in the channel (too much glue) or no good bonding (no enough glue)

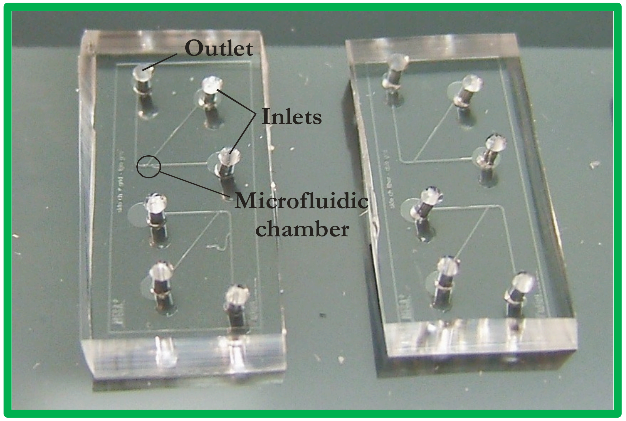
Arayanarakool et al., 2010

Focus on polymer materials

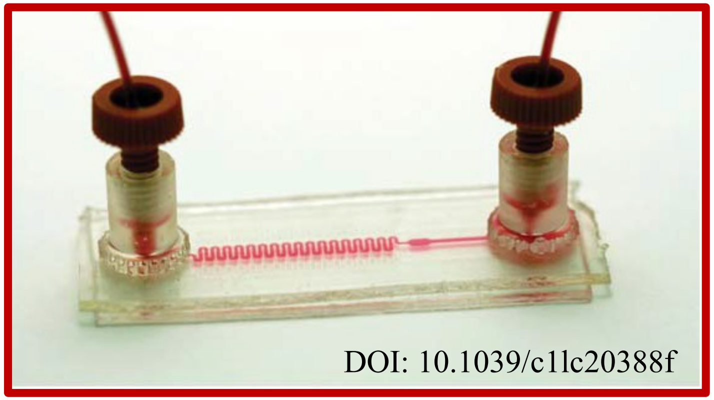
Cleanroom - photoresists



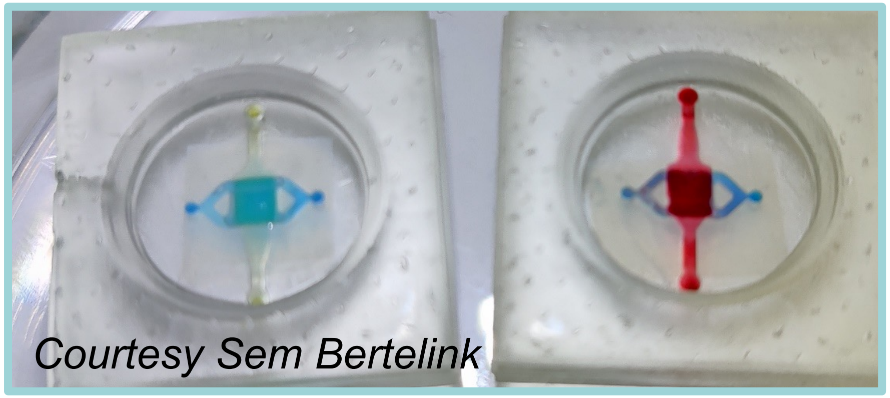
Thermoplastics material



Soft-lithography - PDMS



Thiol-ene material



3D printing technique

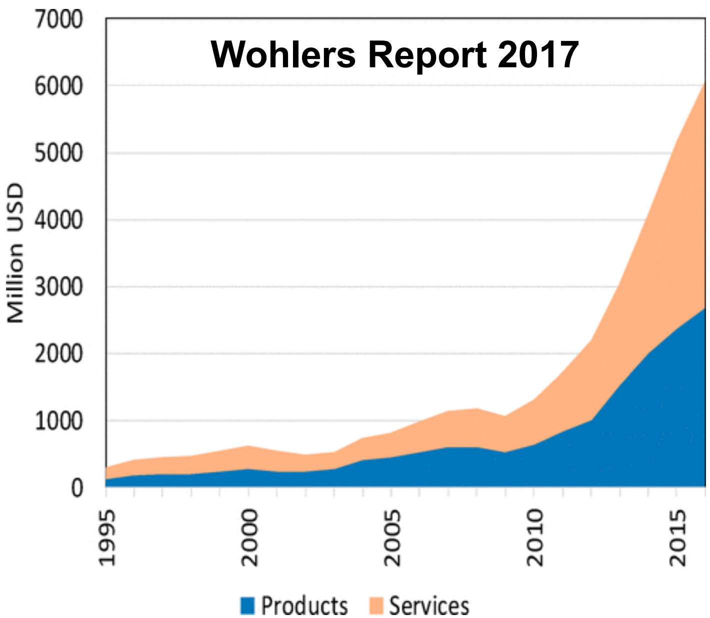
Additive manufacturing or 3D printing

Cleanroom-based approaches

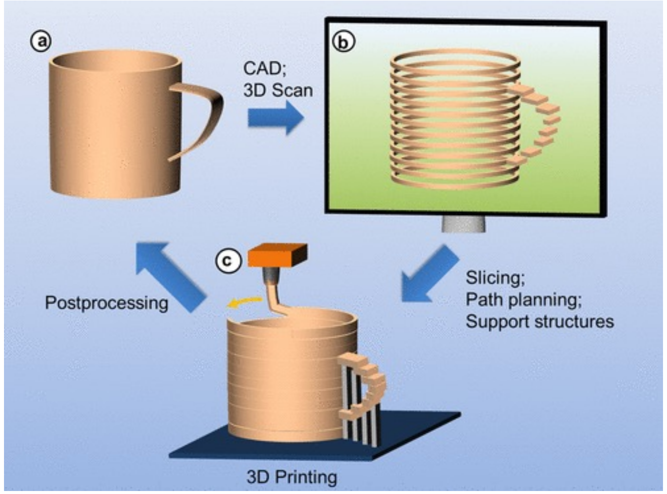
- Long turn-around time: idea-to-device > weeks
- Structures limited to "2D" designs and mostly simple designs (no 3D)

Additive manufacturing

- Introduced in the 80's
- 3D printer now accessible to "anybody"
- Broad range of applications: medical field, automobile, airplanes, clothes, etc.



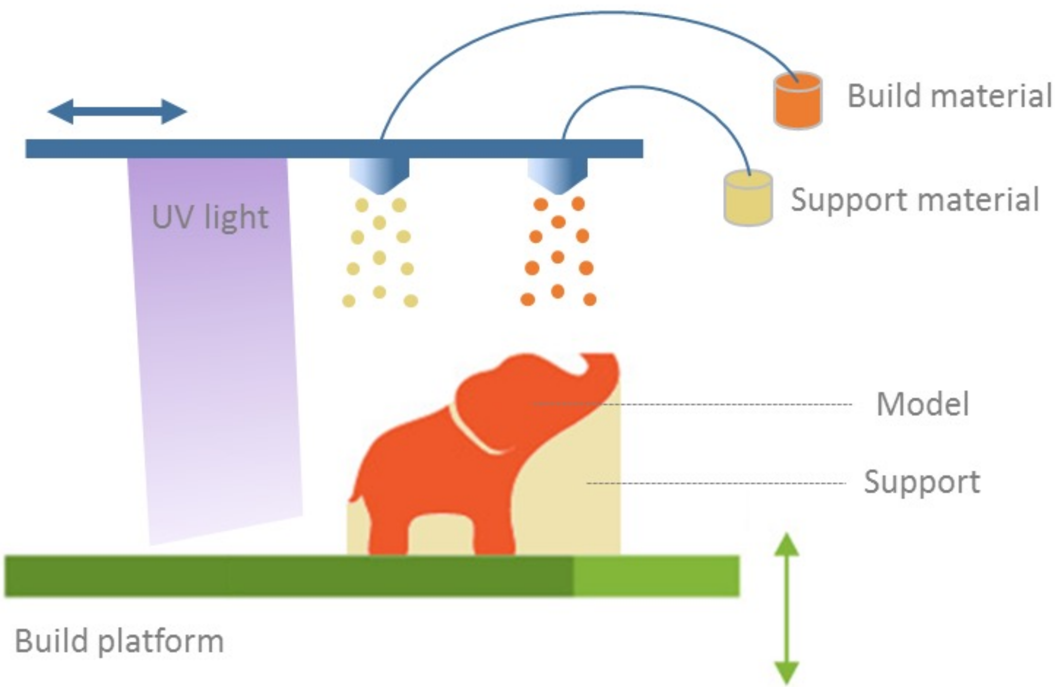
- Possibility to create 3D complex structures (incl. fluidic connections)
- Possibility to use a broad variety of materials: variety of polymers, ceramics, metals, etc.
- Rapid prototyping: CAD design ⇨ 3D object in < 1-2 h (idea-to-device time of ~ 1 day)



doi.org/10.1021/acs.chemrev.7b00074

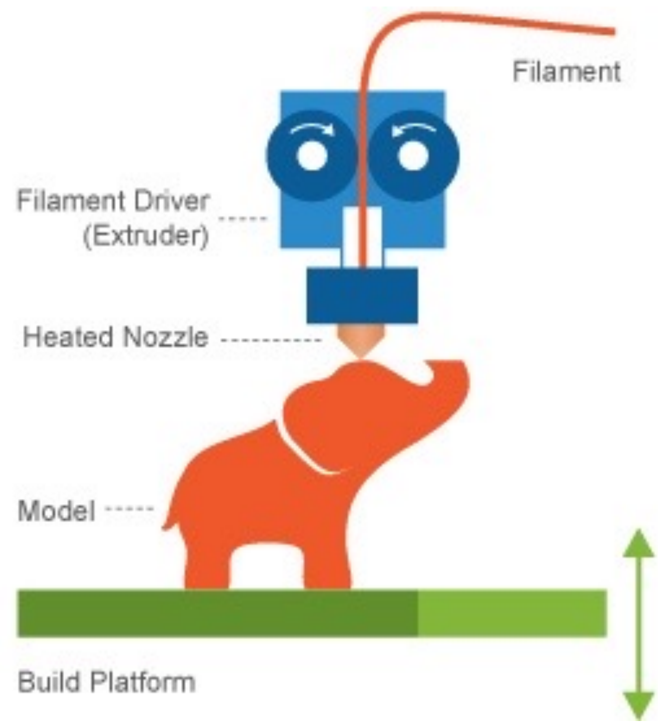
3D printing approaches

Inkjet-like 3D printing



Photopolymerization process

Fused deposition modeling



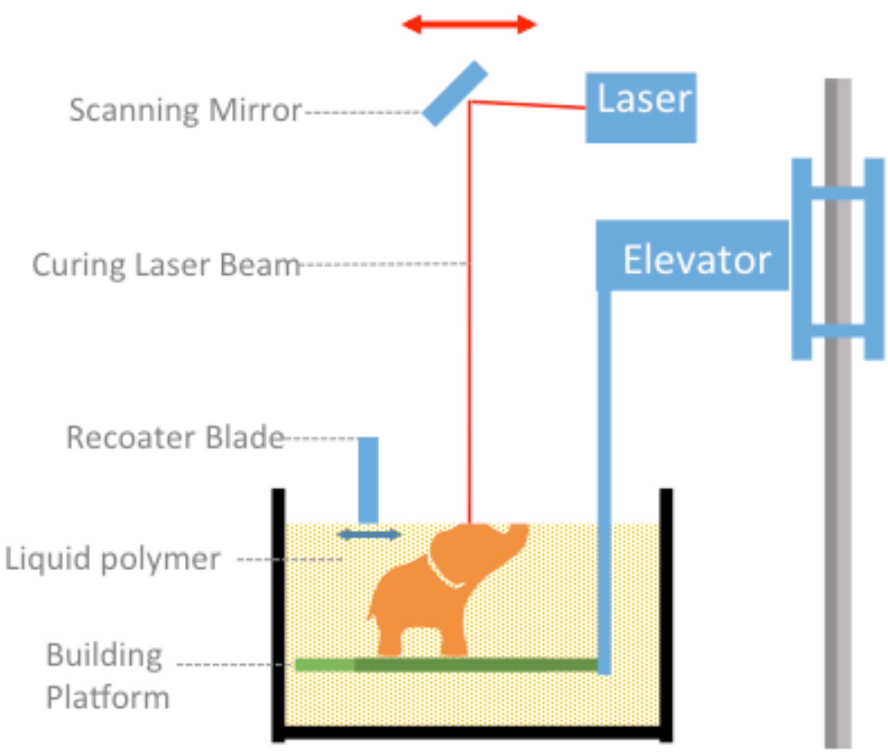
No polymerization process (thermoplastics)

Cartoons: courtesy Dr. Christophe Marquette

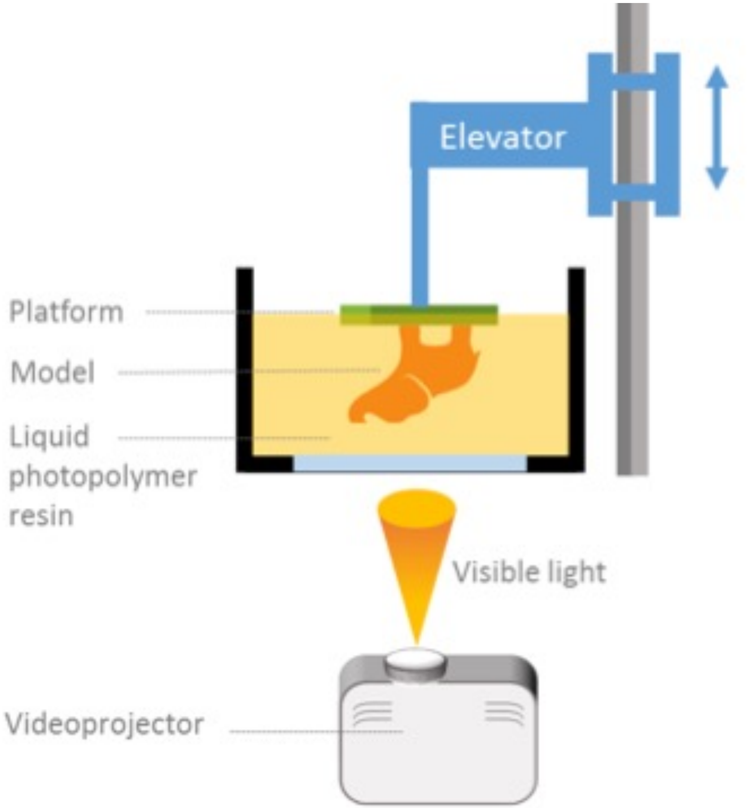
3D printing approaches

Stereolithography (SLA)

Laser writing



Digital light processing (DLD)

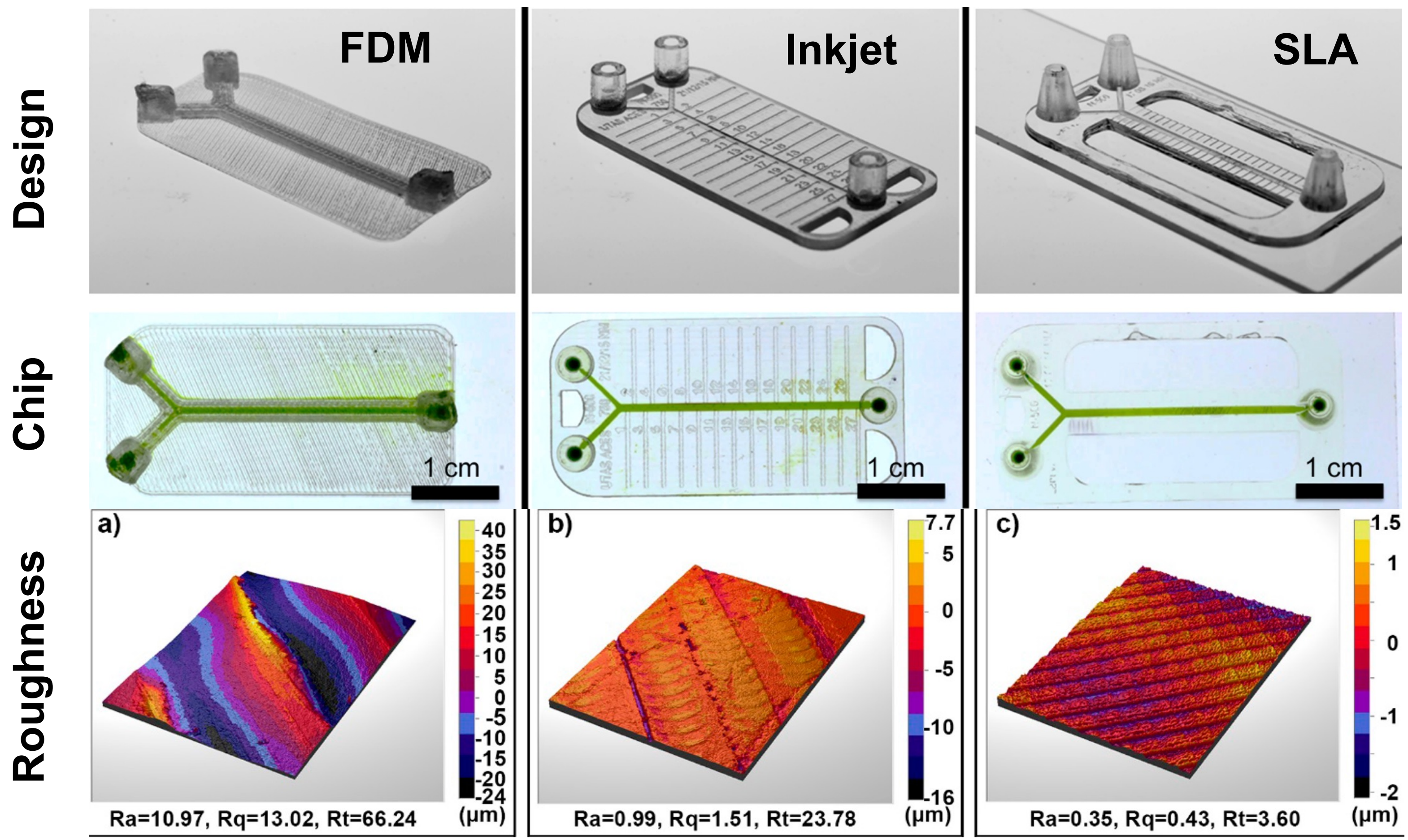


Photopolymerization process

Cartoons: courtesy
Dr. Christophe Marquette

3D printing approaches - Comparison

- Comparison of three main 3D printing approaches (FDM, inkjet-like, SLA)
- Comparison points: smallest features, roughness, channel appearance

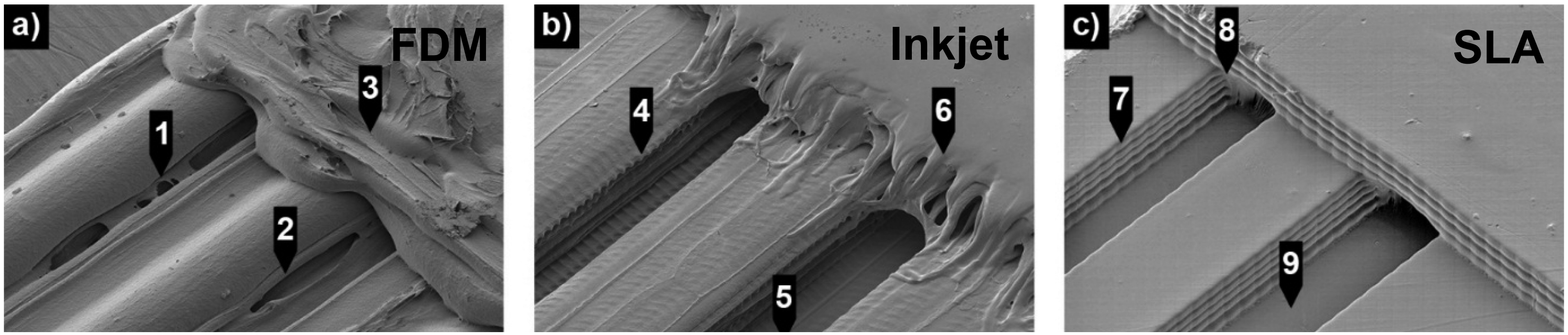


R = 10.97 µm　　R = 0.99 µm　　R = 0.35 µm

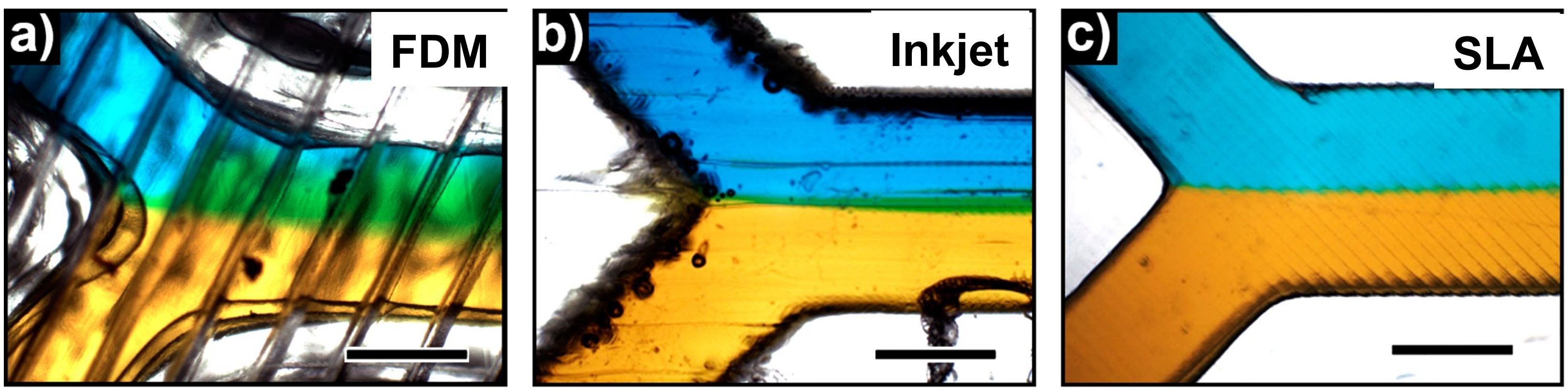
DOI: 10.1021/acs.analchem.7b00136

3D printing approaches - Comparison

Attempt 1: Fabrication of a channel of 250 µm x 350 µm



Attempt 2: Identification of the minimal dimensions that can be created



FDM:
- Width = 321 ± 5 µm
- **Smaller** than design by 107 ± 36 µm

Inkjet:
- Width = 205 ± 13 µm
- **Smaller** than design by 40 ± 36 µm

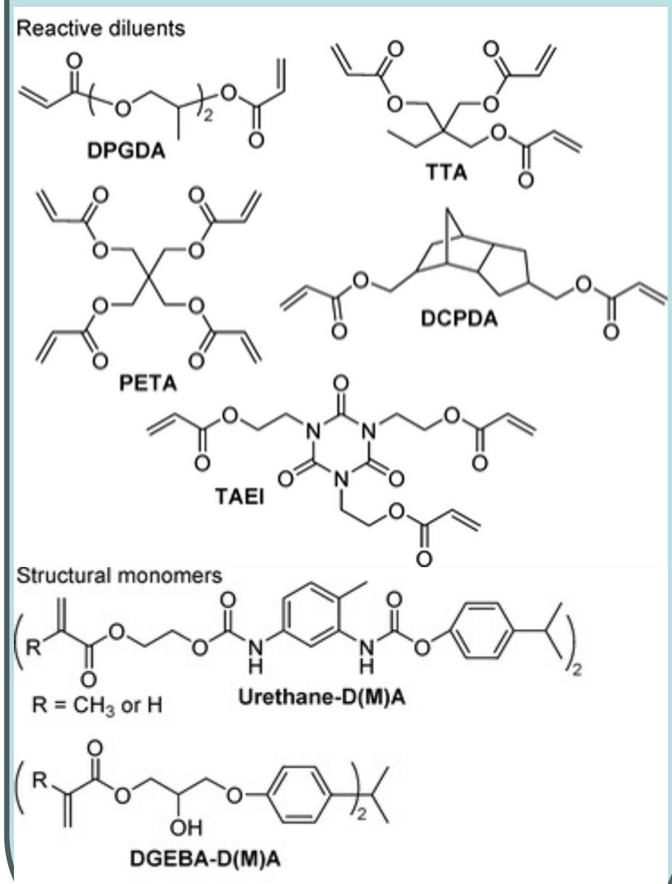
SLA:
- Width = 154 ± 10 µm
- Width = 94 ± 7 µm (inverted design)
- **Larger** than design by 26 ± 20 µm (half pixel size)

DOI: 10.1021/acs.analchem.7b00136

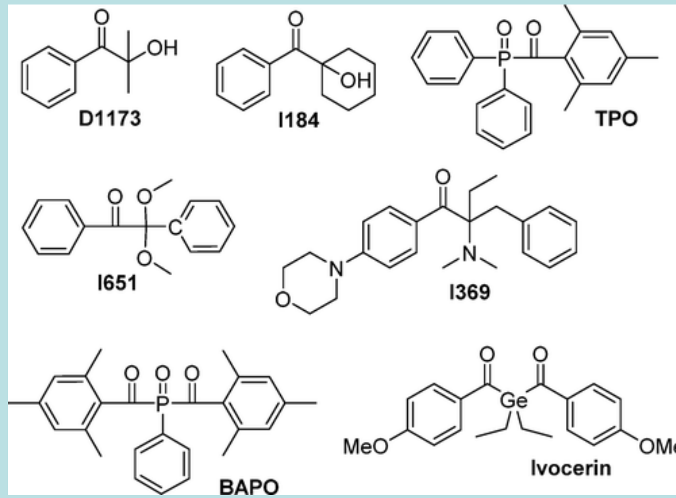
Some more about stereolithography

- Resin formulation mostly **proprietary**, and comprising various components

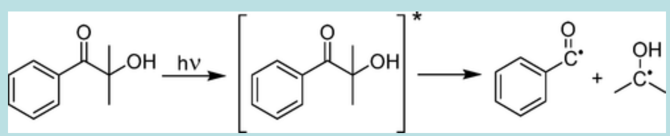
Acrylate/ methacrylate-based resins



Photoinitiators

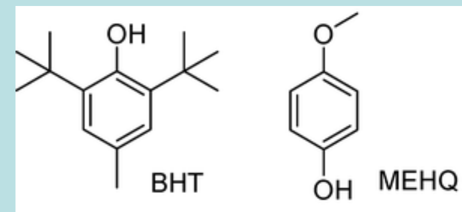


Photocleavage of Darocur 1173

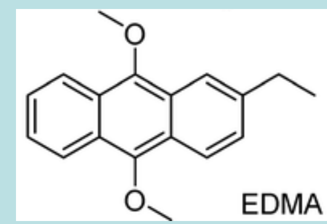


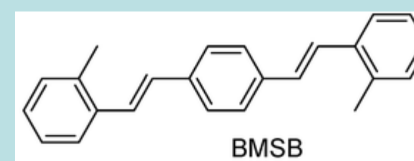
Others…

Stabilizers
(Radical inhibitors)



Light absorbers



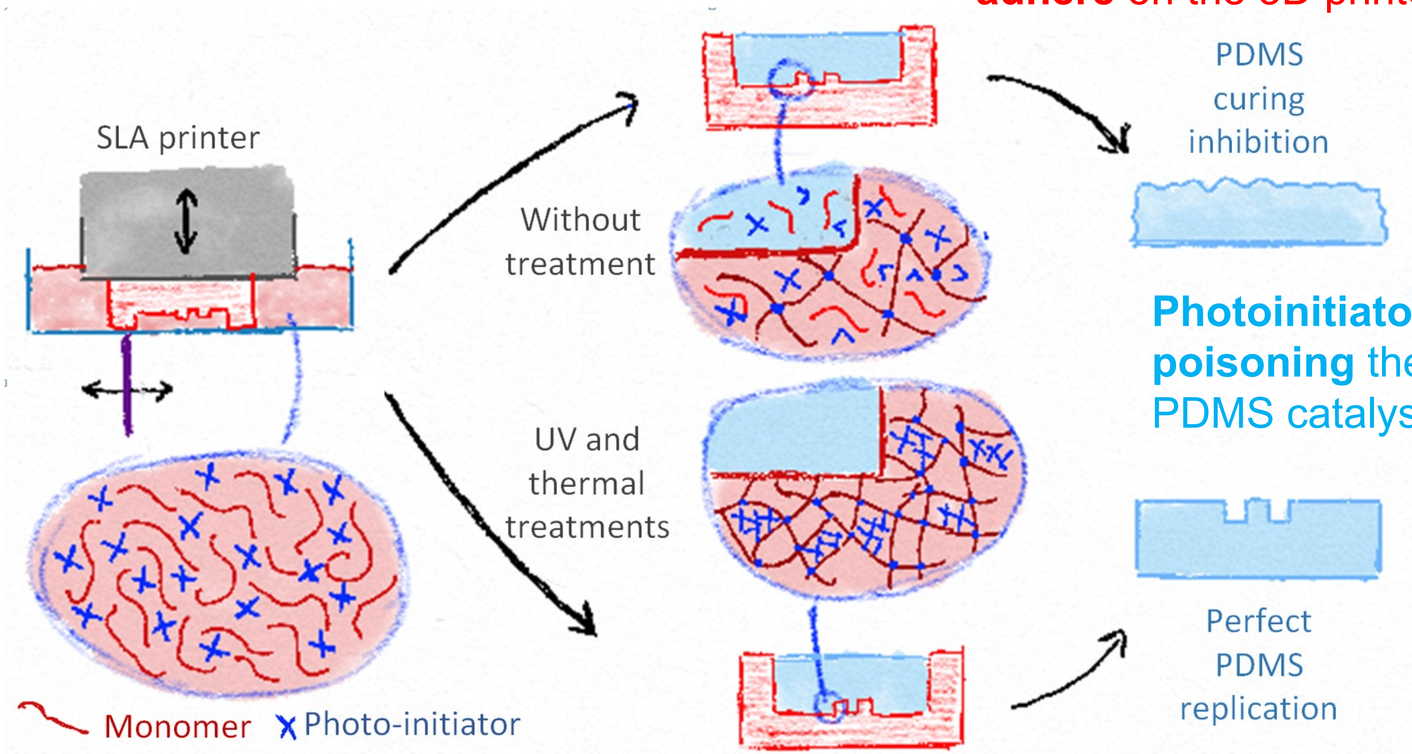


Source: doi.org/10.1021/acs.chemrev.7b00074

3D printed molds for soft-lithography

- PDMS curing inhibition (sticky material)
- PDMS adhesion on the mold

Monomers (acrylate) diffusing into the PDMS causing the PDMS to **adhere** on the 3D printed mold



Photoinitiator poisoning the PDMS catalyst

Post-treatment

- Further **polymerization**
- **Evaporation / vaporization** of small fragments
- **Recombination** of photoinitiator fragments into non-volatile compounds (larger MW)

SLA - stereolithography

Venzac et al., *Anal Chem, 2021*
doi.org/10.1021/acs.analchem.0c04944

Conclusion

- Late appearance of polymer-based devices in the field of LOC
- Development driven by the needs of a “single-use”-disposable-cheap-easy-fast produced device
- **Nowadays**: competitive and highly integrated polymer-based systems
- **Academic** research: mostly PDMS (cell applications…), casting-based fabrication with novel emerging fabrication method but also more and more hot embossing of thermoplastics, and 3D printing…
- **Industrial** applications (commercial LOC): mostly use of the polymer materials and large-scale production fabrication process: injection molding, injection compression molding
  - faster production
  - no back-processing
  - tunable surface chemistry (laser treatment)