Lecture Notes for 10.491
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Soft Lithography

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SOFT LITHOGRAPHY
Microfluidic Systems

micro total analysis systems (μTAS)
high-throughput chemical screening
biological assays
chemical/biological warfare detection
point-of-care testing
chemical synthesis

Harrison (U. Alberta)

Lab-on-a-chip (Caliper)

GeneChip (Affymetrix)
Advantages of Microfluidic Systems

- smaller volumes -- less reagent/sample consumption
- shorter analysis time
- increased throughput -- parallel analysis
- increased automation
- improved integration of sample steps
- easier fabrication
**Why not Silicon?**

- fabrication requires regular access to a cleanroom
- processing costs can be high and cycle times long
- limited range of materials can be patterned
- only planar structures formed
- chemical compatibility, physical and optical properties can be problematic for some applications

micro turbine engine (MIT)  multiphase microreactor (Losey)
**Fabrication in Glass**

- **Step 1:** Coat wafer with photoresist (1 - 2 microns).
- **Step 2:** Photoresist exposure; deposit Cr; lift-off metal.
- **Step 3:** Etch glass to form channel.
- **Step 4:** Anodically bond wafer to second wafer.

**Properties:**
- Compatible with silicon fabrication.
- Transparent.
- Insulating.
- Low autofluorescence.
- Cheaper than Si (?).
- Amorphous material.
- Incompatible with high T.

(Source: Microlyne)
Fabrication in Plastics...

- is cheap!
- doesn’t require routine access to cleanroom
- enables single use, disposable devices
- is performed in batch

but...

can have problems with dimensional stability
some autofluoresce

Micropatterned by:

- injection molding
- embossing
- molding
- (lithography)
Embossing Microfluidic Systems
PDMS-Based Microfluidic Channels

Courtesy of P. Kenis
Polydimethylsiloxane (PDMS) -- A Moldable Elastomer

\[
\begin{array}{c}
\text{CH}_3 \quad \text{Si} \quad \text{O} \quad \left( \text{Si} \quad \text{O} \right)_n \quad \text{Si} \quad \text{CH}_3 \\
\text{CH}_3 \quad \text{Si} \quad \text{O} \quad \left( \text{Si} \quad \text{O} \right)_n \quad \text{Si} \quad \text{CH}_3
\end{array}
\]

**Properties**
- moldable
- deformable
- chemically unreactive
- hydrophobic
- transparent in uv-vis
- insulating

**Applications**
- sealants
- adhesives
- protective coatings
- biomedical uses
- electrical potting
- microfluidics / microchemical reactors
Molding Plastics -- Soft Lithography

1. Photoresist on silicon wafer
2. Photolithography or advanced lithographic technique
3. “Master”
4. Cast PDMS (elastomer)
5. Remove elastomer from master
6. Elastomeric element

replica molding, microcontact printing, microreactor systems, near-field phase shift lithography, microtransfer molding, “dry” patterning, micromolding in capillaries

Rapid Prototyping

Create design in a CAD program

Print design on high resolution transparency

Use transparency to create photolithographic master

SU-8 Resist -- An Alternative to DRIE?

- negative resist
- aspect ratios ~15:1
- thickness > 700 microns
- line width > 25 microns (with R.P.)
Fabrication of Microfluidic Components by Replica Molding

1. Place posts on master to define reservoirs
2. Cast prepolymer and cure
3. Remove PDMS replica from master
4. Oxidize PDMS replica and flat in plasma to seal

**Irreversible Sealing of Polydimethylsiloxane (PDMS)**

- PDMS seals to itself, glass, silicon, silicon nitride, LDPE, PS
- PDMS seals after exposure to plasma of air, dry air or oxygen
Rapid Prototyping of Microfluidic Systems in PDMS

1. Idea

2. CAD File

3. Transparency Mask

4. Mold with Channels

5. Microfluidic Device

- high resolution printing (5080 dpi)
- 24 hours
- replica molding
- SU-8 photoresist (10-500 μm)

1. align
2. seal
Laminar Flow in Microfluidic Channels

\[ \text{Re} = \frac{l \cdot v \cdot \rho}{\eta} \]

- \( l \) = diameter channel (m)
- \( v \) = flow velocity (m/s)
- \( \rho \) = density (g/m³)
- \( \eta \) = viscosity (Pa.s or kg/m.s)
Fabrication Using Multi-Stream Laminar Flow

Apply different chemistries from different streams

From separate streams

Au etch
water

At the interface of streams

AgX
reductant

Fabrication of an In-Channel Three-Electrode System

Etch Au

Deposit Ag wire

AgX

reductant

H₂O

Au etch

PDMS mold placed on glass slide

100 µm

working electrode

counter electrode

reference electrode

Ag contact pad

to Au contact pad

In-Channel Three-Electrode System

Cyclic Voltammetry:

10 pmole Ru(NH$_3$)$_6$Cl$_3$
in 5 nL of H$_2$O
How to pump fluids through Microfluidic Channels?

• syringe pump (pressure driven flow)

• applied potential (electro-osmotic flow)

velocity = mobility * electric field
charged particles separated based on mass and charge (electrophoresis)
**Lab-on-a-Chip Based on Capillary Electrophoresis**

fixed charge on glass wall

anode (+)

reservoir

cathode (-)

microchannel (50 microns)

glass

net flow

electro-osmosis

molecules separated on based on charge to mass ratio

electrophoresis

mobile ions in solution

wall of channel

fixed charge on glass wall

mobile ions in solution
Capillary Electrophoresis

Typical system for CE:

- typical applied fields: ~100 - >1000 V/cm
- increase plug size with double-T injector
- detection typically by fluorescence

“racetrack” effect -- band of analyte become sloped around turn
Separation of Charge Ladder of Carbonic Anhydrase

Beckman CE spectrometer

PDMS CE-chip

detection
(confocal microscope)

injection

Gnd

+ kV

1 cm

Keeping Devices Compact -- How to make a turn?

how to keep devices compact?

Square Turn Motif

Tapered-Turn Motif

Replica Molding to form Liquid Phase Reactors

Si reactor mold
PDMS
PDMS
PDMS
Epoxy
Epoxy

62 µm
66 µm
Integrated Optics for Signal Acquisition

Decreasing flowrate, Increasing contact time

Absorbance

Wavelength (nm)

0.25 mL/min
0.1 mL/min
0.05 mL/min
0.01 mL/min
0.005 mL/min
0.001 mL/min
unmixed

Fiberoptic light source
Fiber optic detector
SU-8: An Alternative to Deep Reactive Ion Etching?

• epoxy-based, negative resist developed at IBM
• standard mask aligner used for patterning
• IC-compatible processing conditions

- thick layers are possible -- up to about 700 µm in a single coat
- high-aspect ratio (<15:1) structures can be achieved
- chemically resistant material
- multilayered structures are possible
- contoured surfaces can be planarized
Bonding with SU-8 to form Sealed Microchannels

1. Coat transparent substrate with layer of SU-8; partially pre-bake layer.
2. Bring wafers into contact at elevated T; blanket expose resist through pyrex; post-bake.
3. If necessary, dissolve release layer or perform fabrication on surface having poor adhesion.
4. All SU-8 structure (supported on pyrex).
**Bonding with SU-8 to form Sealed Microchannels**

- maintains dimensions and integrity of multilayered structure

- interface between bonded layers is not apparent

- SU-8 will bond other materials -- requires one uv-transparent layer for exposure step

- exact profile of resulting channel depends on bonding conditions
**SU-8 Based Microreactors**

- produced all SU-8 micromixer with minimum feature size $\sim 50 \, \mu m$
- demonstrated channels are sealed and fluid flow is possible

Photograph by Scott Brittain
**Hybrid Microreactor Devices for Electrochemistry**

- electrochemistry provides **direct control** of chemical reaction through applied voltage
- **dimensions** of microfluidic channels can be on the same order as diffusion lengths
- high surface-to-volume ratio maximizes area of electrode available for reaction
- **anodic oxidations** are reasonable candidates for model reactions
## Some Materials

<table>
<thead>
<tr>
<th>Fabrication</th>
<th>Optical</th>
<th>Structural</th>
<th>Bonding</th>
<th>Permeability</th>
<th>Pumping</th>
<th>Pressure</th>
<th>EOF</th>
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</thead>
<tbody>
<tr>
<td>Silicon</td>
<td>etching</td>
<td>rigid</td>
<td>anodic</td>
<td>-</td>
<td>-</td>
<td>EOF</td>
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<tr>
<td>Glass</td>
<td>etching</td>
<td>rigid</td>
<td>thermal</td>
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<td>pressure</td>
<td>EOF</td>
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<tr>
<td>Mylar</td>
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<td>'rigid'</td>
<td>thermal</td>
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<td>heat</td>
<td>vacuum</td>
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<tr>
<td>PDMS</td>
<td>molding</td>
<td>elastomeric</td>
<td>self-sealing</td>
<td>organics, gasses</td>
<td></td>
<td>pneumatic</td>
<td>EOF</td>
</tr>
</tbody>
</table>

**Material of choice depends on:**
- Application
- Prototyping vs. Mass production

Courtesy of P. Kenis