Review of Fabrication Techniques of X-ray Transparent Microfluidic Chips

Carried out in the CNSI μFL by Andrew Furst with funding from BioPACIFIC MIP; oversight provided by Dave Bothman.

Project goals

- Facilitate research for groups exploring X-ray microscopy of microfluidic devices
- Evaluate published channel construction processes using µFL resources
  - Direct Milling
  - Laser Cutting
  - Embossing
  - Thermal Pressure Molding
- Evaluate published bonding processes using µFL resources
  - Thermal Bonding
  - Solvent Bonding

Constraints

1. Material
    a. X-ray transparent
    b. Bondable with available resources
2. Geometric
    a. Y-mixer
    b. 2:1 or 3:1 depth to width ratio specified by Prof. Helgeson
    c. 500 micron to 2mm channel width
    d. Approx microscope slide dimensions
    e. Convenient connection to pumps
3. Scientific
    a. Minimize top/bottom channel thickness to reduce X-ray scattering/absorption
4. Manufacturing
    a. Maintain optical clarity of COC

Material Selection

- Typical Microfluidic devices Constructed from of glass and PDMS
  - Allows for casting at room temperature as PDMS is thermoset polymer
  - Not X-ray transparent
  - Relatively easy to bond utilizing ozone or plasma surface activation
- COC
  - X-ray transparent
  - 2 grades tested
    - 6013M-07 w/ Tg of 142 °C
    - 8007X-04 w/ Tg of 78 °C
  - Difficult to bond
  - Thermoplastic

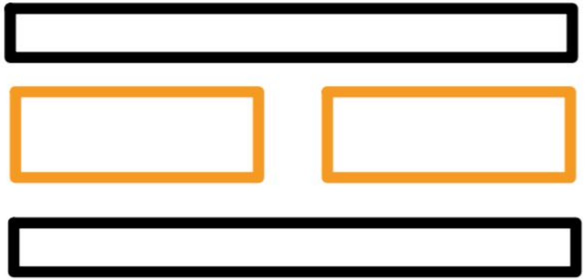
Two vs. Three Layer Chip Design

Two Layer Chips

- Fewer bonds/failure points
- Requires polishing of channel floor
- Able to take advantage of mixing COC grades
- Construction methods:
  - Direct Milling
  - Thermal Embossing
  - Thermal Pressure Molding

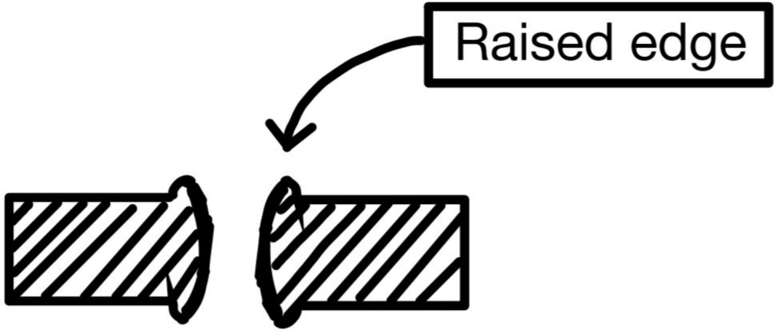
Three Layer Chips

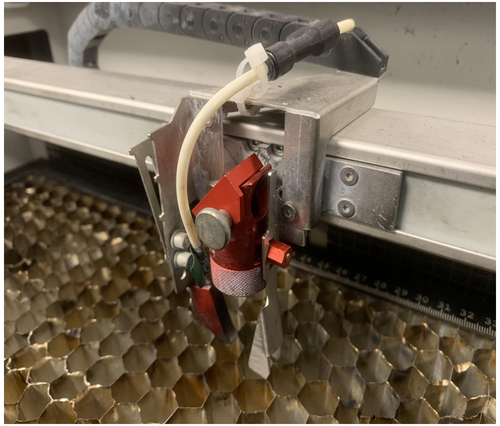
- Through channels
- Able to take advantage of mixing COC grades
- Allows use of non transparent channel plate
- Construction Methods
  - Laser Cutting
  - Direct Milling
  - Thermal Pressure Molding



Laser cutting

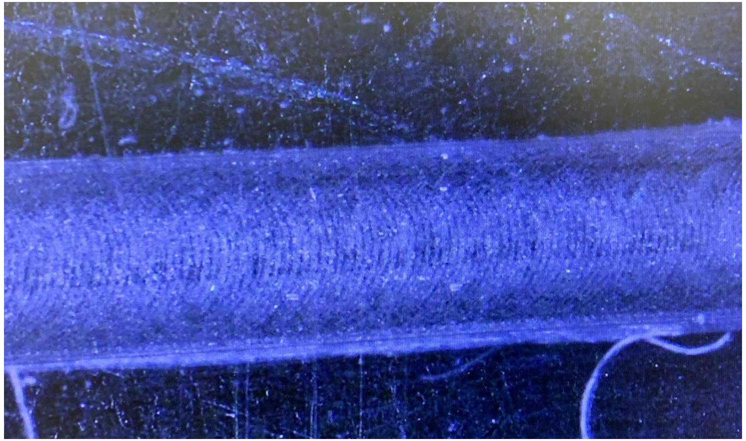
- Capable of creating through channels
- Creates raised edge which must be removed before bonding
- Induces thermal stresses into base material causing crazing if exposed to non polar solvents
    - Can be reduced if annealed





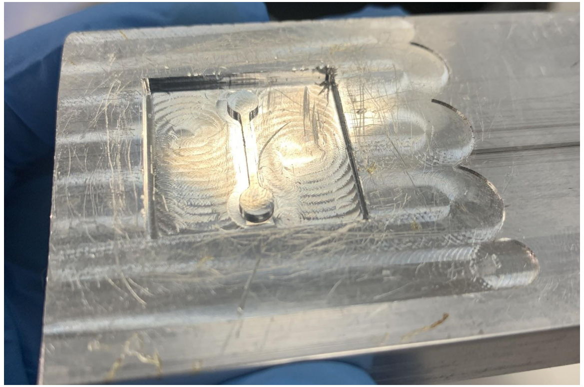
Milling

- Creates sharpest and most accurate channels
- Limited by tool length and tool diameter
- Requires coolant while milling to avoid melting of base material
- Capable of creating both through and partial depth channels



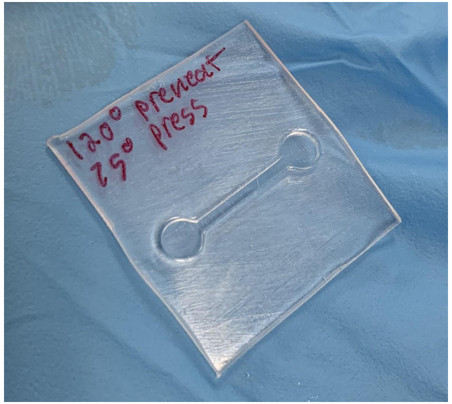
Hot press pressure molding of 8007X-04 COC pellets

- Mimicking injection molding commonly used in mass manufacturing
- Requires construction of metal master mold for each design
- COC preheat of 210° C and 60° C press temp
- Requires pressure exceeding 2 tons
- Increased risk of trapping bubbles



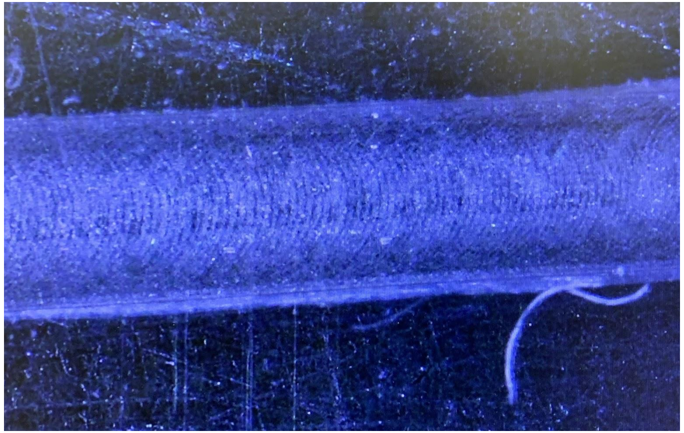
Hot press embossing of 8007X-04 COC sheet

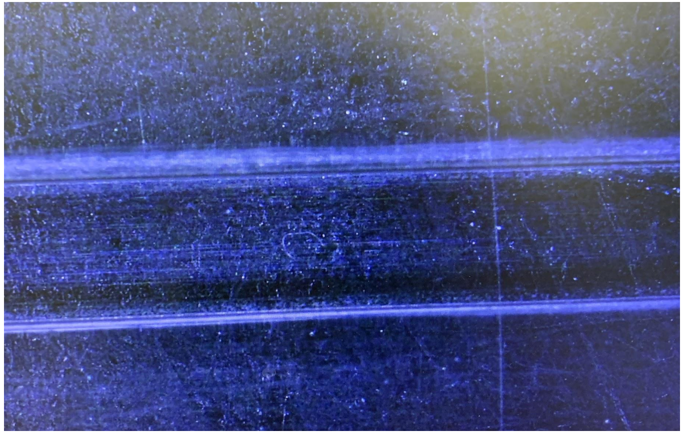
- Requires construction of master mold for each design
- COC preheat of 120° C and 60° C press temp
- Variety of available mold materials including 3D printed options
- Requires less pressure than pressure molding



COC Polishing

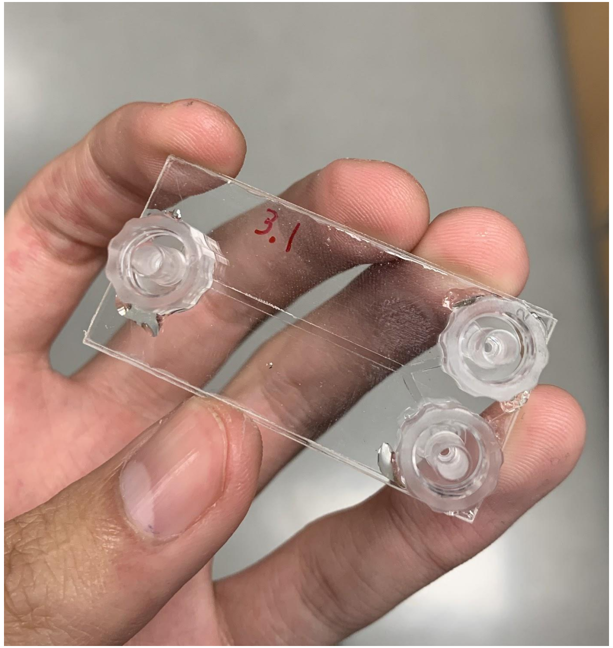
- Required for all partial channels to improve channel floor clarity
- COC sheet polished with NOVUS plastic polish
- Progressive polishing from NOVUS 3 to NOVUS 1
- Polishing done by hand, documentation references rotary polishing





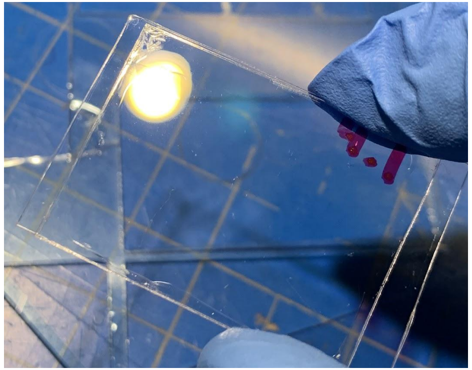
Thermal Bonding

- Preferred method of bonding due to consistency
- Occurs below the Tg for minimal distortion of channels
- Required ozone treatment before bonding
- Able to bond both sides of a three sided chip simultaneously
- Can take advantage of different Tg during bonding
  - Higher Tg for top/bottom plate resulting in less warping of thin sheet



Solvent Bonding

- 40% cyclohexane in acetone by volume
  - Over exposure of COC to cyclohexane results in pitting and fogging of surface
- Difficult to achieve consistent bonding without trapping air bubbles
- Only necessary to expose one bond surface
  - Allows for patterning of immobilized bacteria or proteins on channel surface without risk of denaturing
  - Only channel plate exposed reducing risk of pitting on channel floor/ceiling
- Less pressure required than thermal bonding < (½ ton)



Optical sample of solvent bonded COC

Choosing Fabrication processes

Channel Construction

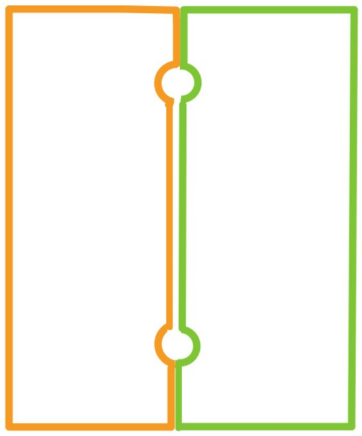
- Laser cutting of through channels is acceptable if COC sheet matches channel depth
- CNC milling of channels has the advantage of consistency and reduced post processing at the expense of requiring a skilled machinist
- Embossing or pressure molding channels are preferred if large numbers of identical devices are required to compensate for the expense of the initial set up
- Embossing is preferred over pressure molding due to time and chip consistency

Bonding processes

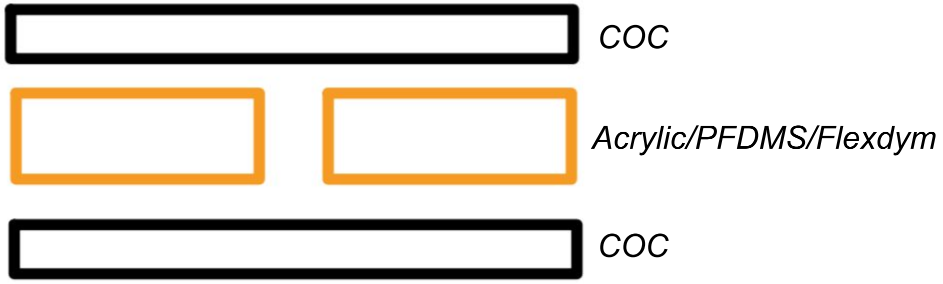
- Thermal bonding is generally preferred as it is more consistent and requires less preparation than solvent bonding
- Solvent bonding is preferred if patterning of immobilized organic material is required
- Solvent bonding has the advantage of only exposing one bond surface

Unexplored territory

- Multi part channel plates
- Polishing mold to improve COC channel floor surface finish
- X-ray opaque channel plate
  - 3 layer chip
  - Wider range of available channel plate material
- Laminating sheets for deeper channels



Multi part channel plate example



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- GDenz, M.; Brehm, Gerrit and Hémonnot. Cyclic olefin copolymer as an X-ray compatible material for microfluidic devices. *Proceedings* **2018**, http://dx.doi.org/10.1039/C7LC00824D

Material Introduction

COC Grade	Industry Name	Supplier	Tg °C	Thickness (micron)	Quantity
8007X-04	EUROPLEX OF304	Roehm America LLC	78	1000	1 x A4 sheets
8007X-04	EUROPLEX OF304	Roehm America LLC	78	240	2 x A4 sheets
6013M-07	EUROPLEX OF305	Roehm America LLC	142	240	1 x A4 sheets
8007X-04	TOPAS	PolyPlastics	78	NA	.4 kg
6013M-07	TOPAS	Microfluidic Chipshop	142	1000	20 slides

Mold Material Spreadsheet

Mold Material	Supplier	Machine	HDT, °C @ 1.82MPa	HDT, °C @ .45 MPa	Tg	Tensile Strength (mpa)	Notes
RGD 450	Stratasys	Objet	47		50	43	
RGD 525	Stratasys	Objet	80		63	75	Requires post processing to reach 80 °C HDT
High Temp	FormLabs	FormLabs V2/3	101	238		48.7	Requires post processing to reach 101 °C HDT
LOCTITE® IND147	Henkel	MiiCraft	107	238		72	Requires post processing to reach 107 °C HDT
Aluminum	McMaster	HAAS	NA	NA	NA	241	