Shrink-based Device for Protein Purification
Product and Purpose

Current Protein Ultrafiltration Methods
- Direct/Dead End Filtration
- Cross Flow Filtration

Problems
- Formation & Size Control of Membrane Pores
- Biofouling of Pores by Protein Adhesion

Target: Shrinkable Polyolefin Microchannels for Direct Microfluidic Filtration
- 1 µm minimum feature size
- Sperm, the smallest cells in the human body, have a diameter of approx. 3 µm
- Direct filtration of paracrine signaling molecules from organ-on-a-chip cell culture for ELISA analysis
Fabrication Methods

- Fabrication of microscale mold by silicon RIE or even low cost 3D SLA printing
- Hot emboss of shrink polyolefin
- Abrasion to change shape memory
- Surface modification to prevent biofouling
- Heat shrink reduces horizontal features by a factor of 4-5
Design - Hot Emboss and Functionalization
Design - Hot Emboss and Functionalization

- Simple Pattern
- Oversized Channels
- Easy Functionalization
Design - Isotropic Shrinkage
Design - Isotropic Shrinkage

Channel Size Meets Design Specification

Surface Retains Functionality

Bond Points for Rigid Reservoirs
Design - Bonded Silicon Reservoirs
Design - Bonded Silicon Reservoirs

Channels Designed to Align with Reservoirs

Identical Silicon Reservoirs
Design - Glass Bonding

- Built in Reservoir
- Access Ports
- Glass Top Bonds and Seals Components
Fouling and Biocompatibility

- TiO2 layer thickness can be adjusted to finely tune hydrophobicity, which plays a large factor in reducing fouling and protein adsorption\(^1\)
  - The thinner the layer, the more hydrophobic the surface will be
- Heat shrink temperature also plays a role in the wetting of the surface due the rate of crystallization
  - The higher the temperature, the more hydrophobic the surface will be
To further reduce the fouling of the device, and to ensure that the proteins never adhere to the surface, we will also be making the surface inert using the PEGylation (polyethylene glycol) method discussed in class.

While typically it would be difficult to modify the surface of such a small device, we are able to do it large scale, and then shrink the device down.

All of these changes will result in a device that will not be fouled by proteins, which will reduce the rate at which it needs to be replaced.
Testing

- Device flow rate can easily be determined from simple calculations involving pressure, volume, and time.
- The reservoirs can be designed to easily accommodate for current characterization techniques.
- Biofouling resistance could be tested by continuously running material through the device and measuring the flow over time.
Limits of Technology

- One uncertainty of the device is how the surface modifications made on the large scale device, mainly PEGylation, will react when the device is heated and the polymers are pushed closer together.
- The material being shrunk down is limited to shrink polyolefin.
Current Anti-Protein Fouling Methods

- Polyethylene glycol (PEG) Surface Coating (et al., Upadhyayula)
  - Suppress adhesion between glass surfaces and polymers.
- Polymer Coatings for paper (Munch et al., 2018)
  - Copolymers were grafted onto cellulose model layers and filter paper.
  - The layers were synthesized using cellulose films that were fabricated on silicon wafers.
  - Cell adhesion experiments on the cellulose film show anti-fouling against gram positive and gram negative bacteria.
- Fish Protein Coating (Pillai et al., 2009)
  - Protein extracted from fish reduced bacterial adhesion on a variety of surfaces like tissue culturing polystyrene.
    - The study tested its effect on human serum albumin (HSA) and fibrinogen (Fg) repellency.
    - Fg = involved in blood clotting and inflammation.
Current Filtrations on a Chip

- White Blood Cell Filtration (Cheng et al., 2016):
  - Used bidirectional micropump & polycarbonate microporous membranes to prevent clogging
  - 72.1% of WBC were recovered.
  - Throughout of $37.3 \mu l/min$
  - Recovery Rate was recorded to measure the amount of retention or leakage within the chip.
  - Purity was calculated to determine the separation ratio.
  - Results:
    - 1858 -fold enrichment, 90.9% purity, 99.9% removal efficiency.
Questions??