Biomimetic Intestine for Traction Force Studies

BME Design 300/200

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Client Information

Figure 1: Professor Murrell
(Image taken from http://directory.engr.wisc.edu)

Professor Michael Murrell

- Biomedical Engineering
- Material Science and Engineering
- Interests
  - Molecular, Cellular, and Tissue Biomechanics
  - Systems Biology
  - Cellular Engineering
  - Cell Motility and Tissue Dynamics

Problem Statement

Fabricate a micro-scale model of the 3D structure of villi in the intestines. The goal of the project is to create rounded villi structures of varying diameters and heights on collagen scaffold. This scaffold will then be seeded with epithelial cells in order to create a biomimetic intestine model. This project seeks to create a model in which the cell-to-cell forces that cause progressive movement on villi can be measured

Biological Background

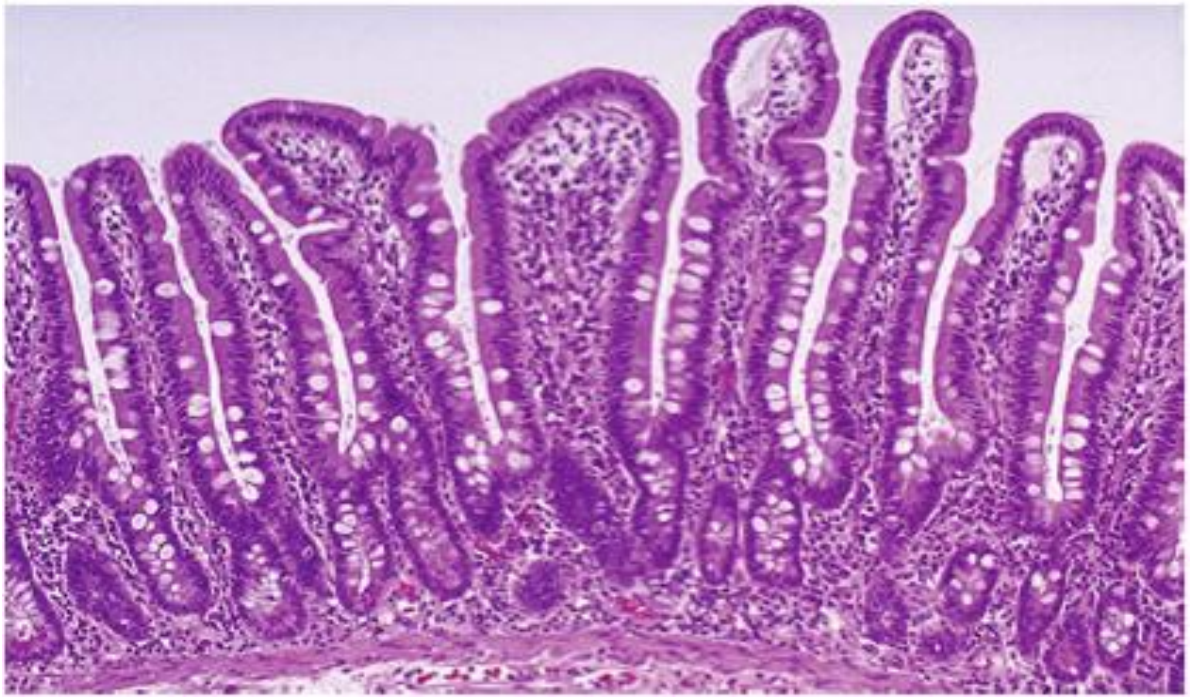
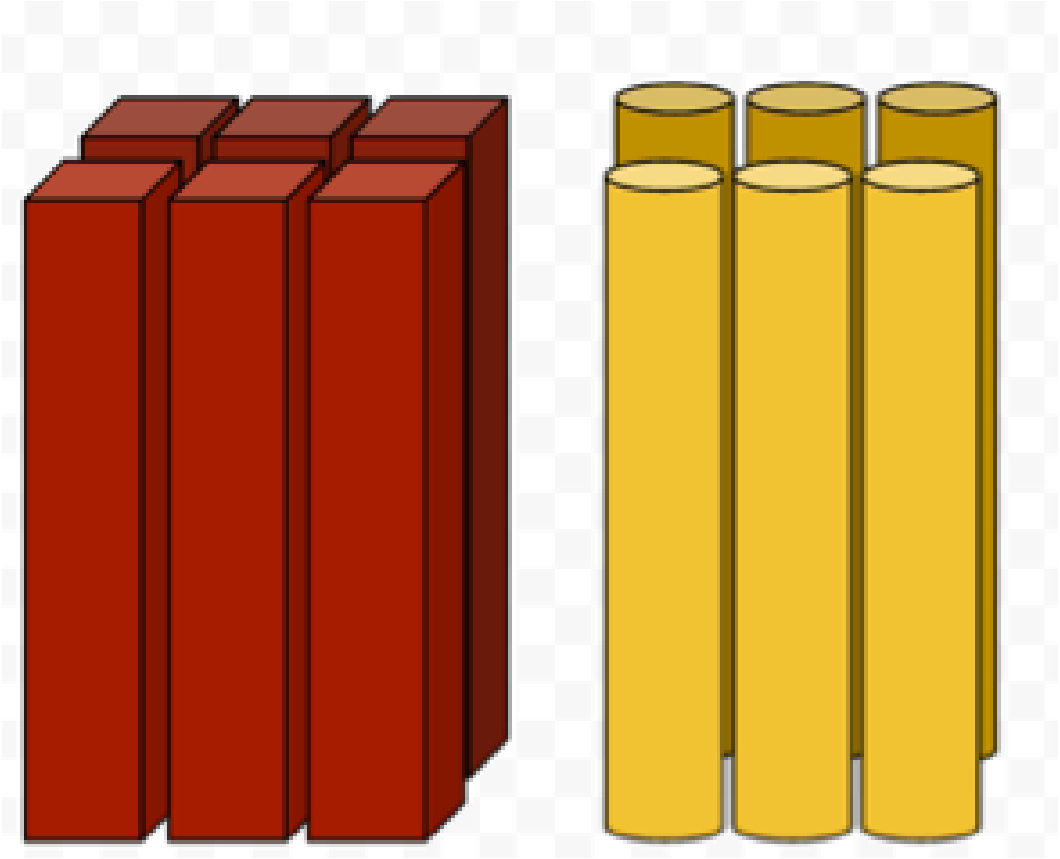


Figure 2: Light microscopy image of crystal violet stained, human small intestinal villi (Image from http://www.medical-terms-glossary.com/Images/celiac-sprue.jpg)

- Villi in small intestine
- Coordinated movement from crypt to point
- Lifecycle 24-48 hours

Conventional Methods for 3D Topography Generation



- Replica Molding
- Photo-polymerization
- Micro-contact printing

Figure 3: Standard 3D topography (Image generated using Google Draw)

Client Goals

- 3D Topography of intestinal villi
  - Tapered/rounded top cylinder
- Master mold
- Seeding of stem cells onto final collagen scaffold

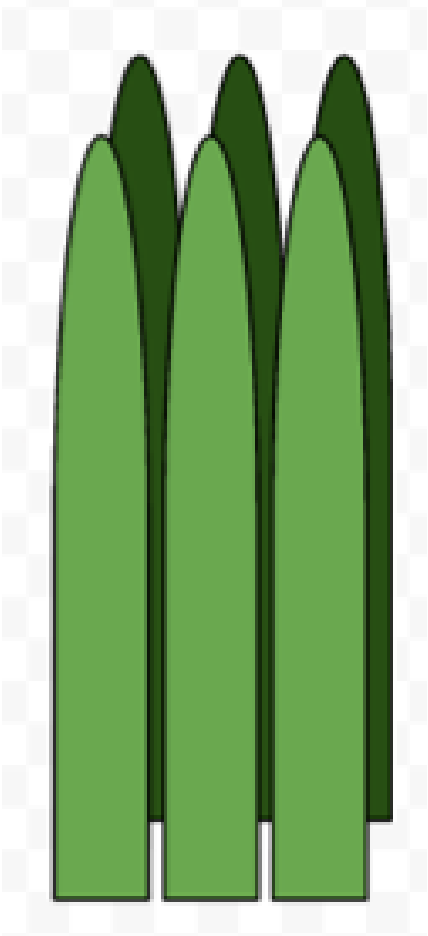


Figure 4: Villi topography (Image generated using Google Draw)

Client Specifications

- 250 um spacing
- Diameter: 5-500 um
  - (10, 50, 100, 200, 300, 400 um in 1 cm^2 sections)
- Height: ~1mm
- 7x1 cm^2 master mold
- Budget: $1000

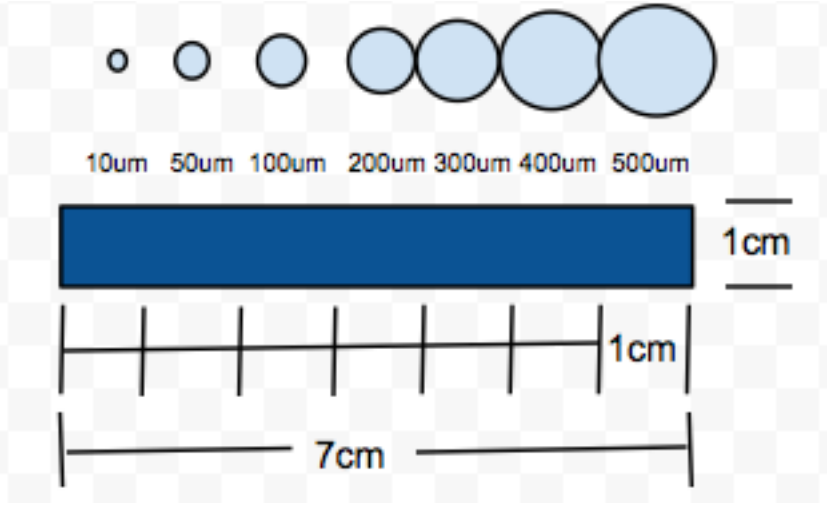


Figure 5: Master mold with 1cm^2 of each diameter (Image generated from Google Draw)

Methods for Collagen Scaffold Generation

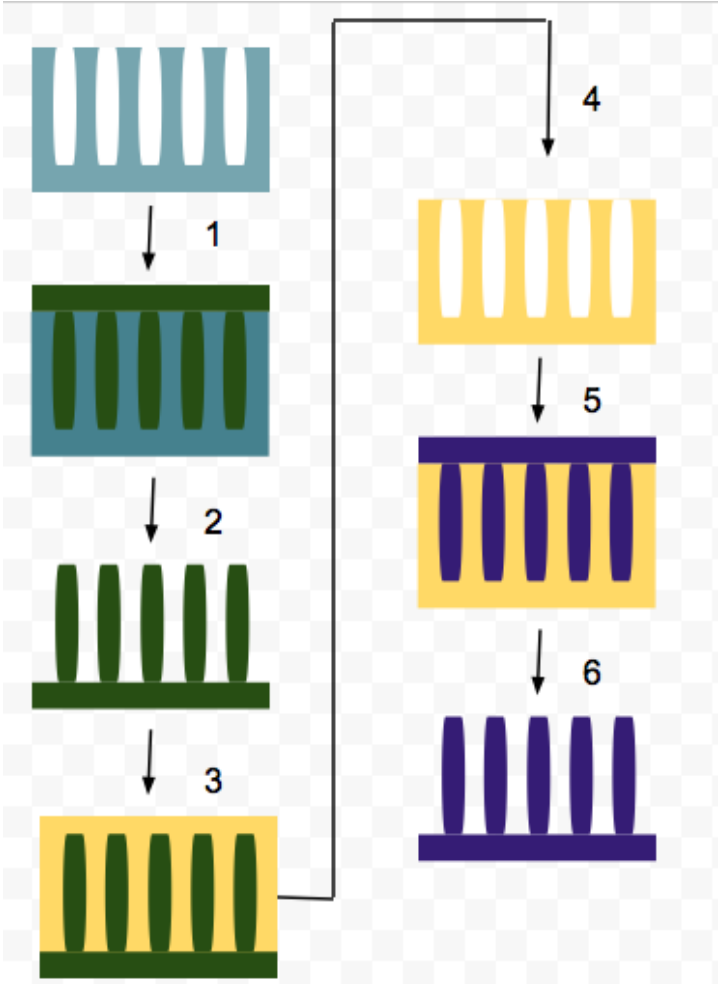


Figure 6: Methods for collagen mold generation (Image generated on Google Draw)

- **Master Mold**
- **PDMS**
- **Alginate**
- **Collagen**

Legend:
Blue = Master Mold
Green = PDMS
Yellow = Calcium Alginate
Purple = Type II Collagen

Multi-photon Excited (MPE) Photochemistry

- Campagnola lab
- Possible dimensions
  - Height: 1-1000 um
  - Diameter: 1-500 um
- Can be formed with SU-8

CO2/UV Laser Ablation

- Polymethyl methacrylate (PMMA)
- Software controlled laser etching
- Time = height

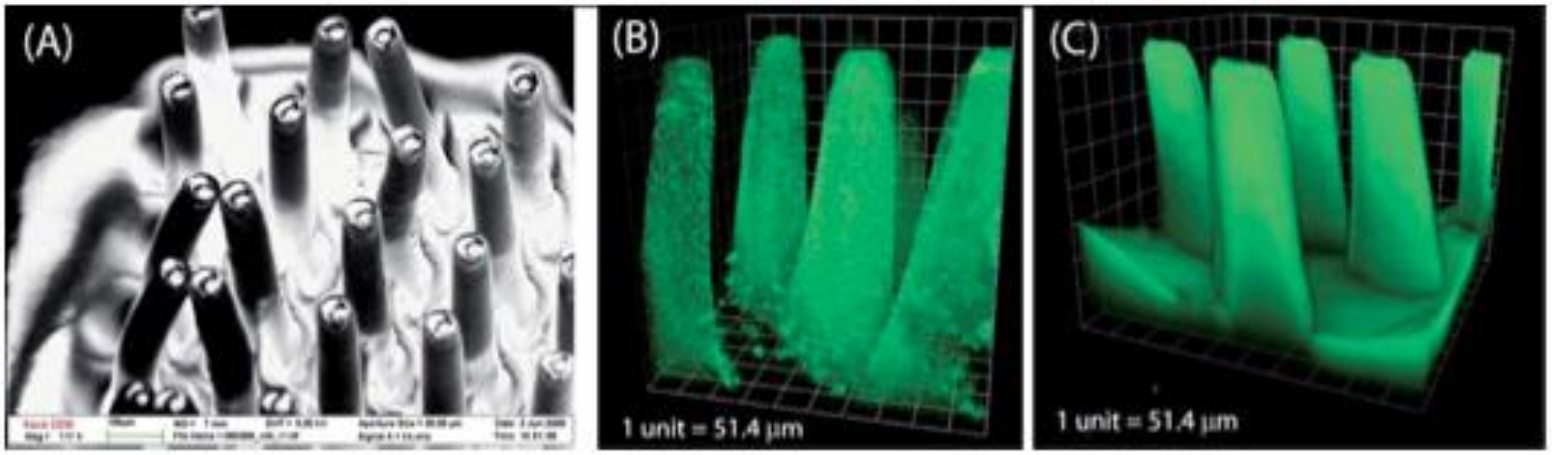


Figure 7: (A) SEM of PDMS (B & C) Confocal microscopy of collagen (Image from Sung et al., 2011)

CO2/UV Laser Ablation

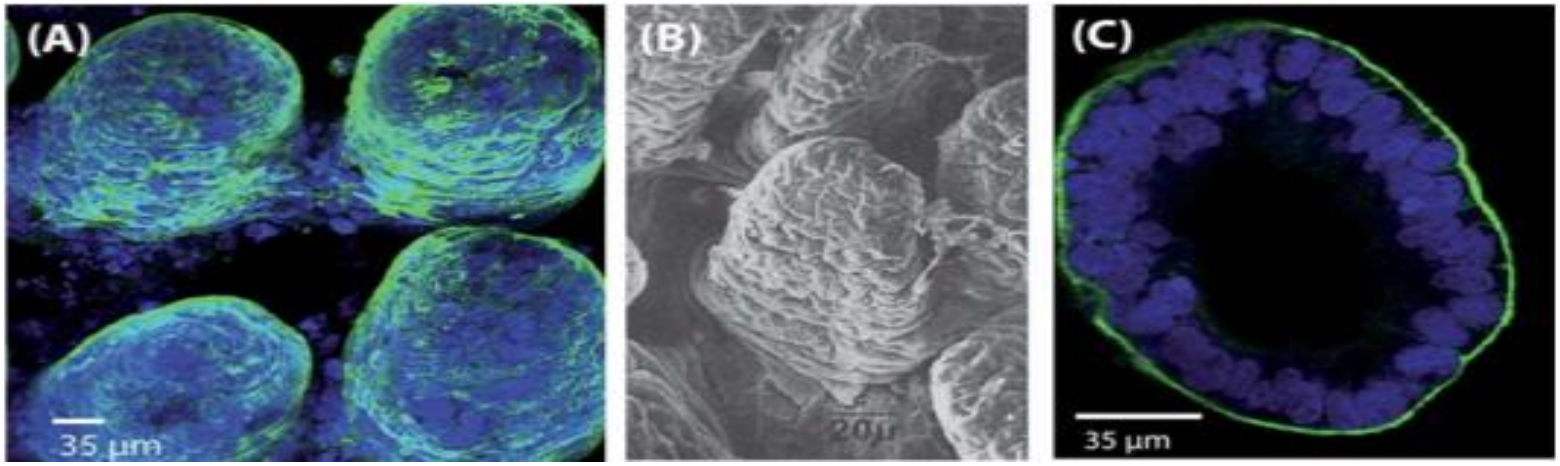


Figure 8: (A) Confocal of cells on collagen (B) SEM of human (C) Confocal of collagen (Image from Sung et al., 2011)

UV-LIGA

- Photo-mask
- Ti/Au coating
- UV-lithography
- SU-8 microarray

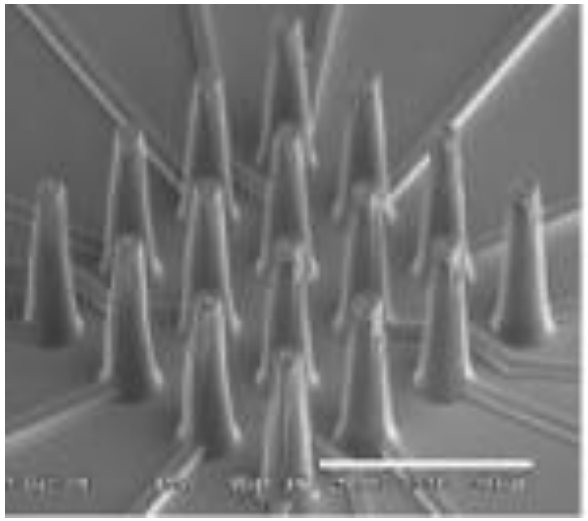


Figure 9: SEM micrograph of UV-LIGA fabricated micro-needle array (Image from Yang et al., 2012)

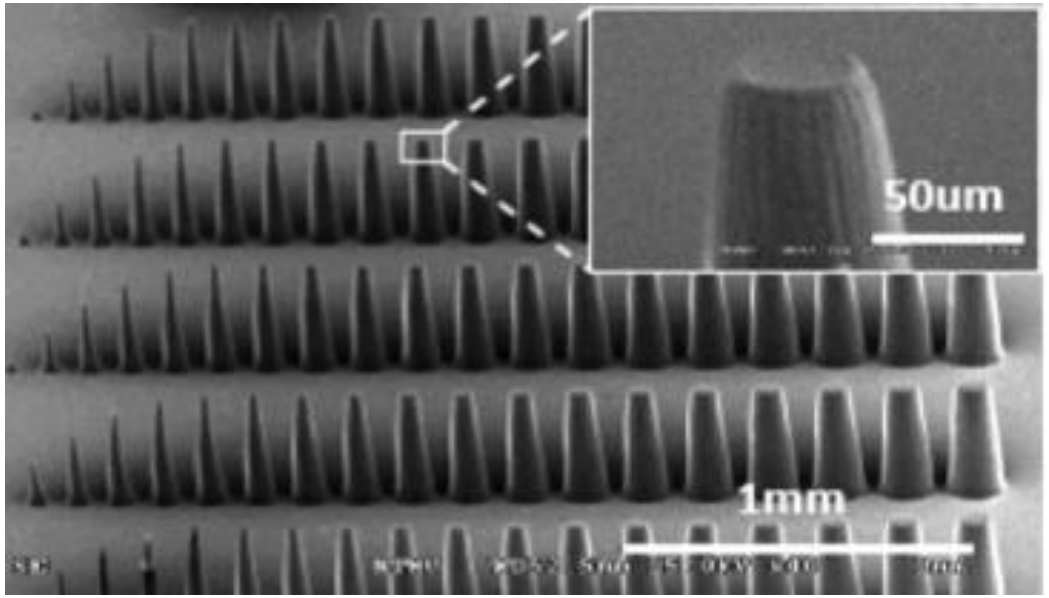


Figure 10: SEM micrograph of UV-LIGA fabricated SU-8 (Image from Yang et al., 2012)

Design Matrix

Design Criteria (Weight)	Laser Ablation		MPE Photochemistry		UV-LIGA	
Ease of Fabrication (25)	4	20	3	15	2	10
Access to Equipment (15)	3	9	5	15	1	3
Reproduceability (15)	5	15	1	3	4	12
Training (15)	4	12	5	15	2	6
Time (10)	5	10	3	6	2	4
Cost (10)	5	10	3	6	2	4
Durability (5)	3	3	3	3	3	3
Safety (5)	3	3	4	4	3	3
Total (100)		**82**		**67**		**45**

Future Challenges

- Deformation of diameter and height
  - Cell seeding
  - Methods
- Removal of PDMS from master mold
- Locating equipment

Literature Cited

- Sung, J.H., Yu, J., Luo, D., Shuler, M.L., March, J.C. 2011. Microscale 3-D hydrogel scaffold for biomimetic gastrointestinal (GI) tract model. Lab Chip 11: p389-392
- Yang, W., Chen, Y., Huang, Y., Fu, Y., Tang, S., Fu, C. 2012. Engineering a biomimetic villus array for in vitro three-dimensional culture of intestinal epithelial cells. Journal of Microelectromechanical systems 21(6): p1418-1425
- Yu, J., Peng, S., Luo, D., March, J.C. 2012. In vitro 3D human small intestinal villous model for drug permeability determination. Biotechnology and Bioengineering 109: p2173-2178