Synthetically Tuned Gut-Brain-Axis Communication
Human Performance and Biosystems Program Review
October 15, 2020

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Optogenetically Activated, Cross-Kingdom Signaling in an ENS-and-Gut-on-a-Chip
Part I: Engineering the Bacteria Delivery System
Synthetically Engineered Bacteria on U-Shapes Robot

Previous approaches of others (Ron Weiss and Vijay Kumar groups.)
Controlling Particle Location in Microfluidic Devices

Behrens et al., *Scientific Reports*, 2020.
Potential for Point-of-Care Diagnostics

Outreach: Five Pitt students completed paid summer internships, building and programming these at their homes across PA. All 5 have abstracts/posters at the annual BMES meeting this week! 4/5 = women.

Behrens et al., *Scientific Reports*, 2020.
Endothelial Cell Response to Generated Flow

Behrens et al., *Scientific Reports*, 2020.
Upgrade Particle to Steerable mini/μRobot

Fuller et al., *Micromachines* (in review).
Magnetic Robots to Steer in an Organ-on-a-Chip
Motion Control of Robot

Basic Joystick Control
Motion Control of Robot
(Similar to OpenAI and Robot Hand Rubik’s Solver)

1: Read frame
2: Convolutional neural network
   - Raw pixels
   - Convolution and max pooling
   - Dense network
   - Output Actions
3: Return commands to electromagnetic coils

Behrens et al., in preparation.
Machine Learning Step

1: Read frame
2: Convolutional neural network
3: Return commands to electromagnetic coils

Behrens et al., in preparation.
Organ-on-a-Chip Translational Applications

Potential Applications

A  Organ-on-a-Chip Technologies as a Testbed for Microrobots

B  An Organ-on-a-Chip

C  Drug-carrying Microbiorobot

Fuller et al., Micromachines (in review).
Part II: Engineering the Mammalian On-Chip Environment
FRESH 3D Bioprinting

• **Freeform Reversible Embedding of Suspended Hydrogels (FRESH)**

• Gelling fluid bioink is embedded into sacrificial support material

• Bath behaves as a yield stress fluid

• BioInk is uniformly supported during printing while it gels

• Support is melted to retrieve print

CAD file design to be printed with alginate and the three scored outputs: (a) grids, (b) free-floating printed fiber diameter, and (c) corner radius.
Printed alginate features.
Printability plots representing the interplay of the two strongest variables, flow rate Q and translational speed VT.
Using Machine Learning to Diagnose Decidual Vasculopathy

• Pre-eclampsia is one of the most common diseases in pregnancy
• Disease indicated by lesions caused by lack of oxygen through placenta – called decidual vasculopathy (DV)
• Analysis of maternal region can predict pre-eclampsia in subsequent pregnancies
  • In large hospitals, placentas from healthy deliveries are typically discarded

Hierarchical Framework

Assessment: 35 of 181 slides

181 slides:
11610 low-resolution patches
25% with DV

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Vessel Classification Data

• Principal component analysis to map latent space into two orthogonal dimensions with the highest variance of the data
• Useful to visualize potential clusters of high dimensional data
Labral tear MRI analysis
• Can deep learning be used effectively with small imaging datasets?
• How can transfer learning improve algorithm training?
• Medical images, 3D images
• Cartilage-like ring around shoulder socket • Commonly torn in overhead throwing athletics • Current diagnosis achieved with contrast enhanced MR arthrogram • Goal: achieve comparable results by analyzing unenhanced MRI
Objectives:

(1) Create a signaling pathway between programmable bacterial and neural cells for gut reprogramming.

(2) Develop a microbiome-and-innervated-gut-on-a-chip system.

(3) Discover and determine optimal interkingdom signaling motifs in the innervated microbiome-gut model system.

Technical Approach:

• Create and probe an interkingdom synthetic bacteria – mammalian cell pathway.

• Discover and determine interkingdom signaling motifs between gut and brain using synthetic biology and organ-on-a-chip technologies.

• Recent: Optimization with AI-Machine Learning

Accomplishments:

• 17 journal articles published, in press, or submitted citing AF award

• Expanded our approach to include Artificial Intelligence/Machine Learning for Organ-on-a-Chip Systems

• Developing new microrobotic techniques for modulating cross-kingdom interactions in organs-on-a-chip.

DoD Benefit: Interkingdom synthetic pathways in a microdevice are the cutting edge of biomimetics. Personalized Devices would ultimately lead to optimized individual human performance. AI-ML applications to patient injury characterization.
PUBLISHED, IN PRESS, OR SUBMITTED ARCHIVAL JOURNAL PUBLICATIONS

- **Bone, J.M., Childs, C.M., Menon, A., Póczos, B., Feinberg, A.W., LeDuc, P.R., Washburn, N.R.,** Hierarchical Machine Learning for High-fidelity 3D Printed Biopolymers *ACS Biomaterials Science & Engineering* (submitted)
2019-2020 Archival Publications Citing AFOSR Support (Page 2)

- **PUBLISHED, IN PRESS, OR SUBMITTED ARCHIVAL JOURNAL PUBLICATIONS**
Thanks and Acknowledgements

- Our fantastic students and research staff.
- University of Pittsburgh and Carnegie Mellon University
- Funding Sources:
  - AFOSR and Dr. Pat Bradshaw

Thank you for your time, and interest!
Questions?