Electrodes fabricated on cell culture substrates have direct, real-time access to molecular dynamics

Motivation and Significance

- The Gut-Brain Axis (GBA) connects the Gastrointestinal (GI) tract and the brain via Enteric Nervous System (ENS) and the vagus nerve.
- Neural disease development is highly correlated with GI tract dysbiosis.
- Proposed pathway: Luminal stimuli induce serotonin (5-HT) release from enteric microorganisms, which activates enteric nerves and propagates signals to the brain.

We have a limited understanding of this dynamic pathway due to a lack of technology capable of real-time in situ serotonin monitoring from relevant tissue.

Electrodes fabricated directly on a cell culture substrate can monitor gut cells and their 5-HT release dynamics, to correlate specific stimuli with their influence on the GBA pathway.

Electrodes for 5-HT Detection

- 3D printed housing with cell-interfacial electronics
- Electrodes are integrated on a flexible, porous Transwell electrode, Au
- Cultured Enterochromaffin RIN14B cells
- ECIS: non-invasively monitor cell growth and reserve through CV: detect chemically-stimulated RIN14B basolateral release of 5-HT and diffusion through membrane
- 3-Dimensional Multimodal Sensing
- Top: Electric Cell-substrate Impedance Sensing (ECIS)
- Bottom: Cyclic Voltammetry (CV)

Functional In Vitro Sensing

Dynamic 5-HT detection

- Interfacial electrodes have close local proximity to the site of molecular release: real-time detection
- 5-HT released into nanoliter pore volumes: high local concentrations

RIN14B cell-released 5-HT

- Detection of 5-HT released from T75-cultured RIN14B cells. (Left) Schematic (Right) 5-HT measurement from cell supernatant before (blue) and after (red) stimulation with 10mM butyrate. Concentration calculated against standard curve: 1µg 5-HT released over 1 hour.

Multimodal measurements

Significance:

- Close proximity to molecular events – high time resolution of molecular dynamics
- Low pore volumes – high concentrations
- Multiple on-site electrode integration

Future Work

- Optimization of RIN14B cell culture and molecular detection on electrode-integrated membrane
- In vitro gut model: incorporate other epithelial cell types and gut bacteria
- Use EIS + CV monitoring to correlate bacterial colonization/degradation of the mucosa with effects on 5-HT release patterns → Uncover real-time GMBA signaling

References


Acknowledgements

This work was funded by the Brain and Behavior Initiative—BBI Seed grant. Travel funding was provided by the International Conference Student Support Award—KSSA. The authors would like to thank the staff at the Maryland Nanocenter for support in fabrication and imaging.

* Corresponding Author: Raja Ghodssi, Tel:+1-301-405-8166, E-mail: rhodssi@umd.edu