CARNEGIE MELLON UNIVERSITY
BME 2023 SPRING SEMINAR SERIES

Hybrid cardiac tissues: bioelectronic interfaces for monitoring and modulating cardiac function

PRESENTED BY

Brian Timko, PhD
Assistant Professor
Biomedical Engineering
Tufts University

SCHEDULE

Hall of Arts (HOA) 160

Thursday,
April 27, 2023
(11:00AM-12:00PM)

Hybrid bioelectronic systems offer a unique route toward two-way electronic communication with living cells and tissues. Recent advances in bioelectronics and bioactive materials have enabled multiplexed, stable and seamless interfaces with surrounding cells and tissues, representing a distinct advantage over conventional systems such as patch clamp and optical dyes.

We recently developed a multi-electrode array (MEA) platform that could integrate with cardiac monolayers at up to 32 spatially-distinct locations in vitro. In the first part of this talk we will discuss our recent heart-on-a-chip platform which integrated both extra- and intracellular recording elements for monitoring cardiac electrophysiology during episodes of acute hypoxia. This system allowed us to monitor not only cell-cell communication (e.g., wavefront propagation) but also action potentials (APs) at several spatially-distinct regions simultaneously. Our platform provided a unique route toward understanding the role of hypoxia on ion channel dynamics. For example, we found that APs narrowed during hypoxia, consistent with proposed mechanisms by which oxygen deficits activate ATP-dependent K + channels that promote membrane repolarization.

In the second part of this talk we discuss an integrated optogenetic and bioelectronic platform for stable and long-term modulation and monitoring of cardiomyocyte function. Optogenetic inputs were achieved through expression of a photoactivatable adenylyl cyclase (bPAC), that when exposed to blue light caused a dose-dependent and time-limited increase in intracellular cyclic AMP concentration and, subsequently, autonomous cardiomyocyte beat rate.Bioelectronic outputs from the MEA provided real-time readouts of cardiomyocyte behavior in response to optical modulation. Irradiation at 24 µW/mm 2 resulted in a ca. 17% increase in beat rate within 20-25 minutes of irradiation. Multiplexed readouts revealed that wavefront propagation rates throughout the monolayer remained constant between “on” and “off” states, demonstrating that optical modulation did not affect intercellular coupling. In addition, bPAC activation could be cycled through repeated “on” and “off” states via time-limited illumination or in a gradient fashion with 0.03-24 µW/mm 2 illumination. Cardiomyocytes could be modulated reproducibly over at least four days, demonstrating that bPAC expression as well as the bioelectronic interface were stable throughout that period.

Taken together, our studies demonstrate the feasibility of bioelectronic and optical techniques for monitoring and modulating cardiac function. We will discuss recent efforts in our lab toward 3D bioelectronics-embedded tissues and closed-loop feedback systems. We will also discuss potential clinical applications for cardiac regulation including arrythmia diagnosis and intervention.

BIOMEDICAL ENGINEERING
Carnegie Mellon University