#305 Jessica Feldman Advisor(s): William Lytton

Modeling network dynamics of cardiac right atrial ganglionic plexus towards enabling in silico testing of vagal neurostimulation

We present single-compartment computational models of right atrial ganglionic plexus (RAGP) neurons that incorporate ion channel models derived from transcriptomic data towards multiscale modeling of an intrinsic cardiac network (ICN) circuit. RAGP cells innervate the sino-atrial node (SAN) and are modulated by vagal input. We defined 3 initial RAGP principal neuron (PN) models based on different transcriptomic patterns identified in pig RAGP. Electrophysiological single compartment models were developed in NEURON utilizing previously developed ion channel models corresponding to particular channel isoforms identified in the transcriptomes. We were able to produce comparable spiking models with all 3 transcriptomes tested and are investigating differences across these. We also establish technical workflows to connect our neural modeling efforts to the NIH's O2S2PARC platform. We first implemented PN models in MATLAB, Python, and NetPyNE. In order to create similarly constructed RAGP neuron models, we mined the available raw RNAseq data for > 500 single RAGP cells (Moss et al., 2020), identifying relevant genes and surveying kinetic models for ion channels that correspond to those genes. We then constructed single-compartment models of theoretic RAGP cells based on gene expression in the transcriptomics data. Each model represents a novel combination of ion channels derived from transcriptomics data that follow the Hodgkin-Huxley gating formalism. These models consist of combinations of 8 ion channels and a leak channel to date and generate action potentials in response to modeled current clamp inputs. As experimental RAGP data demonstrate the presence of both cholinergic and catecholaminergic milieus, future directions include tuning our models to reflect behaviors based on differential inputs. This is relevant ultimately to control the SAN via vagal neuromodulation, with myriad potential applications to treatment of cardiac pathologies.