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Biophysical Models of Minipig Right Atrial Ganglionic Plexus Principal Neurons Identified from Transcriptomics Data

The Right Atrial Ganglionic Plexus (RAGP) is a component of the intrinsic cardiac nervous system. Its neurons are critical to the cardiac pacemaker response to vagal stimulation, regulating sino-atrial node activity. We developed single-compartment computational models of RAGP principal neurons by incorporating ion channels identified from transcriptomics data from HT-qPCR (High Throughput quantitative Polymerase Chain Reaction) and RNA-sequencing of 405 principal neurons in Yucatan minipig RAGP. Out of the ~200 genes in the transcriptomics map, we identified 13 genes that encode ion channel proteins, namely: Naf (Scn1a, Nav 1.1), KDR (Kcnc1, Kv 3.1; Kcna1, Kv 1.1), P-, N-, L-, T-type Ca2+ (Cacna1a, Cav 2.1; Cacna1b, Cav 2.2; Cacna1c, Cav 1.2; Cacna1g, Cav 3.1; Cacna1i, Cav 3.3), KA (Kcnd2) and HCN1, HCN2, HCN3, HCN4. The corresponding Hodgkin-Huxley-based kinetic models of these ion channel isoforms were mined from Ion Channel Genealogy, Channelpedia, and ModelDB. Since each ion channel gene had several kinetic models associated with it, we ran multiple simulations on the NetPyNE software to identify a single model per gene that would best represent the channel's dynamic behaviour in the assembled electrophysiological model. A binary transcriptomic map of the 13 genes showed 101 distinct ion channel combinations. Our 505 electrophysiological models (5 sets of the 101 cells) elicited two primary firing profiles. 65% elicited a single-spike phasic response, ~32% elicited a tonic firing in response to a current clamp stimulus, and ~3% produced tonic firing that continued after the stimulus. The firing frequencies increased by ~13 Hz for every 0.1 nA increase in the current clamp stimulus and decreased by ~11 Hz for every 0.01 S/cm2 increase in KA channel conductance. The models exhibit phasic and tonic excitability profiles with phasic being more prevalent. We next aim to incorporate neuromodulatory inputs and simulate a network of these neuronal models.