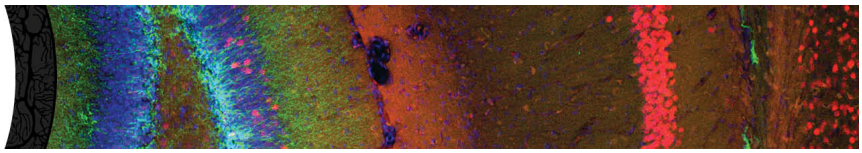

(https://www.abstractsonline.com/pp8/#!/10485)

Session P097 - Ion Channels: Modulation, Behavior, and Disease

Add to Itinerary

P097.12 - Ion-channel degeneracy and plasticity manifolds govern the emergence of circadian oscillations of neuronal intrinsic properties in the suprachiasmatic nucleus

November 11, 2021, 9:00 AM - 10:00 AM | Virtual Only

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Abstract

Organismal adaptation to the day-night cycle is achieved by circadian oscillators in most organs, which are synchronized by the suprachiasmatic nucleus (SCN). Neurons in the SCN undergo autonomous oscillations in their intrinsic physiological properties through changes in a subset of ion channels they express. However, it is not known if characteristic physiology of SCN neurons could be achieved through multiple ion-channel combinations or if there are several routes to achieve the circadian transitions in their physiological properties. In this study, we first employed an unbiased stochastic search (spanning 13 parameters involving 11 SCN neuronal ion channels) to construct a biophysically realistic population of SCN neurons with day-like phenotypes. We generated 30,000 models and found a subset of 128 valid models that manifested 9 different characteristic signatures of day-like SCN neurons. We found these valid models to manifest ion-channel degeneracy, whereby disparate ion-channel combinations were able to elicit similar characteristic functional outcomes, also expressing weak pairwise dependencies across model parameters. We next chose 20 day-like neuron models and subjected a specific subset of 6 ion channels to physiologically established directions of transitions, with transition magnitudes defined by an unbiased stochastic search algorithm. We validated these transitions employing 9 night-like physiological features, and found 719 valid night-like SCN models that manifested ion-channel degeneracy. We performed nonlinear dimensionality reduction analyses on these transitions and found the manifestation of ***plasticity manifolds***, structured low-dimensional manifolds in the space of all permitted changes, underlying day-to-night transitions. Finally, towards completing the circadian cycle, we picked 26 night-like neurons and performed an unbiased stochastic search on the magnitude of changes in the same subset of 6 ion-channel conductances, with directions of changes opposite to those for day-to-night transitions. Validation against day-like phenotypes yielded 1184 valid transitions, with the emergent day-like neurons showing ion-channel degeneracy but with a notable absence of structured plasticity manifolds in the associated transitions. These results pointed to the possibility that night-to-day transitions might have greater flexibility relative to their day-to-night counterparts. Together, our analyses demonstrate the expression of ion channel degeneracy in SCN neurons and points to the existence of structured plasticity manifolds in defining ion-channel transitions during circadian oscillations.