JOHNS HOPKINS UNIVERSITY

Kavli NEUROSCIENCE DISCOVERY INSTITUTE

"AP inference with Biophysical GECI Models"

Kavli Neuroscience Discovery Institute
Seminar by:

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Date: **Tuesday, March 6, 2018**

Time: 4:30 pm

Location: Clark Hall, Kavli NDI North, Room 316

Host: **Joshua Vogelstein**

Abstract: By detecting the calcium influx caused by action potentials (APs), multiphoton imaging of genetically encoded calcium indicators (GECIs) can record from the same spatially resolved neurons over multiple days in vivo. However, quantitatively inferring APs requires understanding their relationship to GECI fluorescence, which can be nonlinear and variable over neurons. Inference methods have been proposed based on thresholding, deconvolution, phenomenological modeling and deep learning, but these techniques do not incorporate existing knowledge of the biophysical processes linking APs to fluorescence and produce high error rates for many neurons. Here we introduce a sequential binding model (SBM) describing APs, calcium influx and extrusion, GECI binding state transitions, endogenous buffering and fluorescence generation. By imaging the calcium sensor GCaMP6s while electrically recording single neurons' APs in mouse visual cortex in vivo, we show that this model predicts AP-evoked fluorescence while capturing nonlinearity and neuron-to-neuron variability. Because all SBM parameters have physical interpretations, the parameters that vary over neurons can be chosen rationally and the same parameters can fit in vivo imaging and in vitro binding assays. To use the SBM for AP inference, we introduce a sequential Monte Carlo algorithm that identifies AP sequences consistent with fluorescence data given the model. This approach outperforms existing AP inference methods with more accurate firing rates, AP counts and AP times. With fewer parameters than "black-box" statistical methods, the SBM is less susceptible to overfitting, and can be fit on a single neuron of training data with only minimal reduction of AP inference accuracy. These results allow for more accurate optical interrogation of neural activity and serve to validate a model-based, biophysically grounded approach to the analysis of complex biological data.

Speaker Bio: David Greenberg is a postdoc in the Department of Brain and Behavior Organization at the CAESAR research institute in Bonn, Germany. He studied mathematics at Brown University before receiving his PhD in Neuroscience from Tuebingen University. He has worked on image and signal processing algorithms for AP inference and motion correction in two photon calcium imaging data, and on eye and head tracking methods for freely moving rodents.