Statistics in Neuroscience

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This quarter, I learned and applied various statistical techniques to find out how neurons respond to classical conditioning. The data we worked with were collected by researchers in the NAPE (Neurobiology of Addiction, Pain, and Emotion) lab at the UW using a novel technique called 2-photon calcium imaging. The dataset contained calcium presence measurements (dF/F) for several hundred neurons across several hundred time points and multiple trials. In the data collected, higher dF/F values meant more calcium was measured in the neuron at that time point. And higher calcium levels meant the neuron was firing more rapidly. Therefore, we can think of dF/F as measuring how active a neuron is at a certain time point. The goal of the analysis was to determine if the dF/F values in the pre-event window and post-event window are significantly different.

My first instinct for analyzing the data was to focus on a time-series approach. The reason was simple, the neuron data were recorded uniformly and sequentially over a period, which match the characteristics of a time series. I hoped to find a way of comparing the parameters of the time-series models to determine how similar/different two neuron signals are. I modeled the data with various time-series models including exponential smoothing, holt-winters, autoregressive integrated moving average (ARIMA), and locally estimated scatterplot smoothing (LOESS). However, I realized one challenge to this approach was I did not know a proper way of comparing the parameters of the fitted models. In the future, it would be interesting to explore unsupervised clustering approaches for model parameters.

After my initial time-series exploration, I changed directions and began looking from a statistical testing approach. The question of interest was if the mean dF/F was different in the pre-event and post-event windows. The first approach I used was the two-sample t-test. Unfortunately, the neuron data violated the independence assumption required for the test to be valid. Thus, I needed to find another approach to obtain valid p-values. My mentor introduced randomization tests and restricted randomization schemes to me. Randomization is a powerful way of approximating unknown distributions. I used randomization to create a distribution of t-statistics obtained from repeatedly shuffling the data. However, this approach had its own problem; the permutation test assumes the data is exchangeable. Exchangeability assumes any permutation of the sequence has the same joint probability distribution. Unfortunately, neurons tend to activate/deactivate gradually rather than jump volatilely between active and inactive states thus violating the exchangeability assumption.

Next, Ethan introduced me to restricted randomization schemes. Here, I got to be a little more creative. I came up with a few of my own randomization schemes including “k-chunking” and “criss-cross with uniform wrapping”. “k-chunking” is a restricted randomization scheme that breaks the data into chunks and shuffles the chunks before recalculating the t-statistic between pre/post event windows. The benefit of this approach is there is a large “palette” to draw the null distribution and the autocorrelation structure of the data is mostly preserved. However, this approach overrepresents neural spikes if such spikes are present in the data. To work around this, I decided to only compare pre-windows between different trials of the same neuron to obtain t-statistics that best resemble a null distribution of t-statistics. I named this approach “criss-cross with uniform wrapping”. More details of the restricted randomization schemes can be found in the slides.

Through the SPA DRP, I learned so much about the challenges and workarounds in statistical testing. Through Ethan’s guidance, I learned about many statistical and mathematical concepts previously daunting to me. My confidence in approaching new mathematical material has grown significantly throughout the quarter. I have so grateful to have had this wonderful experience and to have worked with such a supportive mentor. Thank you for having me!