Transmembrane voltage is often recorded during physiological study of biological neurons. However, voltage-gated ion channel activity and neurotransmitter levels are quite difficult to measure directly and are usually unobserved in such studies. In addition, there is a great diversity of neuron morphology, protein expression, and plasticity which may affect voltage dynamics and synaptic transmission (DeCarli et al., 2012; Kollins and Davenport, 2005). Early development and senescence may also be major determinants of voltage response profiles (Yeoman et al., 2012; Liu et al., 2012). Synaptic tuning in particular is thought to be an essential mediator of learning, stimulus response integration, and memory. There is evidence that memory and learning may depend critically on several distinct types of dynamic behavior in the voltage of neurons. In this project, we will develop parameter inference methods for coupled Morris-Lecar (ML) model neurons. Yu et al. (2008) have shown that this modest model can exhibit a wide range of oscillating or non-oscillating voltage depending on the values of just a few parameters.

In work resulting from the mentor’s previous REU, Cameron and Saladin (2012) show how to use cumulative power to build a conditioned likelihood for the ML model. For a twice differentiable signal $m(t)$, cumulative power $P(t)$ is defined as

$$P(t) = \int_0^t (m''(s))^2 \, ds$$

for real finite $t$. $P(t)$ is a useful feature statistic for a variety of models. For example, square-integrable functions, including bump functions, maxima/minima curves, and saturation curves all have $P(t) \in O(1)$. In contrast, any finite sum of sines and cosines have $P(t) \in O(t)$ (Quinn, 2011). By way of Fourier representation, this $O(t)$ behavior characterizes a broad array of continuous periodic functions (see proof in Appendix). Surprisingly, it has even been shown that $P(t) \in O(t)$ in a class of linear stochastic dynamical systems lacking differentiability at countably many times (Bates et al., 2012). In all such cases $P(t) \in O(t)$ has the intuitive notion that dynamical systems exhibiting consistent (stationary) duty cycle will accumulate power (on average) at an constant rate. For periodic oscillating functions such as the voltage in the ML model, the graph of the cumulative power is linear. In this proposed project we will expand on these previous results to a variation of the model where synaptic noise or stochasticity is present.

In this project, participants will be introduced to Matlab\textsuperscript{TM}, become comfortable generating and working with data sets, and become acquainted with conditional likelihood procedures in Markov Chain Monte Carlo (MCMC). Participants will be introduced to various features which can be measured on canonical dynamical systems. These include statistics like frequency, peak amplitude, inter-peak intervals, and more complex measures such as phase synchrony (Hurtado et al., 2004; Thiel et al., 2006) and cumulative power (Bates et al., 2012; Cameron and Saladin, 2012). Participants will learn how to construct conditioned likelihoods within the Bayesian paradigm. Specifically, participants will be expected to become proficient across four task categories:

**Generate synthetic data sets:** Participants will be expected to use software including Matlab ODE solvers and Statistics Toolbox to generate synthetic data sets from some canonical ODE/SDE

**Learn basic probability:** Participants will be expected to learn some basic probability including likelihood, independence, Bayes Rule, and expectations

**Perform bifurcation continuation analyses:** Participants will learn to use the software XPPAUT to determine location of Hopf bifurcations, stable limit cycles etc. Regions in parameter space associated with certain bifurcation behavior will be used to establish rejection proposal and prior probability distributions for MCMC.

**Obtain MCMC parameter estimates:** Participants will use pre-existing software to compute MCMC estimates of the parameters in their systems. Their challenge will be to address probability model construction and elicitation of prior distributions.
Statistical estimation problems in dynamical systems are nearly always over-determined due to certain variables being unobserved or to model errors and simplifying assumptions which prevent the data from being spanned by the model. It is not surprising that approaches begin by adding conditions to the penalty functions being optimized (minimized) during estimation. However choice of condition can drastically affect the robustness of the estimation procedure. The anticipated outcomes of these projects will be promotion of computational, statistical, and visualization skills in participants and a greater level of mathematical independence.

References


