Potassium Channel Kinetics and Signal Propagation in Axons - Mikhail Shvartsman

Hodgkin and Huxley [26,27,29] proposed a model to describe the ionic and electrical events during the transmission of an impulse through the surface membrane and the propagation of voltage impulse through a nerve axon. In particular, they modeled the axon as a long cylindrical cable with a conducting core and a partially insulating shell submerged into a large volume of conducting fluid. The Hodgkin Huxley model consists of four differential equations and is yet difficult for rigorous mathematical analysis [37]. In particular, even though the chemical and electrical changes take place concurrently as action potential moves through the axon, the equations for voltage and concentration are coupled only via the first order chemical kinetics where the rate parameters depend on voltage. In this case the concentration of open ionic channels at a particular time gives description of only one firing cycle and does not reflect the oscillating nature of channel behavior. A distinctive feature of potassium channels is that they are non-activating to potential conductance. The coupling of the equations for ionic conductance and the partial differential equation for the potential implies that different concentrations will propagate at a different velocity [37,36,44]. It allows to answer some questions about connection between firing frequency, wave velocity, and output frequency. Output frequency is important since it is controls subsequent synaptic behavior [38,53]). Such multiple waves are observed also in experiment [36]).

The student projects will focus on analysis of the dispersion relation for traveling waves resulting in loss of shape for some signals (spikes) and to instability of the potassium channel kinetics. It was shown that finite traveling waves in Nagumo equation allow distinct finite waves profiles moving at different speeds and in the same direction [32]. Finite waves have bounded spatial support on the half-line corresponding to the direction of propagation. The divergence form of the model is

$$n_t = (n^m n_x)_x + f(n)$$

where $n(x,t)$ is the concentration of potassium channels at time t and where m is a parameter. Scaling is important here since $0 \leq n(t) \leq 1$. The goal of the student group project is to carry out a computational analysis of finite waves corresponding to potassium dynamics and compare it with available experimental data.

The group project would consist of the following stages:

To study the Hodgkin–Huxley model, its Nagumo counterpart and channel kinetics involved in action potential

To search for biological data related to potassium channel properties of action potentials for specific axon types

To test computational tools on traveling waves for infinite interval (where analytic solution is available)

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To carry out a computational analysis of the forced waves in a finite domain for the different forms of the term $f(n) = cn^{\alpha}(1-n)^{\beta}$

To find velocities for the double-speed wave trains [30], where solutions have to satisfy the integral condition

$$\int_0^1 n^m f(n)\, dn > 0$$

for all times. Analytically, the double-speed solutions are described [28] on the infinite interval. For the finite length membranes a computational approach has to be used. Students would implement shooting methods to solve the reduced ODE problem on the finite interval.