Ion Concentration and Temperature Effects on the Hodgkin-Huxley Model

Simulation Project

Report due on Friday, December 22, 2017, by noon (12:00 pm)
Late reports: 20% will be deducted for each hour after the deadline.

The MATLAB scripts and functions you wrote as part of Homework Assignments 8, 9, and 10 are the starting point. You will modify your scripts and/or functions, and possibly create new ones, to conduct this experiment and analyze the results.

Report: Your report should be targeted to an audience that understands the Hodgkin-Huxley model, but not your topic of study. The report must include a statement of the problem (or the question being studied), the methods used to solve the problem (including equations and numerical algorithms), and the results of your investigation. Figures or graphics may be integrated with the text or arranged sequentially immediately after the references. The report must close with a discussion section, where the results and their implications are described. Plots must show appropriately labeled axes, including units. Appendices will contain your scripts and any lengthy derivations. Full citations to any reference materials used in your study must be included.

Score: The projects will be graded 80% for your analysis (the content of the report) and 20% for the style of the report. Superior reports will include analysis beyond what is required.

The “classical” Hodgkin-Huxley model was developed to describe the electrical behavior of the squid giant axon at ion concentrations found in sea water and 6.3 °Celsius. Most of the nonlinear conductance data was collected by altering the ion concentrations on either side of the membrane. The experimental preparations also varied in temperature, and these variations must be taken into account by the model.

This purpose of this study is to quantify the differences in the membrane currents and action potential caused by changes in the intra- and extracellular ion concentrations, and temperature. The baseline (“normal”) conditions for this study are:

- $[\text{Na}^+]_i = 50 \text{ mM}$
- $[\text{Na}^+]_o = 491 \text{ mM}$
- $[\text{K}^+]_i = 400 \text{ mM}$
- $[\text{K}^+]_o = 20.11 \text{ mM}$
- $E_L = -49.2 \text{ mV}$
- temperature = 6.3 °Celsius
- stimulus current = 50 $\mu$A/cm$^2$
- stimulus duration = 0.15 msec
- time step $\Delta t = 0.005$ msec
- simulation time = 50 msec

Temperature Effects  Ion currents change at different temperatures, and this greatly affects the action potential. Among other things, the rate constants governing the channel conductances can accelerate or
decelerate the gate kinetics. A temperature factor, $Q_{10}$, scales the time dependence of the rate factors:

\[
\frac{dh}{dt} = \left[ \alpha_h (1 - h) - \beta_h h \right] Q_{10}
\]

\[
\frac{dm}{dt} = \left[ \alpha_m (1 - m) - \beta_m m \right] Q_{10}
\]

\[
\frac{dn}{dt} = \left[ \alpha_n (1 - n) - \beta_n n \right] Q_{10}
\]

where $Q_{10} = 3^{(T_C - 6.3)/10}$, and $T_C$ is the temperature of the preparation in degrees Celsius. Note that at 6.3 °C the temperature factor is one.

Modify the Hodgkin-Huxley model to account for variations in temperature. Run the model with temperatures ranging from 0 °C to 30 °C. Determine within ±0.5 °C the temperature of thermal block, where action potentials are no longer generated. Compute the action potential duration at 90% repolarization (APD$_{90}$) and the maximum upstroke velocity ($dV/dt_{\text{max}}$) and plot these versus temperature.

Is the membrane more or less excitable at high temperatures? That is, does the threshold current (the minimum amount of stimulus current needed to generate an action potential) increase or decrease with temperature? Why?

**Ion Concentrations Effects**  Vary the intracellular potassium concentration from 80% to 110% of the baseline concentration. Compute APD$_{90}$ and $dV/dt_{\text{max}}$. Next, with $[K^+]_i$ at baseline, vary $[Na^+]_o$ from 70% to 140% of its baseline concentration. Again compute APD$_{90}$ and $dV/dt_{\text{max}}$. How does the action potential duration change with changes in the concentrations? Does it always increase, always decrease, or is it not affected? Is the trend the same regardless of the ion being changed? What happens if the intracellular and extracellular concentrations (of the same ion) simultaneously increased (or decreased) by the same percentage?

**Combined Effects**  What happens when the external sodium concentration increases and the temperature increases? At what temperature does thermal block occur? Is it different than the thermal block temperature found above? Can the ion concentrations be altered to offset the temperature effects?