The Brain Pyramidal Neuron Model (Traub 1991)
Simulation Project

Report due on Wednesday, December 23, 2015, by 2:30 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 15% for your analysis (the content of the report) and 5% for the style of the report. Superior reports will include analysis beyond what is required.

Pyramidal neurons are cells found in brain of mammals, fish, reptiles, and birds. These neurons can exhibit different action potentials depending on the input stimulus; the action potential may have a single fast upstroke (like in the squid giant axon), or multiple upstrokes when “burst firing.”

The Hodgkin-Huxley model includes a single potassium current. While that model can demonstrate repetitive action potentials in response to a constant stimulus, the results are unrealistic. Traub and colleagues [1, 2] developed a more complex model of the neuron using the approach of Hodgkin and Huxley. Their formulation follows that of the squid giant axon model: nonlinear membrane conductances are modeled using a saturation value with activation and inactivation gates governed by voltage-dependent opening and closing rates. This model will respond with realistic voltage spikes in response to a constant stimulus current. A second potassium current regulates the firing rate, which can vary by several hundred milliseconds.

The purpose of this study is to implement the Traub pyramidal neuron model and compare its repetitive firing rate and overall electrical characteristics to those in the squid giant axon.

The Traub model uses nine state variables:

1. \( V_m \), membrane potential
2. \( m \), Na\(^+\) activation gate
3. \( h \), Na\(^+\) inactivation gate
4. \( n \), K\(^+\) activation gate
5. \( y \), K\(^+\) inactivation gate
6. \( s \), \( \text{Ca}^{2+} \) activation gate
7. \( r \), \( \text{Ca}^{2+} \) inactivation gate
8. \( q \), \( \text{Ca}^{2+} \)-dependent K\(^+\) inactivation gate
9. \([\text{Ca}^{2+}]_i\), intracellular Ca\(^{2+}\) concentration
Figure 1: Left: The action potential $V_m$ and intracellular calcium concentration $[\text{Ca}^{2+}]_i$ from the Traub pyramidal neuron model. The 2 nA stimulus current was applied for 20 milliseconds, starting at 5 milliseconds. Right: The four ion currents in the model.

These state variables are handled much the same way as those in the Hodgkin-Huxley model, except for the diffusive transport of calcium. The soma portion of Traub model is listed below. The simulation will generate a membrane action potential (a non-propagating action potential at a point).

Modify the Hodgkin-Huxley scripts to implement the Traub model. The first simulation should cover 40 milliseconds using a time step $\Delta t = 0.02$ milliseconds. Use a stimulus current of 2 nA applied for 20 milliseconds starting at $t = 5$ milliseconds; this should generate the action potential, intracellular calcium concentration, and ion currents shown in Figure 1.

With the stimulus conditions above, create plots of the membrane potential, currents, gates, and the calcium concentration. Plot the time contants for gates $n$ and $y$ versus $V_m$. Compute the action potential amplitude, duration at 90% repolarization ($\text{APD}_{90}$) and the maximum upstroke velocity, $dV/dt_{\text{max}}$.

Investigate how the number of action potential spikes changes with the stimulus current duration. Apply the stimulus current over a range of durations, from 5 to 75 milliseconds, in 5 millisecond steps. Count the number of spikes exceeding $+75$ mV, and plot the count versus stimulus current duration. Finally, run a simulation for 200 milliseconds with a stimulus current duration of 150 milliseconds. What happens to the spikes? You may want to consult chapter 4 in the original book [1] for more information.


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Currents are given in nA, conductances in \( \mu \text{S} \), and potentials in mV. Note that l’Hôpital’s rule must be applied to \( \beta_r \) and \( \alpha_q \) (with respect to \([\text{Ca}^{2+}]_i\)) in addition to some opening and closing rates (with respect to \( V_m \)).

\[
I_{\text{ion}} = I_Na + I_K + I_{Ca} + I_{KCa}
\]

ion current

\[
I_{Na} = \overline{g}_{Na} \cdot m^3 \cdot h \cdot (V_m - E_{Na})
\]

Na\(^+\) current

\[
I_K = \overline{g}_{K} \cdot n^4 \cdot y \cdot (V_m - E_K)
\]

K\(^+\) current

\[
I_{Ca} = \overline{g}_{Ca} \cdot s^5 \cdot r \cdot (V_m - E_{Ca})
\]

Ca\(^2+\) current

\[
I_{KCa} = \overline{g}_{KCa} \cdot q \cdot (V_m - E_K)
\]

slow Ca\(^2+\)-dependent K\(^+\) current

Nernst potentials, conductances, and membrane capacitance:

\[
E_{Na} = 115 \\
E_K = -15 \\
E_{Ca} = 140 \\
C_m = 0.104 \text{ nF}
\]

\[
\overline{g}_{Na} = 3.32 \\
\overline{g}_K = 3.98 \\
\overline{g}_{Ca} = 6.64 \\
\overline{g}_{KCa} = 0.10
\]

The initial values of the state variables are:

\[
V_m = -15 \text{ mV} \\
m = 0.00053 \\
h = 0.99991 \\
n = 0.00042 \\
y = 0.99220 \\
[\text{Ca}^{2+}]_i = 0.0 \text{ mmol/Liter} \\
q = 0.01286 \\
r = 0.95657 \\
s = 0.00549
\]

The intracellular calcium concentration \([\text{Ca}^{2+}]_i\) is governed by the state equation

\[
\frac{d}{dt}[\text{Ca}^{2+}]_i = -\frac{c}{A \cdot d} I_{Ca} - \beta_x [\text{Ca}^{2+}]_i
\]

where: \( c = 5.2 \) [the conversion from nA/\( \mu \text{m}^3 \) to mmol/(Liter-msec)]

\[
A = 3320 \ \mu \text{m}^2, \ \text{cell membrane area}
\]

\[
d = 5 \times 10^{-4} \ \mu \text{m}, \ \text{soma membrane thickness}
\]

\[
\beta_x = 0.1 \ \text{per msec}
\]
The gates are governed by the opening and closing rates (in msec⁻¹):

\[ \alpha_m = \frac{0.32 (13 - V_m)}{\exp[0.25 (13 - V_m)] - 1} \]

\[ \beta_m = \frac{0.28 (V_m - 40)}{\exp[0.2(V_m - 40)] - 1} \]

\[ \alpha_h = 0.128 \exp[(17 - V_m)/18] \]

\[ \beta_h = \frac{4}{1 + \exp[0.2(40 - V_m)]} \]

\[ \alpha_n = \frac{0.032 (15 - V_m)}{\exp[0.2(15 - V_m)] - 1} \]

\[ \beta_n = 0.5 \exp[(10 - V_m)/40] \]

\[ \alpha_y = 0.028 \exp[(15 - V_m)/15] + \frac{2}{\exp[0.1(85 - V_m)] + 1} \]

\[ \beta_y = \frac{0.4}{\exp[0.1(40 - V_m)] + 1} \]

\[ \alpha_r = 0.005 \]

\[ \beta_r = \frac{0.025 (200 - [Ca^{2+}]_i)}{\exp[0.05 (200 - [Ca^{2+}]_i)] - 1} \]

\[ \alpha_s = \frac{0.04 (60 - V_m)}{\exp[0.1(60 - V_m)] - 1} \]

\[ \beta_s = \frac{0.005 (V_m - 45)}{\exp[0.1(V_m - 45)] - 1} \]

\[ \alpha_q = \frac{0.005 (200 - [Ca^{2+}]_i) \exp(V_m/27)}{\exp[0.05 (200 - [Ca^{2+}]_i)] - 1} \]

\[ \beta_q = 0.002 \]