Tutorial: electrophysiology, and the Hodgkin-Huxley model

Warm up

1. Familiarise yourself with driver.m and HodgkinHuxley.m. Read carefully the documentation, and the code. We expect that your submissions will have a similar level of documentation.
2. Run driver.m, and verify that the cell achieves its rest state.
3. Estimate the proportion of open Na and K channels at rest.
4. In the folder, you will find an html file with our own answers to the questions so far. We created it using Matlab's Publish feature. To see this in action, open driver.m in Matlab, go to the Publish menu, and then the press the Publish button. This creates an html file, which can be visualised from a browser, and contains your code and your results, nicely formatted. You can also add LaTeX equations in there (see how we did it in driver.m). It may be useful to get into this workflow, as it may save you time submitting reports, or sharing your work with us and others.

Small depolarisation

1. Star the system at rest and, at some later time, inject an applied current of $2\mu A/cm^2$ for $2ms$. This can be done with the following function

$$I(t) = 2\chi_{[16,18]}(t) \begin{cases} 2 & \text{if } t \in [16, 18] \\ 0 & \text{otherwise} \end{cases}$$

   where $\chi_{[a,b]}(t)$ is the indicator function.
2. Plot all state variables as a function of time. At approximately which times do you see a small depolarisation, a repolarisation, a hyperpolarisation, respectively?

Spike generation - all or none response

1. Increase the intensity of the stimulus progressively, from 2 to 10 ($\mu A/cm^2$), and plot the membrane potentials. You should observe a typical all-or-none response: if the stimulus is sufficiently strong, a spike is elicited. Compare your plots with Figure 1.13 in ET book (left panel).

Sustained periodic response

1. Produce a sustained periodic response, as shown in Figure 1.13 of the ET book (right panel).
2. Produce numerical evidence to substantiate the following claim: in a sustained periodic response, the intensity of the injected current influences the period and amplitude of the oscillations. Write down a description of your findings, and compare your results with the image taken from Saito & Isa, 1999, included in the lecture notes.

Revisiting the spike mechanism

1. Start the system at rest and generate a single action potential (a spike) injecting a 25 $\mu A/\text{cm}^2$ current for 2 ms. Produce the following plots:
   - The voltage, plotted together with two horizontal reference lines, for the sodium and potassium Nernst potentials, respectively;
   - All gating variables.
   - The conductances $g_\alpha(t) = \bar{g}_\alpha p_\alpha(t)$ where p_α is the percentage of open channels for voltage-gated α-channels, with $\alpha \in \{\text{K}^+, \text{Na}^+\}$.
   - All currents, as functions of time.
2. Go through the phases of a spike (see lecture notes). Find numerical evidence of the claims below (or answer the questions)
   - During an upstroke, sodium channels open; this ignites a regenerative mechanism: as the cell depolarises, even more sodium channels open, and this induces further depolarisation.
   - Sodium and potassium channels open at different speeds. Which channels are fast, which are slow? You may want to produce additional plots of the respective $\tau(V)$ in support of your answer.
   - The repolarisation in a downstroke is caused by potassium channels
   - What is the sign of the sodium and potassium current? What determines their sign?

Further exercises

1. Superimpose graphs of the steady-state activation functions $m_\infty(V)$ and $h_\infty(V)$, as functions of V. Deduce that there is a window in which a nonzero current is produced. This is what is commonly referred to as "window current".
2. At $10^\circ C$ a cell contains 80mM sodium inside and has only 100mM sodium outside. What is the equilibrium potential for sodium.
3. Derive the Nernst potential equation (including constants and units)
4. A neuronal membrane with capacitance C has channels for the following ions: Na^+, Ca^{2+}, K^+, Cl^-. Assume the channels are purely Ohmic (passive), and that there is no external input to the cell. Write down an ODE for the evolution of the voltage membrane.
   - Prove that the system admits a unique equilibrium, given by

$$V_* = \frac{g_{Na} E_{Na} + g_{Ca} E_{Na} + g_K E_{Na} + g_{Cl} E_{Cl}}{g_{Na} + g_{Ca} + g_K + g_{Cl}}$$

   - Let $I: \mathbb{R} \to \mathbb{R}$ model a time dependent external stimulus. Prove that the membranal voltage evolves according to the following ODE

$$C\dot{V}(t) = I(t) - g_*(V(t) - V_*), \qquad V(0) = V_0.$$

     where g_* is a suitably-defnied constant. Find an analytical solution to this ODE.
   - Let $b > a > 0$, and take $I(t) = A\chi_{[a,b]}(t)$, where $\chi_{[a,b]}$ is the indicator function. Sketch the solution $V(t)$ to the ODE written above. Can this neuronal model produce a spike?