1. Passive membrane

The ionic current across a membrane is given by the sum of two terms: one diffusive term due to the concentration gradient, and one drift term due to the charge of the particles:

\[ I = I_{\text{diff}} - I_{\text{drift}} \]

(this is called the Nernst-Planck equation). \( I_{\text{diff}} \) is proportional to the concentration gradient across the membrane: \( I_{\text{diff}} = k_c \frac{d[C]}{dx} \) (\( x \) is position along membrane, \( [C] \) is concentration), whereas the drift term is proportional to the product of concentration and the gradient of the voltage across the membrane: \( I_{\text{drift}} = k_v [C] \frac{dV}{dx} \).

The nasty constants here are: \( k_v = -uz^2F \) and \( k_c = uzRT \), where \( u \) is an index of the mobility of the ion inside the membrane (in cm\(^2\)/V-s-mol – the value depends on the channel / pore), \( R \) is the gas constant (1.98 cal/K-mol), \( T \) is the absolute temperature (K), \( F \) is Faraday’s constant (96480 C/mol) and \( z \) is the valence of the ion (C).

- The Nernst equation describes the resting potential of a membrane. It is given by the integral of the equation for the current above from \( x_{in} \) on the inside of the membrane to \( x_{out} \) on the outside of the membrane when the total current \( I = 0 \). Show that in that case

\[ V_{\text{out}} - V_{\text{in}} = V_{\text{Nernst}} = \frac{k_c}{k_v} \log \frac{C_{\text{out}}}{C_{\text{in}}} = \frac{RT}{zF} \log \frac{C_{\text{out}}}{C_{\text{in}}}. \]

Here, \( V_{\text{out}} = V(x_{\text{out}}) \) and equally so for \( [C] \). Hint: You’ll have to do a change of variables. What is the Nernst potential for \( K^+ \)? For \( Na^+ \)?

- The Goldman-Hodgkin-Katz equation is a solution to the Nernst-Planck equation which describes ion flux through a simple membrane with constant electric field. In short, the change we make is \( dV/dx = V/l \) (\( l \) is the thickness of the membrane \( x_{out} - x_{in} \), i.e. we don’t bother integrating out a possibly complex electric field but just write: \( I_{\text{drift}} = k_v [C] V/l \). Thus we now have

\[ I = k_v [C] \frac{V}{l} - k_c \frac{d[C]}{dx}. \]

It looks as if the total current were a linear function of the voltage here, but in fact it isn’t because the total current depends on \( [C] \), too. Derive the steady state total current \( (dI/dx = 0) \) as a function of the voltage. Hint: Show that

\[ \frac{dw}{dx} = -\frac{k_v V}{k_c l} w \quad \text{where } w = I - I_{\text{drift}} \]
and integrate from \(x_{in}\) to \(x_{out}\). Neglecting the scale factors, plot the current versus the voltage (this plot is the famous I-V plot). What do you notice? The I-V curve depends on the ratio between \(C_{out}\) and \(C_{in}\). In what regime of this ratio is the description of the relationship between current and voltage used in the Hodgkin-Huxley model \((CdV/dt = -I = -g(V - E))\) a good approximation? Are we in this regime? Why might the Hodgkin and Huxley formalism still be good?

2. Linear passive membrane

Let

\[
\frac{dV}{dt} = -\bar{g}(V - E) + I(t).
\]

Write down an expression for \(V(t)\) as a function of \(I(t)\). Implement this equation in a discretized manner on the computer and drive the membrane with white noise (i.e. \(I(t)\) is gaussian white noise). Plot the power spectra of the input and the voltage trace. What does this membrane do to its input?

3. Active membrane

Numerically integrate the Hodgkin-Huxley equations with matlab. Best idea is to use the \texttt{ode15s} function. Hodgkin and Huxly defined the resting potential to be at -65mV. If we shift their equations by this amount we get:

\[
C \frac{dV}{dt} = -\bar{g}_{Na}m^3h(V - E_{Na}) - \bar{g}_K n^4(V - E_K) - \bar{g}_L (V - E_L) + I_{stim}
\]

\[
\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x \quad \text{where } x \text{ is } m, n \text{ or } h
\]

\[
\alpha_m(V) = 0.1(V + 40)/[1 - \exp(-(V + 40)/10)]
\]

\[
\beta_m(V) = 4 \exp(-(V + 65)/18)
\]

\[
\alpha_h(V) = 0.07 \exp(-(V + 65)/20)
\]

\[
\beta_h(V) = 1/ [\exp(-(V + 35)/10) + 1]
\]

\[
\alpha_n(V) = 0.01(V + 55)/[1 - \exp(-(V + 55)/10)]
\]

\[
\beta_n(V) = 0.125 \exp(-(V + 65)/80)
\]

Let \(C = 1\mu\text{F/cm}^2, \bar{g}_L = 0.003\text{mS/mm}^2, \bar{g}_K = 0.36\text{mS/mm}^2, \bar{g}_{Na} = 1.2\text{mS/mm}^2, E_K = -77\text{mV}, E_L = -54.387\text{mV} \text{ and } E_{Na} = 50\text{mV}. \) Use an integration time step of 0.1 ms. Hint: Choose a surface for your membrane and make sure you get all the constants right.

- Plot a spike (V vs time). Plot the gating variables as a function of time during a spike. What happens?
- Plot the gating variables as a function of voltage.
- Plot the firing rate vs. \(I_{stim}\). The firing rate should suddenly jump from zero to a non-zero value. This is called a type II behaviour. Type I behaviour is when the firing rate begins at zero and increases smoothly without any jumps.
- Apply negative current for 5ms in the middle of a spike train. What happens? Why?
- What happens as you decrease \(\bar{g}_K\)?
- Spikes are initiated at the axon hillock, where the axon meets the soma. One reason for this might be that \(\bar{g}_{Na}\) is very high. What happens as you increase \(\bar{g}_{Na}\)?

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