Assignment 1
Theoretical Neuroscience

Quentin Huys

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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:

   $$I = I_{drift} - I_{diff}$$

   (this is called the Nernst-Planck equation). I_{diff} is proportional to the concentration gradient across the membrane: $I_{diff} = k_c d[C]/dx$ (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: $I_{drift} = k_v [C] dV/dx$.

   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

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

     Here, $V_{out} = V(x_{out})$ 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: $I_{drift} = k_v[C]V/l$. 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

     $$\frac{dw}{dx} = -\frac{k_v V}{k_c l} w \qquad \text{where } w = I - I_{drift}$$

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

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

   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 `ode15s` function. Hodgkin and Huxly defined the resting potential to be at -65mV. If we shift their equations by this amount we get:

   $$\begin{aligned}
C\frac{dV}{dt} &= -\bar{g}_{Na}m^3h(V - E_{Na}) - \bar{g}_K n^4(V - E_K) - \bar{g}_L(V - E_L) + I_{stim} && (1)\\
\frac{dx}{dt} &= \alpha_x(1 - x) - \beta_x x \qquad \text{where } x \text{ is } m, n \text{ or } h && (2)\\
\alpha_m(V) &= 0.1(V + 40)/\left[1 - \exp(-(V + 40)/10)\right] && (3)\\
\beta_m(V) &= 4\exp(-(V + 65)/18) && (4)\\
\alpha_h(V) &= 0.07\exp(-(V + 65)/20) && (5)\\
\beta_h(V) &= 1/\left[\exp(-(V + 35)/10) + 1\right] && (6)\\
\alpha_n(V) &= 0.01(V + 55)/\left[1 - \exp(-(V + 55)/10)\right] && (7)\\
\beta_n(V) &= 0.125\exp(-(V + 65)/80) && (8)\\
& && (9)
\end{aligned}$$

   Let $\mathrm{C} = 1\mu\mathrm{F/cm^2}, \bar{\mathrm{g}}_\mathrm{L} = .003\mathrm{mS/mm^2}, \bar{\mathrm{g}}_\mathrm{K} = 0.36\mathrm{mS/mm^2}, \bar{\mathrm{g}}_\mathrm{Na} = 1.2\mathrm{mS/mm^2}, \mathrm{E_K} = -77\mathrm{mV}, \mathrm{E_L} = -54.387\mathrm{mV} \quad \text{and} \quad \mathrm{E_{Na}} = 50\mathrm{mV}$. 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 $\bar{g}_{Na}$?