Subthreshold Voltage Gated Channels: Questions

• Q1. Emergence of oscillations

On the P, Q phase diagram it was seen that a system with complex eigenvalues and decaying voltage oscillations, can destabilise to give a spontaneously oscillating neuron if $P < -1$. However, it was noted that for the case of a neuron with only one kind of voltage-gated channel $P = \tau_n/\tau_v$, so that $P > 0$. This showed that a neuron with a single voltage-gated channel cannot go into oscillation. Nevertheless, oscillating voltages are seen in neurons *in vivo*. How can this be explained? Consider a neuron with two voltage-gated channels. The linearised equations are

$$\tau_v \frac{dv}{dt} = \kappa_1 y_1 + \kappa_2 y_2 - v, \quad \tau_{n1} \frac{dy_1}{dt} = v - y_1, \quad \tau_{n2} \frac{dy_2}{dt} = v - y_2 \tag{1}$$

[Q] Assume that the second variable equilibrates very quickly, i.e. set $\tau_{n2} = 0$. Reduce the three dynamic equations to two.
[A]

$$\tau_v \frac{dv}{dt} = \kappa_1 y_1 + (\kappa_2 - 1)v, \quad \tau_{n1} \frac{dy_1}{dt} = v - y_1 \tag{2}$$

[Q] Rescale time $s = t/\tau_{n1}$. Show that $P = (1 - \kappa_2)\tau_{n1}/\tau_v$.
[A] This is straightforward given the definitions in the lecture notes.
[Q] What conditions on κ_1 and κ_2 will destabilise the neuron and cause spontaneous oscillations? What kind of currents could this correspond to? What is the physical interpretation of the actions of the currents?
[A] For damped oscillations we require that $Q < -(P-1)^2/4$ which means that the first voltage-gated channel must give strong negative feedback, and so $\kappa_1 < 0$. This could arise from a depolarisation-activated hyperpolarising current or a hyperpolarisation-activated depolarising current. For oscillations $P < -1$ so we must have $\kappa_2 > 1 + \tau_v/\tau_n$. Because κ_2 is required to positive it must be a depolarisation-activated depolarising current or a hyperpolarisation activated hyperpolarising current. The interpretation is that the first kind of voltage-gated channel provides the negative feedback with delay (non-zero τ_{n1}) which is quickly amplified by the fast positive feedback of the second current.

• Q2. H-current effects in the response to square-current pulses

The h-current, or I_h, is a common feature of neurons with large dendritic structure. It is a hyperpolarisation-activated, depolarising current, and as such can protect neurons from too-strong a hyperpolarisation. Its signature is seen in the response to square-current pulses as a non-monotonic overshoot or sag, depending on the sign of the current. The activation time constant of I_h is much longer than the voltage time constant. So $\tau_n/\tau_v \gg 1$ and $\kappa < 0$.
[Q] Using the linear forms of the voltage equation,

$$\tau_v \frac{dv}{dt} = -v + \kappa y + RI_{app} \tag{3}$$

$$\tau_n \frac{dy}{dt} = v - y, \tag{4}$$

show that, in the large τ_n/τ_v, if I_{app} is zero before $t = 0$ and a constant I_0 afterwards then the early-time voltage change is

$$v \simeq RI_0 \left(1 - e^{-t/\tau_v}\right). \tag{5}$$

[A] The dynamics of y are slow, so it can be assumed to remain at its initial value $y = 0$ while the voltage equilibrates. The early-time voltage comes from solving the voltage equation with $y = 0$.
[Q] For the late-time dynamics the voltage can be assumed to be at its equilibrium, $\tau_v dv/dt = 0$. Use this result to express y as a function of v and solve the equation for y and show that it follows

$$y \simeq \frac{RI_0}{1-\kappa}\left(1 - e^{-\frac{t}{\tau_n}(1-\kappa)}\right) \tag{6}$$

[A] If τ_v is zero then $y = (v - RI_0)/\kappa$. Inserting this into the equation for the y dynamics with the initial condition $y = 0$ yields the required result.
[Q] Using the formula relating y and v from the $\tau_v dv/dt = 0$ approximation, show that the late-time voltage follows

$$v \simeq \frac{RI_0}{1-\kappa}\left(1 - \kappa e^{-\frac{t}{\tau_n}(1-\kappa)}\right). \tag{7}$$

[A] Inserting the result for y into the steady-state voltage relation $v = RI_0 + \kappa y$ gives the required result.
[Q] Sketch the form of the voltage response.
[A] It has a rapid rise to a value RI_0 and then decays to the new resting voltage $RI_0/(1-\kappa)$.

• Q3. Eigenvalues for a neuron with the H-current

We now derive the eigenvalues in the same limit just considered with $\tau_n/\tau_v \gg 1$.
[Q] In the previous question, what were the two decay time constants identified in this approximation?
[A]

$$\text{fast decay: } \tau_v \qquad \text{slow decay: } \frac{\tau_n}{1-\kappa} \tag{8}$$

[Q] Using the forms for P and Q given in the lecture notes, show that in the large τ_n/τ_v limit both $P \gg 1$ and $Q \gg 1$.
[A] This follows because both are proportional to τ_n/τ_v.
[Q] Expand the eigenvalue equation to show that the two roots take the form

$$\lambda_+ = -\frac{1}{\tau_n}\left(1 - \frac{Q}{P}\right) \quad \text{and} \quad \lambda_= - \frac{1}{\tau_n}\left(P + \frac{Q}{P}\right). \tag{9}$$

[A] This comes from an expansion

$$\lambda = \frac{1}{2}\left(-(P+1) \pm P\left(1 - \frac{2}{P} + \frac{4Q}{P^2} + \frac{1}{P^2}\right)^{1/2}\right) \tag{10}$$

$$\lambda \simeq \frac{1}{2}\left(-(P+1) \pm \left(P - 1 + \frac{2Q}{P}\right)\right) \tag{11}$$

The τ_n^{-1} prefactors come from putting the correct time scaling in, $t = s\tau_n$.
[Q] Show that these two eigenvalues are consistent to leading order with the time constants derived above.
[A] This is straightforward to show using the definitions for P and Q given in the lecture notes.