Frequency Adaptation and Bursting

In the last lab, we explored spiking due to sodium channels. In this lab, we explore adaptation and bursting due to potassium and calcium channels. To realize adaptation the model uses a population of slow potassium channels (M current). During the spike, the neuron’s depolarized potential activates the potassium channels. These channels hyperpolarize the membrane, which delays subsequent spikes, adapting the neuron’s spike rate.

To realize bursting, the neuron uses a population of calcium channels. During the spike, these calcium channels activate, and remain active for a short time. While they are active they strongly excite the neuron, causing a high frequency train of spikes. Each spike also increases the potassium channels’ conductance, which overcomes the calcium current after several spikes, terminating the burst until potassium activation decreases enough to allow another burst of spikes.

We will analyze and experiment with the adapting–bursting neuron, observing the role of the potassium and calcium channels in spiking behavior, focusing on:

- The adapted spike rate
- The interaction between spike frequency and potassium conductance in bursting

3.1 Reading

Adaptation and bursting come in several varieties and can be realized by many combinations of ion channels. The book below introduces adaptation and explains the requirements for the type of bursting neuron in this lab (Section 7.3). It also reviews bursting in general, emphasizing its utility and the relevant mathematics (Section 9.2).


3.2 Prelab

This prelab analyzes the frequency behavior of the adapting–bursting neuron.

1. M Current

   (a) We model potassium channels (K) as a conductance in parallel with the leak conductance, G (to zero potential) (Figure 3.1). A spike causes a change in K
Figure 3.1: A potassium conductance, $G_K$, in parallel with a leak conductance, $G$, produces adaptation. Adding a Ca current ($I_{Ca}$) results in bursting.

A potassium conductance similar to our synapse model, a brief rise followed by an exponential decay. Here we approximate the rise as instantaneous, thus, if $G_K(t_n)$ is the value of the conductance immediately before the nth spike, which occurs at $t_n$, we have:

$$G_K(t) = (G_K(t_n) + \Delta G_K)e^{-(t-t_n)/\tau_K}$$  \hspace{1cm} (3.1)

where $\tau_K$ is the time constant and $G_K(t)$ increases by $\Delta G_K$ immediately after the nth spike. A neuron spikes regularly with period $T$ in steady-state. Solve for the conductance, $G_K(t_\infty)$, by obtaining $G_K(t_n + T)$ from Equation 3.1 and setting it equal to $G_K(t_n)$.

(b) The potassium conductance increases the minimum input required to elicit a spike, $\gamma$. Determine the minimum input, given that

$$\tau_m \dot{x} = r - x \left(1 + \frac{G_K(t)}{G} \right) + \frac{x^3}{3}$$  \hspace{1cm} (3.2)

by finding the value of $r$ that makes $\dot{x}$’s minimum value zero.

(c) We can obtain the steady-state spike frequency using our previous results if we assume spike generation is instantaneous. Using your result for $\gamma(G_K)$, find the value of $G_K$ that makes $\gamma$ equal to $r$. Using your result for $G_K(t_\infty)$, show that the corresponding steady-state period is given by:

$$T = \tau_K \log \left( \frac{\Delta G_K/G}{(3r/2)^{2/3} - 1} + 1 \right)$$  \hspace{1cm} (3.3)

If the log’s argument is only slightly larger than 1, we can use the approximation

$$\log(1+x) \approx \frac{1}{2} + \frac{1}{x}$$

to obtain the steady-state frequency:

$$f \approx \frac{1}{\tau_K} \left( \frac{(3r/2)^{2/3}}{\Delta G_K/G} + \frac{1}{2} \right)$$  \hspace{1cm} (3.4)

What additional approximation did we make?

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2. Bursting

(a) We model calcium channels (Ca) as an excitatory current ($I_{Ca}$) in parallel with the sodium current (Figure 3.1). A spike causes a change in Ca as in the synapse and potassium models, a brief rise followed by an exponential decay. The Ca current is similar to the potassium conductance but expresses a faster decay. The effect of Ca current ($r_{Ca}$) is to add to the neuron’s input current, causing a rapid train of spikes, until the potassium overcomes it, ending the burst. To visualize the complex interaction between the calcium and potassium that results
Figure 3.2: A neuron’s behavior is set by the strength of its calcium current ($\Delta r_{Ca}$). When the calcium current is weak ($\Delta r_{Ca} = 2$) the neuron adapts, settling at a stable spike frequency. When the calcium current is strong ($\Delta r_{Ca} = 7$) the neuron bursts, alternating between high frequency spiking and quiescence.

in bursting, we use a phase portrait, which depicts the relationships between variables (Figure 3.2). We consider two cases: one adapting and the other bursting. In the adapting case, the Ca current increases a small amount after each spike ($\Delta r_{Ca} = 2$); in the bursting case, the Ca current increases a large amount ($\Delta r_{Ca} = 7$). The other parameters are: $r = 1.0$, $\Delta G_K/G = 0.3$, $\tau_K = 60$ms, $\tau_{Ca} = 10$ms, and $\tau_m = 10$ms.

(b) The adapting neuron reaches steady-state when its frequency decreases, reaching the steady-state (normalized) potassium conductance at that frequency. The normalized steady-state potassium conductance, $G_K(t_\infty)/G$, is plotted as a dashed line (Figure 3.2), using the function of $G_K(t_\infty)$ found in Prelab Question 1a and the parameters given in Question 2a. What happens when the neuron’s frequency reaches the $G_K(t_\infty)/G$ curve in the adapting and bursting cases?

(c) The bursting neuron terminates its burst when it reaches frequency $f_{\text{min}}$, at $f_{\text{min}}$ the sum of its input current $r$ and its calcium current $r_{Ca}$ fall below $\gamma(G_K/G)$, given by:

$$\gamma \left( \frac{G_K}{G} \right) = \frac{2}{3} \left( 1 + \frac{G_K}{G} \right)^{3/2}$$

Set $r + r_{Ca} = \gamma(G_K/G)$ and solve for $f_{\text{min}}(G_K/G)$, given $r_{Ca} = f_{\text{min}}(G_K/G)$ is plotted for the given parameter values for both values of $\Delta r_{Ca}$ as dotted lines. Does the neuron’s frequency decrease below $f_{\text{min}}$ in the adapting case? What happens when the frequency decrease below $f_{\text{min}}$ in the bursting case?

(d) After a burst terminates, it is followed by a silent period during which $\Delta r_{Ca}$ approaches zero and $G_K/G$ decays. When the potassium conductance reaches a minimum value, $G_{K\text{min}}/G$, $\gamma(G_K/G)$ decreases below $r$, starting another burst.
Set \( \gamma(G_{\text{Kmin}}/G) = r \) and show:

\[
\frac{G_{\text{Kmin}}}{G} = \left( \frac{3r}{2} \right)^{2/3} - 1
\]

(3.6)

\( G_{\text{Kmin}}/G \) is plotted for the given parameters as a dotted and dashed vertical line.

### 3.3 Setup

As with previous labs, there will be a folder on the Desktop named **Adapting–Bursting Lab**. This folder contains the instrument control program to acquire and view the neuron membrane potential and spikes in real-time. The TA will instruct you on the use of the software.

In this lab, the contents of *parameters.txt* of interest are:

- Input current \( (I_{\text{IN}}) \)
- Leak conductance \( (G) \)
- Potassium conductance amplitude \( (\Delta G_{K}) \)
- Calcium current amplitude \( (I_{C\text{a}}) \)

As you increase the input current and the leak conductance biases, \( I_{\text{IN}} \) and \( G \) increase exponentially. As you decrease the potassium conductance amplitude and calcium current biases, \( \Delta G_{K} \) and \( I_{C\text{a}} \) increase exponentially. The potassium \( (\tau_K) \) and calcium \( (\tau_{C\text{a}}) \) decay-constants are set to reasonable values such that \( \tau_K \) is about four times \( \tau_{C\text{a}} \). In Experiment 1, \( I_{C\text{a}} \) is fixed at zero. In Experiment 2, \( I_{\text{IN}} \) is fixed at a reasonable value.

### 3.4 Experiments

In the first experiment, we will characterize the neuron’s adapted spike rate in response to K-channel activity. In the second, we will turn on the model’s calcium channels and observe the neuron’s various behaviors—bursting, bursting followed by adapting, and adapting.

**Experiment 1: Spike-Frequency Adaptation**

In this experiment, we will

- Measure the neuron’s adapted spike rate for various (constant) input currents.

Turn on the K channels by decreasing the potassium amplitude bias (to about 1.85V). Calculate the spike frequency for several values of input current (10-20), which we normalize and approximate as:

\[
r = \gamma e^{(V_{\text{IN0}} - V_{\text{IN}}) 0.7/0.0256}
\]

(3.7)
where as before (Lab 2) \( \gamma = 2/3 \); \( V_{IN} \) is the input current bias in volts, and \( V_{IN0} \) is the largest input current bias (smallest input current) that causes the neuron to spike. Plot steady-state \( f \) versus \( r \), fitting the plot with the appropriate equation from the prelab. What are \( \tau_K \) and \( \Delta G_K/G \)?

**Experiment 2: Bursting Phase Portrait**

In this experiment, we will

- Collect phase portraits from a neuron in different regimes.

Turn on the Ca channels by decreasing the calcium amplitude bias (to about 1.45V). Observe the spike frequency versus potassium trajectory for several values (5-10) of calcium amplitude. Ensure that the calcium current amplitude range is sufficient to realize both adapting (small calcium amplitude) and bursting (large calcium amplitude). Measure \( \Delta G_K \) and use it to calculate \( G \) using the value of \( \Delta G_K/G \) determined in Experiment 1. Normalized \( G_K \) by \( G \).

For each calcium current amplitude plot a phase-portrait curve: Plot the inverse of each interspike interval (instantaneous spike frequency) versus the average normalized potassium amplitude during that interval. In the adapting case, plot all interspike intervals until the spike rate reaches steady-state; in the bursting case, plot all intervals for several burst cycles. Label each phase-portrait curve with its corresponding calcium amplitude bias. From the bursting phase portraits estimate \( G_{K_{min}}/G \). From the adapting phase portraits fit \( G_K(t_\infty)/G \) as a function of frequency to an approximation of the expression derived in Prelab Question 1a, given by:

\[
\frac{G_K(t_\infty)}{G} \approx \frac{\Delta G_K \tau_K f}{G}
\]  

(3.8)

Use the slope of this curve and the value of \( \Delta G_K/G \) from Experiment 1 to find \( \tau_K \).

The exact expression for \( f_{min} \) changes, depending on \( \Delta r_{Ca} \). However, the point where each bursting curve intersects it's \( f_{min} \) and terminates the burst follows a trend. From the bursting phase portraits estimate these points and fit \( f_{min} \) versus \( G_K/G \). Try a linear fit; report the slope and intercept and whether it is a good fit of the trend? Does it cross the adapting phase-portrait curves?

### 3.5 Postlab

A fit of Equation 3.3 to the steady-state frequency of a pyramidal neuron in rat neocortex yields \( \tau_K = 36 \text{ms} \) and \( \Delta G_K/G = 4.1 \) (Figure 3.3). Imagine we augment this neuron with sufficient calcium current to cause bursting (\( \Delta r_{Ca} = 20 \) and \( \tau_{Ca} = 9 \text{ms} \)). Based on these parameter values, what value does the model predict for \( f_{min} \) (Prelab Question 2c), using the following approximations?

\[
\frac{r_{Ca}}{G} \approx \frac{\Delta r_{Ca} \tau_{Ca} f_{min}}{G} \gg r
\]

\[
\frac{G_K}{G} \approx \frac{\Delta G_K \tau_K f_{min}}{G} \gg 1
\]  

(3.9)
Figure 3.3: A neocortical pyramidal neuron’s steady-state frequency–current curve is well fit by the equation in the Prelab (Equation 3.3). It’s spike rate exhibits adaptation at various input current levels (inset). Data taken from http://vesicle.nsi.edu/users/izhikevich/publications/dsn/index.htm.