Lab 5   **January 26, 2010**

Synchrony in Inhibitory Recurrent Networks

In Lab 4, we studied the requirements for periodic input to entrain a neuron. In this lab, we expand our study to include many connected, interacting neurons. We will explore a network of inhibitory interneurons. Our goal is to understand the conditions necessary to synchronize a network of heterogeneous neurons.

We will drive a population of 256 inhibitory interneurons with constant input current and have them inhibit each other; the delay determines the period. The phase-response curve (PRC) is also important as it determines how robust synchrony is. When inhibition in most effective in the middle of a neuron's period, neurons that spike out of phase are strongly inhibited, which pushes them into phase in subsequent cycles.

5.1   Prelab

1. Delayed Inhibition

   Consider a population of inhibitory interneurons with all-to-all connectivity. Its activity (total spike rate), $A(t)$, depends on the amount of inhibition, $G(t)$, which in turn depends on the activity, $A(t)$ (Figure 5.1). If inhibition is not delayed, the network settles into a stable equilibrium with $A(t) = $ C and $G(t) = G_{\mathrm{C}}$, $G(t)$'s steady-state value when $A(t) = $ C. If inhibition is delayed (d), then the equilibrium is unstable and the network oscillates about it. In that case,

   $$a(t) = -mg(t) \tag{5.1}$$

   where $a(t) = A(t) - $ C, $g(t) = G(t) - G_{\mathrm{C}}$, and m is the slope (absolute value) of the $A(G)$-curve at $G = G_{\mathrm{C}}$. And

   $$g(t) = \Delta g \tau a(t - d) \tag{5.2}$$

   where Δg and τ are the inhibitory synapse's spike-increment and decay-constant, respectively. Substituting Equation 5.2 into Equation 5.1 shows that $a(t)$ inhibits itself with some delay, a recipe for oscillation.

   (a) Let's look at the oscillation's amplitude. It decays if $m\Delta g\tau < 1$ or grows if $m\Delta g\tau > 1$. What are the upper and lower limits of $a(t)$? (Hint: See Figure 5.1)

   (b) Let's look at the oscillation's period. Setting $m\Delta g\tau = 1$ (approximating the limits' effects), determine the period, T, by assuming $a(t) = a_0 \sin(2\pi t/T)$.

2. Rise-time and Decay-constant

   The synaptic rise-time (T_{r}) and decay-constant (τ) both contribute to the delay. This question explores the decay-constant's contribution, which depends on the oscillation's period, unlike the rise-time's, which is simply $T_{\mathrm{r}}/2$.
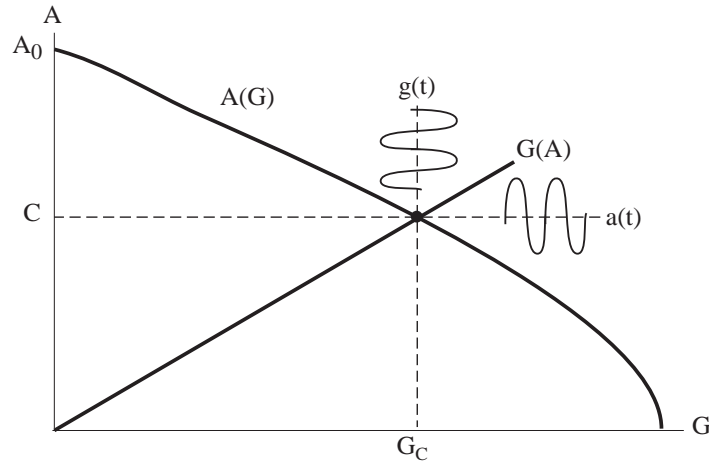
Figure 5.1: Interneuron activity, $A(G)$, depends on the value of inhibition, G and vice versa ($G(A)$ depends on A). At $A = C$ and $G = G_C$ activity is in equilibrium with inhibition. The network activity and inhibition can oscillate about this point ($a(t)$ and $g(t)$).

(a) To calculate τ's influence, we assume the drive to synapses' receptors is sinusoidal, just like we did for the network activity. Thus, the receptors' activation (relative to the value when $A(t) = C$) is described by:

$$\tau \dot{R}(t) + R(t) = R_\infty(t) \tag{5.3}$$

where $R_\infty(t) = \sin(2\pi t/T)$ (with amplitude normalized to one). Plug in $R(t) = R_0 \sin(2\pi(t + s)/T)$ and show that:

$$\frac{2\tau \pi R_0}{T} \cos(2\pi(t + s)/T) + R_0 \sin(2\pi(t + s)/T) = \sin(2\pi t/T) \tag{5.4}$$

τ's contribution to the delay is s. Solve for s and R_0 when $\tau \ll T/(2\pi)$ and when $\tau \gg T/(2\pi)$.

(b) In Prelab Question 1b, we found that T is equal to twice the delay. Including both τ's and T_r's contribution to delay, T is given by:

$$T = 2(T_r/2 + s) \tag{5.5}$$

Using the limits you found for s, solve for T's minimum and maximum, as τ varies.

5.2 Setup

As in previous labs, there will be a folder on the Desktop; this one is named **Synchrony Lab**. This folder contains the instrument control program to acquire and view the interneuron membrane potential and spikes in real-time. The TA will instruct you on the use of the software.

Before each test edit the contents of *parameters.txt*. In this lab, the parameters of interest are:

- Input current (I_{IN})
- Leak conductance (G_{lk})
- Inhibitory rise-time (T_r)
- Inhibitory spread (λ_I)

As you increase the input current, leak conductance, rise-time, and spread biases, I_{IN}, G_{lk}, T_r, and λ_I increase exponentially. Other biases can be changed dynamically while running the program; see the $F1$ key in the program. These can be used to further explore synchrony, but they are not required in the lab.

5.3 Experiments

In the first experiment, we will explore the population of inhibitory interneurons, configured to inhibit only themselves, similar to the M-current K-channels studied in Lab 3. In the second experiment, we will configure the interneurons to inhibit each other globally. Specifically, we will study how the synaptic rise-time influences the synchronous network's period.

Experiment 1: Isolated Interneurons

In this experiment, we will

- Observe variability in isolated interneurons with inhibitory self-feedback

Disconnect the interneurons from each other by setting the inhibitory spread to 0.750V. Leave the other biases at default levels ($G_{lk} = 0.0$; $T_r = 2.286$). Adjust I_{IN} to get a mean network frequency of about 28 Hz (try 0.5V first). Take data for about one second. Calculate each neuron's spike rate. What is the neurons' coefficient of variation (the standard deviation of the rates divided by the mean)? Plot a histogram of the spike rates. Be sure to elimate any non-spiking neurons from the calculations.

Experiment 2: Connected Interneurons

In this experiment, we will

- Observe delay's role in setting the interconnected neurons' period

Globally connect the interneurons by setting the inhibitory spread bias to 1.750V. Keep the same I_{IN} and G_{lk} values from the first experiment. Vary the inhibitory synapse's rise-time (10-20 values). Use rise times from about 1 ms to 50 ms (see equation 5.7). For each rise-time, take data for about one second.

Measure the network activity by calculating the instantaneous firing rate, $F(t)$:

$$F(t) = \frac{N_{spk}(t, t + \Delta t)}{\Delta t} \tag{5.6}$$

where $N_{\text{spk}}(t, t+\Delta t)$ is the count of spikes from all interneurons between times, t and $t+\Delta t$ ($\Delta t = 1$ms). Determine the period of the network, T, by finding the dominant peak in $F(t)$'s FFT.

The rise time of the network can be approximately related to the bias voltage setting by:

$$T_{\text{r}} = 2.0 \, e^{(V_{\text{R}}-2.5)0.616/0.0256} \tag{5.7}$$

where V_{R} is the inhibitory rise-time bias. Assume T is linearly related to T_{r} by:

$$T = n\left(\frac{T_{\text{r}}}{2} + d_0\right) \tag{5.8}$$

where d_0 is delay due to sources other than synaptic rise-time and decay-constant. Plot and fit T as a function of T_{r} for synchronous network states (use vector strength > 0.5, see below). Based on your Prelab, is the value of n reasonable?

The degree to which spikes are in phase (network coherence) can be measured with vector strength (VS):

$$\text{VS} = \frac{1}{\text{N}}\sqrt{\left(\sum_{i=1}^{\text{N}} \cos(\theta_i)\right)^2 + \left(\sum_{i=1}^{\text{N}} \sin(\theta_i)\right)^2} \tag{5.9}$$

where N is the total number of spikes. The phase of the ith spike, θ_i, is given by:

$$\theta_i = 2\pi\left(\frac{\text{t}_i \bmod \text{T}}{\text{T}}\right) \tag{5.10}$$

where t_{i} is the time at which the the ith spike arrived. Plot VS as a function of rise-time.

Calculate the neurons' spike-rate coefficient of variation for each data point, again remembering to remove non-spiking neurons. Plot this on the same figure as VS. Did the minimum CV increase or decrease from the isolated interneurons? Choose a low CV point and a high CV one and plot a spike-rate histogram for each point. Can you explain the change from the isolated interneuron case based on these plots? (Hint: Do highly excitable neurons recieve more or less inhibition in the global coupling case vs. the independent case?)

5.4   Postlab

In Experiment 2, we observed that the network period was proportional to T_{r}, requiring T_{r} to be large for low frequency (20Hz) synchrony. However, even when T_{r} is small (< 1ms), the network can synchronize with a period of 50ms when we use the bursting neurons from Lab 3 (Figure 5.2). Based on the delay model of synchrony developed in the Prelab, calculate what value of delay would achieve this network period. Given $\tau \gg T/(2\pi)$, what is the rise-time's contribution to this delay? Where does this rise-time come from? (Hint: Think about the build up of inhibition during a burst.)
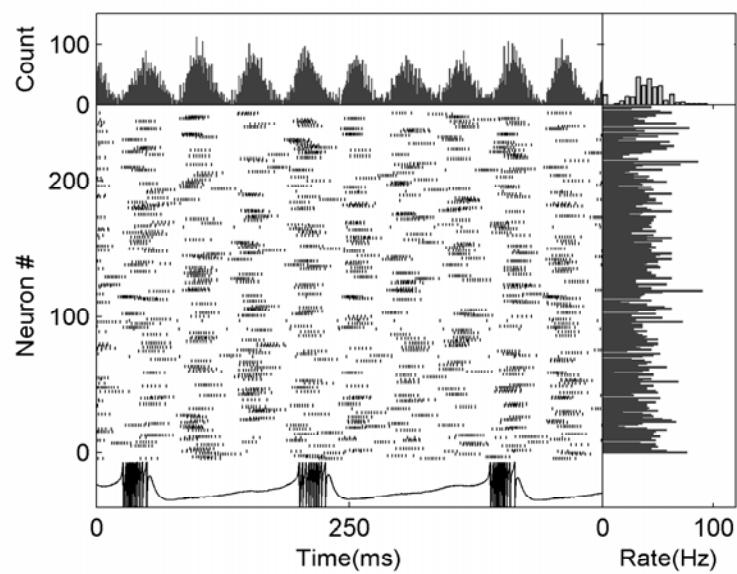
Figure 5.2: Bursting neurons coupled by all-to-all inhibition synchronize with a period of 50ms. Individual neurons have a burst width and period of about 25ms and 125ms, respectively.