Computational Neuroscience Homework 3

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This writeup has referred to some materials mentioned in *Chapter 2: Neurons and Synapses* in Xiao-Jing Wang's book *Theoretical Neuroscience of Cognition*.

1 Part 1

Here we need to simulate the dynamic of AMPA receptor mediated excitation with a short time constant τ_{AMPA}. The first-order kinetics:

$$\frac{ds}{dt} = \alpha_s \sum_j \delta(t - t_j)(1 - s) - \frac{s}{\tau_s} \tag{1}$$

could be simplified to:

$$\frac{ds}{dt} = \alpha_s \sum_j \delta(t - t_j) - \frac{s}{\tau_s} \tag{2}$$

where $\sum_j \delta(t - t_j)$ is a presynaptic spike train and s the gating variable represents the fraction of open synaptic channels. We need to simulate Equation (2) in response to a periodic train at fixed frequency r and calculate the average of s with a long time window T:

$$\langle s \rangle = \frac{1}{T} \int_0^T s(t)dt \tag{3}$$

Figure 1 shows an example of $s(t)$ when $r = 50Hz$ when the simulation time is $100ms$. Figure 2 shows the relationship between the stimulus frequency with the time average of s for AMPA receptor. We purposefully choose some r (not uniformly distributed) so that the grid of t is fine enough to capture each spike time t_j. The relationship itself is monotonic and smooth. Specifically, when $r = 10Hz$, $\langle s \rangle \approx 0.02$; when $r = 50Hz$, $\langle s \rangle \approx 0.10$. Here the simulation time $T = 10s$.

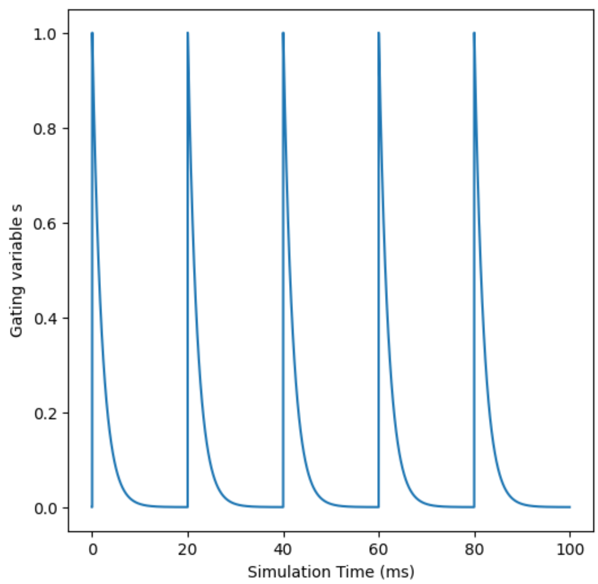

Figure 1: $s(t)$ when the firing frequency $r = 50Hz$ and simulation time is $100ms$.

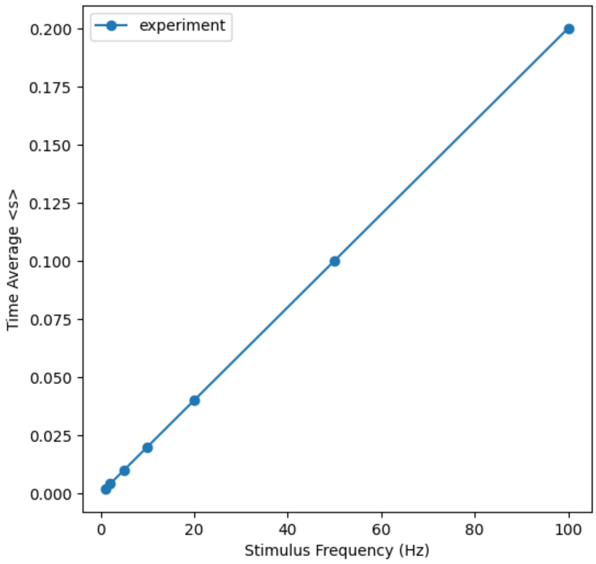

Figure 2: $\langle s \rangle$ as the function of the stimulus frequency r for AMPA receptor.

Here we provide two approaches of calculating $\langle s \rangle$ analytically, one use Equation (1) as the general form and one use Equation (2) directly. As the first approach, for the time just before and after the jth spike, we know that the spike, formulated as the Delta function, would dominate:

$$\frac{ds}{dt} = \alpha_s \delta(t - t_j)(1 - s) \tag{4}$$

Also:

$$\int_{t_j^-}^{t_j^+} \frac{1}{1-s}\frac{ds}{dt} = \int_{t_j^-}^{t_j^+} \alpha_s \delta(t - t_j) \tag{5}$$

$$\ln(1 - s(t_j^-)) - \ln(1 - s(t_j^+)) = \alpha_s \tag{6}$$

$$s(t_j^+) = 1 + (s(t_j^-) - 1)\exp(-\alpha_s) \tag{7}$$

Now for the periodic train with frequency $r = 1/T$, for each j, we have:

$$t_{j+1} - t_j = T = \frac{1}{r} \tag{8}$$

Combined with:

$$s(t_{j+1}^-) = s(t_j^+)\exp(-(t_{j+1} - t_j)/\tau_s) \tag{9}$$

so that:

$$s(t_{j+1}^-) = s(t_j^+)\exp(-1/(\tau_s r)) \tag{10}$$

For the steady state s^+, we have:

$$\begin{aligned} s(t_{j+1}^-) &= s(t_j^-) = s^- \\ s(t_{j+1}^+) &= s(t_j^+) = s^+ \end{aligned} \tag{11}$$

Plugging the equations, we have:

$$\begin{aligned} s^- &= s^+ \exp(-1/(\tau_s r)) \\ s^+ &= 1 + (s^- - 1)\exp(-\alpha_s) \end{aligned} \tag{12}$$

Thus, solving this simple equation system, we have:

$$s^+ = \frac{1 - \exp(-\alpha_s)}{1 - \exp(-(\alpha_s + 1/(\tau_s r)))} \tag{13}$$

Moreover, we know for the s train in one period time T starting from s^+, we have:

$$s(t) = s^+ \exp(-t/\tau_s),\ 0 \le t \le T \tag{14}$$

Thus, we have:

$$\begin{aligned}
\langle s \rangle &= \frac{1}{T}\int_0^T s(t)dt \\
&= \frac{1}{T}\int_0^T s^+ \exp(-t/\tau_s)dt \\
&= rs^+\tau_s(1-\exp(-1/(\tau_s r))) \\
&= \frac{r\tau_s(1-\exp(-1/(\tau_s r)))(1-\exp(-\alpha_s))}{1-\exp(-(\alpha_s+1/(\tau_s r)))}
\end{aligned} \tag{15}$$

Plug in the values of parameters, we would match up the theoretical result with the numerical simulation result. The second approach[1] focuses on Equation (2) itself, and therefore more concise. Suppose $s(t=0)=0$, then we have:

$$ds = \alpha_s \sum_j \delta(t-t_j)dt - s/\tau_s dt \tag{16}$$

dt is small and at most only 1 spikes can happen during this period. Thus:

$$ds = \alpha_s \delta(t-t_s)dt - \frac{s}{\tau_s}dt \tag{17}$$

t_s is the specific spike time. Suppose $r = 10Hz$, the spike train is denoted as $\delta(t-100n), n \in \mathbb{Z}$. Suppose T large and variable $0 \leq t < T$, for $t=0$, $ds = \int \alpha_s \delta(0)dt = 1$; for $0 < t < T$, $ds = -s/\tau_s dt$. Thus, $s = \exp(-\frac{1}{2}t)$ for $0 \leq t < T$. Suppose $T = 100$ with unit of ms, we have:

$$\langle s \rangle = \frac{1}{100}\int_0^{100} e^{-\frac{1}{2}t} \approx 0.02 \tag{18}$$

Similarly, for $r = 50Hz$, we repeat the previous calculation with period $T = 20ms$ and get $\langle s \rangle \approx 0.10$. These are both consistent with the simulation results.

2 Part 2

From the previous lecture, we know that for the differential equation:

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n \tag{19}$$

we have the time constant $\tau_m = \frac{1}{\alpha_n+\beta_n}$. Thus, for this equation:

$$\frac{ds}{dt} = \alpha_s r(1-s) - \frac{s}{\tau_s} \tag{20}$$

we have time constant $\tau_m = \frac{\tau_s}{\alpha_s r\tau_s+1}$. By plugging in the respective τ_s in the unit of ms and fix $r = 20Hz$, we have $\tau_m = 1.923 \times 10^{-3}$ for AMPA, $\tau_m = 6.897 \times 10^{-3}$ for GABA, and $\tau_m = 0.025$ for NMDA.
Also, to calculate the steady state, s has to satisfy that:

$$\alpha_s r(1-s) - \frac{s}{\tau_s} = 0 \tag{21}$$

so that:

$$s_{ss} = \frac{\alpha_s r}{\frac{1}{\tau_s}+r} = \frac{\alpha_s \tau_s r}{1+\alpha_s\tau_s r} \tag{22}$$

Figure 3 shows the result for steady state s as the function of the stimulus frequency r for these three receptors mediated for excitation or inhibition. Notice that with a small τ (AMPA), s increases with r almost linearly (since $\alpha_s\tau_s r \ll 1$) and with larger τ, s increases with r in a more non-linear fashion (NMDA). The curve of GABA could be considered sublinear. For NMDA, the plateau-like shape starts when the $r \approx 50Hz$. Referred to XJW's arguments in his book: biologically, the unbinding of channels from NMDA is low, so the subsequent transmitter release can only recruit those unbounded closed channels. This effect is stronger with a higher stimulus rate. In other words, there is only a finite amount of total receptors available at a synapse, as the cause of saturation. XJW declares that for NMDA when the firing rate is higher than $\approx 50Hz$, a further increase in presynaptic activity no longer recruits more excitatory drive. That is generally consistent with our result in Figure 3.

[1] I have discussed and consulted with Mingming Chen for this method.

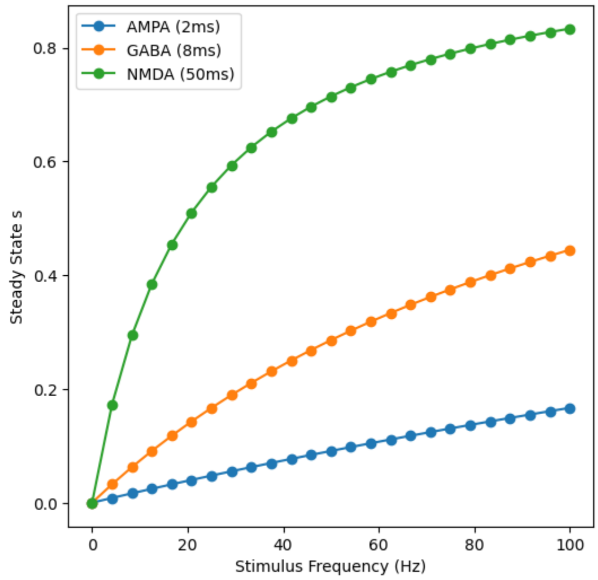

Figure 3: Steady state s as the function of the stimulus frequency r.