Problem Set 7:
Neurons with Conductance-Based Synapses

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As introduced in Lecture 8, one model of neurons with time varying synaptic conductances has the following form:

$$C\frac{\mathrm{d}}{\mathrm{d}t}U(t) + [U(t) - U_r]G_l + [U(t) - U_e]G_e(t) + [U(t) - U_i]G_i(t) = 0, \tag{1}$$

where $U(t)$ is the free membrane potential, C membrane capacitance, G_l membrane leak conductance, and U_r resting membrane potential. $G_e(t)$ and $G_i(t)$ are the synaptic conductances, and U_e and U_i are the synaptic reversal potentials for excitatory and inhibitory synapses, respectively. By defining the total membrane conductance $G_{\mathrm{tot}}(t) \equiv G_l + G_e(t) + G_i(t)$ and effective membrane time constant $\tau_{\mathrm{eff}} \equiv C/G_{\mathrm{tot}}(t)$, this equation can be easily cast into the following form

$$\tau_{\mathrm{eff}}(t)\frac{\mathrm{d}}{\mathrm{d}t}U(t) = -U(t) + \frac{U_r G_l + U_e G_e(t) + U_i G_i(t)}{G_{\mathrm{tot}}(t)}. \tag{2}$$

Note that this model looks vaguely like the leaky integrate-and-fire model, except that the excitatory and inhibitory conductances are functions of time, resulting in time-varying total membrane conductance and effective time constant. The excitatory and inhibitory conductances can be modelled to be linear superpositions of individual responses of the conductance $g_e(t)$ and $g_i(t)$ to synaptic events at times t_j and t_k, respectively:

$$G_e(t) = \sum_j g_e(t - t_j), \quad G_i(t) = \sum_k g_i(t - t_k). \tag{3}$$

While the conductance subsystem is linear, the full system concerning the free membrane potential $U(t)$ given by equations 1 and 2 is obviously not linear. The task is now to predict the dynamics of the model.

Problem 1: Approximation of moments   6 points

To do so, let us first derive how one can approximate moments of a new random variable Y given by the mapping of another random variable X under the function $g(x)$: $Y = g(X)$.

Problem 1.1: The mean   2 points

Remember that the mean of Y is formally

$$\mathbb{E}[Y] = \int_{-\infty}^{\infty} g(x)f_X(x)\mathrm{d}x. \tag{4}$$

This integral is not guaranteed to be easy. More importantly, the exact form of $f_X(x)$ might not be known, such that the integral cannot be performed. If $g(x)$ is well approximated

by the first k-terms of its Taylor expansion (over all $\mathbb{R}$), however, then one does not need to perform the integral and $\mathbb{E}[Y]$ can be well approximated. What do you obtain if one approximates $g(x)$ as a quadratic?

Solution.

Approximating $g(x)$ as a quadratic centred at η: $g(x) \approx g(\eta) + g'(\eta)(x-\eta) + \frac{g''(\eta)}{2}(x-\eta)^2$, and substituting into equation 4:

$$
\begin{aligned}
\mathbb{E}[Y] &= \mathbb{E}[g(X)] \\
&\approx \mathbb{E}\left[g(\eta) + g'(\eta)(X-\eta) + \frac{g''(\eta)}{2}(X-\eta)^2\right] \\
&\approx g(\eta) + g'(\eta)\mathbb{E}[X-\eta] + \frac{g''(\eta)}{2}\mathbb{E}[(X-\eta)^2] \\
&\approx g(\eta) + g''(\eta)\frac{\sigma^2}{2},
\end{aligned}
$$

where $\mathbb{E}[X-\eta] = 0$ and the variance $\sigma^2 = \mathbb{E}[(X-\eta)^2]$ was substituted into the last line.

Problem 1.2: The variance   4 points

Remember that the variance of Y is formally

$$
\mathbb{V}ar[Y] = \mathbb{E}[Y^2] - \mathbb{E}[Y]^2 = \int_{-\infty}^{\infty} (g(x) - \mathbb{E}[Y])^2 f_X(x)\mathrm{d}x. \tag{5}
$$

Use the same approximation of $g(x)$ as in the previous problem to approximate $\mathbb{V}ar[Y]$. If $f_X(x)$ is further known to be sufficiently densely concentrated near its mean η, then the final expression can be reduced to a single term.

Hint: As a trick, it's much easier to use the result from the previous problem, such that you don't have to evaluate the integral on the right hand side of equation 5. Define a new random variable Z given by the mapping under a new function $g_2(x) = g^2(x)$: $Z = g_2(X) = g^2(X)$ then calculate $\mathbb{E}[Z]$ using your result from the previous problem to find $\mathbb{V}ar[Y]$.

Solution.

In the previous problem, we found $\mathbb{E}[g(X)]$ for arbitrary $g(x)$ that could well be approximated by its quadratic Taylor expansion. Assuming this to also be the case for $g_2(X) = g^2(X)$:

$$
\begin{aligned}
\mathbb{V}ar[Y] &= \mathbb{E}[Y^2] - \mathbb{E}[Y]^2 \\
&= \mathbb{E}[g^2(X)] - \mathbb{E}[Y]^2 \\
&= \mathbb{E}[g_2(X)] - \mathbb{E}[Y]^2 \\
&\approx \left[g_2(\eta) + g_2''(\eta)\frac{\sigma^2}{2}\right] - \left[g(\eta) + g''(\eta)\frac{\sigma^2}{2}\right]^2 \tag{$*$}
\end{aligned}
$$

$$\approx \left[g^2(\eta) + \left(2(g'(\eta))^2 + 2g(\eta)g''(\eta) \right) \frac{\sigma^2}{2} \right] - \left[g(\eta) + g''(\eta)\frac{\sigma^2}{2} \right]^2 \qquad (*)$$

$$\approx \left[g^2(\eta) + \left((g'(\eta))^2 + g(\eta)g''(\eta) \right)\sigma^2 \right] - \left[g^2(\eta) + g(\eta)g''(\eta)\sigma^2 + (g''(\eta))^2\frac{\sigma^4}{4} \right]$$

$$\approx \left[(g'(\eta))^2\sigma^2 \right] - \left[(g''(\eta))^2\frac{\sigma^4}{4} \right]$$

$$\approx (g'(\eta))^2\sigma^2 \qquad (\square)$$

where in line $(*)$, the result from the previous problem was substituted in for both terms. In $(\star)$ the calculated differential was substituted in:

$$\begin{aligned}
g_2''(x) &= \frac{\mathrm{d}}{\mathrm{d}x}g_2'(x) \\
&= \frac{\mathrm{d}}{\mathrm{d}x}\left(\frac{\mathrm{d}}{\mathrm{d}x}g^2(x) \right) \\
&= \frac{\mathrm{d}}{\mathrm{d}x}\left(\frac{\mathrm{d}g^2(x)}{\mathrm{d}g(x)}\frac{\mathrm{d}g(x)}{\mathrm{d}x} \right) \\
&= \frac{\mathrm{d}}{\mathrm{d}x}\left(2g(x)g'(x) \right) \\
&= 2(g'(x))^2 + 2g(x)g''(x).
\end{aligned}$$

In the last line $(\square)$, we used the approximation that for a densely concentrated distribution $f_X(x)$, the variance σ^2 is small such that high order powers of the variance tend to zero. In this case, this means that the first term dominates the second term in the second last line such that the last term can be dropped.

Note also that for a sufficiently concentrated distribution $f_X(x)$ near its mean η, such that $f_X(x) \approx 0$ outside some small interval $(\eta - \epsilon, \eta + \epsilon)$, more functions $g(x)$ will be better approximated by their quadratic Taylor expansions in this small interval such that the approximations just calculated for $\mathbb{E}[Y]$ and $\mathbb{V}ar[Y]$ become more accurate.

Problem 2: Analysis of Equation 2   10 points

Now we can see what we can glean from the conductance-based model given by equation 2. In Problem Sheet 5, Problem 2, we derived the mean and variance for shot noise $S(t)$ with kernel response function $g(t)$ and stationary point process intensity λ as:

$$\mu(G) = \lambda \int_0^T g(t)\mathrm{d}t, \qquad \sigma^2(G) = \lambda \int_0^T g^2(t)\mathrm{d}t. \qquad (6)$$

If we model the incoming excitatory and inhibitory synaptic transmissions as separate stationary point processes, we can then easily obtain the means $\mu(G_e)$, $\mu(G_i)$ and variances $\sigma^2(G_e)$, $\sigma^2(G_i)$ of the synaptic conductances G_e, G_i from equation 6. Leaving $g(t)$ and thus these means and variances undefined, let us derive a few results.

Problem 2.1: The moments of G_{tot} and τ_{eff} 4 points

Note that equation 2 is a stochastic differential equation, in that $G_e(t)$, $G_i(t)$ are stochastic processes (shot noise), such that $\tau_{\text{eff}}(t)$, $G_{\text{tot}}(t)$ and ultimately $U(t)$ are also stochastic processes, since they all depend on these stochastic conductances. Using the results from the first problem, derive the means and variances of $\tau_{\text{eff}}(t)$ and $G_{\text{tot}}(t)$, as functions of μ_{G_e}, $\mu_{G_i}, \sigma_{G_e}, \sigma_{G_i}$.

Hint: Remember this property of the variance: $\mathbb{V}ar[aX + bY] = a^2\mathbb{V}ar[X] + b^2\mathbb{V}ar[Y] + 2ab\ Cov[X,Y]$, *for constants* a, b *and random variables* X, Y. *You may assume that excitatory and inhibitory conductances are independent.*

Solution.

Since τ_{eff} is a function of G_{tot}, let us first derive its mean and variance. The mean is just

$$\mathbb{E}[G_{\text{tot}}] = \mathbb{E}[G_l + G_e + G_i]$$
$$= \mathbb{E}[G_l] + \mathbb{E}[G_e] + \mathbb{E}[G_i]$$
$$= G_l + \mu_{G_e} + \mu_{G_i}.$$

Using the hint, its variance is

$$\mathbb{V}ar[G_{\text{tot}}] = \mathbb{V}ar[G_l + G_e + G_i]$$
$$= \mathbb{V}ar[G_l] + \mathbb{V}ar[G_e] + \mathbb{V}ar[G_i]$$
$$= \sigma_{G_e}^2 + \sigma_{G_i}^2.$$

Now, for the effective time constant, using the result from Problem 1.1 for $g(x) = 1/x$:

$$\mathbb{E}[\tau_{\text{eff}}] = \mathbb{E}[C/G_{\text{tot}}]$$
$$= C \cdot \mathbb{E}[1/G_{\text{tot}}]$$
$$\approx C \cdot \left[g(\mu_{G_{\text{tot}}}) + g''(\mu_{G_{\text{tot}}}) \frac{\sigma_{G_{\text{tot}}}^2}{2} \right]$$
$$\approx C \cdot \left[\frac{1}{\mu_{G_{\text{tot}}}} + \frac{2}{\mu_{G_{\text{tot}}}^3} \frac{\sigma_{G_{\text{tot}}}^2}{2} \right]$$
$$\approx \frac{C}{\mu_{G_{\text{tot}}}} \left[1 + \frac{\sigma_{G_{\text{tot}}}^2}{\mu_{G_{\text{tot}}}^2} \right],$$

with $\sigma_{G_{\text{tot}}}^2$ and $\mu_{G_{\text{tot}}}$ given just above. Using the result from Problem 1.2, the variance is

$$\mathbb{V}ar[\tau_{\text{eff}}] = C^2 \cdot \mathbb{V}ar[1/G_{\text{tot}}]$$
$$\approx C^2 \cdot \left[(g'(\mu_{G_{\text{tot}}}))^2 \sigma_{G_{\text{tot}}}^2 \right]$$
$$\approx C^2 \cdot \left[\left(-\frac{1}{\mu_{G_{\text{tot}}}^2} \right)^2 \sigma_{G_{\text{tot}}}^2 \right]$$

$$\approx C^2 \cdot \left[\frac{\sigma^2_{G_{\text{tot}}}}{\mu^4_{G_{\text{tot}}}} \right].$$

Problem 2.2: The stochastic effective time constant   4 points

Given the mean and variance for the effective time constant calculated in the previous problem, predict how these will react to simultaneously increasing input rates λ_e and λ_i. Assume both excitation and inhibitory inputs are Poisson processes. Assume also a form of excitation and inhibitory balance, such that the mean membrane potential $\mu(U(t))$ remains constant. This means that the driving forces (e.g. $U(t) - U_i$) remain approximately constant, such that changes in dynamics can be attributed to changes in conductance. You may also assume high enough input rates such that $\mu_{G_e} + \mu_{G_i} \gg G_l$.

Solution.

Since both $\mathbb{E}[\tau_{\text{eff}}]$ and $\mathbb{V}ar[\tau_{\text{eff}}]$ are functions of $\mu_{G_{\text{tot}}}$ and $\sigma^2_{G_{\text{tot}}}$, we need to see how these react to increasing rates. From equation 3, we know that the excitatory $G_e(t)$ and inhibitory $G_i(t)$ conductances obtain a linear contribution from g_e and g_i, respectively, for each synaptic transmission (spike). These and so the total conductance $G_{\text{tot}}(t)$ thus increase with increasing spike input. For large enough input rates such that $\mu_{G_e} + \mu_{G_i} \gg G_l$, the total expected conductance becomes $\mathbb{E}[G_{\text{tot}}] = \mu_{G_e} + \mu_{G_i}$, which from equation 6 is linear in both λ_e and λ_i since the conductance is a shot noise process. From the last problem and equation 6, we see that the variance $\mathbb{V}ar[G_{\text{tot}}]$ is also linear in both λ_e and λ_i. Thus both mean and variance of the total conductance increases linearly with increasing synaptic input, meaning the following proportionality is observed $\sigma^2_{G_{\text{tot}}} / \mu_{G_{\text{tot}}} \propto 1$.

We can use this to determine the stochastic behaviour of the effective time constant. For the mean, using the proportionality relation, we see that

$$\mu_{\tau_{\text{eff}}} \approx \frac{C}{\mu_{G_{\text{tot}}}} \left[1 + \frac{\sigma^2_{G_{\text{tot}}}}{\mu^2_{G_{\text{tot}}}} \right]$$

$$\propto \frac{1}{\mu_{G_{\text{tot}}}} \left[1 + \frac{1}{\mu_{G_{\text{tot}}}} \right]$$

$$\propto \frac{1}{\mu_{G_{\text{tot}}}},$$

where in the last line we used that for large input rates, $\mu_{G_{\text{tot}}} \gg 1$. Since $\mu_{G_{\text{tot}}}$ is linear in both λ_e and λ_i, we thus expect inverse proportionality with input rates λ_e, λ_i: $\mu_{\tau_{\text{eff}}} \propto 1/\lambda_s$, for $s = e, i$.

As for the variance, again using the proportionality relation:

$$\sigma^2_{\tau_{\text{eff}}} \approx C^2 \cdot \left[\frac{\sigma^2_{G_{\text{tot}}}}{\mu^4_{G_{\text{tot}}}} \right]$$

$$\propto \mu^{-3}_{G_{\text{tot}}}$$

Thus, we expect the variance to decrease even quicker, as in the inverse cubed: $\sigma^2_{\tau_{\text{eff}}} \propto 1/\lambda_s^3$, for $s = e, i$.

Problem 2.3: Effect on the PSPs   2 points

Given that your answers from the previous problem, predict the effect of increasing balanced synaptic input on the shape of the post-synaptic potentials (PSPs). It shouldn't matter whether you consider excitatory or inhibitory PSPs, and the exact functions g_e, g_i. Make reference particularly to the amplitude and width of the PSPs.

Solution.

In the last problem, we saw that increasing input rates decreases the effective time constant. Due to decreasing time constant, all membrane dynamics $U(t)$ will be quicker. That means that all fluctuations away from the resting potential will decay quicker. In terms of induced PSPs, firstly, it means that the membrane will react more quickly to input. Thus, the PSPs will rise to maximum amplitude more quickly. This amplitude will be decreased however. This is because the current height of the PSPs $U(t)$ will already start to decay (rather decay faster) before the full amplitude has even been reached. In other words, more decay occurs at each time step, even during input, such that the rise to the maximum amplitude is made smaller. Lastly, due to faster decay from maximum height, as well as the fast rise to the maximum, the PSP widths will decrease. Thus, PSPs will become shorter and smaller with increasing input rates.

Problem 2.4: Effect on the membrane fluctuations   *Star problem*

Argue, given your answer to the last problem, how increasing balanced synaptic input could first cause an increase in membrane potential fluctuations $\sigma^2(U)$, succeeded by a decrease for higher input rates.

*Hint: Remember that for stationary Poissonian excitatory and inhibitory input, the variance of the membrane potential **for the LIF neuron** is:*

$$\sigma^2(U) = \lambda_e \int EPSP^2(t)\mathrm{d}t + \lambda_i \int IPSP^2(t)\mathrm{d}t.$$

Use this approximation for the non-linear conductance-based neuron model considered here.

Solution.

Note that at low input rates, the conductance will often be able to decay quickly back to low resting values (especially for short functions g_e, g_i), such that the effective time constant will remain quite high and the model can be approximated as the normal LIF neuron in the low conductance regime (that is, all PSPs remain about the same size). In this regime, increasing the input rates will mainly amount to increasing the membrane potential fluctuations in an approximately linear fashion as $\sigma^2(U)$ is linear in the rates as given in the hint (as for the LIF neuron).

As the input rates increase, however, the conductance will increase (linearly as given by equation 6), making the linear approximation no longer accurate. As we found in

the last problem, the PSPs EPSP(t) and IPSP(t) will become smaller and shorter with increasing input rates. Since $\int \text{EPSP}^2(t)\mathrm{d}t$ and $\int \text{IPSP}^2(t)\mathrm{d}t$ are always positive, these terms then become smaller for increasing rates. We can thus expect that membrane fluctuations will thus quickly no longer increase but rather decrease with increasing input rates.

NB: this is a lot of guess work, and to actually determine the shape of $\sigma^2(U)$ as a function of input rates, one needs to explicitly solve equation 3 for spike inputs. This will produce a function of PSPs, which will be a function of τ_{eff} which is a function of G_{tot} which can be cast as a random variable dependent on the input rates.

Problem 2.5: Effect on the firing rate   *Star problem*

Argue, last of all, how increasing balance synaptic input could also caused an initially increasing followed by decreasing firing rate of the neuron. Do you expected the maximum firing rate to occur before, at the same time, or after the maximum membrane fluctuation? In other words, do you expect $\lambda_e(r_{\max}) < \lambda_e(\sigma^2_{\max}(U))$, $\lambda_e(r_{\max}) = \lambda_e(\sigma^2_{\max}(U))$, or $\lambda_e(r_{\max}) > \lambda_e(\sigma^2_{\max}(U))$?

Hint: Remember that the firing rate is dependent on the membrane fluctuations. This dependence of the firing rate r on the amplitude distribution of the membrane potential $P(U)$ can be approximated as

$$r \approx \frac{1}{\tau_{\text{eff}}} \int_{U_\theta}^{\infty} P(U)\mathrm{d}U,$$

where the division by the effective time constant is taken into account as it limits the rapidity of the dynamics and thus how quickly the membrane potential might randomly cross the threshold.

Solution.

From the LIF neuron, one expects a monotonically increasing firing rate of the neuron for increasing excitatory and inhibitory balanced input rate. This is because, though $\mu(U)$ remains constant, $\sigma^2(U)$ increases with increasing input, meaning that the likelihood of the membrane potential crossing the threshold potential U_θ increases.

As discussed in the last problem, however, the width of the pdf $P(U)$ first increases then decreases with increasing input rates (remember we are keeping $\mu(U)$ constant with balanced input). Given the integral in the hint increases for wider $P(U)$, this means that we can expect the firing rate to first increase and then decrease for large enough input rates, as opposed to the LIF neuron.

That said, from the hint, the firing rate is also a function of the effective time constant. Indeed, the firing rate can only be as quick as the dynamics allow, in a similar way that refraction time stops the membrane potential from reaching threshold as quickly.

For example, take two pairs of input rates $\lambda_1^{e,i}$ and $\lambda_2^{e,i}$ either side of the maximum membrane fluctuation $\sigma^2_{\max}(U)$, such that the membrane fluctuations for both these input rates are equal $\sigma^2_1(U) = \sigma^2_2(U)$. The second will be caused by a system with higher input rates and thus lower effective time constant, such that the firing rate will

7

be higher given the equation in the hint. Thus, we can expect the maximum firing rate to occur *after* the maximum membrane fluctuations: $\lambda_e(r_{\max}) > \lambda_e(\sigma^2_{\max}(U))$.

Though this might seem paradoxical, since both pairs have the same pdf $P(U)$ and thus have the same probabilities of crossing the threshold potential and producing spikes, the effective membrane time constant essentially dictates how rapidly the pdf $P(U)$ is sampled from, by causing dynamics to occur more quickly. Thus, one expects a higher firing rate in the same way one expects more sixes to be rolled *per hour* by someone rolling the dice twice as quickly as her neighbour, even though both dice sample from the same distribution seen in the last sheet.