Problem Set 7:
Neurons with Conductance-Based Synapses

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?

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 $\mathbb{V}ar[Y]$.

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:

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

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.

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 $\mu_{G_e} + \mu_{G_i} \gg G_l$.

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.

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.

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

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

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.