

SYNAPTIC FLUCTUATIONS

Neurons in active neural tissue receive a massive, fluctuating synaptic bombardment. The conductance increase can significantly alter the response properties of neurons. In this module we will introduce some of the mathematical tools required to handle stochastic synaptic input.

Spiking Neuron Models, Gerstner and Kistler. Chapter 5 p174-184. Cambridge University Press

• POISSONIAN SPIKE ARRIVAL AND THE GAUSSIAN APPROXIMATION

It is assumed that a neuron has N_s synapses of type $s = e, i$ (for excitatory or inhibitory input) each of which becomes activated at a rate r_s . The total rate of incoming spikes is therefore $R_s = N_s r_s$. Assuming that the synaptic conductance g_s can be considered to sum linearly, and that each pulse causes a step increase of amplitude γ_s that decays exponentially with a constant τ_s , we have

$$\tau_s \frac{dg_s}{dt} = -g_s + \gamma_s \tau_s \sum_{\{t_{sk}\}} \delta(t - t_{sk}) \quad (1)$$

where $\{t_{sk}\}$ is the set of synaptic pulses that arrive at the total rate R_s . This equation can be solved directly to yield

$$g_s = \gamma_s \int_{-\infty}^t dt' e^{-(t-t')/\tau_s} \sum_{\{t_{sk}\}} \delta(t' - t_{sk}) \quad (2)$$

from which it is seen that the conductance is an exponential filter of the synaptic pulses over a time scale τ_s . The sum of delta functions is hard to handle mathematically, but we can smooth it over some time scale less than τ_s , but longer than $1/R_s$ to yield a Gaussian approximation to the Poisson process. This will leave the statistics of the conductance relatively unchanged and leave us with Gaussian random variables which are much easier to handle. We discretise the sum by writing

$$X(t_j) = \frac{1}{\Delta} \int_{t_j}^{t_j+\Delta} dt' \sum_{\{t_{sk}\}} \delta(t' - t_{sk}). \quad (3)$$

The integral itself just counts the number of pulses in a time Δ which is Poisson distributed with a mean and variance $R_s \Delta$. If there are typically many pulses in the time Δ then the excess from the mean will be Gaussian distributed allowing us to write

$$X(t_j) \simeq R_s + \sqrt{R_s} \frac{\phi_j}{\sqrt{\Delta}} \quad (4)$$

where ϕ_j is a Gaussian random number with zero mean $\langle \phi_j \rangle$ and unit variance $\langle \phi_j^2 \rangle = 1$. Hence, we have approximated the Poissonian spike train with a bar-type graph with discretisation constant Δ .

• GAUSSIAN WHITE NOISE

Gaussian white noise comes from taking the limit $\Delta \rightarrow 0$ in the equation (4) above.

$$X(t) = \sum_{\{t_{sk}\}} \delta(t - t_{sk}) \simeq R_s + \sqrt{R_s} \xi(t) \quad \text{where} \quad \xi(t_j) = \lim_{\Delta \rightarrow 0} \frac{\phi_j}{\sqrt{\Delta}}. \quad (5)$$

In itself $\xi(t)$ is not well defined (if in doubt, always go back to the discrete representation) but as will be shown it behaves sensibly under integral signs and provides a powerful tool for the analysis of stochastic systems. First we consider its integral over some time T

$$\int_0^T dt' \xi(t') = \sum_{j=1}^N \Delta \frac{\phi_j}{\sqrt{\Delta}} = \sqrt{\Delta} \sqrt{N} \phi = \sqrt{T} \phi \quad (6)$$

where $N = T/\Delta$ and ϕ is a zero mean unit variance Gaussian random number. The fact that a sum of Gaussian numbers is equal to a Gaussian number with a variance that is a sum of the variances has also been used. It can be noted that though $\xi(t)$ is not defined because it depends on the choice of the arbitrary Δ , its integral is defined and does not depend on Δ . By virtue of the zero mean and independence of the different ϕ_j s we also get the results

$$\langle \xi(t) \rangle = 0 \quad \text{and} \quad \langle \xi(t) \xi(t') \rangle = \frac{\langle \phi_j \phi_{j'} \rangle}{\Delta} = \delta(t - t'). \quad (7)$$

These results now allow the conductance mean and variance to be calculated.

• CONDUCTANCE MEAN AND VARIANCE

On substituting the Poisson process in the conductance equation (1) with the Gaussian approximation (5) we get

$$\tau_s \frac{dg_s}{dt} = \gamma_s \tau_s R_s - g_s + \gamma_s \tau_s \sqrt{R_s} \xi(t). \quad (8)$$

This can be integrated to give

$$g_s = \gamma_s \tau_s R_s + \gamma_s \sqrt{R_s} \int_{-\infty}^t dt' e^{-(t-t')/\tau_s} \xi(t'). \quad (9)$$

Taking the average of both sides, and remembering that $\langle \xi(t) \rangle = 0$, gives the mean conductance directly

$$g_{s0} = \langle g_s \rangle = \gamma_s \tau_s R_s. \quad (10)$$

The variance is calculated by subtracting the mean from both sides of (9) squaring, and taking the average:

$$\begin{aligned} \sigma_s^2 = \langle (g - g_{s0})^2 \rangle &= \gamma_s^2 R_s \int_{-\infty}^t dt' \int_{-\infty}^t dt'' e^{-(t-t')/\tau_s} e^{-(t-t'')/\tau_s} \langle \xi(t') \xi(t'') \rangle \\ &= \gamma_s^2 R_s \int_{-\infty}^t dt' e^{-2(t-t')/\tau_s} = \frac{\gamma_s^2 R_s \tau_s}{2}. \end{aligned} \quad (11)$$

In general the conductance can be written in terms of a mean and a fluctuating component:

$$g_s(t) = g_{s0} + g_{sF} \quad (12)$$

where $g_{sF} \propto \sigma_s$. We can use the values for the mean and standard deviation σ_s to reparameterise equation (8)

$$\tau_s \frac{dg_s}{dt} = g_{s0} - g_s + \sigma_s \sqrt{2\tau_s} \xi(t). \quad (13)$$

This stochastic differential equation is in the form of the Ornstein-Uhlenbeck process.

• THE EFFECT OF SYNAPTIC FLUCTUATIONS ON THE VOLTAGE

We now aim to calculate the effect of the conductance fluctuations on the voltage, which will also fluctuate. Including excitation and inhibition, the voltage obeys

$$C \frac{dV}{dt} = g_L(E_L - V) + g_e(E_e - V) + g_i(E_i - V). \quad (14)$$

On substituting the mean and fluctuating forms for the conductances (12) we get

$$C \frac{dV}{dt} = g_L(E_L - V) + g_{e0}(E_e - V) + g_{i0}(E_i - V) + g_{eF}(E_e - V) + g_{iF}(E_i - V). \quad (15)$$

The first three terms on the RHS may be combined into a single renormalised current $g_0(E_0 - V)$ where

$$g_0 = g_L + g_{e0} + g_{i0} \quad \text{and} \quad E_0 = \frac{E_L g_L + E_e g_{e0} + E_i g_{i0}}{g_L + g_{e0} + g_{i0}}. \quad (16)$$

The total conductance is increased by synaptic drive and so the neuron responds with a smaller voltage amplitude to any input current. However, the new tonic conductance g_0 also gives rise to an effective membrane time constant

$$\tau_0 = C/g_0 \quad (17)$$

that is shorter than $\tau_L = C/g_L$ (sometimes be as much as 4 times shorter). This is an important consequence of synaptic input - it speeds up the dynamics of neurons, giving them a higher temporal resolution. Returning to the equation for voltage we can write

$$\tau_0 \frac{dV}{dt} = E_0 - V + \frac{g_{eF}}{g_0}(E_e - E_0) + \frac{g_{iF}}{g_0}(E_i - E_0) + \frac{g_{eF}}{g_0}(E_0 - V) + \frac{g_{iF}}{g_0}(E_0 - V). \quad (18)$$

If the fluctuations are small relative to the tonic conductance (a biologically realistic assumption) it must be that to leading order $(E_0 - V) \sim g_{sF}/g_0$, which is a statement to the effect that if there are no fluctuations then the voltage is at its rest value E_0 . Hence the second and third terms of the above equation are of the order g_{sF}/g_0 whereas the last two terms are of order $(g_{sF}/g_0)^2$ and therefore less significant. It is justifiable to neglect these terms; it is also desirable as they constitute multiplicative noise and can be delicate to handle analytically. With this approximation in mind we get

$$\tau_0 \frac{dV}{dt} = E_0 - V + \frac{g_{eF}}{g_0} \mathcal{E}_e + \frac{g_{iF}}{g_0} \mathcal{E}_i \quad (19)$$

where we have used the simplifying notation $\mathcal{E}_s = E_s - E_0$. This equation can be solved in terms of the fluctuating g_{sF} to give

$$V = E_0 + \mathcal{E}_e \int_{-\infty}^t \frac{dt'}{\tau_0} e^{-(t-t')/\tau_0} \frac{g_{eF}(t')}{g_0} + \mathcal{E}_i \int_{-\infty}^t \frac{dt'}{\tau_0} e^{-(t-t')/\tau_0} \frac{g_{iF}(t')}{g_0} = E_0 + V_{eF} + V_{iF} \quad (20)$$

where it is directly seen that the voltage fluctuates around its equilibrium $\langle V \rangle = E_0$ because $\langle g_{sF} \rangle = 0$ for both $s = e, i$.

• VOLTAGE FLUCTUATIONS WITH FILTERED SYNAPSES

We can now calculate the variance of the voltage fluctuations by substituting in the form of g_{sF} given implicitly in equation (9).

$$g_{sF} = \sigma_s \sqrt{2\tau_s} \int_{-\infty}^t \frac{dt'}{\tau_s} e^{-(t-t')/\tau_s} \xi_s(t') \quad (21)$$

Considering one of the integral forms of (20) in isolation:

$$V_{sF} = \mathcal{E}_s \frac{\sigma_s}{g_0} \sqrt{2\tau_s} \int_{-\infty}^t \frac{dt''}{\tau_0} e^{-(t-t'')/\tau_0} \int_{-\infty}^{t''} \frac{dt'}{\tau_0} e^{-(t''-t')/\tau_0} \xi(t'). \quad (22)$$

Reversing the order of integration, and performing the inner integral yields

$$V_{sF} = \frac{\sigma_s \mathcal{E}_s \sqrt{2\tau_s}}{g_0 \tau_0 - \tau_s} \int_{-\infty}^t dt' \left(e^{-(t-t')/\tau_0} - e^{-(t-t')/\tau_s} \right) \xi(t'). \quad (23)$$

The argument of this integral can be compared with the form for an isolated PSP (see the notes on synaptic drive): the form is the same but now τ_0 replaces τ_L - the dynamics of the neuron are faster in the presence of synaptic drive.

The variance of the voltage is given by

$$\sigma_V^2 = \langle V_{eF}^2 \rangle + \langle V_{iF}^2 \rangle \quad (24)$$

where it was assumed that the excitatory and inhibitory drive are uncorrelated so that the cross term vanishes. Using the results of Gaussian white noise and performing the remaining integral yields

$$\sigma_V^2 = \left(\frac{\sigma_e}{g_0} \right)^2 (E_e - E_0)^2 \frac{\tau_e}{\tau_e + \tau_0} + \left(\frac{\sigma_i}{g_0} \right)^2 (E_i - E_0)^2 \frac{\tau_i}{\tau_i + \tau_0}. \quad (25)$$

It can be noted that the standard deviation σ_V has a prefactor of $1/g_0$ and hence the increased tonic component of synaptic conductance reduces voltage fluctuations.

• VOLTAGE FLUCTUATIONS WITH FAST SYNAPSES

Though it is possible to calculate the consequences of filtered synaptic drive on the subthreshold voltage of neurons, the firing rate cannot be found in closed form. As we will be interested in calculating the firing rate, we will now consider an approximation in which τ_e and τ_i are both much less than τ_0 and so the closing of the synaptic channels can be assumed to be instantaneously fast $\tau_e = \tau_i \rightarrow 0$. The conductance equation (1) becomes

$$g_s = \gamma_s \tau_s \sum_{\{t_{sk}\}} \delta(t - t_{sk}) = \gamma_s \tau_s R_s + \gamma_s \tau_s \left(\sum_{\{t_{sk}\}} \delta(t - t_{sk}) - R_s \right) \quad (26)$$

where we keep the product $\gamma_s \tau_s$ constant (this is the area under a synaptic pulse and proportional to the total charge delivered into the neuron). In the second equality above we have separated the conductance into its mean and variance. The voltage equation (19) can now be written

$$\frac{dV}{dt} = \frac{E_0 - V}{\tau_0} + a_e \left(\sum_{\{t_{ek}\}} \delta(t - t_{ek}) - R_e \right) + a_i \left(\sum_{\{t_{ik}\}} \delta(t - t_{ik}) - R_i \right) \quad (27)$$

where

$$a_s = \mathcal{E}_s \frac{\gamma_s \tau_s}{g_0 \tau_0} \quad (28)$$

are the amplitudes of the voltage jumps when a synapse pulse arrives. That this is true can be seen by integrating over a short span of time that includes one of the delta functions. We can now make the Gaussian approximation to yield

$$\tau_0 \frac{dV}{dt} = E_0 - V + \tau_0 a_e \sqrt{R_e} \xi_e + \tau_0 a_i \sqrt{R_i} \xi_i = E_0 - V + \tau_0 \sqrt{a_e^2 R_e + a_i^2 R_i} \xi \quad (29)$$

where in the latter equality the summation rule for the variance of Gaussian random numbers has been used. This voltage equation can also be written in terms of the voltage variance for fast synapses

$$\tau_0 \frac{dV}{dt} = E_0 - V + \sigma_V \sqrt{2\tau_0} \xi \quad (30)$$

which takes the same form of as (13). On comparison of equations (29) and (30) we have

$$\tau_0 \sqrt{a_e^2 R_e + a_i^2 R_i} = \sigma_V \sqrt{2\tau_0} \quad (31)$$

so that the voltage variance may be written

$$\sigma_V^2 = \frac{\tau_0}{2} (a_e^2 R_e + a_i^2 R_i). \quad (32)$$

It is straightforward to show that this agrees with the result for synapses with a finite timescale (25) in the limit that the timescale becomes short.