Synaptic Input

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The purpose of this handout is to go a bit beyond the discussion in Ch. 6 of *The Book of Genesis* on synaptic input, and give some examples of how neurons compute things. Read that chapter first.

In this handout, I consider membrane potential to be the key quantity. I take the point of view that action potentials are just a way of encoding (for transmission) the continuous membrane potential signals. In fact, the spike encoding/decoding process may perform important additional processing functions in some neural systems, but I ignore this possibility here. Instead I think of the neural membrane as the brain's primary functional computing element, loosely analogous to a transistor in computer. By wiring transistors together in different ways, you can compute many different functions. Similarly, by using different combinations and spatial arrangements of synapses, a dendritic tree can compute many different functions.

The inputs to the neural membrane are the synaptic conductances $g_j(t)$ evoked by the presynaptic spiking at a number of synapses, and the output is the membrane potential $V_m(t)$. The neural membrane performs two basic functions. First, it acts as a reconstruction filter that transforms the presynaptic spike encoded signal back into a continuous/analog signal. Second, it computes an output membrane potential signal by combining its inputs.

Linear Model of Synaptic Transmission

An approximate model of synaptic transmission is to assume that each spike evokes a change in the conductance of the postsynaptic membrane with a characteristic time-course. For the simulation results in this handout, I used the *alpha function*:

$$\alpha(t) = u(t)\, g_{peak}\, \left(\frac{t}{t_{peak}}\right)\, \exp\left(1 - \frac{t}{t_{peak}}\right), \tag{1}$$

where $\alpha(t)$ is the conductance of the postsynaptic membrane, g_{peak} is the peak conductance change evoked by a single spike, and t_{peak} is the time (after the spike) of the peak conductance change. The $u(t)$ function is the unit step function that makes $\alpha(t)$ causal, i.e., $\alpha(t) = 0$ for all time before $t = 0$. The alpha function is a parametric model that has been fit to approximate experimentally observed synaptic conductance changes. It is not derived from considerations of how ion channels actually work. For some synapses, the alpha function is a poor approximation, so people sometimes use more complicated formulae, but the basic idea is the same.

For a train of spikes, the postsynaptic conductance change is given by a sum of time-shifted alpha functions:

$$g_{syn}(t) = \sum_j \alpha(t - t_j) \tag{2}$$

where t_j are the spike times. The spike train itself $f(t)$ is considered to be a sum of impulses:

$$f(t) = \sum_j \delta(t - t_j),$$

where the $\delta(t - t_j)$ function is the unit impulse signal that is nonzero only when there is a spike. Putting this together with Eq. 2 we see that the postsynaptic conductance is given by a convolving the spike train with an alpha function:

$$\begin{aligned} g_{syn}(t) &= f(t) * \alpha(t) \\ &= \int f(s)\alpha(t-s)ds \\ &= \int \left[\sum_j \delta(s - t_j)\right] \alpha(t-s)\,ds \\ &= \sum_j \left[\int \delta(s-t_j)\,\alpha(t-s)\,ds\right] \\ &= \sum_j \alpha(t - t_j). \end{aligned}$$

The last line follows from the one above it because the integral is zero except when $s = t_j$ for one of the spike times.

This linear model of synaptic transmission assumes that each and every spike evokes the same characteristic conductance change. This not correct in detail for two reasons. First, the effect of each spike is *not* really independent of the others; sometimes a pair or series of spikes spaced closely in time will result in conductance changes that are either bigger or smaller than expected by the linear model, phenomena known as synaptic *facilitation* and *depression*. Second, synapses are unreliable; only a small fraction of spikes (sometimes less than one-tenth) evoke postsynaptic conductance changes. In fact, recent evidence strongly suggests that changes in synaptic reliability may be the cause of synaptic facilitation and depression (Allen and Stevens, 1994; Dobrunz and Stevens, 1997; Tsodyks and Markram, 1997; Abbott *et al.*, 1997). We will stick with the simple linear model for the time being even though it is not completely accurate, but we will cover synaptic reliability, facilitation, and depression later in the course.

Post-Synaptic Potential

The membrane equation, for a passive neural membrane, with a number of synapses is:

$$C\frac{dV_m}{dt} + g_l[V_m(t) - E_l] + g_1(t)[V_m(t) - E_1] + g_2(t)[V_m(t) - E_2] + \ldots + + g_N(t)[V_m(t) - E_N] = 0, \tag{3}$$

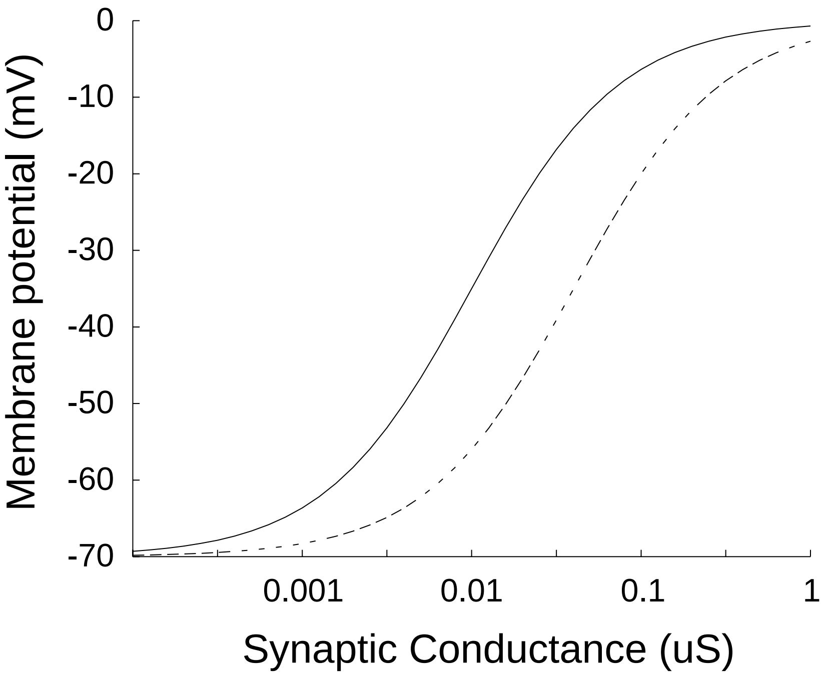

Figure 1: Steady-state postsynaptic potential as a function of postsynaptic conductance. Solid curve: $g_l = 0.01$ uS. Dashed curve: $g_l = 0.04$ uS. Other paramaters: $E_{syn} = 0$ mV, $E_l = -70$ mV.

where $V_m(t)$ is the membrane potential, C is membrane capacitance, $g_j(t)$ is the postsynaptic conductance evoked by each synapse, E_j is the reversal potential of the ion channels in that syanpse, g_l is the constant leak conductance, and E_l is the reversal potential of the leak channel.

In general, the output membrane potential depends nonlinearly on the input conductances. For a simple example, let's assume that there is one synapse with a reversal potential of 0 mV, and that we can hold the conductance of that synapse at a fixed level for some relatively long period of time (long relative to the membrane time constant). Then the membrane potential reaches the following steady state value:

$$V_m = \frac{g_{syn} E_{syn} + g_l E_l}{g_{syn} + g_l}. \tag{4}$$

This function comes from the membrane equation (Eq. 3) by setting $dV_m/dt = 0$, and it is plotted for two different values of g_l in Fig. 1. When g_{syn} is large, the membrane potential saturates:

$$V_m \approx E_{syn}.$$

This, of course, must be the case. There is no way that a synapse could drive the membrane beyond the reversal potential of that synapse. When $g_{syn} = g_l$, the membrane potential is at half the saturating level. When $g_{syn} \ll g_l$, the membrane potential fluctuation is very nearly proportional to g_{syn}:

$$V_m \approx \frac{g_{syn} E_{syn}}{g_l} + E_l.$$

In general, for time-varying synaptic conductances, there is no closed form solution to the membrane equation, Eq. 3. There are closed-form solutions for a handful of interesting special cases (see below), but otherwise we have no recourse but to resort to numerical methods and computer simulations.

Once you know the postsynaptic membrane potential, it is a simple matter to compute the synaptic current:

$$I_{syn}(t) = g_{syn}(t)[V_m(t) - E_{syn}]$$

Temporal Integration and Reconstruction

The inputs to most neurons (other than those in the retina) are in the form of trains of action potentials. But for the purposes of this handout, I do not want to get too hung up on exact timing of individual spikes in spike trains. So I will consider the inputs to be *instantaneous firing rate* signals, denoted $r(t)$, and expressed in units of impulses per second. For example, let's say that a particular input neuron is driven to spike very regularly, at 10 msec intervals, over an extended period of time. Then its instantaneous firing rate is constant over time, $r(t) = 100$ imp/sec.

In most cases, however, we will want to work with time-varying signals. There are (at least) two ways that we could construct an instantaneous firing rate signal from spike trains. The first way to construct an instantaneous firing rate signal is called a post-stimulus time histogram (PSTH), and it involves recording from a neuron for many repeated presentations of the same stimulus (e.g., injected current, visual stimulus, whatever). Break the stimulus presentation period into short time bins, and count the number of spikes that occur in each time bin, collapsed across many repeats of the stimulus. The second way to construct an instantaneous firing rate signal is to record the time of each spike along with its interspike interval (the time interval until the next spike occurs) and plot one over the interspike interval as a function of spike time.

A third method for constructing an instantaneous firing rate signal, available only to the theoretical/computational neuroscientist, is to make it up. That is what we'll do in what follows.

Regardless of how we construct the instantaneous firing rate signals for each of the input neurons, the point I want to make here is that the instantaneous firing rate signals are really all we need because the postsynaptic neural membrane acts as a lowpass, reconstruction filter. Figure 2A shows an example of a theoretical (made-up) instantaneous firing rate signal, and Fig 2B shows a spike train computed from Fig 2A assuming an ideal Poisson spike generator (see the *Poisson Spike Model* handout). Figure 2C shows the postsynaptic conductance computed using the linear (alpha function) model of synaptic transmission discussed above. The thin, noisy curve shows the postsynaptic conductance computed by convolving an alpha function with the spike train (from Fig. 2B). And the bold line shows the postsynaptic conductance computed by convolving an alpha function with the instantaneous firing rate (from Fig. 2A). Finally, Fig. 2D shows the postsynaptic membrane potential computed from both conductances in Fig. 2C. The membrane potential evoked by the spike train is noisy, but otherwise very similar to that computed from the continuous/analog instantaneous firing rate signal. The time constant of the membrane is long relative to the spike and alpha function durations. This results in a temporal summation of the series of inputs. This lowpass filtering property of the membrane acts to reconstruct a continuous, analog signal from the discrete spike events.

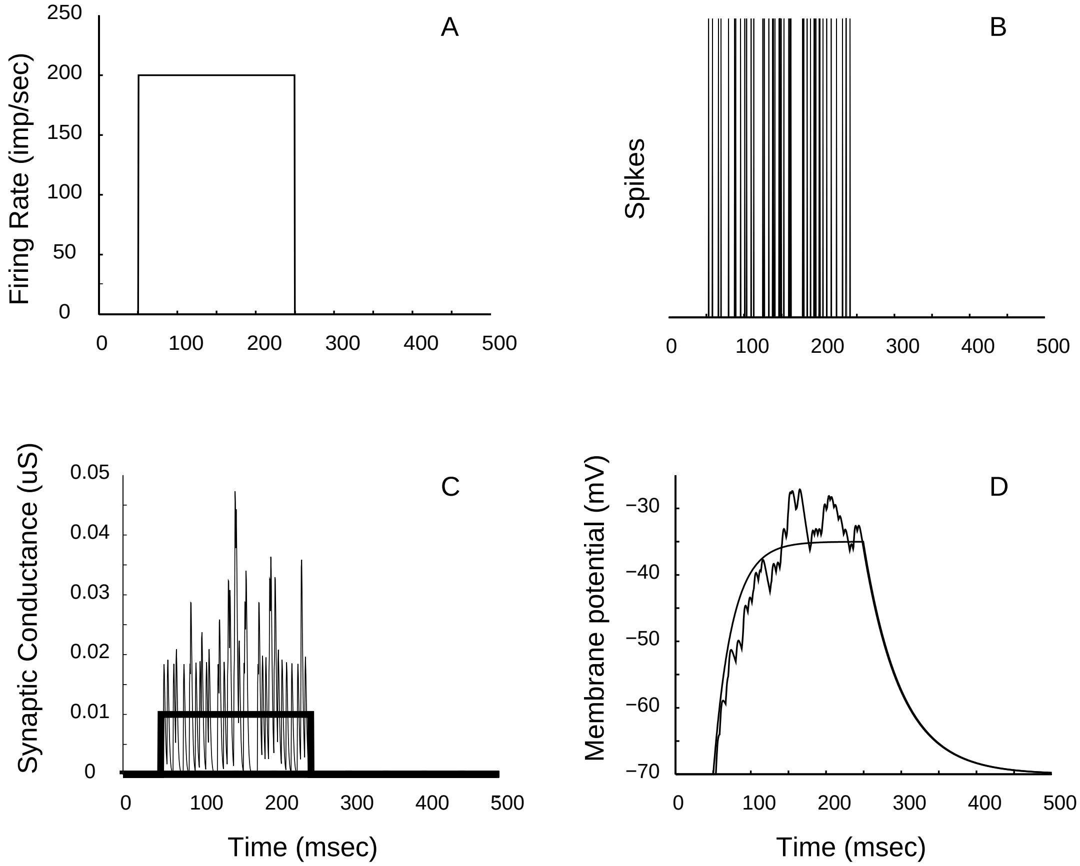

Figure 2: A: Continuous/analog instantaneous firing rate signal. B: Spike train computed from A assuming an ideal Poisson spike generator. C: Postsynaptic conductance. Bold line computed by convolving the instantaneous firing rate signal from A with an alpha function. Thin, noisy curve computed by convolving the spike train from B with the alpha function. D: Postsynaptic membrane potentials computed from C using the membrane equation. Due to the low-pass filtering properties of the membrane, the two curves are very similar. Parameters: $E_l = -70$ mV, $g_l = 0.01$ uS, $C = 0.5$ nF, $E_{syn} = 0$ mV, $g_{peak} = 0.0184$ uS, $t_{peak} = 1$ msec.

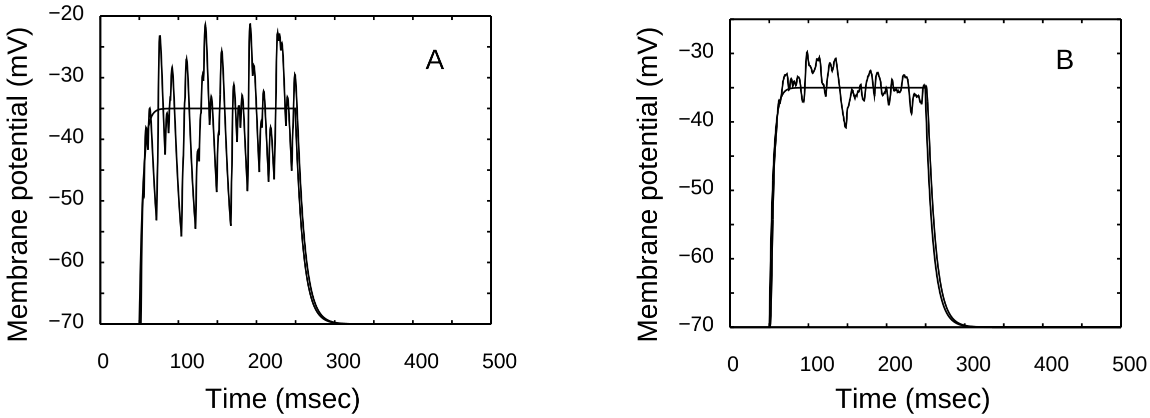

Figure 3: A: Postsynaptic membrane potential, computed as in Fig. 2, except with $C = 0.1$ nF, hence reducing the membrane time constant by a factor of 5. Other parameters are the same as in Fig. 2, e.g., $g_{peak} = 0.0184$ uS. With a short membrane time constant, the evoked membrane potential is much noisier. B: Same as A except with 20 inputs, each an independent Poisson spike process, and each with $g_{peak} = 0.9$ nS, 1/20th as big as in A. With 20 inputs instead of one, the noise is greatly attenuated.

If the time constant is reduced, as demonstrated in Fig. 3A, the evoked membrane potential is very noisy. The noise can be attenuated again by having muliple “copies” of the input. In Fig. 3B there are 20 inputs, each with the same average firing, but generated as independent Poisson processes. Since there are now 20 inputs, each of the synapses has a g_{peak} that is 1/20th as big. This new value, $g_{peak} = 0.9$ nS is close to the actual conductance change at individual synapses.

Computing With Synapses

In this section I give some simple examples of how a neural membrane can do computations. In particular, I show how to compute a linear combination (via addition and subtraction) of a pair of input signals and I show how to multiply/divide a pair of input signals. These examples are not meant to be physiologically realistic. Rather, they should be taken as simplified exercises of working with the equations.

I will use the convention that $V_m(t)$ denotes voltage with respect to the extracellular potential, whereas $V(t)$ denotes voltage with respect to the resting potential. The resting potential in what follows depends both on a leak conductance and on a tonic level of background activity.

Adding and subtracting. We want to use a neural membrane to compute a linear sum of two input signals,

$$V(t) = \beta_1 r_1(t) + \beta_2 r_2(t),$$

where β_2 and β_2 are constants. Equivalently, we can write the desired output membrane potential with respect to the extracellular potential,

$$V_m(t) = \beta_1 r_1(t) + \beta_2 r_2(t) + V_{\mathrm{rest}}. \tag{5}$$

The output, $V(t)$ or $V_m(t)$, is the membrane potential with units of mV. The inputs, $r_1(t)$ and $r_2(t)$, might be instantaneous firing rate signals with units of spikes/sec, or they might be the membrane potentials of a pair of presynaptic neurons (e.g., in the retina where there are no spikes). We'll assume the former (instantaneous firing rates) in what follows.

Equation 5 seems like a relatively simple goal. The inputs give rise to postsynaptic conductance changes which in turn combine to produce the postsynaptic membrane potential. The problem is that the membrane potential is not a linear function of the synaptic conductance (see Eq. 4 above). Synaptic currents are summed, but then divided by the total membrane conductance.

The trick is to use a complementary (push-pull) arrangement of inputs to hold the total conductance at a fixed constant level even though the synaptic currents are varying over time. Such a push-pull arrangement of inputs has been used to model the linearity of retinal ganglion cell responses (e.g., Gaudiano, 1994), and the receptive field properties of V1 simple cells (e.g., Carandini and Heeger, 1994).

In an idealized push-pull model we replace our two inputs with a set of four inputs, two excitatory and two inhibitory:

$$\begin{aligned} r_{e1}(t) &= s + r_1(t) \qquad & r_{i1}(t) &= s - r_1(t) \\ r_{e2}(t) &= s + r_2(t) \qquad & r_{i2}(t) &= s - r_2(t) \end{aligned}$$

where s is the spontaneous firing rate of all four input neurons. Choosing $s > r_1(t)$ and $s > r_2(t)$ guarantees that the four input signals are positive, as firing rates must be. Each of the four inputs gives rise to a postsynaptic conductance:

$$\begin{aligned} g_{e1}(t) &= g_1 + \beta_1' \, r_1(t) \qquad & g_{i1}(t) &= g_1 - \beta_1' \, r_1(t) \\ g_{e2}(t) &= g_2 + \beta_2' \, r_2(t) \qquad & g_{i2}(t) &= g_2 - \beta_2' \, r_2(t) \end{aligned}$$

where β_1', and β_2' are new constants, and where $g_1 = \beta_1' s$ and $g_2 = \beta_2' s$ are the conductances that result from the spontaneous firing.

The membrane equation is:

$$C \frac{dV_m}{dt} + g_l[V_m - E_l] + g_{e1}[V_m - E_e] + g_{i1}[V_m - E_i] + g_{e2}[V_m - E_e] + g_{i2}[V_m - E_i] = 0$$

Here E_e and E_i are, respectively, the reversal potentials of the excitatory and inhibitory synaptic ion channels. In addition, g_l and E_l are, respectively, the leak conductance and leak reversal potential.

The goal now is to show that V_m is a linear summation of the inputs (Eq. 5). To simplify matters, let's begin by assuming that the inputs and the postsynaptic conductances are constant over time. We will return to the general (time-varying) case below. When the postsynaptic conductances are constant over time, then the membrane potential is also constant over time, $\frac{dV_m}{dt} = 0$, hence,

$$\begin{aligned} V_m &= \frac{g_{e1}E_e + g_{i1}E_i + g_{e2}E_e + g_{i2}E_i + g_l E_l}{g_{e1} + g_{i1} + g_{e2} + g_{i2} + g_l} \\ &= \frac{\beta_1' r_1(E_e - E_i) + \beta_2' r_2(E_e - E_i) + (g_1 + g_2)(E_e + E_i) + g_l E_l}{2g_1 + 2g_2 + g_l} \\ &= \beta_1 r_1 + \beta_2 r_2 + V_{\text{rest}} \end{aligned}$$

where

$$\beta_1 = \beta_1' \frac{E_e - E_i}{2g_1 + 2g_2 + g_l} \quad \beta_2 = \beta_2' \frac{E_e - E_i}{2g_1 + 2g_2 + g_l},$$

and where

$$V_{\text{rest}} = \frac{(g_1 + g_2)(E_e + E_i) + g_l E_l}{2g_1 + 2g_2 + g_l}.$$

Or,

$$V = \beta_1 r_1 + \beta_2 r_2,$$

as desired.

The solution for time-vary input signals is:

$$V_m(t) = [u(t)\, \tfrac{1}{C}\, e^{-(t/\tau)}] * [\beta_1 r_1(t) + \beta_2 r_2(t)] + V_{\text{rest}},$$

where $\tau = C/g$ as usual, and $g = 2g_1 + 2g_2 + g_l$ is the total conductance. The membrane potential is simply a lowpass filtered version of the linear sum of the two inputs. It would be a good exercise for you to try to derive this result from the above equations. In deriving this result, it is critical that the total conductance is constant over time even though the conductances of the 4 individual synapses change over time.

The additional lowpass filter is unavoidable because of the capacitance of the membrane. It is, however, a feature, not a bug. In the brain (excluding in the retina), the input signals are spike trains, not the continuous/analog instantaneous firing rate signals that I have used here. The lowpass filtering property of the membrane acts to reconstruct a continuous, analog signal from the discrete spike events (see above).

Figure 4 shows an example. Panel A shows two of the four continuous (instantaneous firing rate) input signals. Panel B shows the spike trains computed from A assuming a Poisson spike generator. Panel C shows the synaptic conductances computed in two ways: (1) using the instantaneous firing rates as inputs, and (2) using the spike trains as the inputs. Panel D shows the postsynaptic membrane potentials computed from C. Notice in comparing C and D how the membrane's lowpass filter greatly attenuates the noise in the postsynaptic conductance.

Multiplying/Dividing. We want to use a neural membrane to compute a ratio of two input signals,

$$V(t) = \frac{\beta_1 r_1(t)}{\beta_2 r_2(t) + \gamma},$$

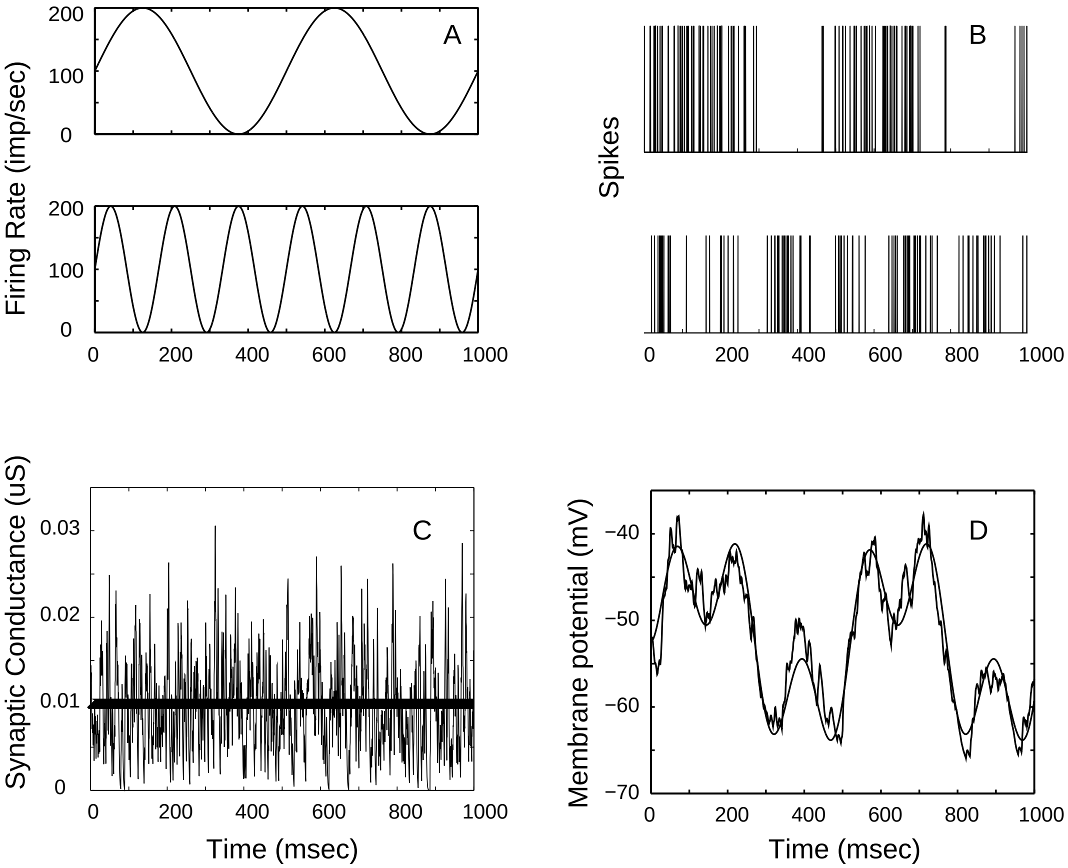

Figure 4: A: Instantaneous firing rates of two of the input signals. B: Spike trains computed from A using a Poisson spike generator. C: Synaptic conductances computed by convolving A and B and an alpha function. D: Postsynaptic membrane potentials computed from A and B. Parameters: $E_l = -70$ mV, $g_l = 0.01$ uS, $C = 0.5$ nF, $E_e = 0$ mV, $E_i = -70$ mV, $g_{peak} = 0.0184$ uS, $t_{peak} = 1$ msec.

for some constants, β_1, β_2, and γ. Equivalently, we can write the desired output membrane potential with respect to the extracellular potential,

$$V_m(t) = \frac{\beta_1 r_1(t)}{\beta_2 r_2(t) + \gamma} + V_{\text{rest}}. \tag{6}$$

As before we replace $r_1(t)$ with a pair of complementary inputs:

$$g_e(t) = g_1 + \beta_1' r_1(t) \quad g_i(t) = g_1 - \beta_1' r_1(t),$$

for a new constant β_1', so that the sum of these two conductances $g_e(t) + g_i(t) = 2g_1$ is constant over time. For the second input, we choose the conductance to be proportional to the presynaptic firing rate:

$$g_{sh}(t) = \beta_2 r_2(t),$$

where the subscript in g_{sh} stands for *shunting*. The membrane equation is:

$$C\frac{dV_m}{dt} + g_l[V_m - E_l] + g_e[V_m - E_e] + g_i[V_m - E_i] + g_{sh}[V_m - E_{sh}] = 0$$

As before, we begin by assuming that the inputs are constant over time, and solve for the steady state membrane potential,

$$\begin{aligned} V_m &= \frac{g_e E_e + g_i E_i + g_{sh} E_{sh} + g_l E_l}{2g_1 + g_{sh} + g_l} \\ &= \frac{\beta_1' r_1 (E_e - E_i) + \beta_2 r_2 E_{sh}}{\beta_2 r_2 + 2g_1 + g_l} + V_{\text{rest}}, \end{aligned}$$

where the resting potential (when $r_1 = r_2 = 0$) is:

$$V_{\text{rest}} = \frac{g_1(E_e + E_i) + g_l E_l}{2g_1 + g_l}.$$

Now we assume that the reversal potential of the shunting synapse is equal to the resting potential, $E_{sh} = V_{\text{rest}}$, and write the membrane potential with respect to V_{rest}:

$$\begin{aligned} V &= \frac{\beta_1' r_1 (E_e - E_i)}{\beta_2 r_2 + 2g_1 + g_l} \\ &= \frac{\beta_1 r_1}{\beta_2 r_2 + \gamma}, \end{aligned}$$

where

$$\beta_1 = \beta_1'(E_e - E_i) \quad \gamma = 2g_1 + g_l.$$

The trick here is that I chose $E_{sh} = V_{\text{rest}} = 0$. Shunting inhibition refers to this situation in which the reversal potential of the synaptic ion channel equals the resting potential, and it is a widely cited proposal for how neurons might perform division (Coombs *et al.*, 1955; Koch and Poggio, 1987). Because the equilibrium potential for chloride, E_{cl}, is close to a cell's resting potential, the GABA-A receptor has been proposed as a potential shunting channel. Chloride shunting, however, only approximates division because E_{cl} is not exactly equal to V_{rest}. Exact division can be implemented with two synaptic conductances, one excitatory and one inhibitory, that increase (and decrease) in proportion. For example, let's assume that shunting is subserved by a combination of chloride and sodium. The synaptic current combining both ion species is the sum of the two (chloride, sodium) components:

$$g_{syn}(V - E_{syn}) = g_K(V - E_k) + g_{Na}(V - E_{Na}),$$

i.e.,

$$g_{syn} = g_K + g_{Na},$$

and

$$g_{syn}E_{syn} = g_K E_k + g_{Na}E_{Na}$$

With $E_{syn} = V_{\text{rest}} = 0$,

$$g_K E_k + g_{Na}E_{Na} = 0,$$

i.e.,

$$\frac{g_{Na}}{g_K} = -\frac{E_K}{E_{Na}}.$$

In words, we can get a perfect shunting channel by choosing the two conductances so that their ratio equals minus the ratio of their reversal potentials (noting that E_K and E_{Na} are specified with respect to V_{rest}, and hence have opposite sign).

Unfortunately, there is no exact solution to the above equations when $r_2(t)$ varies arbitrarily over time. However, we can get an solution by assuming that $r_2(t)$ is piecewise constant, i.e., that it is constant for some period of time (long relative to the membrane time constant), and then it swtiches instantaneously to a new constant value. Then the time-varying solution is:

$$V(t) = [u(t)\,\tfrac{1}{C}\,e^{-(t/\tau)}] * \left[\frac{\beta_1 r_1(t)}{\beta_2 r_2(t) + \gamma}\right],$$

where $\tau = C/g$ as usual, and $g = g_{sh} + 2g_1 + g_l$ is the total conductance. Having $r_1(t)$ vary over time is not problematic because the complementary inputs g_e and g_i guarantee that r_1 has no effect on the total membrane conductance.

The membrane potential is simply a lowpass filtered version of the quotient: $r_1/(r_2 + \gamma)$. The $r_2(t)$ input controls the total conductance of membrane. This has two effects: (1) it changes the gain (sensitivity to the r_1 input) since r_1 is scaled by $r_2 + \gamma$, and (2) it changes the dynamics since the cell's time constant ($\tau = C/g$) is also scaled by conductance.

This link between gain and dynamics is one of the signatures of shunting inhibition. Changes in gain and dynamics are linked in a variety of neural systems including: vestibulo-ocular reflex (Lisberger and Sejnowski, 1992), turtle photoreceptors (Baylor *et al.*, 1974), and in V1 neurons (Carandini and Heeger, 1994).

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