Neural Signaling II – Electrical and Mathematical Modeling

Electrical Model of Membrane

The membrane can be modeled by a lumped electrical circuit for quantitative study of its electrical behaviors. First a patch of membrane without any ion channels can be simply modeled by a *capacitance* C (typically between 0.7 and 1 $\mu F/cm^2$) with negative charge Q stored on the inside (intra-cellular side) and equal amount of positive charge stored on the outside (extra-cellular side), and the potential difference across the capacitor represents the membrane potential V_m:

$$V_m = Q/C$$

Second, an ion channel is modeled by a *resistance* R which allows current to flow through. Finally the resting potential is modeled by a battery of about70 mV. Put together these three elements form a simple circuit as shown in the figure.

../figures/membranemodel.gif

The Membrane Equation and Membrane Dynamics

../figures/membranemodel1.gif

At the rest state, the ionic currents flowing through the ion channels balance each other to reach a dynamic equilibrium of zero net current, and the membrane potential as the voltage across the capacitor is the same as the rest potential of about 70 mV. But when there is an external current source as shown in the figure, either caused by a synaptic stimulus or injected from a intra-cellular microelectrode, the membrane potential will change as a function of time. According *Kirchhoff's current law*, the current source I_{in} is split into the current flowing through R and the current flowing through C:

$$I_{in}(t) = I_R(t) + I_C(t) = \frac{V_m(t) - V_{rest}}{R} + C\frac{dV_m(t)}{dt}$$

This is the *membrane equation*, which is a first order ordinary differential equation for the membrane potential $V_m(t)$:

$$\tau \frac{dV_m(t)}{dt} + V_m(t) = V_{rest} + RI_{in}(t)$$

where $\tau = RC$ is the *time constant* of the membrane which is typically in the range of 10 msec. to 20 msec. Solving this membrane equation one can obtain the membrane potential as a function of time.

If we assume the external current source is a step function

$$I_{in}(t) = \begin{cases} 0 & t < 0 \\ I_{in} & t \geq 0 \end{cases}$$

We assume the *general solution* of the membrane equation to be

$$V_m(t) = c_0 e^{-t/\tau} + c_1$$

from which we also get

$$\frac{dV_m(t)}{dt} = -\frac{c_0}{\tau} e^{-t/\tau}$$

where c_0, c_1 are two constants to be determined by the initial condition that the membrane potential is equal to the rest potential until the moment $t = 0$ when the external current source is applied

$$V_m(0) = V_m(t = 0) = V_{rest}$$

Substituting the general solution of V_m and dV_m/dt above into the membrane equation, we get

$$c_1 = V_{rest} + RI_{in}$$

plugging this c_1 back to V_m, we get

$$V_m(t) = c_0 e^{-t/\tau} + V_{rest} + RI_{in}$$

Applying the initial condition to this, we get

$$V_m(0) = c_0 + V_{rest} + RI_{in} = V_{rest}$$

i.e.,

$$c_0 = -RI_{in}$$

Now the *special solution* of $V_m(t)$ can be obtained as

$$V_m(t) = RI_{in}(1 - e^{-t/\tau}) + V_{rest}$$

As shown in the figure, after the step current into the neuron, it will respond so that its membrane potential $V_m(t)$ will either increased (more positive, or depolarized) or decreased (more negative, or hyperpolarized) depending on the direction of the external current source I_{in}. But this membrane potential change always has an exponential transition, instead of an instant response.

../figures/membraneresponse.gif

Measuring Neuronal Response – the Firing Rate

Neurons respond to external stimuli by generating a train of impulses (spikes) of action potentials. In a typical physiological experiment, the same stimulus is presented multiple times to a neuron and its response recorded (e.g., of 2 second long), as shown in the figure. The detailed compositions of the spike trains vary from trial to trial. To characterize the response of the neuron to the same stimulus, the *average firing rate* $< f(t) >$ is computed by averaging the responses of all trials over a brief time window ΔT of a few msce. However, if the average time is too long, some details in the neuronal signal may be averaged out and thereby some useful information may be lost.

To model the spike trains of the neuronal response, we first treat each spike as a delta function:

$$\delta(t) = \lim_{a \to \infty} \left\{ \begin{array}{ll} 1/a & 0 \le t < a \\ 0 & else \end{array} \right. = \left\{ \begin{array}{ll} \infty & t = 0 \\ 0 & else \end{array} \right.$$

Note that although the value of $\delta(t)$ is infinitely large at $t = 0$, the area underneath the function (representing energy contained in the function) is finite (unit):

$$\int_{-\infty}^{\infty} \delta(t) dt = 1$$

A spike occurs at $t = t_o$ is represented by $\delta(t - t_o)$. Now a train of spikes in the jth trial can be represented as

$$T_j(t) = \sum_{i=1}^{n_j} \delta(t - t_{ij})$$

where n_j is the total number of spikes in the jth trial. If the experiment is repeated k times, the firing rate at time t is computed as the average over all k trials and over a time window of width ΔT:

$$
\begin{aligned}
< f(t) > &= \frac{1}{k}\sum_{j=1}^{k}\frac{1}{\Delta T}\int_{t}^{t+\Delta T} T_j(\tau)d\tau \\
&= \frac{1}{k}\sum_{j=1}^{k}\frac{1}{\Delta T}\int_{t}^{t+\Delta T}\sum_{i=1}^{n_j}\delta(\tau - t_{ij})d\tau
\end{aligned}
$$

Alternatively, we can make the average more smooth over time by using a Gaussian function

$$G(t,\sigma) = \frac{1}{\sqrt{2\pi\sigma^2}}e^{-\frac{t^2}{2\sigma^2}}$$

instead of a constant time window, as the weighting function. Note that $G(t,\sigma)$ also contains unit energy:

$$\int_{-\infty}^{\infty} G(t,\sigma)dt = 1$$

Now the smoothed firing rate as a function of time becomes

$$< f(t) > = \frac{1}{k}\sum_{j=1}^{k}\frac{1}{\sqrt{2\pi\sigma^2}}\int_{-\infty}^{\infty} e^{-\frac{(t-\tau)^2}{2\sigma^2}}\sum_{i=1}^{n_j}\delta(\tau - t_{ij})d\tau$$

The resulting smoothed average firing rate is called *post-stimulus time histogram (PSTH).*

../figures/firingrate.gif

Modeling a Spiking Neuron I – Integrate-and-Fire Model

The generation of a spike train can be modeled by a integrate-and-fire circuit (also called voltage-threshold model) as shown in the figure. Note that case B is more realistic than case A as the resistor R is added to simulate the leakage through the membrane. The circuit is very similar to the electrical membrane model which is also charged by external current. The rectangle represents the spiking mechanism which generates a spike whenever the voltage across the

RC component exceeds a threshold V_{th}, and at the same time the switch is momentarily closed to release all charge stored in C, and the next integration cycle begins and the circuit will be recharged.

../figures/integrateandfiremodel.gif

The RC circuit in case (B) is described by this first order differential equation

$$C\frac{dV(t)}{dt}+\frac{V(t)}{R}=I(t)$$

To solve this equation for $V(t)$, we again first assume the *general solution*

$$V(t)=c_0e^{-t/\tau}+c_1$$

and find its derivative

$$\frac{dV(t)}{dt}=-\frac{c_0}{\tau}e^{-t/\tau}$$

Substituting them in the original equation, we have

$$-c_0e^{-t/\tau}+c_0e^{-t/\tau}+c_1=RI(t)$$

and get

$$c_1=RI(t)$$

We now further assume $V(t)|_{t=0}=V(0)=V_0$ (the initial condition, e.g. $V_0=V_{rest}$), we have

$$V(0)=c_0e^{-0/\tau}+c_1=c_0+c_1=V_0$$

and find

$$c_0=V_0-c_1=V_0-RI(t)$$

Having found both c_0 and c_1, we can finally get the *special solution*

$$V(t)=(V_0-RI(t))e^{-t/\tau}+RI(t)=V_0e^{-t/\tau}+RI(t)(1-e^{-t/\tau})$$

We see that $V(t)$ can be considered as the combination of two independent processes, the discharge of C through the leakage of R from initial V_0 (the first term) and the recharge or discharge of C by $I(t)$ (the second term). Whether $I(t)$ will charge or discharge C depends on its direction, i.e., whether the neuron is excited or inhibited.

If we assume a constant external current $I(t) = I$, then $V(t)$ will asymptotically approach a final value:

$$V(t)|_{t\to\infty} = RI$$

and the rate to reach the final value is

$$\frac{dV(t)}{dt} = \frac{RI}{\tau}e^{-t/\tau} = \frac{I}{C}e^{-t/RC}$$

For $V(t)$ to reach the threshold V_{th} to trigger an action potential, we need

$$RI \geq V_{th}$$

i.e., the minimal sustained current is

$$I_{th} = V_{th}/R$$

Solving the above expression of $V(t)$ (assuming $V_0 = 0$)

$$V(t) = RI(t)(1 - e^{-t/\tau})$$

for t, and replacing $V(t)$ by V_{th}, we find the time to trigger an action potential as a function of any external current $I(t) > I_{th}$:

$$T_{th}(I) = -\tau \; ln(1 - \frac{V_{th}}{RI(t)})$$

With a sustained external current, a spike train will be generated at the frequency

$$\begin{aligned} f &= \frac{1}{t_{refractory} + T_{th}} = \frac{1}{t_{refractory} - \tau \; ln(1 - V_{th}/RI(t))} \\ &= \frac{1}{t_{refractory} - \tau \; ln(1 - I_{th}/I(t))} \end{aligned}$$

where $t_{refractory}$ is the refractory period. When $I(t) < I_{th}$, no spike is triggered. When $I(t) > I_{th}$, this equation relates the stimulus current $I(t)$ and the firing rate f as shown in the f-I plot ($V_{th} = 16mV$, $C = 0.2nF$, $R = 40M\Omega$, $t_{refractory} = 3msec$). We see that the firing rate is a monotonic function of the external current I when $I > I_{th}$.

../figures/leakyintegrateandfire.gif

To summarize, we see that higher firing rate f may be caused by

- low threshold V_{th};
- small refractory period $t_{refractory}$;
- large stimulus current I;
- large R (for high final voltage value);
- small C (for high charge rate $dV(t)/dt$).

Note here R plays double roles in the charging process. An increased R will increase τ and therefore slow down the growth of $1 - exp(-t/\tau)$, but this is not dominant compared to the high final value also caused by increasing R. In the extreme case where $R \to \infty$ (the model becomes perfect or non-leaky), $V(t)$ increases linearly at rate of I/C without bound and reaches V_{th} sooner than any $R < \infty$, as shown here: ../figures/responsetimemodel.gif

../figures/firingratecompare1.gif

Adapting Model

Adaptation is a temporal process in perception which is experienced widely in our everyday life. As an example, if you keep you right hand in cold water for a while, you feel the water is not as cold as you first dip you hand in. Moreover, if you put both hands in hot water right away, your right hand feels the water is much hotter than how you left hand feels. We will see later that adaptation plays an important role in some psychophysical experiments. At the neuronal level, adaptation is represented by the reduced firing rate after a stimulus was first presented. As an example, the followin gis the temporal response of a cat ganglion cell (X-type) to a light turned on for about 2 seconds.

../figures/tempoadaptation.gif

Adaptation can be simulated by modifying the integrate-and-firing model with an added variable resistance R_{adapt} whose value is reduced each time a spike occurs. As a result, R_{adapt} approaches 0 exponentially with a time constant τ_{adapt}. Now the model is described as

$$C\frac{dV(t)}{dt} + \frac{V}{R} + \frac{V}{R_{adapt}(t)} = I(t)$$

where R_{adapt} decreases exponentially

$$R_{adapt}(t) = R_{adapt}(0)e^{-t/\tau_{adapt}}$$

../figures/adaptationmodel.gif

Modeling a Spiking Neuron II – Firing Rate Model

The firing rate model is used in most artificial neural networks. The dynamics of this model is exactly the same as the integrate-and-fire model discussed above. The only difference here is that the firing rate f is assumed to be a continuous and nonlinear function of $V(t)$

$$f = g(V)$$

As function g relates membrane potential (voltage in Volt) to firing rate (frequency in Hertz), it has the dimension of Hertz/Volt. But we could just treat g as a dimensionless function for simplicity if we can accept to treat f as if it is a voltage representing the signal intensity transmitted along the axon (not to be confused with the intensity of the action potentials).

The most commonly used g is a *sigmoidal function* of $V(t)$

$$f = \frac{1}{1 + e^{-c*V}}$$

where c is some constant. The continuous firing rate model is obtained by replacing the switch and the spike generator with a block simulating function g, as shown in the figure.

../figures/continuousfiringmodel.gif

The sigmoidal function is used in many neural network models. Note that the constant c determines the slope of the transition.

../figures/sigmoidal.gif

Several points need to be made regarding this firing rate model:

- The threshold for an action potential to be generated is not accounted for. In fact, any small change in $I(t)$ will affect $V(t)$ and thereby the firing rate f. When $V(t)$ is small (around 0) the firing rate $f = g(V)$ is approximately a linear function of $V(t)$.

- The non-zero firing rate $g(0) = 0.5$ at $V = 0$ represents the spontaneous firing not related to any stimuli. And an excitatory stimulus will cause a positive current I to increase $V(t)$ (depolarization) and thereby a higher firing rate, while an inhibitory stimulus will cause a negative current to decrease $V(t)$ (hyperpolarization) and thereby a lower firing rate.

- $g(V)$ is a saturating function which approaches 1 when $V \to \infty$ and 0 when $V \to -\infty$. This is to model the fact that the firing rate of a neuron can never exceed an upper limit no matter how much a neuron is excited, neither can it be negative.

1 Neural networks

In a neural network composed of a large number (say, n) of synaptically connected neurons, whether and how much a neuron is excited or inhibited depends on the synaptic stimulations it receives from other neurons. The intensity of each synaptic stimulation is in turn determined by (a) the level of excitation (or inhibition) of the neuron transmitting the signal, represented by its firing rate, and (b) the synaptic connectivity between the transmitting and receiving neurons, represented by the *weight* between the two neurons. And the over all evolution of the network, termed *neurodynamics*, can be described by the flowing equation for the ith neuron in the network:

$$C\frac{dV_i(t)}{dt}+\frac{V_i(t)}{R}=I_i+\sum_{j=1}^n w_{ij}f_j(t) \quad (i=1,\cdots,n)$$

where weight w_{ij} represents the synaptic connectivity between the axon of the jth neuron (transmitting) and the dentrite of the ith neuron (receiving), f_j is the firing rate of the jth neuron related to its membrane potential $V_j(t)$ by

$$f_j(t)=g(V_j(t))$$

and I_i is the external current injected into the ith neuron, representing the external stimulation. As mentioned before, if we treat g as dimensionless and f as voltage, then the weight w_{ij} has the dimension of a conductance (current/voltage), representing how easy it is for current to flow through the synapse from the jth neuron to the ith neuron. And the larger w_{ij}, the more the ith neuron is affected by the jth one.

../figures/neuronetworkcircuit.gif

As solving such a large simultaneous differential equation system (of n equations) is in general very difficult, we further simplify the problem by ignoring the temporal behavior of the system and concentrating on the magnitudes of the output of a neuron as a function of the inputs from other neurons. The membrane potential of the ith neuron in this much simplified model becomes

$$a_i=\sum_{j=1}^n x_j w_{ij} \quad (i=1,\cdots,n)$$

where a_i represents the activation of the receiving neuron, x_j represents the signal intensity transmitted by the jth neuron ($i=1,2,\cdots,n$, assuming there are n of them), and w_{ij} represents the synaptic connectivity from the jth neuron to the ith neuron. If the activation level a is higher than the threshold, the neuron is excited to generate action potentials which will travel along its axon to other neurons down stream. The intensity of this output signal, represented by the firing rate, is a function of the activation

$$y = \begin{cases} 0 & \text{if } a < T \\ f(a) & \text{if } a > T \end{cases}$$

where T represents the threshold, y the output signal (firing rate) generated by the neuron, and f is a function such as the sigmoidal function as discussed above.

This model is in the heart of many neural network algorithms. But note that all these algorithms ignore the temporal behaviors of the system.