

The Membrane Equation

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RC Circuits

Figure 1A shows an RC (resistor, capacitor) equivalent circuit model for a patch of passive neural membrane. The capacitor represents the fact that cellular membranes are good electrical insulators. The battery represents the sodium-potassium pump that acts to hold the electrical potential of the inside of the cell below that of the outside. This voltage difference is called the *resting potential* of the neuron. The resistor represents the leakage of current through the membrane.

To understand the behavior of this circuit, we first need to review the behavior of the individual electrical elements. We'll use a water balloon as an analogy to help develop our intuition. Figure 1B shows a leaky water balloon connected to a water pump. When the pump is off, the balloon is empty. When the pump is first turned on, the balloon starts to fill with water. The balloon expands rapidly at first because the force from the incoming water far overpowers the elastic force of the unexpanded balloon. As the balloon is stretched more and more, the elastic force gets greater and greater, so the balloon's size increases ever more slowly, until it reaches equilibrium. At this point, the current flowing into the balloon from the pump is equal to the current spurting out through the holes, and the water pressure inside the balloon is equal to the pressure exerted by the pump. Increasing the number (or size) of the holes would cause more water current to spurt out. Also, if there were more (or bigger) holes, then the balloon would not inflate quite as much. The behavior of the water balloon is expressed in terms of: (1) water volume, (2) water current, (3) water pressure inside the balloon, (4) the size/number of holes, and (5) the elasticity of the balloon.

In the electrical RC circuit, the analogous quantities are: (1) electrical charge, (2) electrical current, (3) electrical potential, (4) electrical conductance, and (5) capacitance. Electrical charge (analogous to water volume), is measured in coulombs. Electrical current is the rate of flow of charge (analogous to the rate of flow of the water in and out of the balloon), and is measured in amperes or amps ($1 \text{ amp} = 1 \text{ coul/sec}$). Electrical resistance (analogous to the size/number of holes in the balloon) is measured in ohms. Electrical conductance is the reciprocal of resistance, and is measured in siemens ($\text{siemens} = 1/\text{ohms}$). Electrical potential (analogous to the water pressure) is measured in volts. One volt will move 1 amp of current through a 1 siemen conductor.

When we say that a neuron is "at rest", it is actually in a state of dynamic equilibrium. There is always some current leaking out of the cell. But when at rest, that leak current is exactly balanced

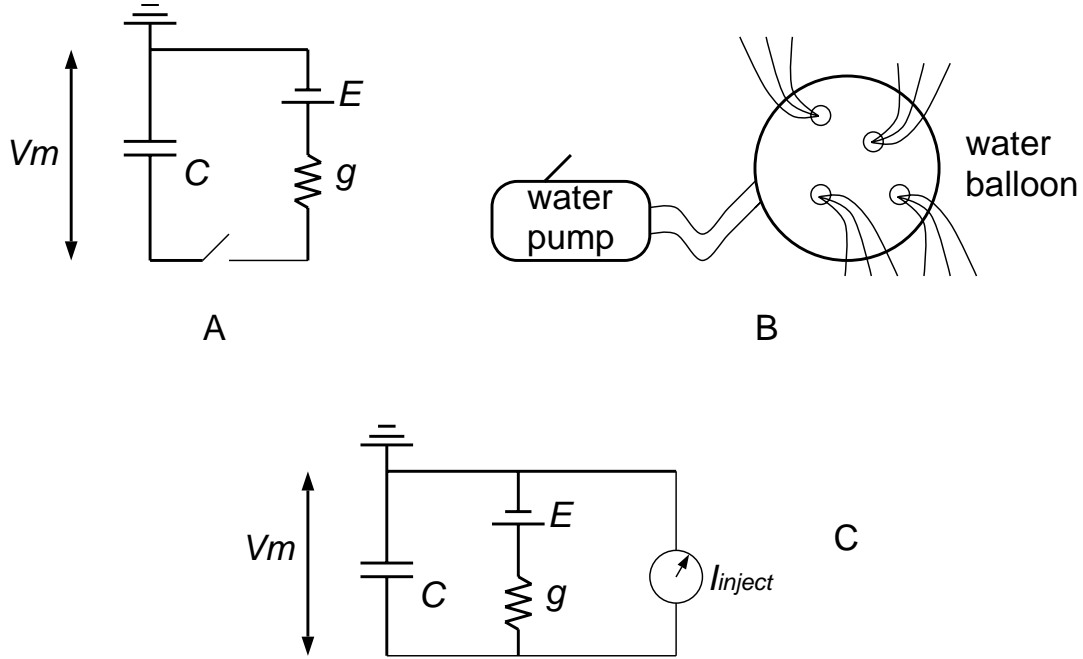


Figure 1: A: RC circuit model of a passive neural membrane. B: Water balloon model of a passive neural membrane. C: RC circuit model of a passive neural membrane, with a current source added.

by the current provided by the sodium-potassium pump so that the net current in/out of the cell is zero. Likewise, once the water balloon is fully inflated, the current provided by the water pump equals the current spurting out through the holes and the net current in/out of the balloon is zero.

We can think about the net current in/out of the balloon/cell in two different ways; one is analogous to the current through the battery/resistor branch of the electrical circuit and the other is analogous to the current through the capacitor of the electrical circuit. We'll consider these in turn.

The net current in/out of the balloon depends on the difference between the pressure in the balloon and the pressure exerted by the pump. When these two pressures are equal, the balloon is in equilibrium, and the net current is zero. The net current also depends on the size/number of holes. If the pressure in the balloon is greater than that exerted by the pump, then the net current will be outward. If the holes are big, then this net outward current will be large. The net current out of the balloon, therefore, increases with increased pressure difference and it increases if the holes are made bigger. In electrical circuits, this is called *Ohm's Law*:

$$I_g = g(V_m - E), \quad (1)$$

where I_g is current through the resistor, V_m is the membrane potential (i.e., the voltage between inside and outside of the neuron, modeled as the voltage drop across both the resistor and the battery), and g is conductance.

The water balloon stores water. We can define the “capacitance” of the water balloon as the volume of water it stores per unit of applied pressure, and it depends on the elasticity of the balloon. Given the same amount of water pressure from the pump, a very elastic balloon will store more water than a very stiff balloon. Likewise, an electrical capacitor stores charge. The capacitance,

measured in farads, is the charge per unit applied voltage:

$$C = q/V_m \quad \text{or} \quad q = CV_m,$$

where C is the capacitance, q is charge, and V_m is again the membrane potential.

As mentioned above, when the pump is turned on the balloon expands rapidly at first, then ever more slowly as it approaches equilibrium. While the balloon is still expanding much of the incoming water goes to fill the balloon. The net current in/out of the balloon changes over time; it is a large inward current at first (when the pump is first turned on) and then decreases eventually to zero. The water pressure in the balloon also changes over time; it is zero at first and then increases eventually to equal the pressure exerted by the pump.

For the electrical circuit, likewise, the voltage across the capacitor and the current through the capacitor both change over time. When the switch is closed, the current through the capacitor is large at first. Then this current drops off slowly as the capacitor charges. The voltage across the capacitor is zero when the switch is first closed, but it increases rapidly at first. Once in equilibrium, the voltage across the capacitor equals the voltage across the battery. It turns out that the current through the capacitor depends on the rate of change of the voltage across the capacitor:

$$I_c = \frac{dq}{dt} = \frac{d}{dt}(CV_m) = C \frac{dV_m}{dt}, \quad (2)$$

where I_c is current through the capacitor. When you look at an equation like this, it is always a good idea to check that units are correct. Electrical capacitance (C) is charge per unit voltage (coulombs/volt). Current (I_c) is the rate of flow of charge per unit time (amps = coulombs/sec). The time-derivative of voltage ($\frac{dV_m}{dt}$) is the rate of change in voltage per unit time (volts/sec). Altogether, $I_c = C \frac{dV_m}{dt}$, that is, amps equals coulombs/volt times volts/sec.

We have formalized two different ways of thinking about the net current in/out of the balloon. Equation 1 expresses the net current (I_g) out of the balloon in terms of pressure difference and conductance. Equation 2 expresses the net current (I_c) into the balloon in terms of rate of pressure change and capacitance. Of course, the net current into the balloon plus the net current out of the balloon must equal zero, that is, $I_c + I_g = 0$, or:

$$C \frac{dV_m}{dt} + g(V_m - E) = 0. \quad (3)$$

This is a first-order, linear, ordinary differential equation that captures the full behavior of the RC circuit. We would like to know exactly how the voltage V_m changes over time when the switch is closed. In other words, we would like to know the solution of this equation. Let $t = 0$ be the time when the switch is closed. Then, by inspection (i.e., a good guess), the solution to this equation is:

$$V_m(t) = u(t) E \left[1 - e^{-(t/\tau)} \right], \quad (4)$$

where $\tau = C/g$, and where $u(t)$ is the unit step function, $u(t)$ is zero for $t < 0$ and $u(t)$ is one for $t > 0$.

Let's double check that this is the correct solution. First, take the derivative of Eq. 4:

$$\frac{dV_m}{dt} = \delta(t) E \left[1 - e^{-(t/\tau)} \right] + u(t) E \frac{1}{\tau} e^{-(t/\tau)},$$

where $\delta(t)$ is the unit impulse, that is, the derivative of the unit step $u(t)$, $\delta(t) = 1$ only for $t = 0$, and $\delta(t) = 0$ otherwise. Note that the first term is zero because the factor in brackets is zero when $t = 0$ and $\delta(t)$ is zero for all other values of t . Then with some algebraic manipulation:

$$\begin{aligned}\frac{dV_m}{dt} &= u(t) E \frac{1}{\tau} e^{-(t/\tau)} \\ &= -\frac{1}{\tau} \left\{ u(t) E \left[1 - e^{-(t/\tau)} \right] - u(t) E \right\} \\ &= -\frac{1}{\tau} (V_m - u(t) E) \\ &= -\frac{g}{C} (V_m - u(t) E),\end{aligned}$$

So, for $t \geq 0$:

$$C \frac{dV_m}{dt} = -g (V_m - E),$$

which is the same as Eq. 3.

Injecting Current

Figure 1C shows another RC circuit, this time with the switch removed and a current clamp added. A current clamp is actually a hard thing to build. For our water balloon the current clamp consists of a second special water pump¹ that can be controlled to produce variable pressure, and a current meter (a mini water wheel). The measurement from the current meter can be used to vary the pressure exerted by the pump. For example, if the current measured by the meter is lower than desired, then it will increase the pressure.

With such a fancy current source, we can inject as much current as we like at any time we like. In fact, the injected current can be varied over time in any way we like. Also, the current clamp allows us to pump water both in (positive currents) and out (negative currents) of the balloon. Try to imagine what will happen to the balloon when we turn on a negative (outward flowing) current. We will derive this below.

There are now three branches in our circuit, each contributing a current either in or out of the balloon/neuron. As before, the sum of these three currents must be zero:

$$C \frac{dV_m}{dt} + g(V_m - E) - I_{\text{inject}} = 0, \quad (5)$$

where I_{inject} is the current provided by the current clamp. Note that the injected current is subtracted from the other two. This is minor detail, but you have to choose a convention for what you mean by positive current. We are following the convention that the current is positive when positive charge flows out of the neuron/balloon.

We would like to solve this differential equation, meaning that we want to know how the membrane potential V_m varies over time in response to any time-varying current injection. We will do this below, but before solving for the general case we will start with an example: a current step.

¹We have been using the water pump as a pressure source (not a current source), analogous to the sodium-potassium pump and the battery that both act as voltage sources. In fact, this is the right way to think about a water pump. If you plug up the pump's hose really tightly, then the pump will work really hard exerting pressure (perhaps eventually overheating) but no current will flow.

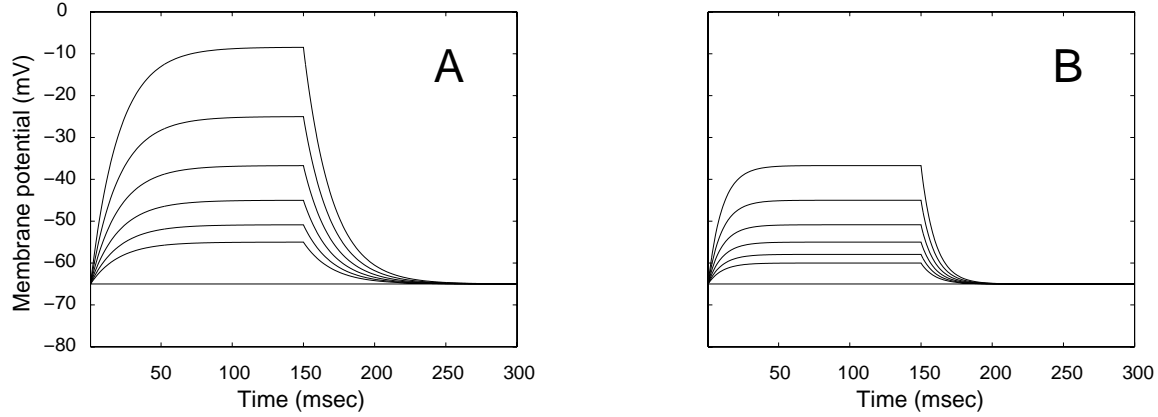


Figure 2: Responses of an RC circuit model of a passive neural membrane to current steps. A: $g = 0.025$ uS. B: $g = 0.05$ uS. Other parameters: $E = -65$ mV, $C = 0.5$ nF. Current amplitudes are: 0, 0.25, 0.3536, 0.5, 0.707, 1, 1.41 nA.

In a current step experiment, the injected current has been zero for some long enough period of time that the membrane potential is at rest, $V_m(0) = E$. Then the current is stepped up or down to some fixed value. After a while, the membrane potential achieves a new steady state value, $V_m(\infty) = V_s$. We want to know what this new steady state value will be, and we want to characterize the time-course of the membrane potential as it changes from E to V_s . Once in steady state, $\frac{dV_m}{dt} = 0$, so the steady state membrane potential V_s can be easily derived from Eq. 5:

$$g(V_s - E) - I_{\text{inject}} = 0,$$

or

$$V_s = E + \frac{1}{g} I_{\text{inject}}.$$

What about the time-course? As you might guess, from what we did earlier, the membrane potential changes exponentially over time from its starting value E to its final value V_s :

$$V_m(t) = u(t) V_s [1 - e^{-(t/\tau)}] + u(t) E [e^{-(t/\tau)}]. \quad (6)$$

At the instant when the current is first turned on ($t = 0$) the first term in square brackets is zero and $V_m(0) = E$. A while later ($t \gg 0$) the second term in square brackets is zero and $V_m(\infty) = V_s$. It would be a good exercise for you to verify that Eq. 6 indeed the solution to Eq. 5 for the case when I_{inject} is a current step.

The voltage time-course given by Eq. 6 is plotted in Fig. 2 for each of several different current step sizes. The current is turned on at time zero and then turned off again 150 msec later. As expected, the voltage V_m rises with an exponential time course to its steady state value, then falls with an exponential time course back to the resting potential. When the conductance is doubled (in Fig. 2B), the response is attenuated (steady state voltages are reduced), but the rise/fall time is quicker. You should check Eq. 6 to verify that this is the expected behavior.

Above, I asked you to imagine what would happen to the balloon by turning on a negative (outward flowing) current. Now we know the answer. At first, just before the current source is turned on, the balloon is at rest meaning that the pressure inside the balloon is equal to the pressure

exerted by the pump, $V_m(0) = E$. A long time after the current source is turned on, the pressure in the balloon is $V_m(\infty) = V_s = E + \frac{1}{g}I_{\text{inject}}$. Since I_{inject} is negative, $V_s < E$, i.e., the balloon shrinks after the current is turned on. The amount of shrinkage depends on both the conductance and the injected current. A larger negative current would result in more shrinkage. A larger conductance (more holes) would result in less shrinkage.

The balloon pressure changes from E to V_s with an exponential time course. The time constant of the exponential, $\tau = C/g$ depends on both the capacitance and the conductance. A larger conductance (more holes) would yield a shorter time constant, i.e., the balloon would shrink more quickly. A larger capacitance (more elasticity) would yield a longer time constant, i.e., the balloon would shrink less quickly.

Now that we've analyzed what happens when injecting a current step, it is time to tackle the solution of Eq. 5 for the general case of an arbitrary time-varying current injection. Let's say that the membrane starts off at rest, $V_m(0) = E$. In the parlance of differential equations, this is called the initial condition. Then a time-varying current $I_{\text{inject}}(t)$ is injected. The solution is:

$$V_m(t) = E + \left\{ [I_{\text{inject}}(t)] * \left[u(t) \frac{1}{C} e^{-(t/\tau)} \right] \right\}, \quad (7)$$

where the $*$ means convolution, and where the $u(t)$ is there to remind us that $I_{\text{inject}}(t)$ is zero for $t < 0$. Equivalently, we can write the desired output membrane potential with respect to the resting potential by adopting the convention that $V(t)$ denotes voltage with respect to the resting potential, $V(t) = V_m(t) - E$:

$$V(t) = [I_{\text{inject}}(t)] * \left[u(t) \frac{1}{C} e^{-(t/\tau)} \right]. \quad (8)$$

This equation is derived in the Appendix I. It would be a good exercise for you to verify that Eq. 7 reduces to Eq. 6 in the case when I_{inject} is a current step.

The RC circuit (passive neural membrane) acts as a shift-invariant linear system; the output membrane potential is a blurred copy of the input injected current. Specifically, $I_{\text{inject}}(t)$ is convolved with an exponential lowpass filter. As the injected current fluctuates positive and negative, the membrane potential fluctuates above and below rest, but the membrane is sluggish so it does not follow high frequency modulations in the injected current.

Frequency Response

A passive neural membrane is a shift-invariant linear system. According to Eq. 8, the membrane potential fluctuations (above and below E) may be predicted by convolving the injected current with a low-pass filter. The parameters of that low-pass filter, g and C , completely determine the behavior of the membrane.

Since the passive membrane is a shift-invariant linear system, we know that we have two alternative methods for determining its parameters: (1) measure the impulse response, or (2) measure the frequency response. Following the first approach, one would inject a very brief pulse of current and fit an exponential to the measured membrane potential fluctuations. However, the membrane

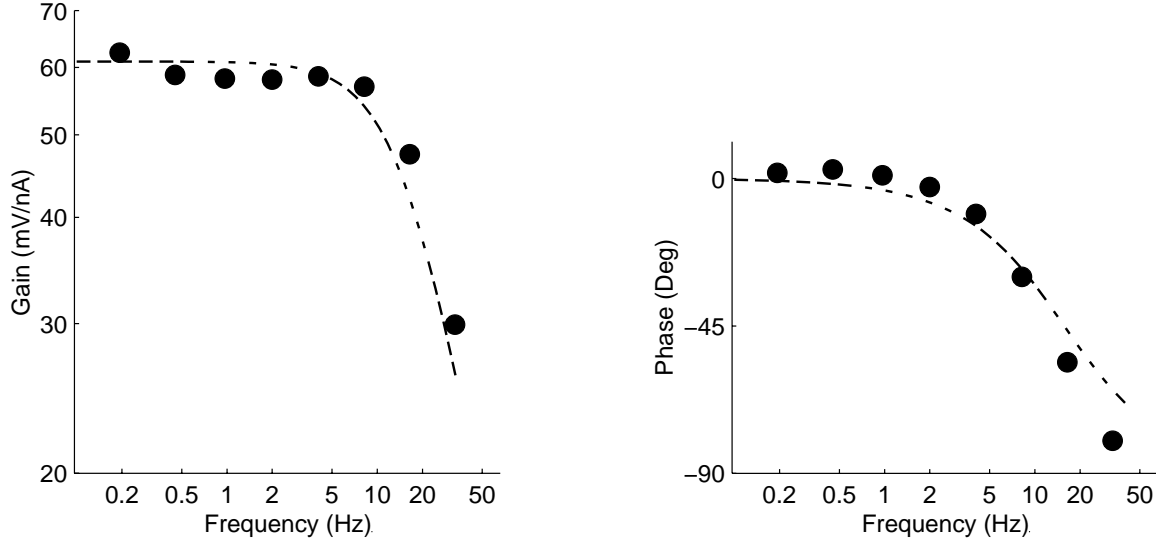


Figure 3: Gain (left) and phase (right) of membrane potential fluctuations in response to sinusoidal current injections of various frequencies. The dashed curves indicate the fit of a single-compartment RC circuit model to the data. Fitted parameters are: $g = 0.017$ uS, $C = 0.1595$ nF (redrawn from Carandini *et al.*, *J. Neurophysiol.*, 76:3425-3441, 1996).

potential fluctuations will be very small and perhaps difficult to measure accurately for very brief current pulses.

Following the second approach, one would inject sinusoidal current modulations, and fit the amplitude and phase of the measured sinusoidal membrane potential fluctuations, for several different frequencies. Data of this sort is plotted in Fig. 3. The data points represent amplitude and phase measurements for different current frequencies. That is, each data point represents the amplitude/phase of the best fitting sinusoid to the membrane potential measurements. The dashed curves are the best fit RC circuit model, that is, they are the frequency response curves for an RC circuit with the best choices for the g and C parameters. As you can see, the fits are quite good.

To determine the best fit g and C parameters, we need a mathematical expression for the frequency response of an RC circuit. The input is a sinusoidally modulating current injection:

$$I_{\text{inject}}(t) = \sin(2\pi\omega t),$$

where ω is the frequency of modulation (in Hz), and where for simplicity we've taken the amplitude of current modulation to be 1 (but it could be anything). The output is a sinusoidally modulating membrane potential (again using the convention that $V(t) = V_m(t) - E$):

$$V(t) = A(\omega) \sin[2\pi\omega t + \phi(\omega)],$$

a sinusoid of the same frequency, but shifted by $\phi(\omega)$ and scaled by $A(\omega)$. The goal is to derive expressions for $A(\omega)$ and $\phi(\omega)$, in terms of g , C , and ω . The answer is:

$$A(\omega) = \frac{1}{\sqrt{g^2 + (2\pi\omega C)^2}} \quad (9)$$

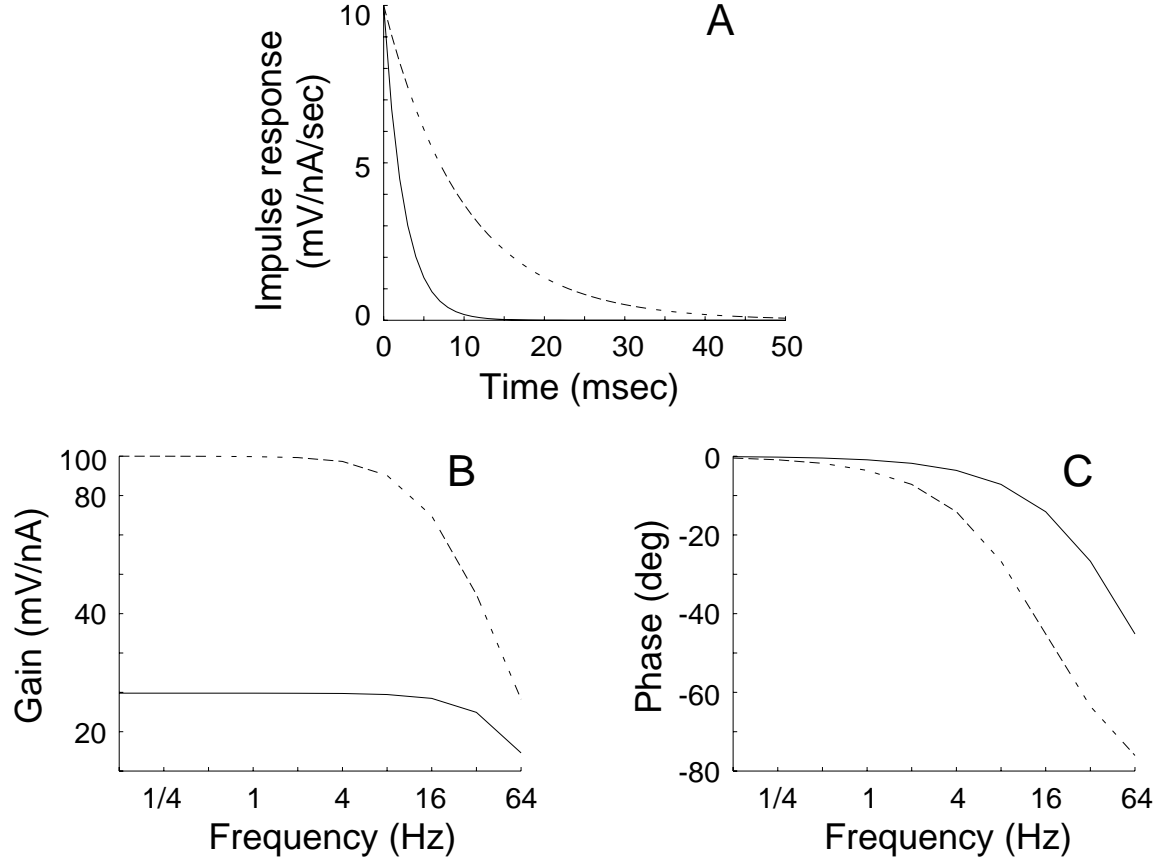


Figure 4: Impulse response (A), gain (B), and phase (C) of a passive neural membrane. Solid curves: $g = 0.04$ uS, $C = 0.1$ nF, and $\tau = 2.5$ msec. Dashed curves: $g = 0.01$ uS, $C = 0.1$ nF, and $\tau = 10$ msec.

$$\phi(\omega) = -\tan^{-1}(2\pi\omega\frac{C}{g}) \quad (10)$$

These equations are derived in Appendix II, and they were used to determine the best values of g and C for fitting the data in Fig. 3.

Figure 4 shows how the membrane's impulse response, amplitude, and phase depend on conductance. The dashed curves correspond to decreasing the conductance by a factor of 4. Decreasing the conductance has two effects. First, it increases the membrane's time constant, i.e., it makes the response more sluggish. This is evident in Fig. 4A since the dashed curve has a longer tail. The change in time constant is also evident in Fig. 4B since the dashed curve starts to turn downward at a lower frequency. And the change in time constant is evident in Fig. 4C since the phase of the dashed curve lags behind that of solid curve. The second effect of decreasing the conductance is to increase the gain. This is evident in Fig. 4B since the dashed curve is above the solid curve. Even though the peaks of the two impulse responses are the same, the gains are different. Note that the dc gain (the y-intercept of each curve in Fig. 4B) equals the integral of the corresponding impulse response (Fig. 4A); the solid curve in Fig. 4A clearly has a smaller integral.

Appendix I: Derivation of Eq. 8

It is convenient to let $V(t)$ denote voltage with respect to the resting potential, $V(t) = V_m(t) - E$. It is also convenient to assume that the injected current is zero for times $t < 0$. Then we begin by rewriting the membrane equation, Eq. 5, in a standard form:

$$\frac{dV}{dt} - aV(t) = f(t), \quad (11)$$

where $a = -\frac{g}{C} = -\frac{1}{\tau}$, and where $f(t)$ depends on the time-varying injected current:

$$f(t) = \frac{1}{\tau}(E + \frac{1}{g}I_{\text{inject}}) = \frac{1}{C}I_{\text{inject}},$$

since $E = 0$. Multiply both sides of the equation by an exponential:

$$e^{-at} \left(\frac{dV}{dt} - aV \right) = e^{-at} f(t). \quad (12)$$

Integrating the left side from 0 to t ,

$$\begin{aligned} \int_0^t e^{-as} \left[\frac{dV}{ds} - aV \right] ds &= e^{-as} V \Big|_0^t \\ &= e^{-at} V - V(0), \end{aligned}$$

where $V(0) = E = 0$ is the initial condition. Hence, integrating both sides of Eq. 12,

$$e^{-at} V = \int_0^t e^{-as} f(s) ds.$$

That is,

$$V(t) = \int_0^t e^{-a(t-s)} f(s) ds$$

This equation can be rewritten as a convolution

$$\begin{aligned} V(t) &= \int_0^\infty u(t-s) e^{-a(t-s)} f(s) ds \\ &= \int_{-\infty}^\infty u(t-s) e^{-a(t-s)} f(s) ds. \end{aligned}$$

The first line follows from the fact that $u(t-s) = 0$ for $s > t$ (the unit step is zero before time zero), and the second line follows from the fact that $f(s) = 0$ for $s < 0$ (there is no current injected before time zero).

Since the last line above is the formula for a convolution we can rewrite it using the $*$ notation:

$$V(t) = f(t) * [u(t)e^{at}]. \quad (13)$$

Equation 13 is the solution for the standard form in Eq. 11. Now we substitute for a and $f(t)$ to get:

$$V(t) = I_{\text{inject}}(t) * \left[u(t) \frac{1}{C} e^{-t/\tau} \right], \quad (14)$$

which is the same as Eq. 8 (when $E = 0$).

Appendix II: Derivation of Eqs. 9 and 10

It is again convenient to let $V(t)$ denote voltage with respect to the resting potential, $V(t) = V_m(t) - E$. Then the membrane equation, Eq. 3, is:

$$C \frac{dV}{dt} + gV = I_{\text{inject}}.$$

Take the Fourier transform of both sides:

$$\mathcal{F} \left\{ C \frac{dV}{dt} + gV \right\} = \mathcal{F} \{ I_{\text{inject}} \},$$

where $\hat{V}(\omega) = \mathcal{F}\{V(t)\}$ denotes the Fourier transform of $V(t)$. The Fourier transform is a linear transform, so we can use additivity and homogeneity to rewrite this equation:

$$C \mathcal{F} \left\{ \frac{dV}{dt} \right\} + g \mathcal{F} \{ V \} = \mathcal{F} \{ I_{\text{inject}} \}.$$

It turns out that there is a very simple relationship between the Fourier transform of a signal and the Fourier transform of the derivative of that signal. In particular,

$$\mathcal{F} \left\{ \frac{dV}{dt} \right\} = 2\pi j\omega \mathcal{F} \{ V \},$$

where j is the square root of -1. Substituting this into the equation that precedes it gives:

$$2\pi j\omega C \hat{V}(\omega) + g \hat{V}(\omega) = \hat{I}_{\text{inject}}(\omega).$$

Rearranging terms gives an expression for the frequency response of the membrane, $\hat{V}(\omega)$:

$$\hat{V}(\omega) = \frac{\hat{I}_{\text{inject}}(\omega)}{g + 2\pi j\omega C} = \hat{I}_{\text{inject}}(\omega) \frac{g - 2\pi j\omega C}{g^2 + (2\pi\omega C)^2}. \quad (15)$$

The last step is to get rid of the complex number notation and write Eq. 15 in terms of its amplitude and phase. Since $\hat{V}(\omega)$ in Eq. 15 is the product of $\hat{I}_{\text{inject}}(\omega)$ times a complex-valued scale factor, the amplitude of $\hat{V}(\omega)$ is the product of the amplitude of $\hat{I}_{\text{inject}}(\omega)$ times the amplitude of that complex number. The squared amplitude of the complex-valued scale factor in Eq. 15 is:

$$\left[\text{amplitude} \left(\frac{1}{g + 2\pi j\omega C} \right) \right]^2 = \left(\frac{1}{g + 2\pi j\omega C} \right) \left(\frac{1}{g - 2\pi j\omega C} \right) = \frac{1}{g^2 + (2\pi\omega C)^2}$$

So the amplitude of $\hat{V}(\omega)$ is:

$$\text{amplitude}[\hat{V}(\omega)] = \frac{\text{amplitude}[\hat{I}_{\text{inject}}(\omega)]}{\sqrt{g^2 + (2\pi\omega C)^2}}. \quad (16)$$

Likewise, the phase of $\hat{V}(\omega)$ is the sum of the phase of $\hat{I}_{\text{inject}}(\omega)$ plus the phase of that complex-valued fraction in Eq. 15 (see the Appendix of the “Signals, Linear Systems, and Convolution” handout). The phase of the complex-valued fraction is:

$$\begin{aligned} \text{phase} \left[\frac{g - 2\pi j\omega C}{g^2 + (2\pi\omega C)^2} \right] &= \tan^{-1} \left(\frac{\frac{-2\pi\omega C}{g^2 + (2\pi\omega C)^2}}{\frac{g}{g^2 + (2\pi\omega C)^2}} \right) \\ &= -\tan^{-1} \left(2\pi\omega \frac{C}{g} \right) \end{aligned}$$

So the phase of $\hat{V}(\omega)$ is:

$$\text{phase}[\hat{V}(\omega)] = \text{phase}[\hat{I}_{\text{inject}}(\omega)] - \tan^{-1} \left(2\pi\omega \frac{C}{g} \right) \quad (17)$$

Choosing the amplitude of the injected current to be one and the phase of the injected current to be zero in Eqs. 16 and 17 gives Eqs. 9 and 10.