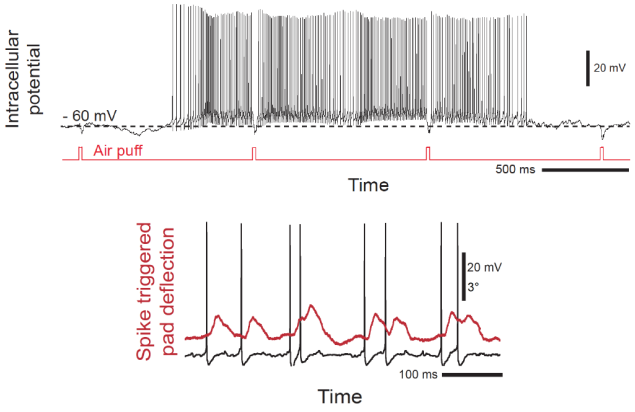
Physics 178/278 - David Kleinfeld - Winter 2022

Lecture 9
Revised 13 Feb 2022 17:44

9 Biophysics of action potentials in "point" neurons

We now step back and visit the nature of spike generation by neurons (Figure 1). We'll do this first in terms of an ad hoc simplified model, then an "exact" model, and then a principled brutalization of the "exact" model. This last step is a critical prelude to a discussion of spike-by-spike synchronization between cells.

Figure 1: Spikes are the currency of neuronal computation and communication. From Bellavance, Takatoh, Lu, Demers, Kleinfeld, Wang and Deschenes, 2017.

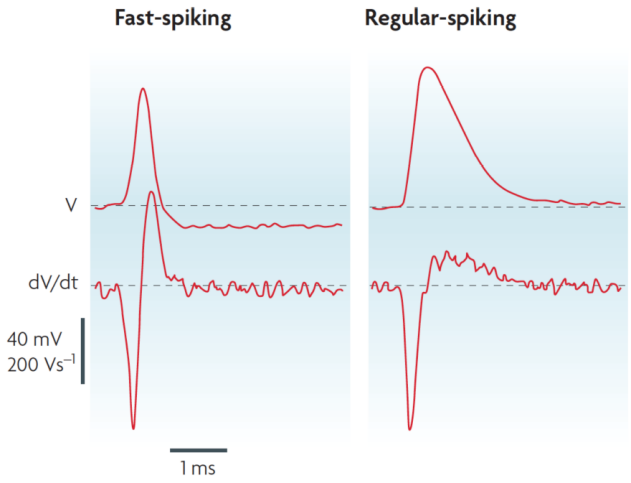


9.1 Fundamental instability for an action potential

The essential ingredient that allows signaling is that the conductance for Na^+ is voltage dependent (Figure 2). That is, the current-voltage relationship has an essential nonlinearity that gives rise to the threshold phenomena in neuronal spiking. This is reminiscent of the drain-to-source conductance in a FET, which is a nonlinear function of the voltage to the gate. The conductance for Na^+ provides the leading edge of the action potential and we thus our point of focus.

For small disturbances of the membrane potential, the cell returns to the resting potential. However, for current injections beyond some critical value, the potential will jump to a new equilibrium point. A simplified model makes use of a voltage dependent

Figure 2: The Na^+ current leads to a similar rise across different classes of neurons. From McCormick, Connors, Lighthall and Prince, 2009.



change in the conductance for one of two ions. To be concrete, we take a cell with a solely Ohmic potassium current, G_{K^+}, and a voltage dependent sodium conductance, $G_{Na^+}(V)$, that has a value of zero below a threshold potential, V_{th}, and that is constant above V_{th} with value $G_{Na^+}(V_\infty)$.

Thus we have a current-voltage relation given by

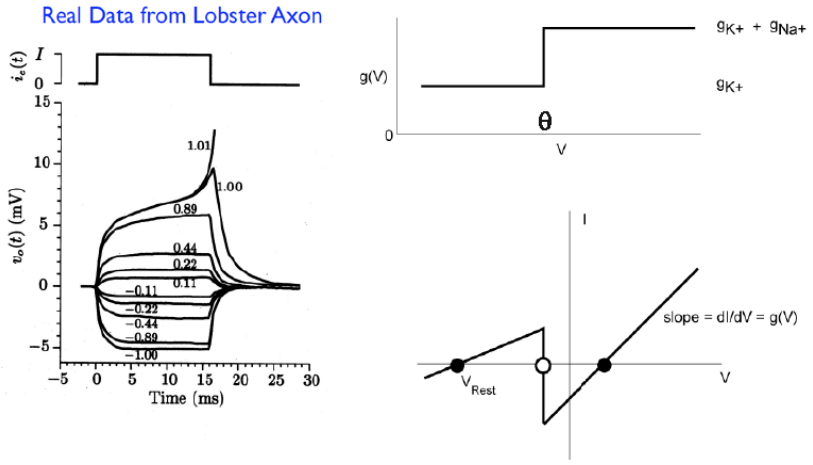
$$I(V) = \begin{cases} G_{K^+}\,(V - V_{K^+}) & \text{if } V < \theta \\ G_{K^+}\,(V - V_{K^+}) + G_{Na^+}(V_\infty)\,(V - V_{Na^+}) & \text{if } V > \theta \end{cases} \tag{9.1}$$

where, V_{Na^+} and V_{K^+} are the Na^+ and K^+ Nernst potential for sodium and potassium, respectfully' we'll return to this. This relation is discontinuous at $V = \theta$ and Ohmic below and above this potential (Figure 3). There are two equilibrium values, one for $V < \theta$ and one for $V > \theta$. These are found by setting $I(V) = 0$, so

$$V_{equil} = \begin{cases} V_{K^+} & \text{if } V < \theta \\ \frac{G_{K^+}V_{K^+} + G_{Na^+}(V_\infty)}{G_{K^+} + G_{Na^+}(V_\infty)} & \text{if } V > \theta \end{cases} \tag{9.2}$$

We consider a pulse of current that causes the cell to change from the lower to the upper curve. This represents the front of the action potential. The shift in equilibrium potential from V_{K^+} to $\frac{G_{K^+}V_{K^+} + G_{Na^+}(V_\infty)}{G_{K^+} + G_{Na^+}(V_\infty)}$ occurs in roughly $10^{-4}s$ (Figure 3). On the longer time scale of $10^{-3}s$, relaxation processes associated with the Na^+ current and the activation of an additional voltage dependent K^+ current cause the front to decay, so we are left with a pulse (Figures 4 and 5). **The critical lesson is that neurons use two voltage levels, and at least one voltage dependent conductance, to shift between the two levels.**

Figure 3: The onset phase of an action potential. The data (left) shows the onset occurs just above a threshold current of $I = 1.00$, while the cartoon shows how a change in the total conductance at threshold voltage, θ, leads to a bistable behavior and switching of the stable point from rest to top of the action potential.



9.2 Review of the Nernst potential

Consider a cell. It consists of two compartments, labeled "inside" and "outside", each filled with Na^+ and Cl^- ions and separated by a lipid membrane. On the inside of the cell, the concentration of ions is denoted $[Na^+]_{in}$ and $[Cl^-]_{in}$ and on the outside they are denoted $[Na^+]_{out}$ and $[Cl^-]_{out}$. To get a feel for the scale of $moles/liter$, letÕs put it into terms relevant for the size of a cell, i.e., ions per cubic micrometer. In a biological cell, the ion concentration is about 0.15 M, so we have about $10^8 ions/\mu m^3$ in a cell.

We set the cell so that, initially, $[Na^+]_{in} = [Cl^-]_{in}$ and $[Na^+]_{out} = [Cl^-]_{out}$ and the two sides are electrically neutral. Further, we impose $[Na^+]_{out} > [Na^+]_{in}$. Suppose we put a sub-nanometer pore that allows only one kind of ion to pass. To be concrete, we open up a hole that allows $[Na^+]$ ions, but not $[Cl^-]$ ions, to pass. This is a Na^+ selective channel. What follows is:

- Initially, the $[Na^+]$ moves down itsÕ concentration gradient, driven by diffusion.
- As Na^+ ions move across the wall, the solutions in the two compartments are no longer electrically neutral. Positive charge (from the Na^+) leaves the outside and builds up on the inside. This leads to an electric field across the wall.
- The electric fields points from the inside to the outside and opposes motion of additional Na^+ ions.
- In time, the electric field caused by the initial movement of ions points from the inside to the outside. This field is the

Figure 4: The slower recovery phase of an action potential. The Na^+-current begins to turn-off and a K^+ current turns on and the membrane potential returns to rest.

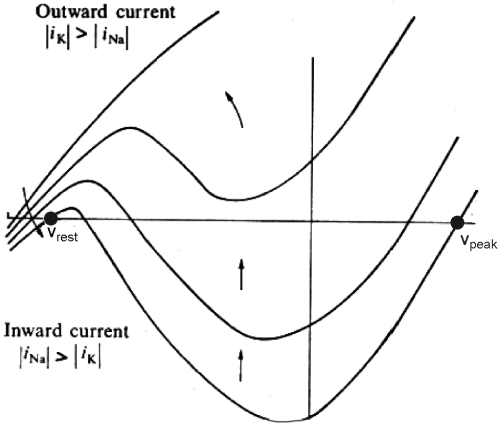
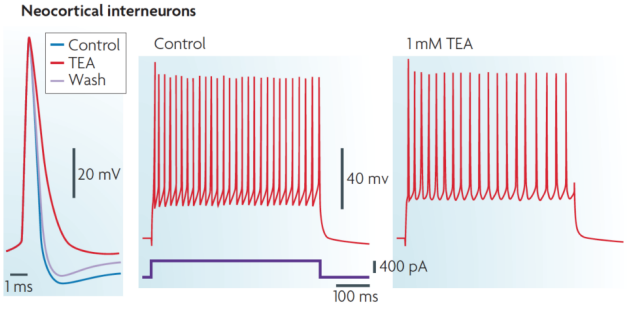


Figure 5: Voltage-gated potassium conductances, which are blocked by TEA, can shape the width of the action potential. From Erisir, Lau, Rudy and Leonard., 1999



direction that opposes motion of additional Na^+ ions and will prevent any more Na^+ ions from moving. As this point the system is in equilibrium.

The result is that the concentration difference in Na^+ ions between the inside and outside of the cell leads a difference in electrical potential across the cell.

The value of the potential is found by equating the chemical potential to move an ion across the membrane, μ, with the electrical potential by $eV = \mu$, i.e.,

$$\begin{aligned} \mu &= \left(\frac{\partial F}{\partial N}\right)_{T,V} \\ &= -k_B T \frac{\partial ln Z}{\partial N} \\ &= -k_B T \frac{\partial ln \frac{\xi^N}{N!}}{\partial N} \\ &= -k_B T \frac{\partial \left(N ln \xi - N ln N\right)}{\partial N} \\ &= k_B T \, ln N \; + \; \text{constant} \end{aligned} \tag{9.3}$$

where Z is the partition function, ζ is the partition function per ion, the denominator of $N!$ accounts for the ways to arrange N identical ions, and we approximated $N! \to N^N$ (Sterling's formula). Thus

$$V = \frac{k_B T}{e} ln \frac{[Na^+]_{out}}{[Na^+]_{in}} \tag{9.4}$$

We see immediately that V is on the order of $\frac{k_B T}{e} \approx 25$ mV.

Review of Goldman-Katz (I-V) relation

In the presence of a weak electric field the motion of ions is limited by the collisions so that the velocity, as opposed to acceleration, is proportional to the force. We have

$$\begin{aligned} \vec{v}_D(x,t) &= \mu \vec{E}(x,t) \\ &= -\mu \frac{\partial V(x,t)}{\partial x} \hat{x} \end{aligned} \tag{9.5}$$

where $\vec{v}_D(x,t)$ is known as the drift velocity, albeit we take the one-dimensional case at present, and μ is the mobility. We can now calculate the flux due to the electric field as

$$\begin{aligned} \vec{J}_D(x,t) &= [Ion](x,t)\ \vec{v}_D(x,t) \\ &= \mu [Ion](x,t)\ \vec{E} \\ &= -\mu [Ion](x,t) \frac{\partial\ V(x,t)}{\partial x} \hat{x}. \end{aligned} \tag{9.6}$$

The total flux includes diffusion down a concentration gradient as well as the electric force. For simplicity, we drop vector notation as all movement is along the $\hat{x}$-axis. Then

$$J(x,t) = -D \frac{\partial [Ion](x,t)}{\partial x} - \mu [Ion](x,t)\ \frac{\partial V(x,t)}{\partial x}. \tag{9.7}$$

At equilibrium, $J(x,t) = 0$. Then

$$\int_{V(x')}^{V(x)} dV = -\frac{D}{\mu} \int_{x'}^{x} \frac{d[Ion](x)}{[Ion](x)} \tag{9.8}$$

and thus

$$\begin{aligned} \Delta V &= V(x) - V(x') \\ &= \frac{D}{\mu} ln \left(\frac{[Ion](x)}{[Ion](x')} \right). \end{aligned} \tag{9.9}$$

But we showed that this equilibrium potential is just given by the Nernst formula, i.e.,

$$\begin{aligned} \Delta V &= V_{Nernst} \\ &= -\frac{k_B T}{ze} ln \left(\frac{[Ion](x)}{[Ion](x')} \right) \end{aligned} \tag{9.10}$$

where include the possibility of a polyvalent ion and write ze for the charge. Thus

$$\mu = D\frac{ze}{k_BT}. \tag{9.11}$$

We can now put all of the formalism together to get a final equation for the flux in terms of a single transport coefficient, D, i.e,

$$J(x,t) = -D\left(\frac{\partial[Ion](x,t)}{\partial x} + \frac{ze}{k_BT}[Ion](x,t)\frac{\partial V(x,t)}{\partial x}\right). \tag{9.12}$$

We focus on the case of current through a pore of cross sectional area A that spans a membrane of thickness L. We further assume that the electric field is uniform (not true, but it allows us to make some uncluttered progress) and that we are in steady state, so that $V(x) = \Delta V \cdot x/L$. We have an equation for the electrical current, I, *i.e.*,

$$\begin{aligned} I &= -zeJ(x)A \qquad (9.13)\\ &= zeDA\left(\frac{d[Ion](x)}{dx} + \frac{ze}{k_BT}[Ion](x)\frac{\Delta V}{L}\right). \end{aligned}$$

or

$$L\frac{d[Ion](x)}{dx} + \frac{ze\Delta V}{k_BT}[Ion](x) = \frac{IL}{zeDA} \tag{9.14}$$

which we can solve directly to obtain

$$I = ze\frac{DA}{L}\ \frac{zeV}{k_BT}\ \frac{[ion]_{in} - [ion]_{out}e^{-\frac{zeV}{k_BT}}}{1 - e^{-\frac{zeV}{k_BT}}} \tag{9.15}$$

where we took the voltage to be $V = 0$ on the outside on the cell and this replace $\Delta V \leftarrow V$ (Figure 6).

The essential feature is that the $I - V$ curve is nonlinear for voltage changes on the order of $\frac{k_BT}{ze} \approx 25/z\ mV$ away from the reversal potential.

In the limit that $V >> 0$ we see that $I \to (ze)^2[ion]_{in}\frac{DA}{L}\ \frac{1}{k_BT}V$ and in the limit In the limit that $V << 0$ we see that $I \to (ze)^2[ion]_{out}\frac{DA}{L}\ \frac{1}{k_BT}V$. Thus in the limits of large and small voltages Ohm's Law, i.e., $I = GV$, is obeyed and the conductance is greater when the current flows from high concentration of ions to low concentrations of ions. The $I - V$ relation is often expressed in terms of the Nernst potential, i.e.,

$$\begin{aligned} I &= ze\frac{DA}{L}\ [ion]_{in}\ \frac{zeV}{k_BT}\ \frac{1 - \frac{[ion]_{out}}{[ion]_{in}}e^{-\frac{zeV}{k_BT}}}{1 - e^{-\frac{zeV}{k_BT}}} \qquad (9.16)\\ &= ze\frac{DA}{L}\ [ion]_{in}\ \frac{zeV}{k_BT}\ \frac{1 - e^{-\frac{ze(V - V_{Nerst})}{k_BT}}}{1 - e^{-\frac{zeV}{k_BT}}} \end{aligned}$$

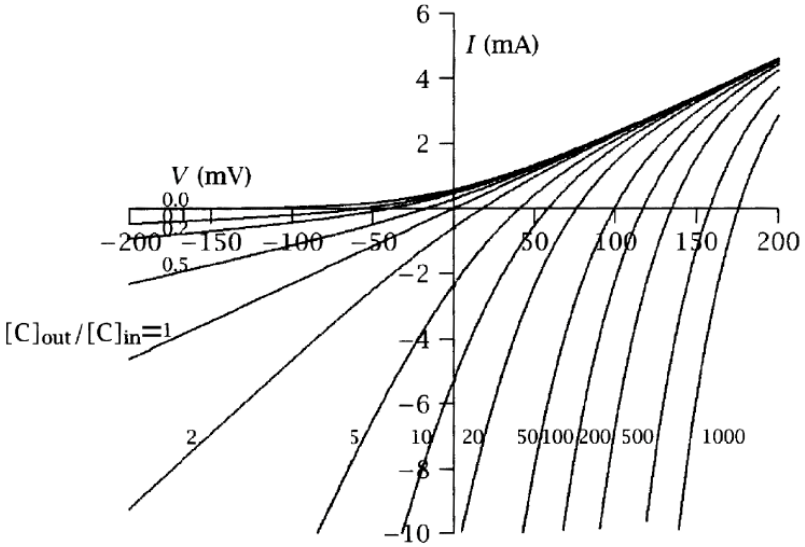
and is known as the Goldman-Katz relation. The essential feature is that the $I-V$ curve is nonlinear for voltage changes on the order of $\frac{k_BT}{ze} \approx 25/z\ mV$ away from the reversal potential.

We can pack all of the prefactors together as a single conductance, $g_{ion}(V)$ where we include the possibility that the pores, or conductances, can be modulated by the transmembrane voltage through $D = D(V,t)$. We write

$$I = g_{ion}(V,t) \left[V \frac{1 - e^{-\frac{ze(V-V_{Nerst})}{k_BT}}}{1 - e^{-\frac{zeV}{k_BT}}} \right]. \qquad (9.17)$$

Figure 6: The I-V relation for ions is nonlinear. Convention is to ignore this and take I = g $(V - V_{Nernst})$

$$I(V) \rightarrow \begin{cases} z^2 e \frac{D}{L} \left(\frac{eV}{k_BT}\right) AC(L) & \text{if } V >> \frac{k_BT}{e} \\ z^2 e \frac{D}{L} \left(\frac{eV}{k_BT}\right) AC(0) & \text{if } V << -\frac{k_BT}{e} \end{cases}$$



.

9.3 Cell circuit with active currents

Let's develop the framework for the physics and electrochemistry of the action potential $V(t)$ for a cell with no spatial extent. We start in the most general manner by adding active currents to the equation for a leaky capacitor,

$$\tau \frac{dV(t)}{dt} - V(t) \;=\; -R_m g_{Na^+}(V,t)\, V\, \frac{1 - e^{-\frac{e(V-V_{Na^+})}{k_BT}}}{1 - e^{-\frac{zeV}{k_BT}}} \qquad (9.18)$$

$$- \quad R_m g_{K^+}(V,t)\; V\; \frac{1-e^{-\frac{e(V-V_{K^+})}{k_BT}}}{1-e^{-\frac{zeV}{k_BT}}}$$

$$- \quad R_m g_{Cl^-}(V,t)\; V\; \frac{1-e^{-\frac{e(V-V_{Cl^-})}{k_BT}}}{1-e^{-\frac{zeV}{k_BT}}} + I^{ext}(t)$$

where τ is the time constant of the passive membrane, R_m is the resistance of the membrane, and $I^{ext}(t)$ includes all external inputs. The sign convention is that positive current flows out.

All of the interesting physics is in the form of the conductances $g_{ion}(V,t)$ so the apparently complicated form of Goldman-Katz is irrelevant. But Hodgkin and Huxley ignored Goldman-Katz for unclear historical reasons and chose to approximate the I-V relation in terms of a voltage and time dependent conductance and a term where the voltage relative to a battery at the Nernst potential. Thus yields a circuit equation (Figure 7). Of course, one can expand Goldman-Katz near $V = V_{Nerst}$, which gives

$$I = \left[g_{ion}(V,t)\; \frac{zeV_{Nerst}/k_BT}{1-e^{-zeV_{Nerst}/k_BT}} \right] (V - V_{Nerst})\,. \tag{9.19}$$

where the terms in the square brackets are just a rescaled conductance. The rectifying form of Goldman-Katz is only impotant if one swings on both sides of the reversal potential; this only occurs for Cl^-1. All told, this dubious approximation reduces the equations into a circuit formulation (Figure 7).

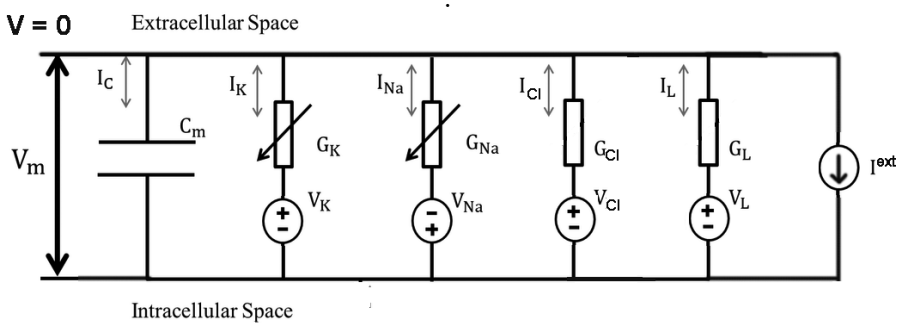
$$\begin{aligned} \tau\frac{dV(t)}{dt} \; - \; V(t) \quad &= \quad R_m g_{Na^+}(V,t)\,[V(t) - V_{Na^+}] \\ &- \quad R_m g_{K^+}(V,t)\,[V(t) - V_{K^+}] \\ &- \quad R_m g_{leak}\,[V(t) - V_{leak}] \; + \; R_m I^{ext}(t). \end{aligned} \tag{9.20}$$

9.4 Functional form of the conductances

The business end is the form of the conductances $g_{ion}(V,t)$, although in the laboratory one measures the current which is proportional to the product $g_{ion}(V,t)[(V,t) - V_{ion}]$. The expectation is that the conductance is in the form of a a maximum conductance, $\bar{g}$, times voltage and time dependent terms for the activation, i.e., the opening of channels designated by $P_{activate}(V,t)$, and the inactivations, i.e., the closing of channels designated by $P_{inactivate}(V,t)$. This allows for transient behavior by the sequential flow and stopage of currents. Recall that all probabilities vary between 0 and 1. Thus

$$g_{Ion}(V,t) \equiv \bar{g}_{Ion} \times P_{activate}(V,t) \times P_{inactivate}(V,t). \tag{9.21}$$

Figure 7: A circuit model for the conductance-based equations of Hodgkin-Huxley equations



9.4.1 A differential equation for $P_{activate}(V,t)$

In general, the activation and inactivation terms are governed by a first order equation that describes their dynamics. We have

$$P_{act}^{open}(V,t) + P_{act}^{closed}(V,t) = 1 \tag{9.22}$$

and

$$\begin{aligned} \frac{dP_{act}^{open}(V,t)}{dt} &= k_{open}(V)P_{act}^{closed}(V,t) - k_{closed}(V)P_{act}^{open}(V,t) \\ &= -\left[k_{open}(V) + k_{closed}(V)\right] P_{act}^{open}(V,t) + k_{open}(V) \\ &= -\left[k_{open}(V) + k_{closed}(V)\right] \times \left[P_{act}^{open}(V,t) - P_{act}^{open}(V,\infty)\right] \end{aligned} \tag{9.23}$$

where $P_{act}^{open}(V,\infty)$ is the steady value of the activation. Thus

$$\frac{dP_{act}(V,t)}{dt} = -k_{obs}\left(P_{act}(V,t) - P_{act}(V,\infty)\right). \tag{9.24}$$

where $k_{obs}(V) = k_{open}(V) + k_{closed}(V)$. There are two inherently voltage dependent terms, the steady state value and the observed time constant. We consider the steady-state behavior and kinetics of a two-state system as a means to understand and parameterize the basic physics of these terms . The idea is that a thermal average or a population of two-state systems is a reasonable portrayal of ionic currents. In fact, the decomposition of macroscopic currents in terms of channels is a justification for this view.

9.4.2 The form of $P_{activate}(V,\infty)$

For sake of argument, let's say that the activation sensor works by having a dipole interact with the transmembrane potential. Dipole

is of the form $\vec{p} = q\vec{d}$ and the dipole experiences a torque from the electric field in the membrane that results in an energy

$$\begin{aligned} Energy &= -\vec{p}\cdot\vec{E} = qd\ cos\phi\ \frac{\partial V}{\partial x} \approx \left(q\frac{dcos\theta}{L}\right)V \\ &\equiv z'e\ V \end{aligned} \tag{9.25}$$

where ϕ is the angle between the dipole and the normal to the membrane, and we have lumped all factors into the charge $z'e$.

The steady state extent of activation to inactivation is given by the usual Boltzmann relation

$$\frac{P_{act}^{open}(V,\infty)}{P_{act}^{closed}(V,\infty)} = e^{\frac{z'e(V-V_{bias})}{k_BT}} \tag{9.26}$$

where V_{bias} is the internal potential drop across the activation sensor. Thus

$$P_{act}^{open}(V,\infty) = \frac{1}{1+e^{-\frac{z'e(V-V_{bias})}{k_BT}}} \tag{9.27}$$

and

$$P_{act}^{closed}(V,\infty) = \frac{e^{\frac{z'e(V-V_{bias})}{k_BT}}}{1+e^{-\frac{z'e(V-V_{bias})}{k_BT}}} \tag{9.28}$$

$P_{act}^{open}(V,\infty)$ is in the form of the logisitic function.

9.4.3 The form of $k_{open}(V)$

We now come to the issue of the observed rate constant or the channel. In general, from a classical view point, the rate is determined by the time it takes for the dipole sensors to rearrange themselves in the activated versus inactivated state. The rate-constants $k_{open}(V)$ and $k_{closed}(V)$, in the absence of an applied electric field, i.e., $V = 0$, are of the form

$$k_{open}(0) = \nu e^{\frac{-\Delta G_o}{k_BT}} \tag{9.29}$$

where ν is an attempt frequency to jump over the barrier and ΔG_o is a barrier height. Then

$$\begin{aligned} k_{closed}(0) &= \nu e^{\frac{-\Delta G_o - z'eV_{bias}}{k_BT}} \\ &= k_{open}(0)e^{\frac{-z'eV_{bias}}{k_BT}} \end{aligned} \tag{9.30}$$

where ν is a molecular attempt frequency and clearly $k_{inact}(0) < k_{act}(0)$ With the addition of an electric field, the activation barrier is modified. The simplest assumption is that the energy of the closed state is raise as much as that of the open state is lowered. Thus

$$k_{open}(V) = k_{open}(0)e^{\frac{-z'eV}{2k_BT}} \tag{9.31}$$

and

$$k_{closed}(V) = k_{open}(0) e^{\frac{-z'eV_{bias}}{k_BT}} e^{\frac{z'eV}{2k_BT}}. \tag{9.32}$$

Thus

$$\begin{aligned} k_{obs}(V) &= k_{open}(V) + k_{closed}(V) \\ &= k_{open}(0) \left(e^{\frac{-z'eV}{2k_BT}} + e^{\frac{-z'eV_{bias}}{k_BT}} e^{\frac{z'eV}{2k_BT}} \right) \\ &= k_{open}(0) e^{\frac{-z'eV_{bias}}{2k_BT}} \left(e^{\frac{-z'e(V-V_{bias})}{2k_BT}} + e^{\frac{z'e(V-V_{bias})}{2k_BT}} \right) \\ &= k'_{open}(0)\ cosh\left(\frac{z'e(V-V_{bias})}{2k_BT} \right). \end{aligned} \tag{9.33}$$

This functional form has the shape of a bowl with a minimum at $V = V_{bias}$. Thus the larger the magnitude of the voltage change, the faster the rate of the shorter the opening time.

9.4.4 Synopsis

The bottom line is that the above forms for $P_{act}^{open}(V, \infty)$ and $k_{obs}(0)$ provide a formulation of the ionic basis for the action potentials. The measured currents for one volttage sensor is

$$I^{\text{active}} = \bar{g}_{Ion} \times P_{activate}(V,t) \times \left[V - V^{\text{Nernst}} \right] \tag{9.34}$$

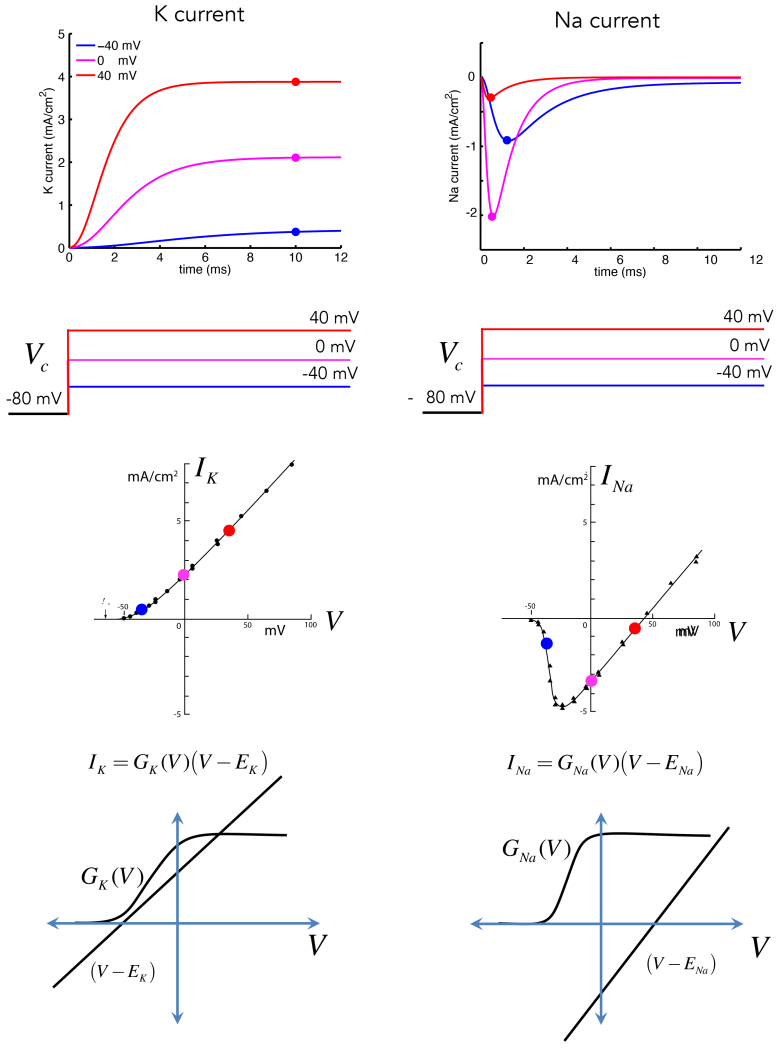
from which one extracts $P_{activate}(V,t)$ by measuring the current as a function of voltage. This is a nontrivial procedure, as all currents but one must be blocked while $P_{activate}(V,t)$ as well as a potential $P_{inactivate}(V,t)$ must be measured. Currently, the measurements are best done by measuring "tail" currents to avoid the contributions of leakage currents. This is now a standard art and we urge you to look in a Neurobiology text. Our focus is on where the Physics takes hold.

9.5 Experimental self-consistency of the Hodgkin-Huxley model

From a formal point of view, the transmembrane voltage, $V(x,t)$ and the activation parameters for each current, $P_{act}^{open}(V,t)$, form the state variables for the the system. For the Hodgkin-Huxley model there are four state variables total, while for models of thalamic relay neurons the number of state variables is (presently) 13.One arrives at measured currents for each ion that can be used to parameterize $P_{act}^{open}(V,x,\infty)$ and $\tau_{obs}(V,x)$ for that ion.

The Hodgkin-Huxley equations are functions of 4 variables.

Figure 8: Logic of the onset activation parameter derived for the Hodgkin Huxley K^+ and Na^+ currents from data. From Hodgkin and Huxley1952 as summarized by Fee class notes.



.

- $V(x,t) \leftarrow$ the transmembrane potential
- $m(V,t) \leftarrow$ the activation function ($P_{act}(V,t)$) for Na^+ current
- $h(V,t) \leftarrow$ the inactivation function (a separate function, $P'_{inact}(V,t) = 1 - P'_{act}(V,t)$) for Na^+ current
- $n(V,t) \leftarrow$ the activation function ($P''_{act}(V,t)$) for K^+ current

The exact fitting parameters are in standard texts and we will not show them. The functional dependencies on V that we expect are clearly seen. This framework includes the observation that the peak of the time constants and the midpoint of the activation functions

occur at nominally the same potential. The dynamic equations are

$$\begin{aligned} \tau \frac{dV(x,t)}{dt} &= -r_m \overline{g}_{Na^+} m^3(V) h(V) \left(V - V_{Na^+}\right) \\ &- r_m \overline{g}_{Ka^+} n^4(V) \left(V - V_{K^+}\right) \\ &- -r_m \overline{g}_{leak} \left(V - V_l\right) + r_m I^{ext}(t). \end{aligned} \tag{9.35}$$

which has 7 independent biophysical parameters, i.e., τ, r_m, $\overline{g}_{Na^+}$, $\overline{g}_{K^+}$, $\overline{g}_{leak}$, V_{Na^+}, V_{K^+}, and V_{leak} as well as 12 (or more in principle) fitting parameters as exponents on the activation and inactivation functions.

$$\frac{dh(V,t)}{dt} = \frac{h_\infty(V) - h(V,t)}{\tau_h(V)} \tag{9.36}$$

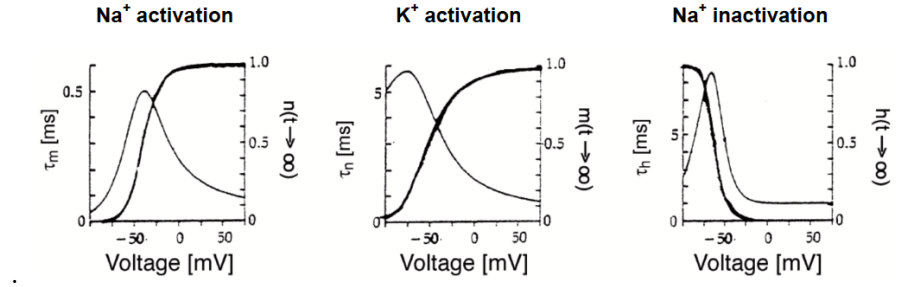
$$\frac{dm(V,t)}{dt} = \frac{m_\infty(V) - m(V,t)}{\tau_m(V)} \tag{9.37}$$

$$\frac{dn(V,t)}{dt} = \frac{n_\infty(V) - n(V,t)}{\tau_n(V)} \tag{9.38}$$

where $n_\infty(V) \equiv n(V, t \to \infty)$ and the parameterization for each rate expression has three fitting parameters, i.e., z', V_b, $\tau_{obs}(0)$, for a total of 9 parameters (Figure 9).

These circuit equations, derived from current clamp data, were used to predict the shape of the action potential in both the space clamped and, as we will discuss later, in the non-space clamped propagating place. The results showed self consistency about the ionic currents and the voltage changes (Figure 10)

Figure 9: The parameters experimentally derived for the Hodgkin Huxley equation, from data. From Hodgkin and Huxley1952.



.

To recap, the action potential results from an instability in the conductance such that the direction of the membrane current transiently reverses in response to a perturbative current. Eventually, the conductance saturates and recovers to a linear response. In both cases, the cell is leaky and the effective time-constant is transiently very short, so that the width of the action potential is small, less than one millisecond.

Figure 10: Computtation shows the form of the currents throughout the action potential.