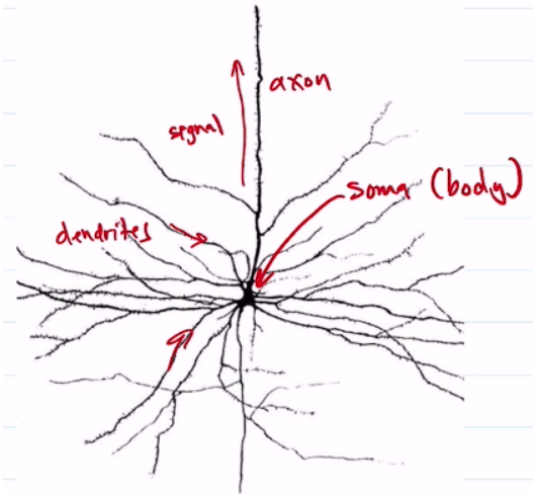
1 Topic 1.

1.1 The Hodgkin-Huxley Neuron Model.

1.1.1 Neurons

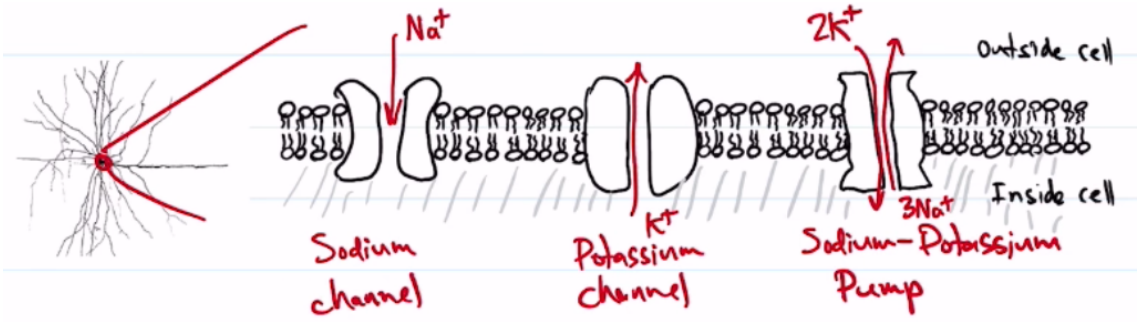
A **neuron** is a special cell that can send and receive signals from other neurons.



- **Soma**: generate electrical signals.
- **Axon**: transmit electrical signals.
- **Dendrites**: receive electrical signals.
- **Synapses**: send electrical signals.

1.1.2 Neuron Membrane Potential

Ions are molecules or atoms in which the number of electrons (-) does not match the number of protons (+), resulting in a net charge. Many ions float around your cells. The cell's **membrane**, a lipid bi-layer, stops most ions from crossing. However, ion channels embedded in the cell membrane allow ions to pass. There exist **sodium** and **potassium channels** which permits Na^+ and K^+ ions to move across the cell membrane, respectively.



The Na^+ channel moves Na^+ ions into the cell while the K^+ channel moves K^+ ions out of the cell. The **sodium-potassium pump** exchanges 3 Na^+ inside the cell for 2 K^+ ions outside the cell. This causes a higher concentration of Na^+ outside the cell and a higher concentration of K^+ inside the cell. It also creates a net positive charge outside and a net negative charge inside the cell. This difference in charge across the membrane induces a voltage difference and is called the **membrane potential**.

1.1.3 Action Potential

Neurons have a peculiar behavior: they can produce a **spike** of electrical activity called an **action potential**. This electrical burst travels along the neuron's **axon** to its **synapses**, where it passes signals to other neurons.

1.1.4 The Hodgkin-Huxley Model

The **Hodgkin-Huxley models** describes how action potentials in neurons are initiated and propagated. Their model is based on the non-linear interaction between membrane potential (aka **voltage**) and the opening/closing of Na^+ and K^+ ion channels. Both Na^+ and K^+ ion channels are voltage-dependent, so their opening and closing changes with the membrane potential.

Let v denote the membrane potential. A neuron usually keeps a membrane potential of around -70mV. We now wish to model the opening/closing of the channels.

Potassium Channels

The fraction of K^+ channels that are open is $n^4(t)$,[1] where

$$\frac{dn}{dt} = \frac{1}{\tau_n(v)}(n_\infty(v) - n).$$

n here is the dynamic variable. Both $\tau_n(v)$ and $n_\infty(v)$ depend on voltage. Thus, the dynamics of the K^+ channel depends on the voltage and varies over time.

As a remark, the DE converges to level n_∞; the rate of convergence is inversely proportional to τ, i.e., it converges faster if τ is smaller.

Sodium Channels

The fraction of Na^+ ion channels open is $(m(t))^3 h(t)$, [2] where

$$\frac{dm}{dt} = \frac{1}{\tau_m(v)}(m_\infty(v) - m)$$
$$\frac{dh}{dt} = \frac{1}{\tau_h(v)}(h_\infty(v) - h)$$

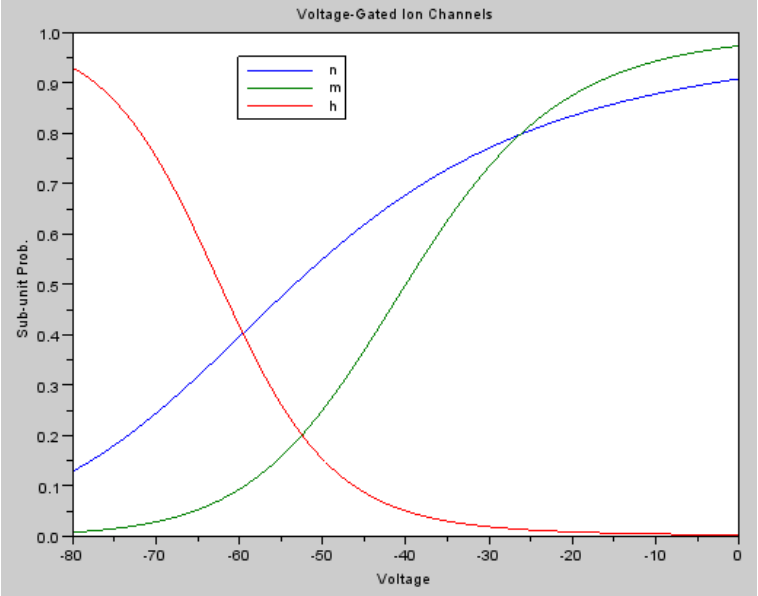
All quantities like τ_m, τ_h, τ_n, etc., are measured empirically.

[1] The intuition is that each K^+ channel is controlled by four gates wherein the probability of one gate being open is n, hence the probability of all gates being open is n^4.

[2] Similar to above, we can interpret this as the Na^+ channel is controlled by three gates with probability m being open and one gate with probability h being open.

Making Sense of DEs

Below is a graph showing how $h(v), m(v), n(v)$ change as functions of voltage. As we can see, as voltage increases (move rightward) the n-gates and m-gates tend to open while the h-gate tend to close. To see how the DEs work, fix membrane potential at $v = -40$. Then we have $m(-40) \approx 0.5$ and $h(-40) \approx 0.05$. With this, you can compute the number (fraction) of sodium channels that are open as $(m(t))^3 h(t)$.



Channels and Membrane Potential

Now these two types of channels allow ions to flow into and out of the cell, inducing a current, which affects the membrane potential V. We can thus describe the membrane potential as a DE in terms of the fraction of K^+ and Na^+ channels that are open:

$$C\frac{dV}{dt} = J_{in} - g_L(V - V_L) - g_{\text{Na}} m^3 h(V - V_{\text{Na}}) - g_{\text{K}} n^3 (V - V_{\text{K}}).$$

- C: **capacitance**.
- $\frac{dV}{dt}$: time rate of change in voltage, or **current**.
- J_{in}: **input current**, usually from other neurons.
- $V_L, V_{\text{Na}}, V_{\text{K}}$: **zero-current potentials**.
- $g_L, g_{\text{Na}}, g_{\text{K}}$: **maximum conductance**.
- $g_L(V - V_L)$: **leak current**.
- $g_{\text{Na}} m^3 h(V - V_{\text{Na}})$: **sodium current**.
- $g_{\text{Na}} m^3 h(V - V_{\text{Na}})$: **potassium current**.

This system of four DEs governs the dynamics of the membrane potential.

1.2 Leaky Integrate-and-Fire Model.

The HH model is already greatly simplified:

- A neuron is treated as a point in space.
- Conductances are approximated with formulas.
- Only considers K^+, Na^+, and generic leak currents.

But to model a single action potential (spike) takes many time steps of this 4-D system. However, spikes are fairly generic, and it is thought that the *presence* of a spike is more important than its specific shape.

1.2.1 The Leaky Integrate-and-Fire Model

The **leak integrate-and-fire** (LIF) model only considers the sub-threshold membrane potential (voltage), but does NOT model the spike itself. Instead, it simply records when a spike occurs (i.e., when the voltage reached the threshold). We express it as

$$C\frac{dV}{dt} = J_{in} - g_L(V - V_L)$$

- C: capacitance.
- g_L: conductance.
- J_{in}: input current.

Note that $g_L = 1/R$ where R is the resistance, so we have

$$RC\frac{dV}{dt} = RJ_{in} - (V - V_L)$$

Let $\tau_m := RC$ denote the time constant. By Ohm's Law (resistance $\times$ current = voltage), let $V_{in} = RJ_{in}$. Thus, the voltage can be modelled as

$$\tau_m\frac{dV}{dt} = V_{in} - (V - V_L).$$

Note this model is valid only when $V < V_{th}$ (later). Define $v := \dfrac{V - V_L}{V_{th} - V_L}$. Then $v \to 0$ if $V_{in} = 0$ and $v = 1$ is the threshold. With this change of variable, we get

$$\tau_m\frac{dV}{dt} = v_{in} - v.$$

Note that unlike in HH, our simplified time constant τ_m is not a function of v.

We integrate the DE for a given input current (or voltage) until v reaches the threshold of 1. Then we record a spike at that time. After it spikes, it remains dormant during its refractory period (denoted by τ_{ref}, often just a few ms). Then it can start integrating again (more on this below).

1.2.2 LIF Firing Rate

Suppose we hold the input v_{in} constant. We can solve the DE analytically between spikes.

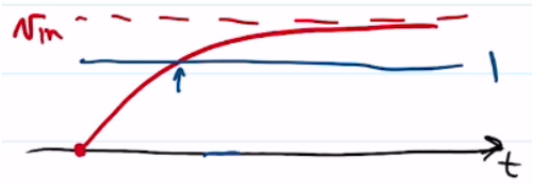
Claim. *$v(t) := v_{in}(1 - e^{-t/\tau})$ is a solution for*

$$\tau \frac{dV}{dt} = v_{in} - v$$

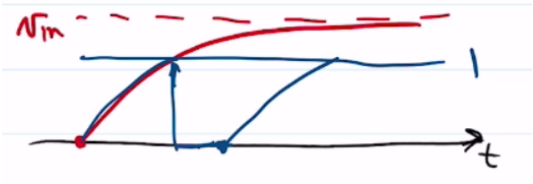
with initial value $v(0) = 0$.

In words, starting at a voltage of 0, follow the dynamics described by the DE, you get $v(t)$ as specified. To prove the claim, plug in the solution to the DE and show that LHS = RHS.

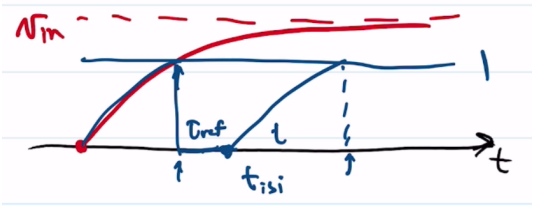
The graph of $v(t)$ looks like this:



Note v_{in} must be above 1 or the neuron never spikes. The blue arrow points to the intersection of $v(t)$ and 1; at this time the neuron spikes. It then enters the refractory period and reinitiate the curve:



To solve for the firing rate, we need to solve for the time the spike occurs (as a function of v_{in}). Let t_{isi} denote the **inter-spike interval**. Note this value is the reciprocal of the fire rate. Now t_{isi} has two components, the refractory time constant τ_{ref}, plus the time it takes to go from $v = 0$ to $v = 1$, call it t^*.



We need to find t^* where $v(t^*) = 1$. From our above solution,

$$v(t^*) = 1 = v_{in}(1 - e^{-t/\tau}) \implies t^* = -\tau \ln\left(1 - \frac{1}{v_{in}}\right), \qquad v_{in} > 1.$$

Therefore, the firing rate is given by

$$G(v_{in}) = \begin{cases} \dfrac{1}{\tau_{ref} - \tau_n \ln(1 - 1/v_{in})} & v_{in} > 1 \\ 0 & v_{in} \leq 1. \end{cases}$$

Typical values for *cortical neurons*:

- τ_{ref} = 0.002s or 2ms.
- τ_m = 0.02s or 20ms.

Below is the graph of the firing rate as a function of v_{in}.