

A neural cell is very ***complicated system***, in order to determine the dynamics of Neuron , we need to define the objective of our model .HODGKIN - HUXLEY had simplified the **spiking** of neuron cell with a model containing four **state variable**.These four state variable define the whole dynamics of neural spike (electric signal) generation. It tell how the system will evolve over time . Figure: State variables (V, m, h, n)

V: Membrane voltage — represents the electrical potential of the neuron. m: Sodium activation gate — controls how quickly sodium channels open. h: Sodium inactivation gate — controls how sodium channels close after a spike. n: Potassium activation gate — controls how potassium channels open to reset the voltage.

If Neuron Cell as bag (shown in the image) it contains water and various dissolved particles both in and out. Particles in and outside the cells are called ions and they carry electric charge .These ions are separated by cell membrane.The composition of ions on each side is different

- Inside highly negative
- outside highly positive

Separation of these ion through the cell membrane generates electric potential

Like the potential energy stored in the water of the dam.

- If the charged ion pass through the membrane(permiable membrane) then the potential is converted in kinetic energy
- If ion does not pass through the membrane the potential energy is stored ---> the phenomenon is called -

$$CAPACITANCE: Q = CV$$

- This formula \$ Q = CV \$ helps us to understand the neural dynamics
- Taking the derivative of both side

Derivative of (Q = C V)

If both (C) and (V) depend on time (t):

$$\frac{dQ}{dt} = \frac{d}{dt}(CV) = C \frac{dV}{dt} + V \frac{dC}{dt}$$

If (C) is constant (does not change with time):

$$\frac{dQ}{dt} = C \frac{dV}{dt}$$

- it describes how voltage changes as charge redistributed across the membrane

- membrane is not completely impermeable it is semi-permeable with proteins channel allowing only specific ion to flow through the membrane

We can think this pathways as register , working along with capacitor. When the ions pass through this channel they create electric current that changes the distribution of charge. Since **current** is defined as the rate of change of charge(rate of flow of charge)

- **from the above statement**

$$\text{as we know : } \frac{dQ}{dt} = C \frac{dV}{dt}$$

- since current is defined as the rate of change of electric charge, we can replace $dQ/dt = I$

$$I = C \frac{dV}{dt}$$

$$C \frac{dV}{dt} = \sum I_{\text{ion}} \quad (\text{sum of all the ionic current flowing through the membrane})$$

- **this Equation is one of the most fundamental for Hodgkin-Huxley model**

- It links the membrane voltage with different ionic current flowing through the different ion channels

Action potential

: Think of it as a brief electrical pulse of increased membrane voltage , created by precisely coordinated way of these ions moving through different channels in the membrane. There are two types of ions that play a very important role in the action potential (spiking) of the neurons

In Figure 2, The membrane voltage slowly rises from resting level , crossing certain threshold this DEPOLARISATION causes the sodium channels to begin opening allowing sodium ion (+ charge) to flow inside the cell causing even more depolarization after brief period of opening the sodium channel closes . Blocking the influx of sodium charge . At the same time channels of another kind open causing the (+)potassium ion to leave the cell , driving the membrane voltage back down to resting . The entire signal happens in milliseconds and this is the fundamental signal that neuron uses to transmit information

How does the flow of ion within the channel takes place

- Number of ion channels open
- The driving force for these ions

As we have already discussed that there is a excess of (+) charge outside the neuron cell and (-) charge inside the cell

Taking POTASSIUM as an example

There is more potassium ion inside the cell as compared to outside , Diffusion tends to push the K^{+} ion outward as the charge inside the cell is (-ve) the electric force tends to pull it inwards .

- Which force wins depend on concentration of ion and membrane voltage
- For any given concentration ratio there exist a special membrane voltage called **EQUILIBRIUM POTENTIAL** (E_{eq}) : where electric force exactly balances the diffusion force . At this point although there is a few ion flow in and outward of the cell , but the net flow is zero
 - when the membrane voltage differs from this **EQUILIBRIUM POTENTIAL** , there is a net flow of ions that tends to drive the membrane potential towards the equilibrium

We can represent the above phenomenon mathematically

$$I_{ion} = g_{ion}(E_{ion} - V)$$

- g_{ion} --> it is conductance [how many channels are open and how many ions flow through them]
- this equation is same as ohm's law
 - with conductance being reverse of resistance $I = \frac{\Delta V}{R}$ { $R=1/g$ }

In Real world this conductance is not constant , which means many of the channels opening and closing depend on the membrane voltage itself so we have to come up with an expression where g is the function of voltage completing our description

$$I_{ion} = g_{ion}(V)(E_{ion} - V)$$

- The formula for voltage dependant - conductance is same for every ion

Now break the conductance into two parts

$$I = \dot{g} p (E - V)$$

- Where \dot{g} : Maximum conductance possible if all the channels were open(hypothetically).It is const, that is determined by the total number of channels present in the cell * conductance of each channel when it is open .Does not change with time
- p = Fraction of ion channels that are open at any given time , which depends on membrane voltage
 - Fraction of open ion channel is same thing as [the probability of channel being open]

Each ion channel is a complex protein machine that changes its shape according to membrane voltage , either allowing or blocking the flow of ion (how -- all mechanism is not fully resolved)

Lets n be the probability of the single gate being present in the permissive state

- They come up with an differential equation that tells , how fast the number of permissive gates changes (we can think of it as transition between permission of non-permissive state)
 - When n increases ,there are $(1-n)$ non permissive gates that move --> permission (at a rate moving to permissive state α)
 - When n decreases ,there are (n) permissive gates that move -->non-permission (at a rate moving to permissive non-state β)

Above phenomena led to the result of differential equation the defines the dynamics of opening and closing of these gates , where there rate depends on voltage

$$\frac{dn}{dt} = \alpha(1-n) - \beta(n)$$

$$\alpha_n(V) = 0.01 \frac{(V+10)}{e^{\frac{V+10}{10}} - 1}$$

$$\beta_n(V) = 0.125 e^{\frac{V}{80}}$$

$$\alpha(V) = \frac{A + BV}{C + e^{\frac{V+D}{F}}}$$

(same for β)

- With these empirical expression of alpha and beta as functions of voltage we can numerically solve the Differential Equation that governs the fraction of individual gate in the permissive state

What about the channels that requires the combination of multiple gates to allow the ion flow?

- Here comes the probability theory
 - probability of single gate to be in permissive state is n
 - of for such independent gate $p(4 \text{ independent gate}) = n^4$
- This is exactly what HODGKIN-HUXLEY found through their experiments , the conductance was directly proportional to the 4th power of n

- what is truly remarkable is at the time , when these experiments were performed the molecular structure of potassium ion was completely unknown. The 4th power totally emerge from fitting curve to their experimental data
- Decades later researcher when examined the channel structure through X-Ray crystallography, They indeed confirm that each potassium channel contains 4 identical gates, which work together to control the flow of ions

So far

- Till now we have come with two equations

$$C \frac{dV}{dt} = g_K n^4 (E_K - V)$$

- Change in membrane voltage as function of potassium current

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$$

- potassium conductance as the function of membrane voltage

Only Potassium does not alone , responsible for generation action potential .Sodium and equally responsible

- The formula to describe sodium current is almost same as potassium but with few differences
- Sodium has gates of two types m and h with different conductance
 - $m \rightarrow$ activating gates ($\times 3$)
 - $h \rightarrow$ inactivating gates ($\times 1$)
 - both have their own distinct properties
- m gate responds to increased voltage making the channel more likely to conduct, h gate does something opposite .It closes with sustained depolarization in a process known as inactivation , but the underlying differential equation is almost same with different constants in α and β constants

$$\frac{dn}{dt} = \alpha_m(1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h$$

Each of the above gating mechanism follows its own Differential Equation

$$\frac{dx}{dt} = \alpha(1-x) - \beta x$$

$$x \in \{n, m, h\}$$

- α and β are voltage dependent rate constants determined experimentally

$$C \frac{dV}{dt} = \sum I_{ion} \quad (\text{sum of all the ionic current flowing through the membrane})$$

We can summarize the above all the phenomena as

$$I_{ion} = g_{ion}(V)(E_{ion} - V)$$

$$I = C \frac{dV}{dt}$$

$$C \frac{dV}{dt} = \sum I_{ion} \quad (\text{sum of all the ionic current flowing through the membrane})$$

- For more realistic dynamics we include "LEAKY CURRENT", which corresponds to various ions moving through the channel that are permanently open and has a constant conductance, such as Cl^-

$$C \frac{dV_m}{dt} = I_K + I_{Na} + I_{leak}$$

$$I_{leak} = g_{leak}(E_{leak} - V)$$

Till now we have considered the neuron as a single point, assuming membrane voltage same everywhere at the same time, but real neurons have complex branching structure with dendrites that receive inputs and axons that transmit signals. Membrane voltage can vary differently across different locations

- To handle this complexity we divide neurons into many small segments and applying HODGKIN-HUXLEY to each segment leading to more complex differential equation
 - The core principle remains the same. Everything is still governed by ion flowing through voltage dependent channels this spread through whole neuron elaborate morphology

HODGKIN-HUXLEY MODEL

- This model tells us how neurons generate and propagate electrical signals known as action potentials (also spikes)

This model contains 4 sets of differential equations to determine the NEURAL DYNAMICS OF THE SYSTEM

Those are as follows

$$C_m \frac{dV}{dt} = g_{Na} m^3(V) h(V)(E_{Na} - V)$$

- $C_m \frac{dV}{dt}$: The capacitive current (change in voltage)

- ***It describe change in membrane voltage driven by ionic current flowing through the membrane***

\$\$ \begin{cases} \frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m \\ \frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h \\ \frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n \end{cases} \$\$

- The other three equation monitor the proportion of open ion channels which themselves depend on voltage creating an feedback loop

V = is membrane voltage electric potential across the neuron's cell membrane

- The rate of change of voltage (electric potential) across the cell membrane is $\frac{dV}{dt}$
- Cm = capacitance of the cell membrane that act as small capacitor, storing electrical charges. Charged Ion^{+} are separated by cell membrane create a capacitance inside the neuron cell
- The voltage change is driven by sum of all the ionic current flowing across the membrane.
- The model simplify this into three main currents flowing across the cell membrane

Lets simplify the HODGKIN-HUXLEY model to specifically just two variable

- n = fraction of open potassium channel
 - We derived to this euqation

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n(n)$$

THE SIMPLIFIED VERSION FOR THE ABOVE CODE IN 2 SET OF DIFFERENTIAL EQUATION TO DETERMINE THE NEURAL DYNMAICS OF THE SYSTEM

$$C_m \frac{dV}{dt} = g_{Na} m_\infty^3(V) h_\infty(V) (E_{Na} - V)$$

- $\frac{dn}{dt} = \frac{n_\infty(V) - n(V)}{\tau_n(V)}$
- Imagine if we freeze the voltage to some value α and β becomes +(ve) numbers the n and $(n-1)$ gates tends to reach equilibrium

□ Reduction of the Gating Variable Equation

In the Hodgkin–Huxley model, each gating variable (like (n, m, h)) follows the dynamic:

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n$$

This describes two competing processes:

$\alpha_n(V)(1-n)$: opening of gates

$\beta_n(V)n$: closing of gates

⚙ Step 1: Expand and Rearrange

$$\frac{dn}{dt} = \alpha_n(V) - (\alpha_n(V) + \beta_n(V))n$$

Now we can see (n) decreases at a rate proportional to itself and increases toward a voltage-dependent constant.

⚙ Step 2: Factor Common Terms

$$\frac{dn}{dt} = (\alpha_n(V) + \beta_n(V)) \left[\frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} - n \right]$$

This shows that the rate of change of (n) depends on how far it is from a certain **target value**.

⚙ Step 3: Define Steady-State and Time Constant

Let:

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}, \tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

Substitute them into the equation:

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

□ Interpretation

- ($n_{\infty}(V)$): steady-state (equilibrium) value toward which (n) relaxes.
- ($\tau_n(V)$): time constant controlling how fast it relaxes.

Thus the solution takes the familiar exponential form:

$$n(t) = n_{\infty}(V) + (n_0 - n_{\infty}(V))e^{-t/\tau_n(V)}$$

□ Final Insight

The transformation:

$$\alpha(1-n) - \beta n \Rightarrow \frac{n_{\infty} - n}{\tau_n}$$

isn't just algebraic — it shows that gating variables follow **exponential relaxation dynamics** toward equilibrium states.

This reduction turns messy biological kinetics into clean geometric flows — the true *elegance* of the Hodgkin–Huxley formulation.

$$n_{\infty}$$

- An equilibrium point where rate of opening and closing of gate is constant value alpha = beta
- tau determines how fast the system reaches the equilibrium value
 - small tau , rise fast
 - large tau , rise slow
 - $n(t) = n_{\infty} + (n_0 - n_{\infty})e^{-t/\tau_n}$

Symbol	Meaning	Effect
(n_{∞})	The final equilibrium value of n	Where it's going
(τ_n)	The time constant	How fast it gets there
Small τ_n	Fast approach	Quick gating
Large τ_n	Slow approach	Sluggish gating

□ The Setup

In the **Hodgkin–Huxley model**, we have **three gating variables**:

$$n(t), m(t), h(t)$$

Each follows the same type of equation:

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}$$

where (x) is (n), (m), or (h).

- $x_\infty(V)$: steady-state (final) value at a given voltage
 - $\tau_x(V)$: time constant — how quickly (x) reaches equilibrium
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⚙️ What the Graph Shows

Each curve shows **how fast** each gating variable responds when voltage changes:

Variable	τ (time constant)	Meaning
$\tau_n = 3.7 \text{ ms}$	Slow	Potassium gate opens slowly
$\tau_m = 0.009 \text{ ms}$	Extremely fast	Sodium activation gate reacts almost instantly
$\tau_h = 0.71 \text{ ms}$	Medium	Sodium inactivation gate reacts moderately fast

☐ The Key Idea — Why ($m(t)$) and ($h(t)$) Can Be **Simplified**

Look at the **middle graph** — ($m(t)$) rises to its final value **almost instantly** because:

$$\tau_m = 0.009 \text{ ms}$$

is extremely small.

That means:

$$m(t) \approx m_\infty(V)$$

In plain English:

The sodium activation variable (m) changes so fast that it's practically *always* at its steady-state value for the current voltage.

⚡ So What Happens in the Equations?

Normally, we'd have to **solve**:

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

But since τ_m is very small, m catches up to $m_\infty(V)$ almost instantly.

So we **approximate**:

$$m(t) \approx m_\infty(V)$$

and **remove** the differential equation for (m).

This greatly simplifies the system — instead of tracking how (m) *changes*, we just assume it's already at its equilibrium for that voltage.

□ What About ($h(t)$) and ($n(t)$)?

- $h(t)$: has a moderate $\tau_h \rightarrow$ we still model it dynamically.
- $n(t)$: slowest $\tau_n = 3.7\{ms\} \rightarrow$ we definitely need its time evolution.

So:

- Keep **n** and **h** as dynamic variables.
 - Approximate $m \approx m_\infty(V)$.
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* Result — The Simplified Equations

After this approximation, the **membrane current equations** simplify:

$$I_{Na} = g_{Na} m^3 h (V - E_{Na}) \Rightarrow I_{Na} \approx g_{Na} m_\infty(V)^3 h (V - E_{Na})$$

Now only (h) and (n) need differential equations — (m) is replaced by ($m_\infty(V)$), a direct function of voltage.

□ In Short

Variable	Time Constant	Behavior	What We Do
(m)	Very small	Instantaneous	Replace ($m(t)$) with ($m_\infty(V)$)
(h)	Medium	Dynamic	Keep differential equation
(n)	Slow	Dynamic	Keep differential equation

□ Why h Can Be Removed

In many *reduced* Hodgkin–Huxley models we **remove** m and **also remove** h (or replace $h(t)$ by its steady-state value) because of these simplifying assumptions:

- m is extremely fast → set $m(t) \approx m_\infty(V)$
- h is either fast enough (or tightly voltage-dependent) that we approximate it by its steady-state value $h_\infty(V)$ (or by a simple function of V or n) → this eliminates the differential equation for h and replaces $h(t)$ by a direct function of V
- The result: only **membrane voltage** $V(t)$ and one gating variable (typically $n(t)$) remain dynamic — giving a **2D system** that's much simpler to analyze and still captures main excitability behavior.

⚠ *Tradeoff*: you lose some fine timescale structure of sodium inactivation, but still capture the qualitative spike dynamics.

⊗ Final Two Differential Equations

(*Standard 2-variable Hodgkin–Huxley reduction*)

Assume $m \approx m_\infty(V)$ and $h \approx h_\infty(V)$. Then the reduced system becomes:

$$C_m \frac{dV}{dt} = -g_{Na} m_\infty(V)^3 h_\infty(V)(V - E_{Na}) - g_K n^4 (V - E_K) - g_L (V - E_L) + I_{\text{ext}}$$
$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)}$$

□ Parameter Definitions

- C_m : membrane capacitance
- g_{Na}, g_K, g_L : maximum conductances
- E_{Na}, E_K, E_L : reversal potentials

And the voltage-dependent steady-state functions:

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)}, h_\infty(V) = \frac{\alpha_h(V)}{\alpha_h(V) + \beta_h(V)}, n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}$$

Time constant for n :

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

□ **Result:** We now have a **two-dimensional system** of ODEs — $V(t)$ and $n(t)$ are dynamic, while m and h are algebraic functions of V .