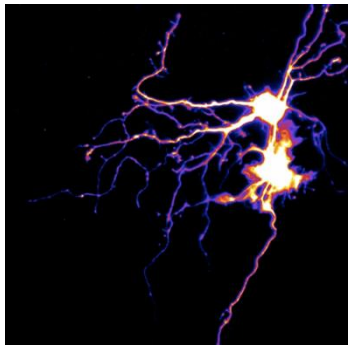

Foundations of Computational Neuroscience (2): Models of Neurons

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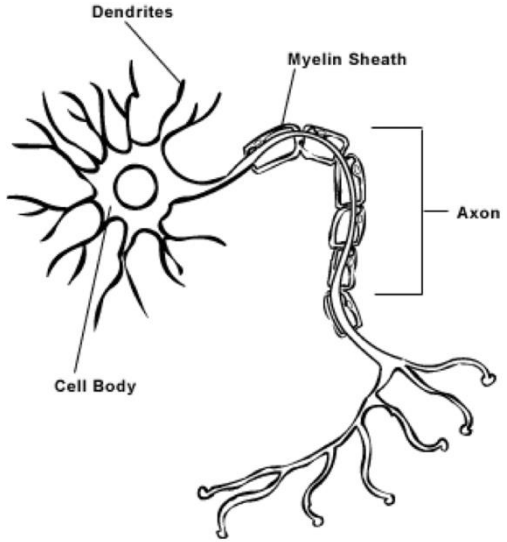
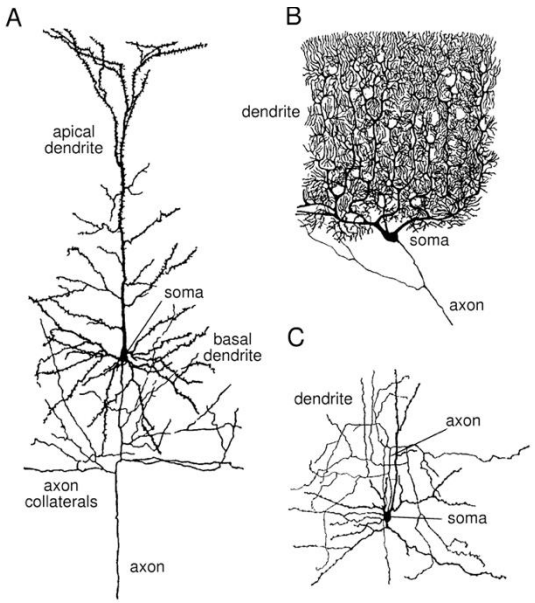
CCN 2026 lecture 3

Neurons





Neuron = cell, diverse morphologies

Dendrites: receive inputs from other cells, mediated via synapses.

Soma (cell body): integrates signals from dendrites. 4-100 micrometers.
Action potential: All-or-nothing event generated if signals in soma exceed threshold.

Axon: transfers signal to other neurons.

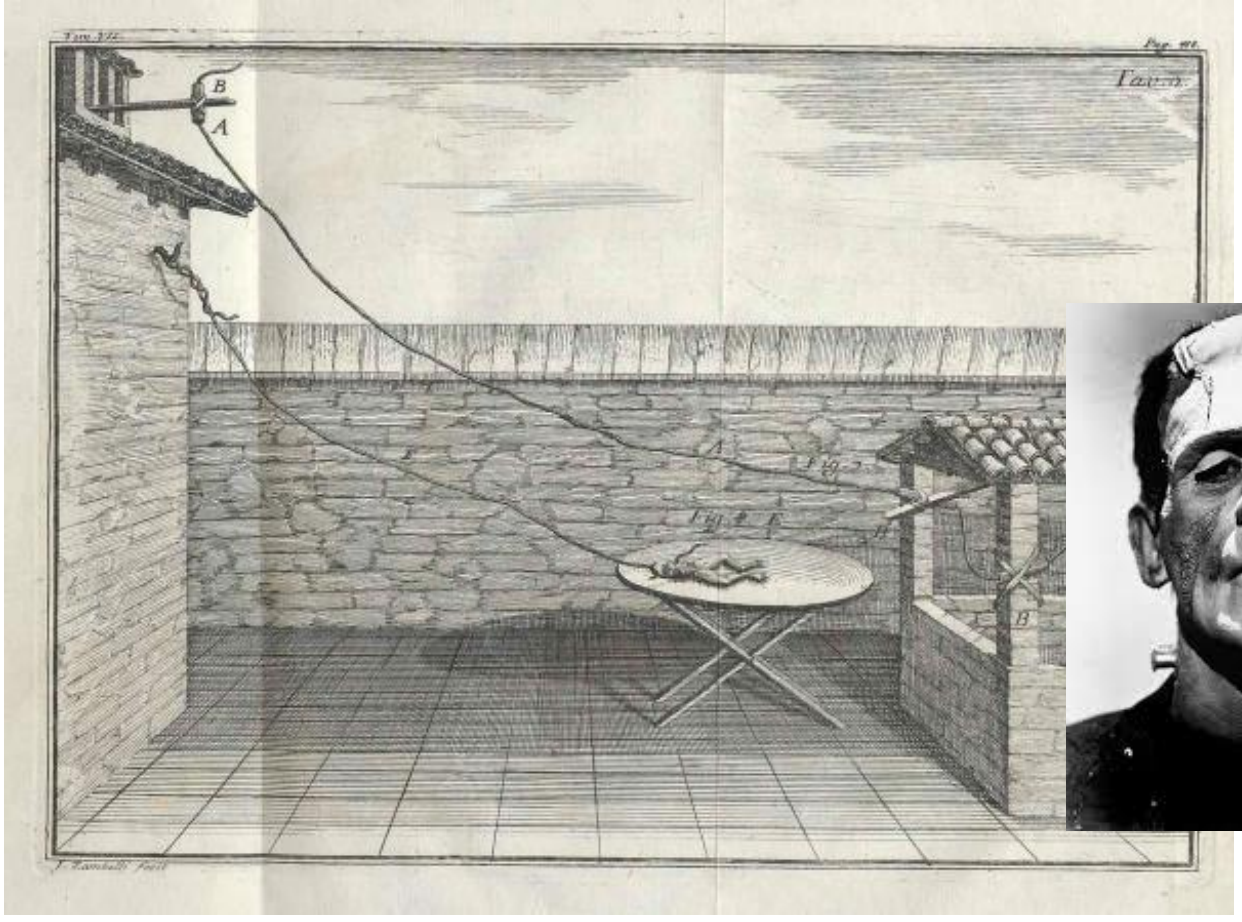
Synapse: contact between pre- and postsynaptic cell.
- Efficacy of transmission can vary over time.
- Excitatory or inhibitory.
- Chemical or electrical.

10^16 synapses in young children (decreasing with age --1-5x10^15)

A Bit of History

- 1791-1797: **Galvani** describes electrical activity in nerves (“ animal electricity”): Dead frogs legs jump when electrically stimulated.

This inspired **Volta’s** first battery 1800 - and Mary Shelley’s Frankenstein.

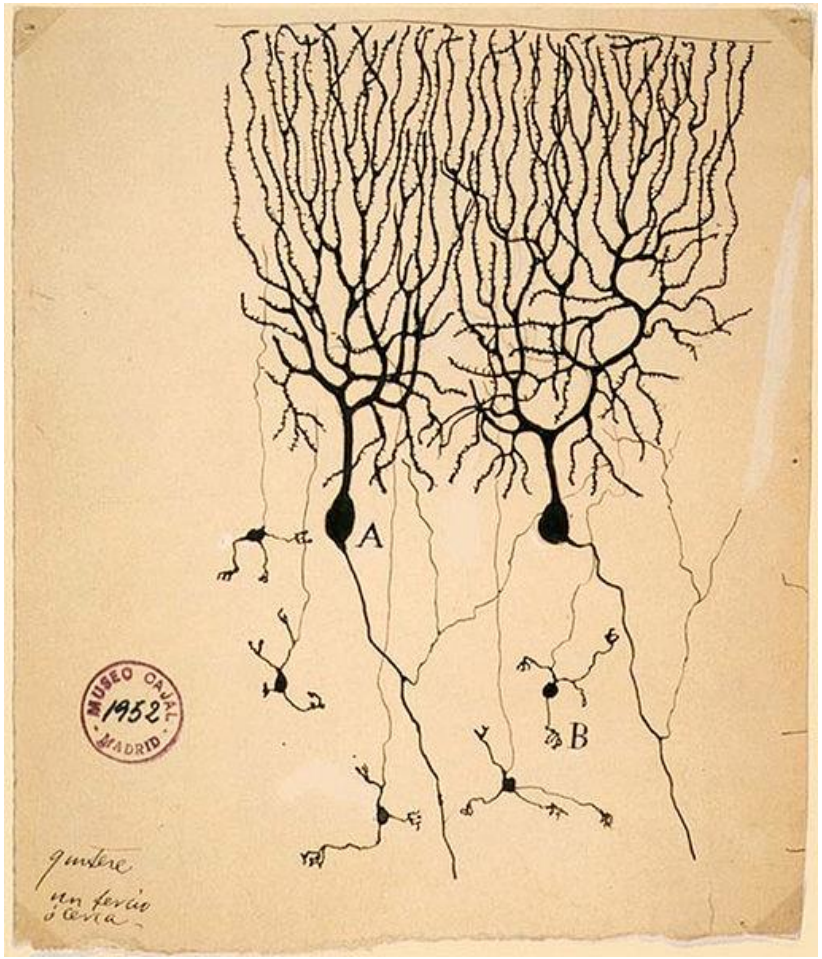


A Bit of History

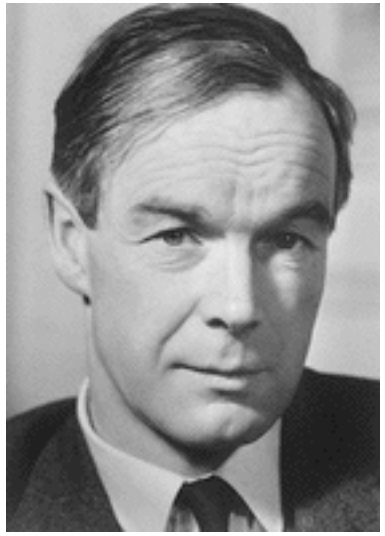
- 1848 **Emil du Bois Reymond** discovered the action potential in frogs' muscles

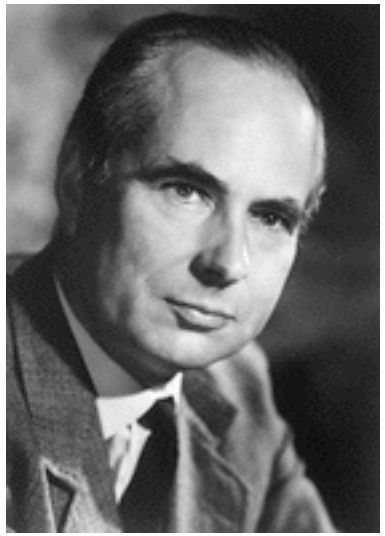
- **Ramon y Cajal** (Nobel prize 1906) established that nervous tissue is made up of discrete cells

- In 1902 and 1912, **Bernstein** advanced the hypothesis that the action potential resulted from a change in the permeability of the axonal membrane to ions.



Hodgkin & Huxley (1952)

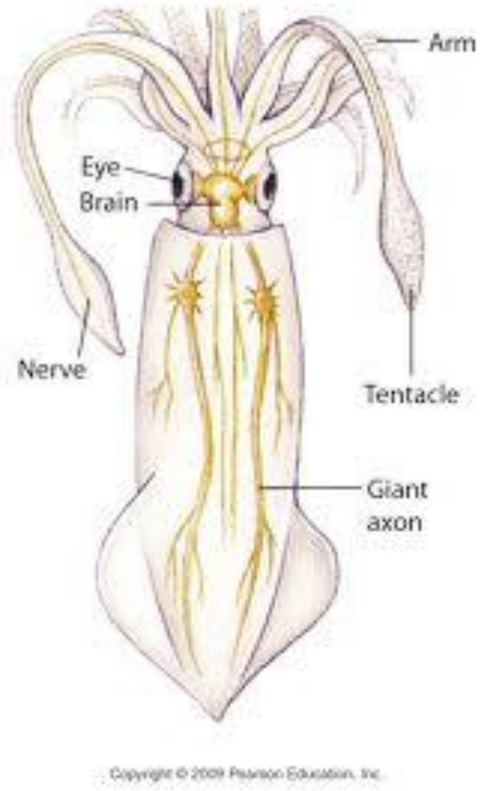




- Cambridge (1935-1952)
- experimental measurements theory of the action potential
- Used the giant axon of the squid which enabled them to record ionic currents
- voltage clamp technique: to measure ionic currents across membrane by holding potential constant.

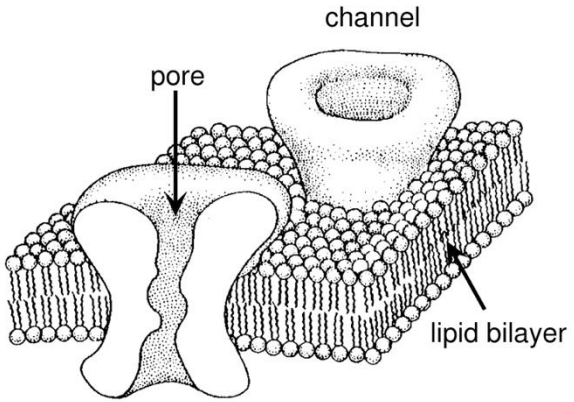
Nobel Prize 1963

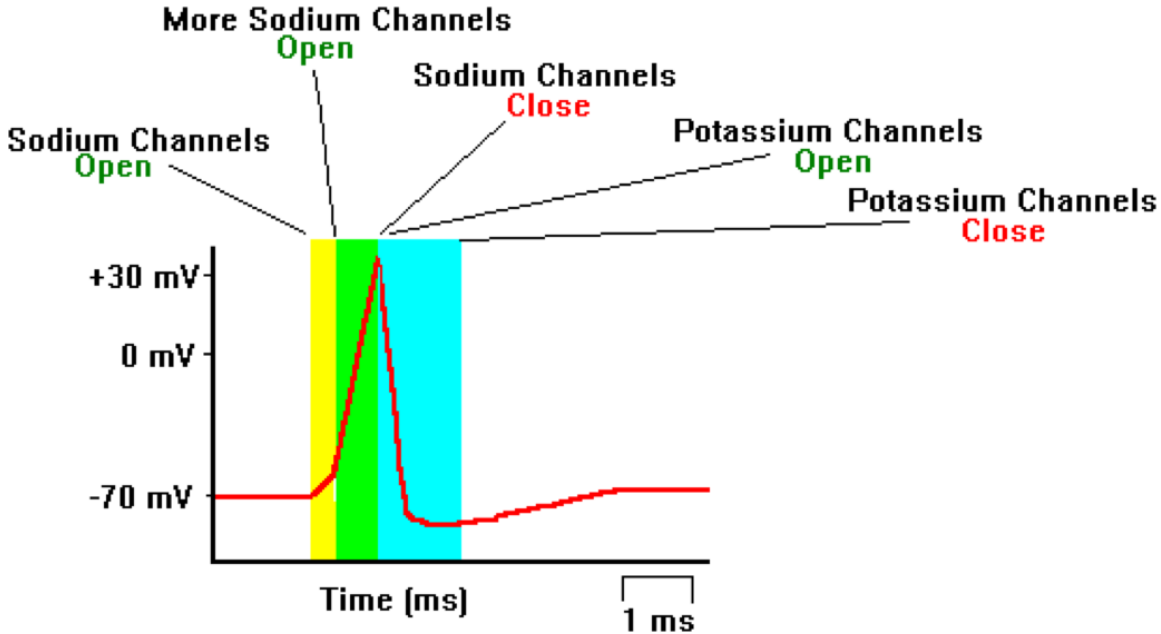
http://www.youtube.com/watch?v=k48jXzFGMc8

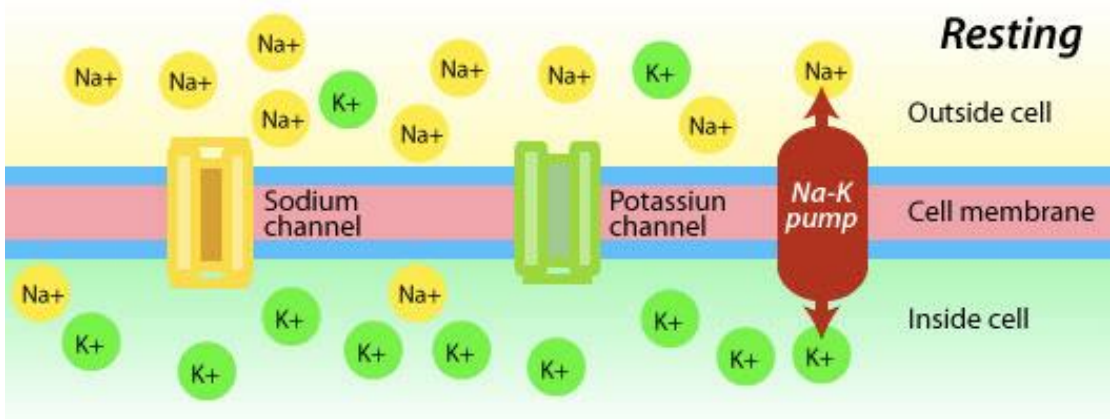


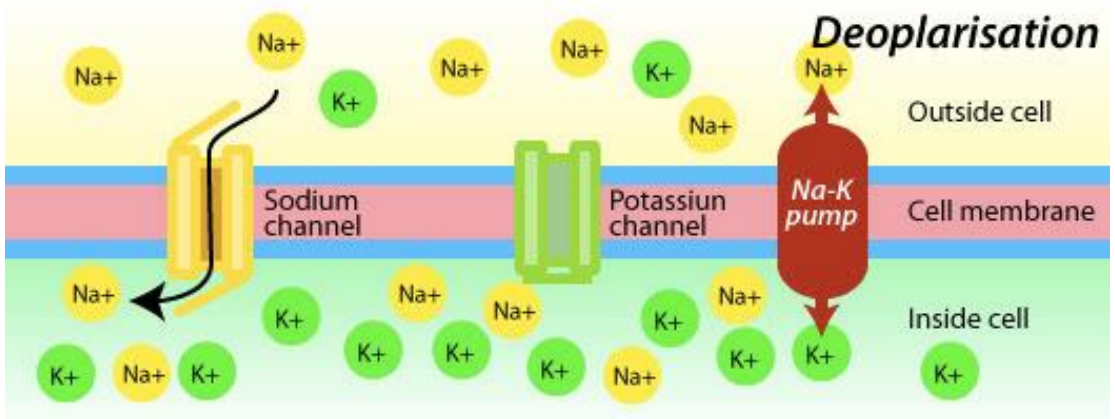
Membrane Potential and Action Potential

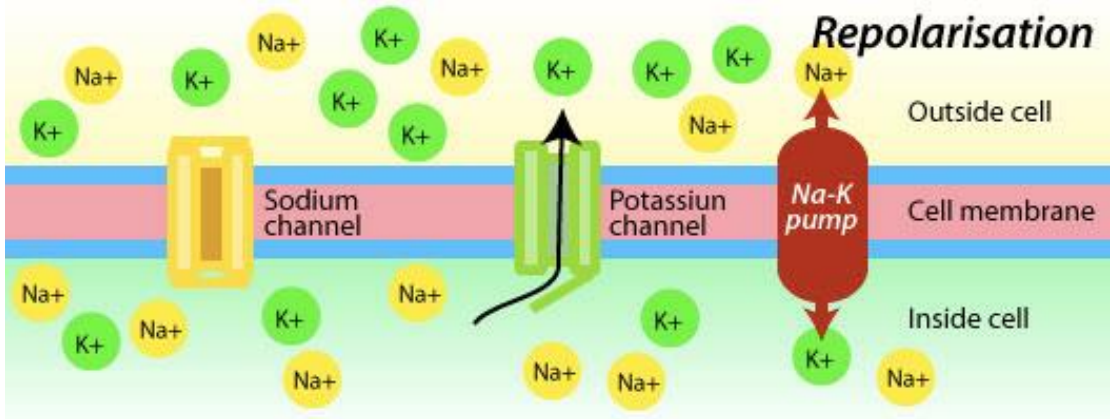
- Ions channels across the membrane, allowing ions to move in and out, with selective permeability (mainly Na+, K+, Ca2+,Cl-)
- Vm: difference in potential between interior and exterior of the neuron.
- at rest, Vm~-70 mV (more Na+ outside, more K+ inside, due to N+/K+ pump)
- Following activation of (Glutamatergic) synapses, depolarization occurs.
- if depolarization > threshold, neuron generates an action potential (spike) (fast 100 mv depolarization that propagates along the axon, over long distances).

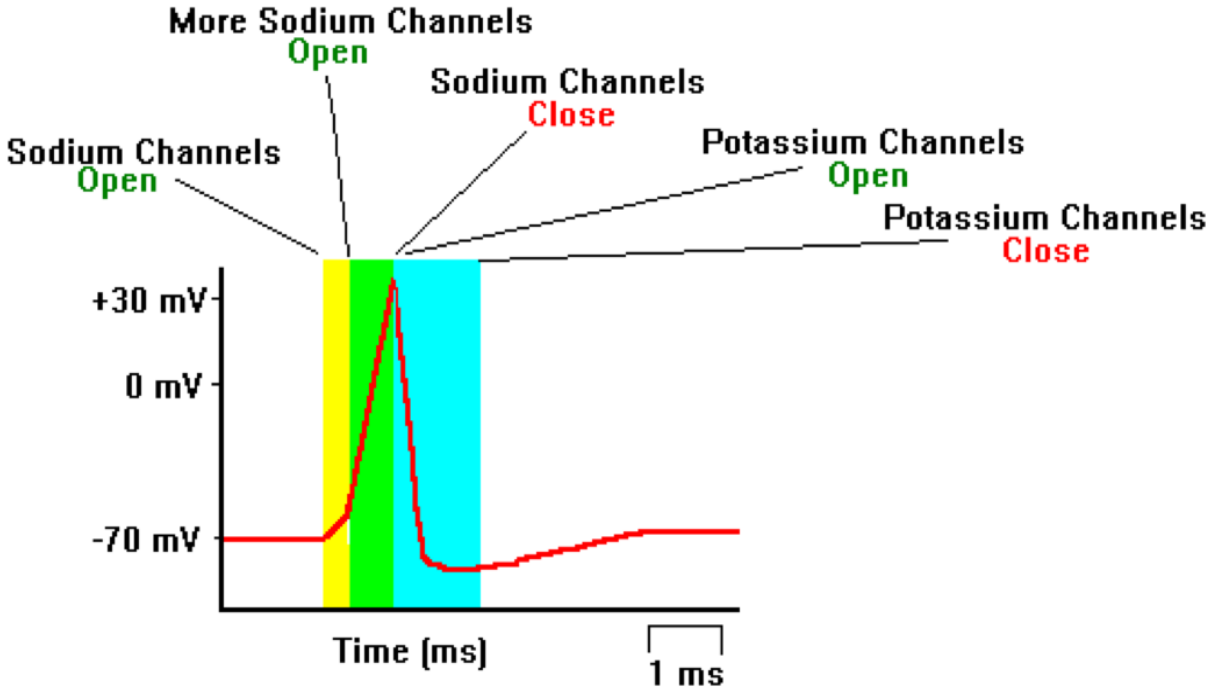





Resting
Outside cell
Sodium channel
Potassiun channel
Na-K pump
Cell membrane
Inside cell


Deoplarisation
Outside cell
Sodium channel
Potassiun channel
Na-K pump
Cell membrane
Inside cell


Repolarisation
Outside cell
Sodium channel
Potassiun channel
Na-K pump
Cell membrane
Inside cell


More Sodium Channels Open
Sodium Channels Close
Sodium Channels Open
Potassium Channels Open
Potassium Channels Close
+30 mV
0 mV
-70 mV
Time (ms)
1 ms

Point Neurons (1)

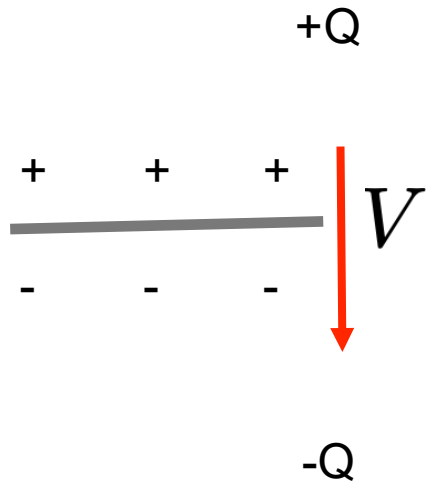
- We describe the membrane potential by a single variable V.
- Membrane capacitance: Due to excess of negative charges inside the neuron & positive charges outside the neuron, membrane acts like a capacitor
- V and the amount of charges Q are related by the standard equation for capacitor:

$$Q = C_m V$$

- From this we can determine how V changes when charges change:

$$C_m \frac{dV}{dt} = \frac{dQ}{dt} = -i_m$$

here, by convention i_m is positive outwards



This is the basic equation used to model neurons.

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$

Point Neurons (2)

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$

- The ion movements are due to channels that are open all the time (leakage), or that open at specific times, dependent on V, e.g. to generate action potential, or following synaptic events.

- Each current can be described in terms of a conductance g_i and equilibrium or reversal potential E_i. E_i describes the value of potential at which the current would stop, because the forces driving the ions (diffusion and electric forces) would cancel.

$$I_i = g_i(V - E_i)$$

A conductance with reversal potential E_i will tend to move Vm towards E_i

E_{K+}~-70--90 mV, E_{Na+}~50mV, E_{cl-}~-60mV--65mV.

Hodgkin-Huxley Model (in a nutshell)

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$

$$\bar{g}_{\mathrm{L}}(V - E_{\mathrm{L}}) + \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) + \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})$$

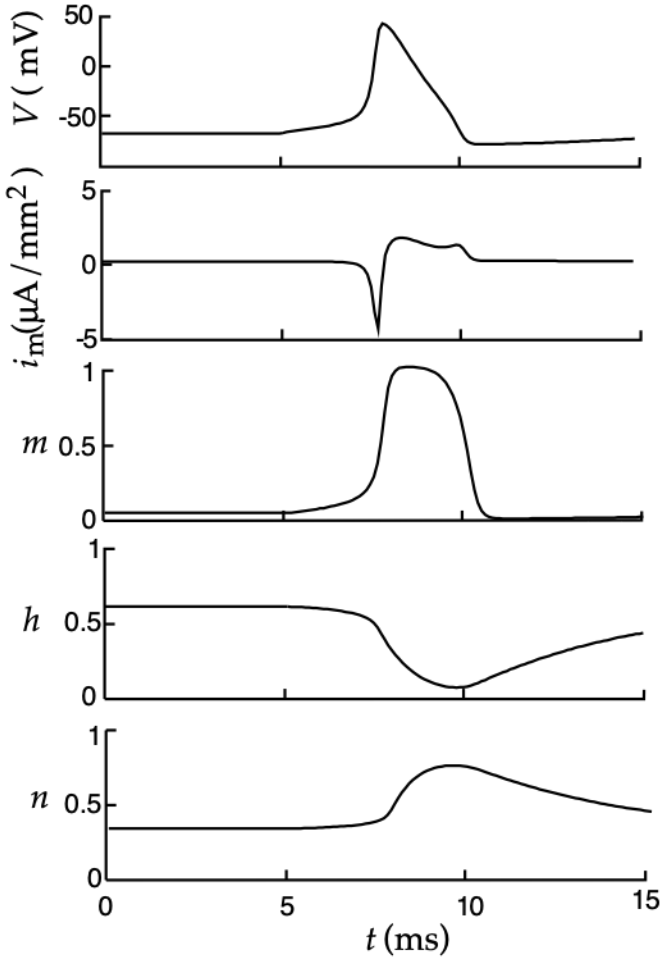
- Describe ionic movements involved in generation of action potential.
- n,m,h are the gating variables describing the dynamics of the K+, and Na+ channels.

m: opening of Na+ (activation)

h: closing of Na+ (inactivation)

n: opening of K+ (activation)

- They depend on V and their evolution (V,t) is described by other differential equations.



Hodgkin-Huxley Model (in a nutshell)

- n,m, and h are also described using differential equations

$dn/dt=a_n(V)(1-n)-b_n(V)n$ $a_n(V)$ = opening rate $b_n(V)$ = closing rate

$dm/dt=a_m(V)(1-m)-b_m(V)m$ $a_m(V)$ = opening rate $b_m(V)$ = closing rate

$dh/dt=a_h(V)(1-h)-b_h(V)h$ $a_h(V)$ = opening rate $b_h(V)$ = closing rate

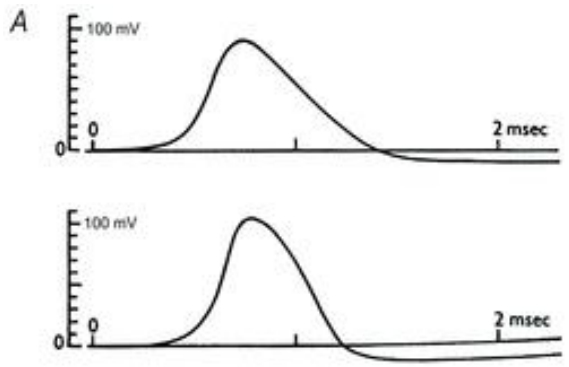
$a_n=(0.01(V+55))/(1-\exp(-0.1(V+55)))$ $b_n=0.125\exp(-0.0125(V+65))$

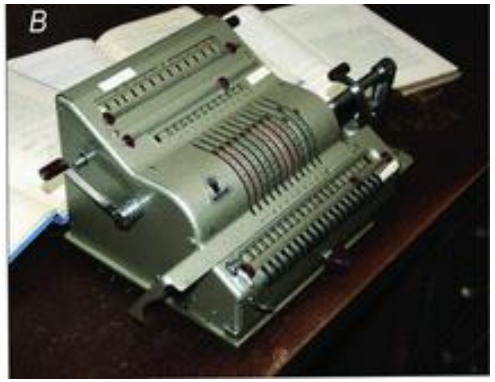
$a_m=(0.1(V+40))/(1-\exp(-0.1(V+40)))$ $b_m=4.00\exp(-0.0556(V+65))$

$a_h=0.07\exp(-0.05(V+65))$ $b_h=1.0/(1+\exp(-0.1(V+35)))$

The iterative solution for the propagating action potential, whose results are shown in **Fig. 6A**, took a few weeks and many thousands of rotations of the mechanical calculator crank (**Fig. 6B**)

https://physoc.onlinelibrary.wiley.com/doi/10.1113/jphysiol.2012.230458





Hodgkin-Huxley model : Conclusion

- The Hodgkin Huxley model : one of the most influential models of computational neuroscience

- In terms of models 3 success: (1) good model system;

(2) introduction of computers (3) right level of details for describing phenomenon --> link microscopic ion channels to macroscopic currents and action potential.

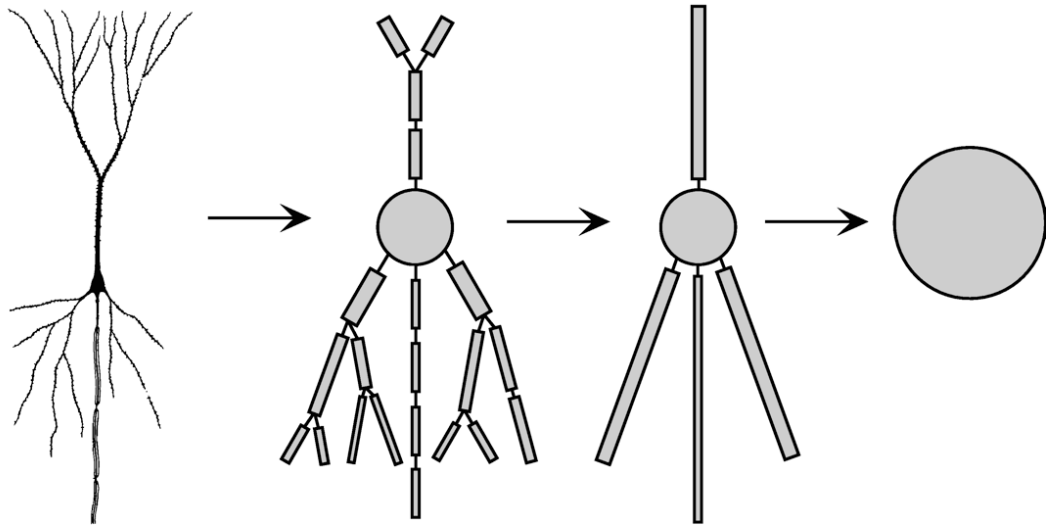
- Led to many predictions and experiments, e.g. gating charge movements, that Na+ and K+ channels were separate molecular identities with different pore sizes, other dynamics.
- most biophysical models of spiking neurons still based on H-H equations.

Models of Neurons

simplify

- One extreme: detailed description of the morphology of the neuron -- multi-compartmental models. Based on cable (differential) equations to solve Vm(x,t), simulations with softwares like NEURON.
- Hodgkin-Huxley neuron: model of spike generation using differential equations to model dynamics of K+ and Na+
- Integrate and fire neurons (family). spike generation replaced by stereotyped form.
- rate model.

this course



Integrate and fire neurons (1)

1. Only describe ion movements due to channels that are open all the time (leakage)= passive properties.

$$C_m \frac{dV}{dt} = -g_l(V - E_L) + I_{ext}(t)$$

Can be also written, using $R_m C_m = \tau_m$

$$\tau_m \frac{dV}{dt} = -V + E_L + R_m * I_{ext}(t)$$

E_L= resting potential;

R_m=1\g_l = membrane resistance;

tau_m= membrane time constant;

2. When $V>V_{thres}$ (e.g. -55 mV) an action potential is triggered (V set to V_{spike} (e.g. 50 mV)) and immediately reset to V_{reset} e.g. -75 mV.

Integrate and fire neurons (2)

Example.

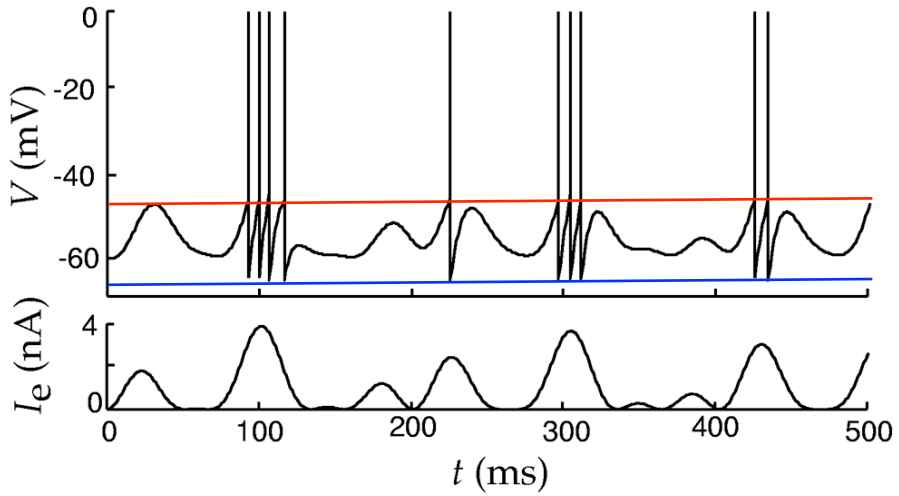


Figure 5.5: A passive integrate-and-fire model driven by a time-varying electrode current. The upper trace is the membrane potential and the bottom trace the driving current. The action potentials in this figure are simply pasted onto the membrane potential trajectory whenever it reaches the threshold value. The parameters of the model are $E_L = V_{reset} = -65$ mV, $V_{th} = -50$ mV, $\tau_m = 10$ ms, and $R_m = 10$ MΩ.

Integrate and fire neurons (3)

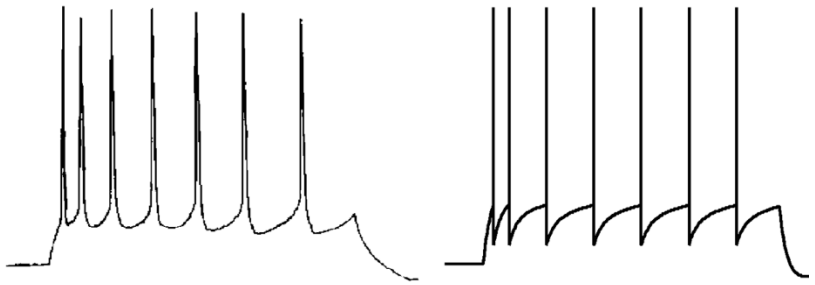
- The firing rate of an integrate and fire neuron in response to a constant injected current can be computed analytically (cf D&A).

- Integrate and fire neurons = a family of models.

  Inputs can be modeled as a current, or conductances (better model of synapses).

- Can be modified to account for a repertoire of dynamics e.g. can include a model of refractoriness and spike rate adaptation (and more)

- conductance-based IAF: these phenomena + inputs are modelled using added conductances.



spike rate adaptation

Integrate and fire neurons (4): adding spike rate adaptation

- spike rate adaptation can be modeled as an hyperpolarizing K+ current

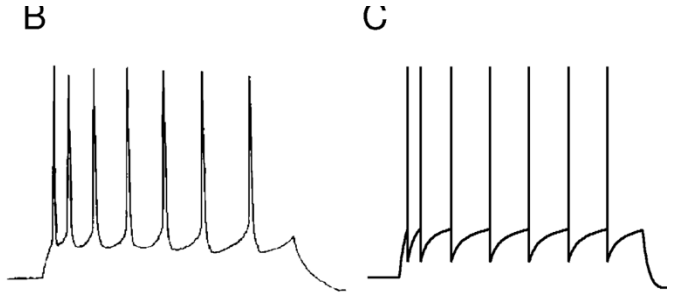
$$\tau_m \frac{dV}{dt} = E_L - V - \boxed{r_m g_{sra}(t)(V - E_K)} + R_m I_e$$

- when neuron spikes, g_{sra} is increased by a given amount:

$$g_{sra} \rightarrow g_{sra} + \Delta g_{sra}$$

- the conductance relaxes to 0 exponentially with time constant τ_{sra}

$$\tau_{sra} \frac{dg_{sra}(t)}{dt} = -g_{sra}(t)$$



spike rate adaptation

Conductances triggered by spiking are used to model refractory period, bursting...
Synaptic input can be modeled similarly (but triggered by presynaptic spike)

Integrate and fire neurons (5): adding synaptic input

- Synaptic inputs are modeled as depolarizing or hyperpolarizing conductances

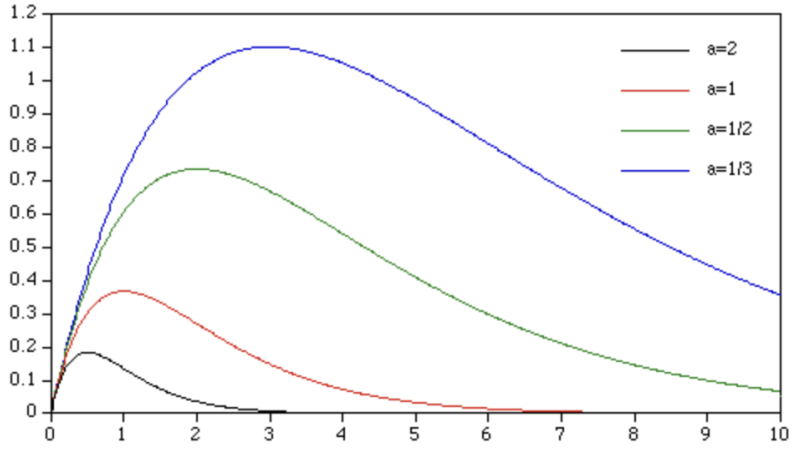
$$\tau_m \frac{dV}{dt} = E_L - V - r_m \bar{g}_s P_s (V - E_s) + R_m I_e .$$

- Each time a presynaptic spike occurs (+ synaptic delay), P_s is modified.

For example, Ps can be modeled using an alpha-function:

$$P_s(t) = \frac{P_{max} t}{\tau_s} \exp(1 - \frac{t}{\tau})$$

$$f(x) = \begin{cases} x\, e^{-ax} & x >= 0 \\ 0 & x < 0 \end{cases}$$

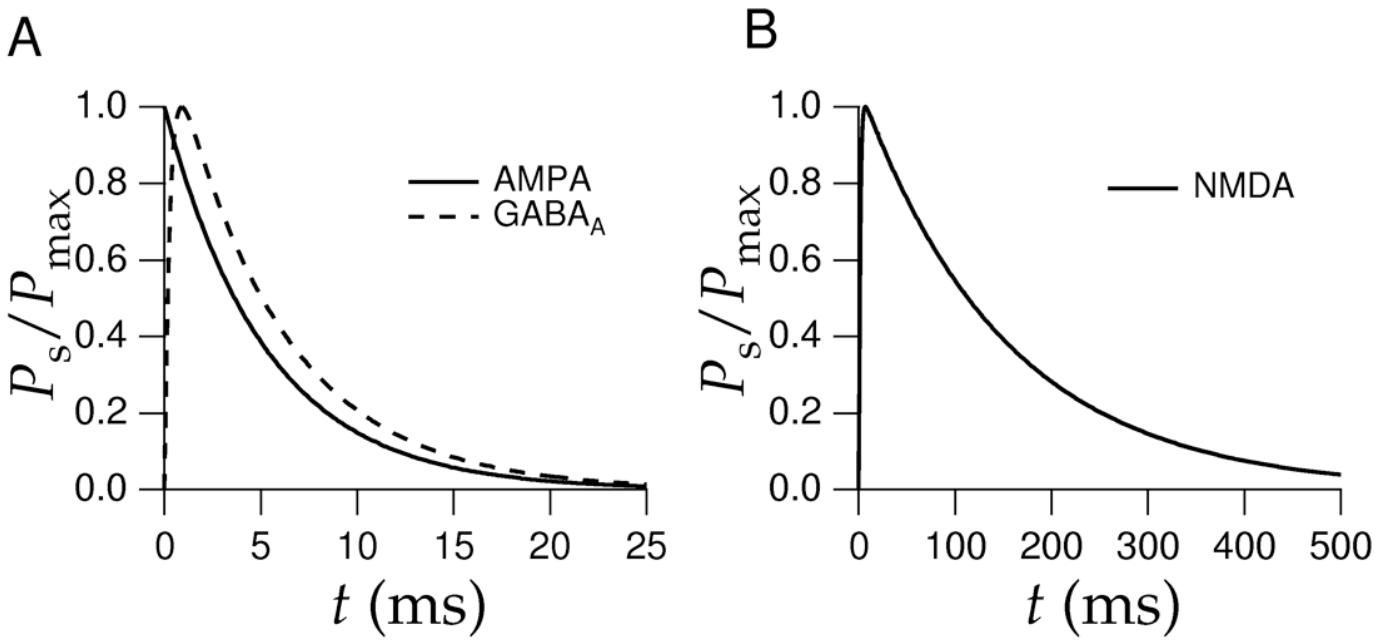


- a variety of models can be used for Ps depending on dynamics that we want to account for (slow/fast synapses)

- Es=0 for excitatory synapses, Es=-70--90 mV for inhibitory synapses.

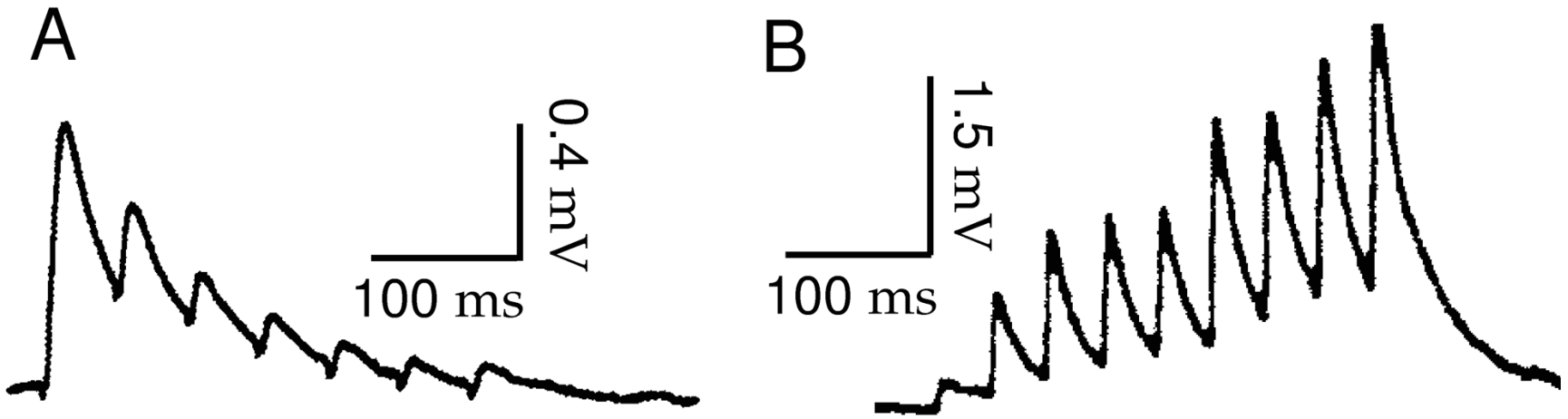
Synaptic input

- Different synapses have different dynamics.
- Excitatory synapses: AMPA is fast, NMDA slow.
- Inhibitory synapses: GABAa are fast, GABAb slower.



Synaptic input

- The amplitude of synaptic EPSPs and IPSPs may vary depending on spiking history: synaptic facilitation and depression.
- They can also vary on a longer time scale : learning. (LTP, LTD)



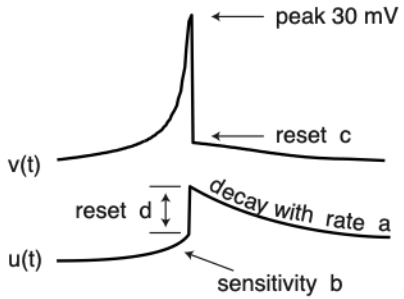
Izhikevich neuron (2003,2004)

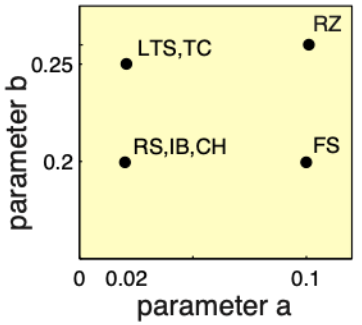
- A more recent and popular alternative to the integrate and fire.

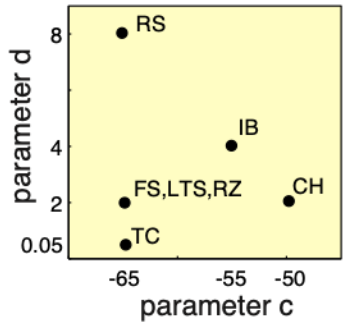
$v' = 0.04v^2 + 5v + 140 - u + I$

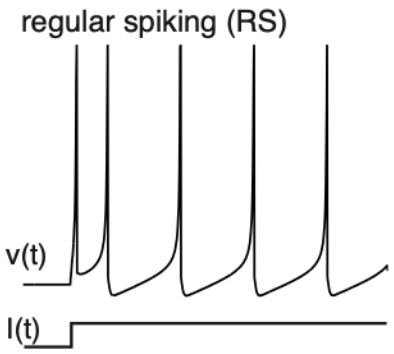
$u' = a(bv - u)$

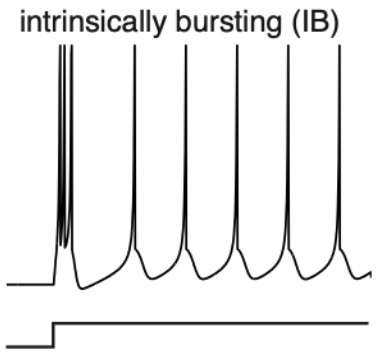
if $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$

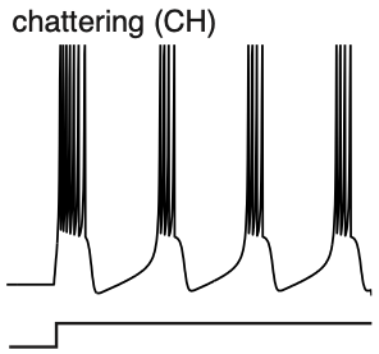


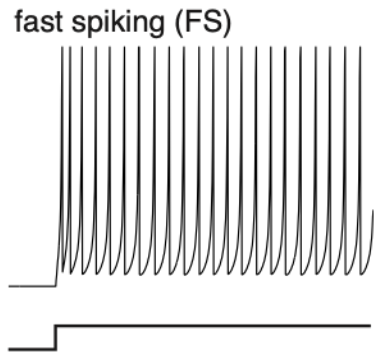


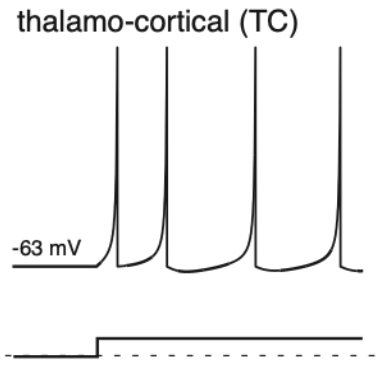


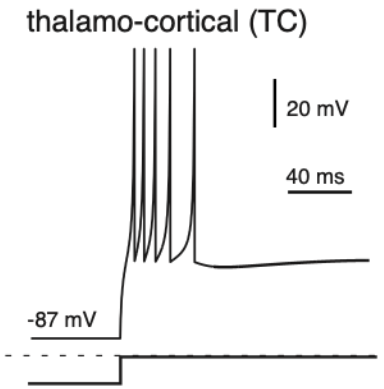


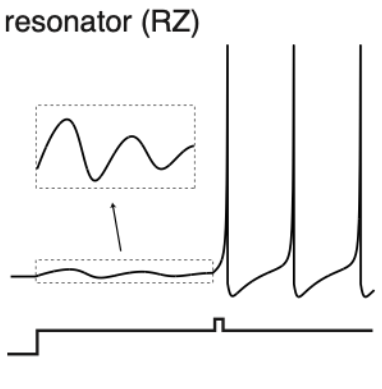


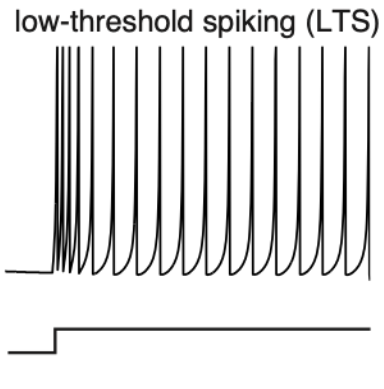












On Numerical Integration

- Sometimes the differential equations can be solved analytically
- Usually though, they are solved numerically
- The simplest method is known as Euler's method: a system

$$\frac{dy}{dt} = f(y)$$

can be simulated by choosing the initial condition y(0) and repeatedly performing the Euler integration step:

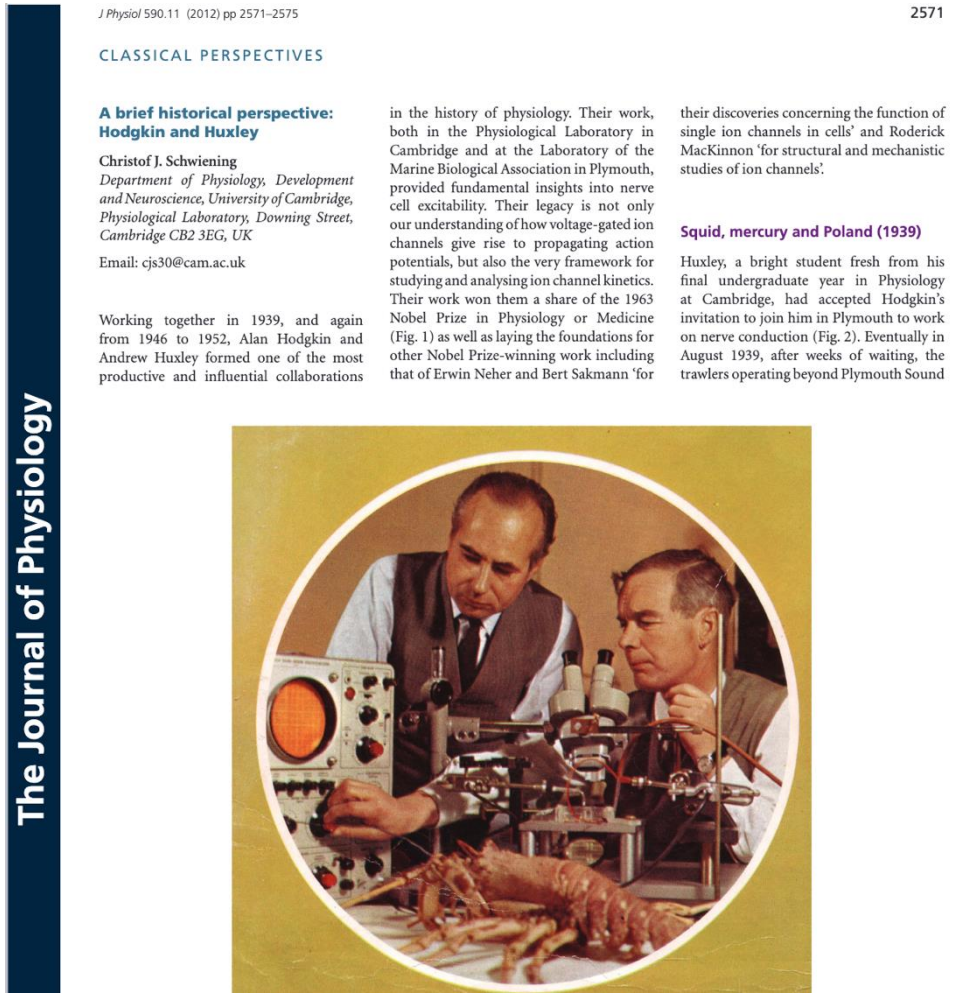
$$y(t + dt) = y(t) + dtf(y)$$

Higher order and adaptive methods, such as Runge-Kutta are commonly used (check 'numerical recipes', matlab ode23, ode45, and Hansel et al 1998 for an evaluation of such methods with IAF neurons).

Readings

- Dayan & Abbott Chapter 5
- Historical perspective

https://physoc.onlinelibrary.wiley.com/doi/epdf/10.1113/jphysiol.2012.230458



The Journal of Physiology

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CLASSICAL PERSPECTIVES

A brief historical perspective: Hodgkin and Huxley

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Working together in 1939, and again from 1946 to 1952, Alan Hodgkin and Andrew Huxley formed one of the most productive and influential collaborations in the history of physiology. Their work, both in the Physiological Laboratory in Cambridge and at the Laboratory of the Marine Biological Association in Plymouth, provided fundamental insights into nerve cell excitability. Their legacy is not only our understanding of how voltage-gated ion channels give rise to propagating action potentials, but also the very framework for studying and analysing ion channel kinetics. Their work won them a share of the 1963 Nobel Prize in Physiology or Medicine (Fig. 1) as well as laying the foundations for other Nobel Prize-winning work including that of Erwin Neher and Bert Sakmann 'for their discoveries concerning the function of single ion channels in cells' and Roderick MacKinnon 'for structural and mechanistic studies of ion channels'.

Squid, mercury and Poland (1939)

Huxley, a bright student fresh from his final undergraduate year in Physiology at Cambridge, had accepted Hodgkin's invitation to join him in Plymouth to work on nerve conduction (Fig. 2). Eventually in August 1939, after weeks of waiting, the trawlers operating beyond Plymouth Sound

Computational Cognitive Neuroscience. Lab 1

Simple Neuron Models. January 2025

Lecturer: Peggy Seriès
Teaching Assistant: Lars Werne

Tutorial Objectives

In this tutorial, you will learn to do the following:

- Implement a model of a single neuron in Python (or Matlab)
- Simulate the model numerically and plot the results
- Interpret your findings and their relevance to biology
- Understand where analytical approximations may be used alongside numerical simulation and how the two approaches complement each other

Introduction

In this tutorial, you will code and simulate a simple neuron model that we discussed at length in Lecture 3: the leaky integrate and fire neuron. You will explore how the spike statistics and membrane potential dynamics of the model depend on the statistics of the input the neuron receives and how analytical approximations can provide insights into this behaviour in limiting situations.

Part 1: Setting up the Model for Passive Dynamics

We first consider how to numerically simulate the passive membrane potential dynamics of a simple neuron model – the leaky integrate and fire neuron.

The membrane potential of the leaky integrate and fire model obeys the following equation while below the spiking threshold:

$$\tau \frac{\mathrm{d}V}{\mathrm{d}t} = -(V - E_m) + \frac{I_{\text{ext}}}{g_m}.$$

Our goal is to solve this equation numerically using the Euler method. This will allow us to explore how the membrane potential evolves over time and how it eventually stabilizes under various conditions. You can review Lecture 3, Slide 22, for a refresher. Follow these steps:

1. **Set up parameters**:
   - Assign values to the parameters: τ, E_m, I_{ext}, g_m.
   - Define the number of iterations, $N_t = 10000$, and the timestep, $\delta t = 0.1\,\text{ms}$, for a total simulation time of 1 second.
2. **Initialize arrays**:
   - Create an array of size $[N_t + 1, 1]$ to store the values of the membrane potential.[1]
3. **Simulate the dynamics**:
   - Use a `for` loop to compute the values of the membrane potential at each time step.
   - Start the simulation with the initial condition $V = E_m$ and the following parameters:
     - time constant $\tau = 10\,\text{ms}$
     - resting potential $E_m = -70\,\text{mV}$
     - membrane conductance $g_m = 1\,\text{S}$
     - external current $I_{\text{ext}} = 20\,\text{A}$
4. **Plot and analyze results**:
   - Check that your simulation runs without errors.
   - Plot the membrane potential as a function of time.
   - Inspect the plot. Did the simulation behave as expected? How can you tell?

[1] After N_t iterations you will have $N_t + 1$ time points

5. **Explore parameter variations**:
    - Vary the input current, time constant, and initial condition. [2] Observe how each affects the evolution of the membrane potential.
6. **Determine steady-state behavior**: In the simulations above, you should observe that the membrane potential converges to a stable, final value (the "steady-state" or "equilibrium" potential). This value of V is reached when $\frac{dV}{dt} = 0$ in the equation:

$$\tau \frac{dV}{dt} = -(V - E_m) + \frac{I_{\text{ext}}}{g_m}.$$

    - Derive an analytical equation for the steady-state membrane potential.
    - Compare the derived equation with your simulations. Do the results agree?

Part 2: Incorporating Spiking Into the Model

Next, we will add spikes to the model and observe how they change its behavior. To model spikes, we introduce the following spike-reset rule:

$$\text{If } V(t) \geq V_{\text{threshold}}, \text{ then set } V(t) \to V_{\text{reset}}.$$

1. **Implement the spike-reset rule**:
    - Modify your code to include the spike-reset rule by adding an `if-then` condition inside the loop over time steps.
    - Ensure that spike times are stored in a separate array for later analysis.
2. **Set parameters for spiking**:
    - Use the following parameter values for spiking behavior:
        - Threshold potential: $V_{\text{threshold}} = -50\,\text{mV}$
        - Reset potential: $V_{\text{reset}} = -75\,\text{mV}$
3. **Run and analyze simulations**:
    - Run the modified simulation with different values of:
        - Input current (I_{ext})
        - Time constant (τ)

Part 3: Adding Noise to the Input

In this part, we will explore how the neuron behaves when driven by noisy, fluctuating input. Initially, we return to the case of purely passive dynamics, as in Part 1. To simulate this, you can modify your spiking code by setting $V_{\text{threshold}} = \infty$, which ensures the neuron never spikes.

The noisy input is modeled as:

$$I_{\text{ext}}(t) = I_0 + \sigma\xi(t),$$

where $\xi(t)$ is a normally distributed random variable with zero mean and unit variance, drawn independently at each timestep.[3]

1. **Simulate passive dynamics with noisy input**:
   - Set $\sigma = 50$ and simulate with different values of I_0.
   - Plot the membrane potential for each input current value.
   - Analyze the plots. How would you expect the noise to influence spiking activity?
2. **Incorporate the spike-reset rule and analyze interspike interval distributions**:
   - Reintroduce the spike-reset rule by setting $V_{\text{threshold}} = -50\,\text{mV}$.
   - Vary both I_0 and σ. Compute interspike interval (ISI) distributions for different parameter combinations.
   - Use `matplotlib.hist` to create histograms of the ISI distributions for various parameter values.
   - Discuss how the shape of the ISI distribution depends on the input parameters. If necessary, increase the number of simulation timesteps to obtain higher sample sizes for better analysis.