COMPUTATIONAL NEUROSCIENCE
Research group at the University of Tartu

Introduction to Computational Neuroscience

Lecture 6: Single neuron models

Lesson	Title	
1	Introduction	Basics
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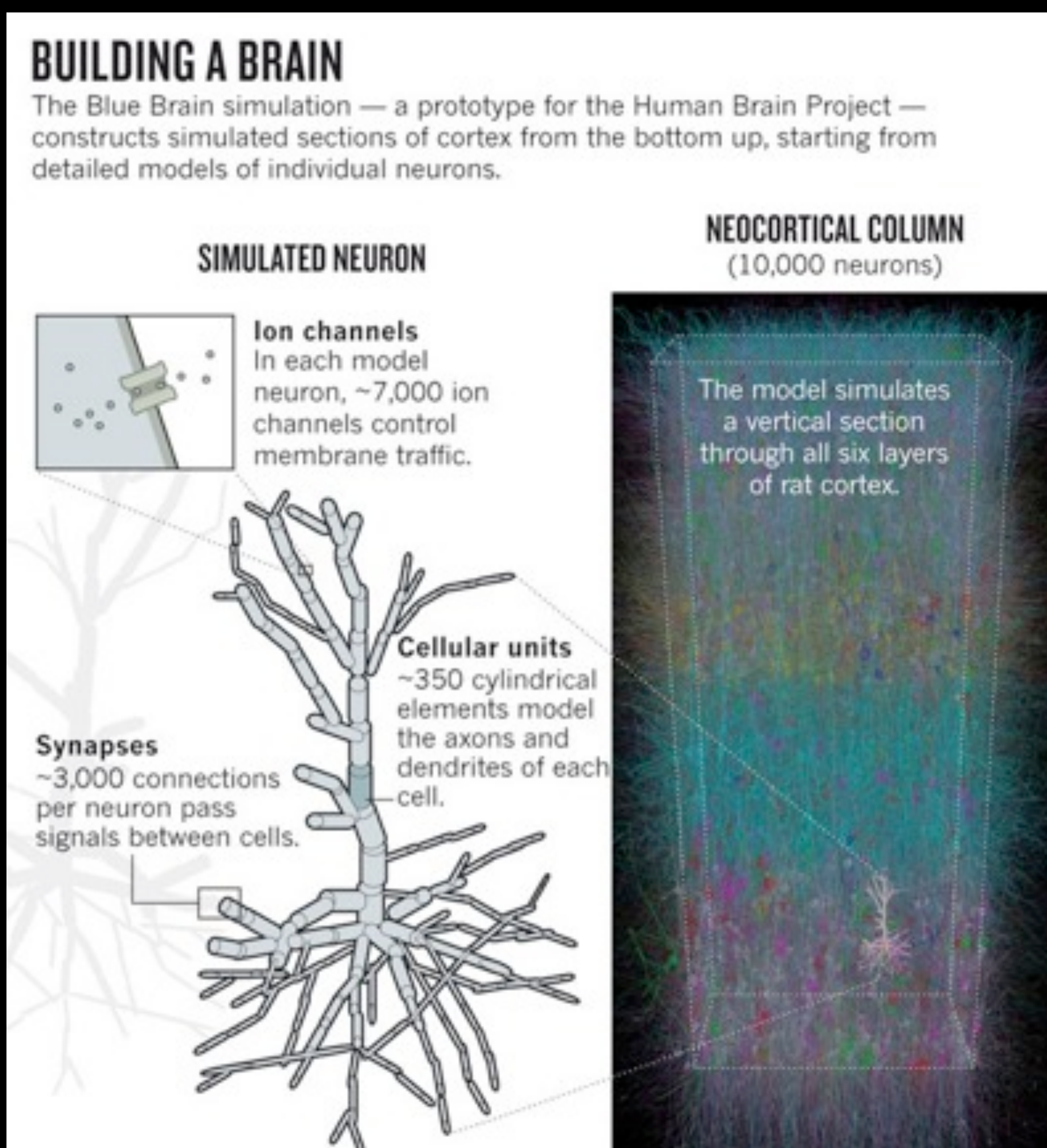
Neurons in silico

Artificial neural networks is a major strand in computational neuroscience, machine learning, and artificial intelligence



Let's start easy... how do we simulate the behavior of a single neuron in a computer?

"Make it as simple as possible but not simpler"
Einstein

Learning objectives

- Understand the different levels of single neuron modeling
- Simulate the most popular single compartment models

Appropriate level of models?

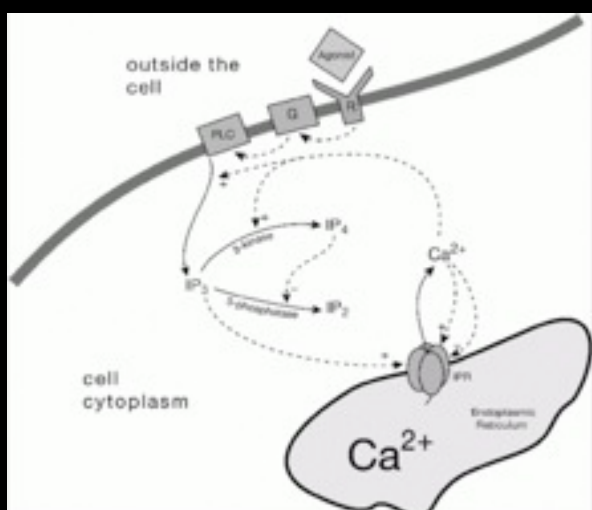
Conferences of computational neuroscience...

* **Biologists** (bottom-uppers) believe that a model that deviates from details of known physiology is inadmissibly inaccurate

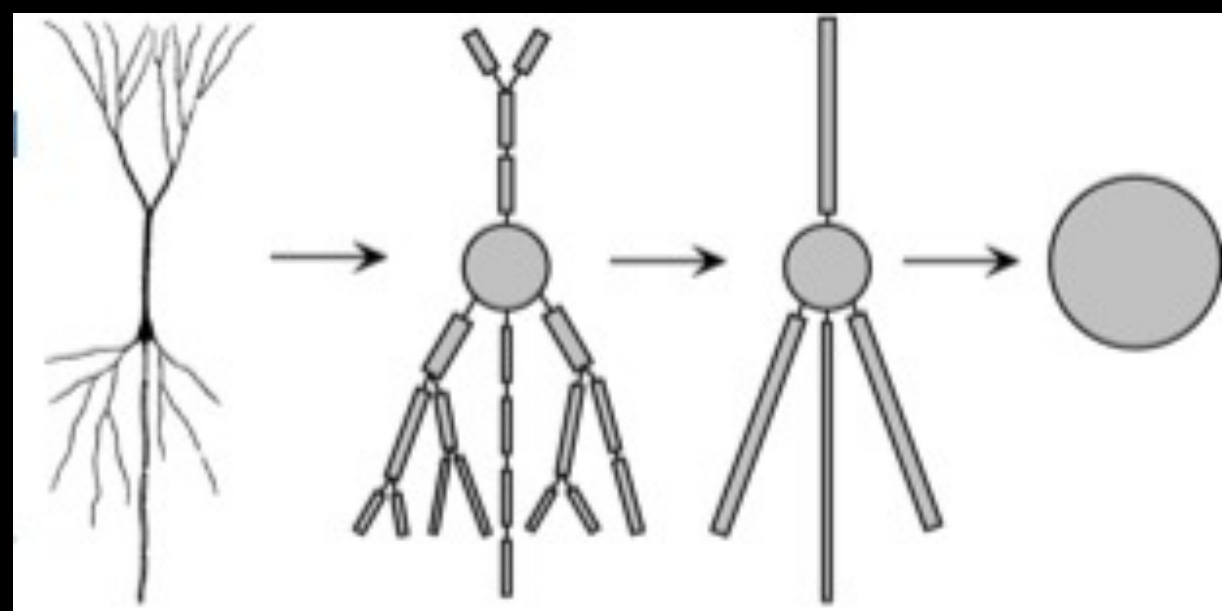
* **CS, physicists, and mathematicians** (top-downers) feel that models that fail to simplify do not allow any useful generalization to be made

Appropriate level of models

Biological detail

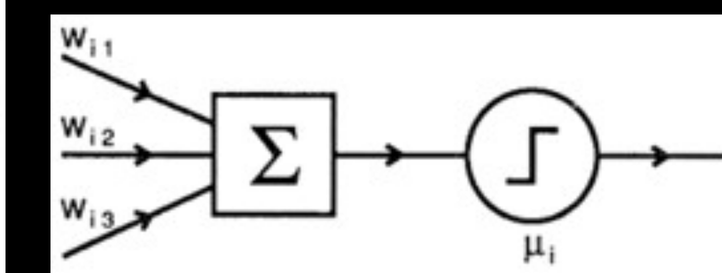


Biological processes (molecular)



Electrical properties (morphology)

Electrical properties (average)



Computational properties (processing)

Classification of neuron models

Point neuron models

Spiking neurons

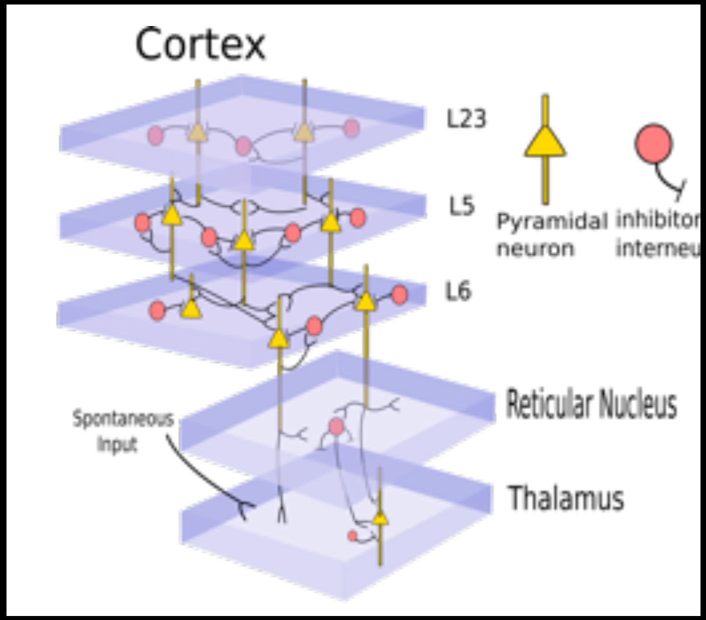
McCulloch-Pitts

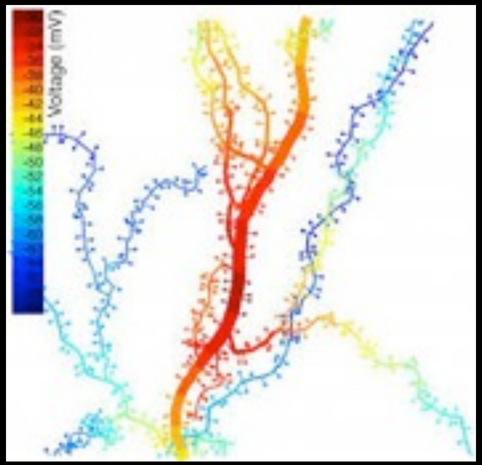
Integrate-and-Fire

Hodgkin-Huxley

Rate neurons

Multi-compartment models





McCulloch-Pitts

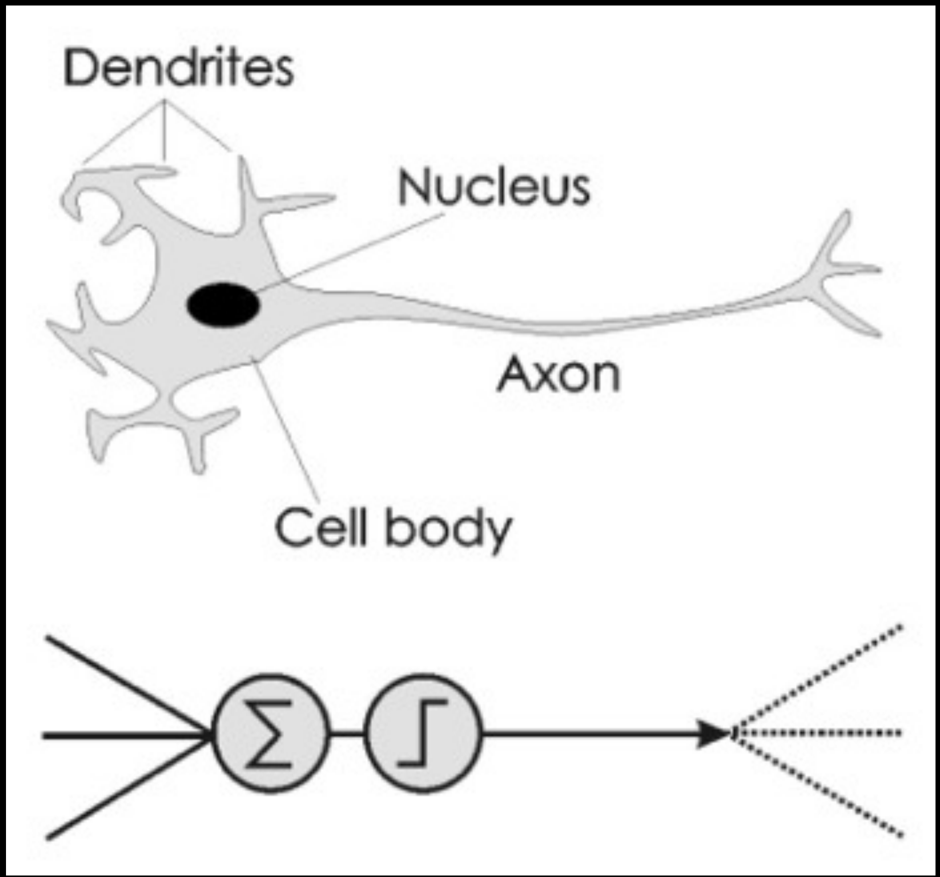
Integrate-and-Fire

Hodgkin-Huxley

McCulloch-Pitts (idea)

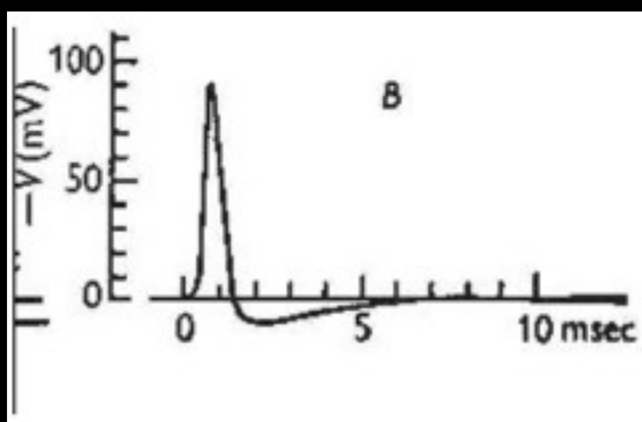
McCulloch and Pitts (1943): pioneers to formally define neurons as computational elements

The idea: explore simplified neural models to get the essence of neural processing by ignoring irrelevant detail and focusing in what is needed to do a computational task



McCulloch-Pitts (idea)

McCulloch and Pitts knew that spikes (action potential) somehow carry information through the brain:



each spike would represent a binary 1

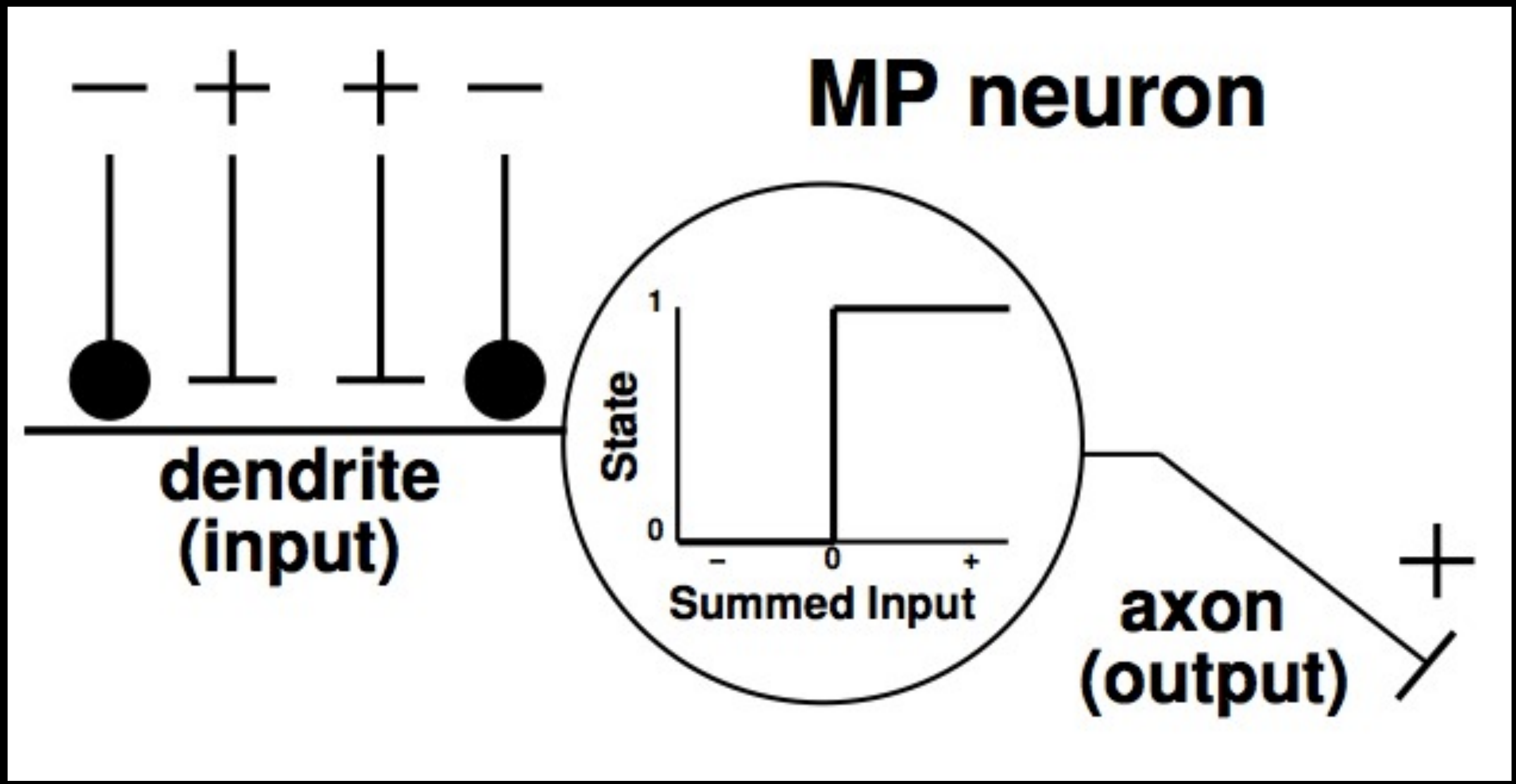
each lack of spike would represent a binary 0

They showed **how spikes could be combined to do logical and arithmetical operations**

From modern perspective there is a design problem for these circuit elements: brevity of a spike (1 ms) compared to the interval between spikes (>50 ms) implies a duty cycle of < 2%

McCulloch-Pitts (rule)

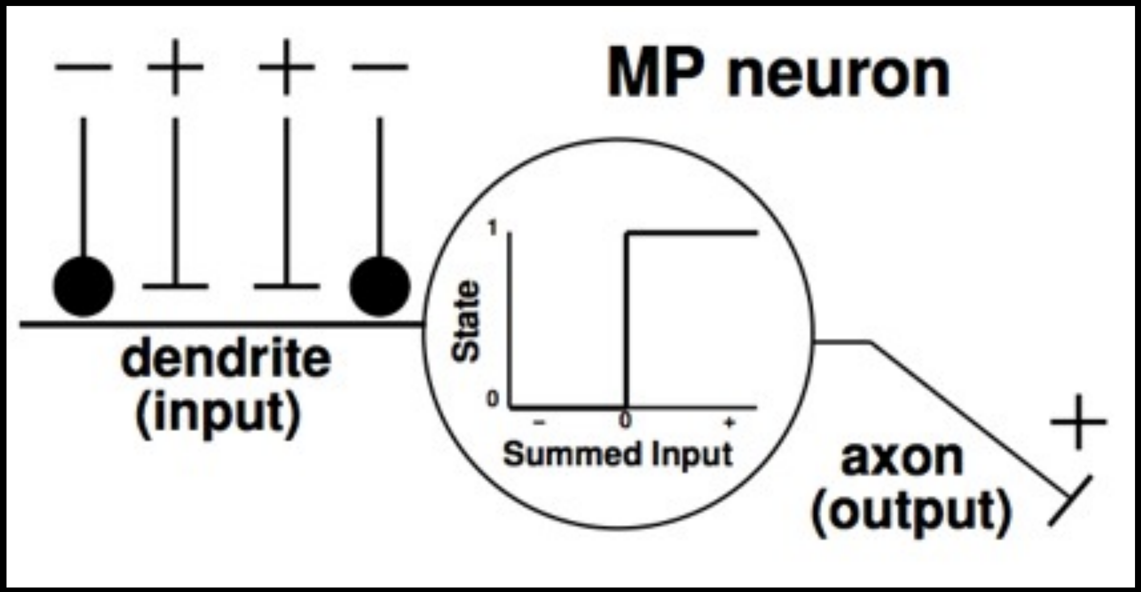
MP neurons are binary: they take as input and produce as output only 0's or 1's

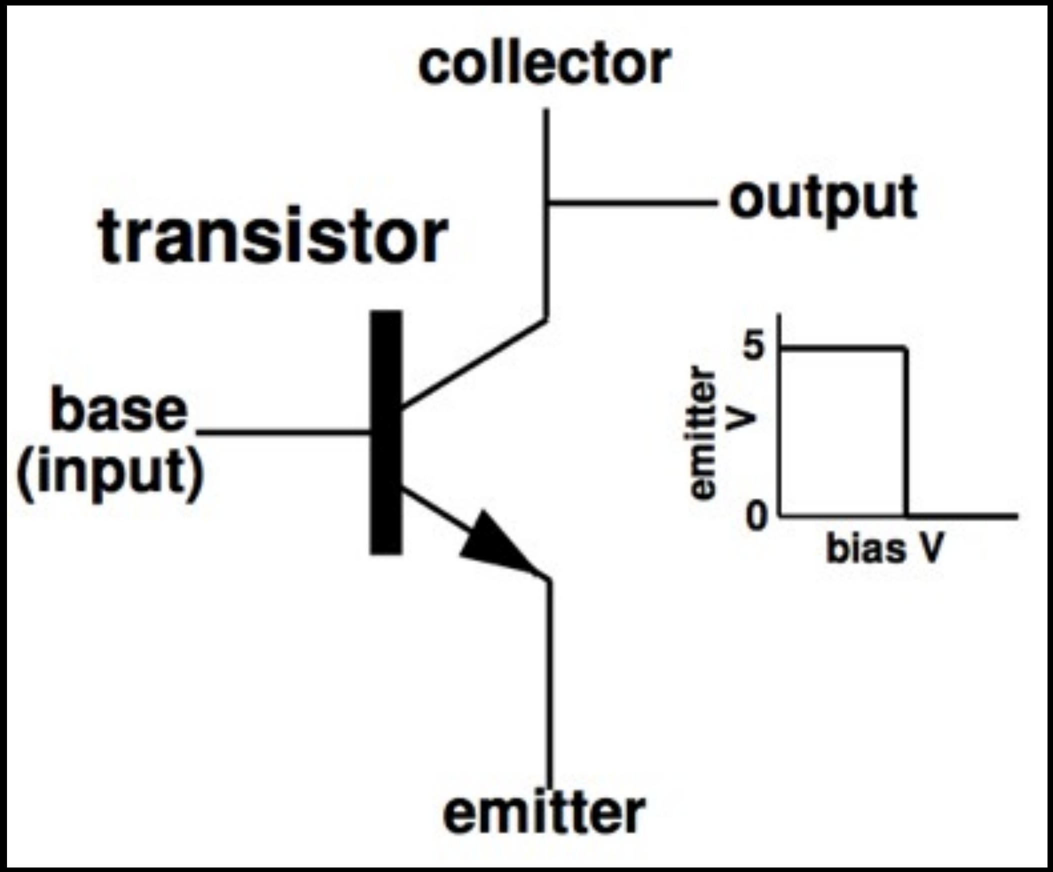


Rule: activations from other neurons are summed at the neuron and outputs 1 if threshold is reached and 0 if not

McCulloch-Pitts (analogy)

MP neurons function much like a transistor:





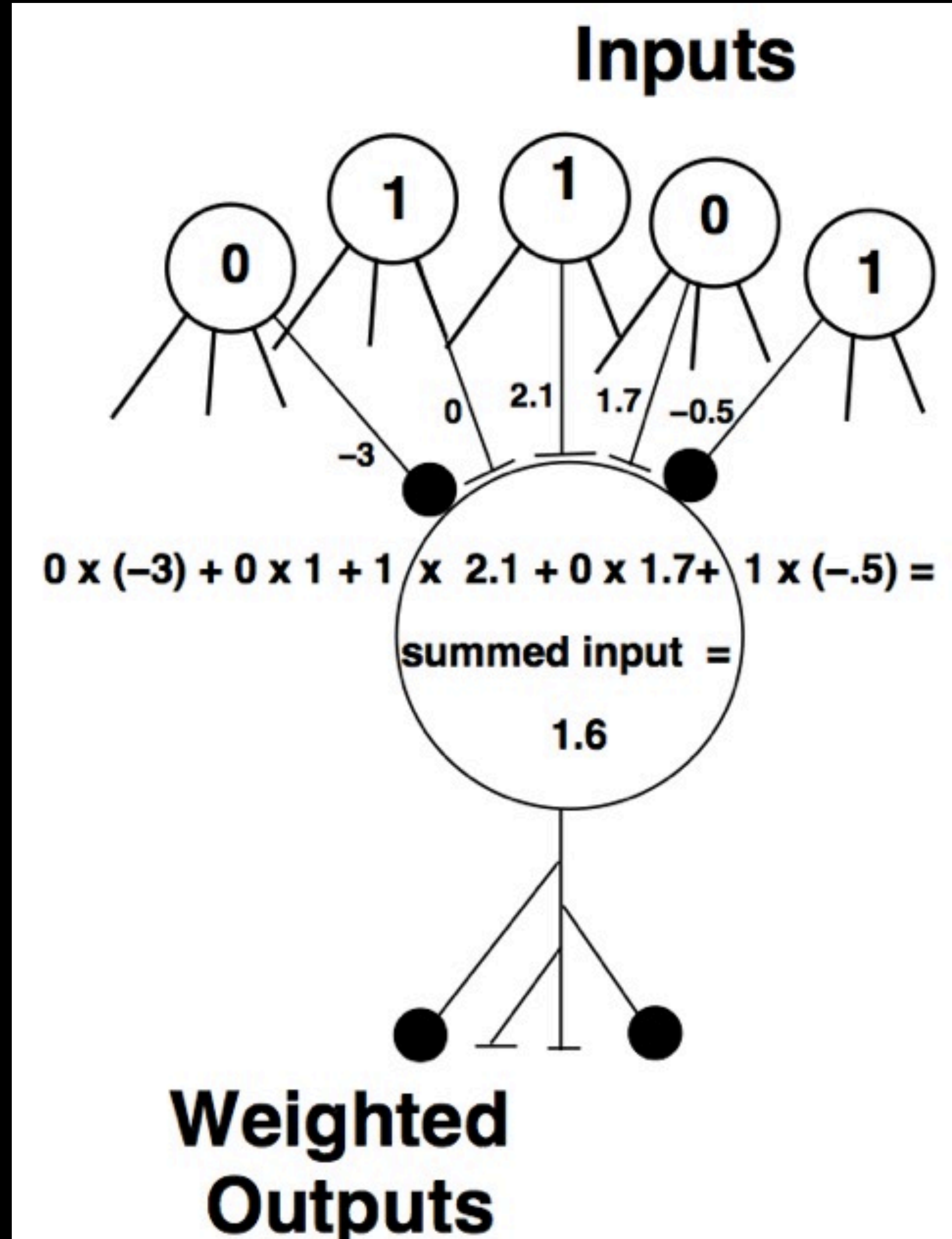
In artificial networks, inputs come from the outputs of other MP neurons (as transistors in a circuit)

McCulloch-Pitts (nomenclature)

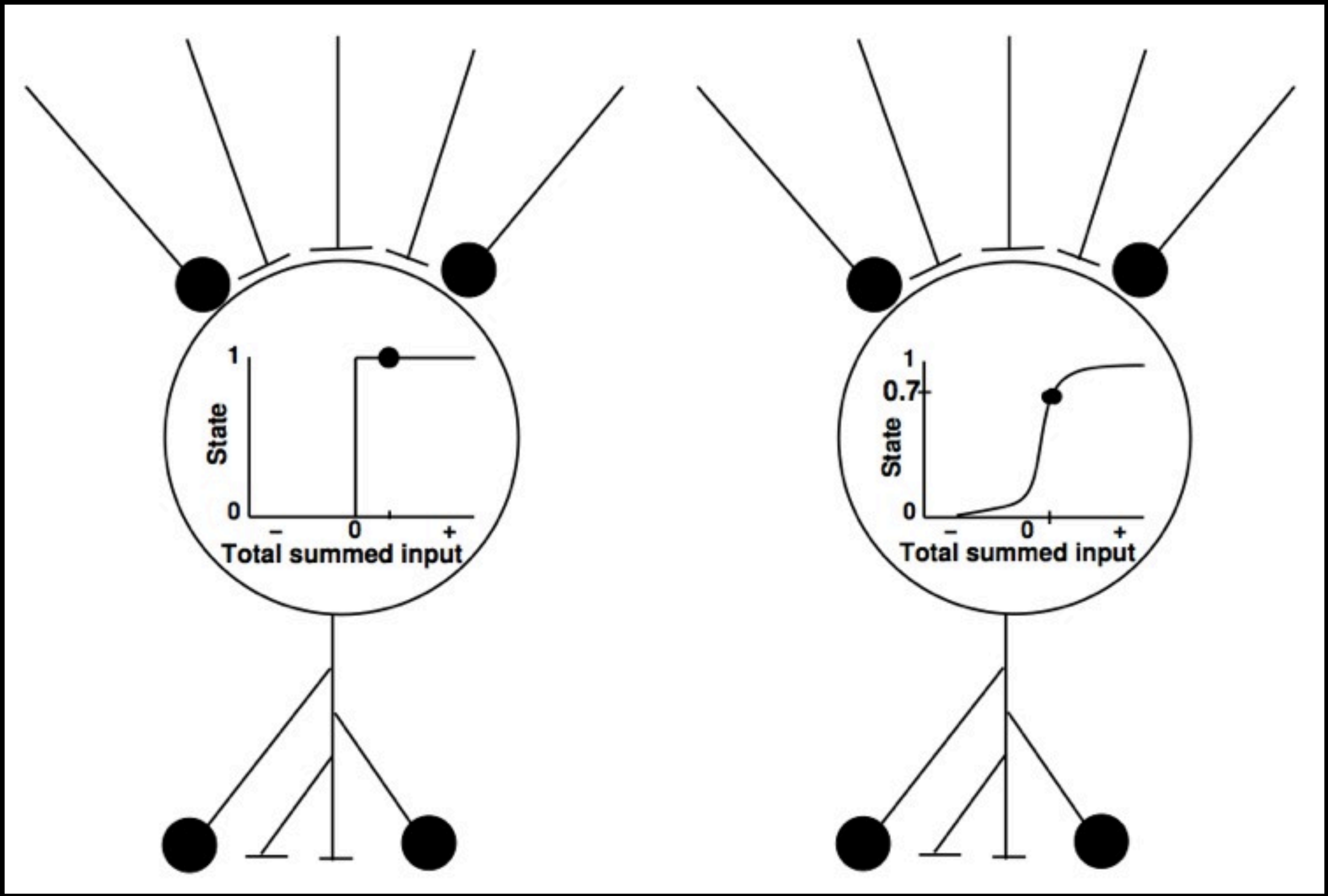
State: is the degree of activation of a single neuron

Weight: is the strength of the connection between two neurons

Update rule: determines how input to a neuron is translated into the state of that neuron



McCulloch-Pitts (states)



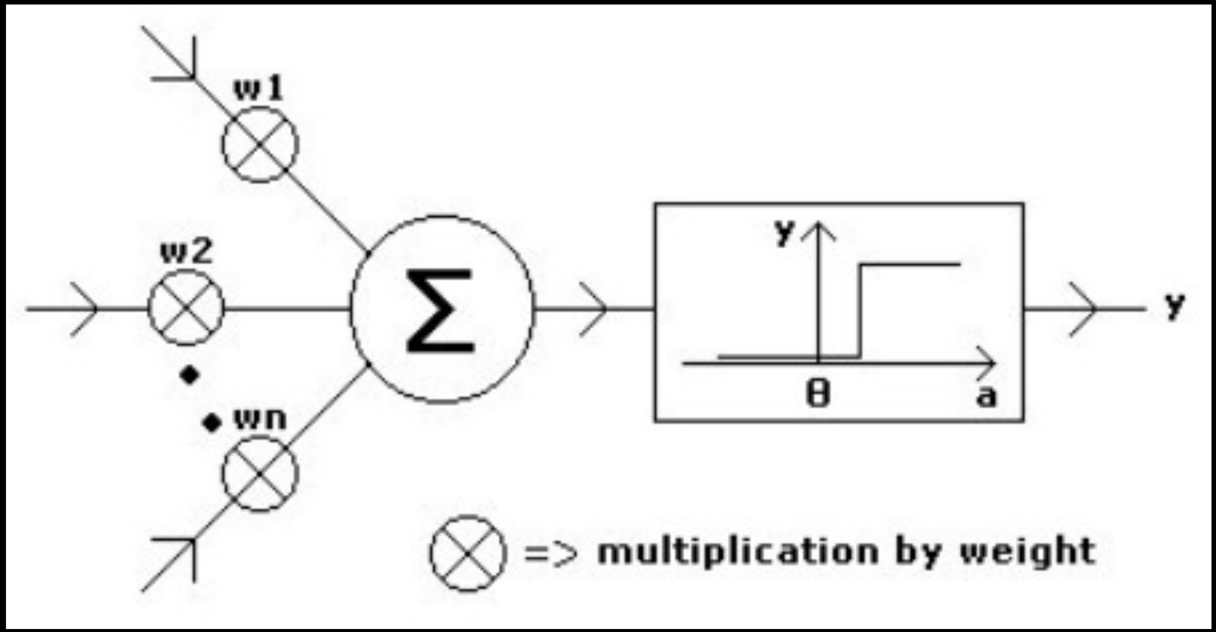
Sharp threshold (digital)

Sigmoid function (analog)

McCulloch-Pitts (states)

In mathematical terms:

$$y = \phi\left(\sum_{i=1}^{n} \omega_i \cdot x_i\right)$$

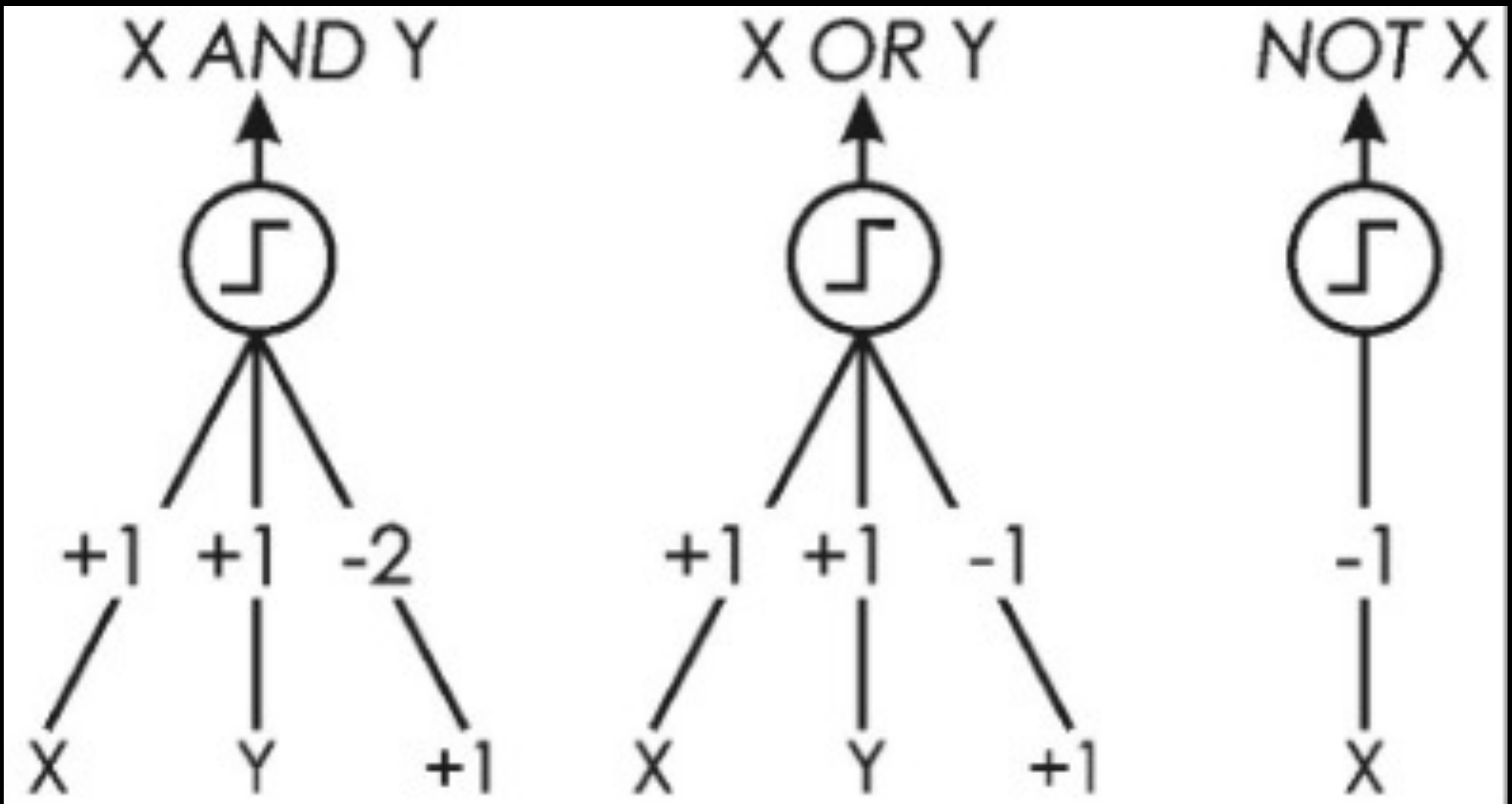


where ϕ represents a threshold or a sigmoid function

```
total_input = sum(w.*x);
if total_input >= 0
   y = 1;
else
   y = 0;
end
```

McCulloch-Pitts (logic)

MP neurons are capable of logic functions



McCulloch-Pitts

Integrate-and-Fire

Hodgkin-Huxley

Prerequisites

Differential equations (1 slide)

Neurons as electronic circuits (4 slides)

Differential equations

The most common and simplest types of dynamic models come in the form of differential equations

They describe the rate of change of some variable, say *u*, as a function *u* and other variables

$$\frac{du}{dt} = \text{change per unit time} = \text{sum of production rates} - \text{sum of removal rates}.$$

$$c_\mathrm{m}\frac{dV}{dt} = -i_\mathrm{m} + \frac{I_\mathrm{e}}{A}\,.$$

Generation of electric potential in neuron's membrane

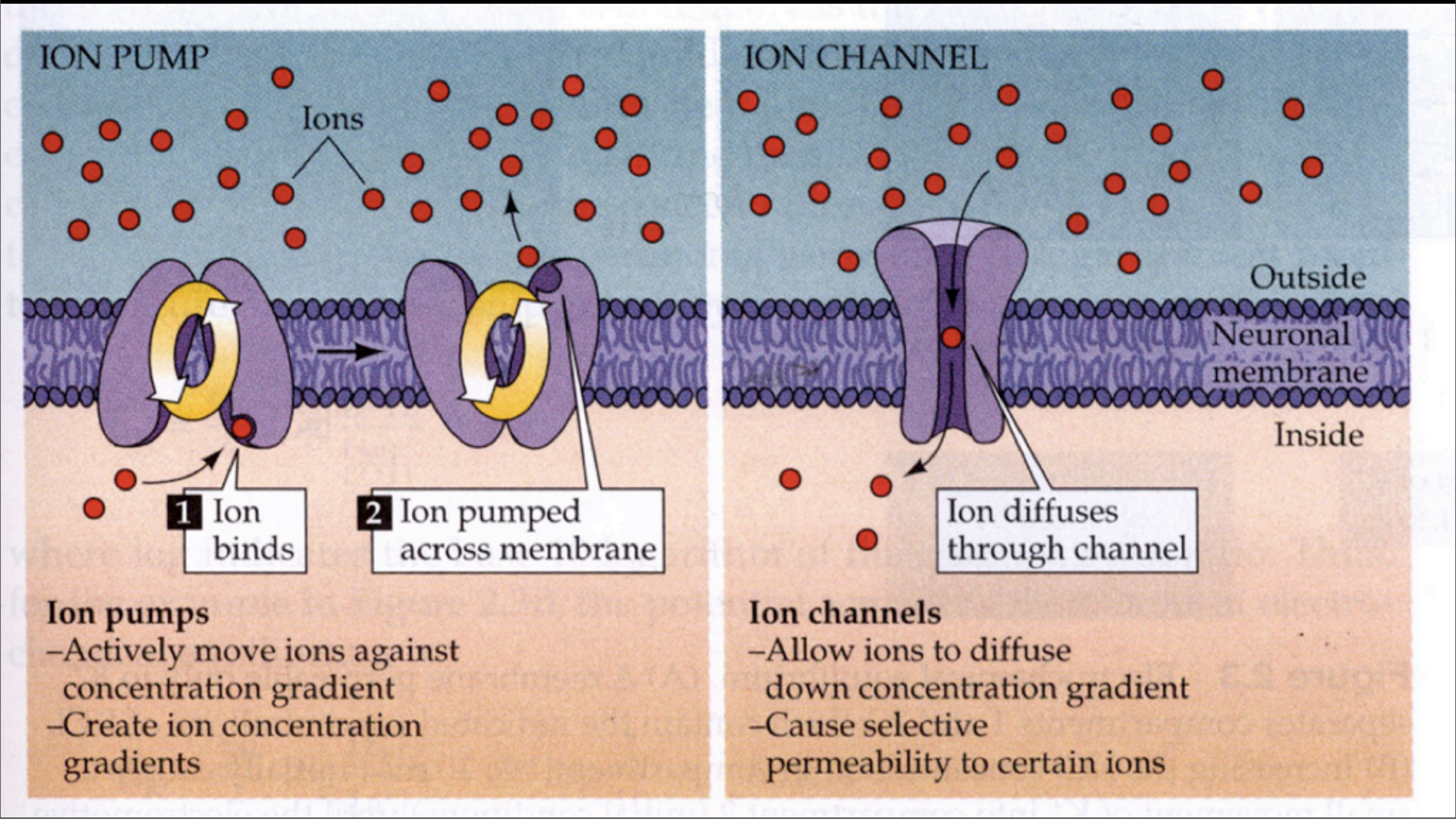
Chief factors that determine the **membrane potential**:

1. The permeability of the membrane to different ions
2. Difference in ionic concentrations

Ion pumps: maintain the concentration difference by actively moving ions against the gradient using metabolic resources

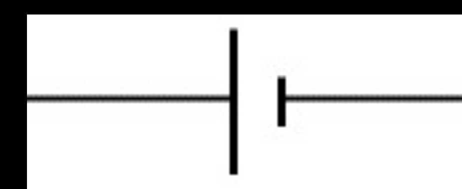
Ion channels: "holes" that allow the passage of ions in the direction of the concentration gradient. Some channels are selective for specific ions and some are not selective

Neuron as an electric circuit

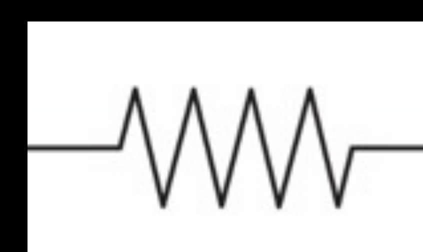


Neuron as an electric circuit

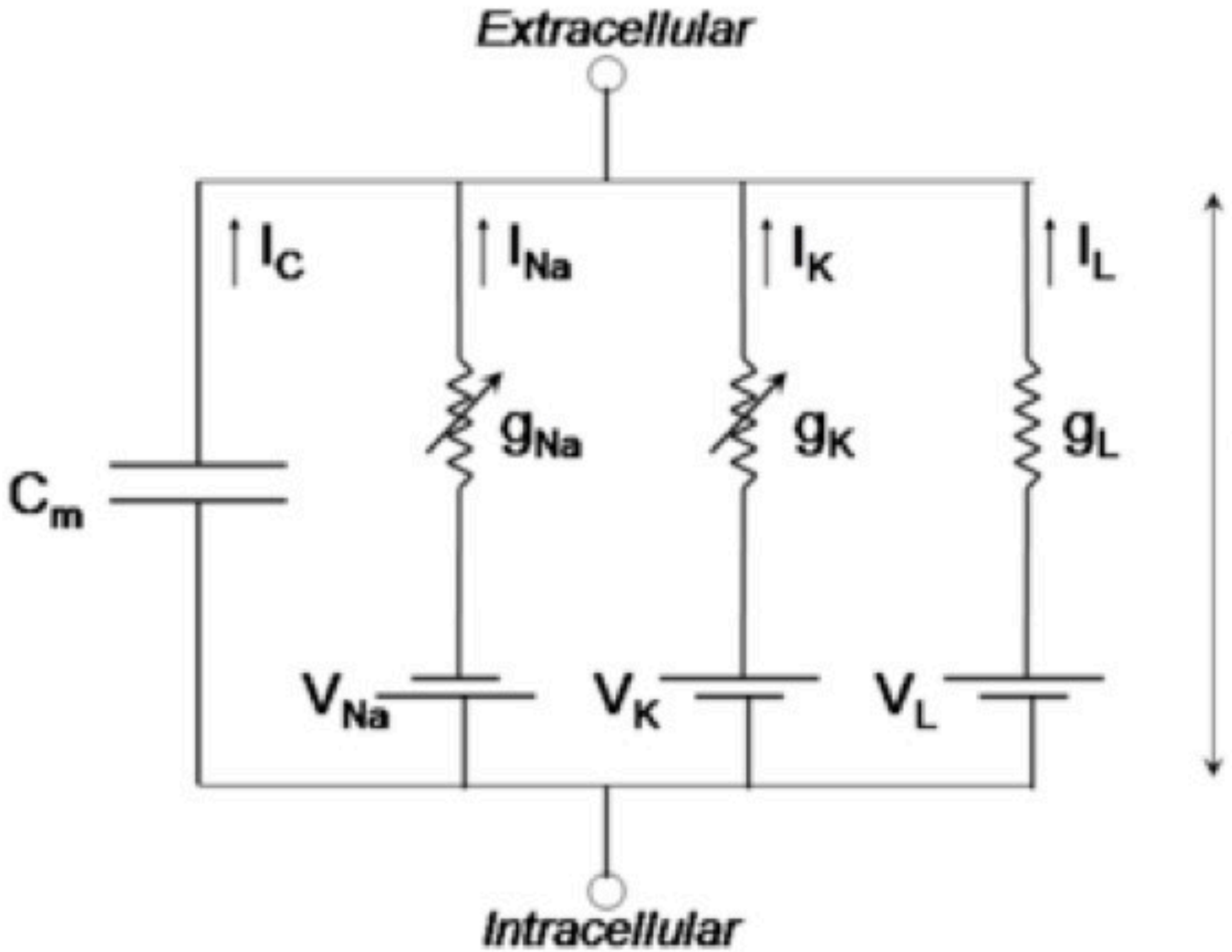
Can we describe an equivalent circuit to calculate the change in membrane potential V?

Differences in ion concentration → **Batteries** → 

Cell membrane → **Capacitor** → 

Ionic channels → **Resistors** → 

Neuron as an electric circuit



Ohm law: $I = \frac{V}{R} = gV$

$$I_{cap} = C\frac{dV}{dt}$$

$$I_{app} = C\frac{dV}{dt} + I_{ion}$$

Kirchoff's law: the total current flowing across the cell membrane is the sum of the capacitive current and the ionic currents

Integrate-and-fire (idea)

One of the most popular neuronal models (simple but capture important neuronal properties)

One of the oldest... proposed by Lapicque (1907) way before the mechanisms that generate action potential we understood

Neurons **integrate** inputs (synaptic currents) from other neurons, and when "enough" are received they **fire** an action potential and reset their membrane voltage

Integrate-and-fire (bath tube)

Analogy: imagine a bath tube with a hole in the bottom, and thus leaking water

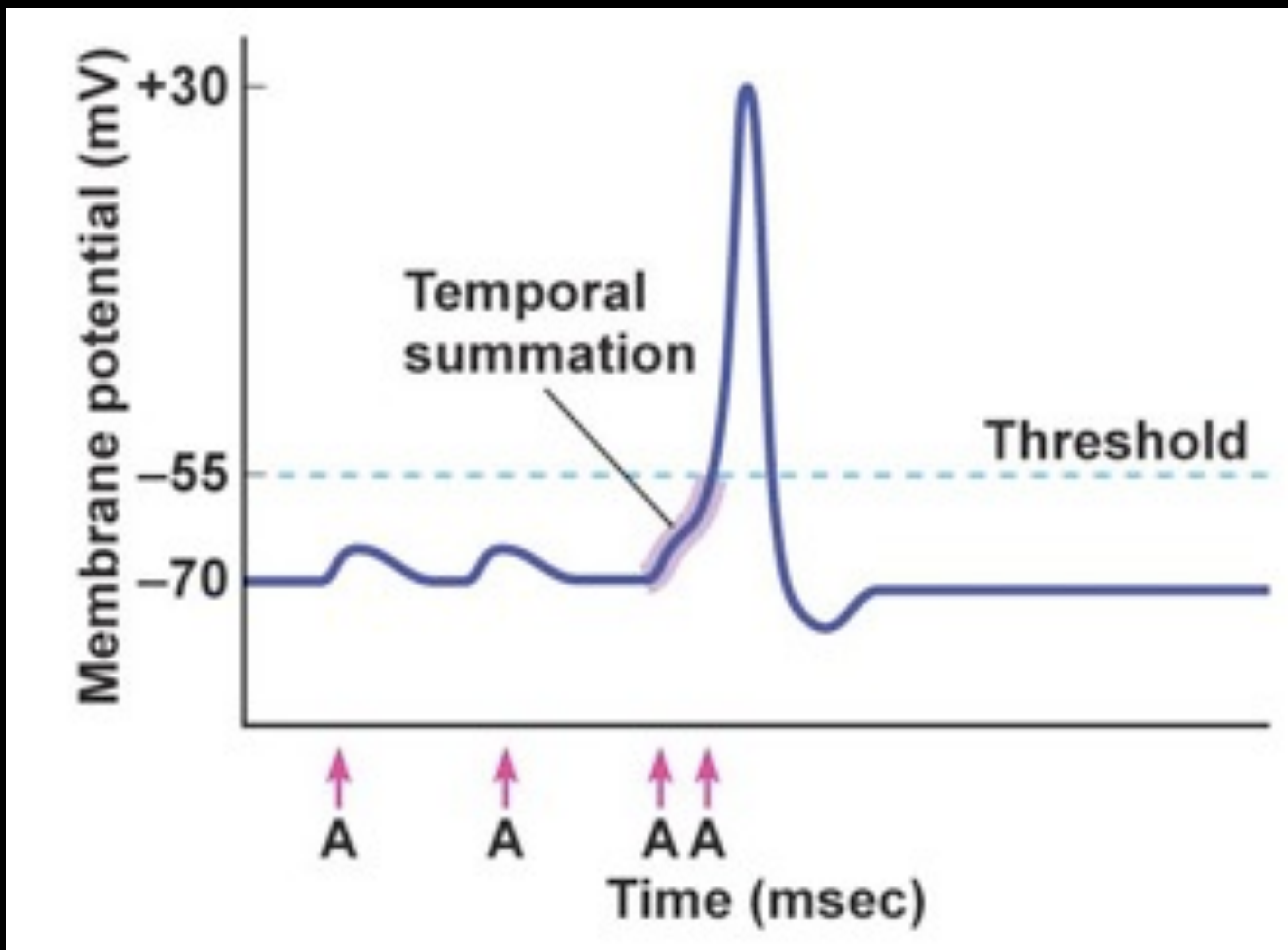
Incoming action potentials are like buckets of water that are poured in time into the bath tube

If enough are coming during a short time, and thus compensating for the leak, water will overflow

At threshold the neuron emits an action potential and its voltage (equivalent to the water level) will be reset to a default value

Integrate-and-fire (threshold)

Threshold mechanism



For $V = V_{Th}$ neuron fires a spike and resets

For $V < V_{Th}$ neuron obeys a passive dynamics

The shape of the action potentials are more or less the same

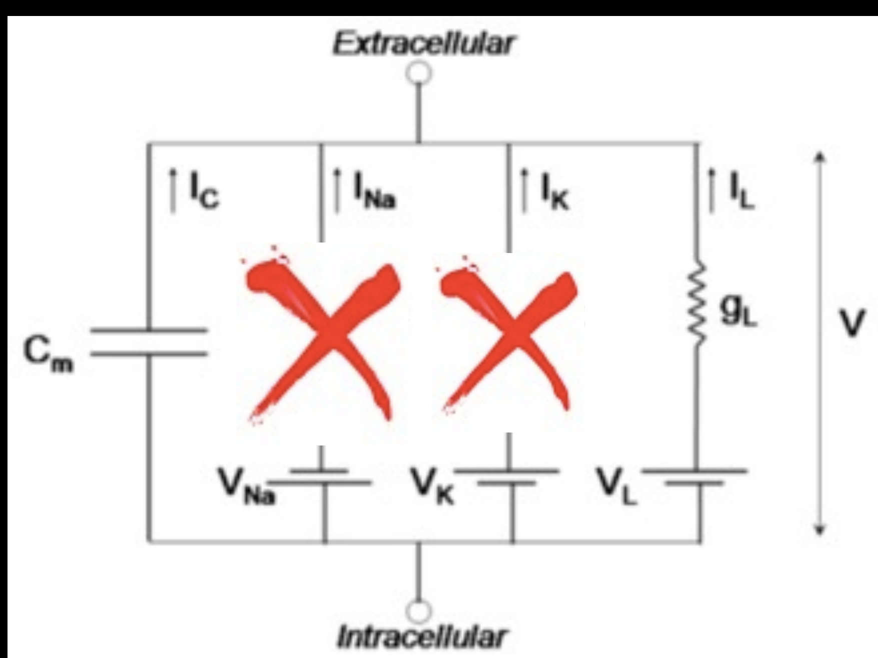
As far as neural communications is concerned, the exact shape of the spike is not important, rather its time of occurrence

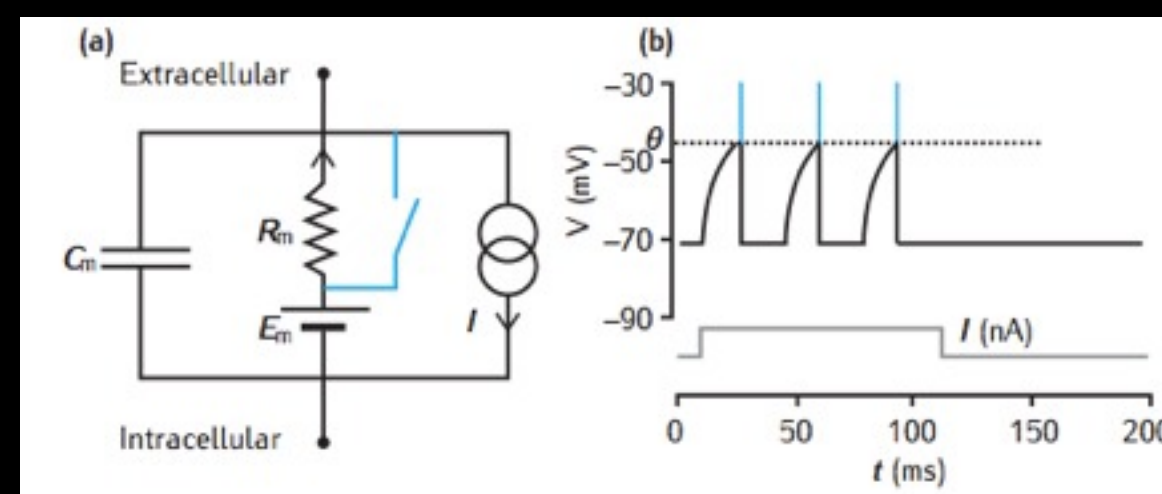
Integrate-and-fire (equation)

Let's divide the behavior of a neuron in two regimes

Supra-threshold (if $V = V_{Th}$ then spike and reset)

Sub-threshold (voltage according to equivalent circuit):



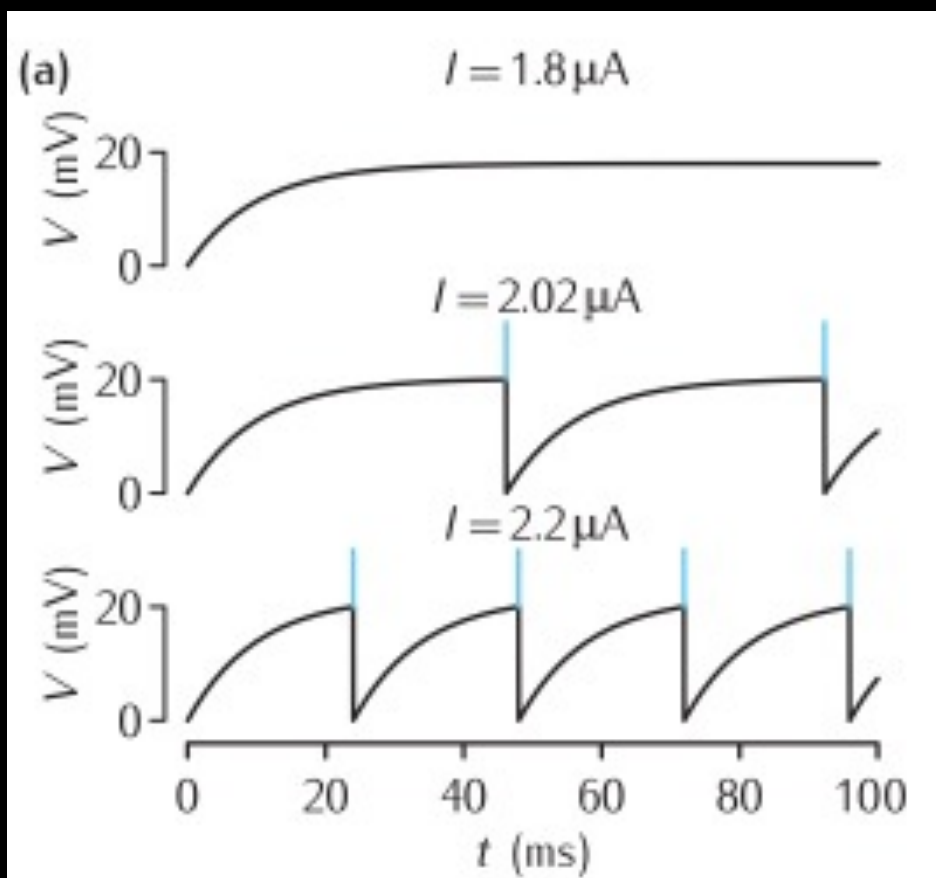


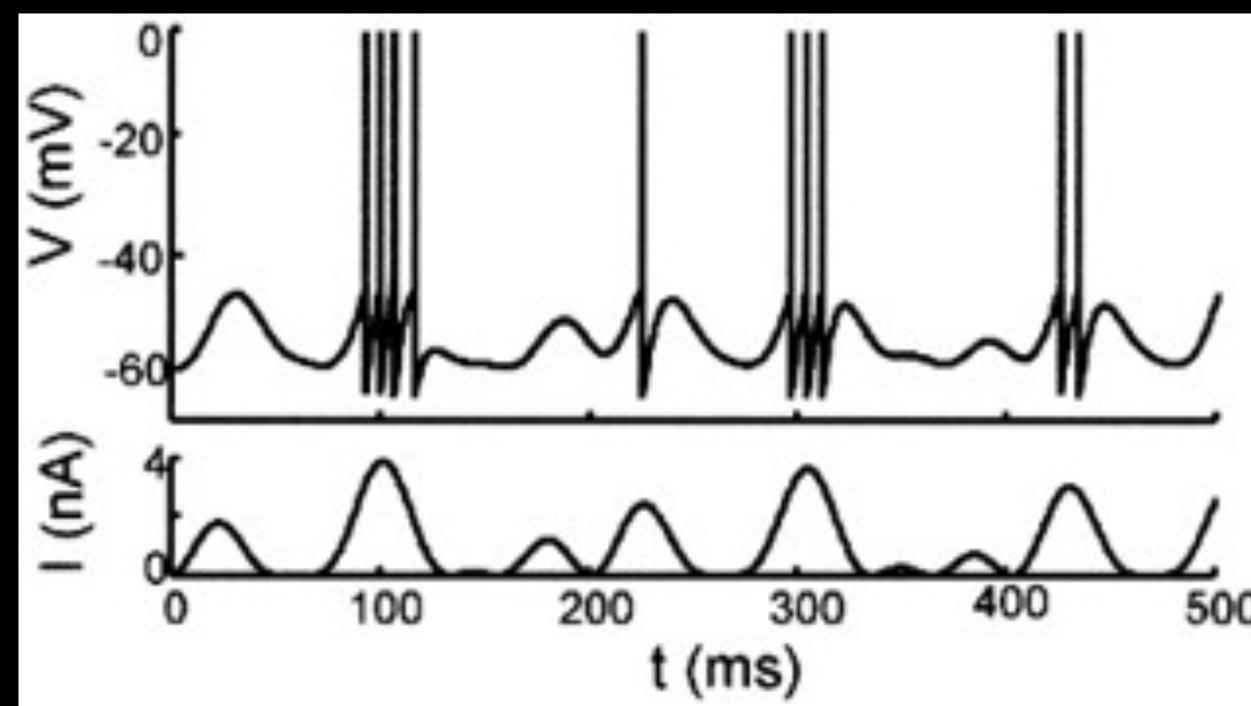
$$C_m \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I$$

Integrate-and-fire (simulation)

Now we are ready to simulate an I&F neuron...

$$C_m \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I$$





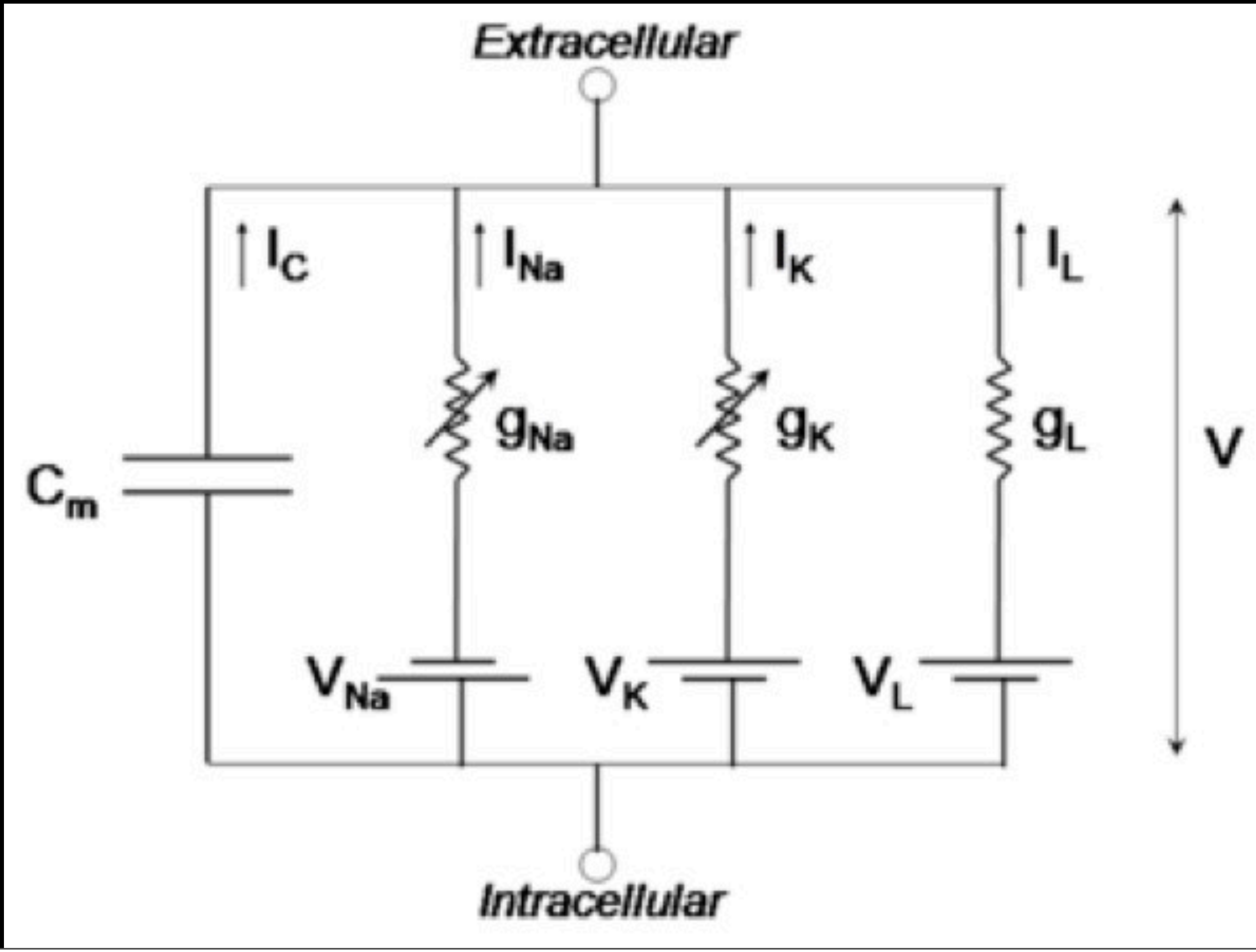
We still lack synaptic currents from other neurons... (later)

McCulloch-Pitts

Integrate-and-Fire

Hodgkin-Huxley

Hodgkin-Huxley



Hodgkin-Huxley (heroic)

Empirical model that describes the ionic conductance and **generation of nerve action potential**

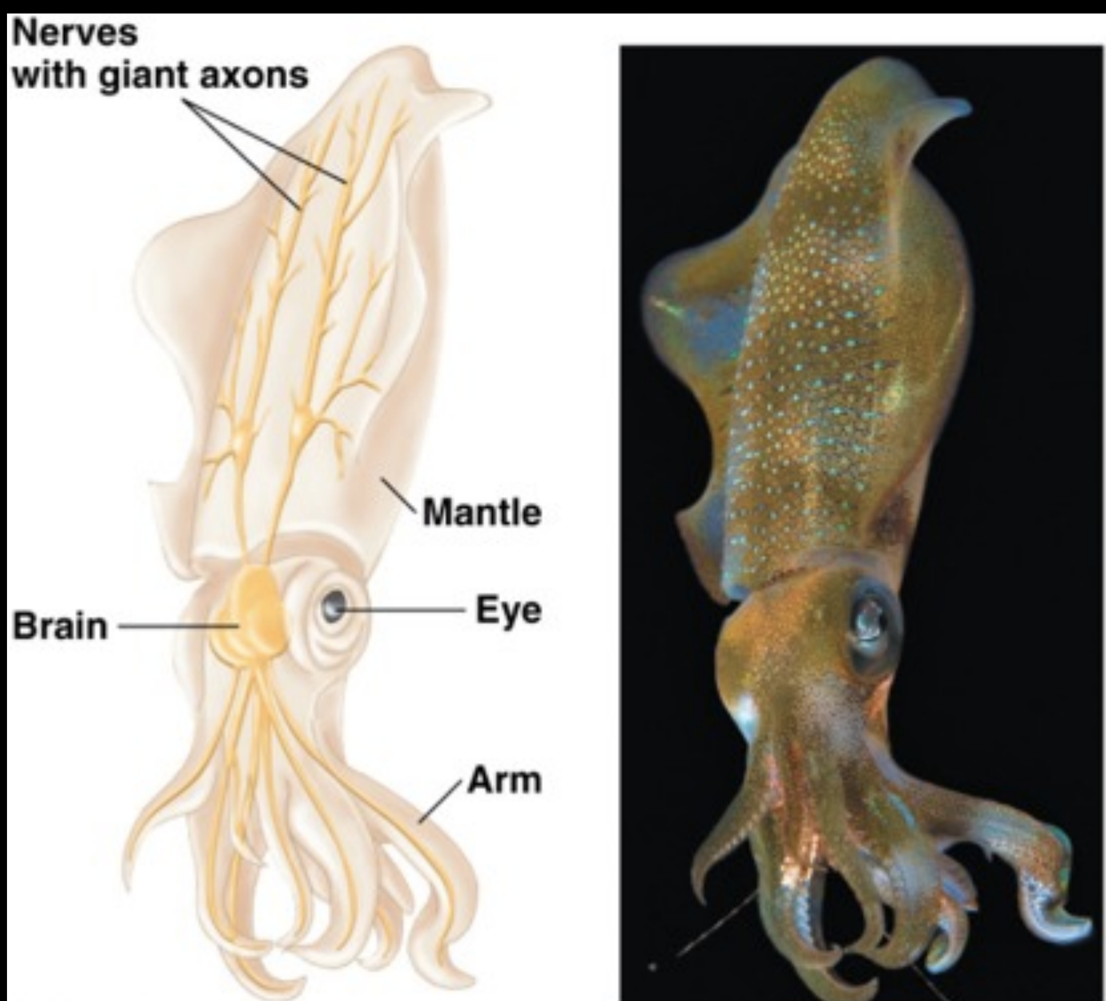
Published in 1952

Nobel Prize in Medicine or Physiology in 1963

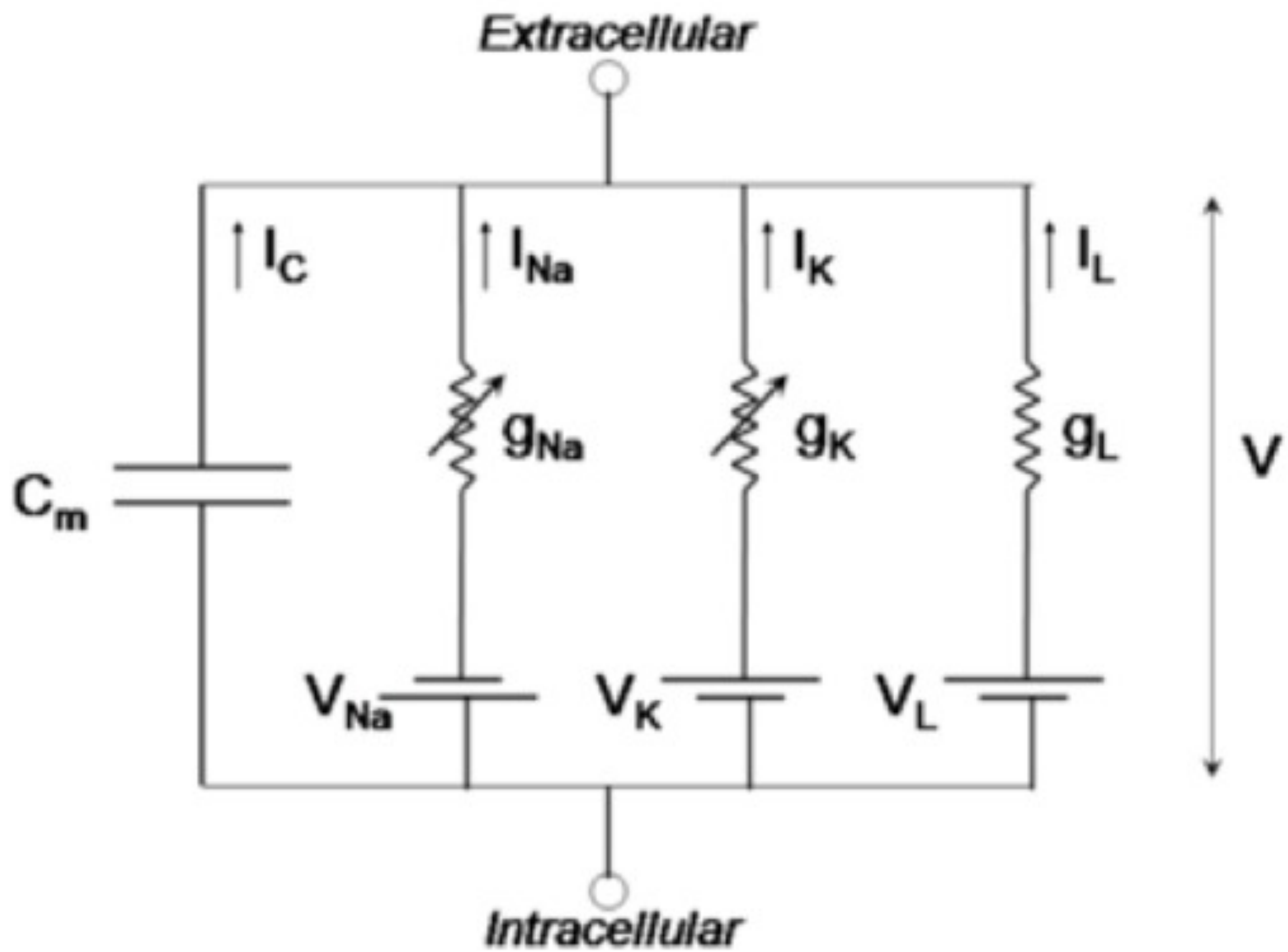
Work reflects a combination of experimental work, theoretical hypothesis, computational data fitting, and model prediction

Hodgkin-Huxley (big is good)

Made their experiments on the squid giant axon, not the giant squid axon!



Hodgkin-Huxley (as a circuit)



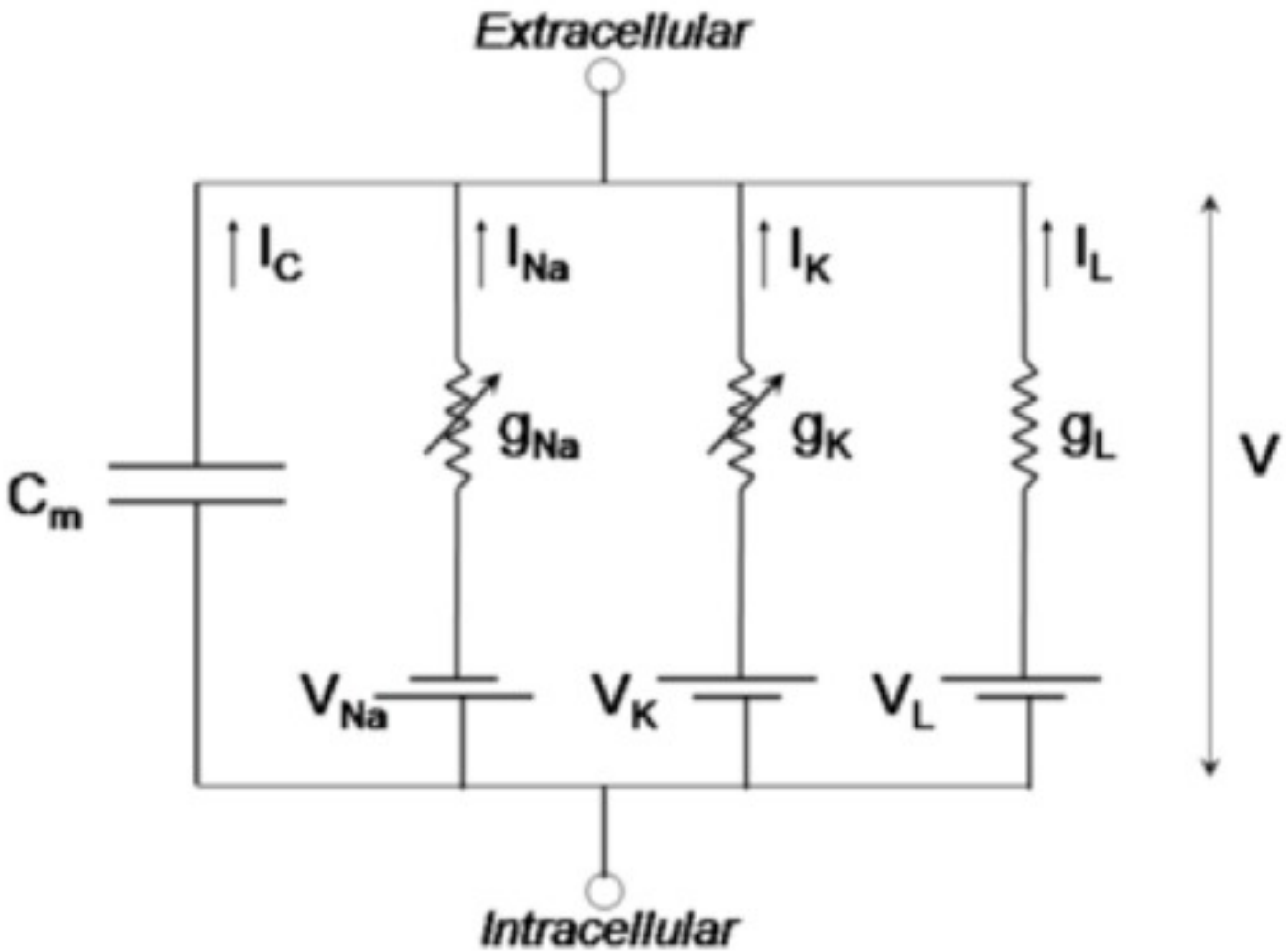
$$I = I_c + I_i = C_m \frac{dV}{dt} + I_i$$

$$I_i = I_{Na} + I_K + I_L$$

$$I_{Na} = g_{Na}(V - E_{Na}),$$
$$I_K = g_K(V - E_K),$$
$$I_L = \overline{g}_L(V - E_L),$$

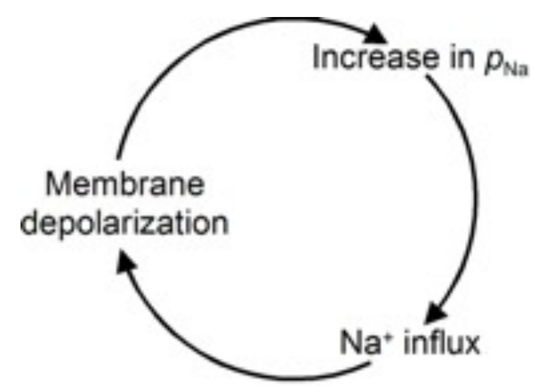
Hodgkin-Huxley (Na and K)

The data of HH indicated that Na and K ion channels conductance (open) depended on voltage



$$g_{Na} = g_{Na}(V)$$

$$g_K = g_K(V)$$



But how exactly?

Hodgkin-Huxley (gating)

HH proposed that **channels** behaved **as a system of gates** or doors

Example for K channels:

g_K = maximal conductance x probability all gates are open

For 1 gate $g_K = \bar{g}_K n$. *n* being the probability gate is open

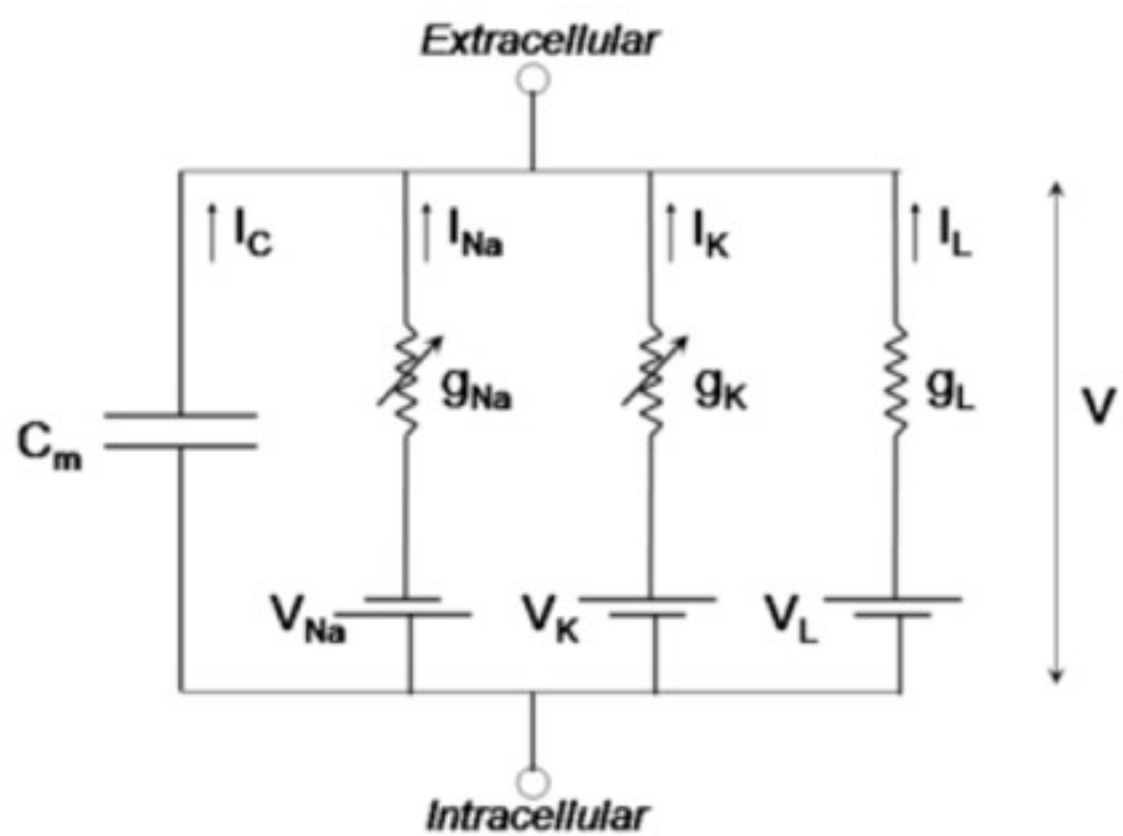
For 4 gates $g_K = \bar{g}_K n^4$.

n changes over time: $\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$.

Hodgkin-Huxley (full model)

Full model: Inserting gating mechanisms of Na and K conductances into current equations...

$$C_{\mathrm{m}}\frac{\mathrm{d}V}{\mathrm{d}t} = -\overline{g}_{\mathrm{L}}(V - E_{\mathrm{L}}) - \overline{g}_{\mathrm{Na}}m^3h(V - E_{\mathrm{Na}}) - \overline{g}_{\mathrm{K}}n^4(V - E_{\mathrm{K}}) + I$$



Hodgkin-Huxley (full model)

$$C_m \frac{dV}{dt} = -\bar{g}_L(V - E_L) - \bar{g}_{Na} m^3 h (V - E_{Na}) - \bar{g}_K n^4 (V - E_K).$$

Sodium activation and inactivation gating variables:

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m, \qquad \frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h,$$

$$\alpha_m = 0.1\ \frac{V + 40}{1 - \exp(-(V + 40)/10)}, \qquad \alpha_h = 0.07\ \exp(-(V + 65)/20),$$

$$\beta_m = 4\ \exp(-(V + 65)/18), \qquad \beta_h = \frac{1}{\exp(-(V + 35)/10) + 1}.$$

Potassium activation gating variable:

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

$$\alpha_n = 0.01 \frac{V + 55}{1 - \exp(-(V + 55)/10)},$$

$$\beta_n = 0.125 \exp(-(V + 65)/80).$$

Parameter values (from Hodgkin and Huxley, 1952d):

$C_m = 1.0\ \mu F\, cm^{-2}$

$E_{Na} = 50\ mV$ $\qquad \bar{g}_{Na} = 120\ mS\, cm^{-2}$

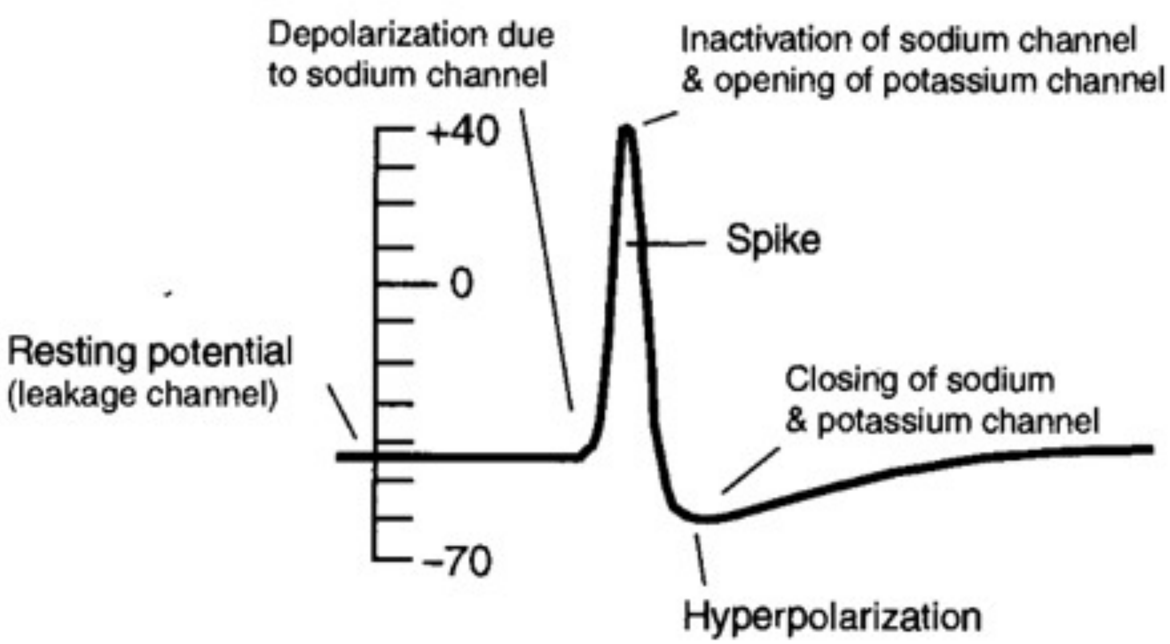
$E_K = -77\ mV$ $\qquad \bar{g}_K = 36\ mS\, cm^{-2}$

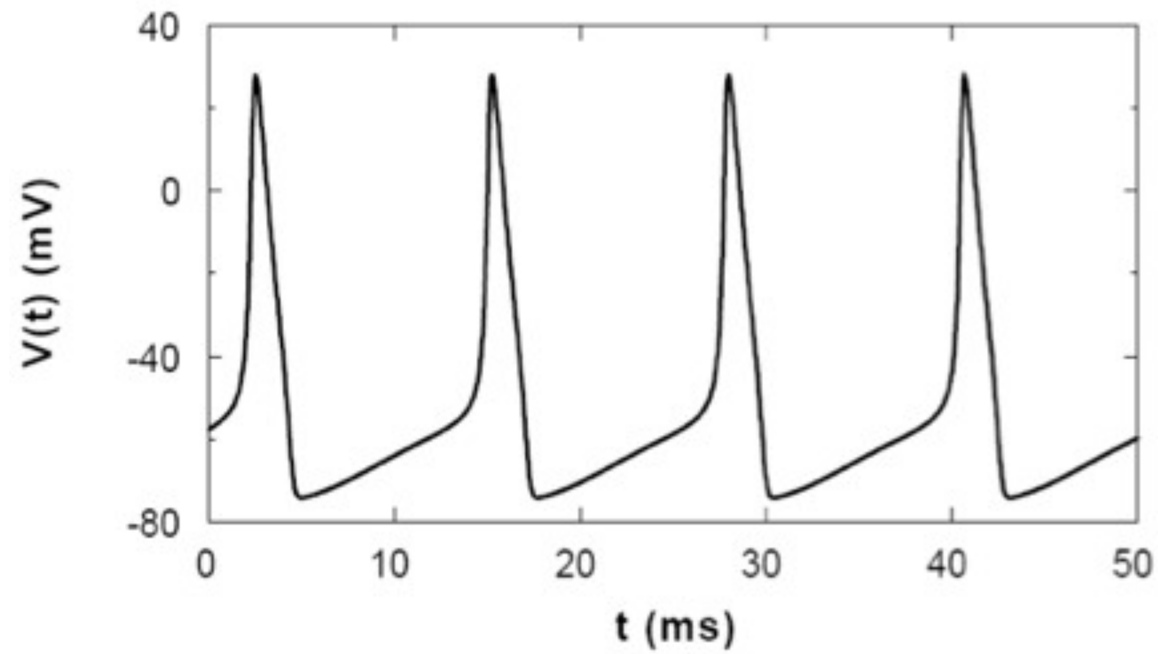
$E_L = -54.4\ mV$ $\qquad \bar{g}_L = 0.3\ mS\, cm^{-2}$

HHsim

Hodgkin-Huxley (full model)

$$C\frac{dV}{dt} = -\sum_i g_i(V - V_i) + I_{app}$$

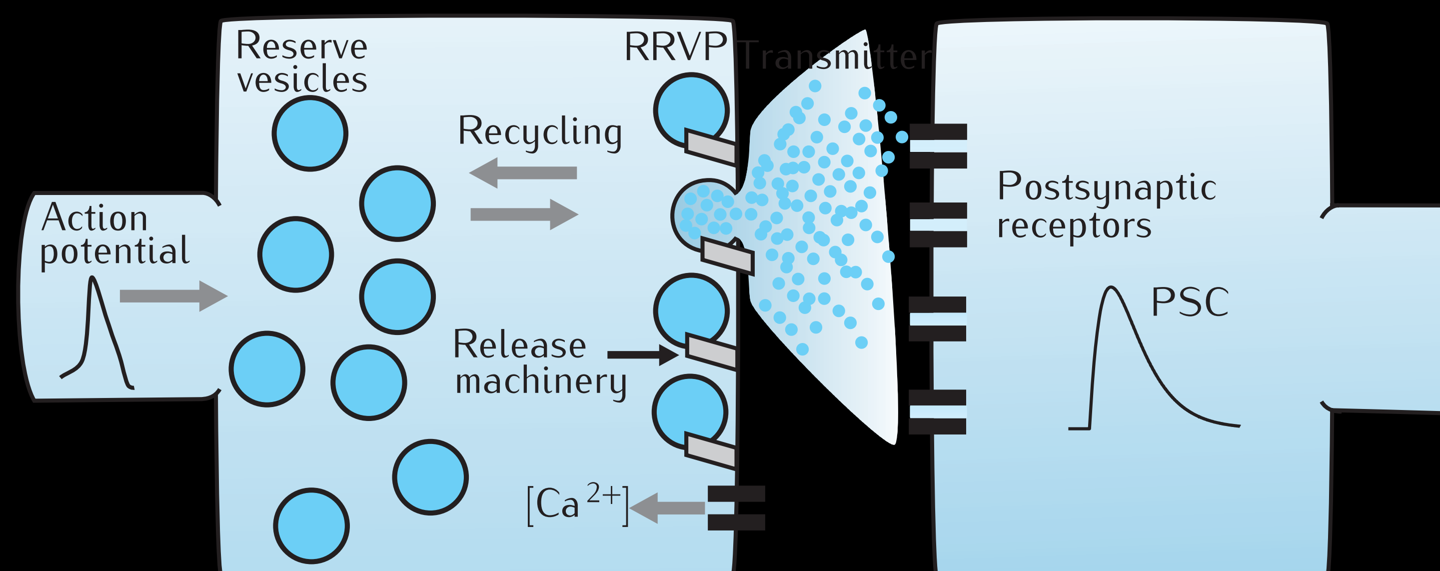




Action potentials come naturally

What about the synapses?

To simulate circuits of neurons we also need to include the synaptic currents (I_{syn})



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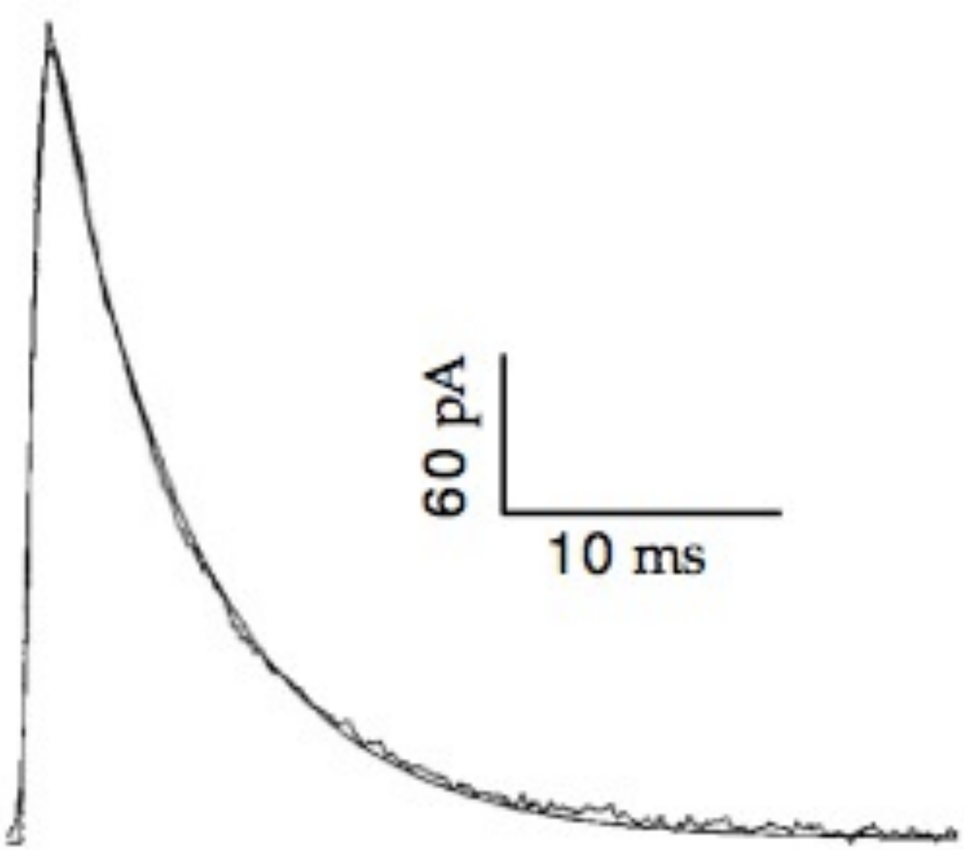


PSC (excitatory)

How do we model synaptic currents?

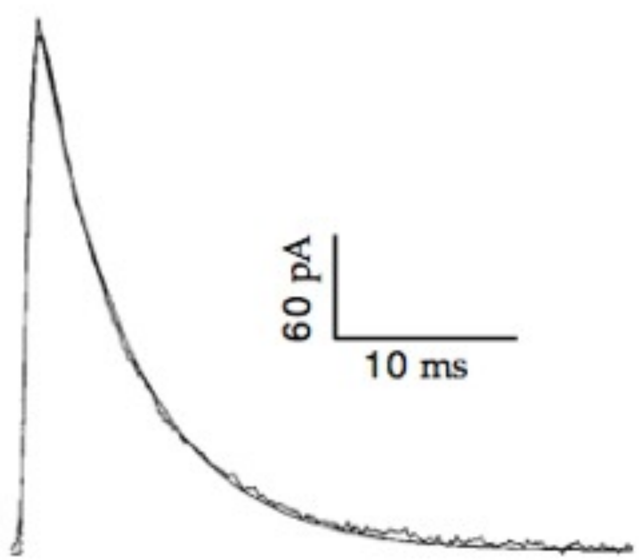
What about the synapses?

Synaptic currents also occur due to the opening and closing of ion channels:

$$I_{syn} = g_{syn}(V - E_R)$$

as with Hodgkin-Huxley the difficulty is to find how *g* changes with time

Solution I:



PSC (excitatory)

Arrival of incoming spike from other neuron:

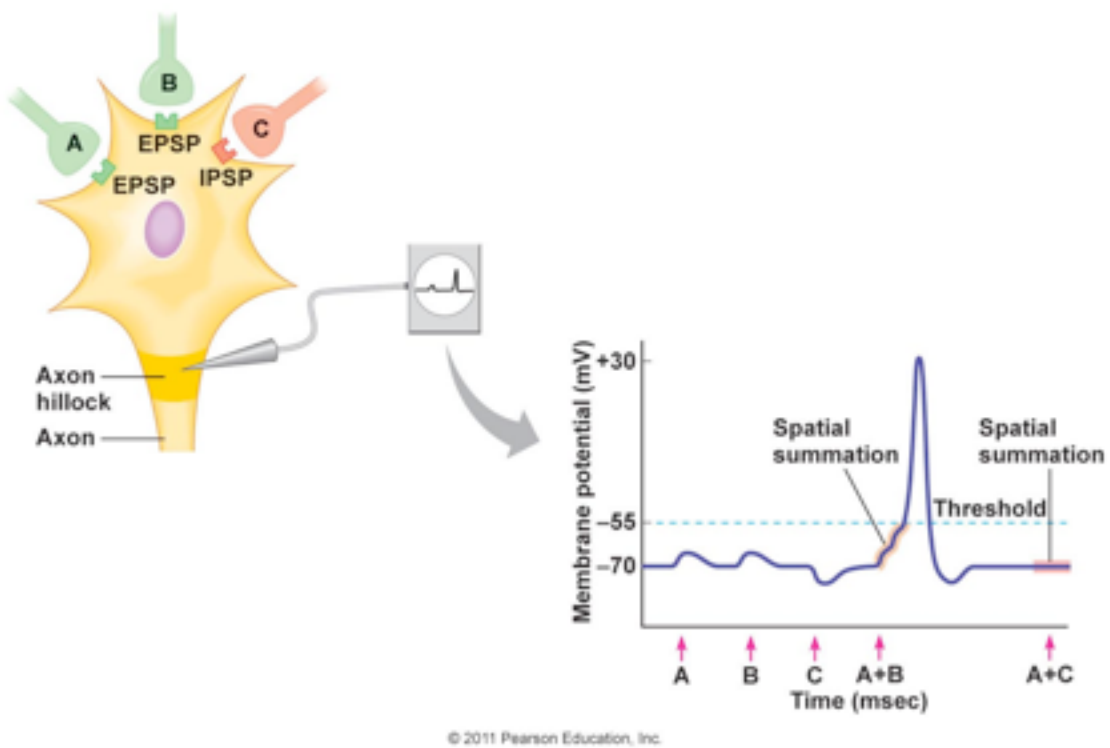
1) $g_{syn} \longrightarrow g_{syn} + dg$

2) exponential decay

What about the synapses?

Two important remarks:

* There are excitatory and inhibitory synapses



$$I_{syn} = I_{exc} + I_{inh}$$

* There MANY synapses

What about the synapses?

Now, we can couple a synaptic model with I&F or HH

I&F

$$\tau_m \frac{dV_m(t)}{dt} = -V_m(t) + RI(t)$$

+

synaptic currents

$$g_{exc}(t)(E_{exc} - V_m(t)) + g_{inh}(t)(E_{inh} - V_m(t))$$

=

Full model

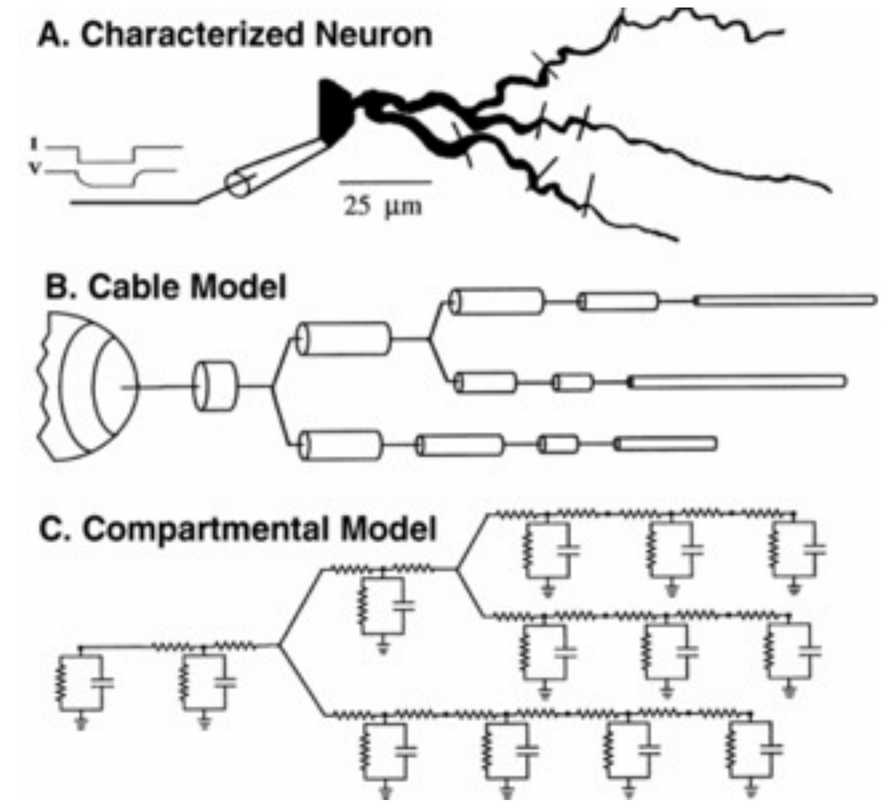
$$\tau_m \frac{dV_m(t)}{dt} = (V_{rest} - V_m(t)) + g_{exc}(t)(E_{exc} - V_m(t)) + g_{inh}(t)(E_{inh} - V_m(t))$$

Ready to simulate any neuronal circuit!

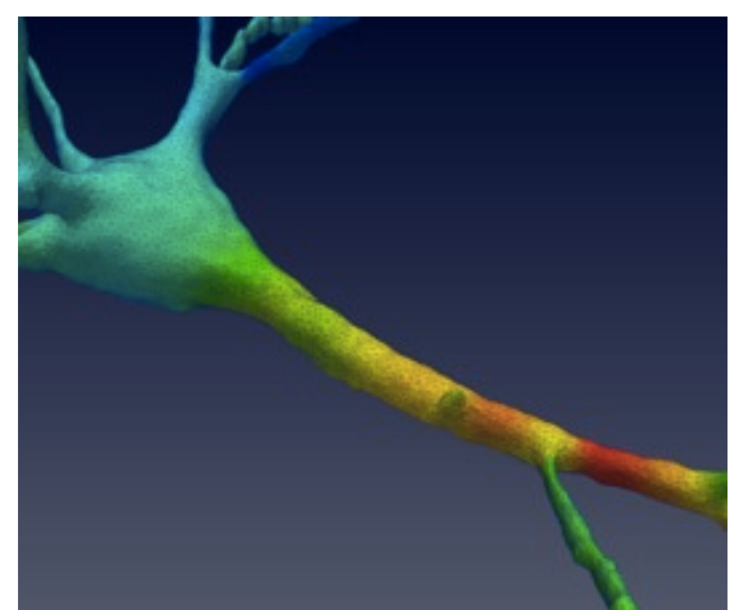
Multicompartment models

Used for very detailed simulations of one or few neurons

Idea: divide a neuron in compartments (with distinct electrical properties) & connect the equivalent circuits



Allows fine study of morphological, pharmacological, or electrical effects



Simulated using NEURON or GENESIS

Summary

- Single compartment models include McCulloc-Pitts, Integrate-and-Fire, and Hodgkin-Huxley
- MP is good for exploring computational properties
- I&F and HH capture important details of neuronal activity and are the basis for simulating realistic neuronal circuits

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Basics

Analyses

Models

Cognitive

Applications