Introduction to computational neuroscience : from single neurons to network dynamics

Michael Graupner

SPPIN, CNRS UMR 8003, Université Paris Cité

slides : on the moodle or https://biomedicale.u-paris.fr/~mgraupe/teaching.php - michael.graupner@u-paris.fr

Lecture outline :

Introduction to Computational Neurosciences

1. Introduction (today) :

- A couple of (fun) brain questions

2. The Neuron (today) :

- Hodgkin-Huxley model
- Integrate-and-Fire model
- Rate model
- Cable theory

3. Neural networks (next course) :

- Rate models
- Spiking neuron models
- Examples

What's the brain good for ?

Tree
no neurons

C.elegans
302 neurons

Fly
1 000 000 neurons

Rat
50 000 000 neurons

Human
80 000 000 000 n.

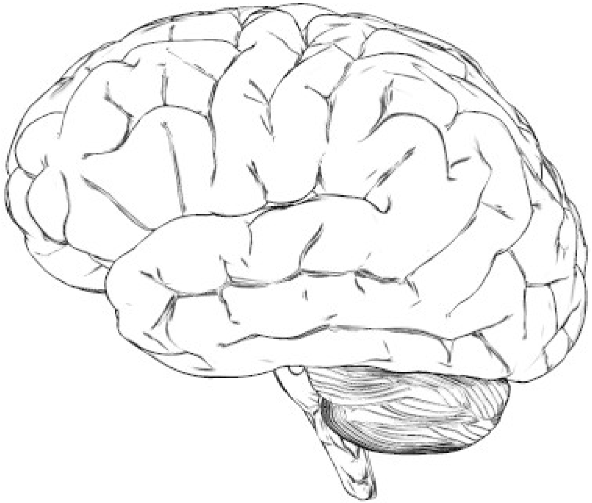
The brain generates motion (=behavior)

more complex brains generate a greater variety of behaviors

more complex brains can learn more behaviors

Cognitive processing

stimulus



response

What's the brain good at ?

			
chess	1	:	0
scrabble	1	:	0
Jeopardy!	1	:	0
video games	1	:	0
Go	1	:	0
Object recognition	1	:	1

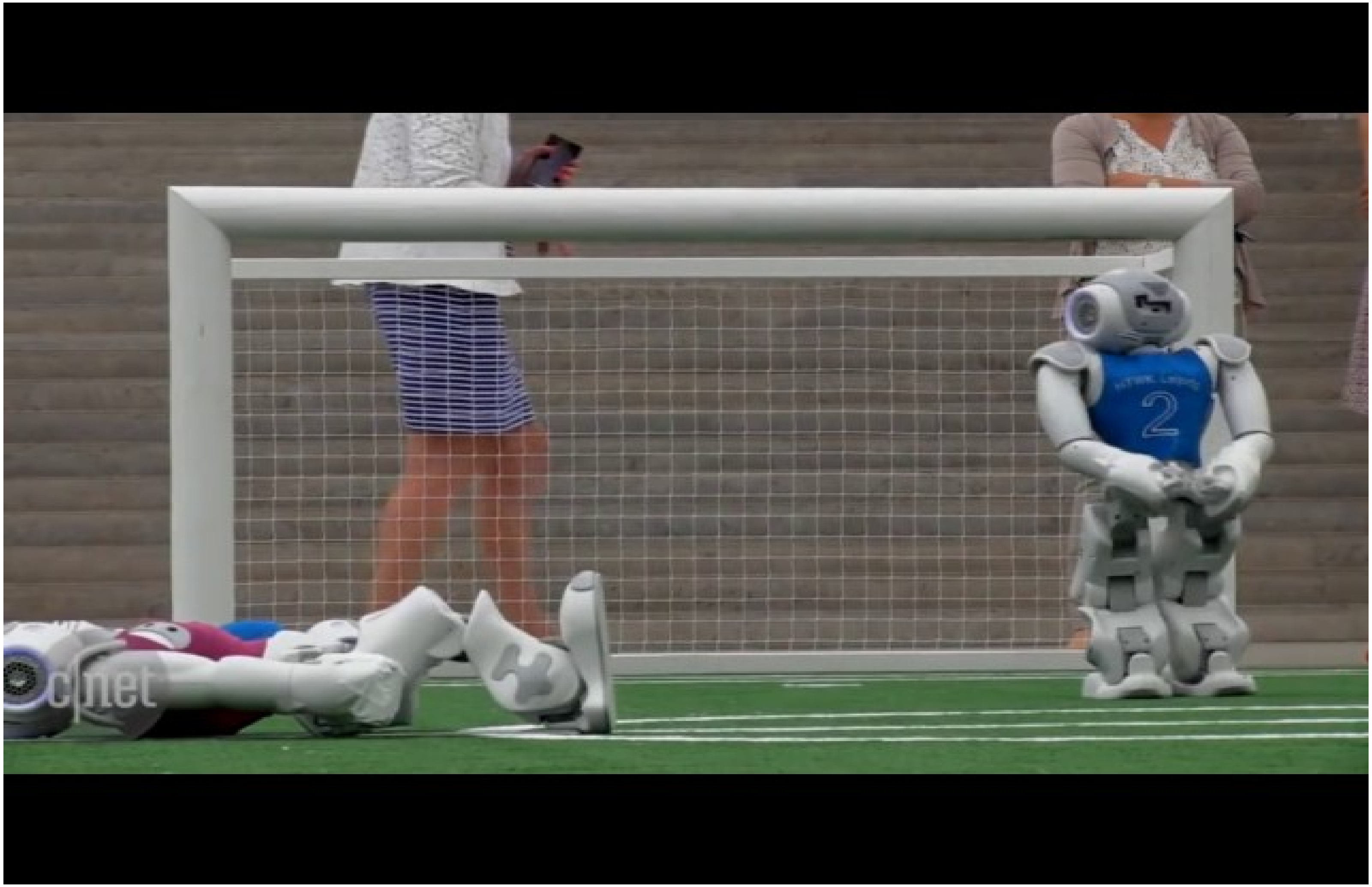
Computers outperform humans in algorithmic tasks and tasks involving database mining.

What's the brain good at ?

Lionel Messi – Barcelona : Getafe CF 2007

What's the brain good at ?

RoboCup 2016



What's the brain good at ?

Boston Dynamics

https://www.youtube.com/watch?v=tF4DML7FIWk&t=7s

What's the brain good at ?

soccer	0	:	1	
numerous motor tasks	0	:	1	(it's getting tight)

Brains are better in tasks involving interactions with the real world.

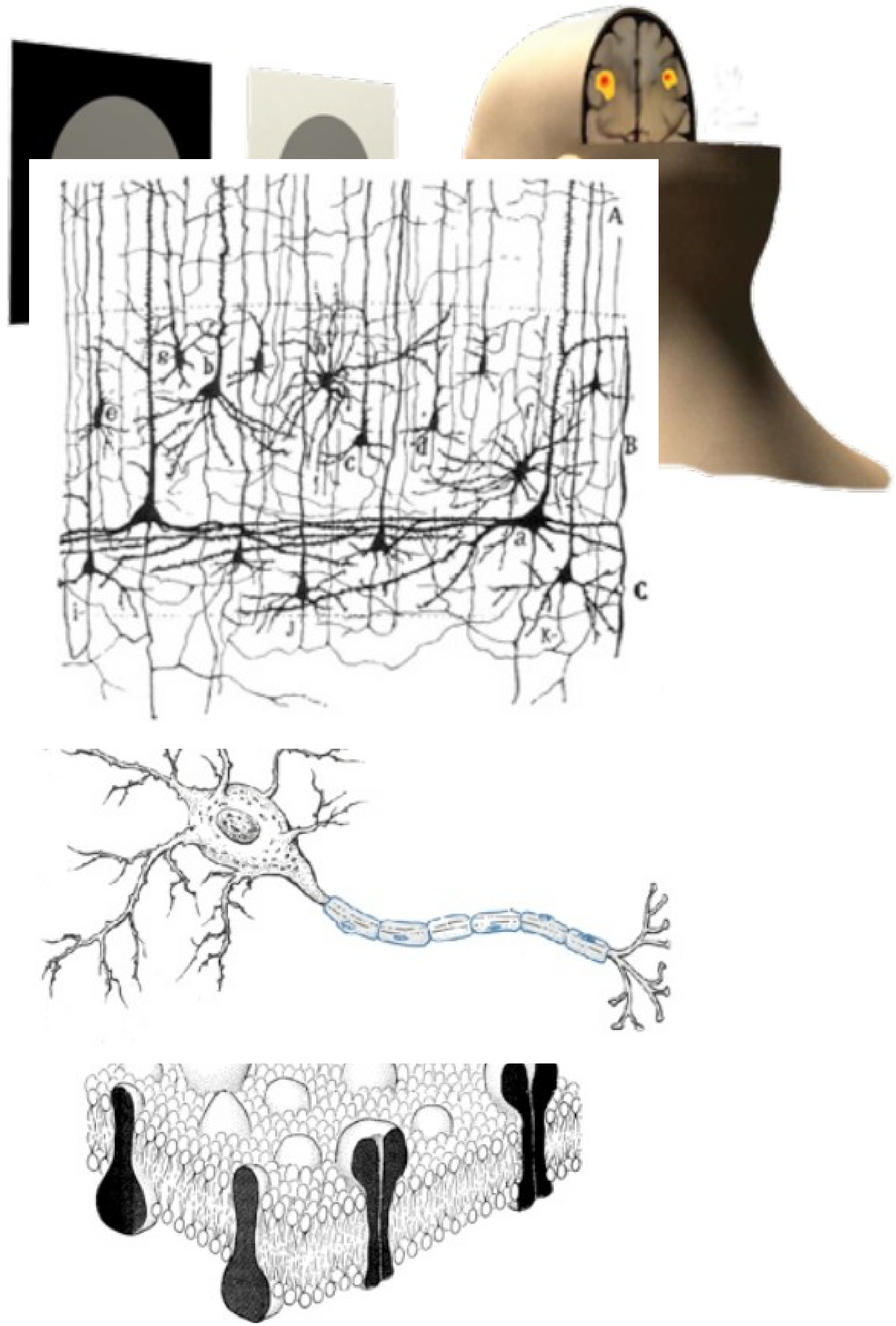
Why model the brain ?

- ➔ to understand it
- ➔ to repair/improve it
- ➔ to get inspired

What makes modeling the brain so complex?

The many spatial scales of the brain

CNS	1 m
Systems	10 cm
Maps	1 cm
Networks	1 mm
Neurons	100 µm
Synapses	1 µm
Molecules	1 nm



How does the

brain work ?

A physics/engineering approach

just rebuild the whole thing

→ reverse engineering the brain

The quest for mechanisms : Constructing the systems from parts

CNS	1 m
Systems	10 cm
Maps	1 cm
Networks	1 mm
Neurons	100 µm
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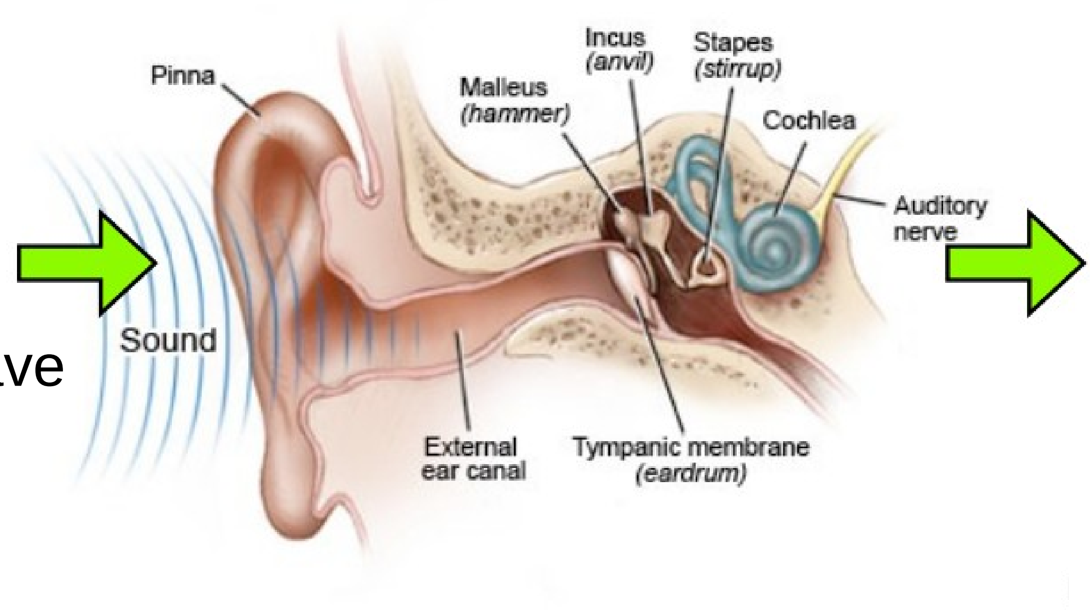
A computer science approach

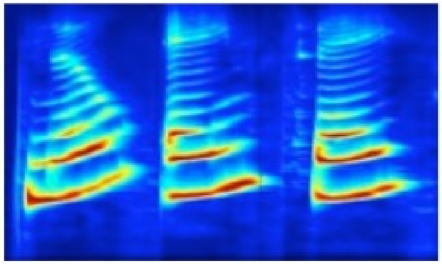
Study the computational problems

Computation : manipulating information

Normal hearing

sound pressure wave

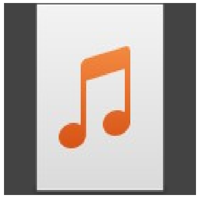




cochleogram (time-frequency representation of sound)

Representation of information

Music example : Art Blakey – Mayreh



Representation of information more or less lossy

How to transmit the music of a jazz concert :

- Partition

- Sound

- CD

- Language

The other day, I went to this cool jazz concert ... .

lossy

Why represent information differently

Example : numbers, twenty-three

XXIII	Roman system
23	Decimal system
00010111	Binary system

Why represent information differently

Example : numbers, twenty-three

XXIII	in ... ?
23	in multiples of 10
00010111	in multiples of 2

Can you add these number ?

```
   29
+  33
 ----
   62
```

simple

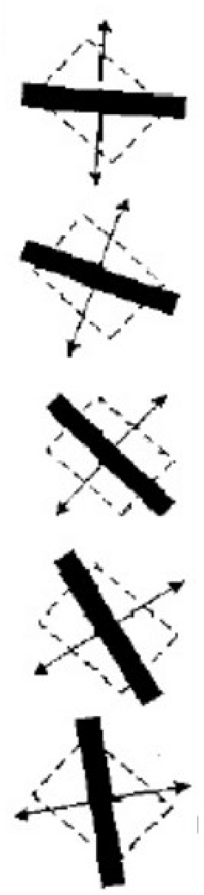
```
   00011101
+  00100001
 ----------
   00111110
```

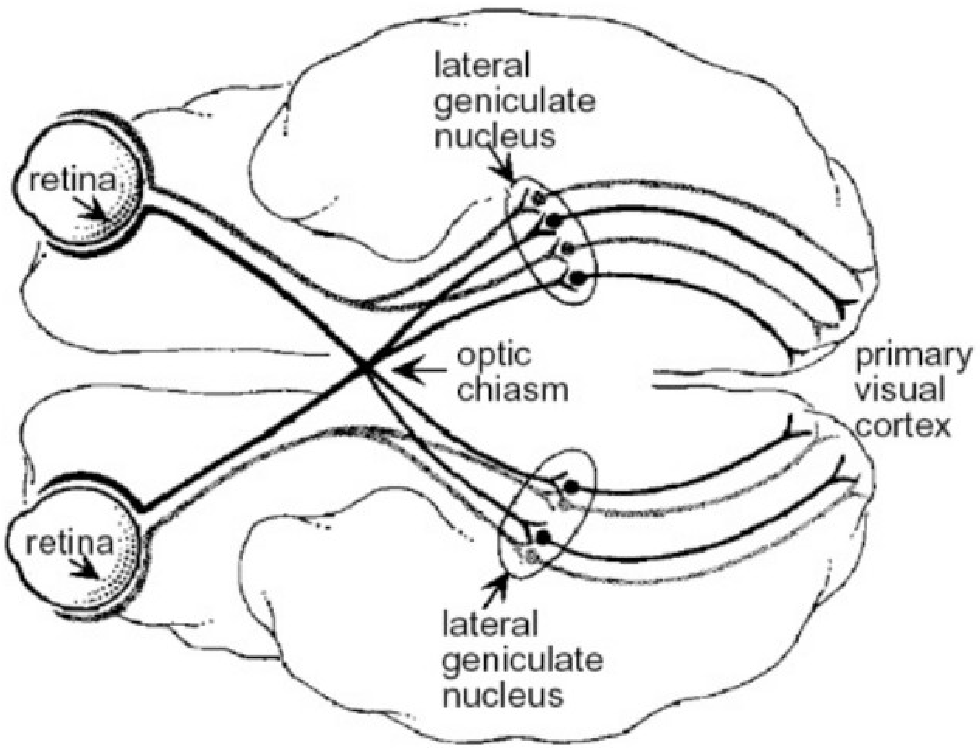
simple

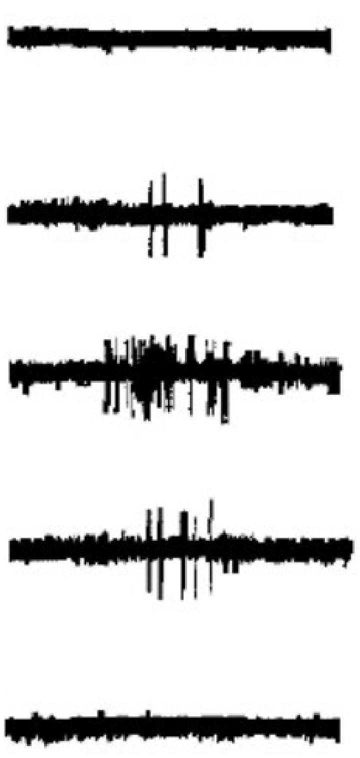
```
     XXIX
+  XXXIII
 --------
     LXII
```

complicated

Most famous example
“edge detectors” in visual cortex





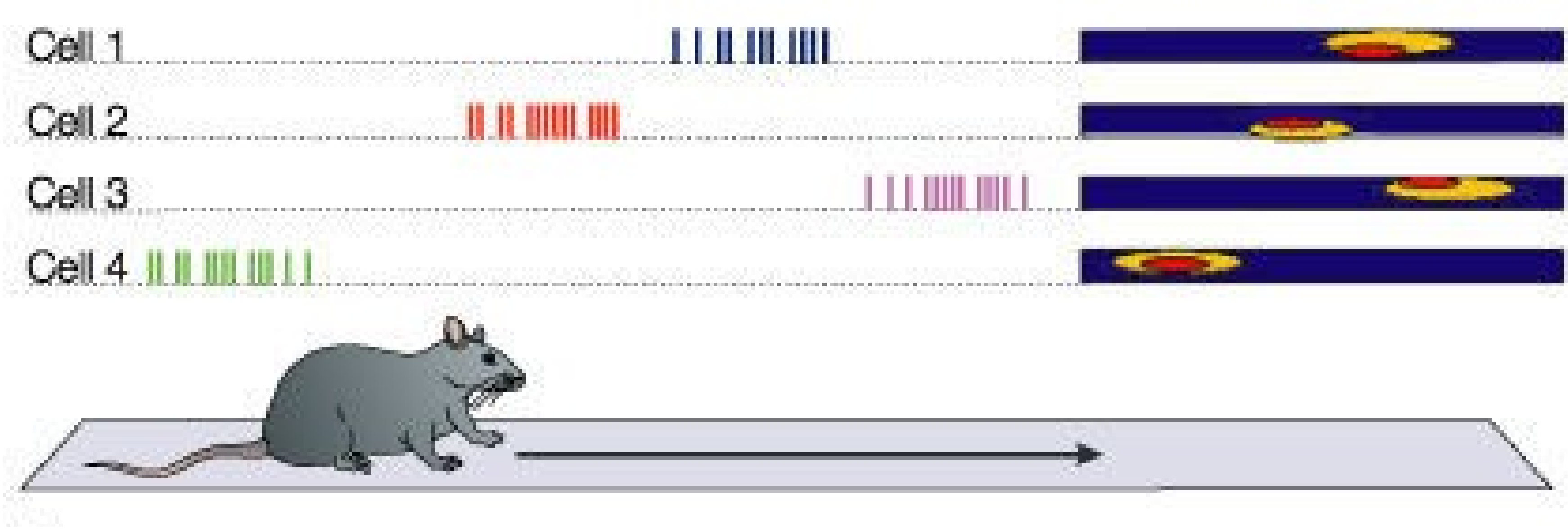


stimulus:
black
bar

Activity of
neuron in
visual cortex
(V1)

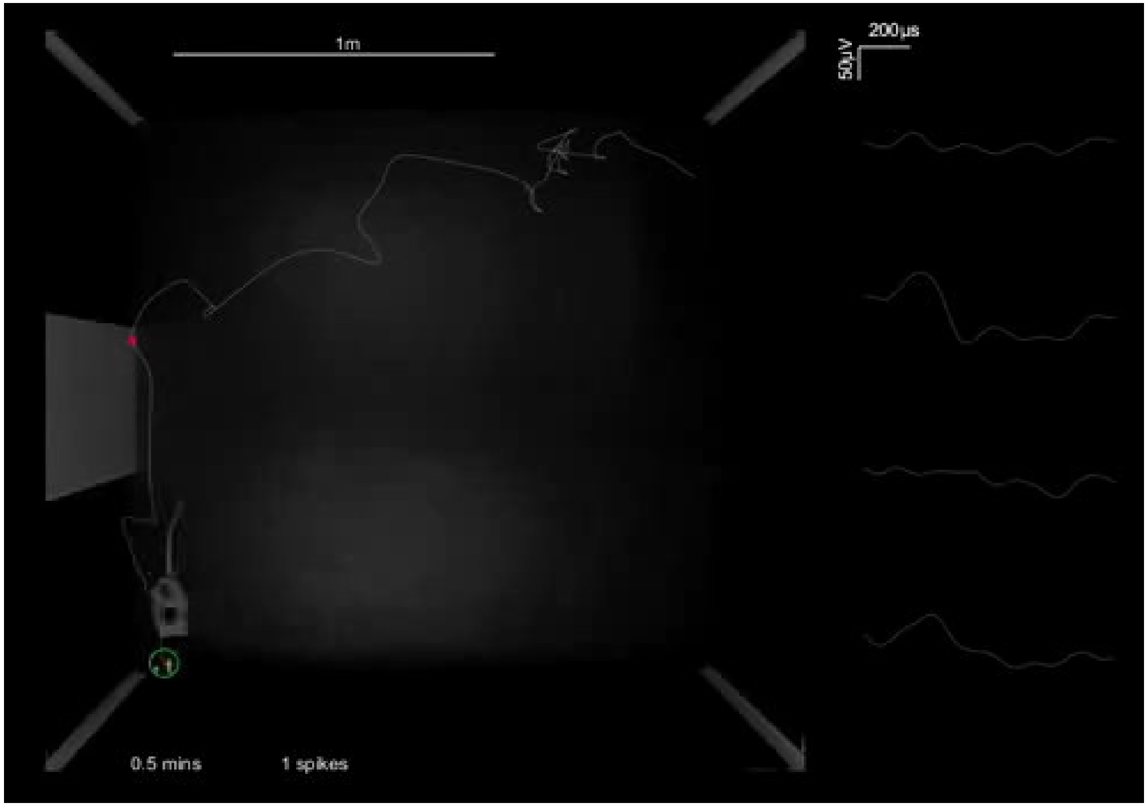
Another famous example
“Place cells” in the hippocampus

Linear track



[Nakazawa et al. 2004]

Another famous example
“Place cells” in the hippocampus



[Nakazawa et al. 2004]

What we understand

very little

What is required

biologists, psychologist

- to probe the brains of animals and humans
- to design and carry out clever experiments
- to investigate and quantify human and animal behavior

physisists, computer scientists, engineers

- to formulate mathematical theories of information processing
- to create biophysical models of neural networks

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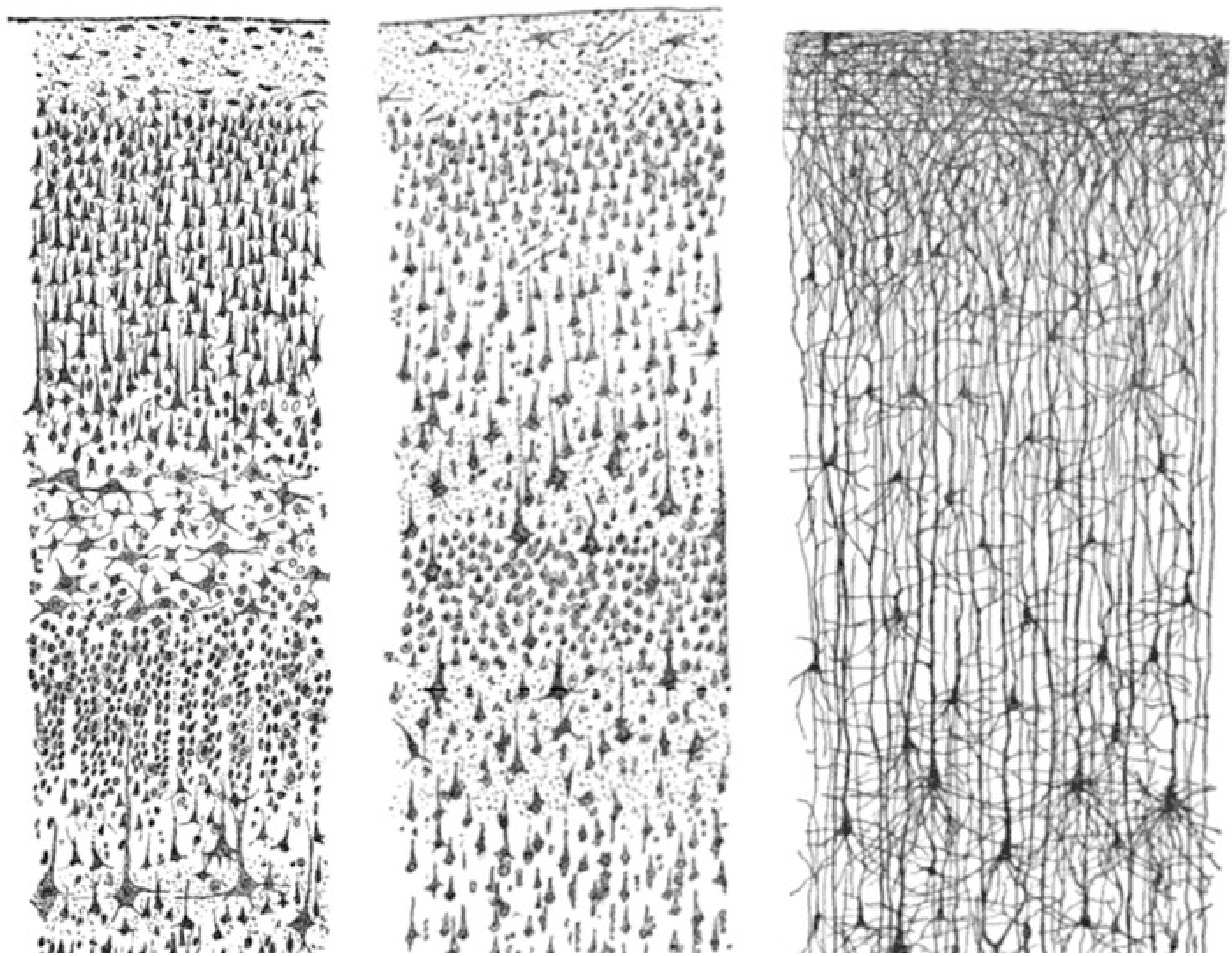
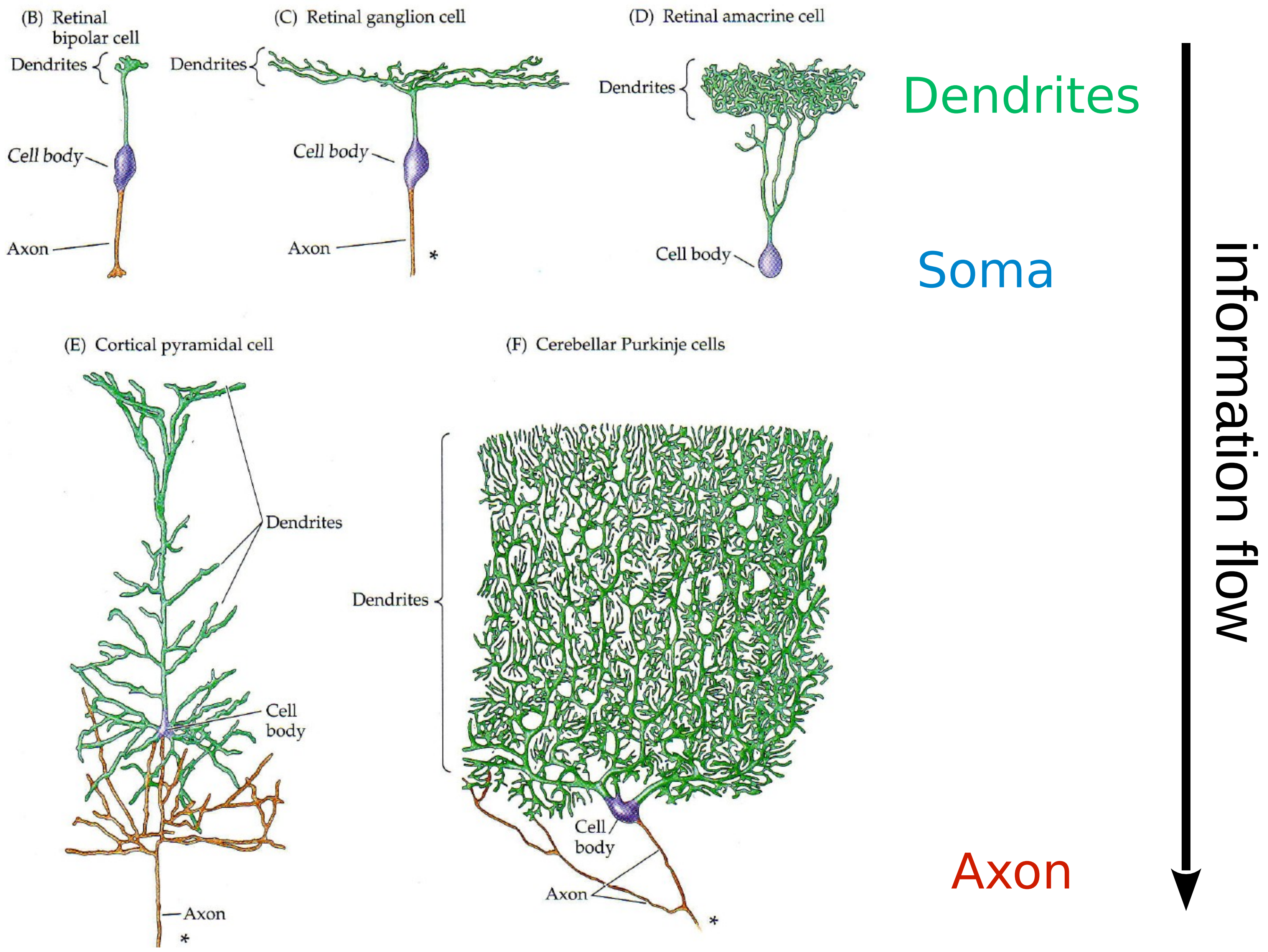
What does the hardware look like ?



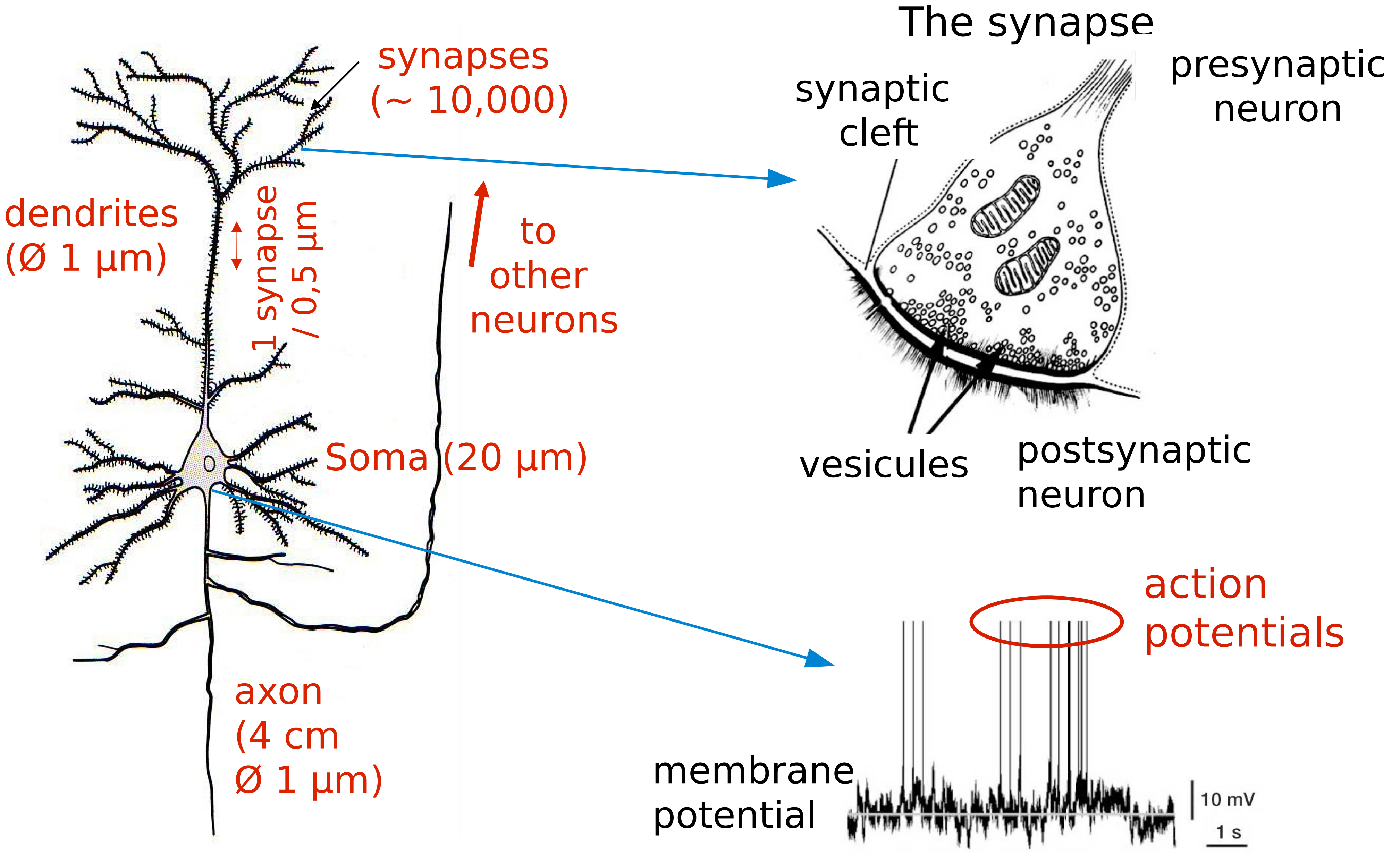
Ramon y Cajal (Nobel Prize 1906) → neuron doctrine

Joseph von Gerlach (1871), Camillo Golgi → ~~Reticular theory~~

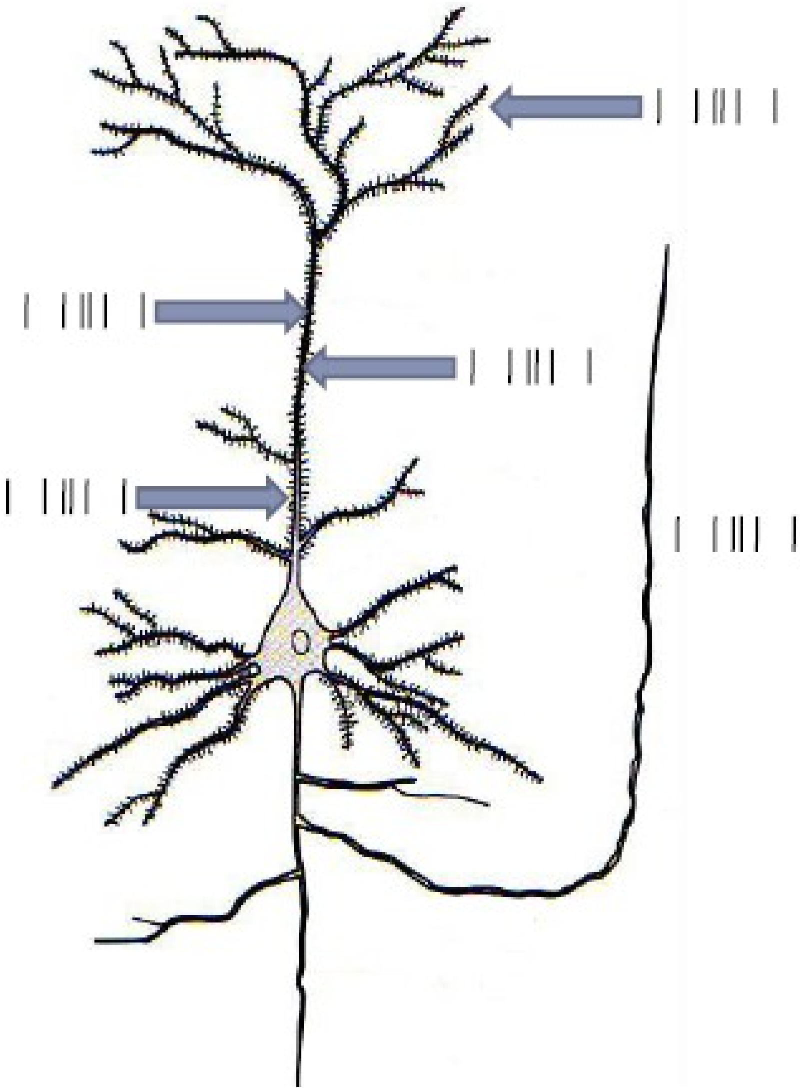
Neurons = basic units of computation

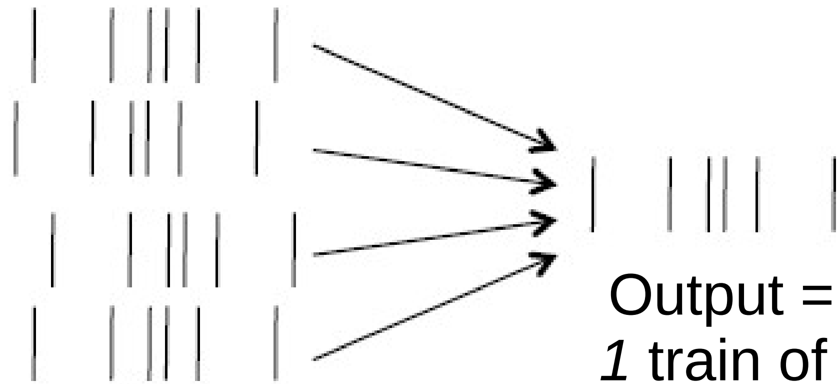


The typical cortical neuron



Neural integration





Input =
N trains of
action potentials

Output =
1 train of
action potentials

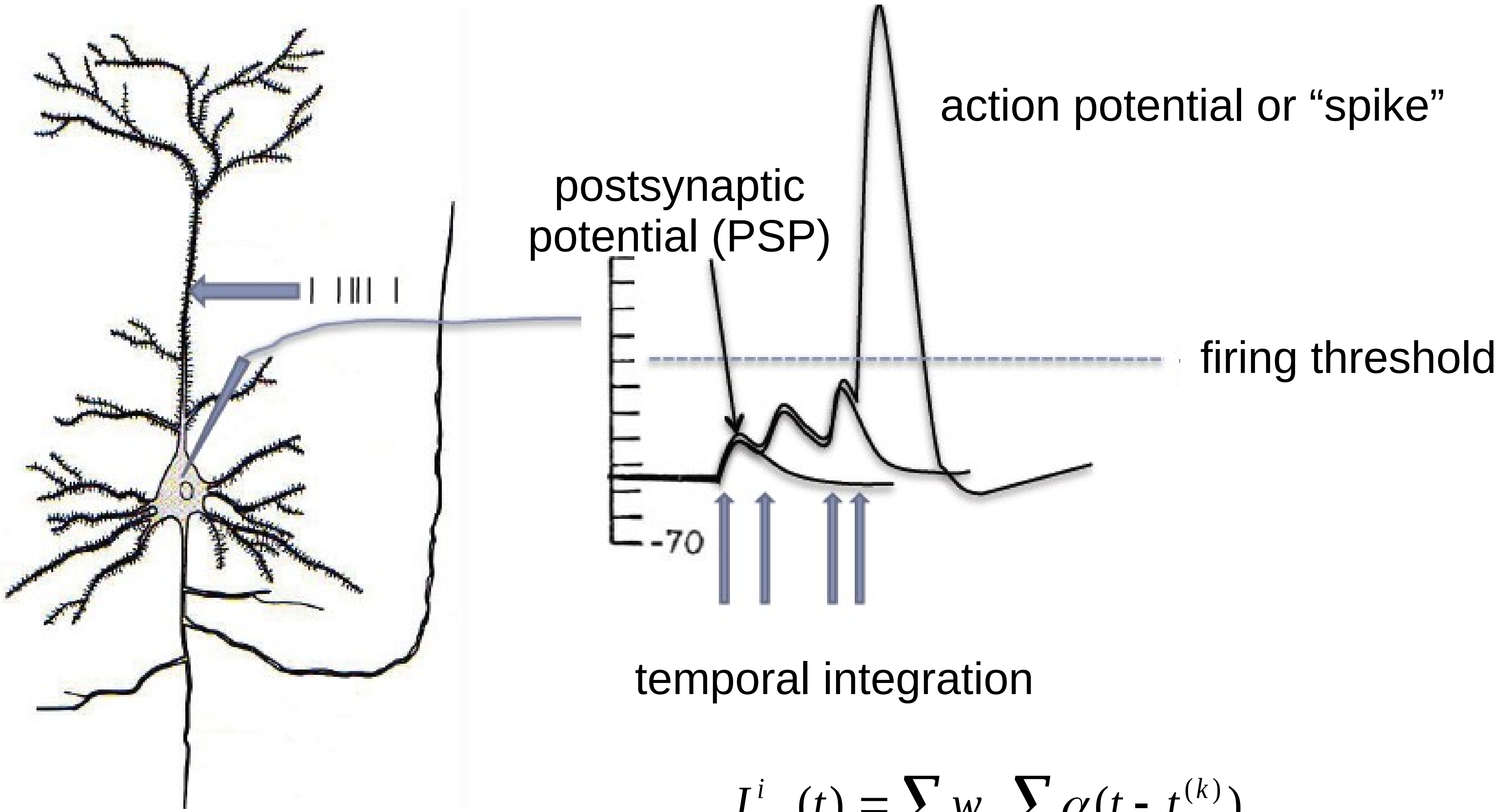
Synaptic current of one specific synapse (*ij*) :

$$I_s = G_{max}\,\Delta V\,\alpha(t) = w_{ij}\,\alpha(t)$$

Total synaptic current in neuron *i* at time *t* :

$$I^{i}_{syn}(t) = \sum_{j} w_{ij} \sum_{k} \alpha(t - t_j^{(k)})$$

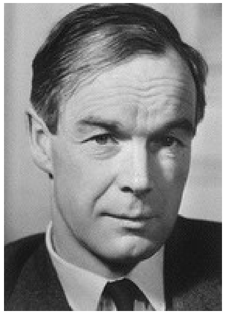
Neural integration



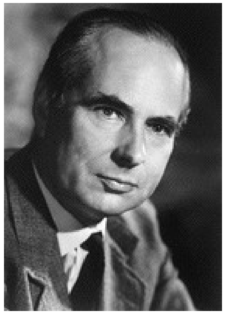
$$I_{syn}^{i}(t) = \sum_{j} w_{ij} \sum_{k} \alpha(t - t_j^{(k)})$$

Single neuron models

- **Hodgkin Huxley model** : description of ion channel dynamics (Hodgkin & Huxley, 1952)



Hodgkin



Huxley

- **integrate-and-fire model** : description of input integration membrane potential dynamics (LaPicque, 1907)

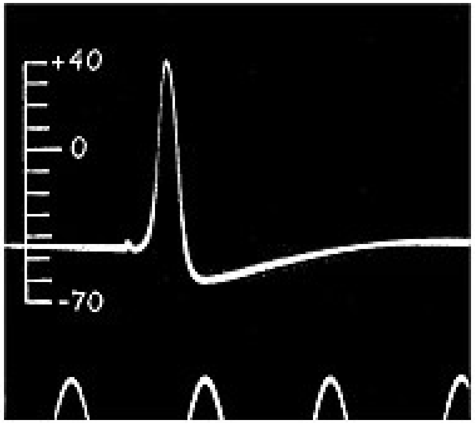
- **rate model** : description of the mean firing rate dynamics

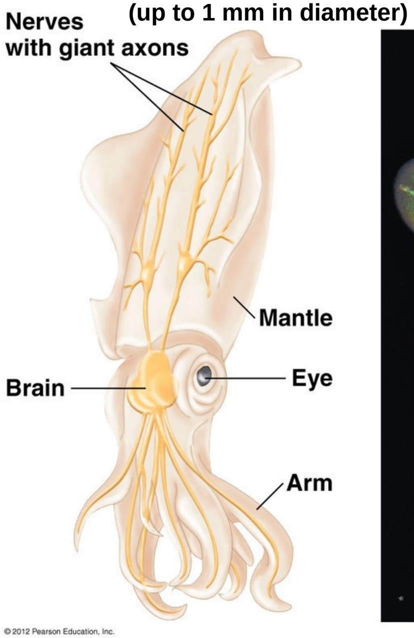
- **cable theory** : description of input propagation along the dendrites (Rall, 1962)

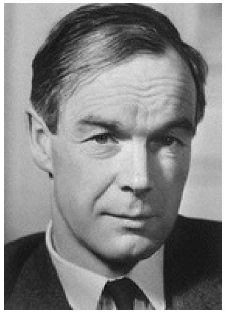
Wilfrid Rall

Significance of the Hodgkin-Huxley model

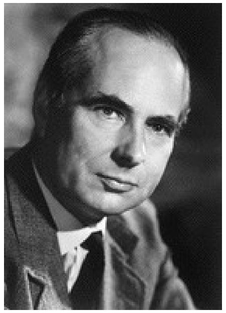
- Hodgkin and Huxley performed first intracellular recording of an action potential







Hodgkin

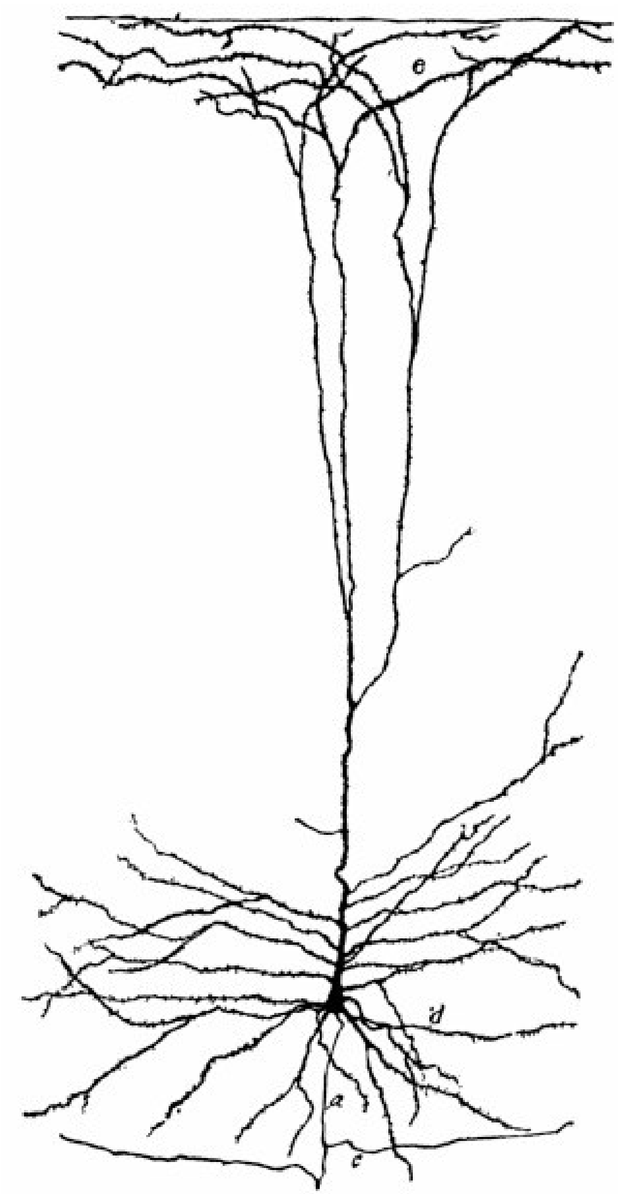


Huxley

- using voltage-clamp protocol : demonstrated that two independent currents are underlying action potential – sodium and potassium

- empirical representation of the experimental data in a quantitative model : the Hodgkin-Huxley model -> links the microscopic level of ion channels to the macroscopic level of currents and action potentials

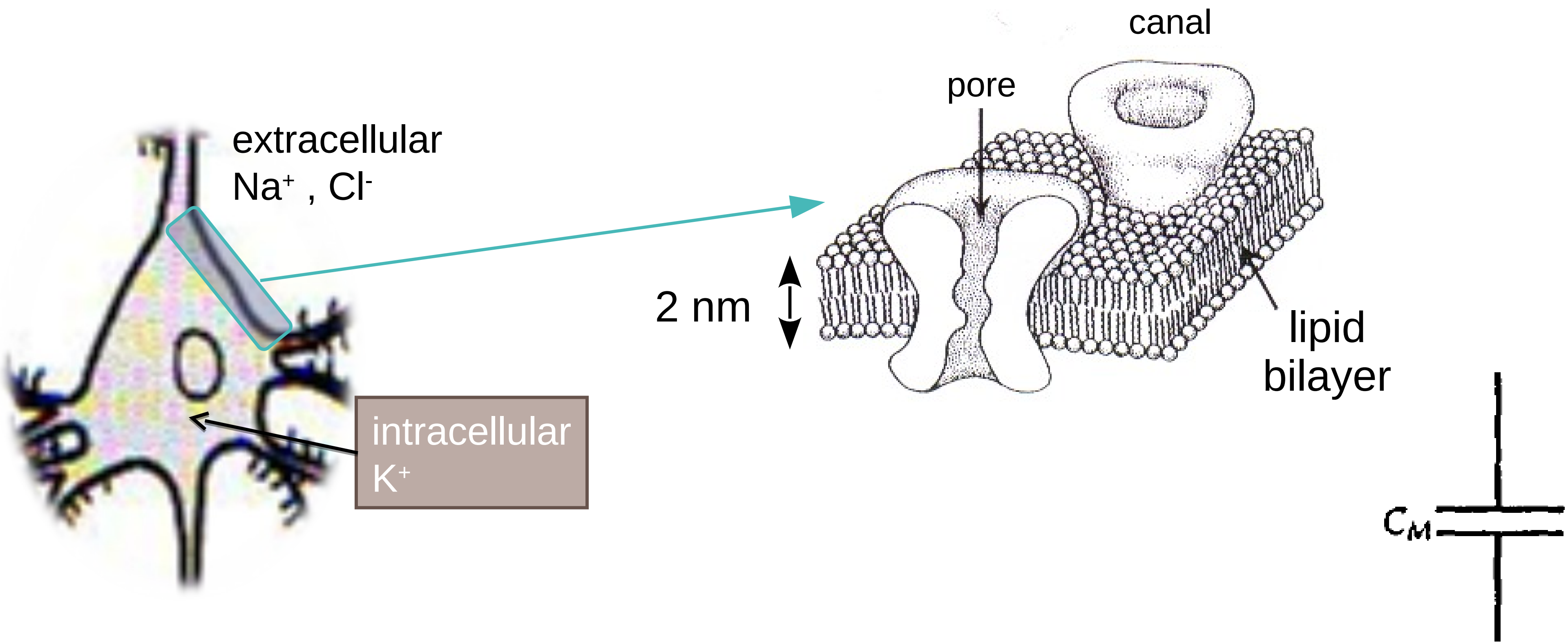
Simplified single neuron : single compartment model



$V(t)$

The membrane

- Lipid bilayer (= capacitance) with pores (channels = proteines)



specific capacitance 1 μF/cm²
total specific capacitance = specific capacitance * surface

Physics reminder

Ohm's law :

The current flowing through a resistor is directly proportional to the voltage drop across the resistor.

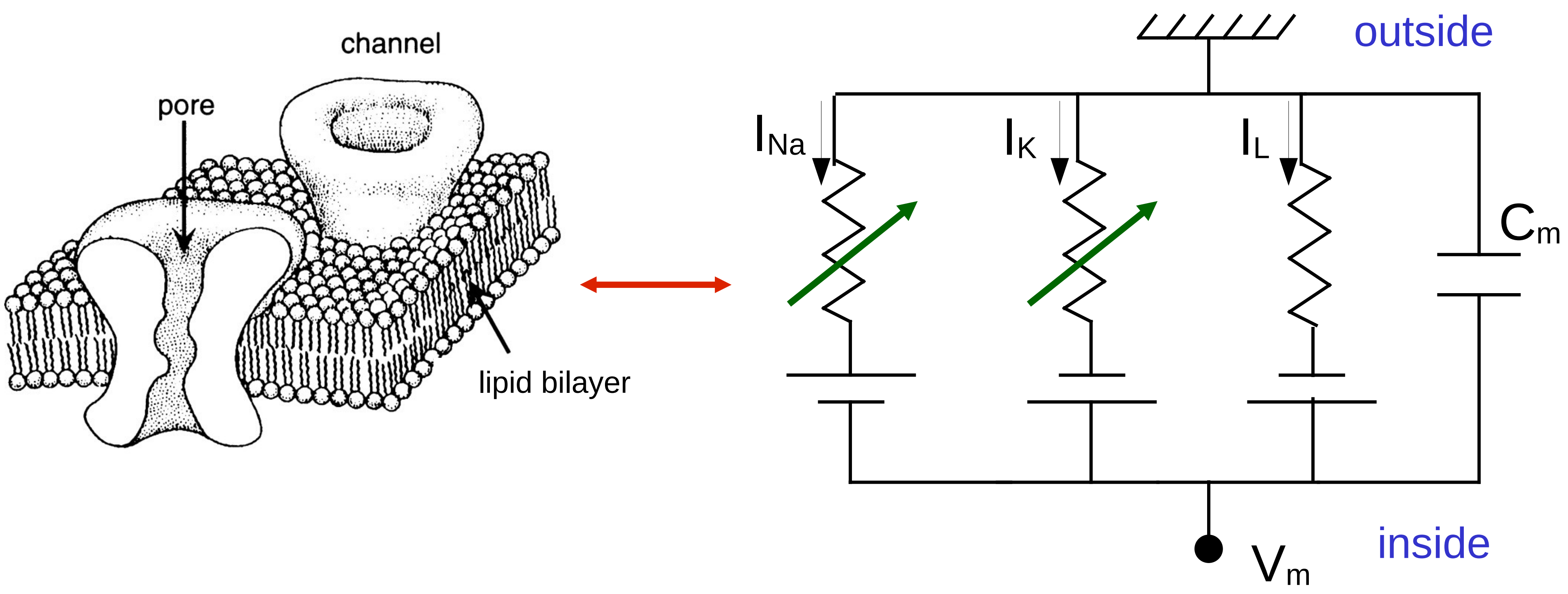
$$I = \frac{V}{R} \qquad R = \frac{1}{g}$$

Kirchoff's law :

The sum of currents flowing into a point is equal to the sum of currents flowing out of that point..

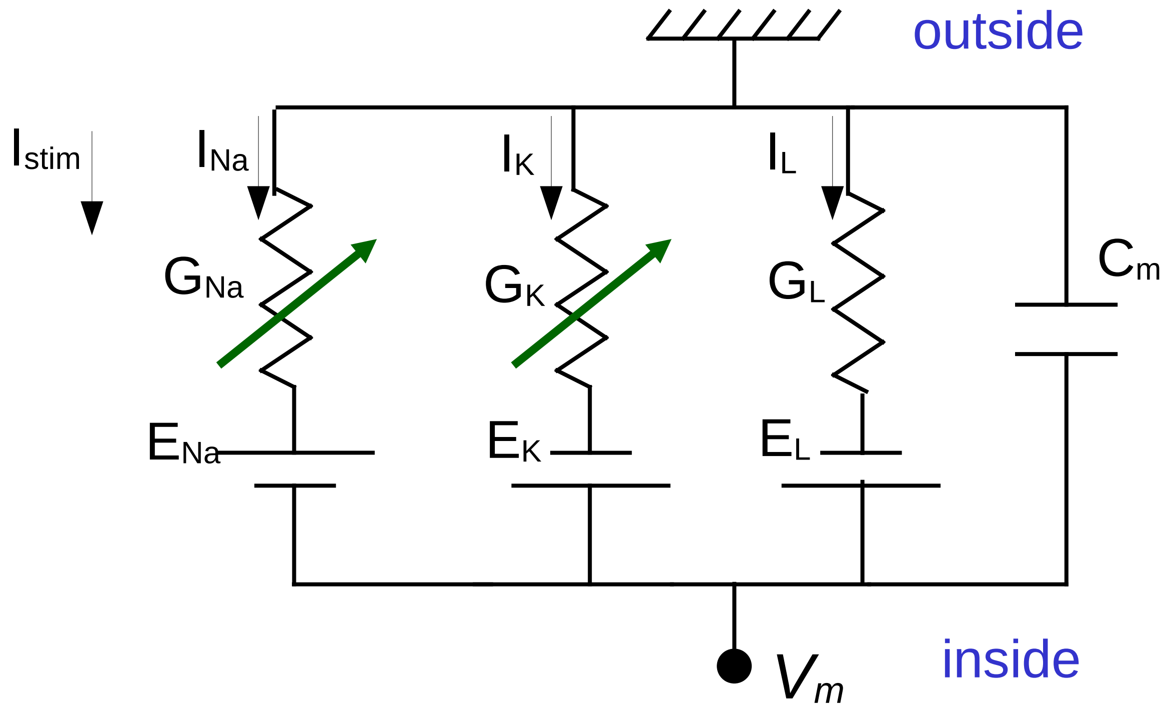
$$I_1 + I_2 + I_3 + \cdots = 0$$

Membrane properties : equivalent circuit



- The membrane potential V_m varies due to the opening/closing of different types of ion channels.
- **"Active membrane"** : Ion channel conductance varies with the membrane potential.

Hodgkin-Huxley model : membrane potential equation



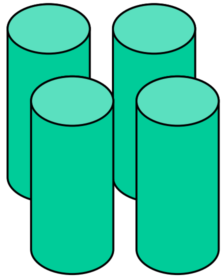
Kirchhoff's law : $$I_{stim} = I_{Na} + I_k + I_L + I_C$$

Ohm's law : $$R = \frac{\Delta V}{I} \rightarrow I = \frac{\Delta V}{R} = g(V_m - V_{rev})$$

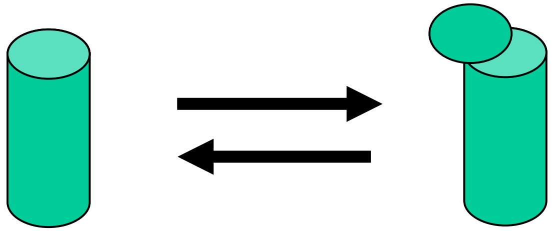
$$\rightarrow I_{stim} = g_{Na}(t)(V_m - V_{Na}) + g_K(t)(V_m - V_K) + g_L(V_m - V_L) + C\frac{dV_m}{dt}$$

Hodgkin-Huxley model : potassium channel

- 4 similar sub-units



- Each subunit can be « open » or « closed » :



- The channel is « open » if and only if all the sub-units are « open »

Hodgkin-Huxley model : potassium channel

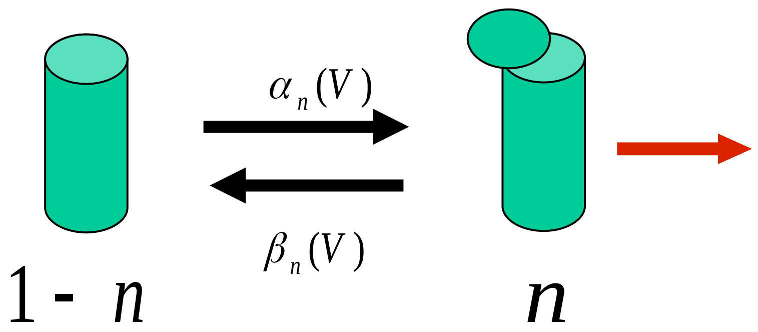
- probability that one sub-unit is « open » : $n(t)$
- probability that all sub-units are « open » : $n(t)^4$
- maximal K+ conductance, when all channels are open : $\bar{g}_K$
- K^+ conductance : $g_k = \bar{g}_K n(t)^4$

$$C\frac{dV}{dt} = g_{Na}(t)(V_{Na} - V) + g_K(t)(V_K - V) + g_L(V_L - V) + I_{stim}$$

$$\Downarrow$$

$$\boxed{C\frac{dV}{dt} = g_{Na}(t)(V_{Na} - V) + \bar{g}_K n(t)^4 (V_K - V) + g_L(V_L - V) + I_{stim}}$$

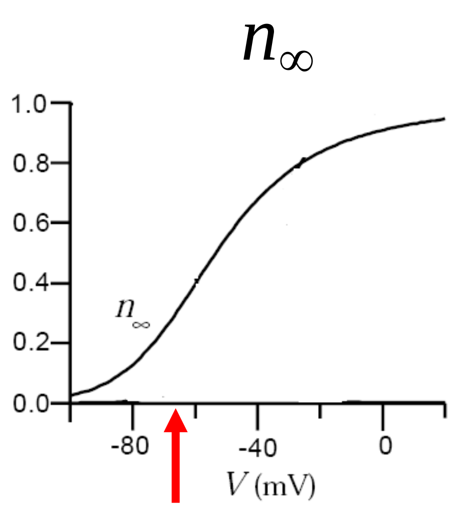
Hodgkin-Huxley model : potassium channel

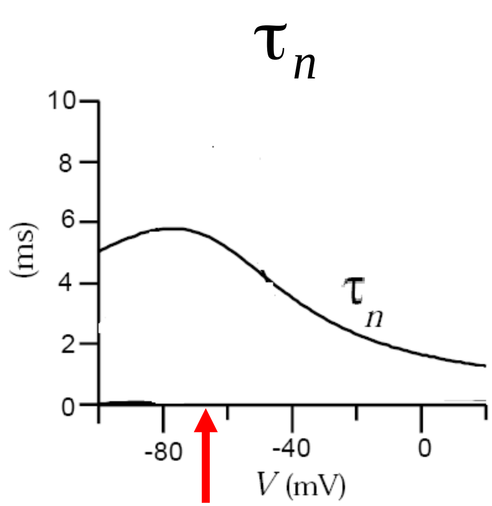


dynamics equation $\quad \tau_n \frac{dn}{dt} = -n + n_\infty$

time constant $\quad \tau_n = \frac{1}{\alpha_n + \beta_n}$

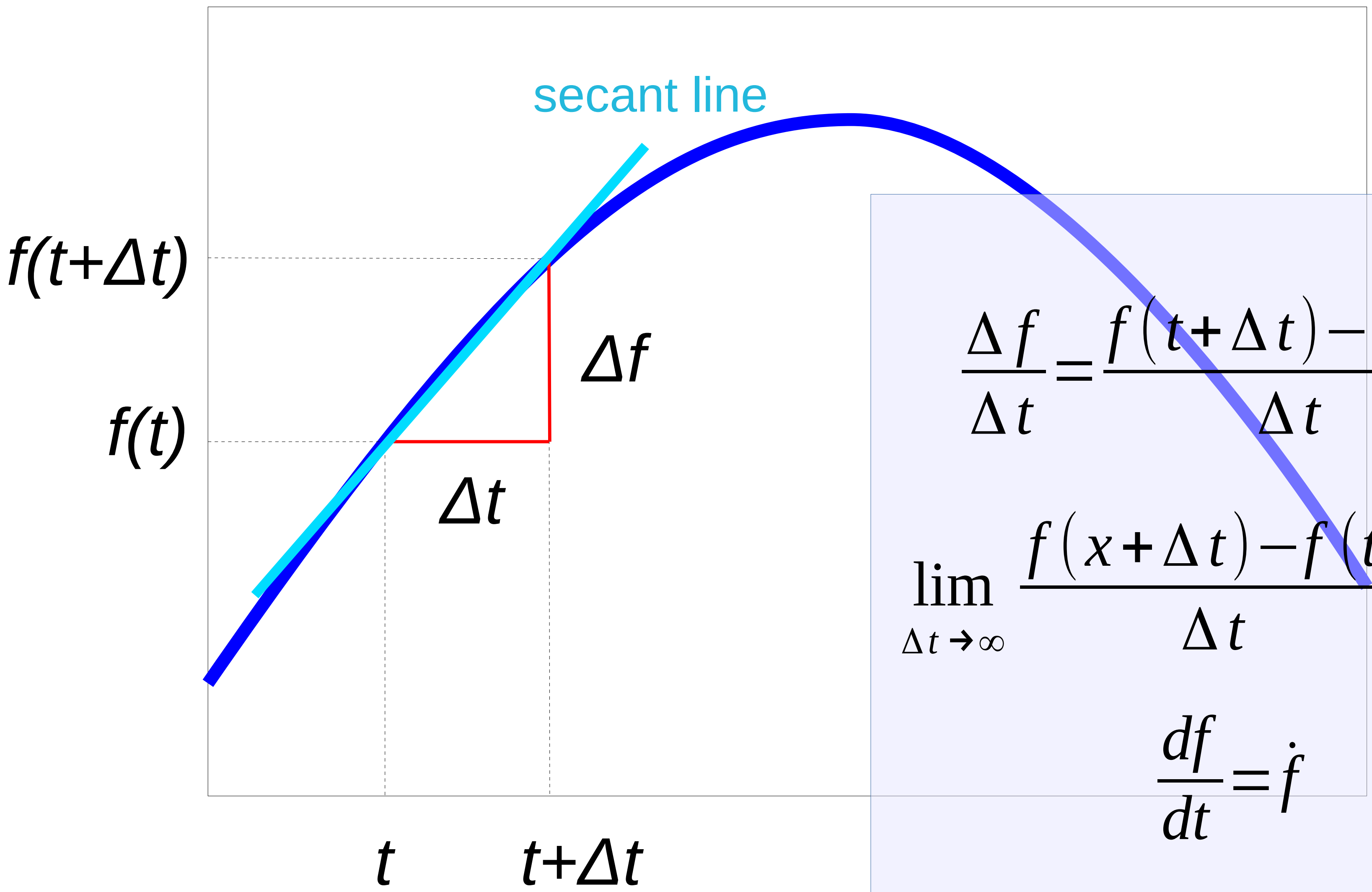
asymptotic value $\quad n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n}$





- The potassium channel is closed at resting potential.

Math reminder : difference quotient



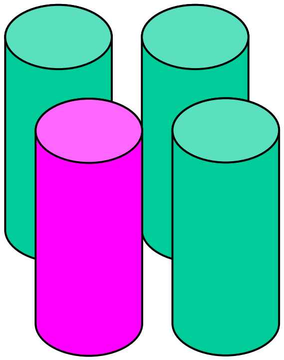
$$\frac{\Delta f}{\Delta t} = \frac{f\left(t + \Delta t\right) - f\left(t\right)}{\Delta t}$$

$$\lim_{\Delta t \to \infty} \frac{f\left(x + \Delta t\right) - f\left(t\right)}{\Delta t} = \frac{df}{dt}$$

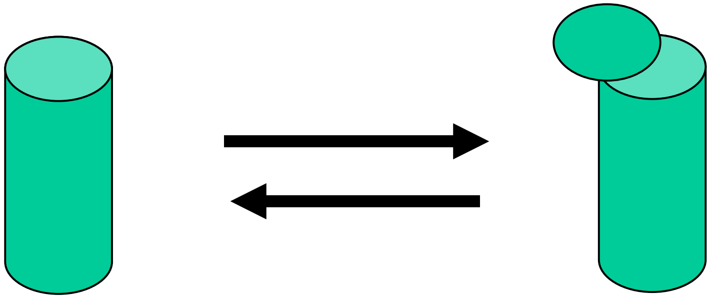
$$\frac{df}{dt} = \dot{f}$$

Hodgkin-Huxley model : sodium channel

- The sodium channel has 3 similar « fast » esub-units and 1 « slow » subunit



- Each sub-unit can be « open » or « closed »



➔ The channel is « open » if and only if all the sub-units are « open »

Hodgkin-Huxley model : sodium channel

- Probability that the « fast « sub-unit is « open » : m
- Probability that the « slow » sub-unit is « open » : h
- Probability that the channel is « open » : $m^3 h$
- Maximal Na+ condutance, when all channels are open : $\bar{g}_{Na}$
- Na+ conductance : $g_{Na} = \bar{g}_{Na} m^3 h$

$$C \frac{dV}{dt} = g_{Na}(V_{Na} - V) + g_K(V_K - V) + g_L(V_L - V) + I_{ext}$$

$$\boxed{C \frac{dV}{dt} = \bar{g}_{Na} m^3 h \left(V_{Na} - V\right) + \bar{g}_K n^4 \left(V_K - V\right) + g_L \left(V_L - V\right) + I_{stim}}$$

Hodgkin-Huxley model : sodium channel

dynamics of the of the fast sub-unit

$$\tau_m \frac{dm}{dt} = -m + m_\infty$$

$$\tau_m = \frac{1}{\alpha_m + \beta_m}$$

$$m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m}$$

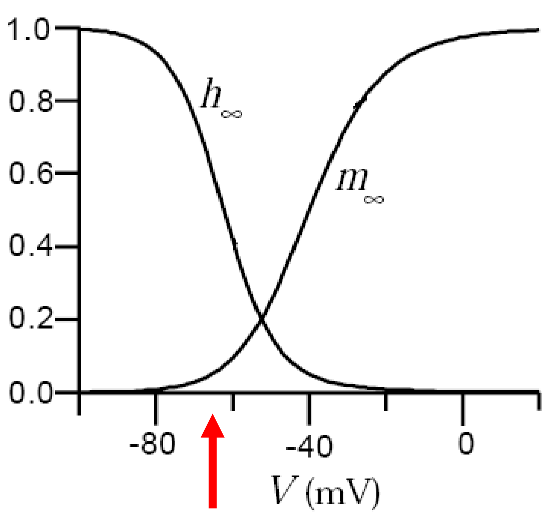
dynamics of the slow sub-unit :

$$\tau_h \frac{dh}{dt} = -h + h_\infty$$

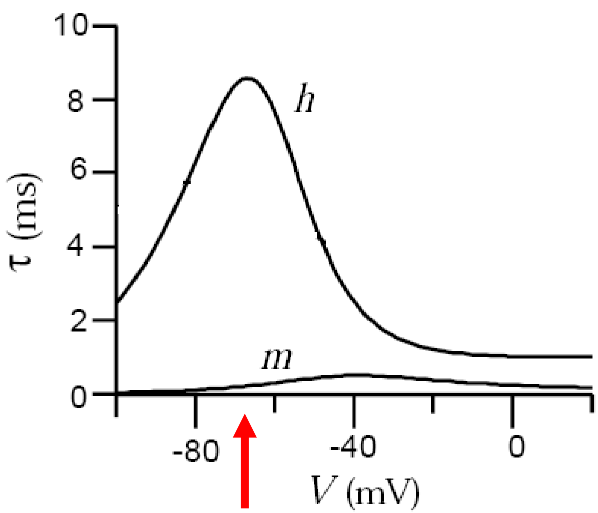
$$\tau_h = \frac{1}{\alpha_h + \beta_h}$$

$$h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h}$$

asymptotic values



time constants



- The fast sub-unit is closed at resting potential.
- The slow sub-unit is open at resting potential.
- The sodium channel is closed at resting potential.

Complete equations of the Hodgkin-Huxley model

$$\boxed{C\frac{dV}{dt}=\bar{g}_{Na}m^3h\left(V_{Na}-V\right)+\bar{g}_K n^4\left(V_K-V\right)+g_L\left(V_L-V\right)+I_{stim}}$$

$$\tau_n\frac{dn}{dt}=-n+n_\infty\ ,\tau_n=\frac{1}{\alpha_n+\beta_n},n_\infty=\frac{\alpha_n}{\alpha_n+\beta_n}$$

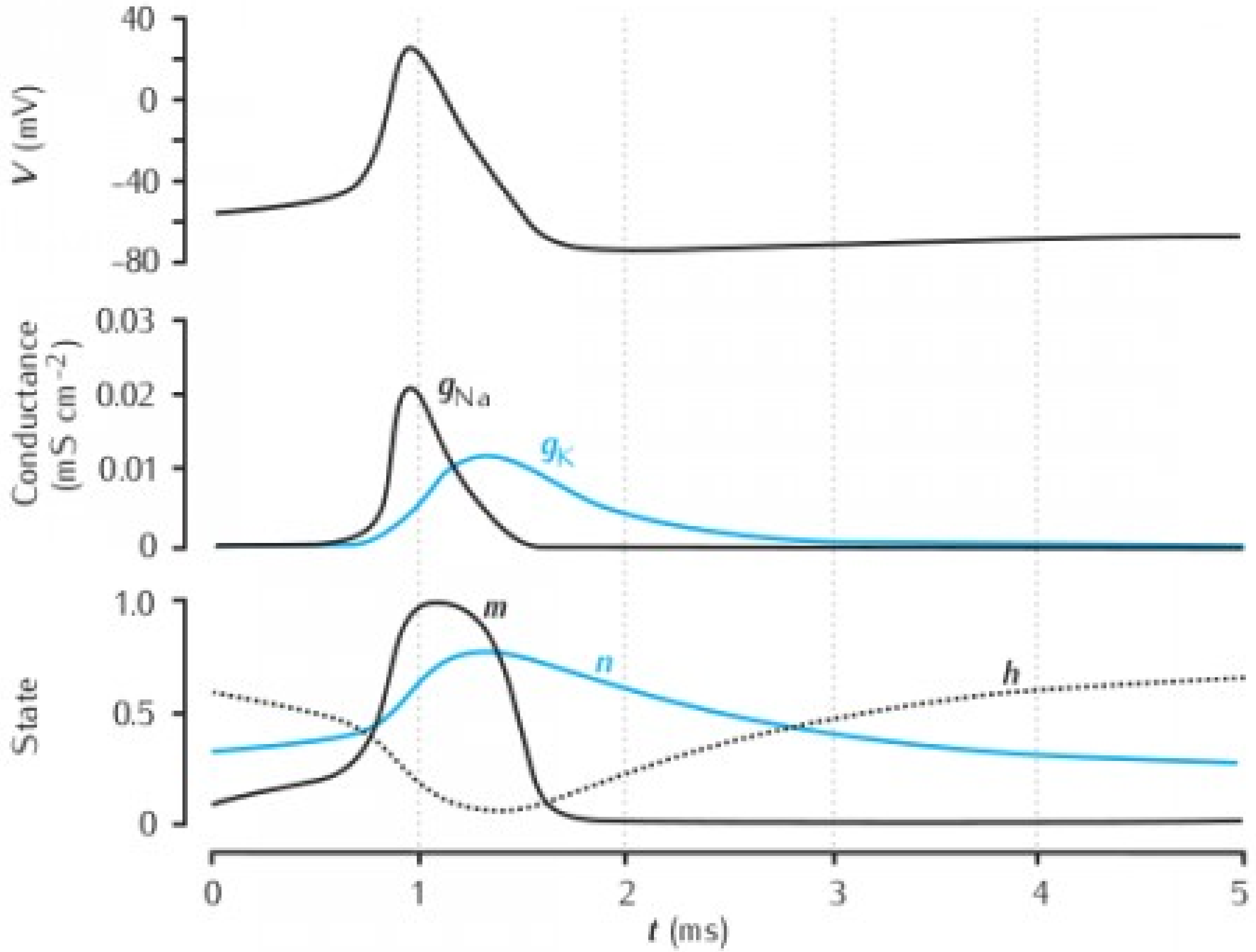
$$\tau_m\frac{dm}{dt}=-m+m_\infty\ ,\tau_m=\frac{1}{\alpha_m+\beta_m},m_\infty=\frac{\alpha_m}{\alpha_m+\beta_m}$$

$$\tau_h\frac{dh}{dt}=-h+h_\infty\ ,\tau_h=\frac{1}{\alpha_h+\beta_h},h_\infty=\frac{\alpha_h}{\alpha_h+\beta_h}$$

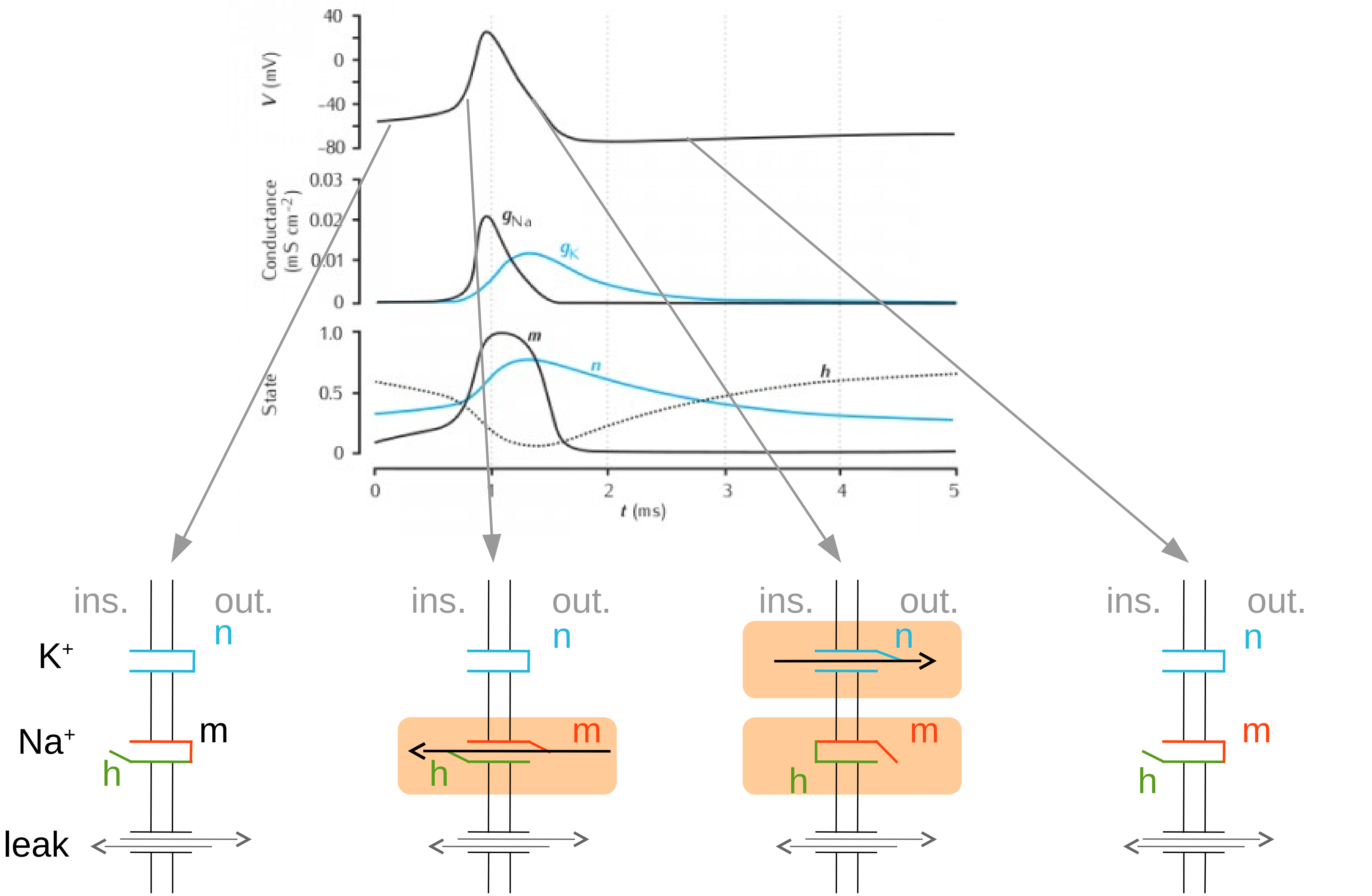
$$\alpha_n(V)=\frac{(0.1-0.01V)}{e^{1-0.1V}-1}\qquad \alpha_m(V)=\frac{(2.5-0.1V)}{e^{2.5-0.1V}-1}\qquad \alpha_h(V)=0.07\,e^{-\frac{V}{20}}$$

$$\beta_n(V)=0.125e^{-\frac{V}{80}}\qquad \beta_m(V)=4e^{-\frac{V}{18}}\qquad \beta_h(V)=\frac{1}{e^{3-0.1V}+1}$$

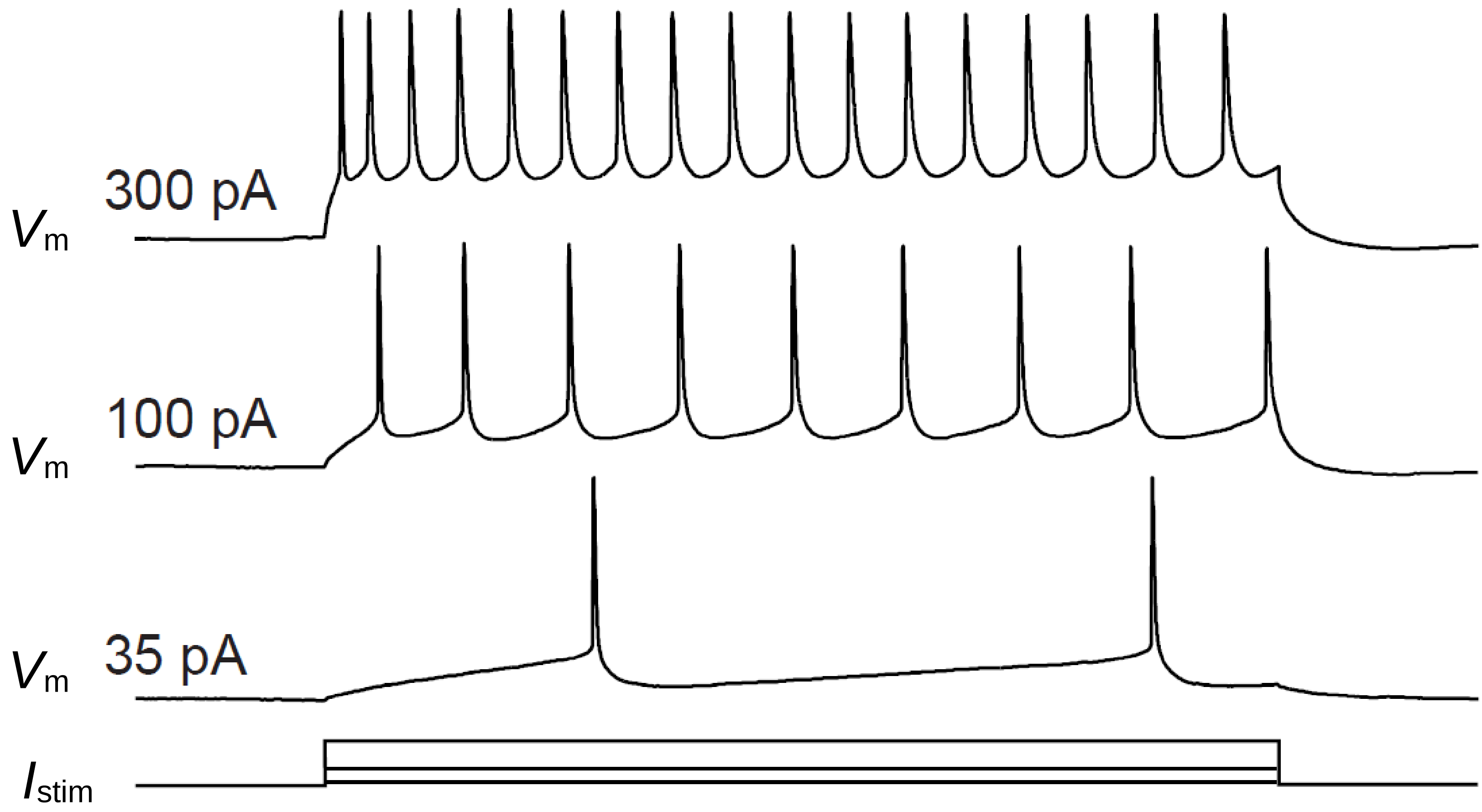
Hodgkin-Huxley model : the action potential



Hodgkin-Huxley model : the action potential

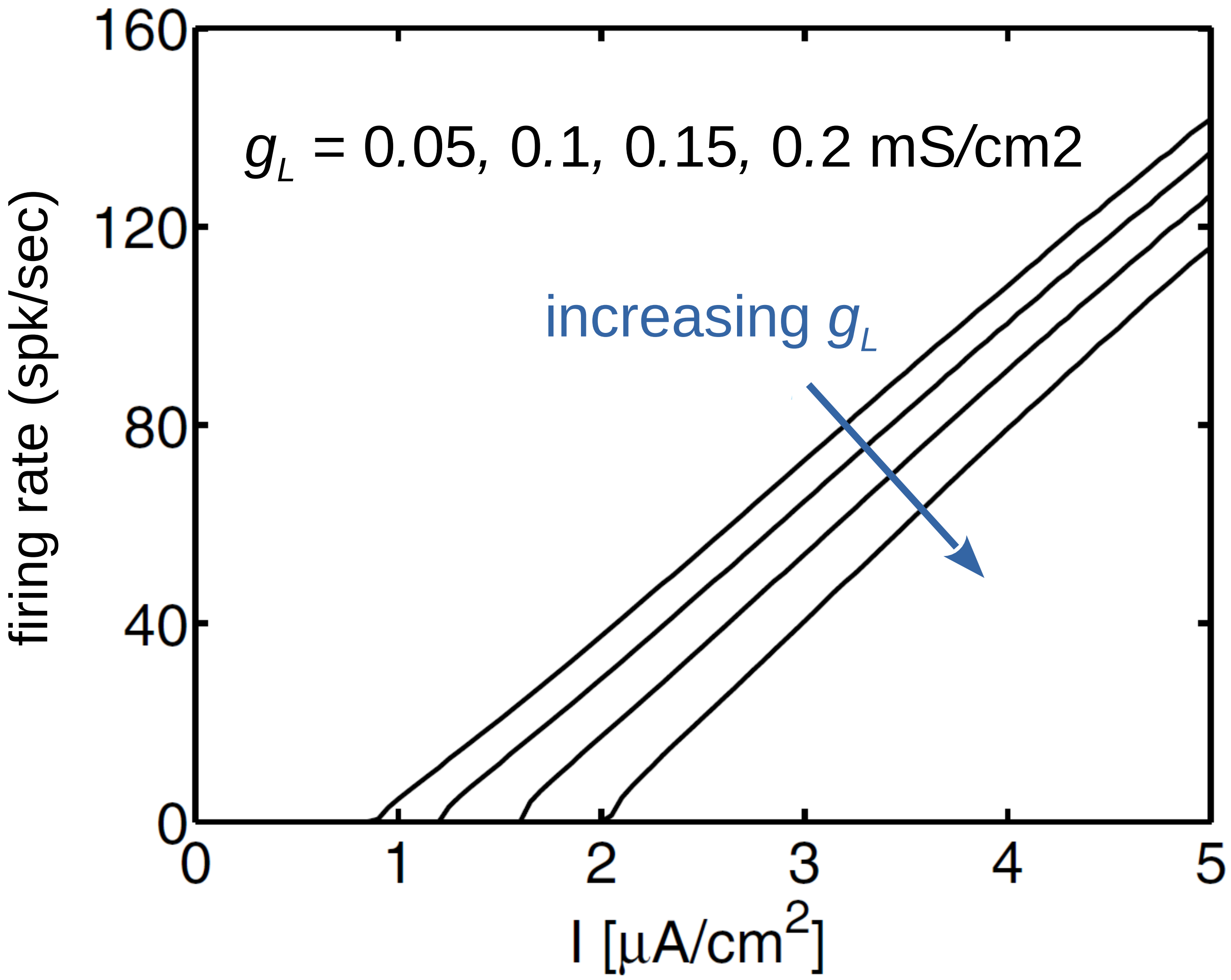


Hodgkin-Huxley model : current injection

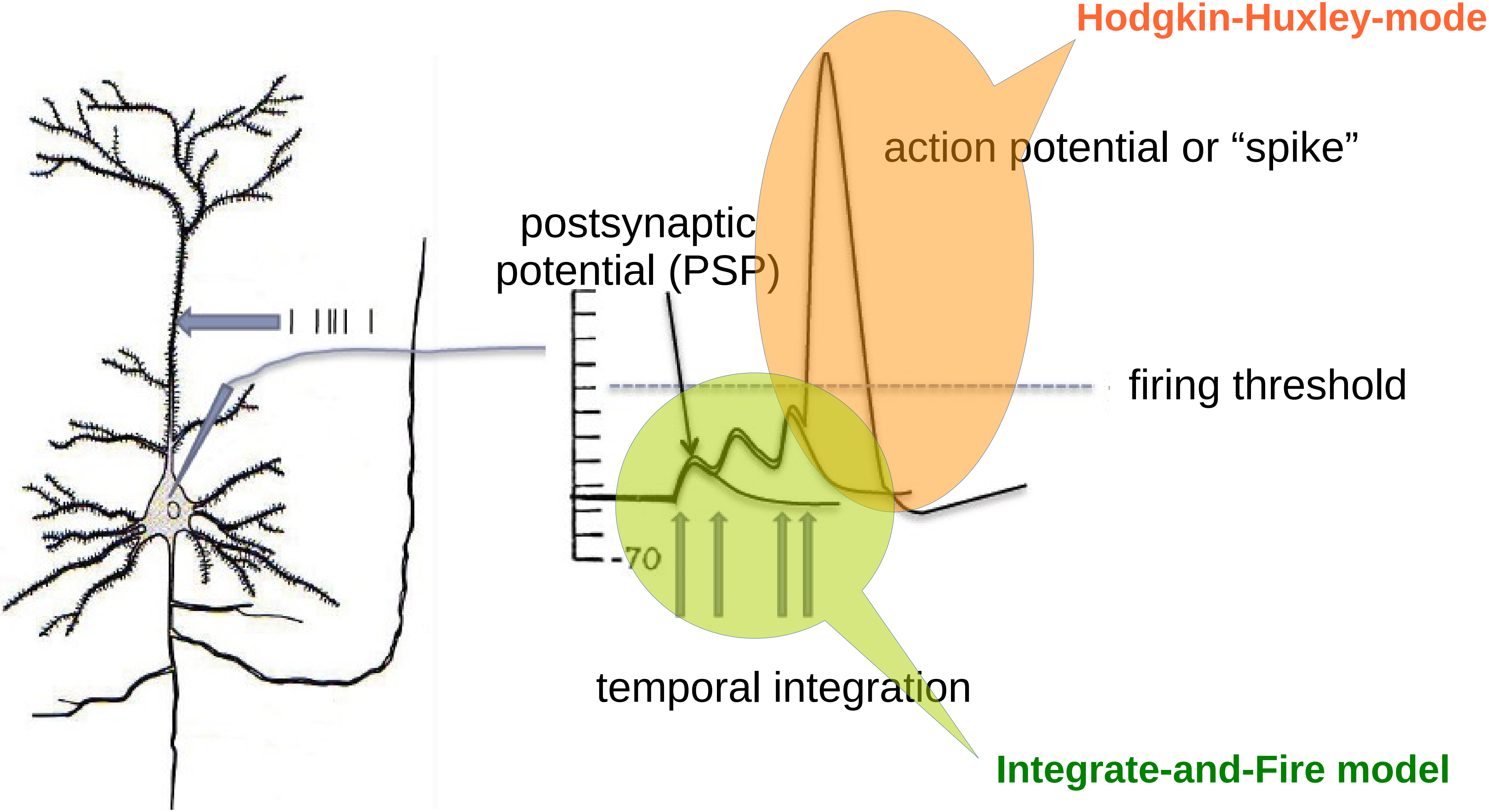


Hodgkin-Huxley model : F-I curve

Example : study the role of the membrane permeability (conductance g_L) on action potential output



Neural integration



Integrate-and-Fire model : derivation

simplification : no active currents → $g(t) = const.$

→ The shape of the action potential is not described !

$$C\frac{dV}{dt} = g_{Na}(V_{Na} - V) + g_K(V_K - V) + g_L(V_L - V) + I_{stim}$$

$$C\frac{dV}{dt} = \underbrace{g_{Na}V_{Na} + g_K V_K + g_L V_L}_{} - (\underbrace{g_{Na} + g_K + g_L}_{G_{tot}})V + I_{stim}$$

$$C\frac{dV}{dt} = G_{tot}(V_0 - V) + I_{stim}$$

$$\tau = \frac{C}{G_{tot}}$$

$$\boxed{\tau\frac{dV}{dt} = (V_0 - V) + \frac{I_{stim}}{G_{tot}}}$$

Integrate-and-Fire model : membrane potential equation

$$\boxed{\tau \frac{dV}{dt} = \left(V_0 - V\right) + \frac{I_{ext}}{G_{tot}}}$$

- V_0 resting membrane potential
- τ membrane time constant
- I_{ext} external current (synaptic)
- G_{tot} total conductance

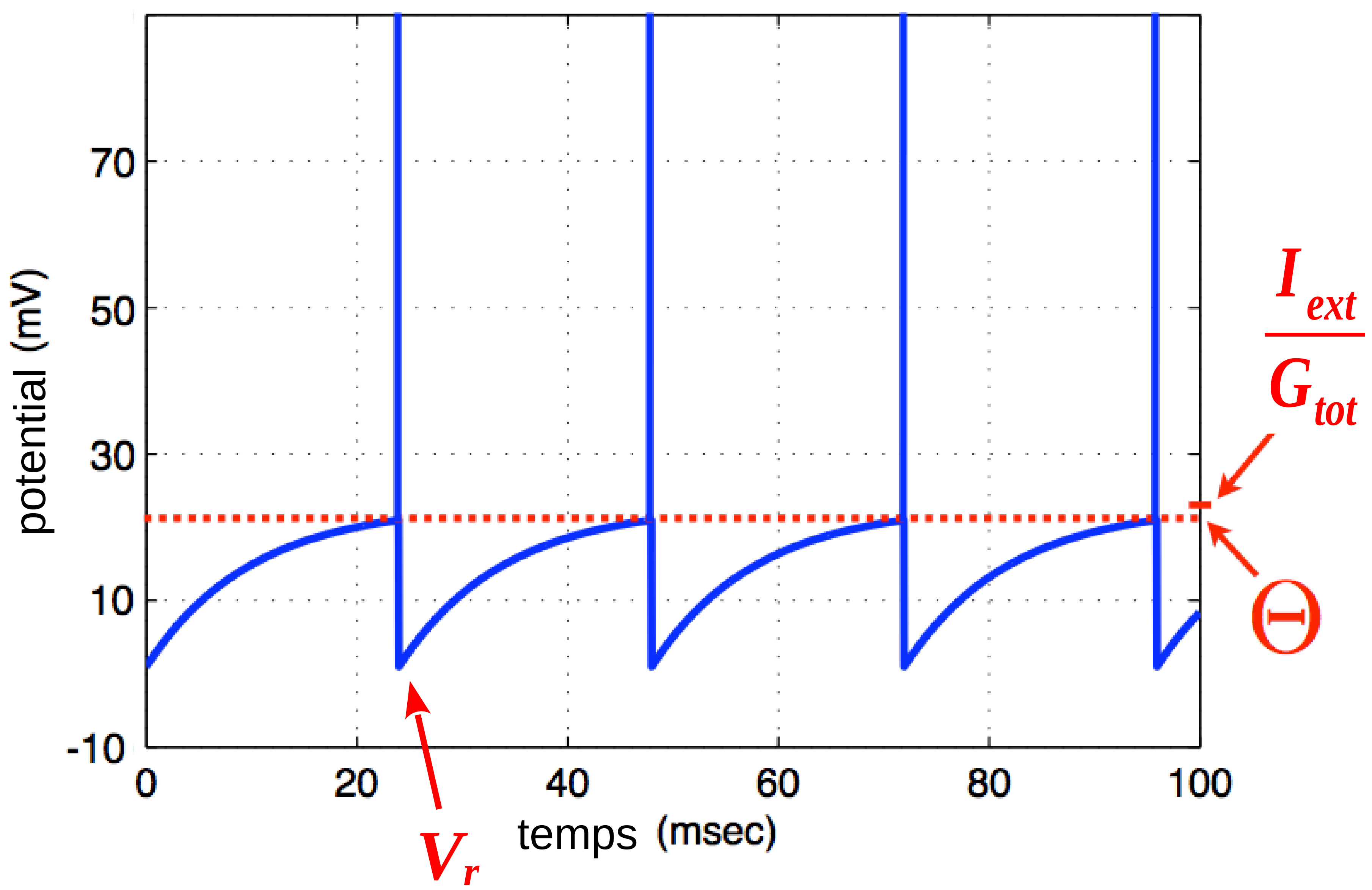
generation of the action potential :

- Θ firing threshold
- V_r reset potential
- if $V > \Theta$:

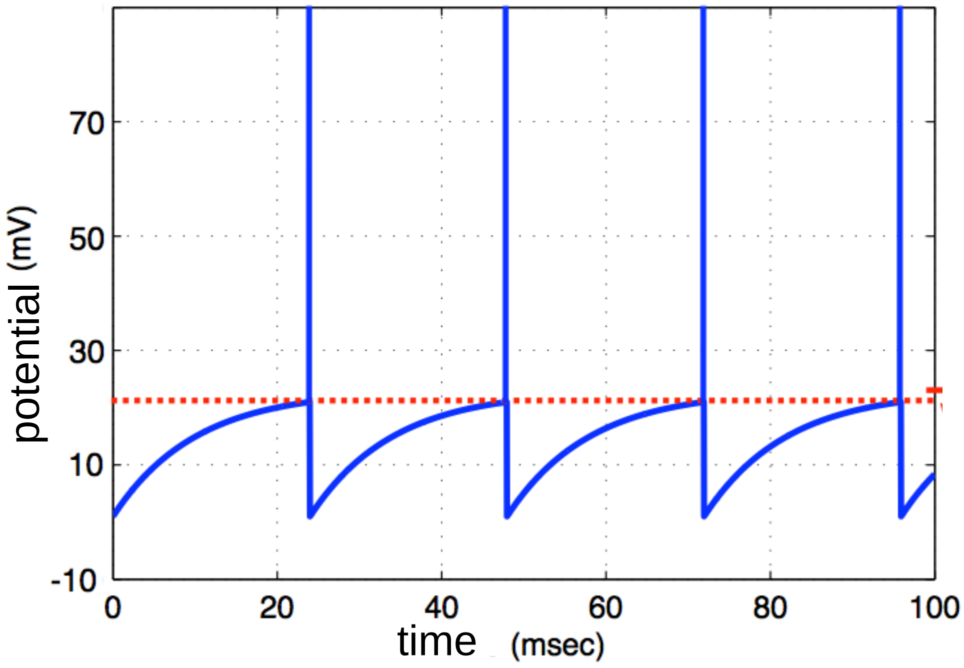
  → the neuron fires an action potential

  → after the action potential, the membrane potential is reset to V_r

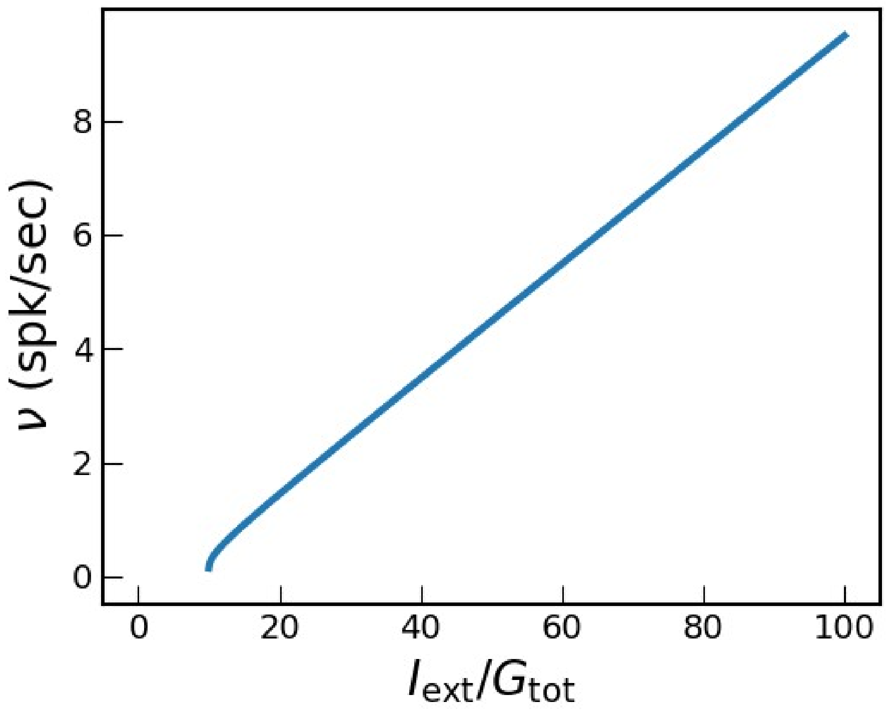
Integrate-and-Fire model : dynamics



Integrate-and-Fire model : dynamics

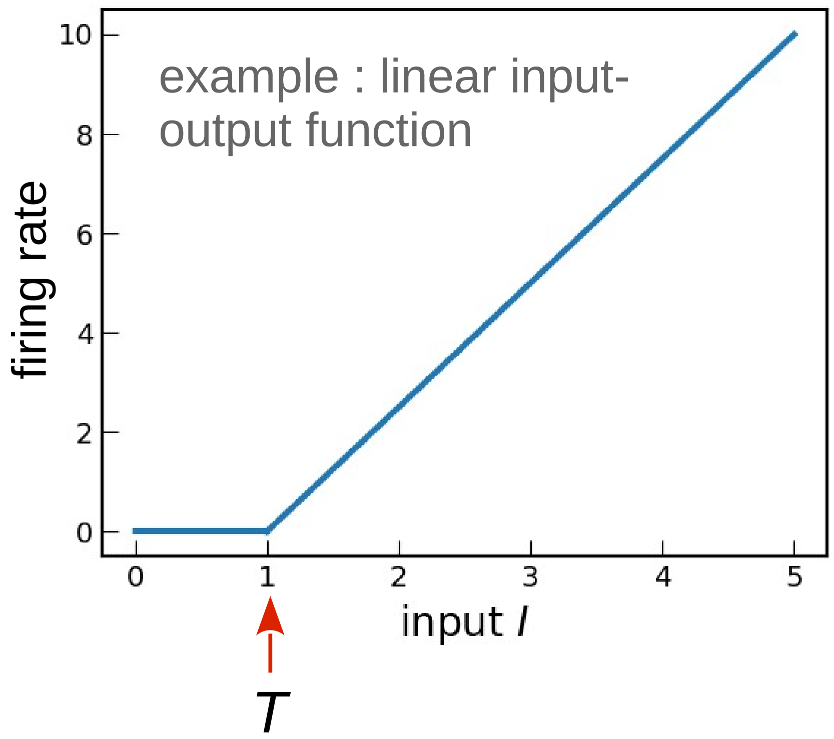


F-I curve



Rate neuron model

Phenomenological description of the input-output function :



$$\boxed{\tau \frac{dm}{dt} = -m + F(I_{syn} + I_{ext} - T)}$$

m: output of the neuron – firing rate

τ : membrane time constant

F : input-output transfer function

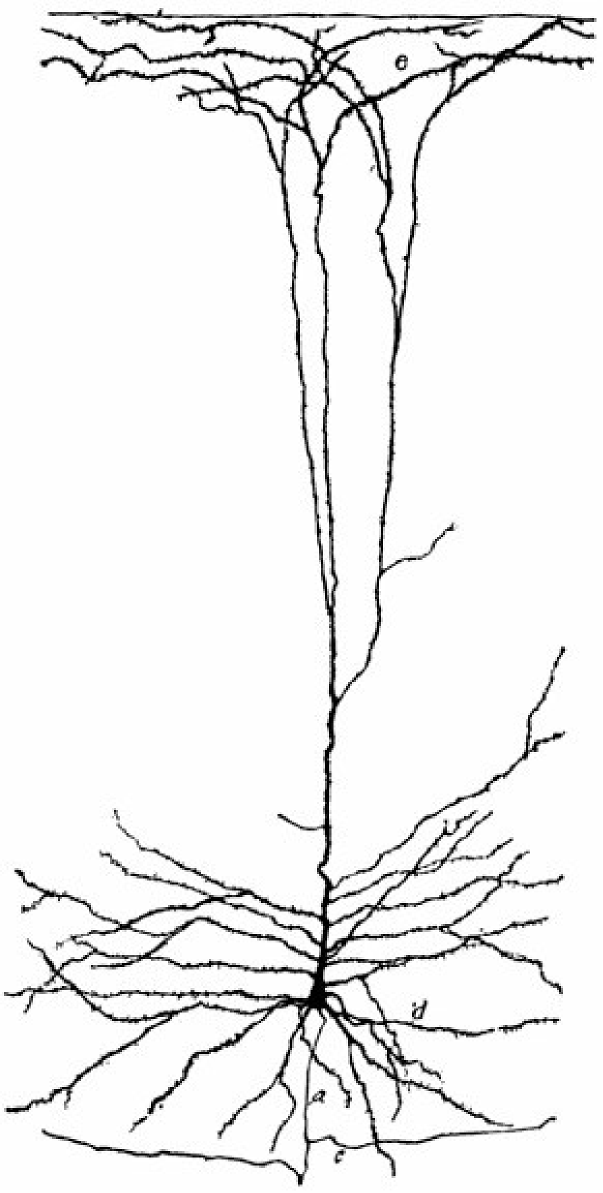
$\boldsymbol{I_{syn}}$: synaptic input

$\boldsymbol{I_{ext}}$: external current

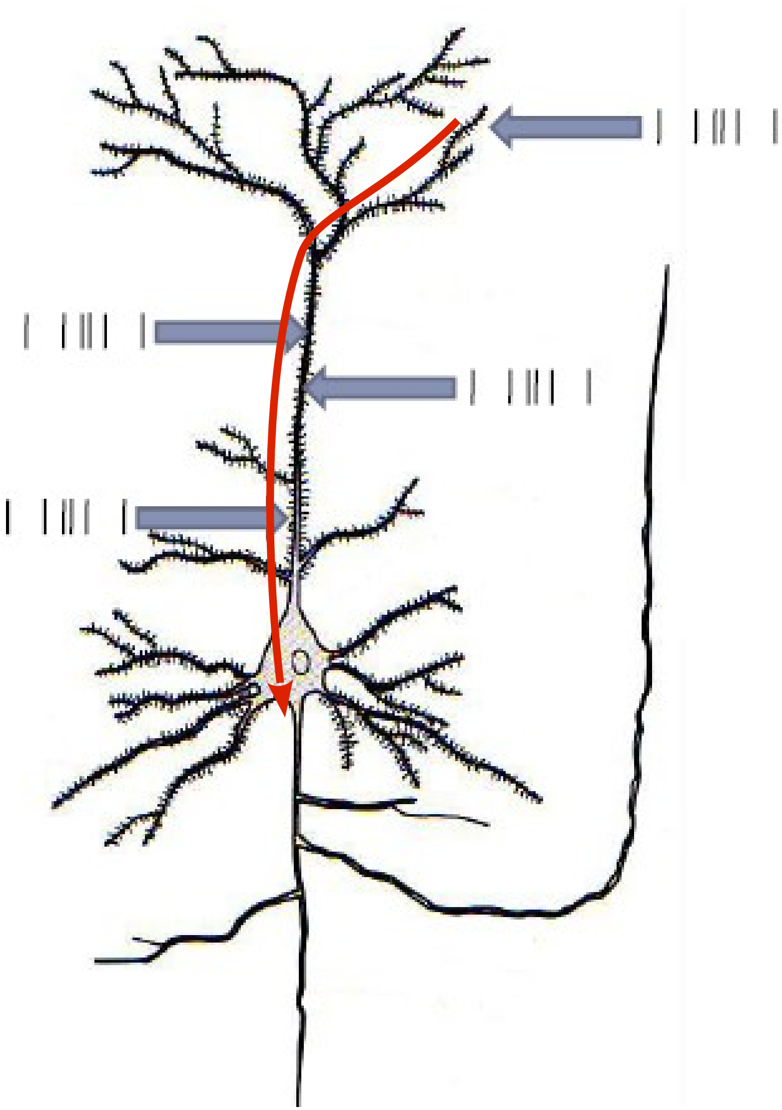
T : firing threshold

How do potentials propagate along the dendritic tree ?

$V(t)$

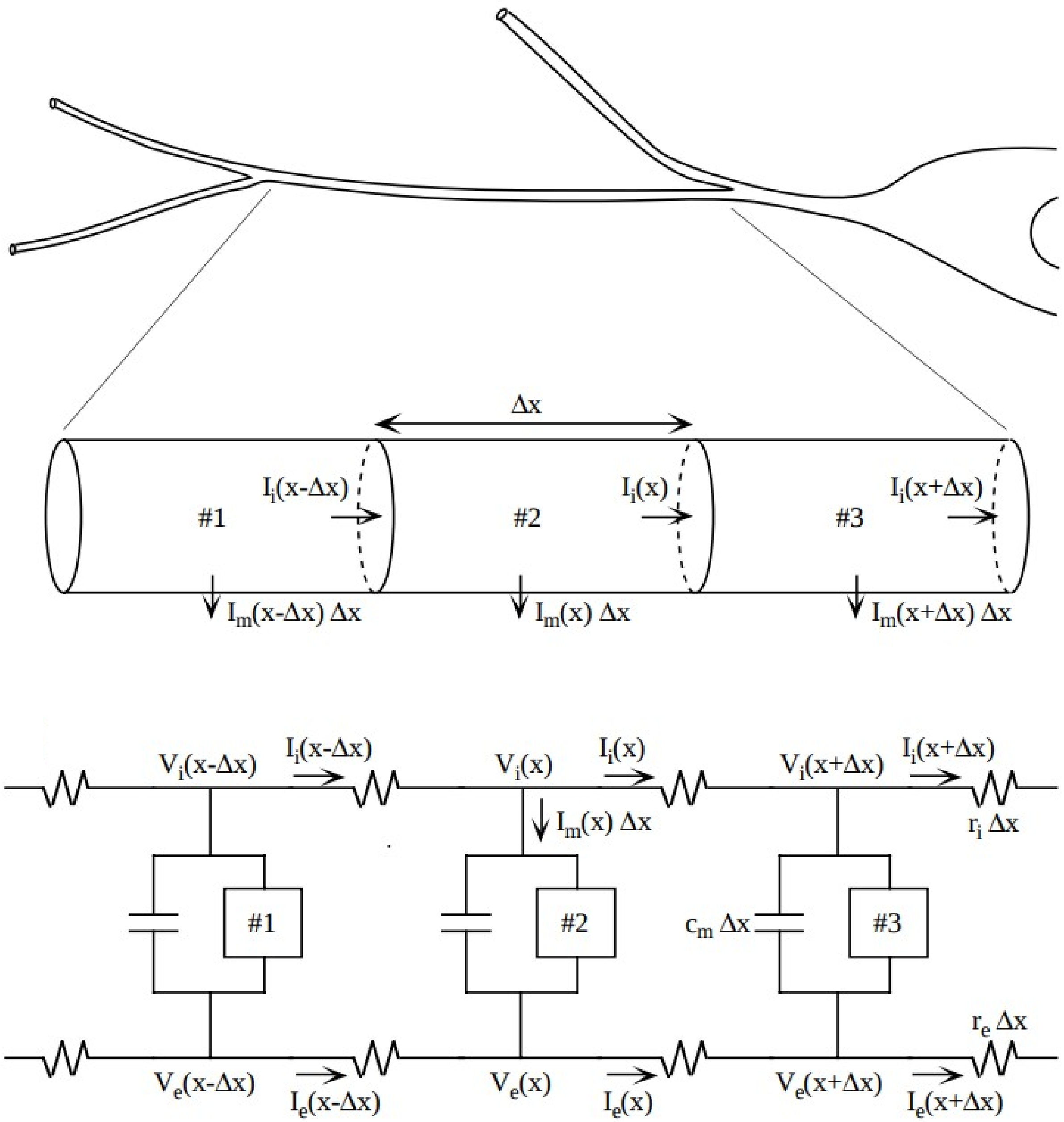


Cable theory



- how do synaptic inputs propagate to the soma or the axon initial segment
- how do input interact between each other
- how does the input location along the dendritic tree impact its functional importance for the neuron

Abstraction of the dendritic membrane of a neuron



Soma and dendritic branch

Portion of the secondary dendrite divided in three sub-cylinders

Discrete electric model of the three sub-cylinders

Non-linear cable equation

models the membrane potential distribution along a membrane cylinder

$V(t) \longrightarrow V(x,t)$

$$\boxed{\underbrace{\frac{1}{r_i+r_e}\frac{\partial V}{\partial x^2}}_{\text{current which propagates between neighboring points along the cylinder}}=\underbrace{c_m\frac{\partial V}{\partial t}+I_{ion}}_{\text{typical membrane potential equation of the point neuron model}}}$$

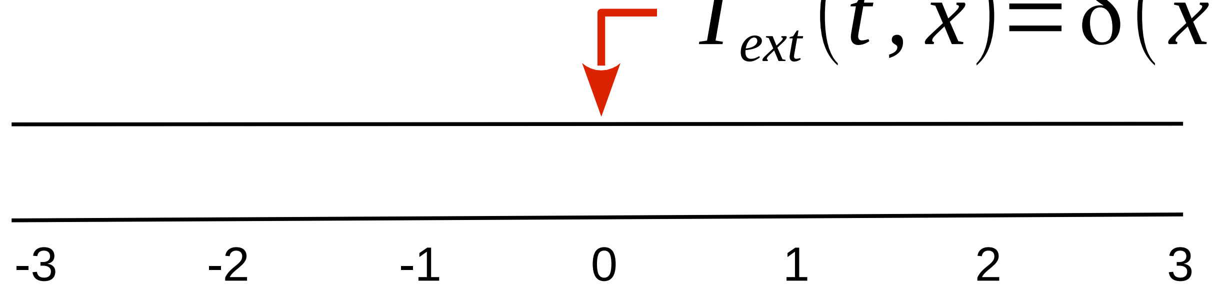
current which propagates between neighboring points along the cylinder

typical membrane potential equation of the point neuron model

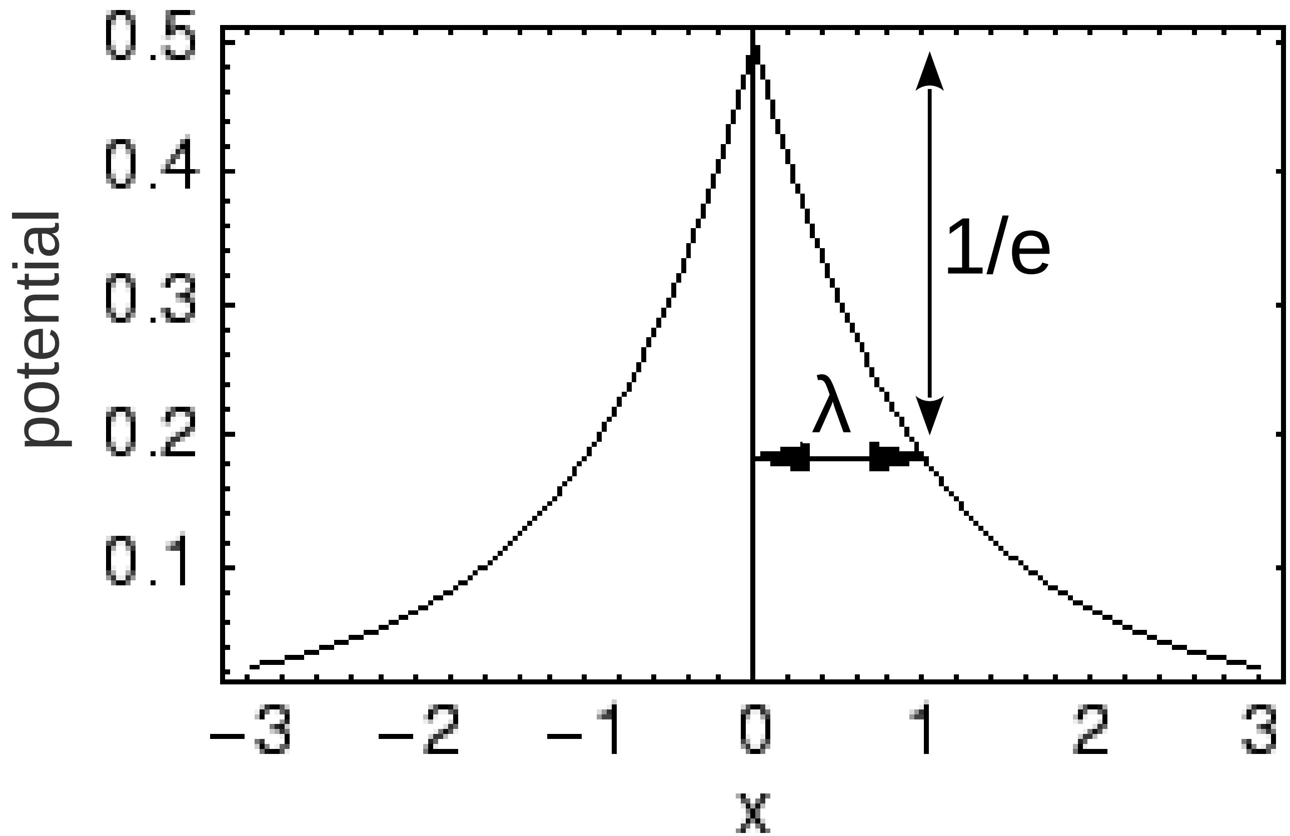
[2^{nd} order partial differential equation]

Stationary solution of the cable equation

$$I_{ext}(t,x)=\delta(x)$$

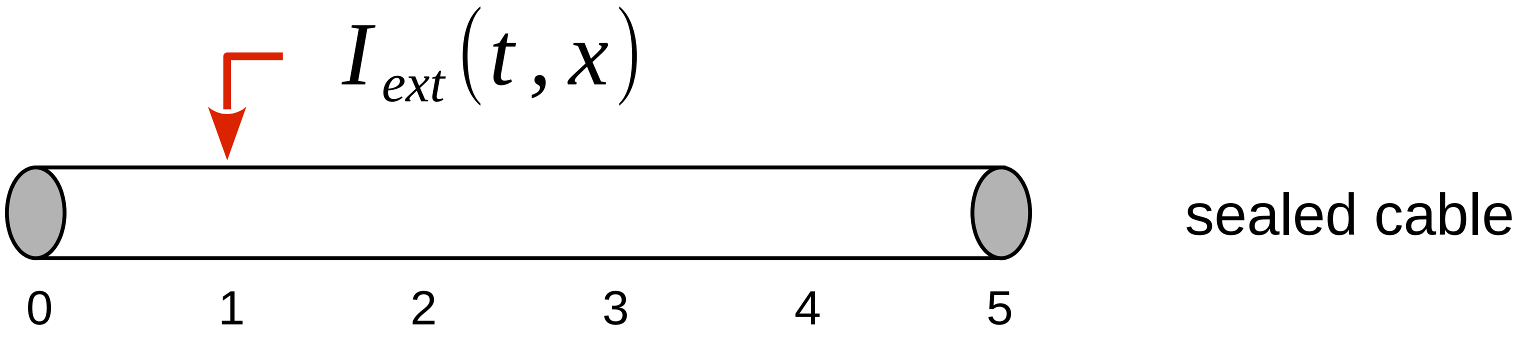


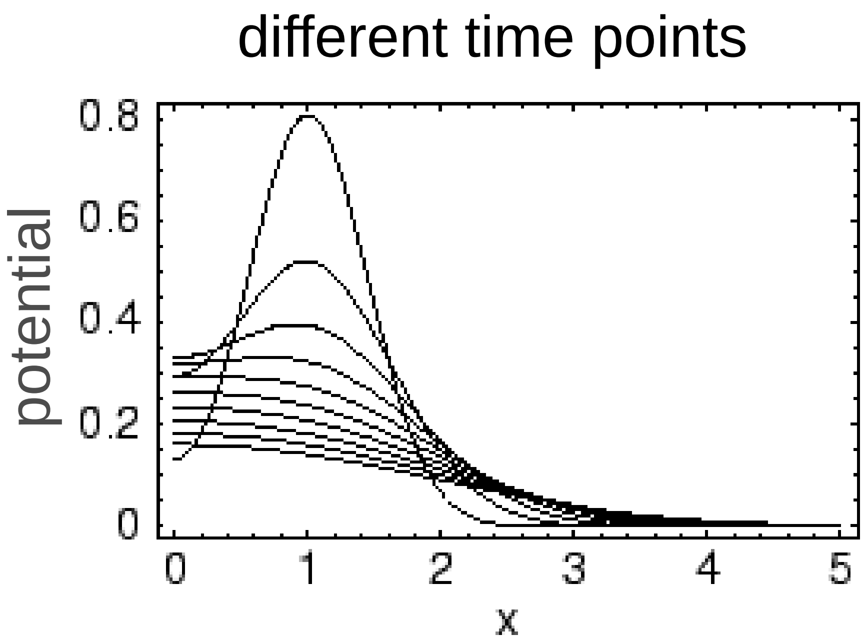
infinite cable
(open ends)



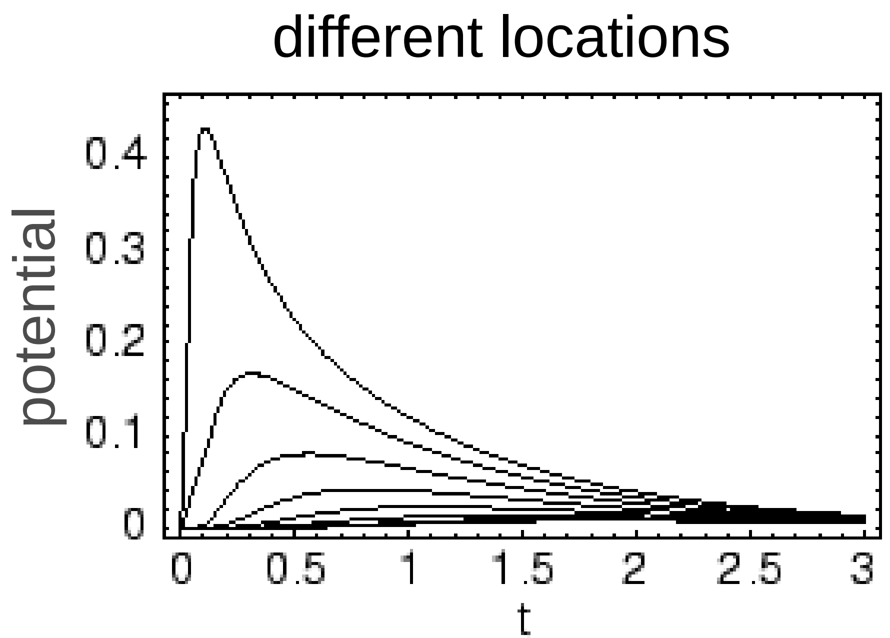
λ electrotonic
length constant

Spatial and temporal distribution of the potential along the membrane





t = 0.1, 0.2, ... , 1.0



x = 1.5, 2.0, 2.5, ... , 5.0

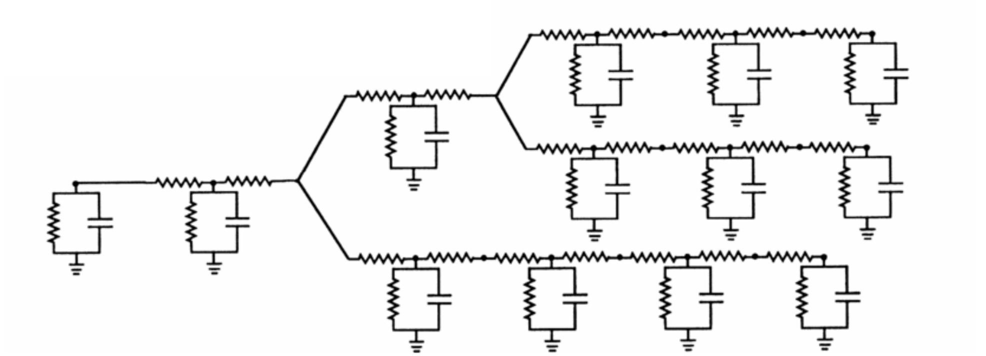
Cable theory and compartmental modeling

Cable theory consists of solving the partial differential equation

$$\boxed{\frac{1}{r_i+r_e}\frac{\partial V}{\partial x^2}=c_m\frac{\partial V}{\partial t}+I_{ion}}$$

- a few cases with analytical solutions
- generally solved using numerical simulations

Compartmental modeling

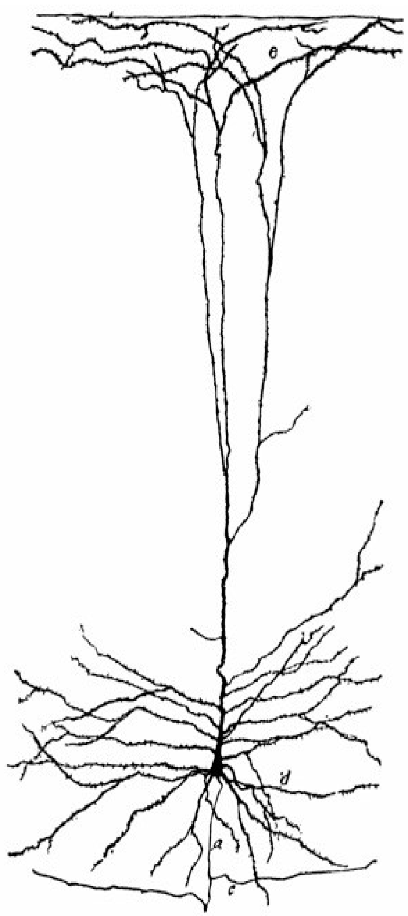


- discretize space → coupled system of ordinary differential equations (with temporal derivative)
- easier to solve numerically
- typically done using the Neuron software

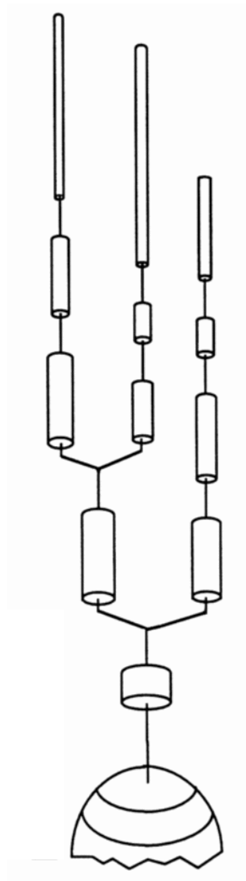
NEURON

for empirically-based simulations of neurons and networks of neurons

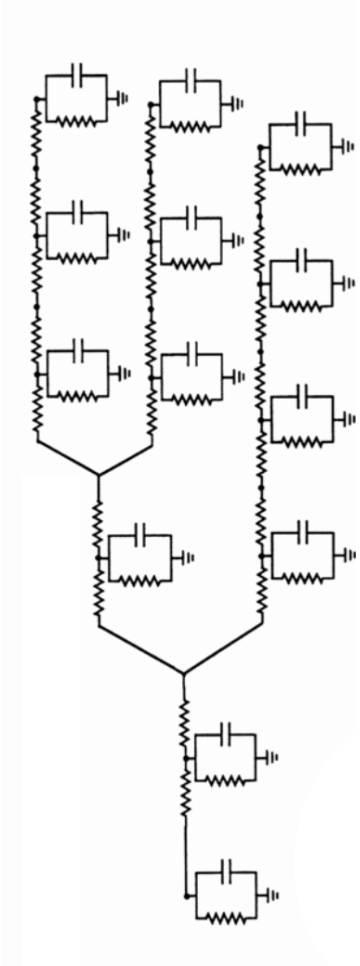
Single neuron models



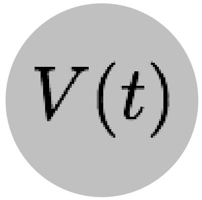
real
neuron



cable
theory

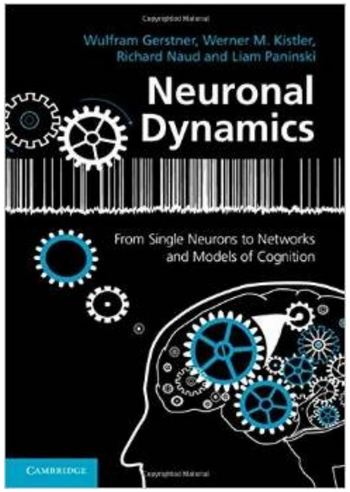


compartmental
model



point
neuron

Resources for further reading

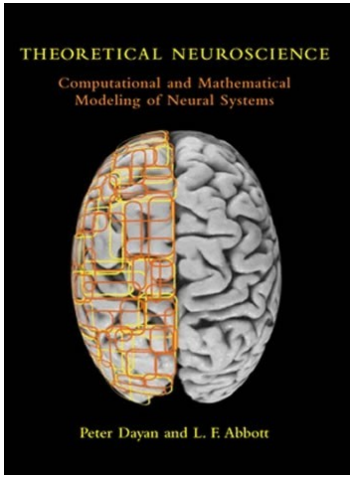


Neuronal Dynamics

From single neurons to networks and models of cognition

Wulfram Gerstner, Werner M. Kistler, Richard Naud and Liam Paninski

online book : https://neuronaldynamics.epfl.ch/online/index.html



Theoretical Neuroscience

Computational and Mathematical Modeling of Neural Systems

Peter Dayan and L. F. Abbott

online book : http://www.gatsby.ucl.ac.uk/~lmate/biblio/dayanabbott.pdf