Le neurone:
des propriétés électriques membranaires à l’excitabilité

General issues

Why focusing on electrical activity?

A brief history of excitability

Information processing in neurons

1. Morpho-functional organisation
2. Electrochemistry and ionic basis of membrane and synaptic potentials
3. Cable properties
4. Initiation and propagation of action potentials
5. “Non-linear” excitability

Conclusions: Three peculiar features of the Brain

1.The brain information is theoretically infinite
2. Brain activity is probabilistic, highly variable and “state-dependent”
3.The brain is a liar

The year 1952

A quoi sert le cerveau?

À rien

“La ferme des célébrités”
(TF1)
(…effets même délétères)

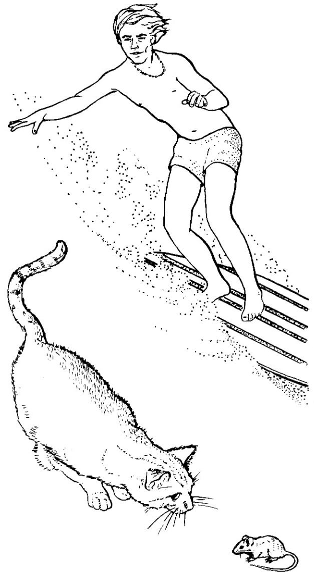
Construction intellectuelle

“…le mouvement est mouvement et agit comme mouvement, en tant qu’il est en relation avec des choses qui en sont privées; mais, pour ce qui concerne les choses qui y participent toutes également, il n’agit nullement et il est comme s’il n’était pas…”
(Galilée, 1632)

“Je chante l’homme vécu à la puissance voluptueuse du grain de tonnerre!”
(T. Tzara, 1931)

Two major roles of the central nervous system

Regulation: short-term compensation to maintain status quo.



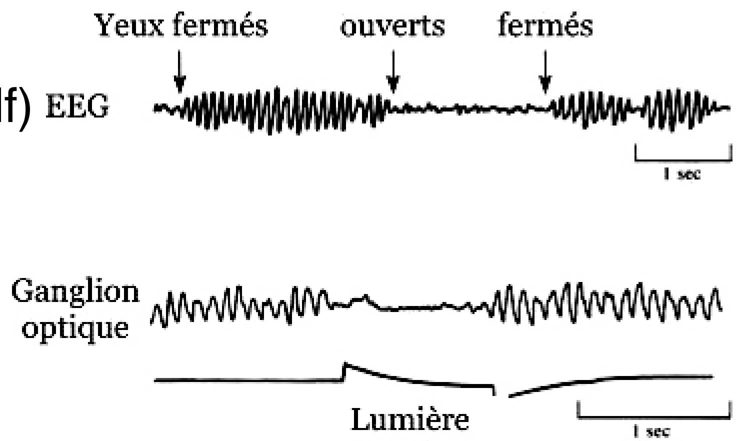
Initiation: longer-term change in the sphere of action.

Why focusing on electrical activity?

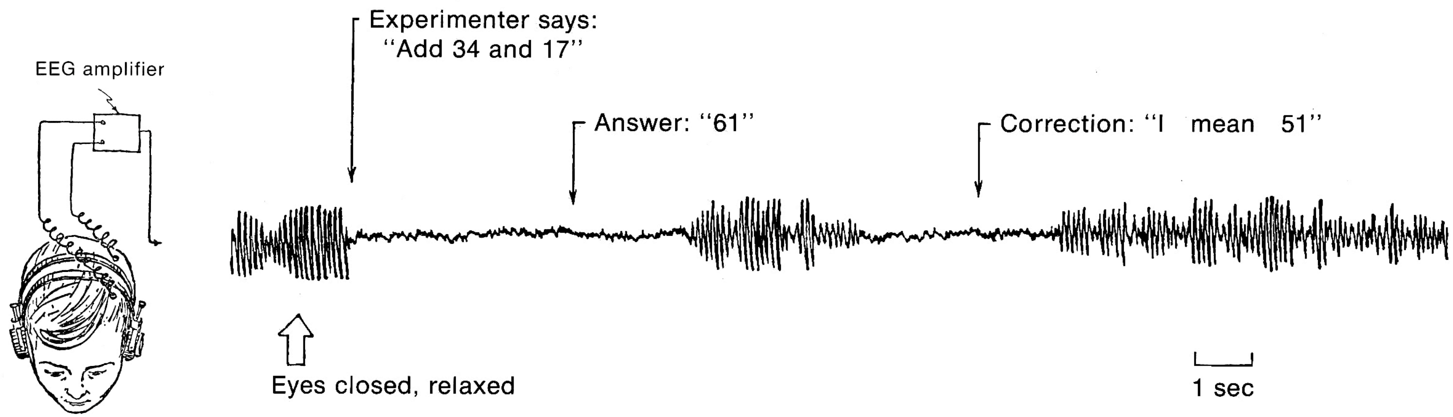
Electrical correlates of brain-mental activity

(E. Adrian himself)

(Beetle)

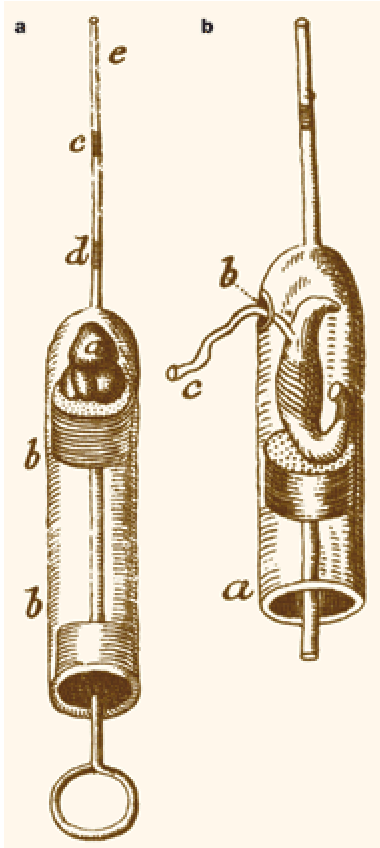


Electrical correlates of brain-mental activity



JAN SWAMMERDAM (1637–1680) ON NERVE FUNCTION:

"Death of animal spirits"



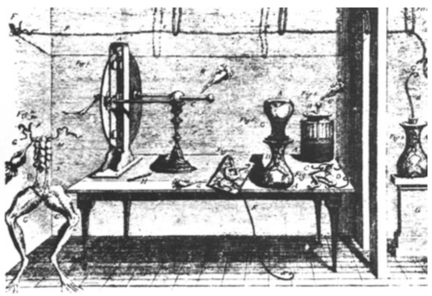
Descartes (1596–1650) ' illustration of his hypothesis of
ıe movement of the 'animal spirits' in response to burning

Swammerdam' experiments

Animal electricity

Luigi Galvani (1737-1798)

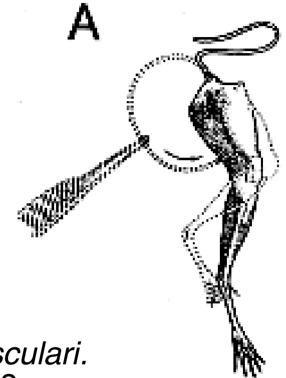
The Galvani's sciatic nerve-muscle preparation



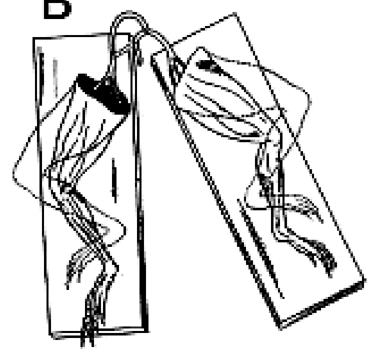
From Galvani L. *Aloysii Galvani de viribus electricitatis in motu musculari.*
De viribus electricitatis artificialis in motu musculari. 1791;7:363–418.

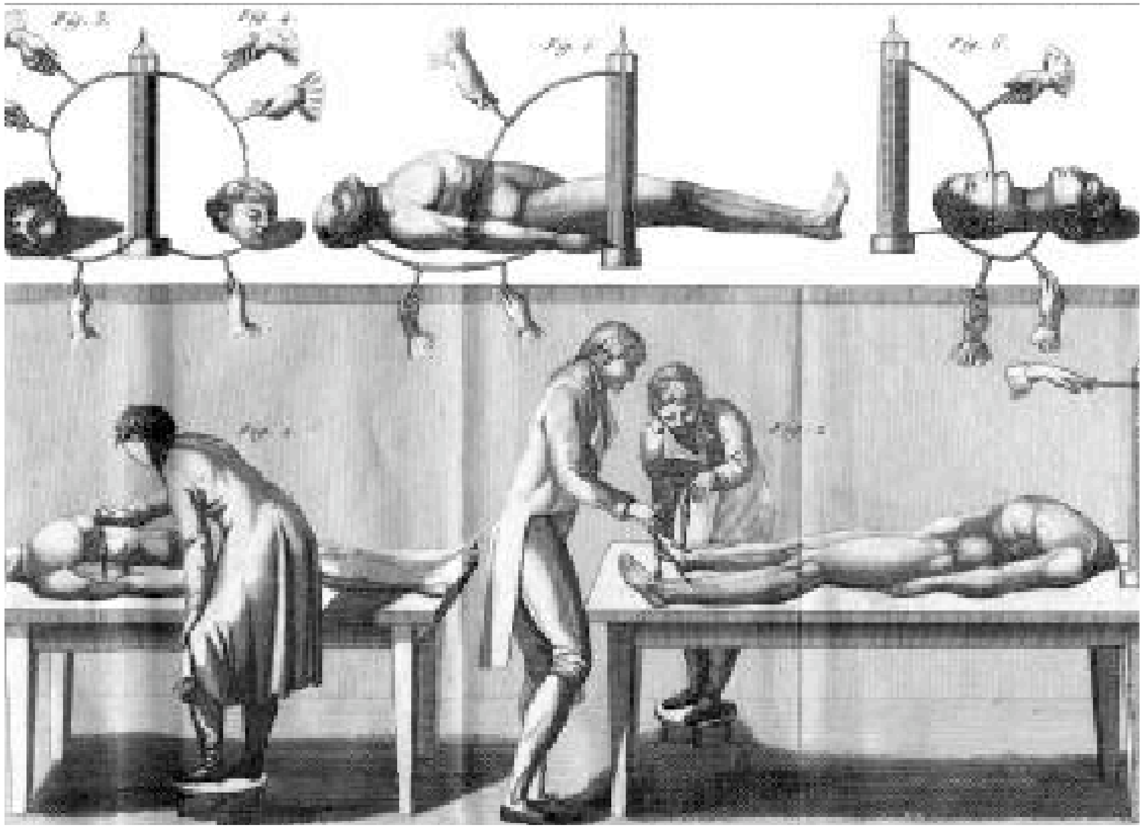
The crucial experiment

A

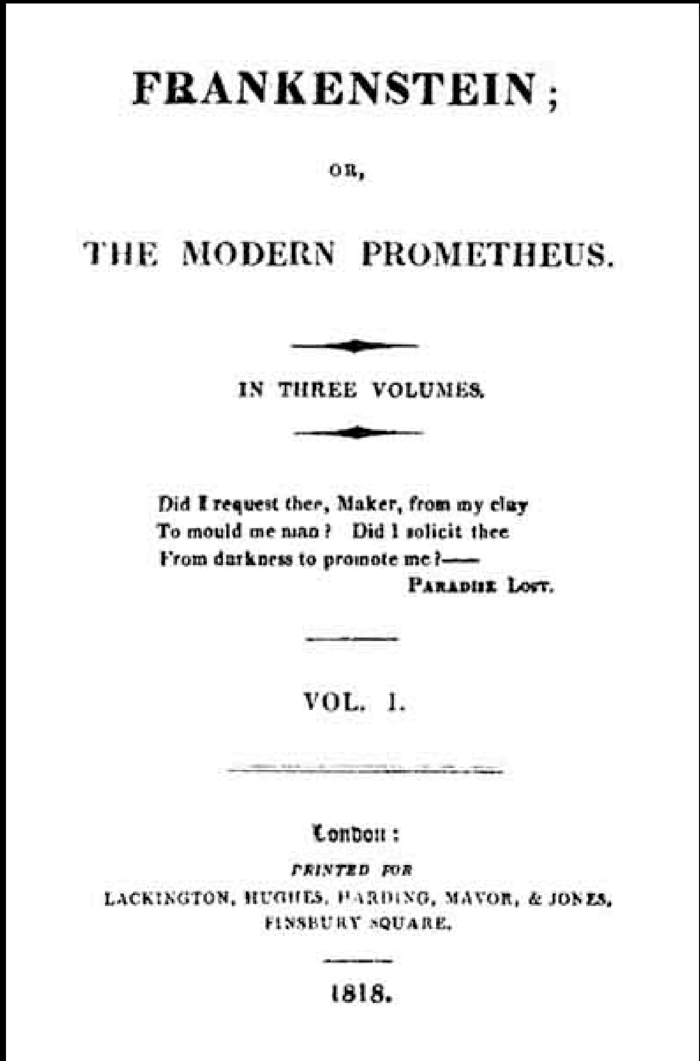


B





Aldini (1762-1834) and his assistants used to electrify corpses of criminals that were decapitated in Bologna in 1802.



FRANKENSTEIN;

OR,

THE MODERN PROMETHEUS.

IN THREE VOLUMES.

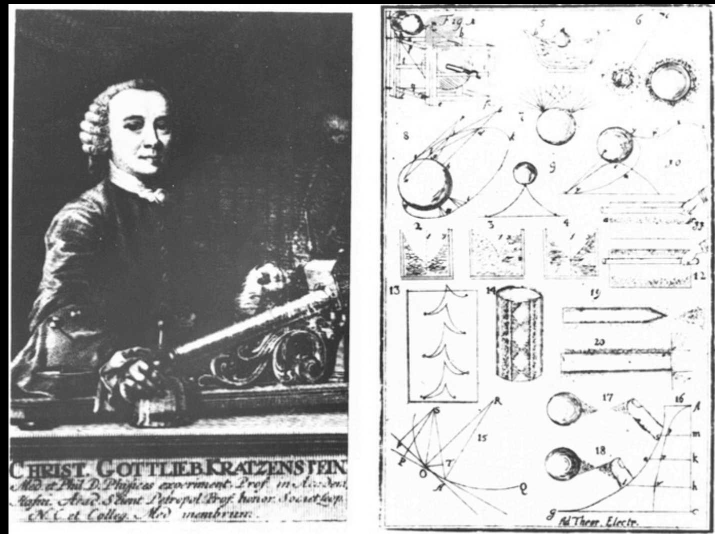
Did I request thee, Maker, from my clay
To mould me man? Did I solicit thee
From darkness to promote me?—
PARADISE LOST.

VOL. I.

London:
PRINTED FOR
LACKINGTON, HUGHES, HARDING, MAVOR, & JONES,
FINSBURY SQUARE.

1818.

(Mary Shelley)



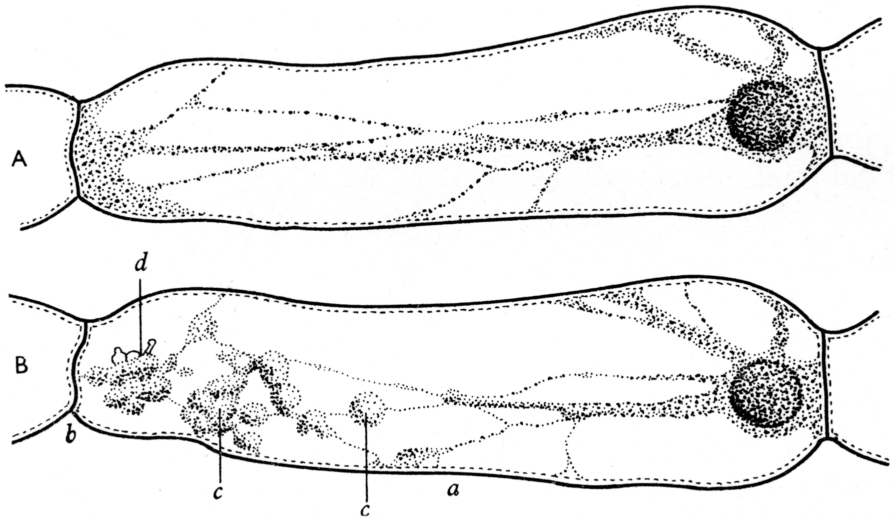
Christian Gottlieb Kratzenstein (1723–1795).

SOME WORDS WITH A MUMMY

by Edgar Allan Poe

1850

Effect of electrical stimulation on plant cells: speed up or stop of “ protoplasming streaming”



CELLS OF STAMINAL HAIRS OF TRADESCANTIA, DRAWN WITH CAMERA LUCIDA

Künhe, 1864

A brief history of excitability

From Du Bois-Reymond to Hodgkin-Huxley

L’excitabilité

Albrecht von Haller (1753)

“Irritability” (muscular contraction) and “sensibility”

Claude Bernard (1879)

«…la propriété de tout élément anatomique d’être mis en activité et de réagir d’une certaine manière sous l’influence d’excitants extérieurs.»

Louis Lapicque (1926)

« L’excitabilité est une *abstraction*. La réalité mesurable c’est l’*excitant,* c’est-à-dire l’action qui provoque la réaction propre à l’objet considéré…L’excitabilité est une valeur *réciproque* de l’action excitante. »

Aujourd’hui

Capacité (relative) d’un élément excitable à décharger un potentiel d’action. Dépend des interactions entre les propriétés électriques « passives », les conductances membranaires actives et les entrées synaptiques.

Stimulating agents used to “reveal” excitability

(reviewed in Bayliss, 1915 and Lapicque, 1926)

- Mechanical disturbances: pinching, tapping, shaking...

  ➡ Graduation in strength and frequency by dropping mercury from different heights (Schafer, 1901)

- Changes in temperature

- Irradiation with U-V light, X-rays, γ-rays, α-particles, neutrons…

- Crystals of salt, glycerol (change in osmotic pressure)

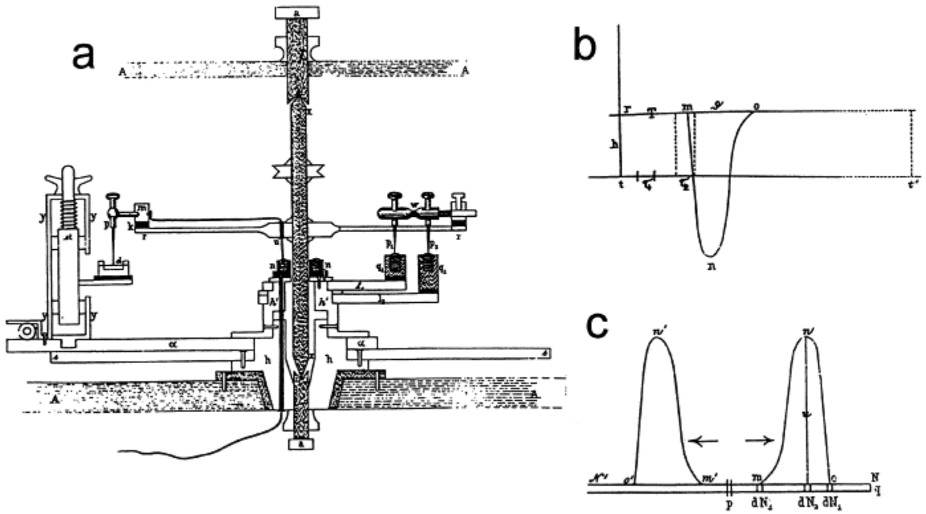
- “True” chemical agents: neurotransmitters and hormones (extracts of supra-renal glands, Schafer and Olivier, 1894).

- Electrical stimuli: duration, strength and frequency can be accurately and conveniently graduated and measured!

Recordings and nature of excitation:
From Du Bois-Reymond to Adrian

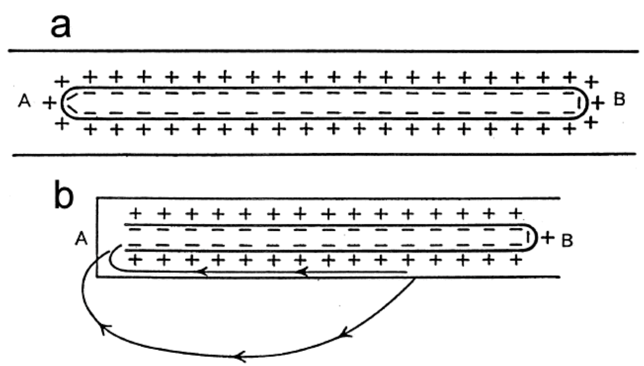
Recording of the “negative Schwankung”
(Du Bois-Reymond , 1848)

Time course of the electrical nerve impulse
(J. Bernstein, 1868)



Measure of conduction velocity
(Von Helmotz, 1850)

Bernstein’s theory of membrane polarization
and excitation (1912)



Time and excitation

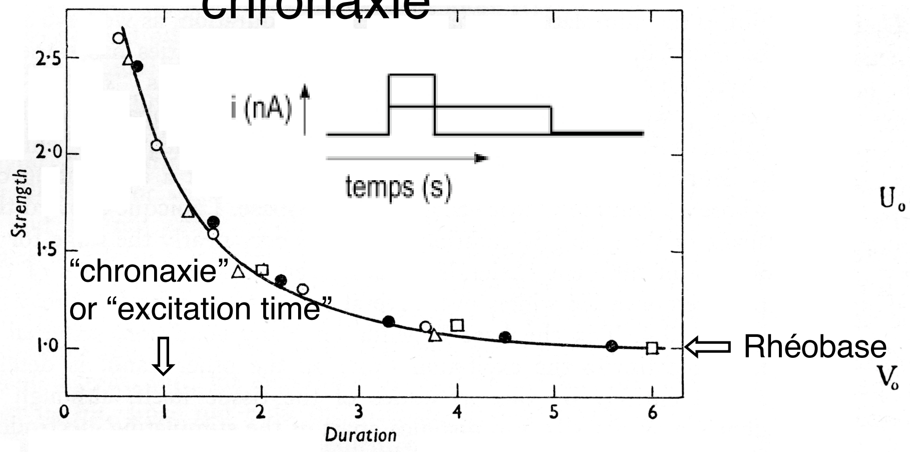
A

$$\varepsilon = f\left(\frac{d\Delta}{dt}\right)$$

Δ = current density

E. Du Bois-Reymond, 1840

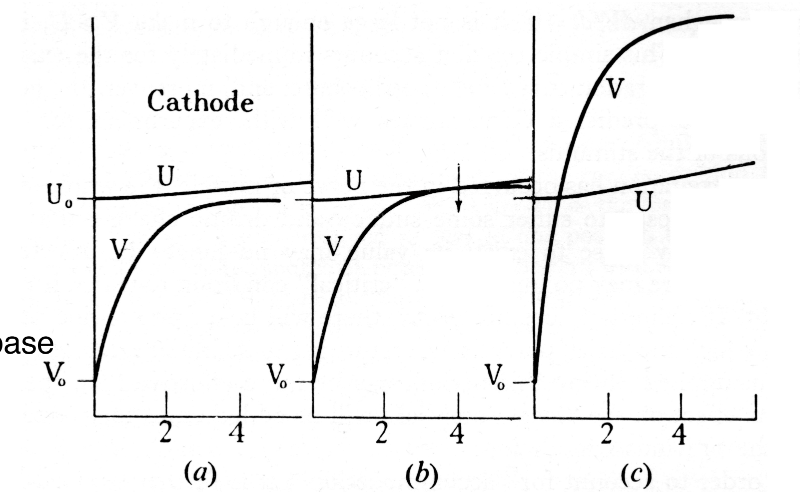
B The "chronaxie"



THE RELATION BETWEEN THE STRENGTH AND THE DURATION OF A THRESHOLD STIMULUS

L. Lapicque and K. Lucas; 1900-1910

C Accommodation



Hill, 1936

The “equivalent circuits” of excitation

A Lapicque, 1907

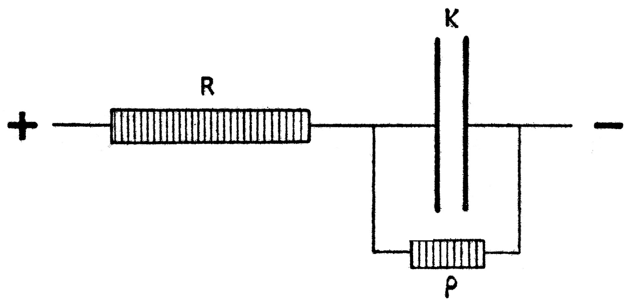


FIG. 1.

B Hodgkin and Huxley, 1952

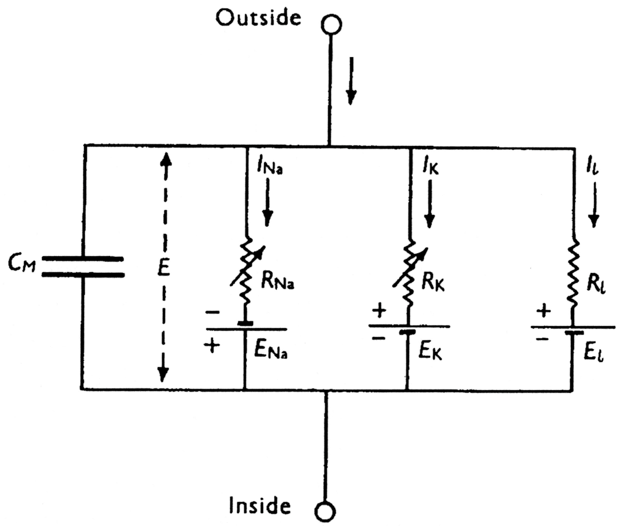
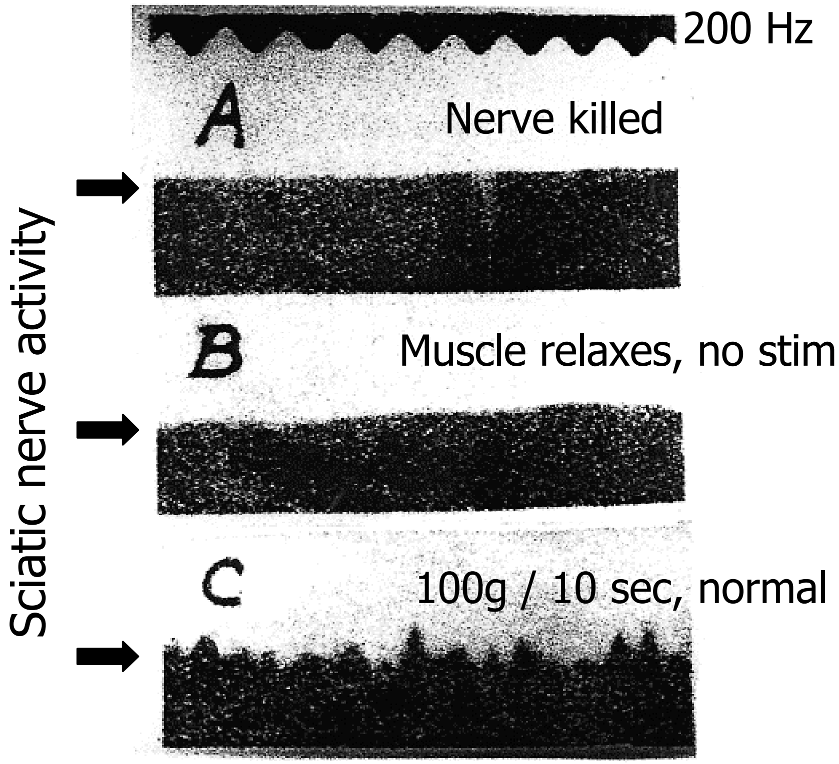


Fig. 1. Electrical circuit representing membrane. $R_{Na}=1/g_{Na}$; $R_K=1/g_K$; $R_l=1/\bar{g}_l$. R_{Na} and R_K vary with time and membrane potential; the other components are constant.

First single axon recording and sensory coding

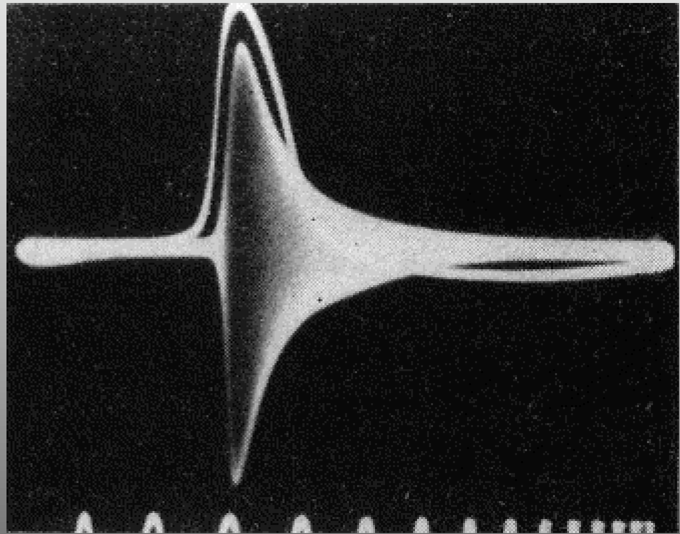
Unitary electrical activity in sensory fibers
during physiological stimuli
(E. Adrian, 1926)



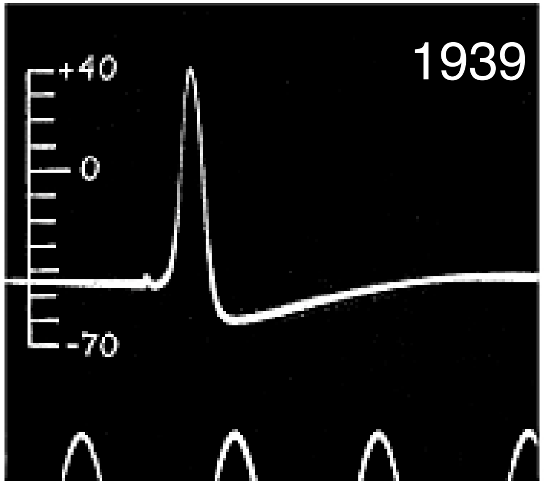
Mechanical stimulus applied to gastrocnemius

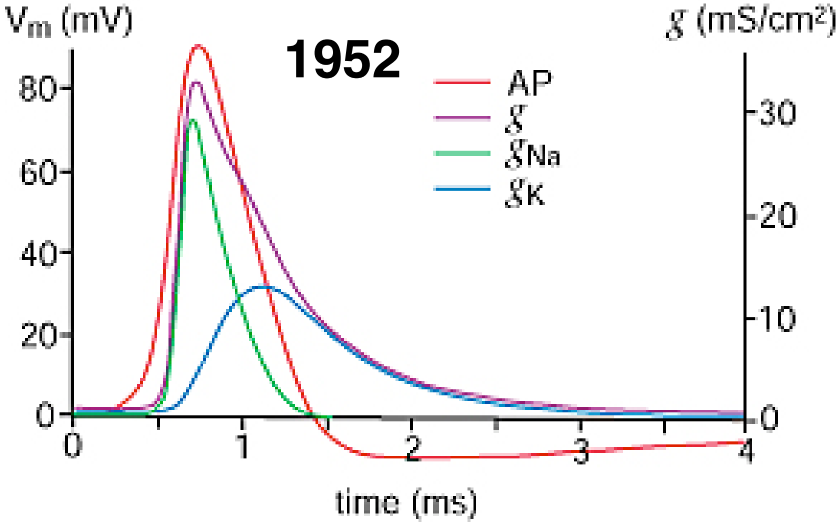
First assessment of conductance changes during an action potential

(Cole KS and Curtis HJ, 1939)



The ionic origin of action potential : the "Hodgkin-Huxley" model





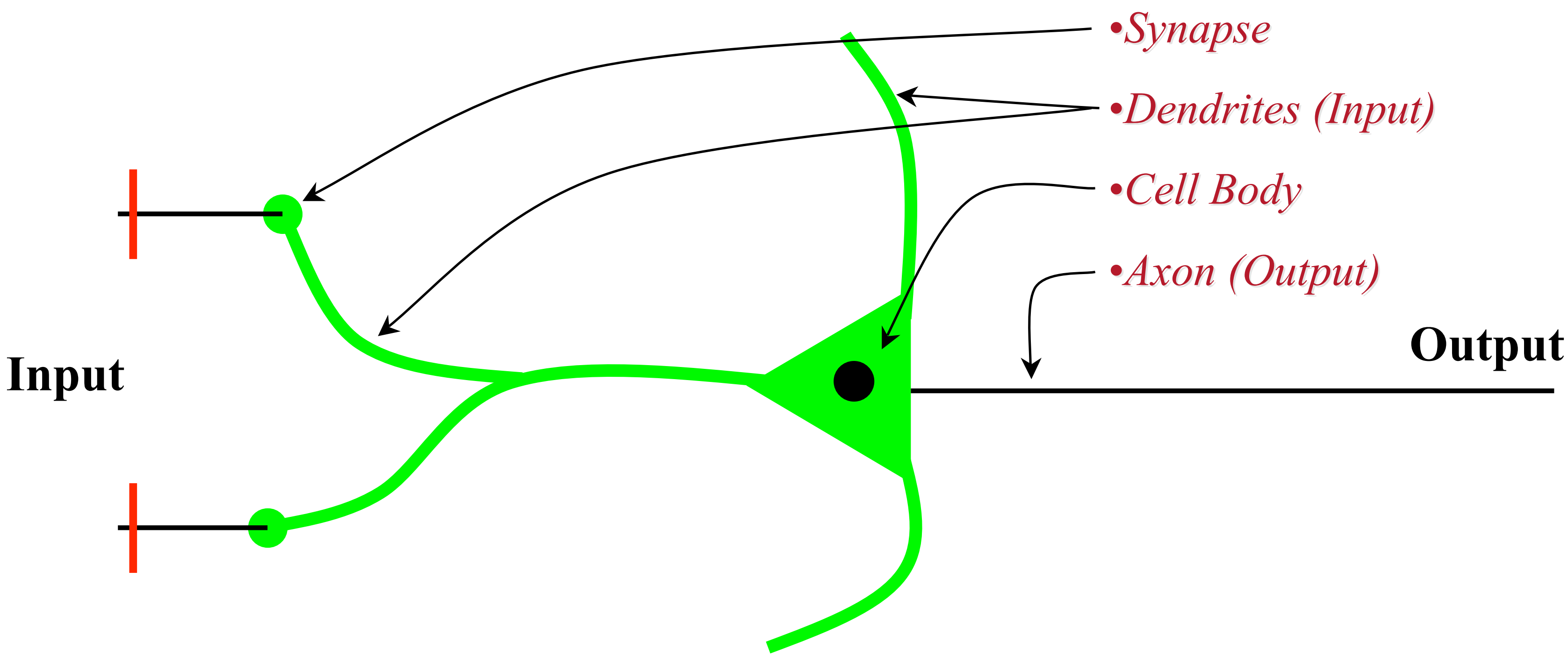
We may first collect the equations which give the total membrane current I as a function of time and voltage. These are:

$$I = C_M \frac{\mathrm{d}V}{\mathrm{d}t} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l), \qquad (26)$$

Information processing in neurons

1. Morpho-functional organization

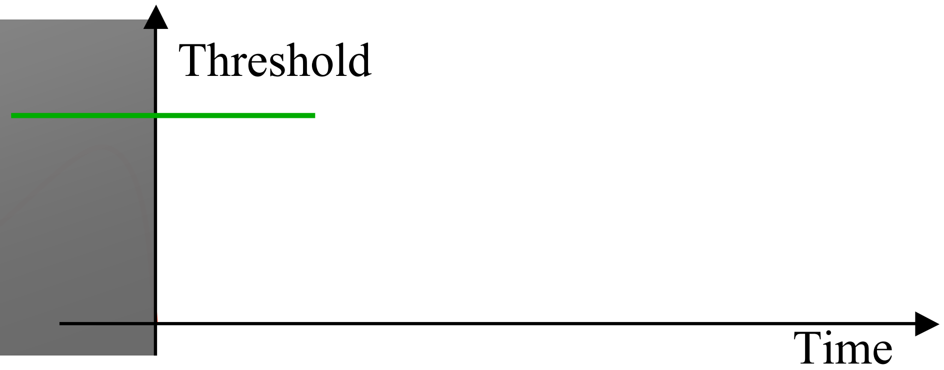
Neuron as a Device



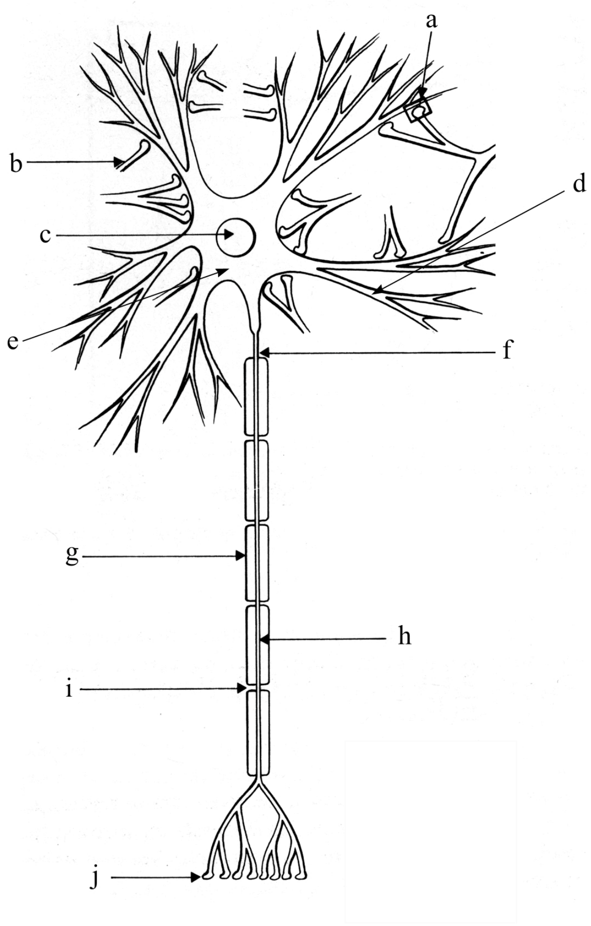
Equilibrium: Membrane Potential

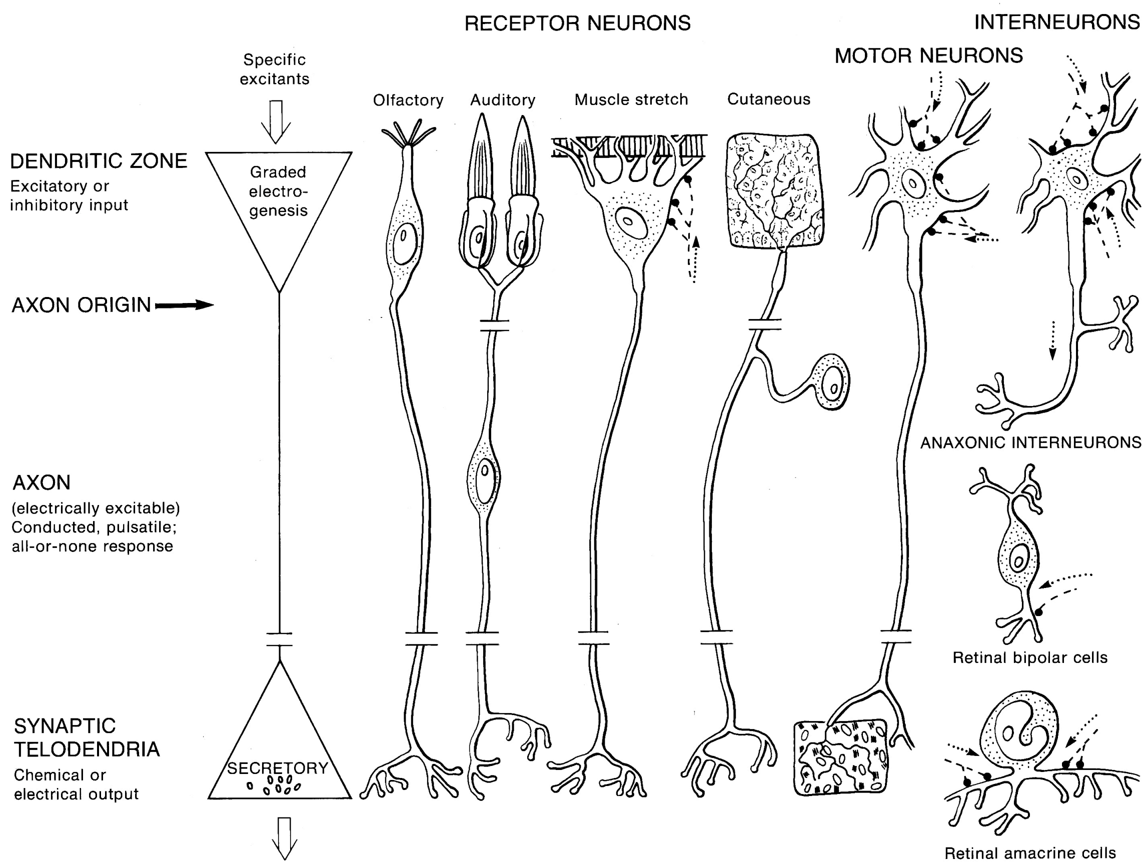
Dendrites: Passive Conductance

Axon: Spikes (Hodgkin Huxley Eqns)

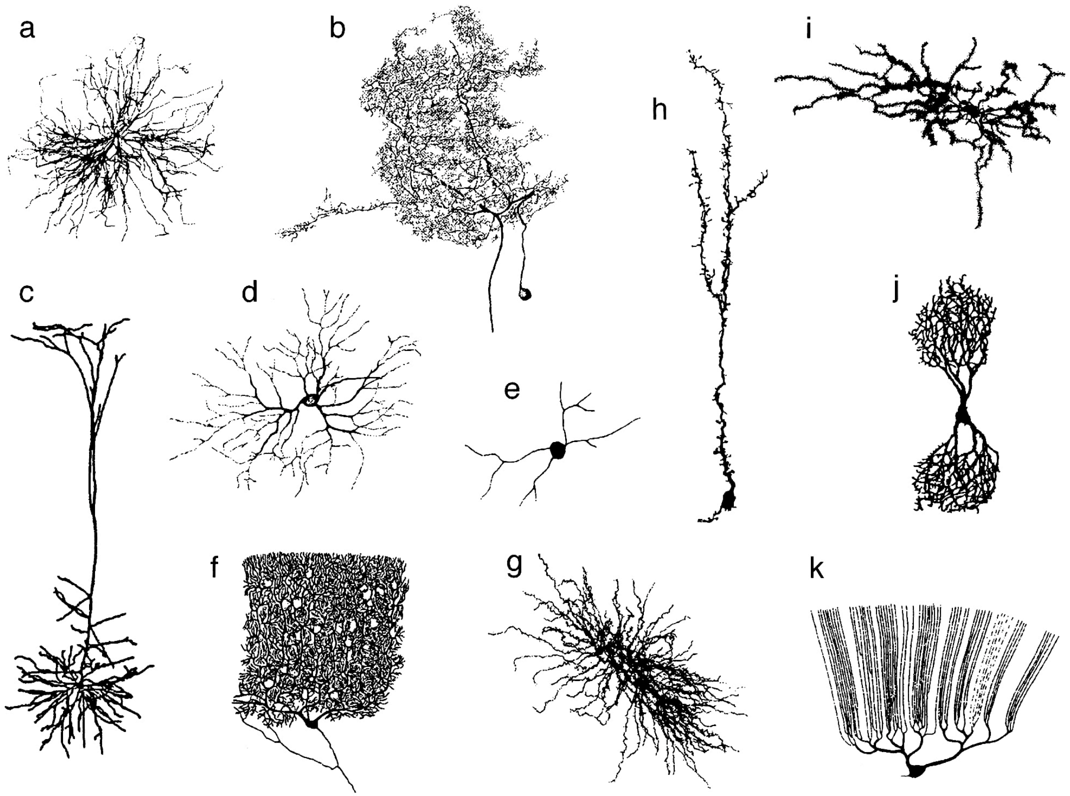


Structural and functional features of neurons





"True" neuron types



Dendritic trees come in different shapes and sizes. The size of the dendritic tree (largest dimension) is given in brackets. (a) Cat spinal motoneuron (2.6 mm). (b) Locust mesothoracic ganglion spiking interneuron (0.54 mm). (c) Rat neocortical layer 5 pyramidal neuron (1.03 mm). (d) Cat retinal ganglion neuron (0.39 mm). (e) Salamander retinal amacrine neuron (0.16 mm). (f) Human cerebellar Purkinje neuron. (g) Rat thalamic relay neuron (0.35 mm). (h) Mouse olfactory granule neuron (0.26 mm). (i) Rat striatal spiny projection neuron (0.37 mm). (j) Human nucleus of Burdach neuron. (k) Fish Purkinje neuron (0.42 mm). Modified from Mel, B. W. (1994). *Neural Computation*, **6**, 1031–1085.

The chemical synapse

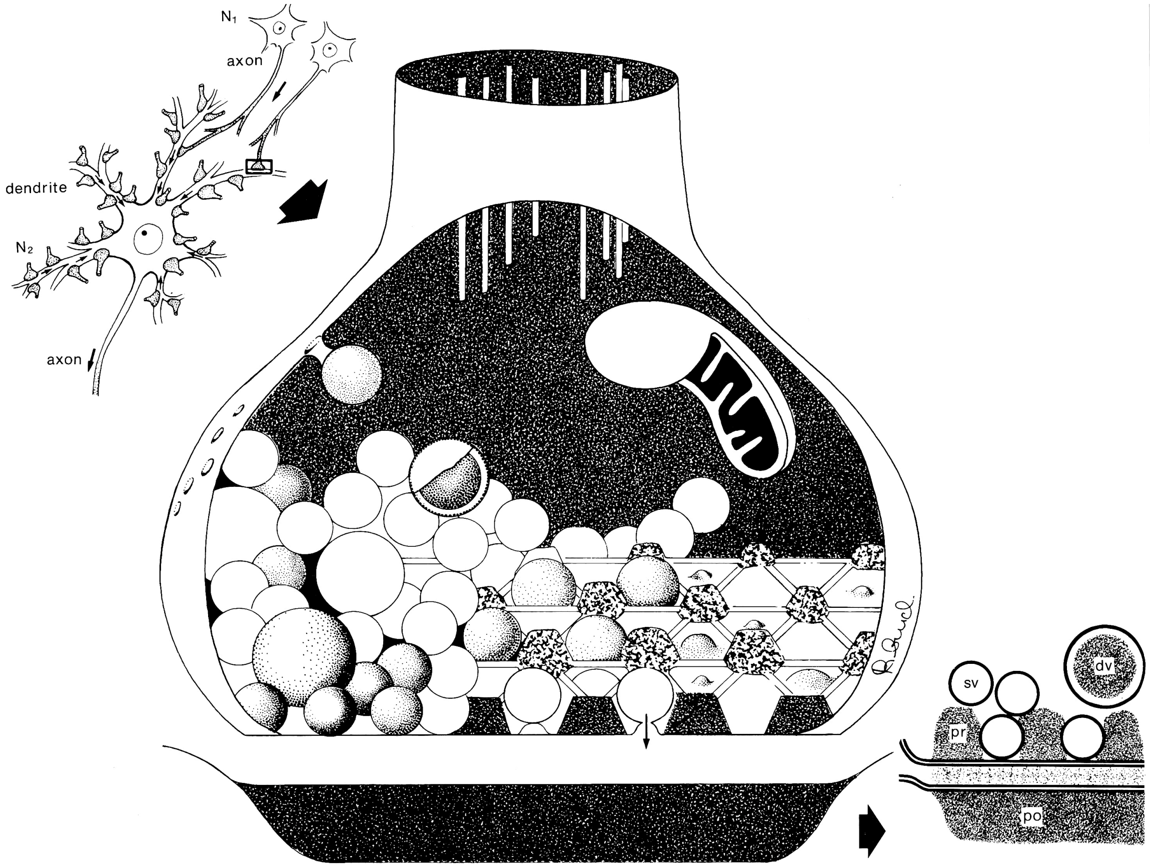


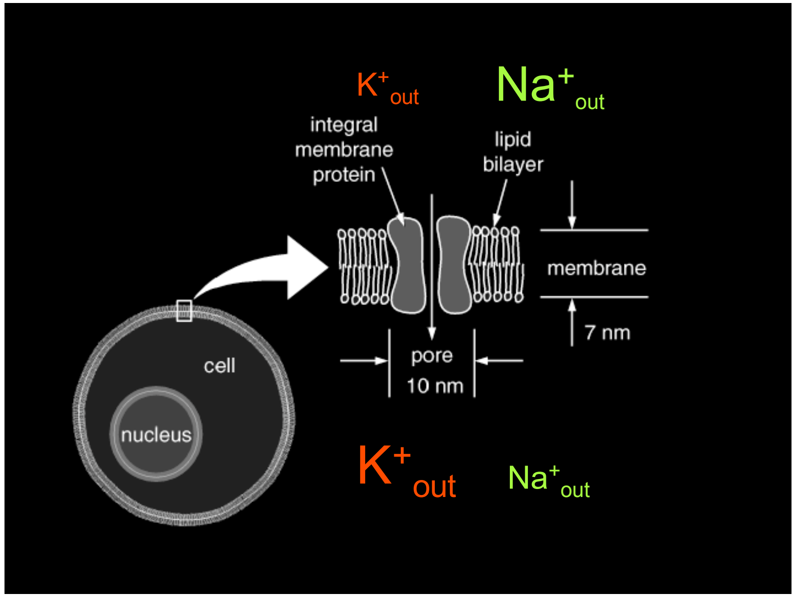
Figure 2.24
Left. Low-power diagram showing a presynaptic terminal within the rectangle. **Center.** An enlarged view of the same terminal, showing the vesicular grid, "synaptophores" and vesicles incorporated into the cell membrane, a single mitochondrion, neurofilaments, and the cleft, but no postsynaptic detail. **Right.** Diagram of terminal at lower magnification than the preceding, as seen with a different fixative: *dv,* dense core vesicle; *sv,* spherical vesicle; *pr,* presynaptic projection; *po,* postsynaptic cytoplasm. [Akert et al., 1972.]

Information processing in neurons

2. Electrochemistry and ionic basis of membrane and synaptic potentials

Nernst equation

$$E_i \equiv V_{in} - V_{out} = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$$

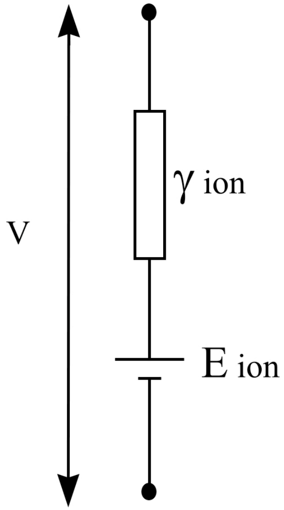


The Variable Definitions
Ei : The equilibrium potential for the ion i.
R : the thermodynamic gas constant
T : the absolute temperature
z : the charge/valence of the ion
F : the Faraday (96485.309 C/mol)

[C] out : the extracellular concentration of the ion i.

[C] in : the intracellular concentration of the ion i.

Driving force and passive currents



$i = \gamma (V - E)$

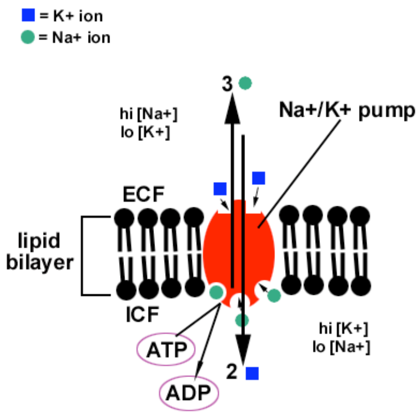
$I = \gamma N Po (V - E)$

$I = N Po\ i$

$i < 0$ => courant entrant

$i > 0$ => courant sortant

$i = 0$ => ion à l'équilibre: $V = E$



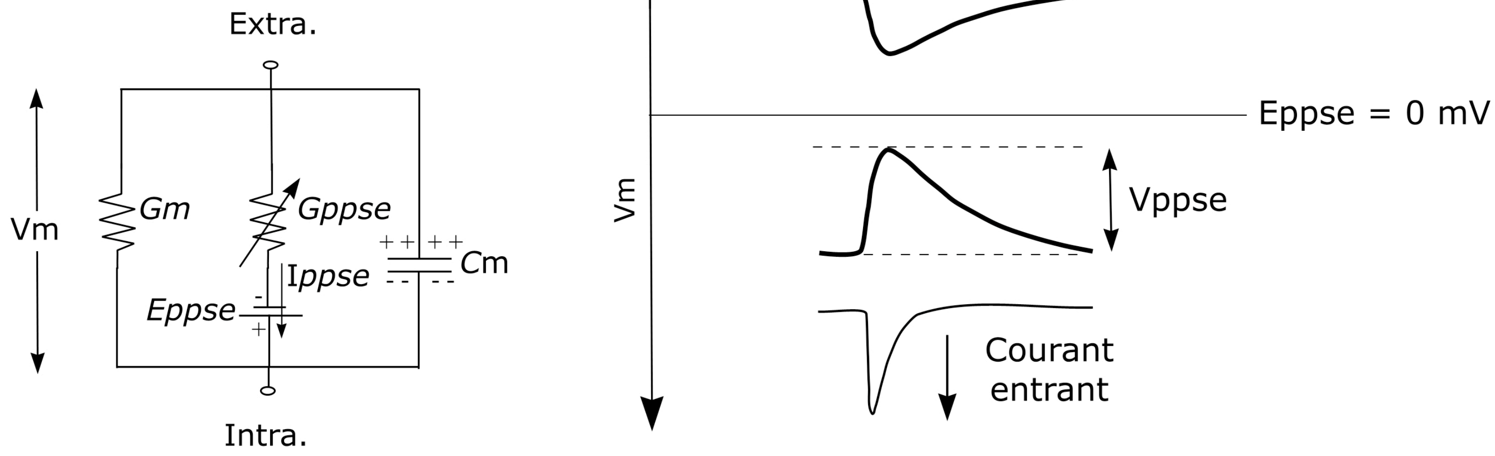
A l'équilibre (potentiel de repos) $\Sigma I_{ion} = 0$

Vm (gion, Eion)= ?

$$Vm\ (gion,\ Eion) = \Sigma\,[G_{ion}.E_{ion}]/\ \Sigma G_{ion}$$

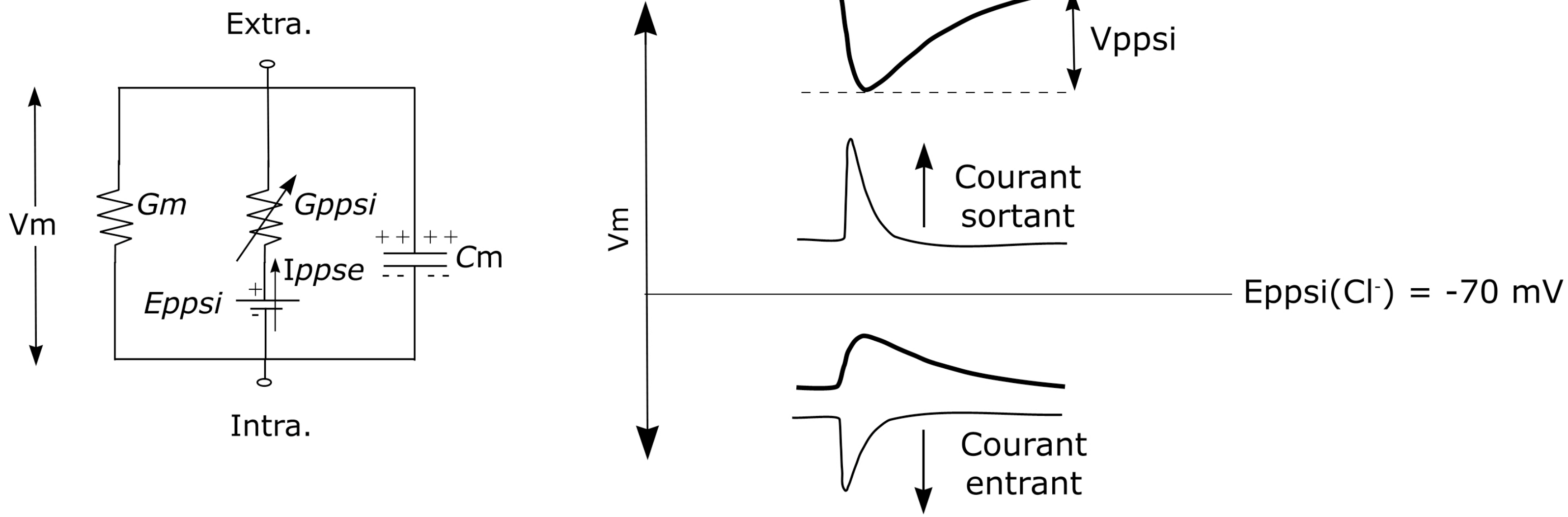
Glu

$$\text{Vppse} = [\text{Gppse}\ (\text{Vm} - \text{Eppse})] / \text{Gm}$$



GABA (R-$GABA_A$)

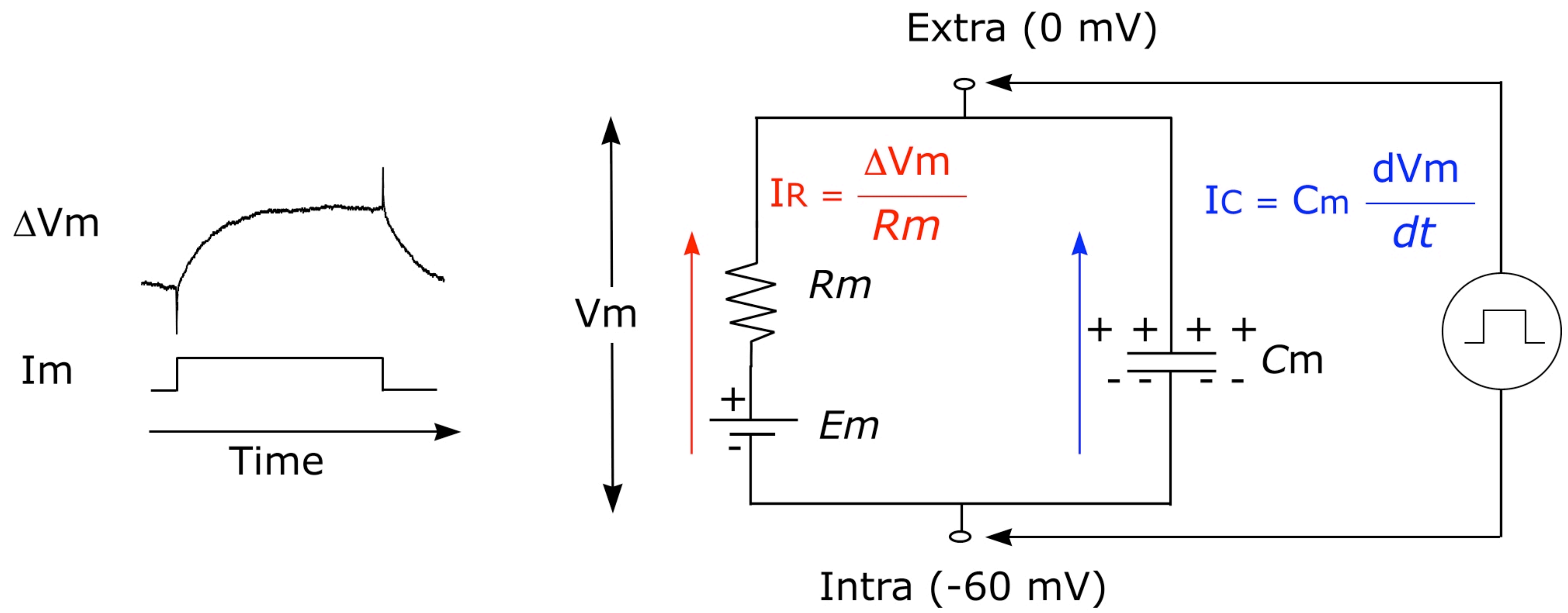
$$\text{Vppsi} = [\text{Gppsi}\ (\text{Vm} - \text{Eppsi})] / \text{Gm}$$



Information processing in neurons

3. Cable properties

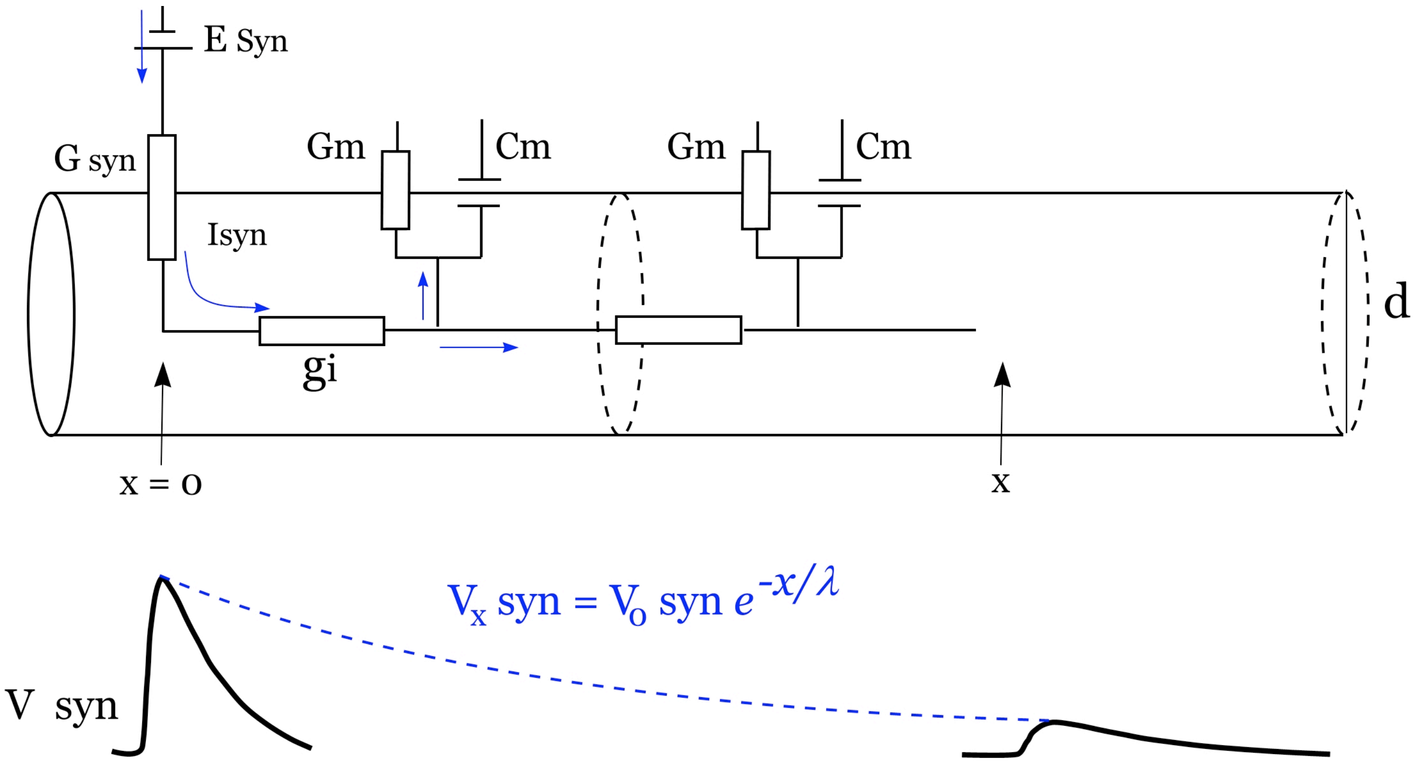
Time constant



$$V(t) = I.Rm\,(1 - e^{-t/Rm.Cm})$$

$$\tau = Rm.Cm$$

Space constant



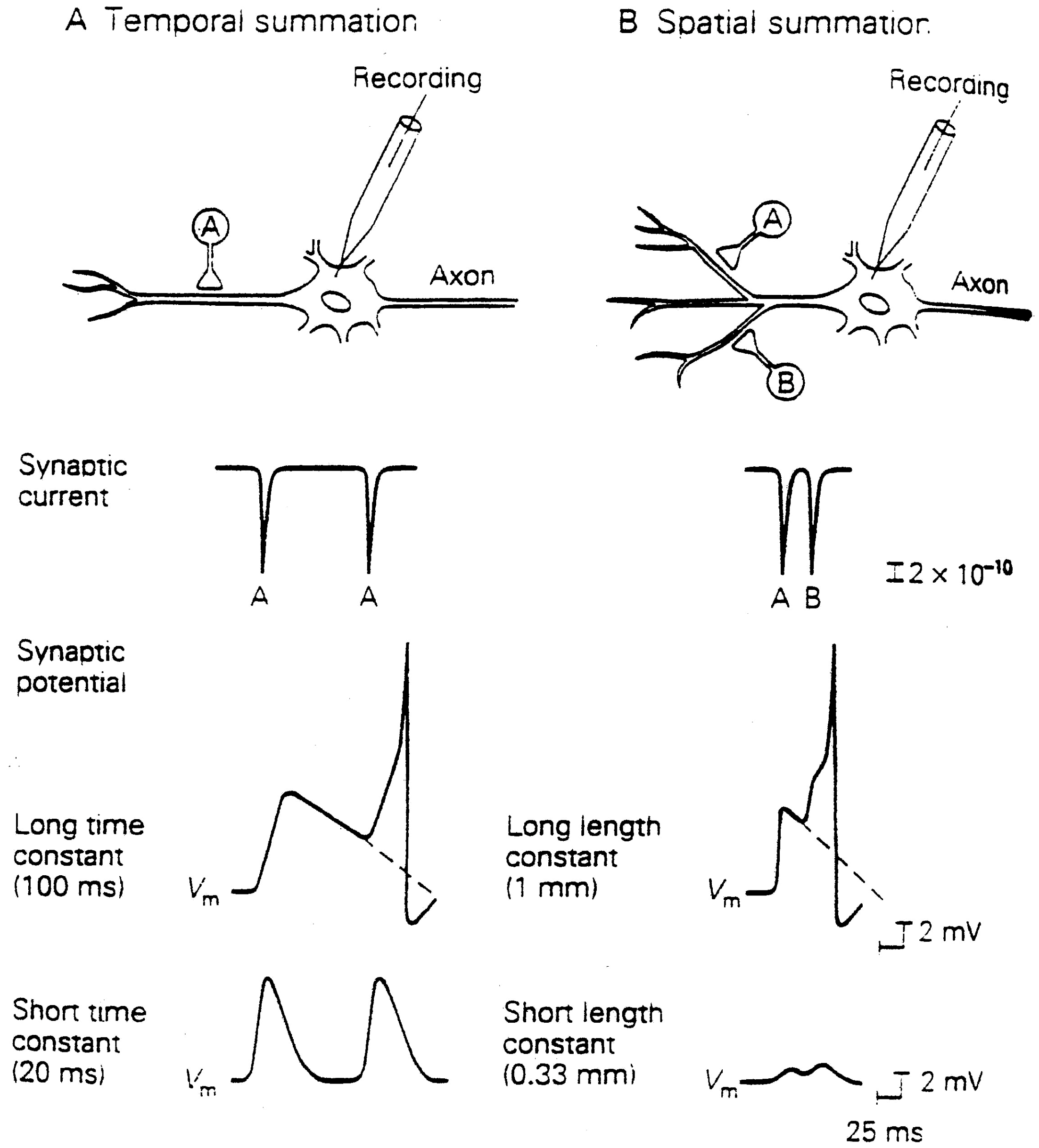
$$V_x \text{ syn} = V_o \text{ syn } e^{-x/\lambda}$$

avec

$$\lambda = \sqrt{d \text{ Gi} / 4 \text{ Gm}}$$

Gi = conductance spécifique axoplasmique

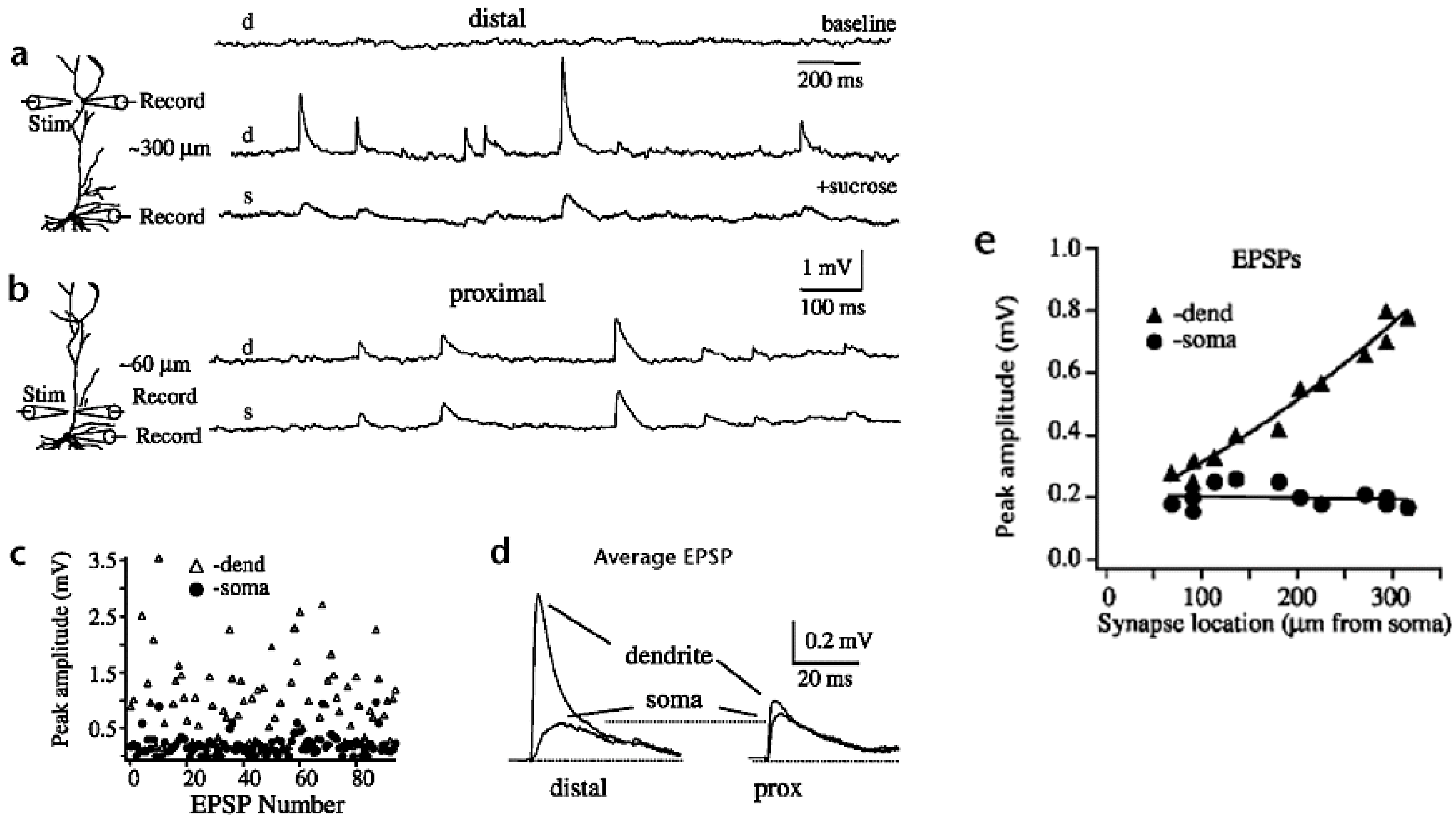
Gm = conductance membranaire


A Temporal summation
B Spatial summation
Recording
Recording
A
A
B
Axon
Axon
Synaptic current
A
A
A B
2 × 10⁻¹⁰
Synaptic potential
Long time constant (100 ms)
Vm
Long length constant (1 mm)
Vm
2 mV
Short time constant (20 ms)
Vm
Short length constant (0.33 mm)
Vm
2 mV
25 ms

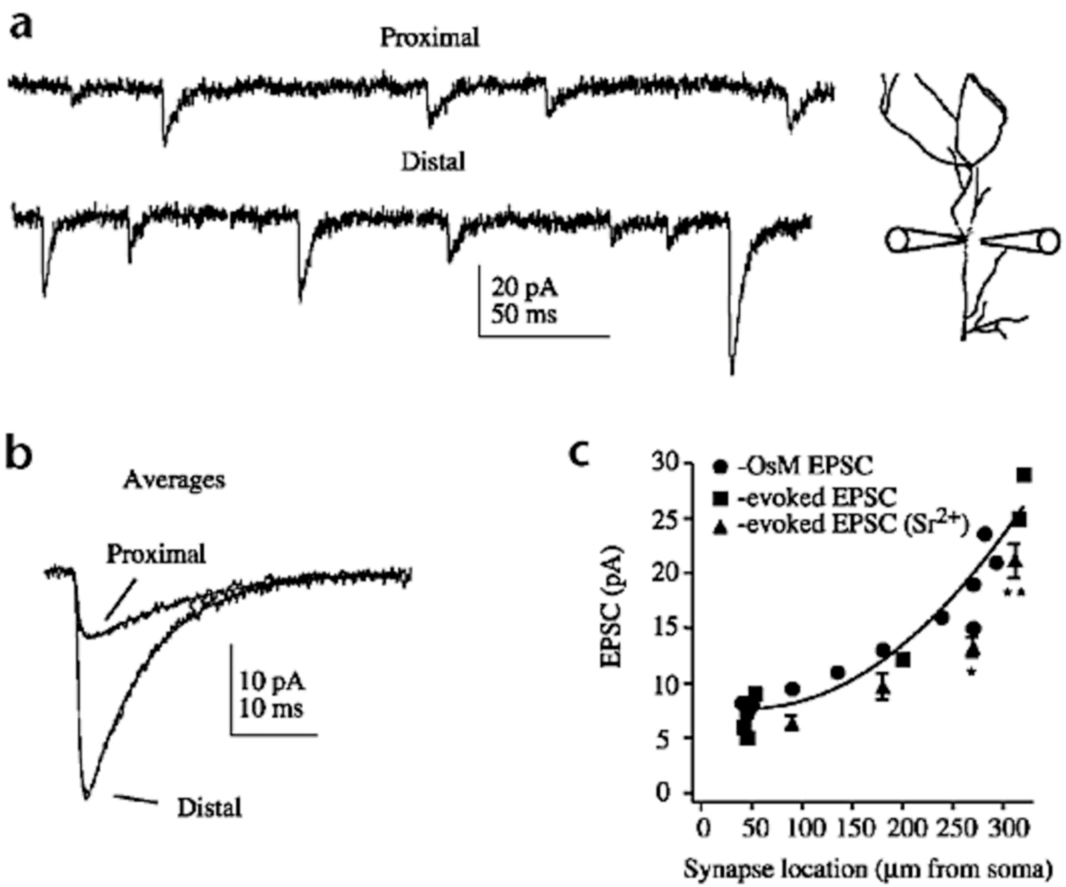
L'amplitude des PPSE somatiques est indépendante de la localisation des synapses

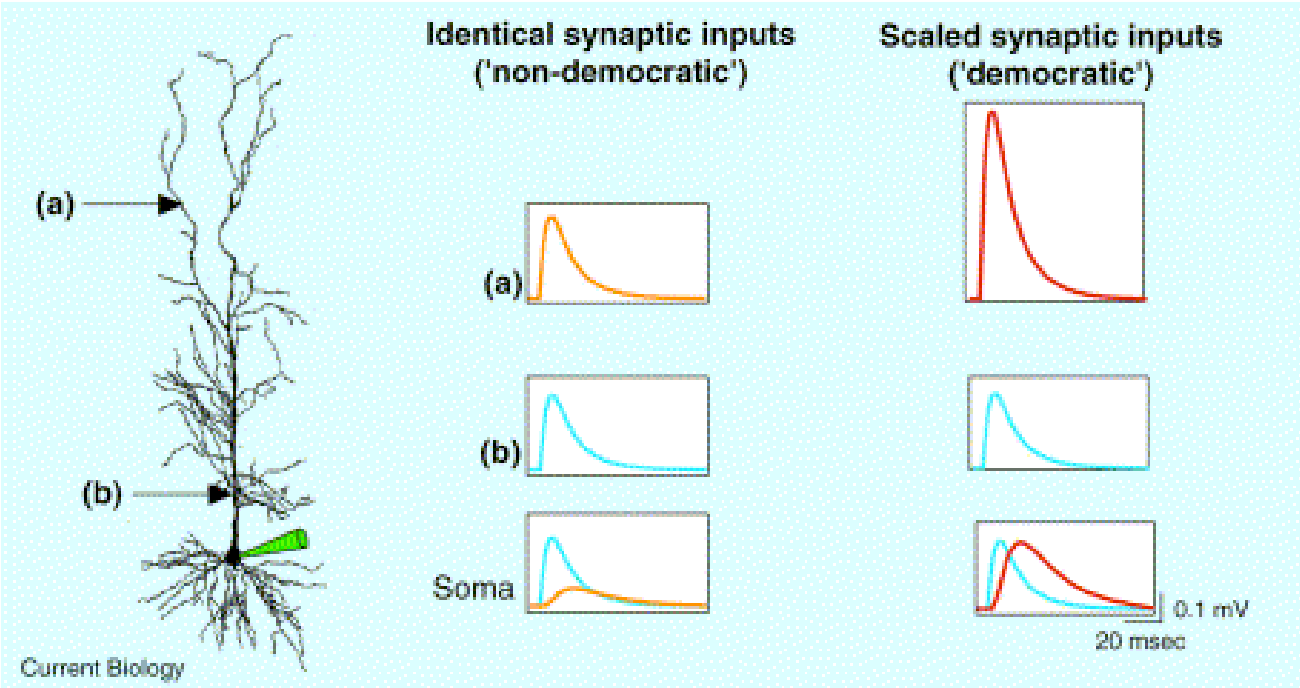
(Neurones pyramidaux CA1, tranches d'hippocampe, enregistrements cellule entière)

Magee & Cook, 2000

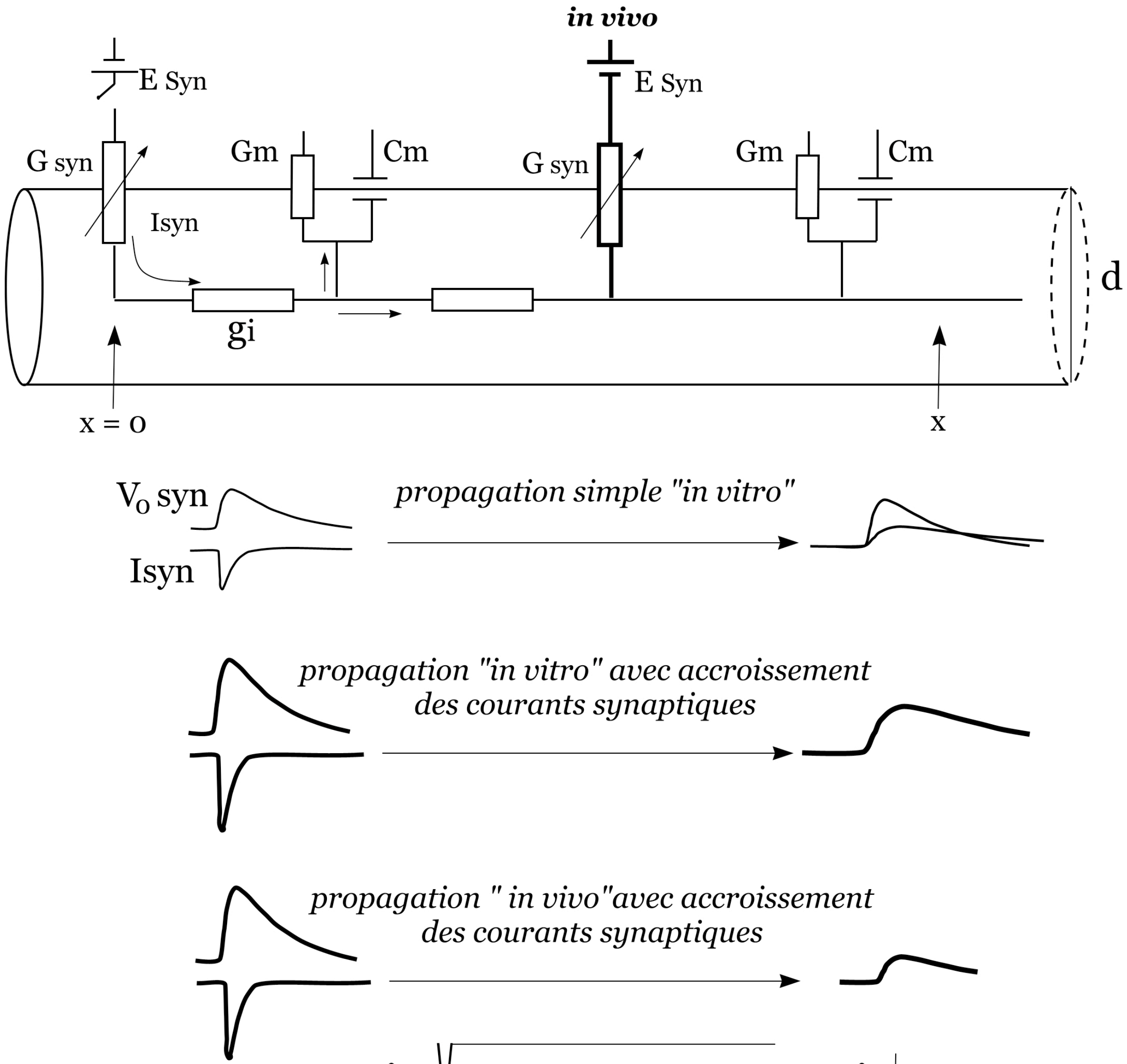


Increase in synaptic currents as a function of the somatic distance




Identical synaptic inputs
('non-democratic')
Scaled synaptic inputs
('democratic')
(a)
(b)
(a)
(b)
Soma
0.1 mV
20 msec
Current Biology

In vivo…?

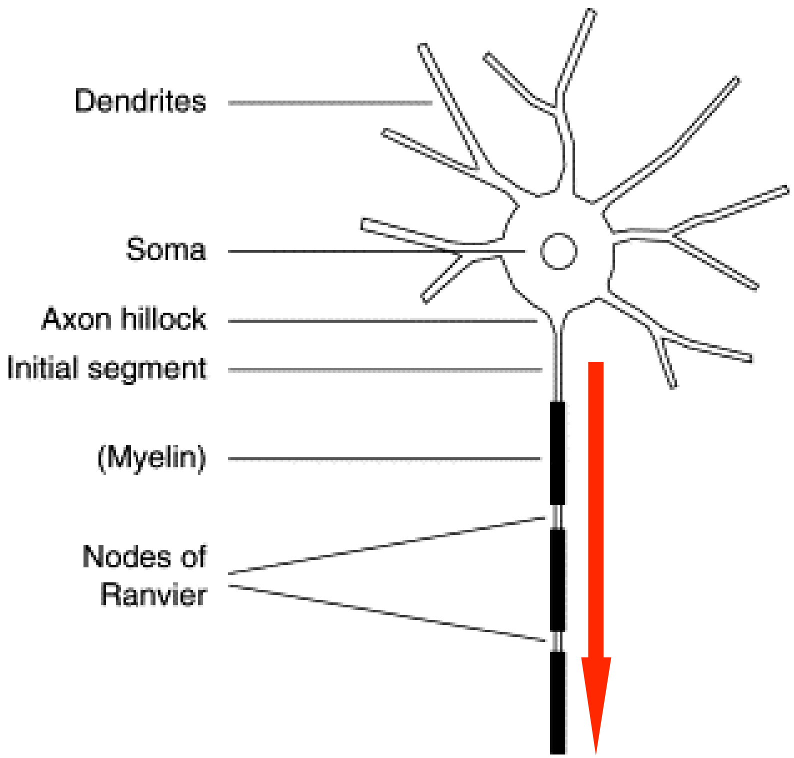


$$\lambda = \sqrt{d\, Gi / 4\, Gm + Gsyn} \Rightarrow \lambda \downarrow$$

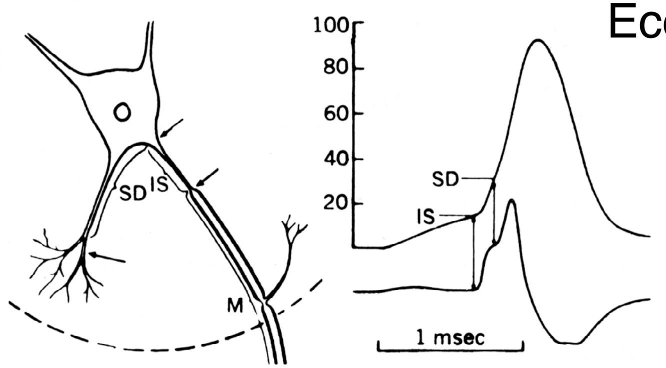
Information processing in neurons

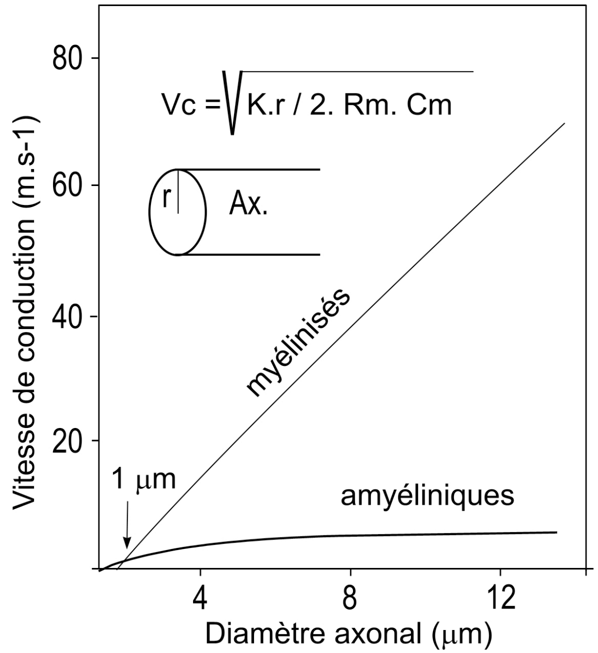
4. Initiation and propagation of action potentials

Initiation and propagation of the action potential: “classical view”

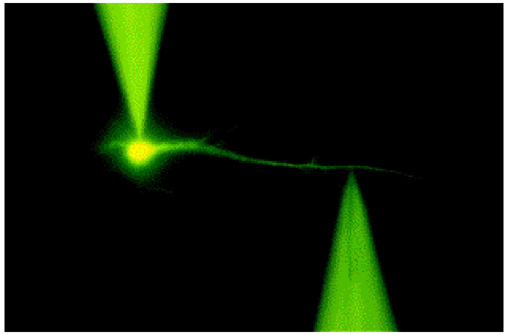


Eccles, 1952



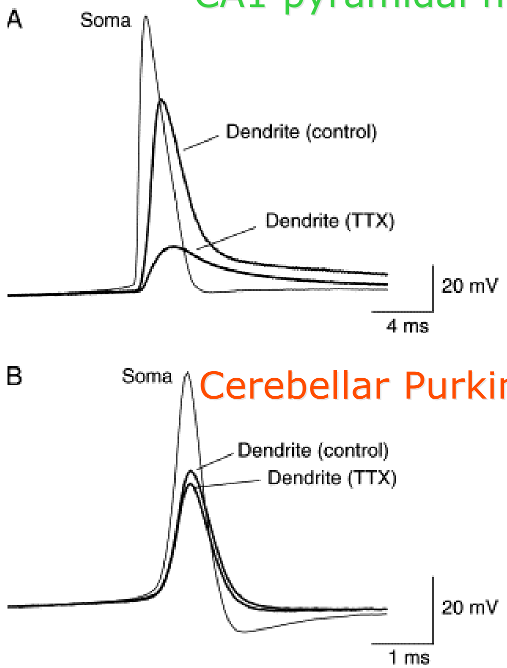


Axonal Initiation and dendritic backpropagation



CA1 pyramidal neuron during simultaneous somatic and dendritic (145 μm from the soma) recording

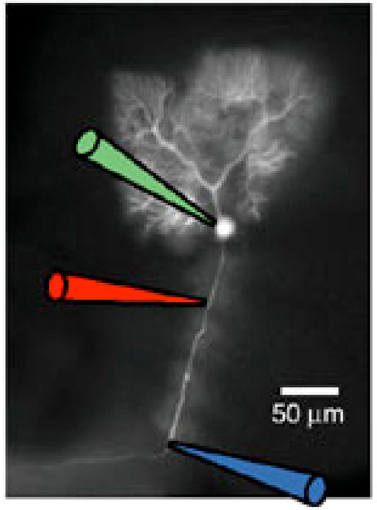
CA1 pyramidal neuron

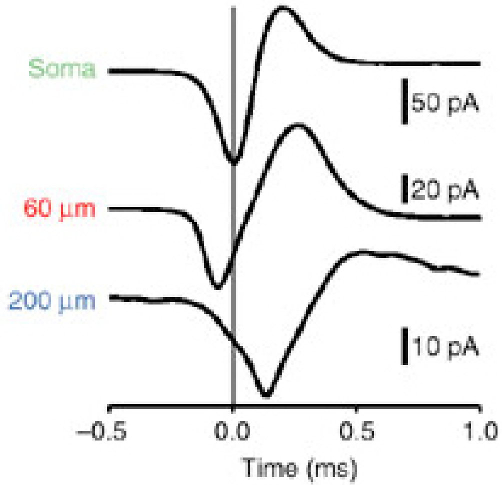


Cerebellar Purkinje neuron

Stuart et al, 1997

Cerebellar Purkinje neuron

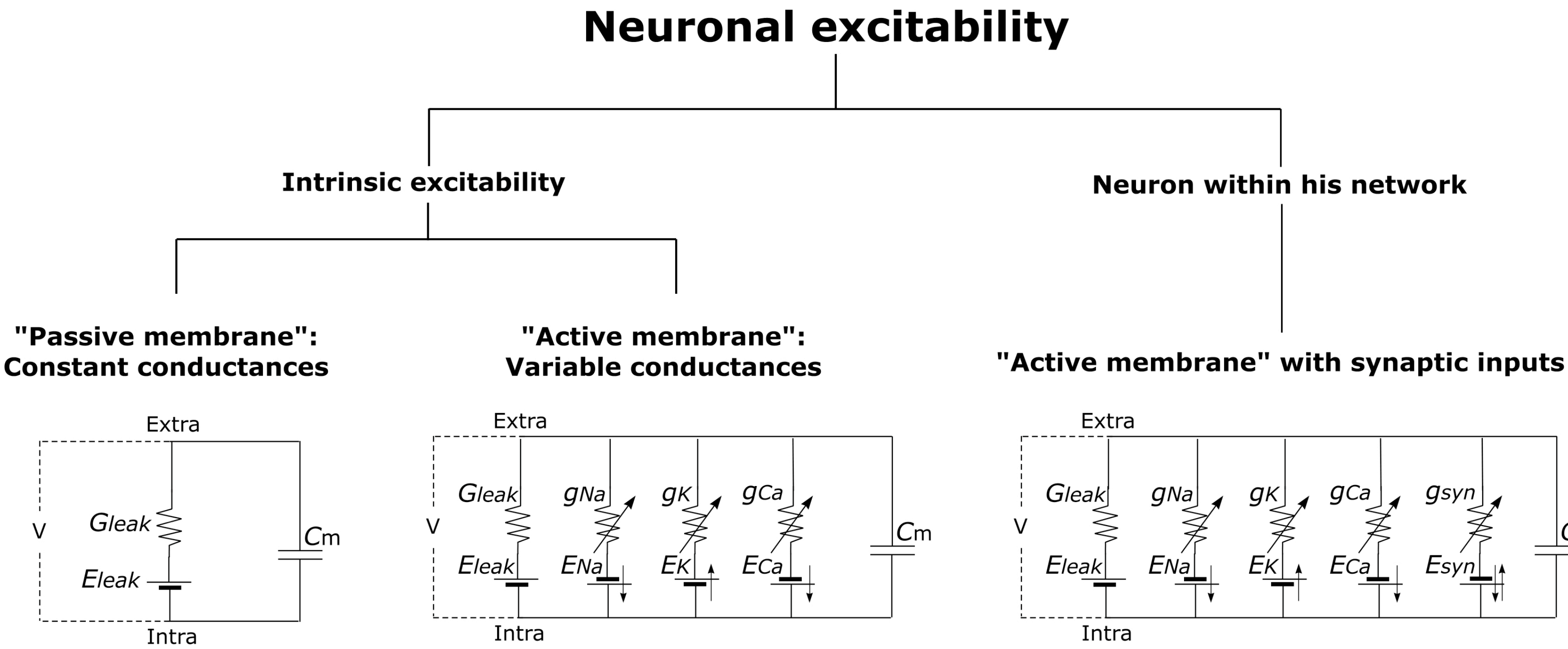




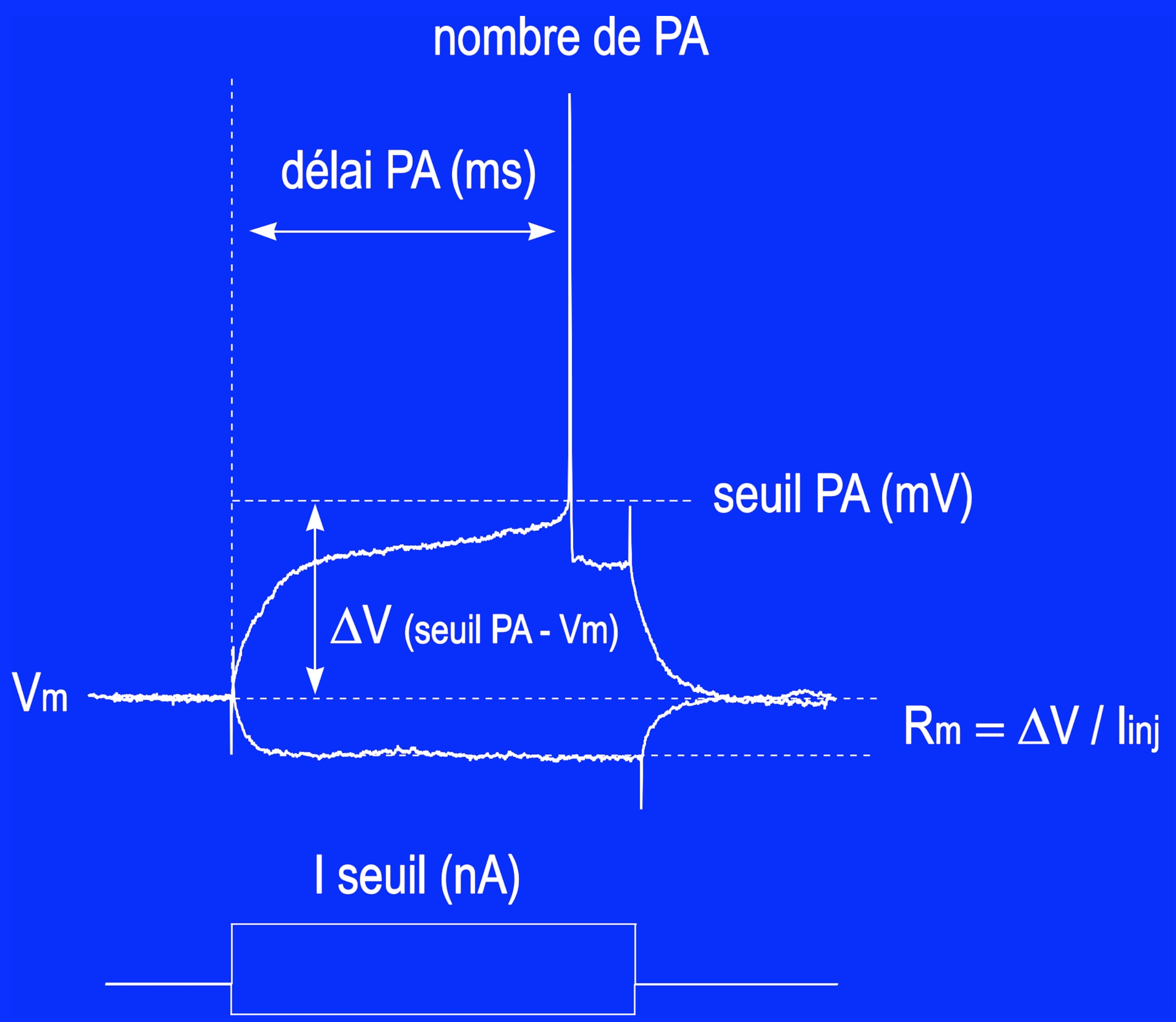
Clark et al, 2005

Information processing in neurons

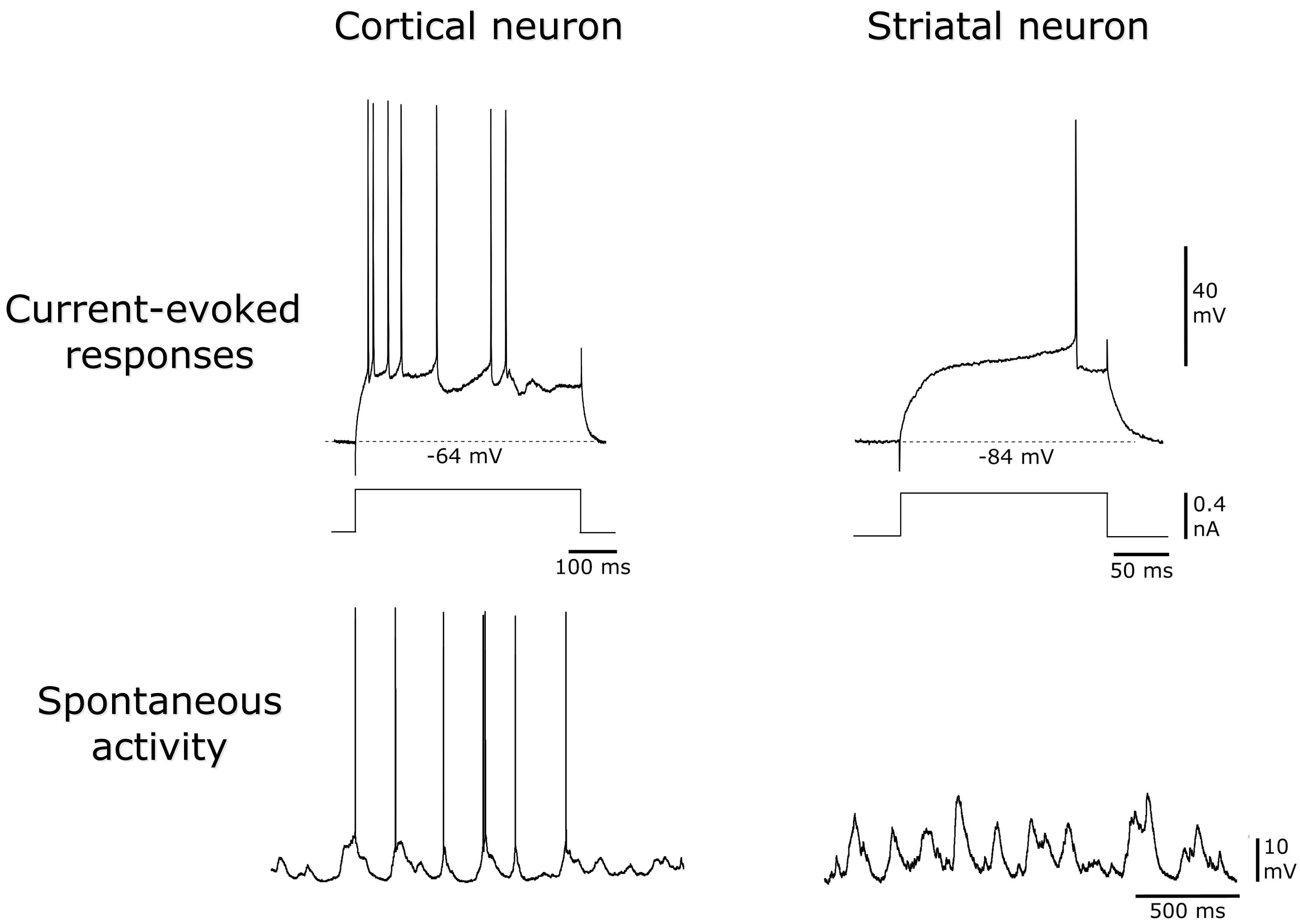
5. “Non-linear” excitability


Neuronal excitability
Intrinsic excitability
Neuron within his network
"Passive membrane":
Constant conductances
"Active membrane":
Variable conductances
"Active membrane" with synaptic inputs
Extra
Intra
V
Gleak
Eleak
Cm
gNa
gK
gCa
gsyn
ENa
EK
ECa
Esyn

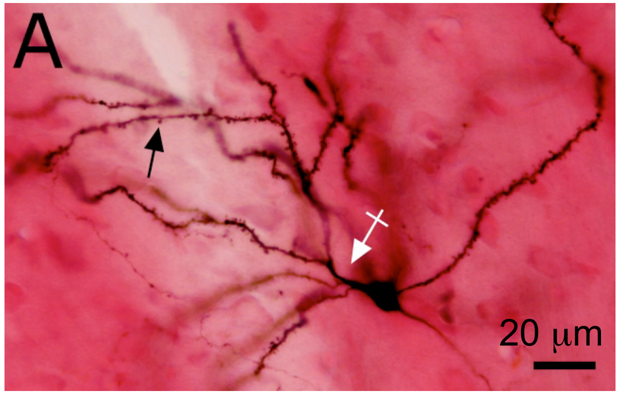
Some parameters relative to membrane excitability

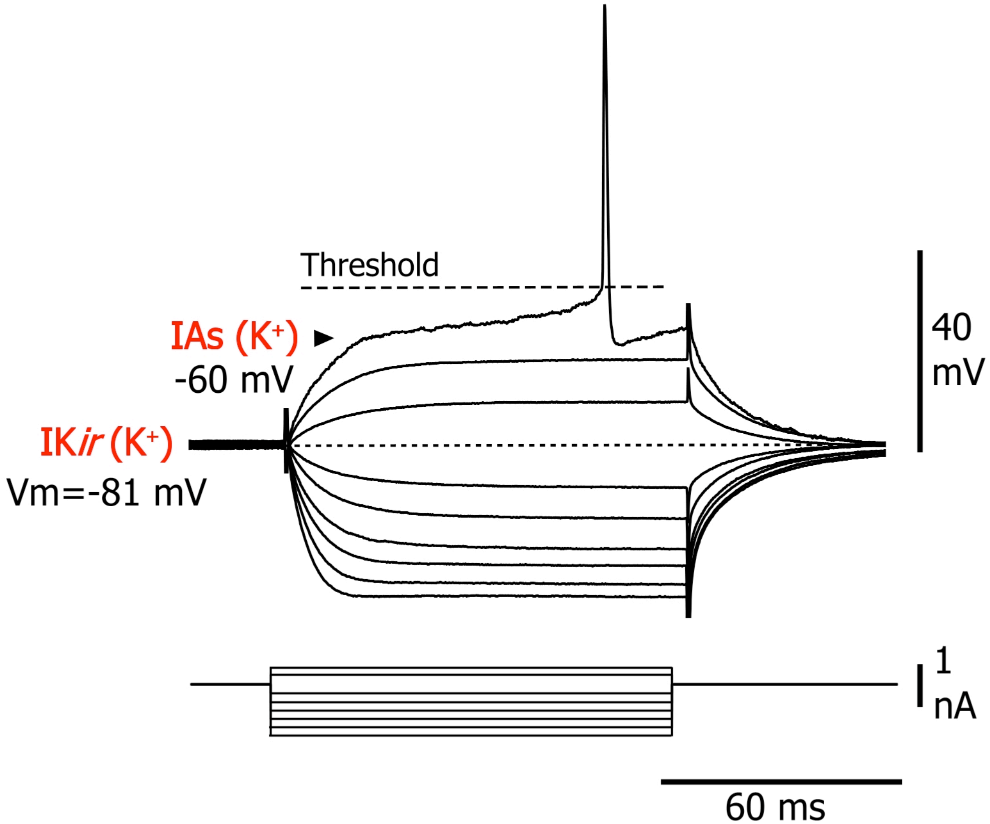


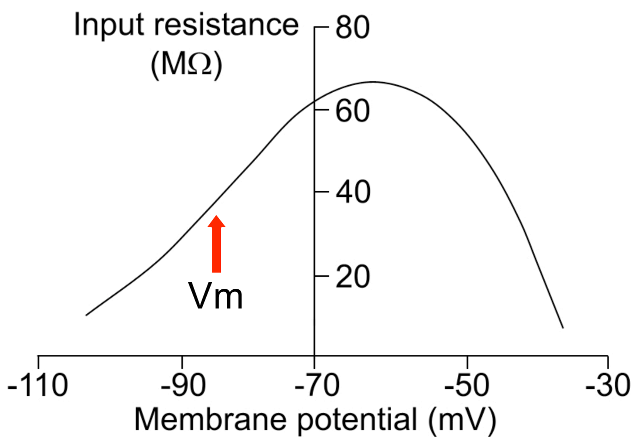
Comparative excitability



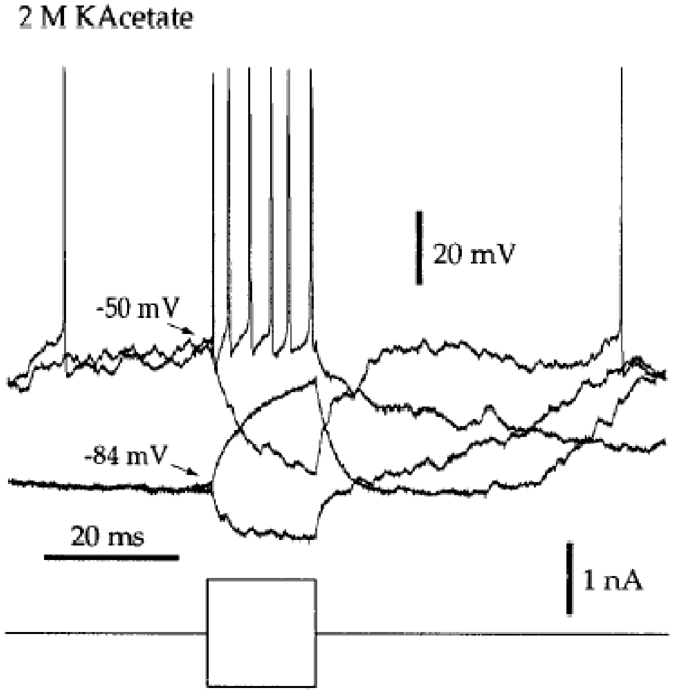
Example of non-linear electrical membrane properties

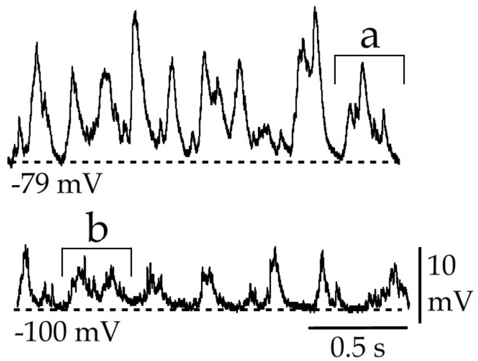


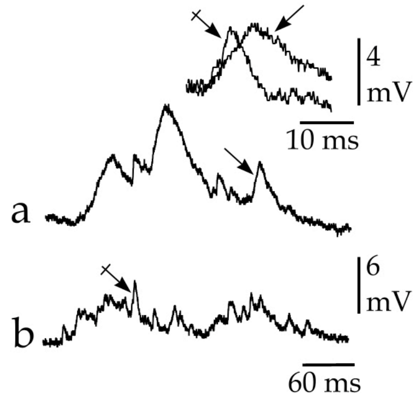




Impact of non-linear electrical membrane properties on synaptic integration







From Charlie Wilson

Conclusions

Three peculiar features of the Brain

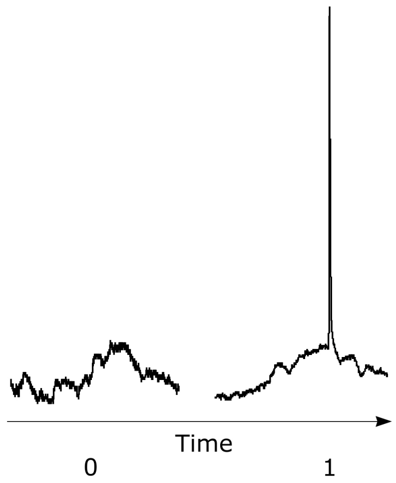
1. The brain information is theoretically infinite

2. Brain activity is probabilistic, highly variable and “state-dependent”

3. The brain is a liar

The brain information is theoretically infinite

Binary code of information (Shannon' theory)



If f_{max} = 1000 Hz (refractory period)

⇓

In one sec, in one cell, 2^{1000} choices…

⇓

In the human brain (10^{12} neurons) => $2^{1000} . 10^{12}$ choices for one sec

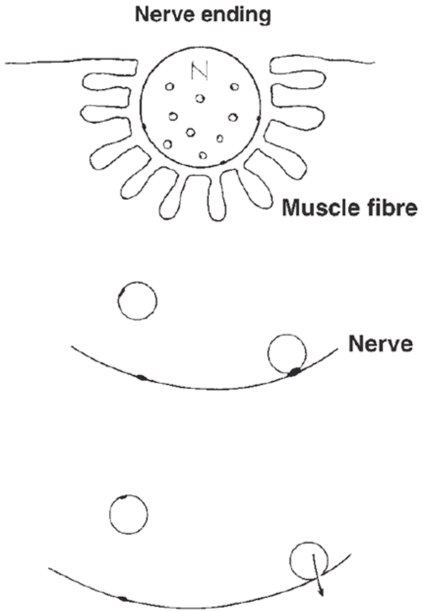
($2. 10^{9}. 2^{1000} . 10^{12}$ for one life)

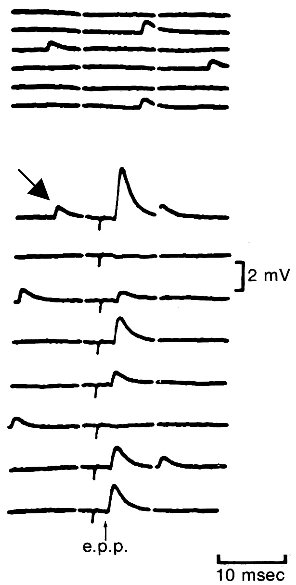
(# of atoms in the Universe = 10^{80})

The synaptic transmission is probabilistic

(Katz, Del Castillo, Fatt; 1952-1954)

Quantal parameters



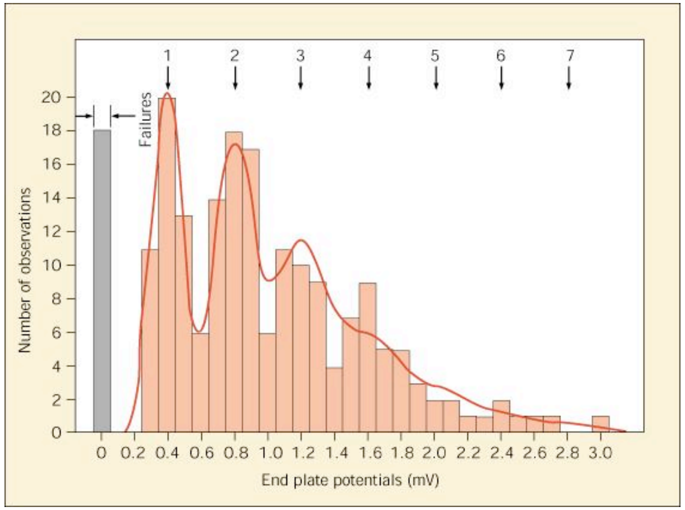


q = miniature eep (“quantum”)
p = probablility of release
n = total # of packets available for release
m = average # of packets released (=n.p)
Thus m = mean response/mean q

Mean response (number trials) = n.p.q
and
# of responses containing x quanta

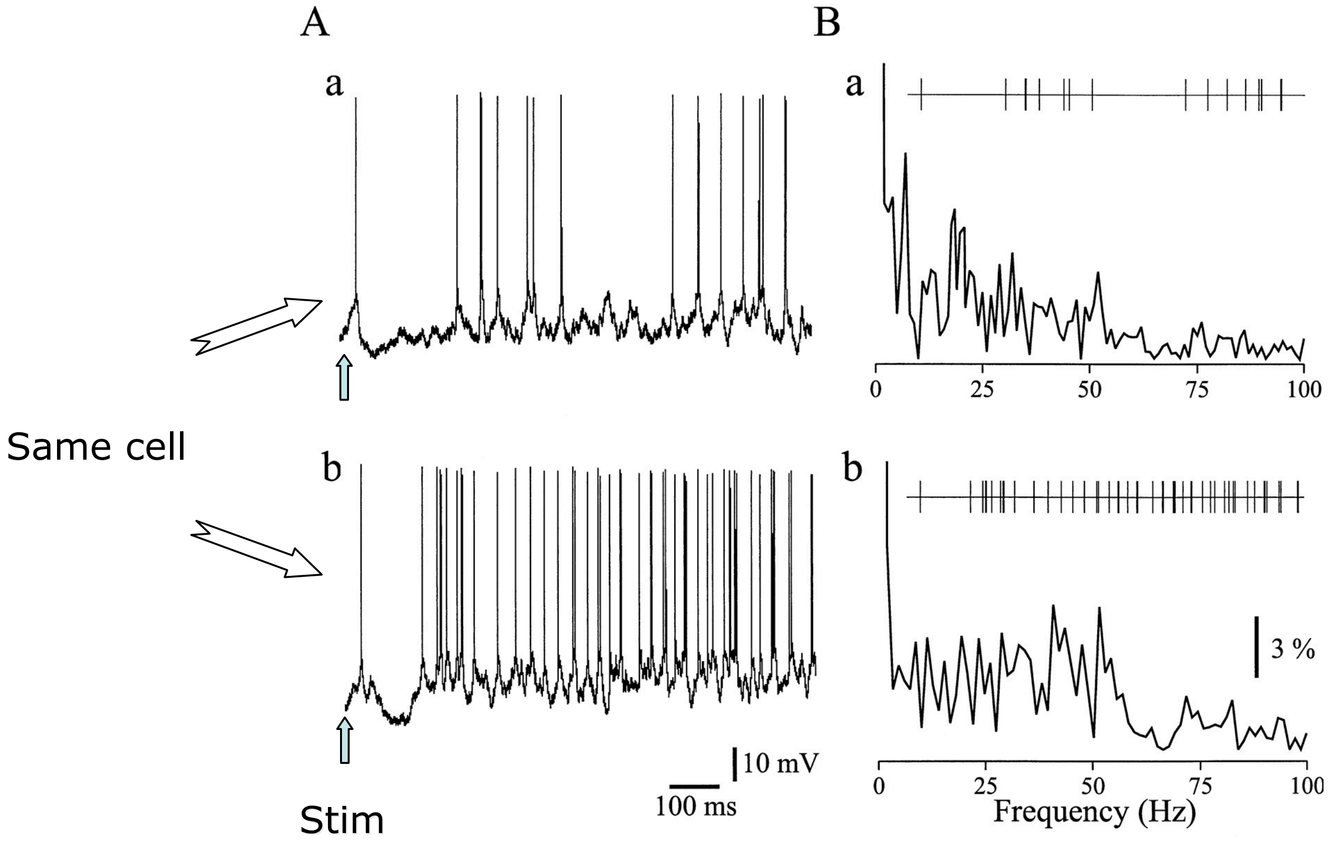
$$n_{x\,=}\ N.\ e^{-m}.\ x\ /\ x!$$

(with N = # of trials)



Brain activity is highly variable and “state”-dependent

Sensory integration in visual cortical neurons

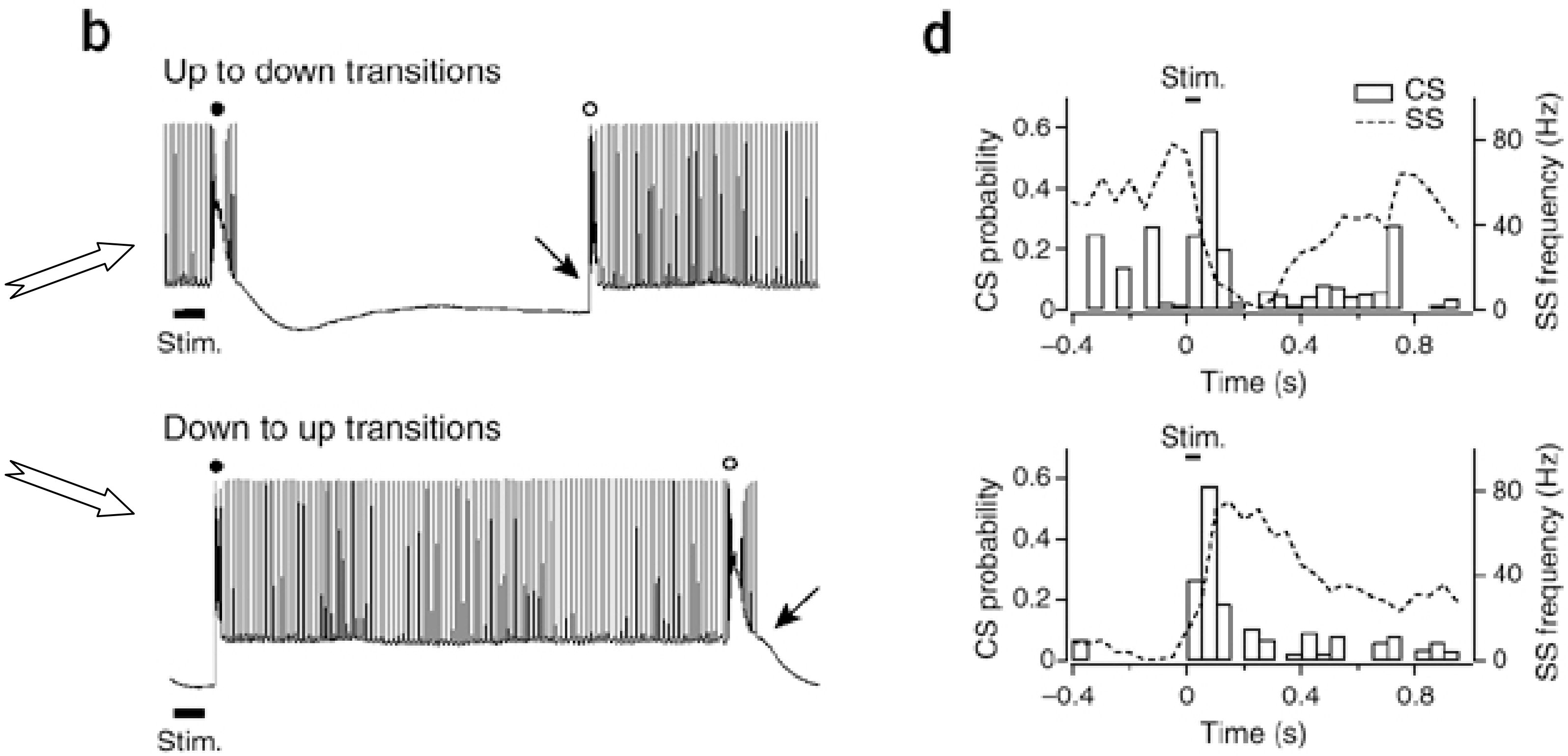


From Azouz and Gray, 199

Brain activity is highly variable and “state-dependent”

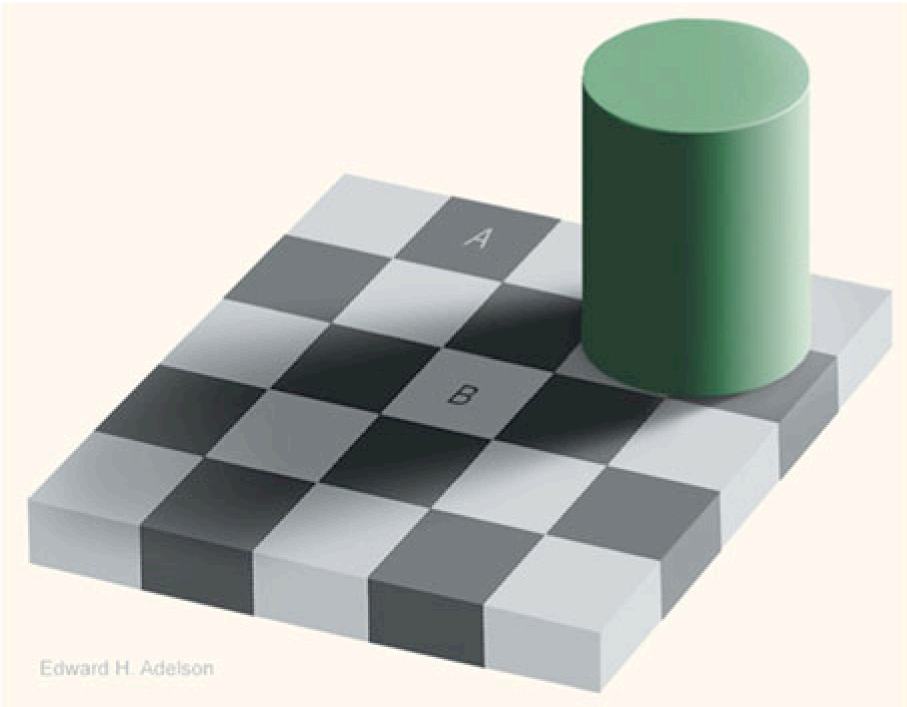
Sensory integration in cerebellar Purkinje neurons

Same cell



(From Mahon et al, 2005

Neural worlds and real worlds
The brain lies



(From Churchland and Churchland,

J. Physiol. (1952) 117, 500–544

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

By A. L. HODGKIN and A. F. HUXLEY
From the Physiological Laboratory, University of Cambridge

(*Received* 10 *March* 1952)

J. Physiol. (1952) 117, 431–460

THE RECORDING OF POTENTIALS FROM MOTONEURONES WITH AN INTRACELLULAR ELECTRODE

By L. G. BROCK, J. S. COOMBS and J. C. ECCLES
From the Departments of Physiology, University of Otago, Dunedin, and Australian National University, Canberra

(*Received* 13 *December* 1951)