# Neurophysiology - seminar

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# Excitable membrane

= ability of a membrane to respond to variations in electric and chemical gradients, to generate and conduct action potentials (AP)

# Types of ion channels

- ***Permanently opened*** - 2P potassium channels with 2 subunits (together with $Cl^-$ channels – resting *MP)*
- ***Voltage gated*** – $Na^+$,$Ca^{2+}$, $K^+$, $Cl^-$, $H^+$ channels- change conformation **with voltage, they are opened** (sometimes closed – e.g.. K+ channels in dendrites of neurons) by depolarization,
- ***Chemically gated*** – **receptor-channel**; **ligand** (receptor), mostly neurotransmitters :
  - **receptors ionotropic**- iont channel
  - **receptor metabotropic** – secondary messanger systems (G-proteins, IP3, etc.)
- ***pH gated*** (pain)
- ***mechanically gated***
- ***gated by other forms of energy***– e.g.. thermal energy

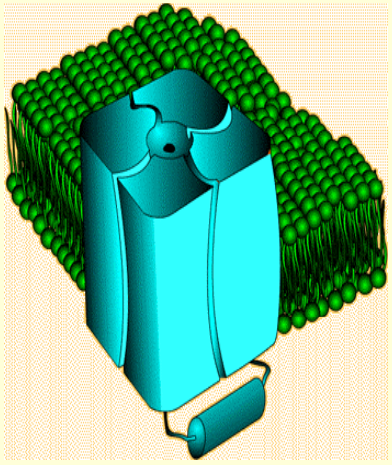
**Paramoecium** –

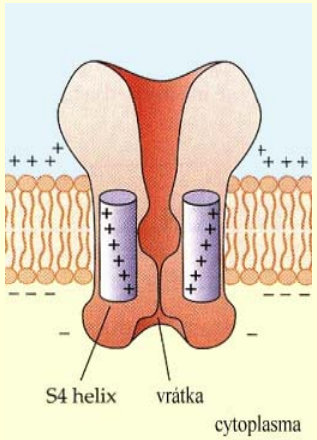
bangs into smt ⇒ $Ca^{+2}$ channels are mechanically opened - membrane depolarization – cillia backward movement
pushed forward ⇒ $K^+$ - hyperpolarization – speed up forward movement

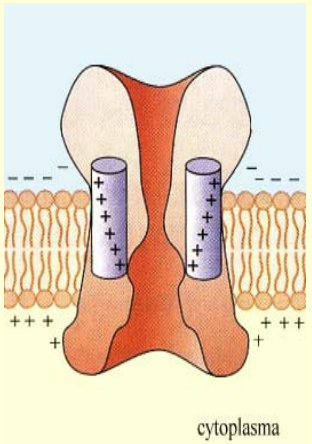
# $K^+$ channels

**opened** (2 subunits) - 2P-K channels – resting MP
**inward rectifiers** (- KIR)
**voltage-modulated** (Kv) (4 subunits)

**voltage-dependent** - 2 main levels :
**closed – opened**
**gated – c**onformation changes



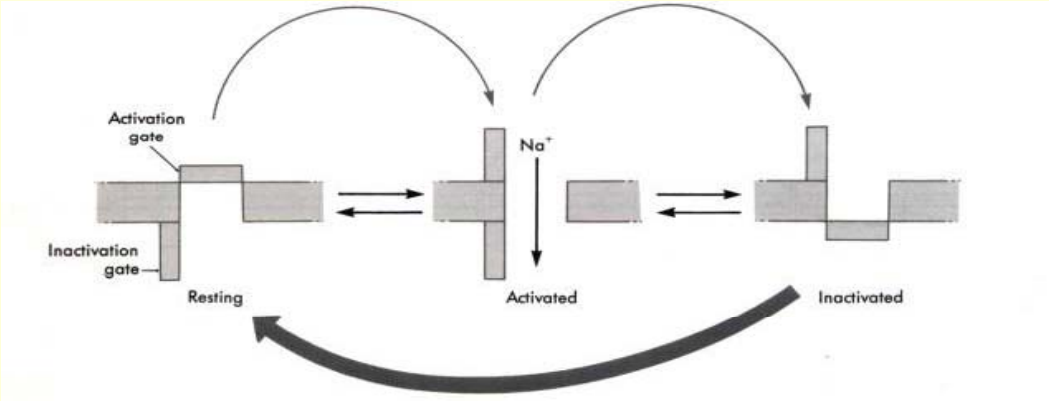



$K^+$ channel closed opened

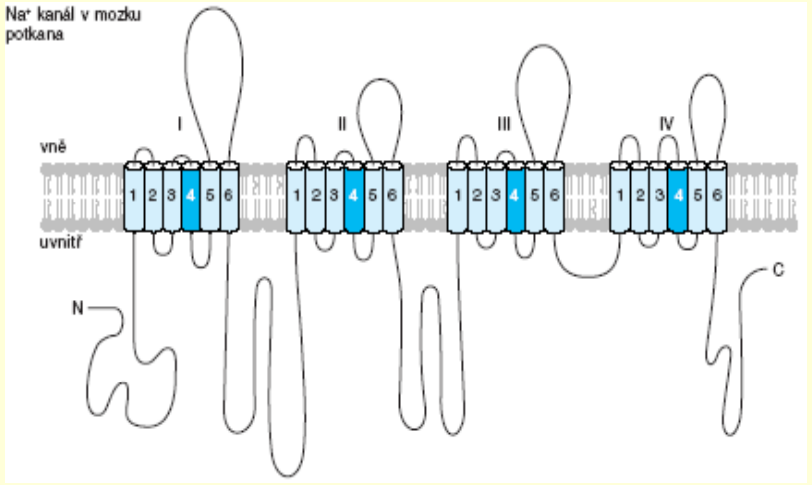
# $Na^+$ channels

Voltage gated




**Epithelial Na channel (ENaC)** – three subunits α, β, γ.

α- transfer of Na+, β a γ assist to subunit α increase transport of Na+
.(i.g. In kidney - regulatetion of ECT volume, aldosteron)



# Diffusion rate

Fick´s low (diffusion rate)

$J = -DA \Delta c / \Delta x$

Stokes – Einstein equilibration

$D = kT/(6 \pi r \eta)$

**Factors determining diffusion rate**

Diffusion surface (area)
Concentration difference
distance of diffusion
size of molecules
Viscosity (friction)
temperature

Lipid solubility
Ion charge

# Origin of resting MP

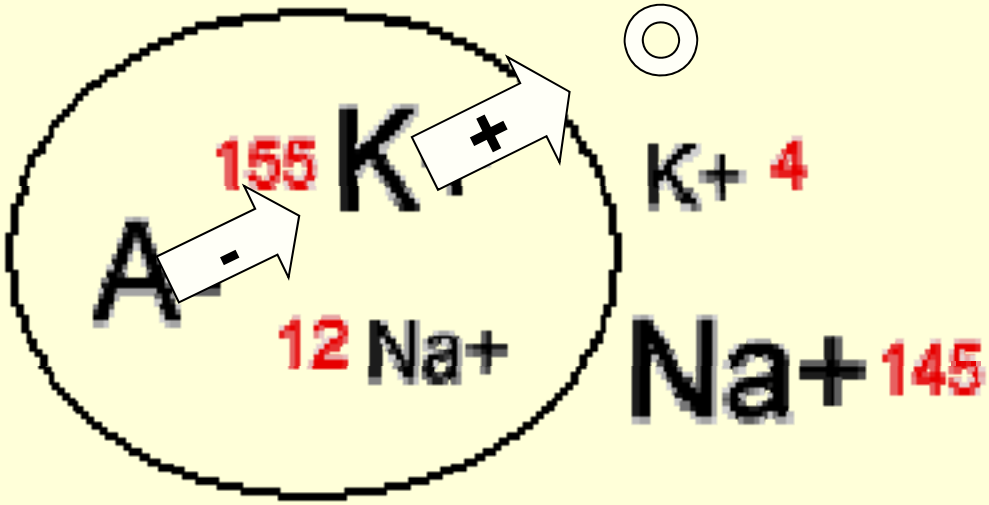
**Membrane = demarcation line between two different environments – shift of electrically charged chemic elements - ions**

**Membrane – resting stage - only $K^+$ ions permeability** (permeability for $Cl^-$ a $Na^+$ non-significant)

$K^+$ ions tendency to diffuse to the place with lower concentration

complementary **$A^-$** cannot accompany $K^+$

Potential – charge difference slows down $K^+$ ions out (Coulomb´s low)




inside - negative outside positive

Osmotic power (chemic gradient) forcing $K^+$ out (down of concentration gradient) reverse power – electric – protecting such movement

**dynamic equilibration = equalizing electric and chemic gradient**

(elektrochemic equilibration)

**http://www2.biomed.cas.cz/d331/vade/**

# Electro-chemic potential

Electrochemic equilibration $\Delta\mu_i$,

Two parts - diffusion (osmotic) work, electric work, replacement of some amount of electric charges between 2 solutions

Electrochemic potential for the ion

$$\Delta\tilde{\mu}_i = RT \ln\frac{[x_i]_{II}}{[x_i]_I} + nF\Delta\psi$$

$[x_i]$ – ion concentration $x_i$ in solutions I a II, F - Faraday´s constant , n (or z) quantivalenceof ion (e.g.. n=+1 for $K^+$ and –1 for $Cl^-$).

$\Delta\Psi$ electric potential in Volts, i.e.

MEMBRANE POTENTIAL.

# Nernst´s equilibration

$$E_{ion} = RT/zF \ln [ion]_{out}/[ion]_{in},$$

where $R$ is the gas constant, $T$ the absolute temperature, $F$ the Faraday constant, and $z$ the charge of the ion. Substituting and converting to base 10 at body temperature,

$$E_{ion} = 61 \ (\log_{10} [ion]_{out}/[ion]_{in} ).$$

$$E_{Cl} = \frac{RT}{FZ_{Cl}} \ln \frac{[Cl_o^-]}{[Cl_i^-]}$$

$$E_{Cl} = 61{,}5 \log \frac{[Cl_i^-]}{[Cl_o^-]} \text{ při } 37\ ^\circ C$$

$E_{Cl}$ = equilibration potential for $Cl^-$
R = gas constant
T = absolut temperature
F = Faraday`s constant
(počet coulombů na mol náboje)
$Z_{Cl}$ = quantivalence $Cl^-$ (–1)
[Clo–] = concentration Cl– out, [Cli–] = concentration Cl– inside of cell

# Goldman´s equilibration

membrane potential

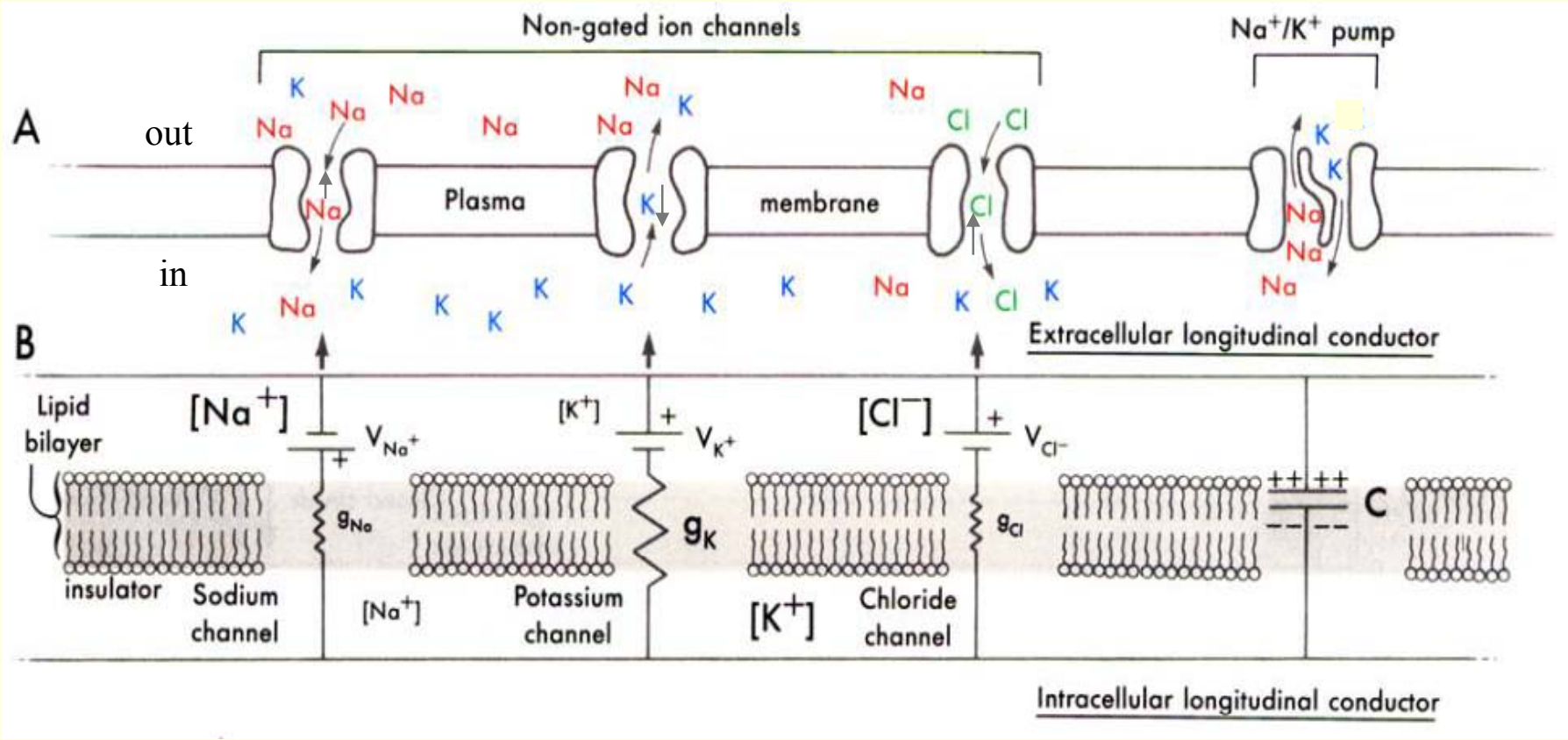
$$V = \frac{RT}{F} \ln \frac{P_{K^+}[K_o^+] + P_{Na^+}[Na_o^+] + P_{Cl^-}[Cl_i^-]}{P_{K^+}[K_i^+] + P_{Na^+}[Na_i^+] + P_{Cl^-}[Cl_o^-]}$$

V - membrane potential,
R – gas constant,
T - absolute temperature,
F - Faraday constant
$P_{K+}$, $P_{Na+}$ a $P_{Cl-}$ permeability for $K^+$, $Na^+$ a $Cl^-$.
[ ] concentration
index *i* and *o* out – in (extra-, intracellular concentration)

# Resting membrane potential

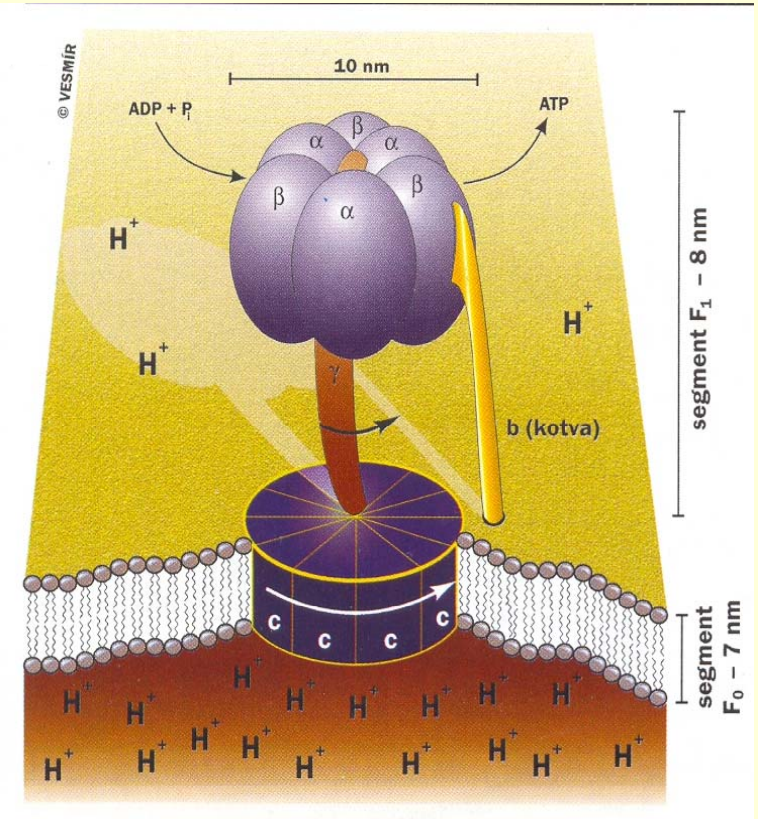
$NaCl \rightleftharpoons Na^+ + Cl^-$

$K^+ + HCO_3^- \rightleftharpoons KHCO_3$




Haines, Fundamentel Neuroscience, 1997, p. 33

# Proton pump




***Difference in electrochemic potencials of protons H+*** (secondarily of other ions) ***is, besides ATP, universal source of energy using by cells***

# Electro-neuro-physiology

# Electric impulses in the NS

1. LOCAL POTENTIALS OR CURRENTS - graded, spreading with decrement (**generator or receptor potentials)**

- sensory terminals – transduction of energy i.e. mechanic or thermal to elektric (graded according to the number of activated receptor cells)
- synapses (**post)synaptic potential** (current), graded according to
  - number of excreted quanta of neuromediators:

    inhibitory (hyperpolarization of postsynaptic membrane several ms - Cl channels)

    excitatory (depolarization – Na and/or Ca cgannels)
  - number of active receptors (postsynaptic membrane)

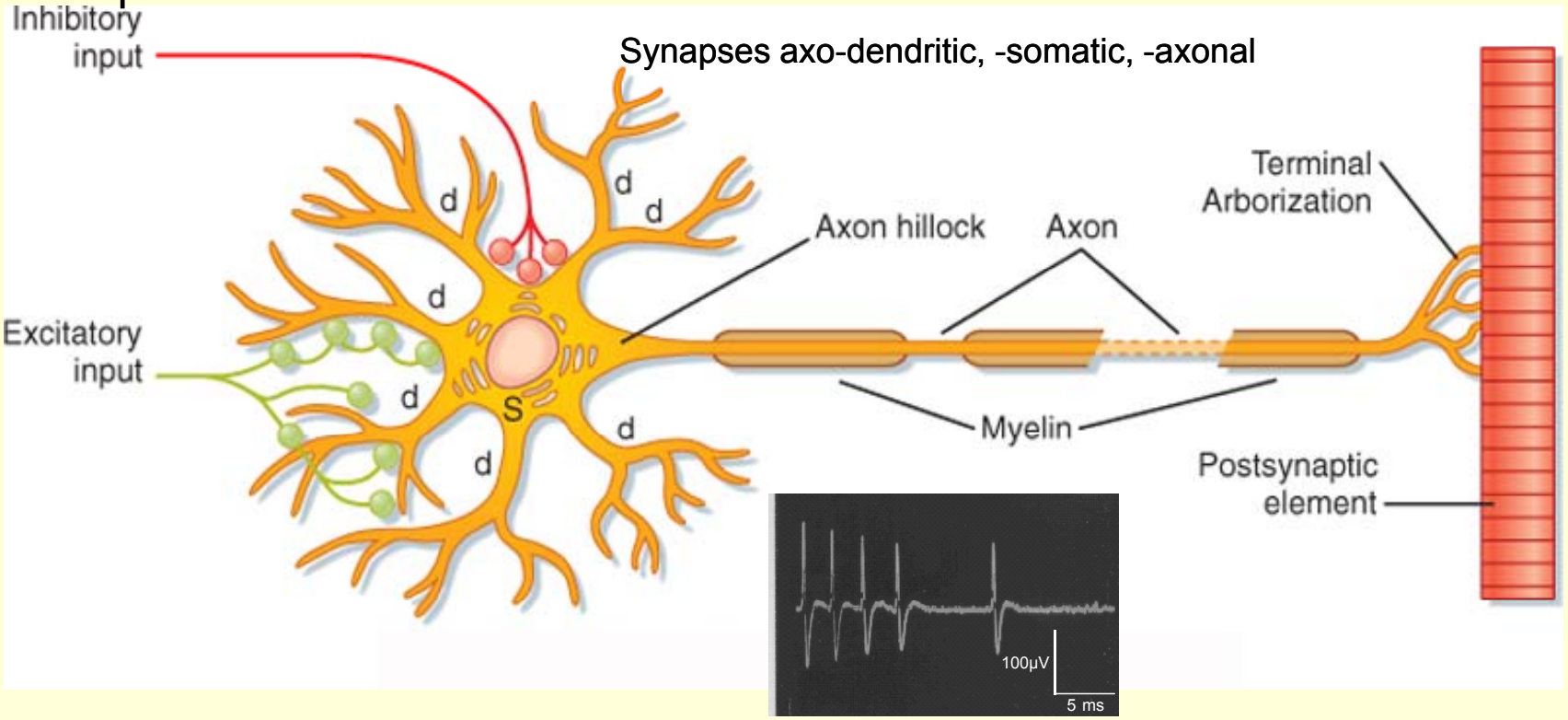
2. ACTION POTENTIALS (spikes)

# Neuron

= analogue-digital convertor evaluate analog inputs – continuous signal - sum of synaptic potentials

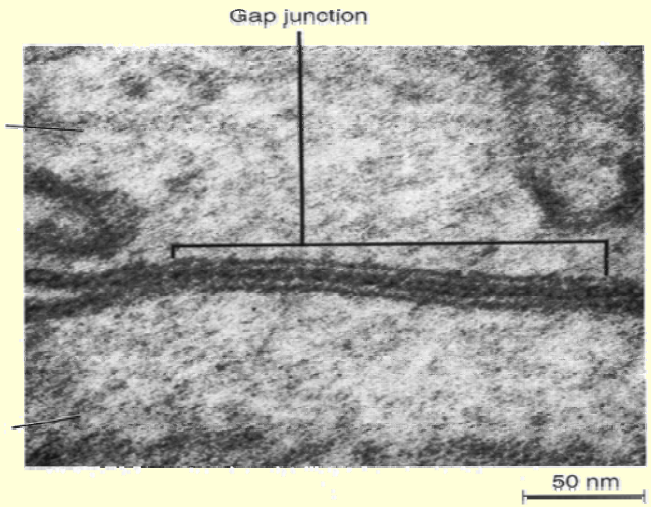
Result – action potential - yes (1) or no (0) ⇒ digital output „ all or nothing “.

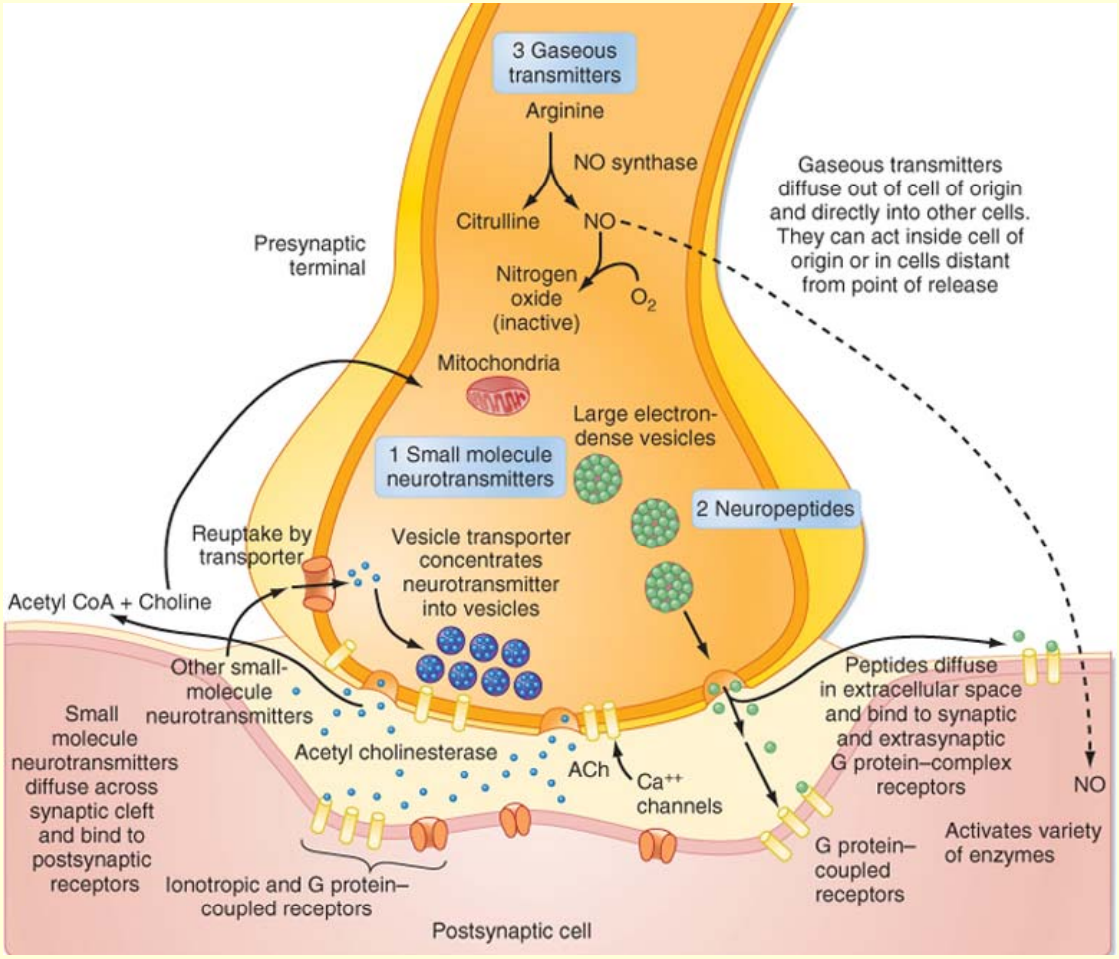
Neuron encods output information by latency, frequentation, amplitude of AP



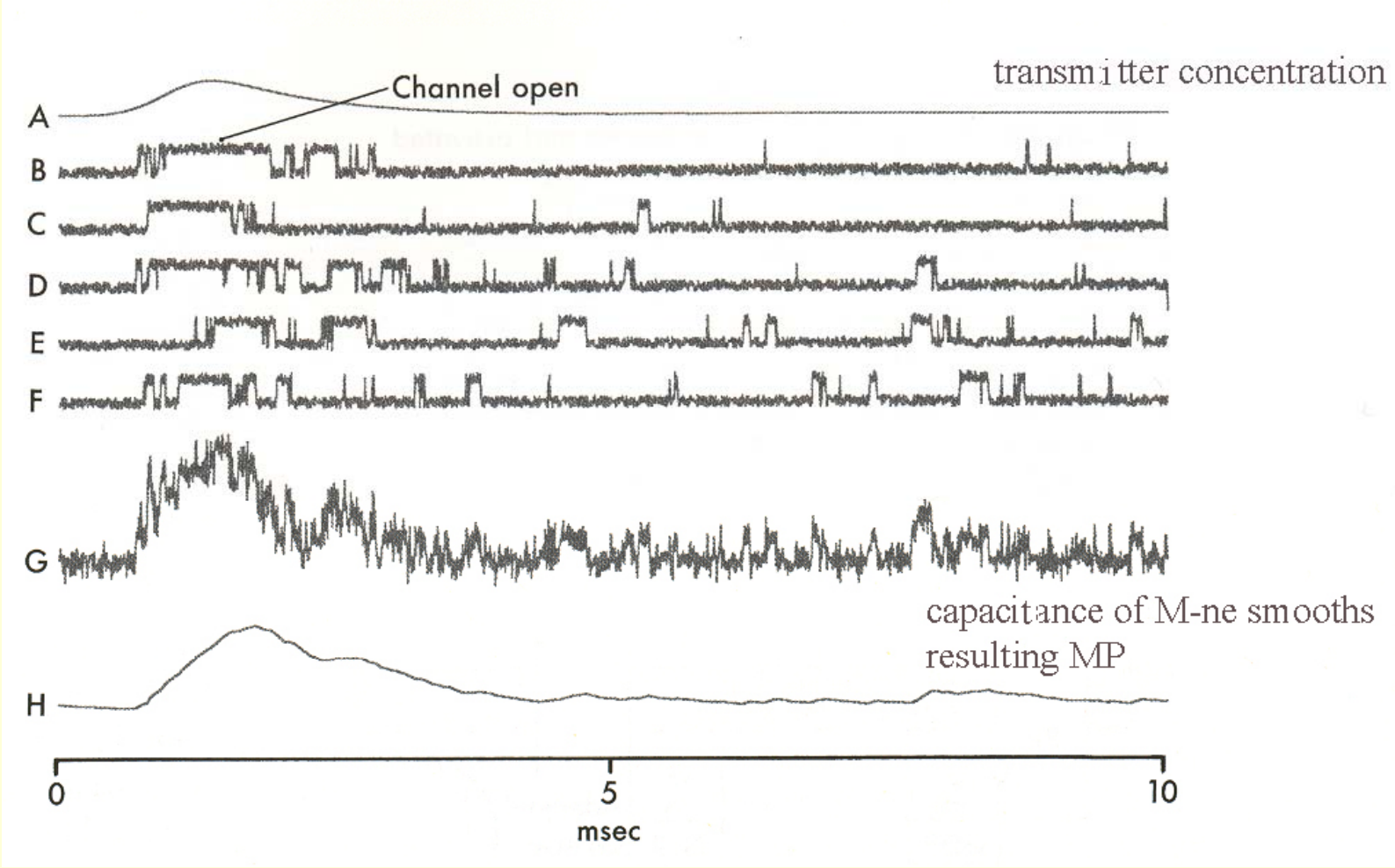
# Synaptic transmission

Electric synapse



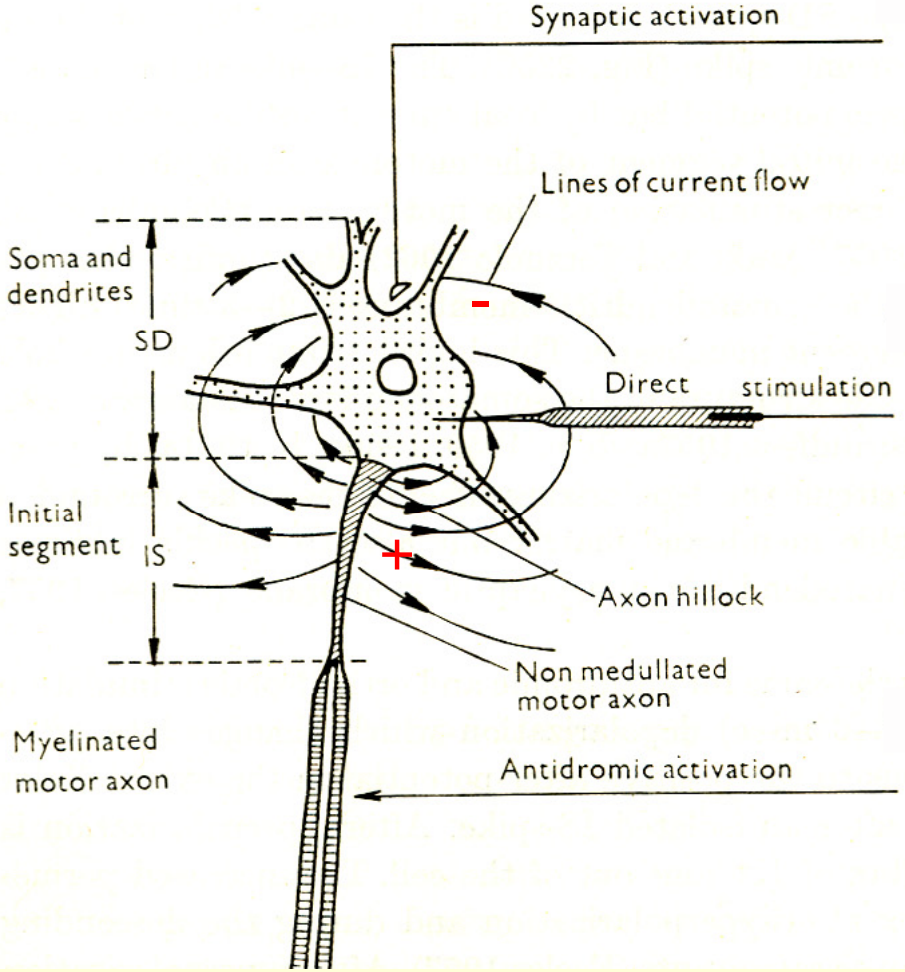



# Synaptic potential – sum of „channels“ potentials

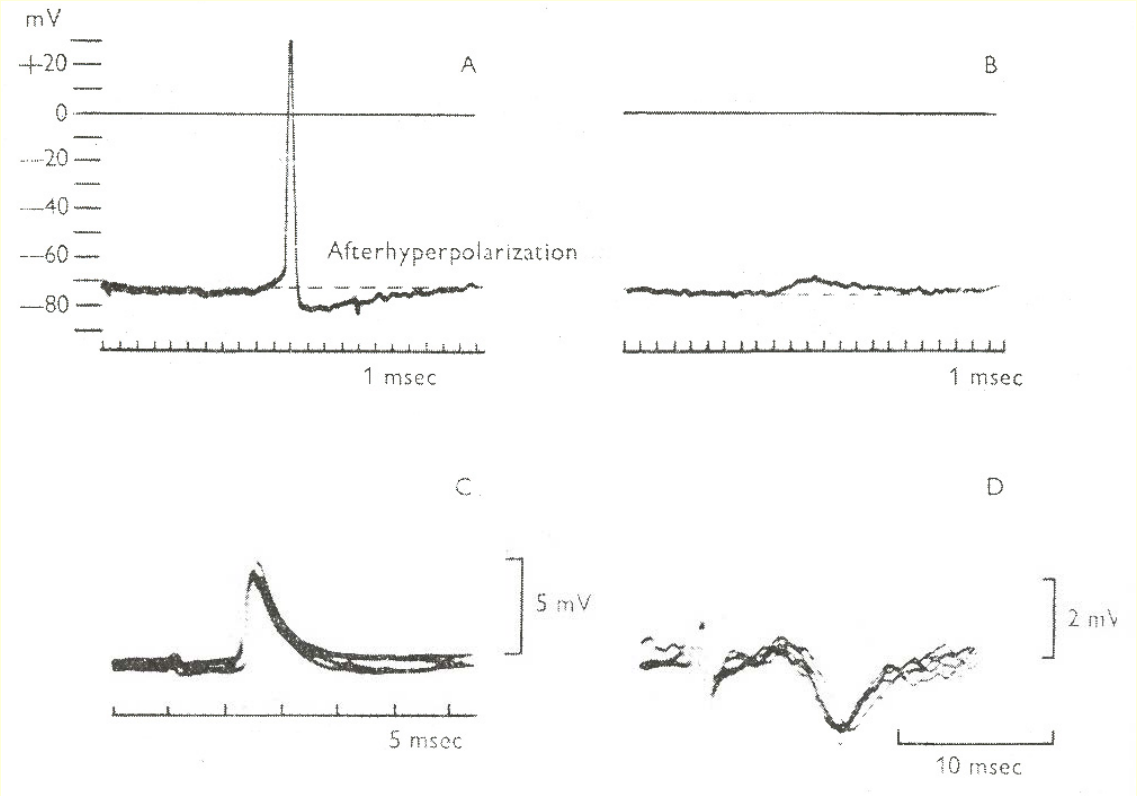



Haines, Fundamentel Neuroscience, 1997, p. 45

# Activation of initial segment



# AP, EPSP, IPSP - motoneuron



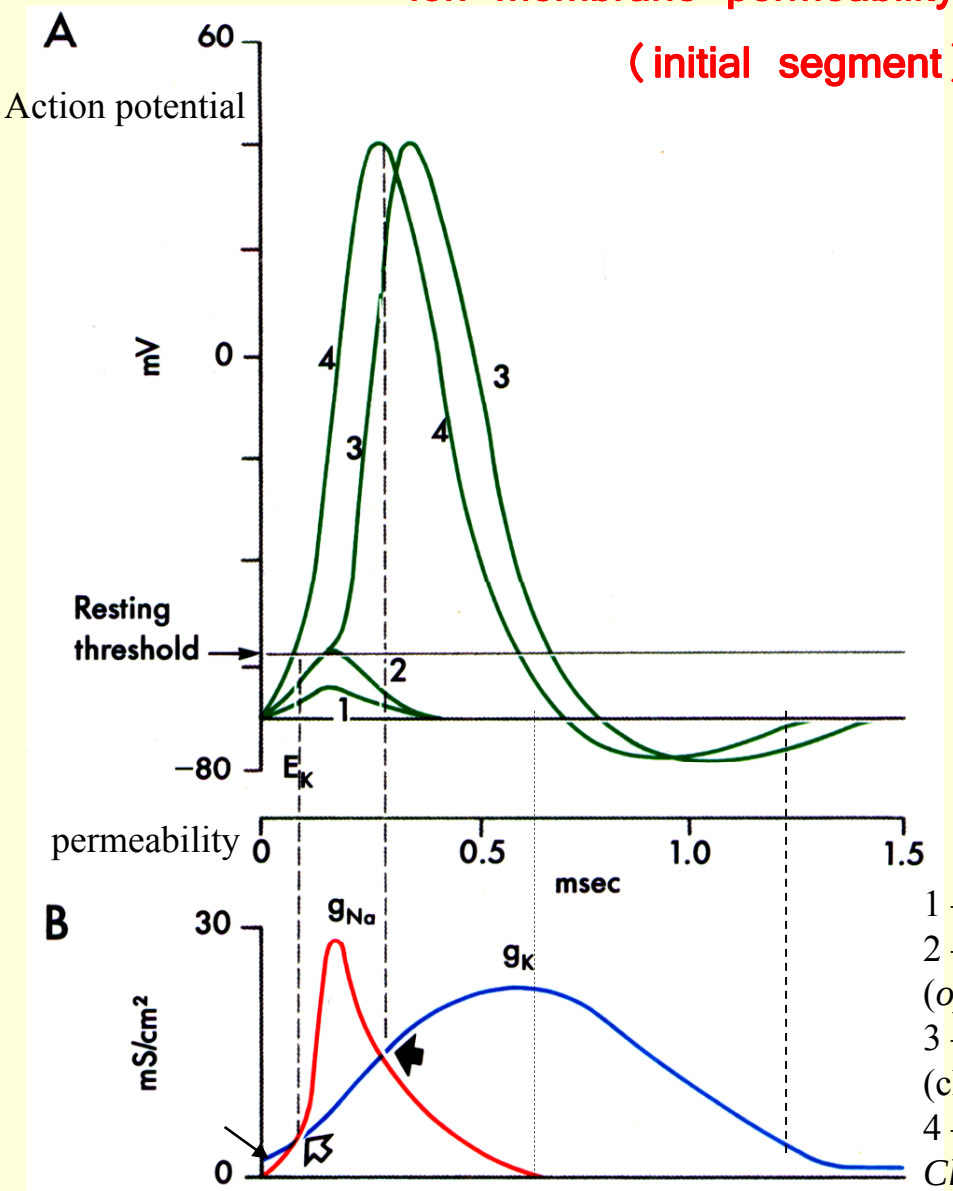

Ortodromic stimulation of n. gastrocnemius

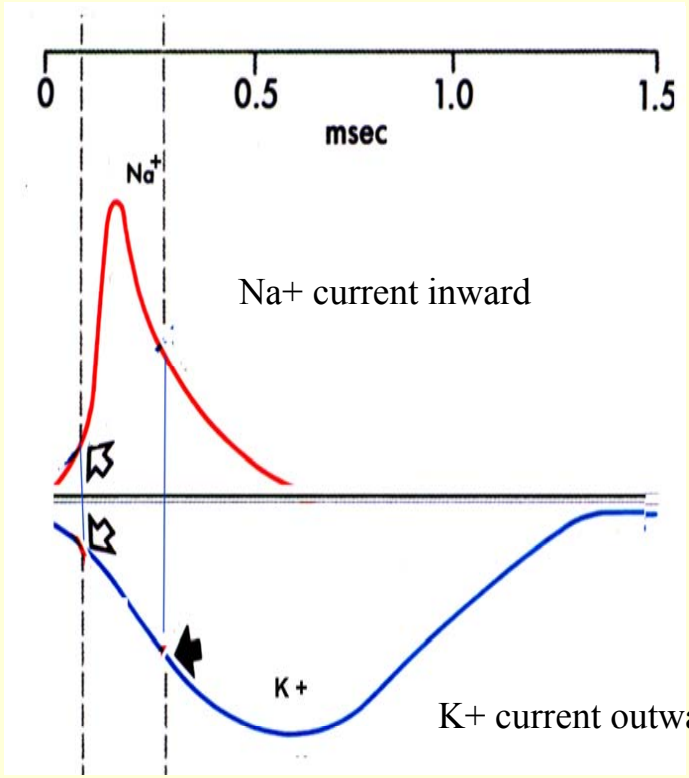
Stimulation of n. tibialis (antagonist)

Intracellularly recorded potentials of a cat motoneurone. A: Spike potential evoked by single orthodromic nerve volley in a cat gastrocnemius motoneurone. B: Excitatory postsynaptic potential (EPSP) in the same motoneurone evoked by single nerve volley of reduced size as compared with that used in A. C: EPSP recorded intracellulary in a medial gastrocnemius motoneurone by an afferent volley from medial gastrocnemius nerve. D: Intracellular record of inhibitory postsynaptic potential (IPSP) of a gastrocnemius motoneurone to a train of four impulses from the anterior tibial nerve. Records C and D are formed by the superposition of about ten faint traces.

# Ion membrane permeability during AP

## (initial segment)

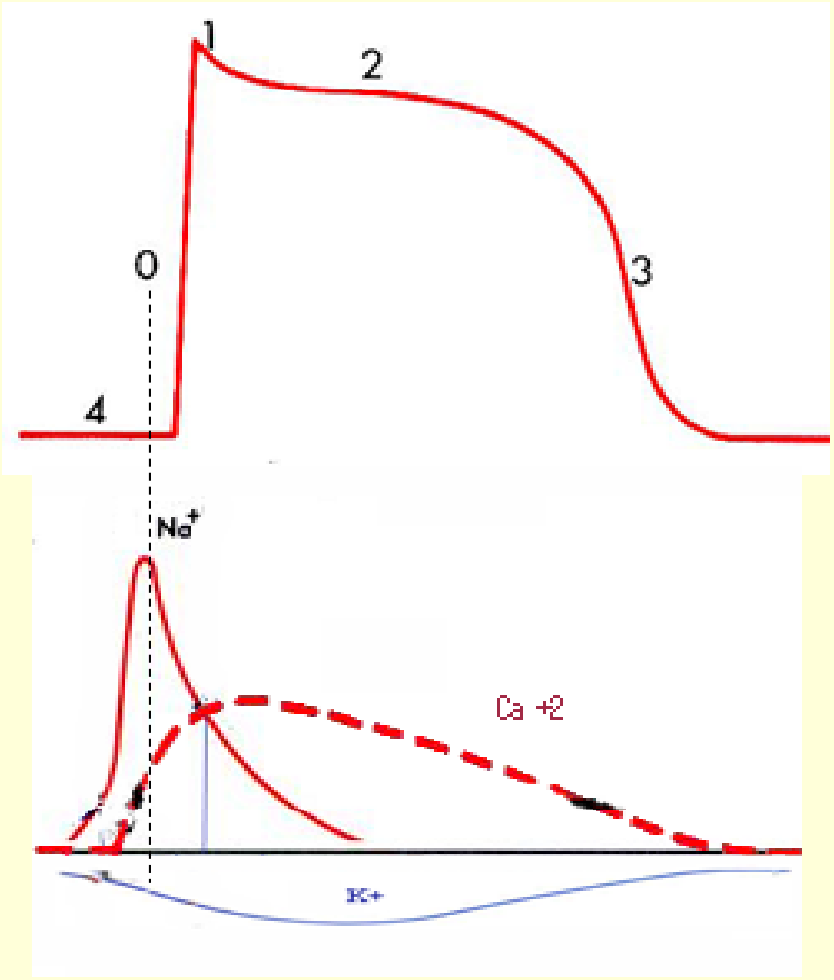


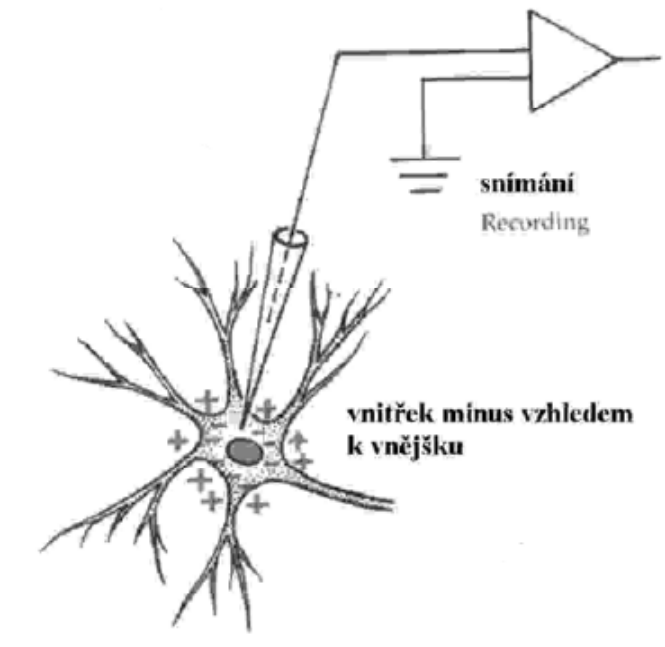

1 – subthreshold depolarization (EPSP) – $K^+ > Na^+$
2 – threshold depol. – $Na^+$ permeability = $K^+$ permeability (*open arrow*)
3 – action potential (AP) – high $Na^+$ permeability (chemic gradient), slowly increases $K^+$ permeability
4 – subthreshold depolarization (EPSP) – shorter latency
*Closed arrow* –peak of AP - permeability $K^+ = Na^+$
Hyperpolarization – permeability $K^+ >> Na^+$

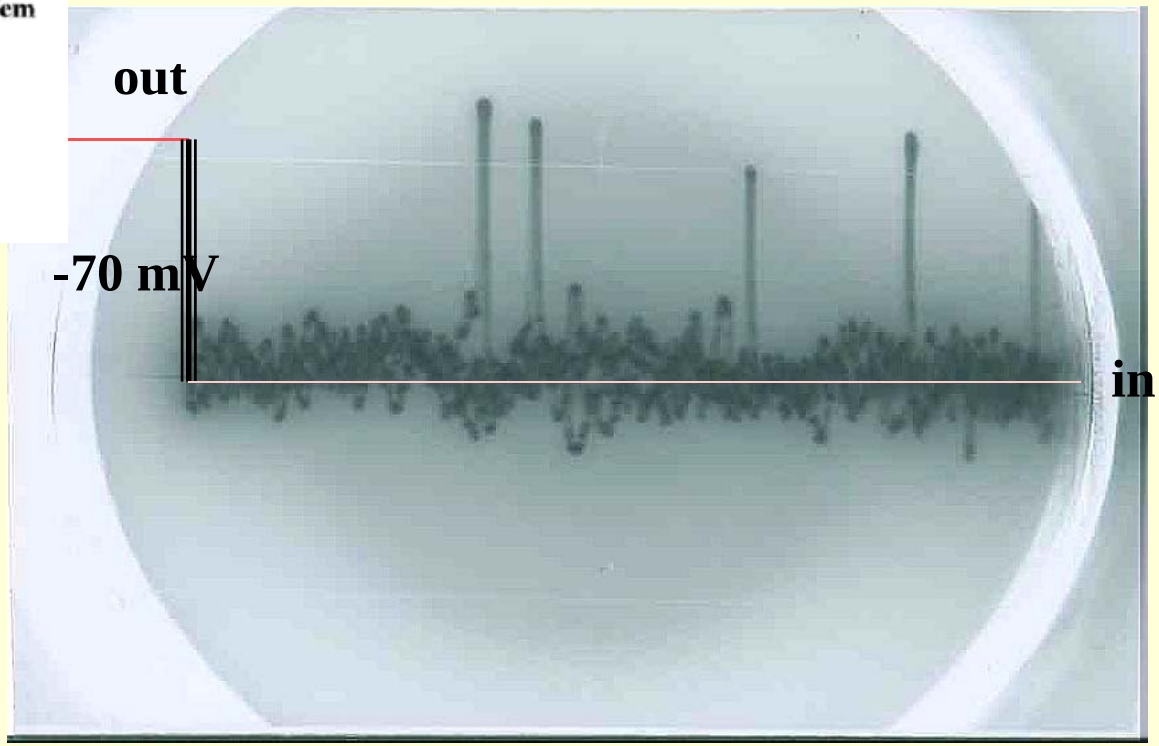
Haines, Fundamental Neuroscience, 1997, p. 37

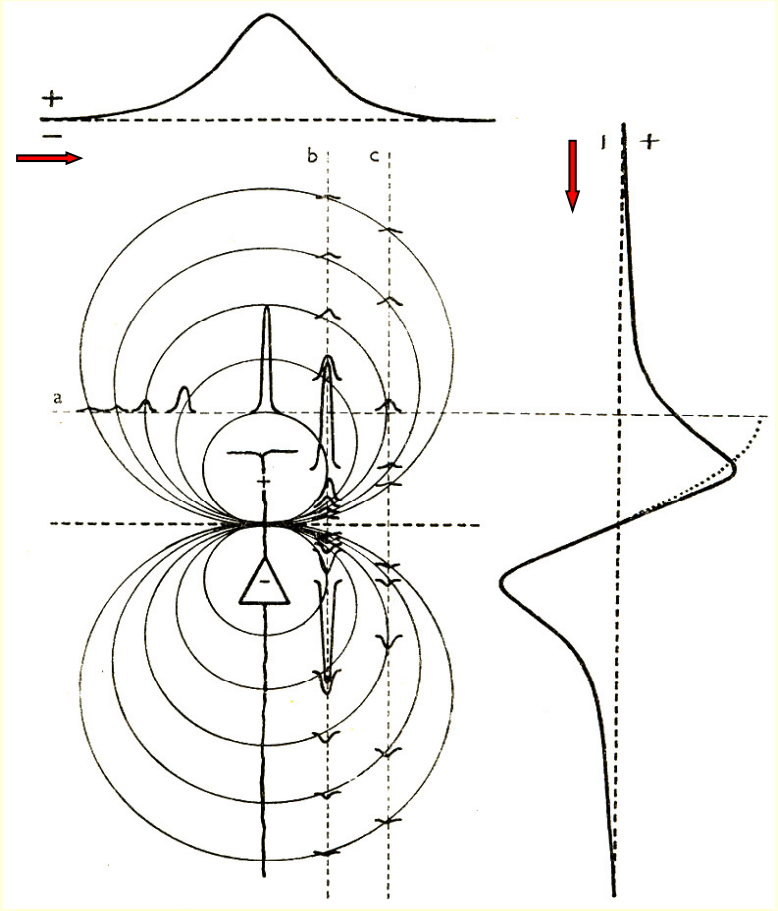
# AP – myocardium （？）



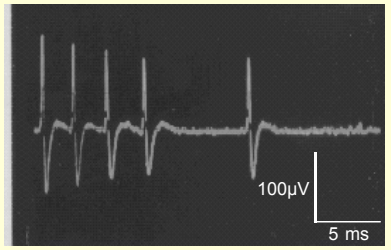
# Spontaneous neuron activity– intracellular registration






# Electric field of dipole




**Large electrode - summation of dipoles - EEG**

The field arising around an electric dipole, and characteristic equipotential lines. The thin, interrupted lines represent sections through this field perpendicular to the axis of the dipole (a) or parallel to it (b, c). The amplitude and polarity of deflections at the corresponding points of the field are illustrated. Top: spatial distribution of the dipole potential in plane *a*. On the side: spatial distribution of the dipole potentials in plane *b*, assuming a medium of indefinite extent (full line) and the actual voltage plot found in the cerebral cortex (dotted line).

# Modulation of signal

## Structural changes during signal reception and signal (information) processing and storage

**Short-term**

-different location and sensitivity of receptors in postsynaptic membrane

-sensitization and inhibition of channels – temporary conformation and configuration changes

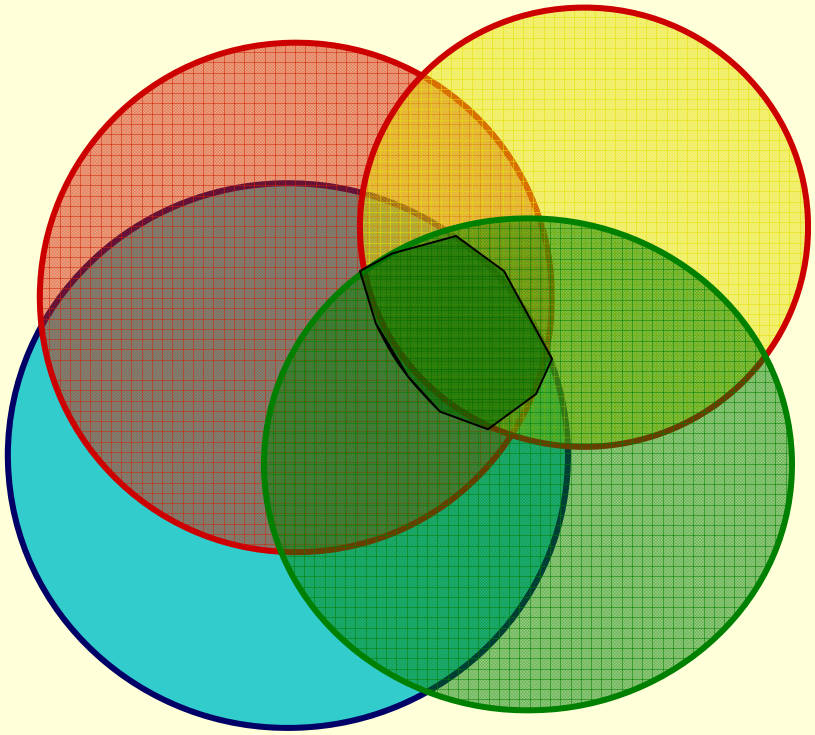
**Long-term**

(proteosyntheses, proteolyses, enzymes = > structural changes – e.g. swelling of dendrite spine – new receptors

Synaptogeneses – synaptic sprouting (GD)

???neurogeneses, gliogeneses ???

# Resulting information signal

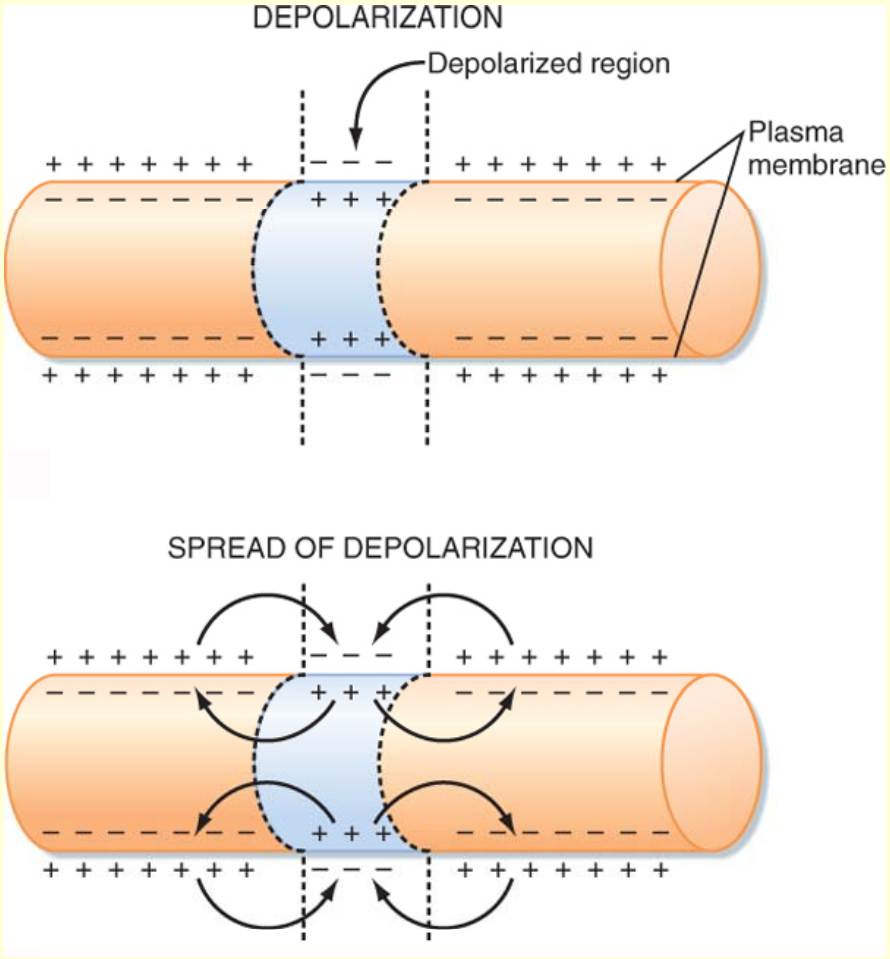


inhibitory
excitatory
chronological
stereometric

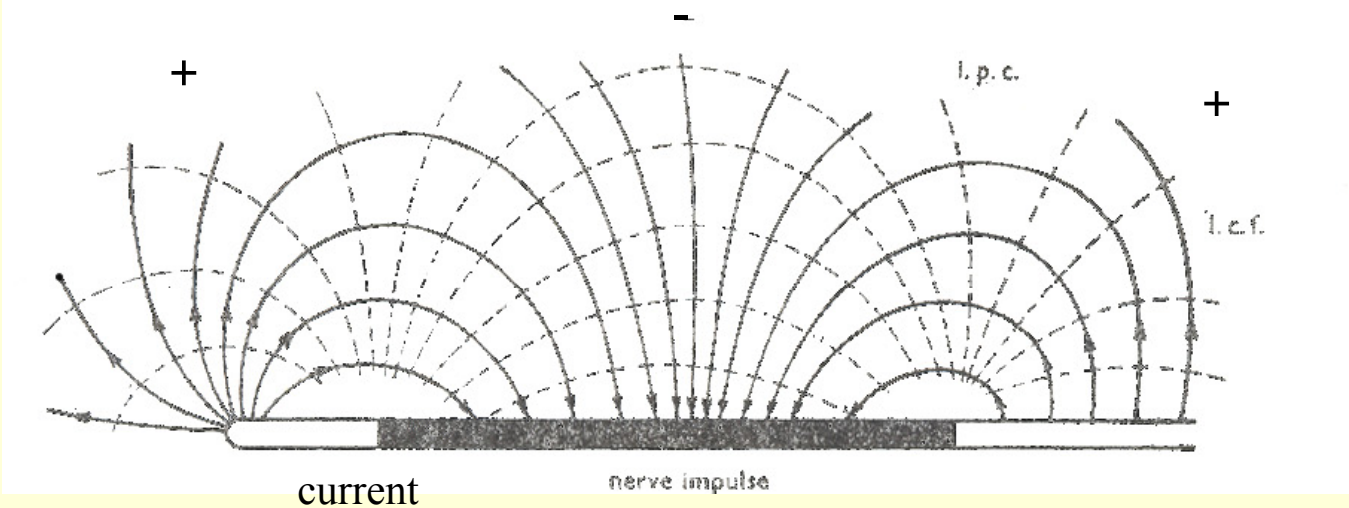
factors

**Trophic and growth factors - GLIa???** **Neuron ⟷ glia**

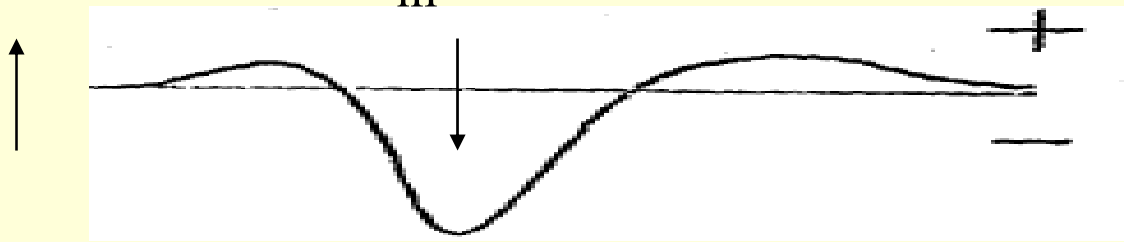
# Axon


DEPOLARIZATION
Depolarized region
Plasma membrane
SPREAD OF DEPOLARIZATION

Diagramatic representation of the distribution of the external current field in the nerve at the moment when the impulse wave is at the marked point, i. p. c. — isopotential contours, l. c. f. — lines of current flow, (diagramatically, according to Lorente de Nó (1947) and Kostyuk 1960).




out in



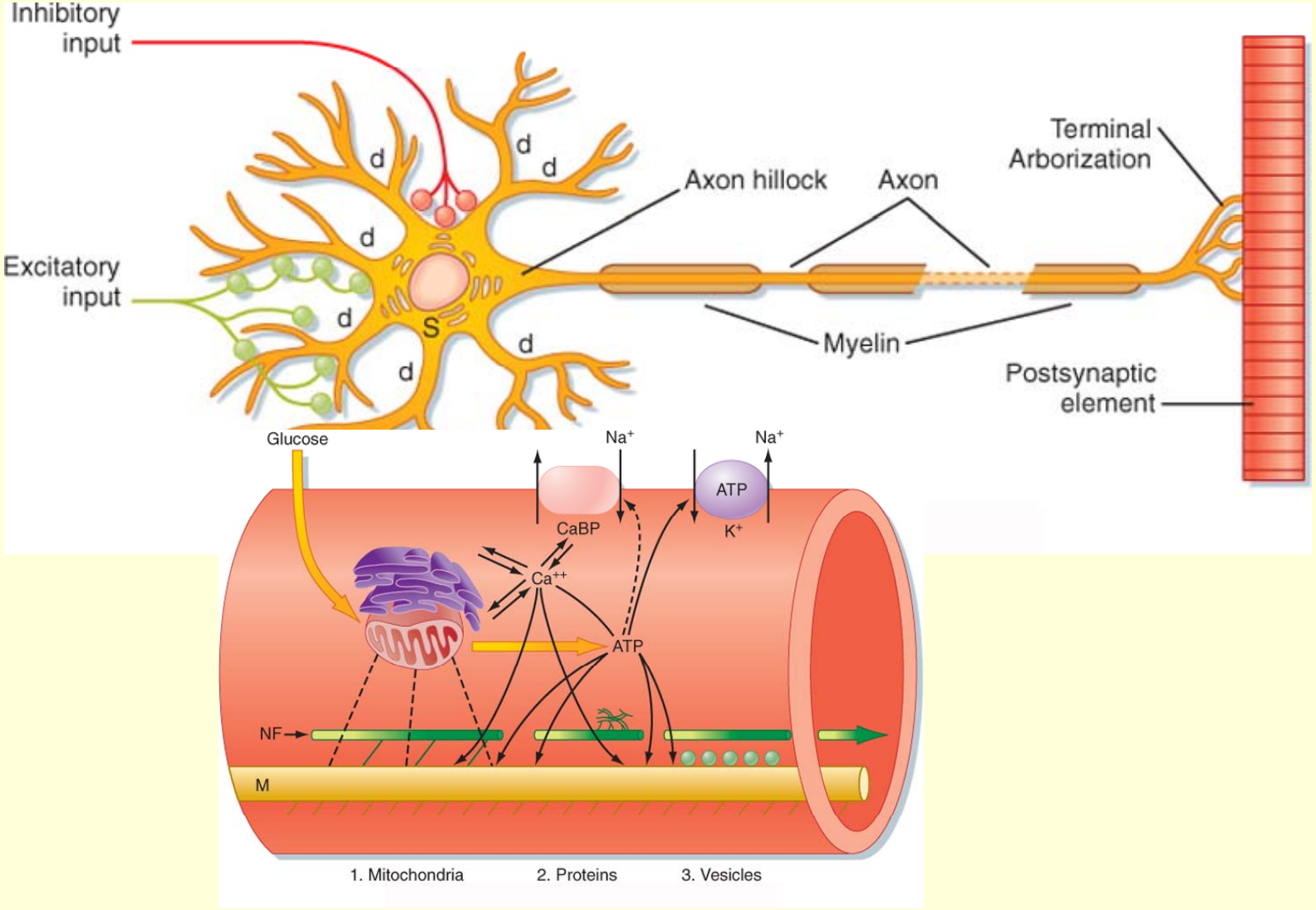
Unipolar registration – active electrode

- positive – if in the point of current outflow - higher M-ne potential than neighbour points

-Negative – current influx

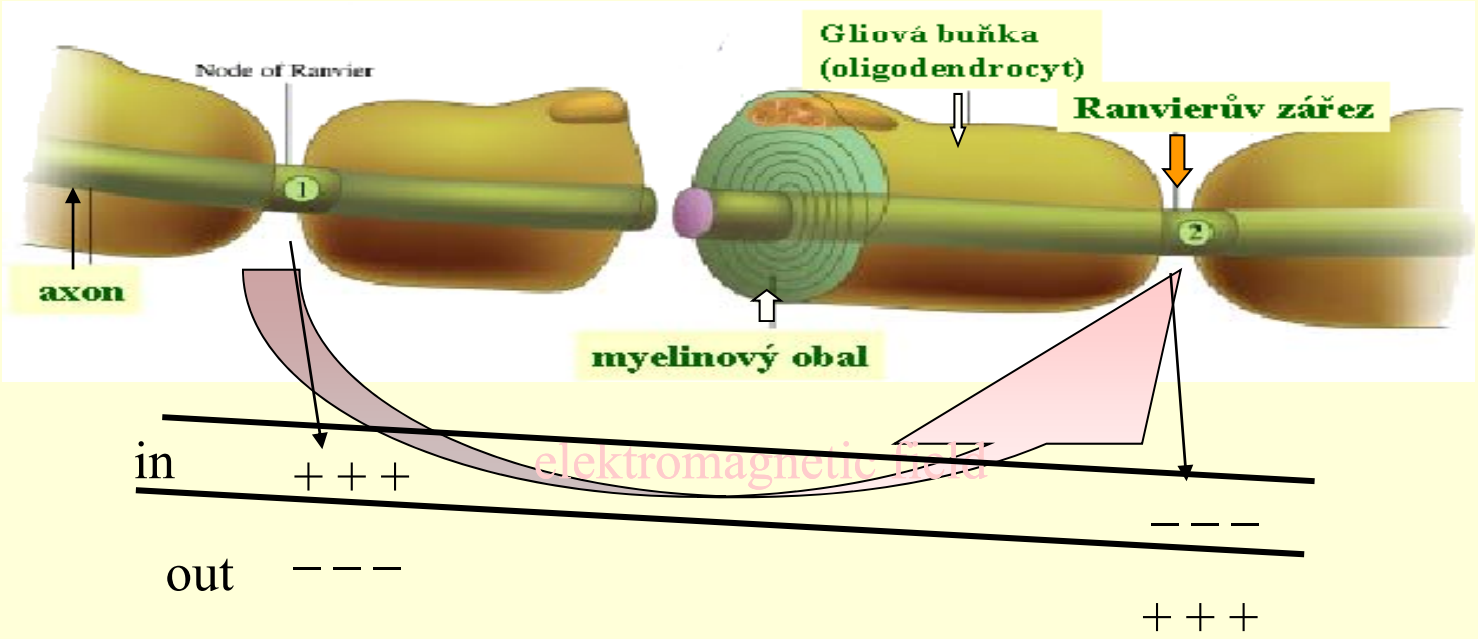
Stimulus moves under electrode ⟹ triphasic wave

# Axonal transport



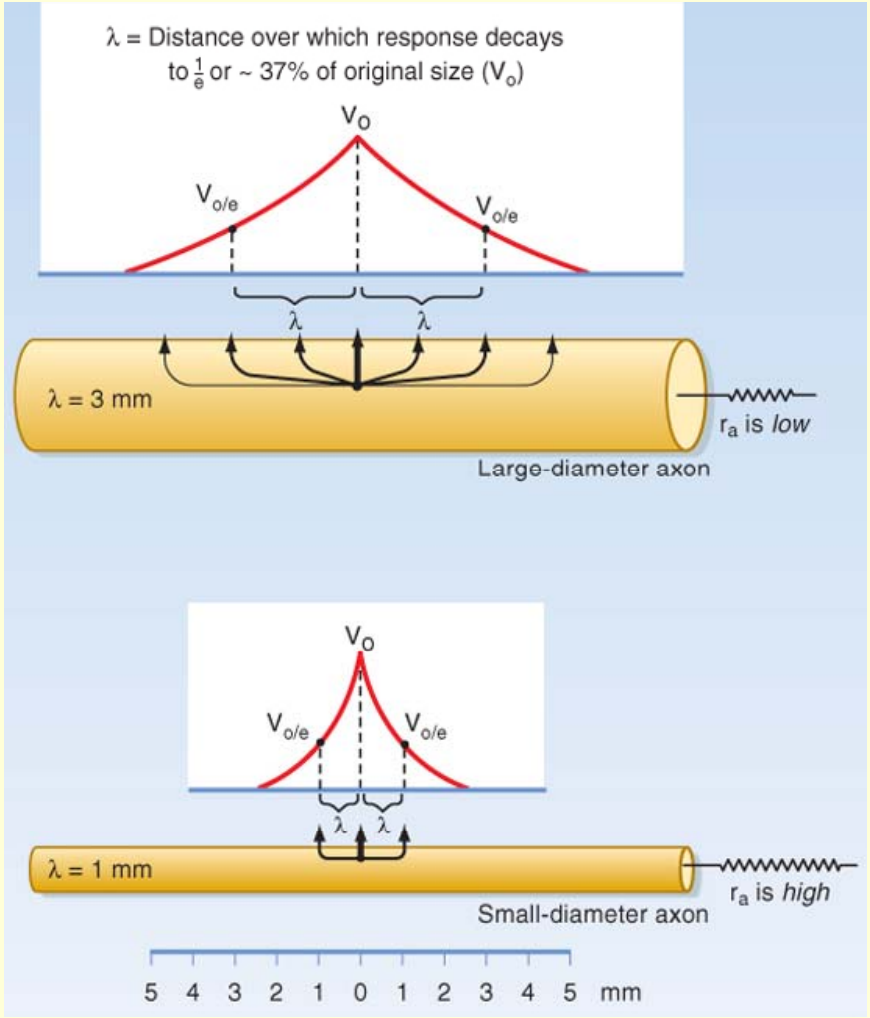
# Spreeding of signal without decrement

Better izolation = increased membrane resistance = minimal decrement
Myelin sheet = oligodendrocyte in the CNS a Schwann cells in periphery
(regeneration)
Node of Ranwier – **saltatory conduction -- next** node (1-2 mm) – high densiy of Na-chanels – **signal amplification** - AP



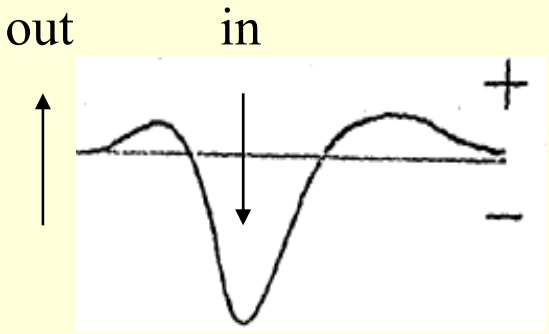

*Myelinizated fibres* - no decrement, fast, in NS about 60%

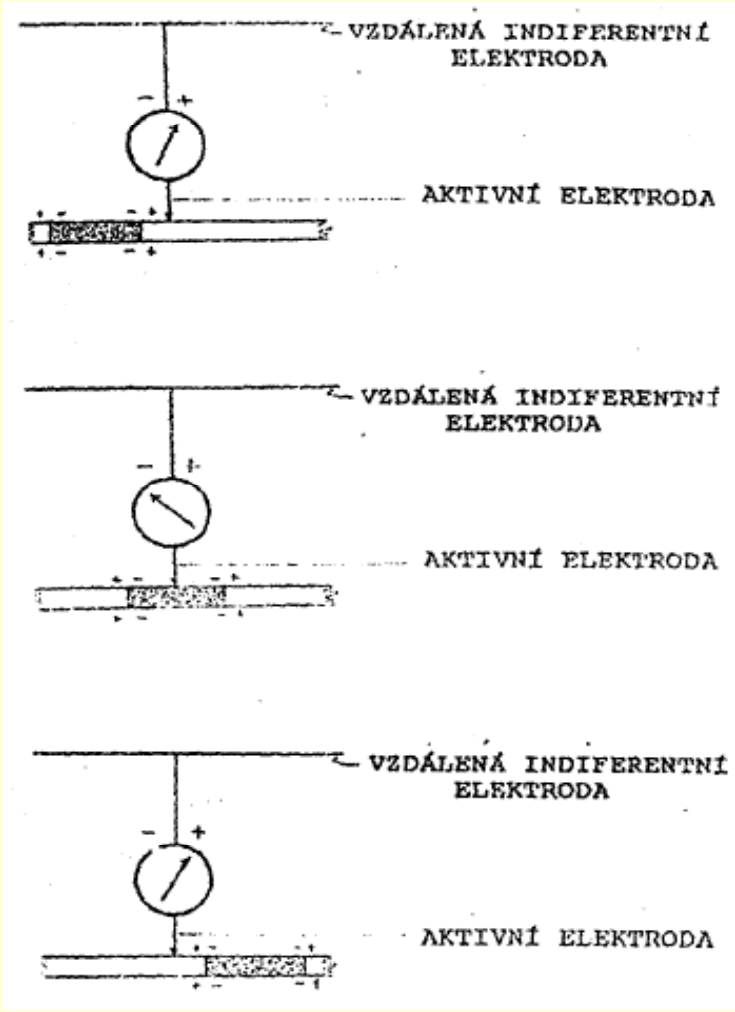
# Velocity of signal propagation – space constant λ



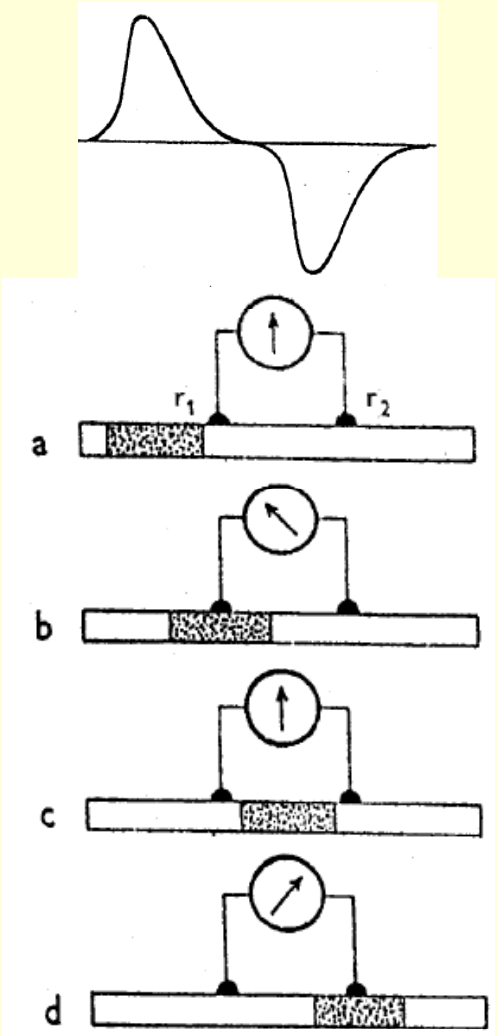
# Unipolar registration

Far-distant electrode – **indifferent** or r**eferent electrode,** close – **active (registration) electrode**



# Axon - bipolar registration of AP

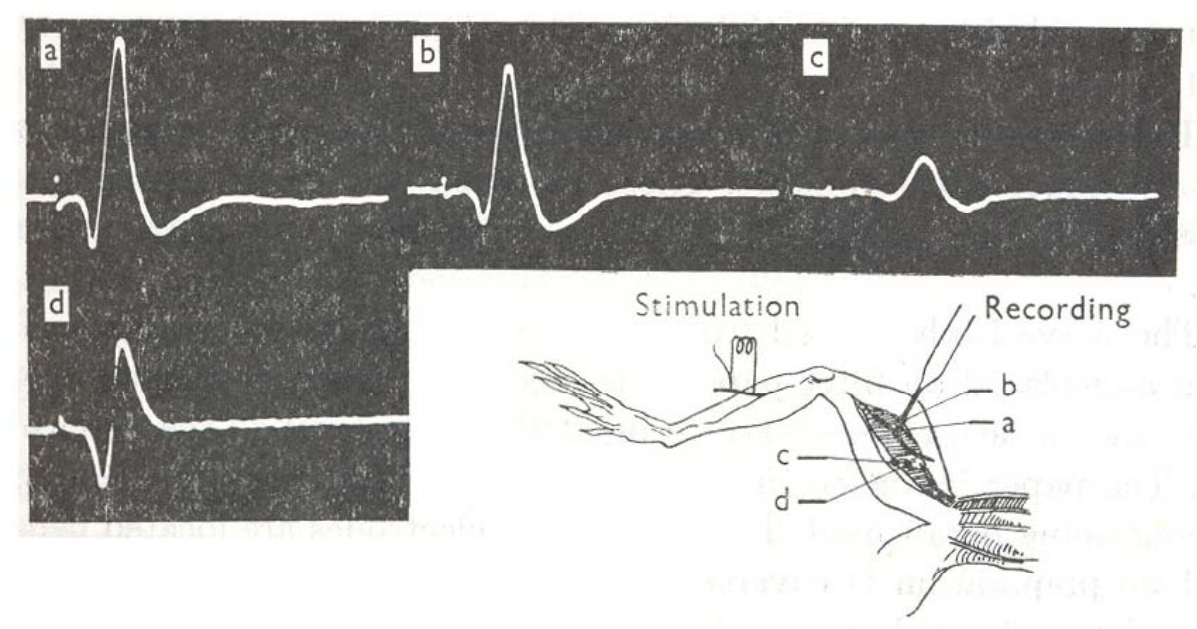



Electrodes very close to a fibre. Impulse - electrode negative then positive in reference to the second

Increasing distance from this fibre, amplitude of wave decreased - biphasic

one electrode far-away - small potential changes => monopolar registration

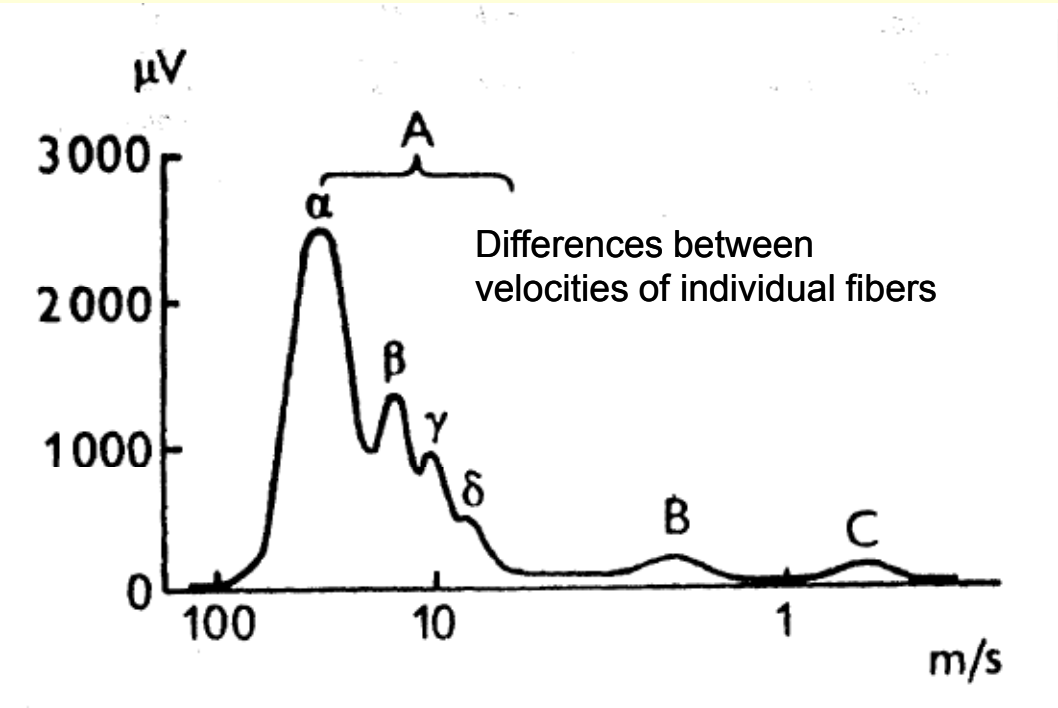
# AP recording - n. sciaticus (frog)

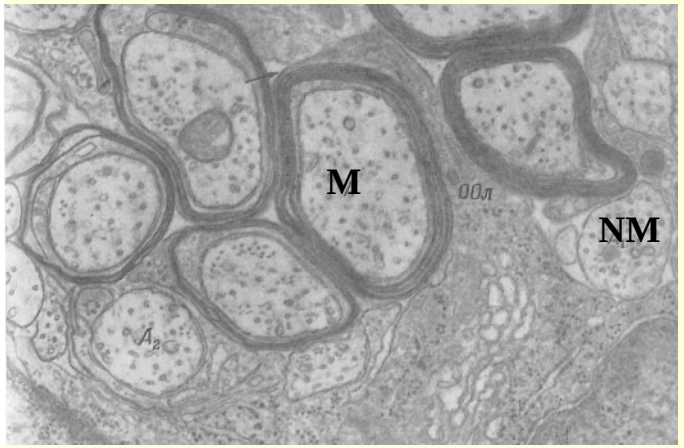



Recording of action potential of the frog sciatic nerve with a volume lead in situ at the site marked on the drawing. Letters a-d in the diagram denote the corresponding oscillogram. Stimulating electrodes are on the peroneal nerve. The indifferent earthed electrode is on the opposite limb.

Bureš et al., 1967
El. Methods in Biol. Res.

# Electroneurogram of mixed nerve




Průřez nervem, zv. 57 tis.x
M-myelinizovaný, NM - nemyelinizovaný axon (Piters a spol. 1972)

Classification according Erlanger and Gasser
Fibers are classify into fibers of category
A –myelinated, 4 subgroups
B –myelinated preganglion autonomic fibers
C –non-myelinated postganglion fibers of sympatic ($C_S$),
centripetal fibers (nocioception) $C_{d.r.}$ – dorsal roots

# Nerve fiber types in a mammalian nerve

(according to Erlanger and Gasser)

| Fiber Type | Function | Fiber Diameter (μm) | Conduction Velocity (m/s) |
|---|---|---|---|
| **A** | | | |
| α | Proprioception; somatic motor | 12–20 | 70–120 |
| β | Touch, pressure (skin afferents) | 5–12 | 30–70 |
| γ | Motor to muscle spindles | 3–6 | 15–30 |
| δ | Pain, cold, touch (skin afferents) | 2–5 | 12–30 |
| **B** | Preganglionic autonomic | <3 | 3–15 |
| **C** | | | |
| Dorsal root | Pain, temperature, some mechanoreception, reflex responses (skin afferents) | 0.4–1.2 | 0.5–2 |
| Sympathetic | Postganglionic sympathetics | 0.3–1.3 | 0.7–2.3 |

A and B fibers are myelinated; C fibers are unmyelinated.

# Numeral classification used for sensory nerves

(according to Lloyd) – seldom use

| Number | Origin | Fiber Type |
|---|---|---|
| Ia | Muscle spindle, annulo-spinal ending. | A α |
| Ib | Golgi tendon organ. | A α |
| II | Muscle spindle, flower-spray ending; touch, pressure. | A β |
| III | Pain and cold receptors; some touch receptors. | A δ |
| IV | Pain, temperature, and other receptors. | Dorsal rout C |

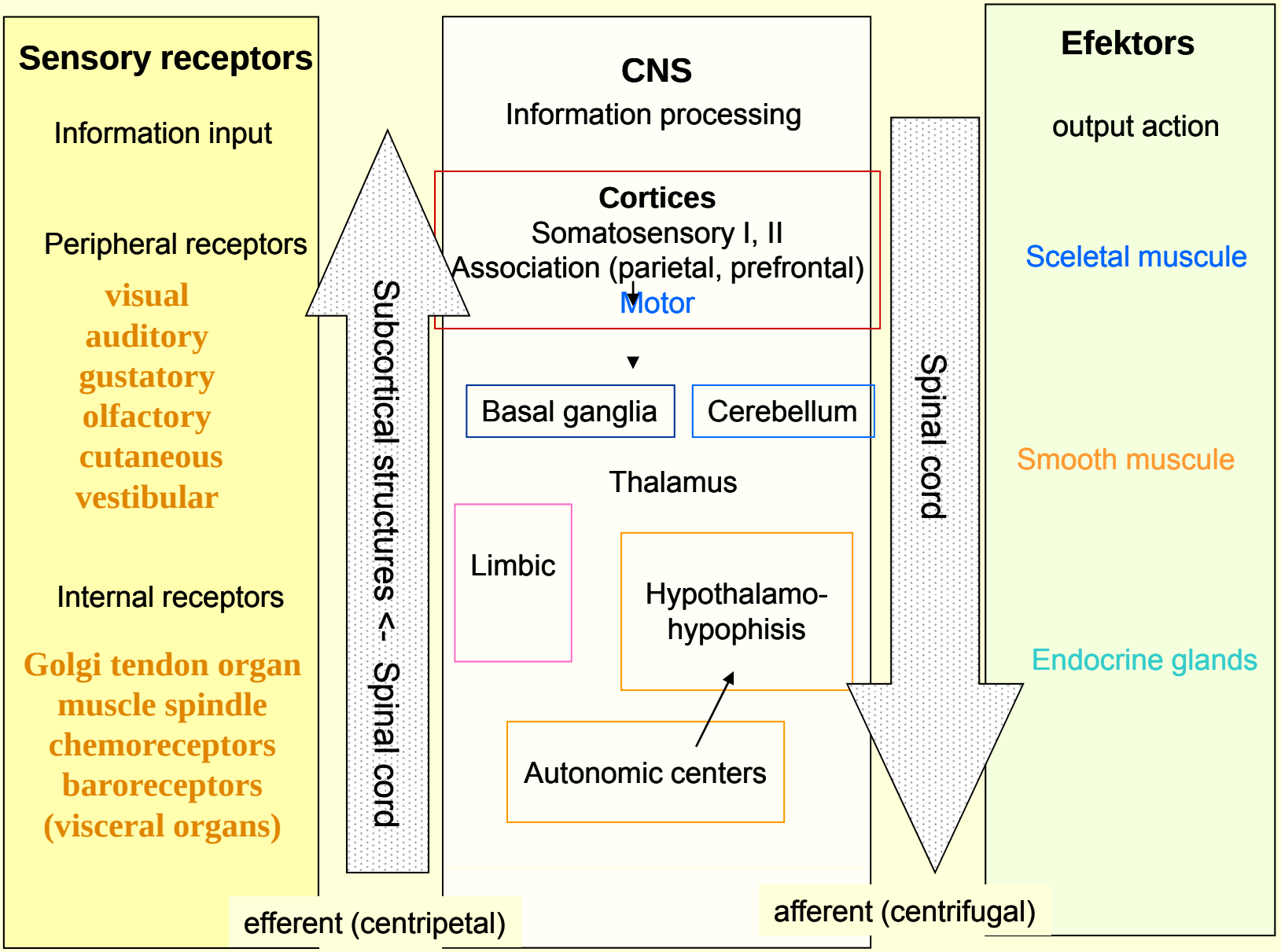
This system is used for afferents from receptors in muscle, which fall into classes I and II; consequently classes III and IV are not in practice used.

# Mammalian nerve fibers

- relative sensitivity of mammalian nerve fibers A, B, C to several influences inhibiting conduction

| Sensitivity to | High sensitivity | Midle sensitivity | The most resistant |
|---|---|---|---|
| hypoxia | B | A | C |
| pressure | A | B | C |
| Local anaesthetic | C | B | A |

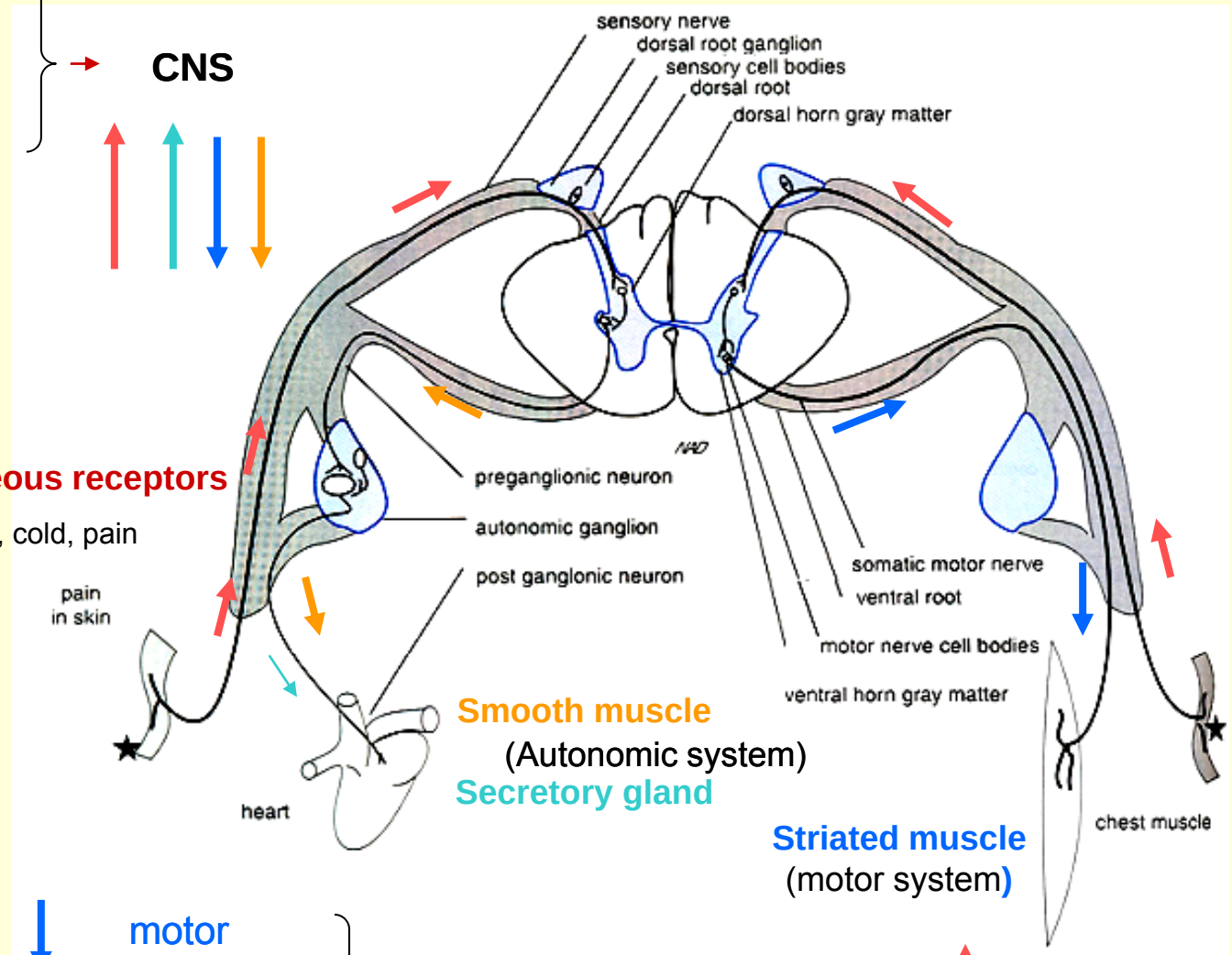
# Organizaion of NS



# Organization of PNS

sight
audition
taste
olfaction
poise

CNS




**(sub)cutaneous receptors**

pressure, worm, cold, pain

**Smooth muscle**
(Autonomic system)
**Secretory gland**

**Striated muscle**
(motor system)

**intero- receptors**

Muscle spindle,
Golgi tendon organ,
chemo-, baro-

motor

autonomic

**afferent** (centripetal) pathways

Sensory **efferent** pathways

# Signal processing

Several levels

Preliminary analyses

↓

Spinal cord
medulla
cerebellum
midbrain – limbic system
Midbrain (thalamus)
Telencephalon (cortex)

detail analyses