Graduate Studies in Biomedical Technology and Medical Physics
University of Patras 02-12-2022

Physiology and Pathophysiology for Engineers and Physisists

part 2 - nervous system

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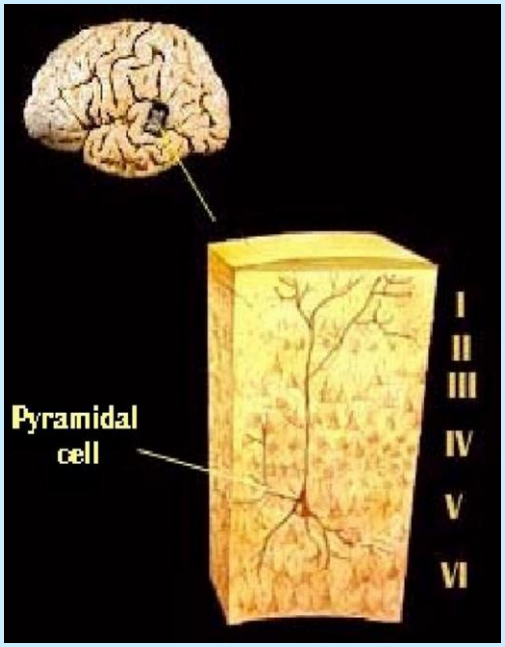
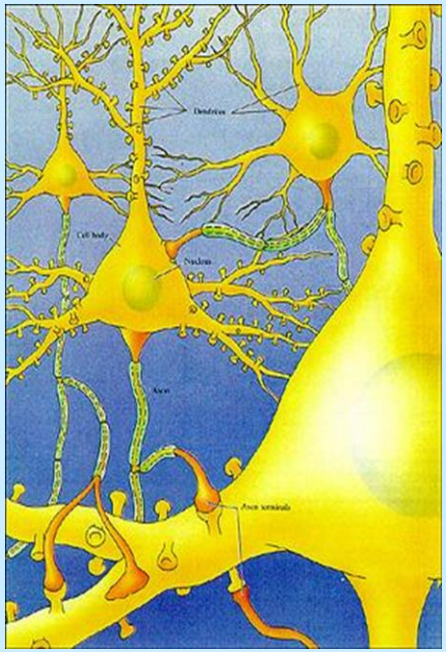
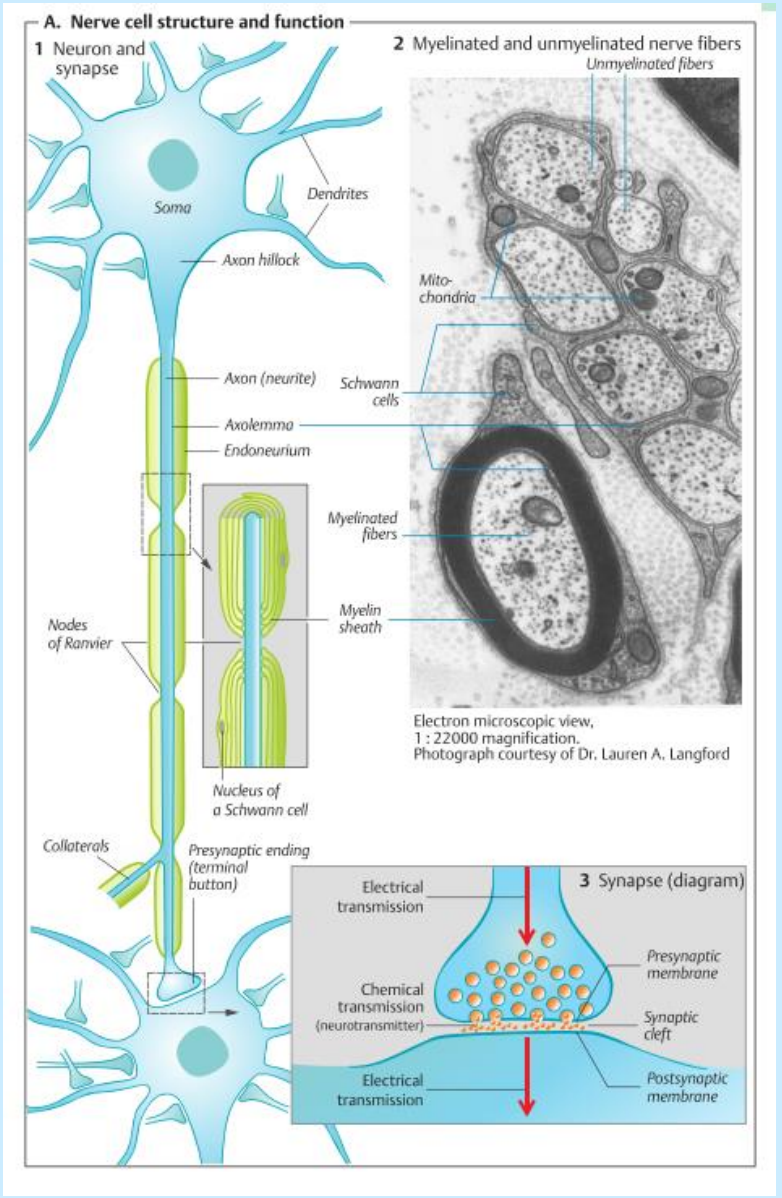
Cells of the Nervous System







Cells of the Nervous System: are of 2 kinds

- Over 100 billion nerve cells **(neuron**s)
- **Supporting cells** - - more numerous (**neuroglia)**

Neurons have 3 properties :

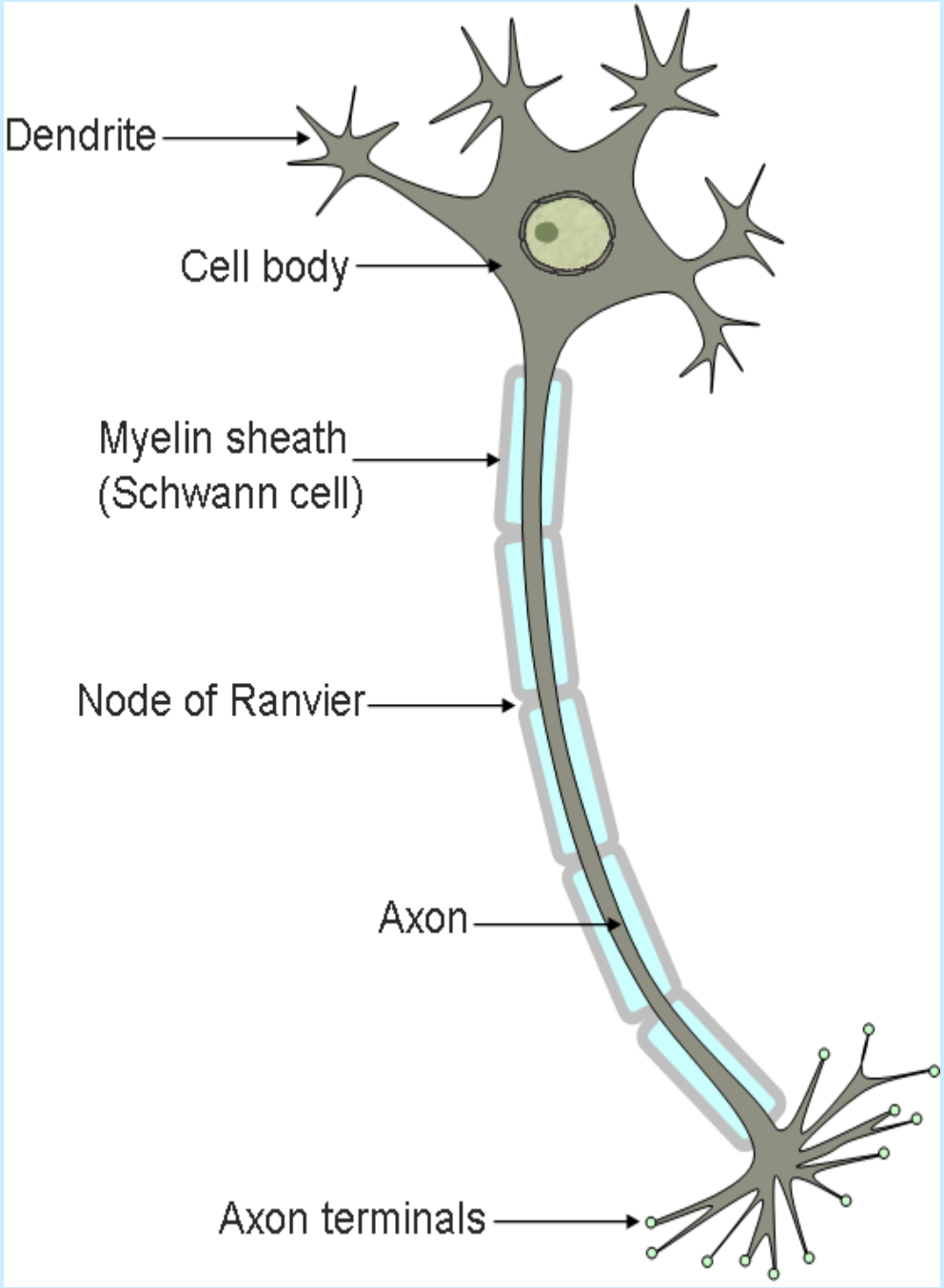
- **Excitability** - ability to respond to stimuli with action potentials.
- **Conductivity** - ability to transmit an action potential.
- **Synaptic transmission**

Nerve Processes

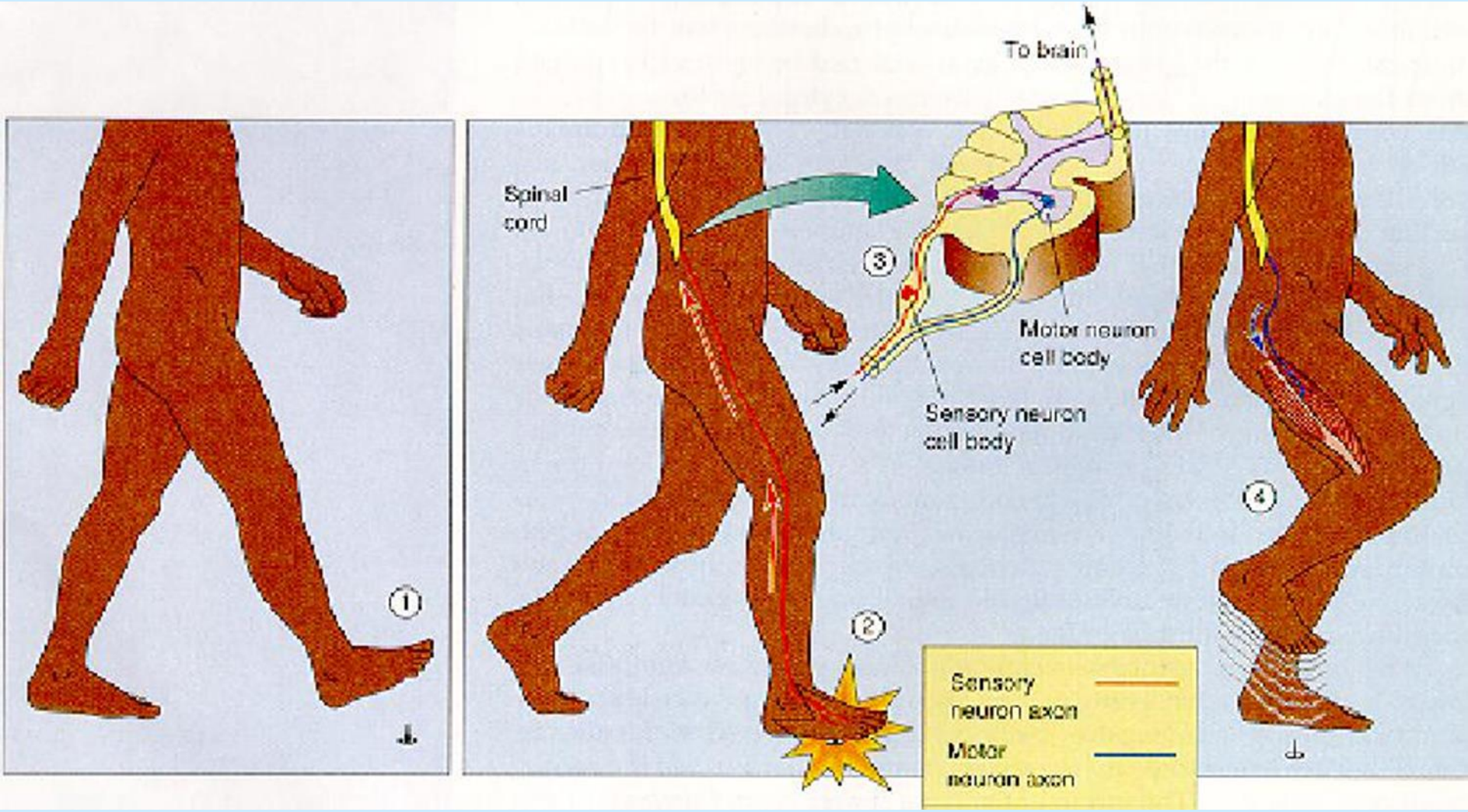
Two kinds - axons and dendrites - also called **nerve fiber**s.

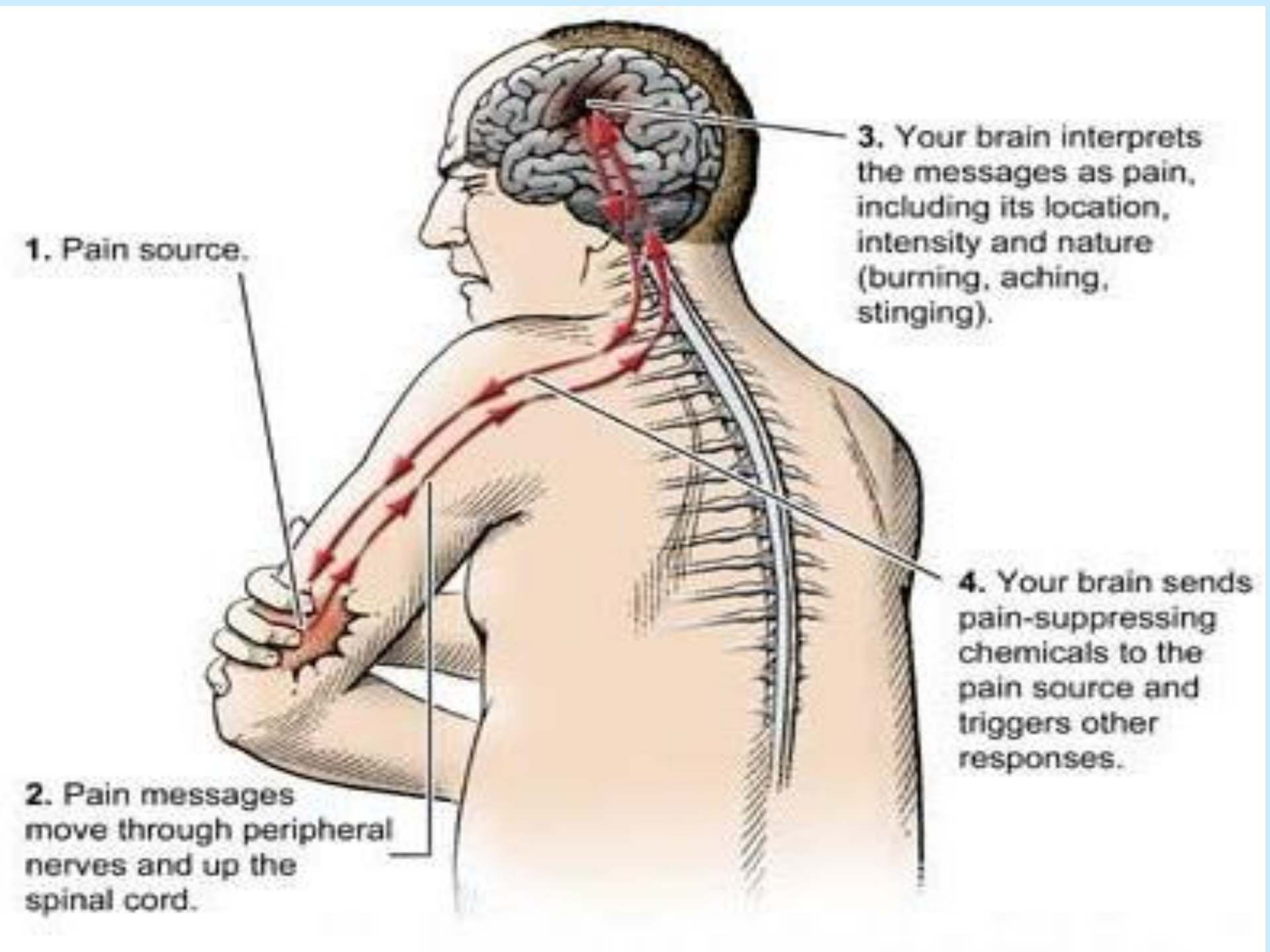
Dendrites - short, threadlike processes that are extensions of the cell body and conduct nerve impulses **toward** the cell body. Can have as many as 200 dendrites in one neuron.

Axon - slender process that extends from the cell body for from less than a millimeter (in the brain) to more than a meter (sciatic nerve). Carries nerve impulses **away** from the cell body. Generally just one.



The function of Neurons




1. Pain source.
2. Pain messages move through peripheral nerves and up the spinal cord.
3. Your brain interprets the messages as pain, including its location, intensity and nature (burning, aching, stinging).
4. Your brain sends pain-suppressing chemicals to the pain source and triggers other responses.

Types of PNS Neurons -

Based on direction in which they transmit nerve impulses.

- Afferent (sensory) neurons - convey information from sensory receptors in the skin, sense organs, muscles, joints, and viscera to the CNS. **Exteroceptors** (monitor external), **proprioceptors** (monitor position), **interoceptors** (monitor internal activities).

- **Efferent (motor) neurons -** convey nerve impulses away from the CNS to the effectors (muscles and glands).

- Interneurons - lie (1) between sensory and motor neurons in neural pathways and transmit signals through pathways of the CNS, where integration occurs, and (2) in autonomic ganglia. About 90% of the neurons of the body are interneurons.

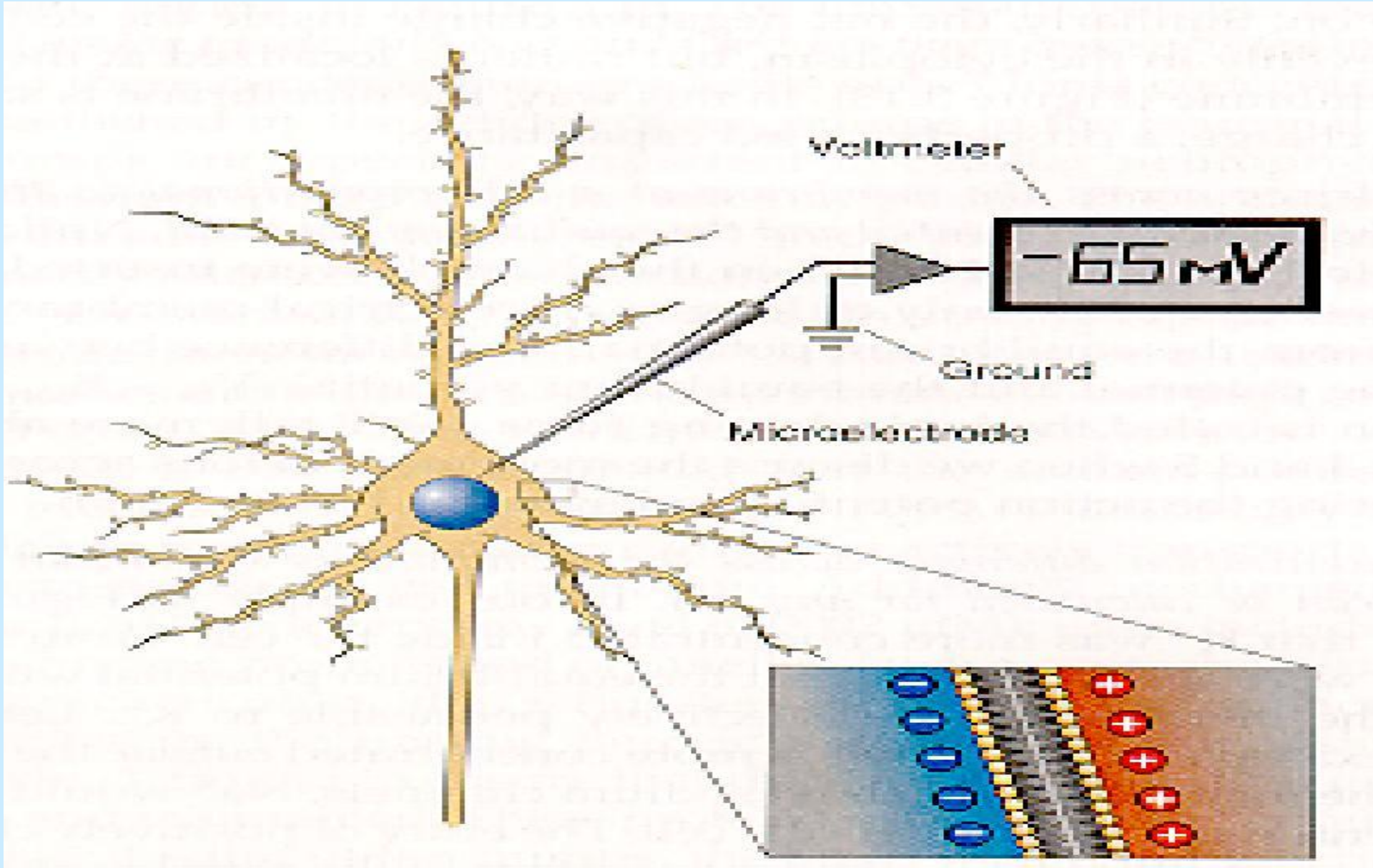
How do neurons accomplish this communication intracellularly (in elongated cells) and intercellularly?

They use 3 unique mechanisms:

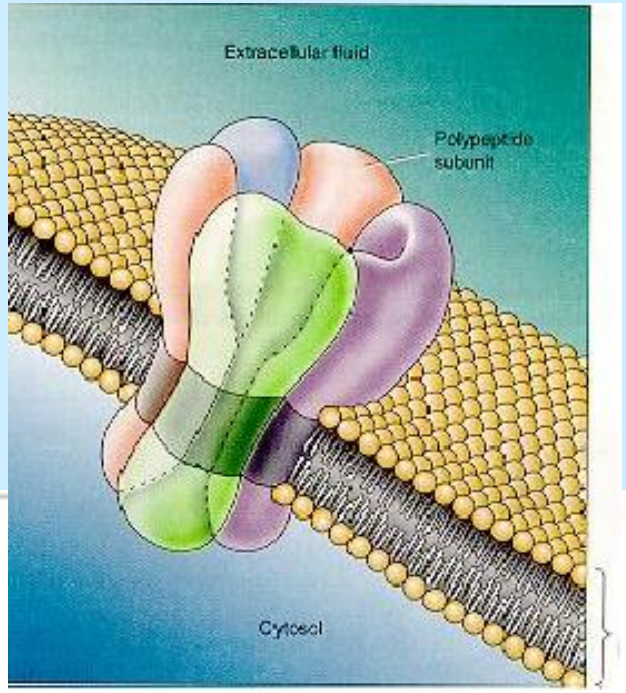
1. Excitability
2. Conductivity
3. Synaptic transmission

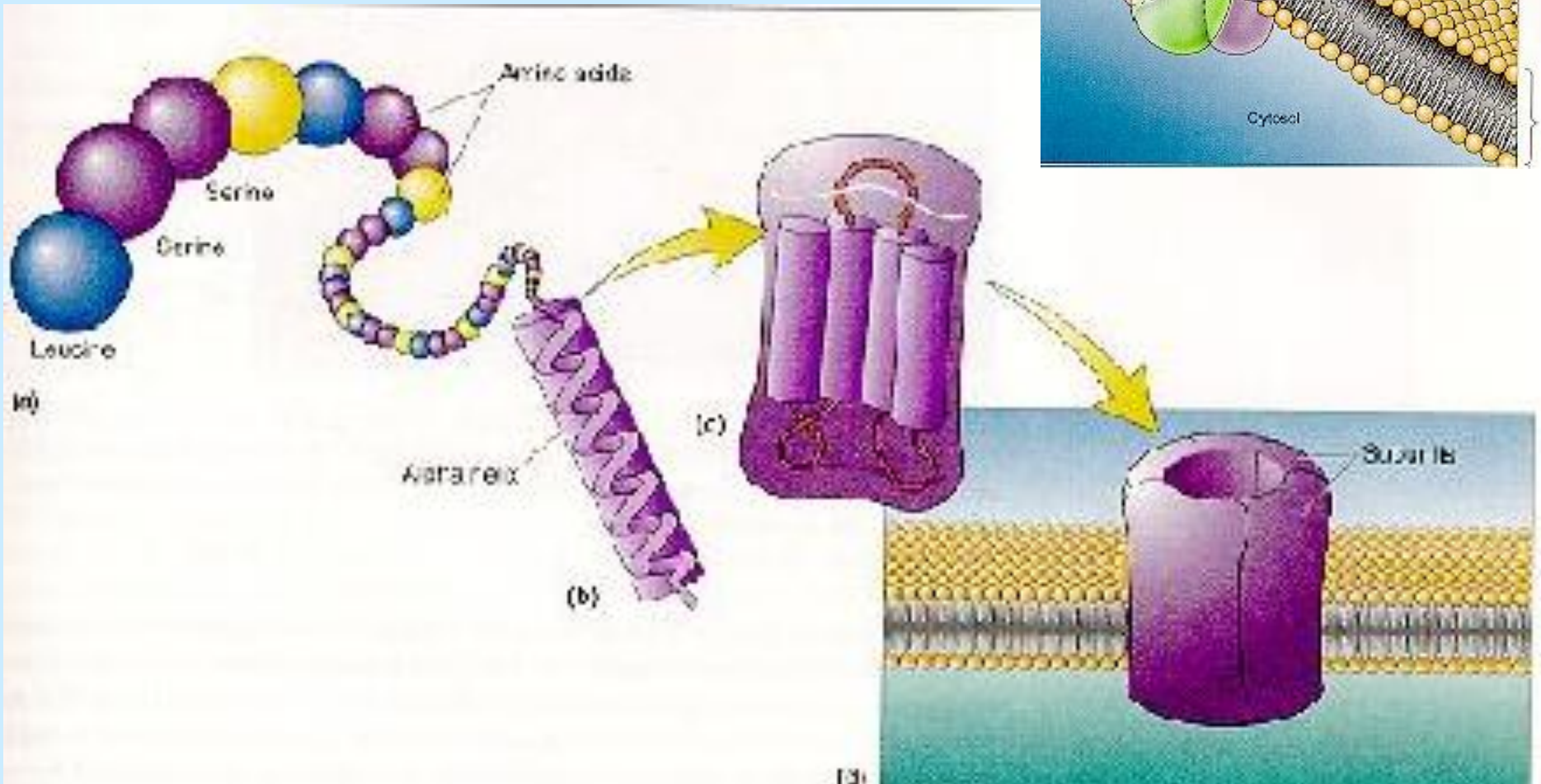
The membranes of all cells are electrically polarized, i.e. they have a resting membrane potential

The membranes of all cells are electrically polarized, i.e. they have a resting membrane potential (RMP)

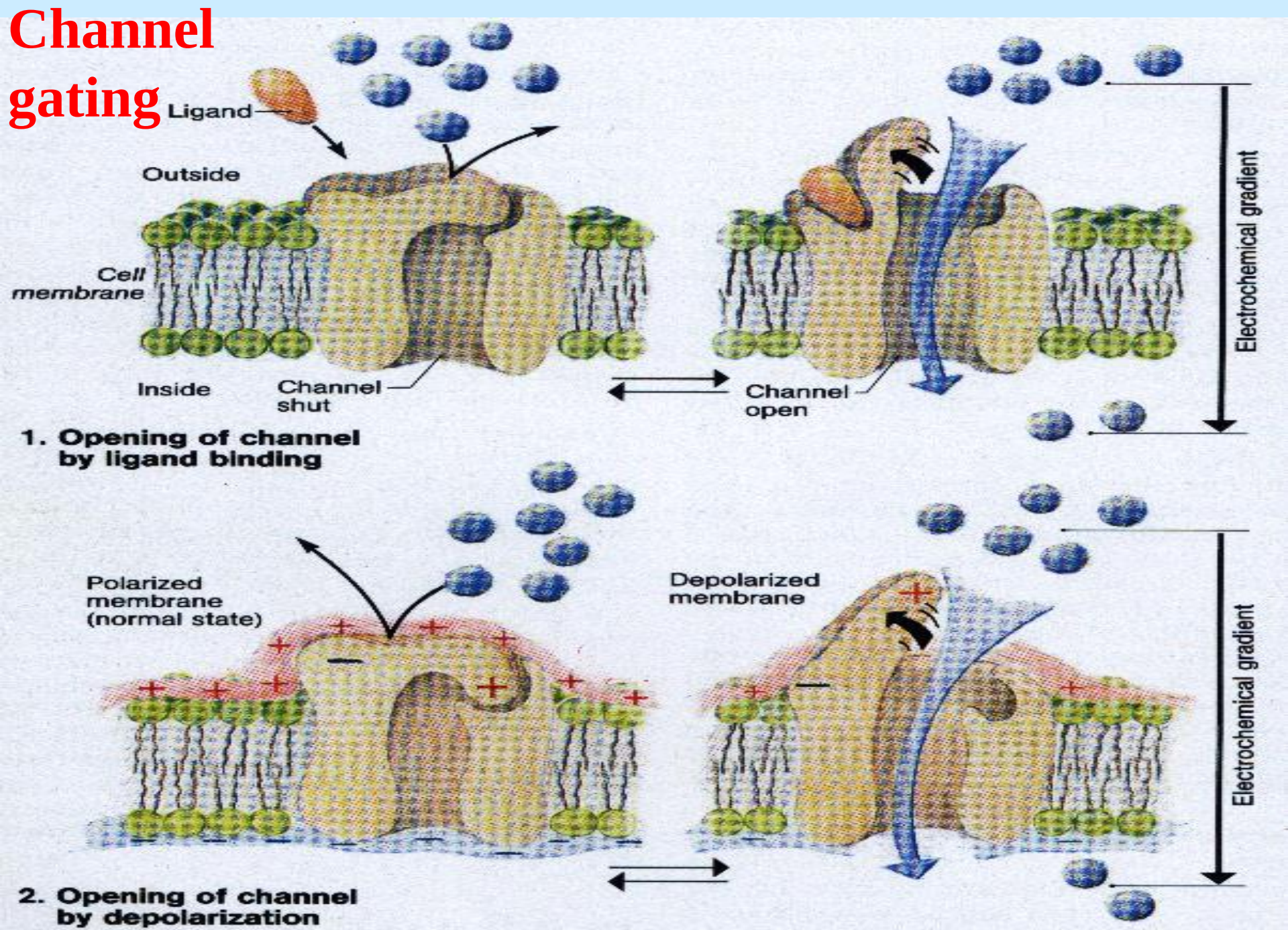


The RMP is created by gated **channels** and ionic **concentration gradients** across the membranes





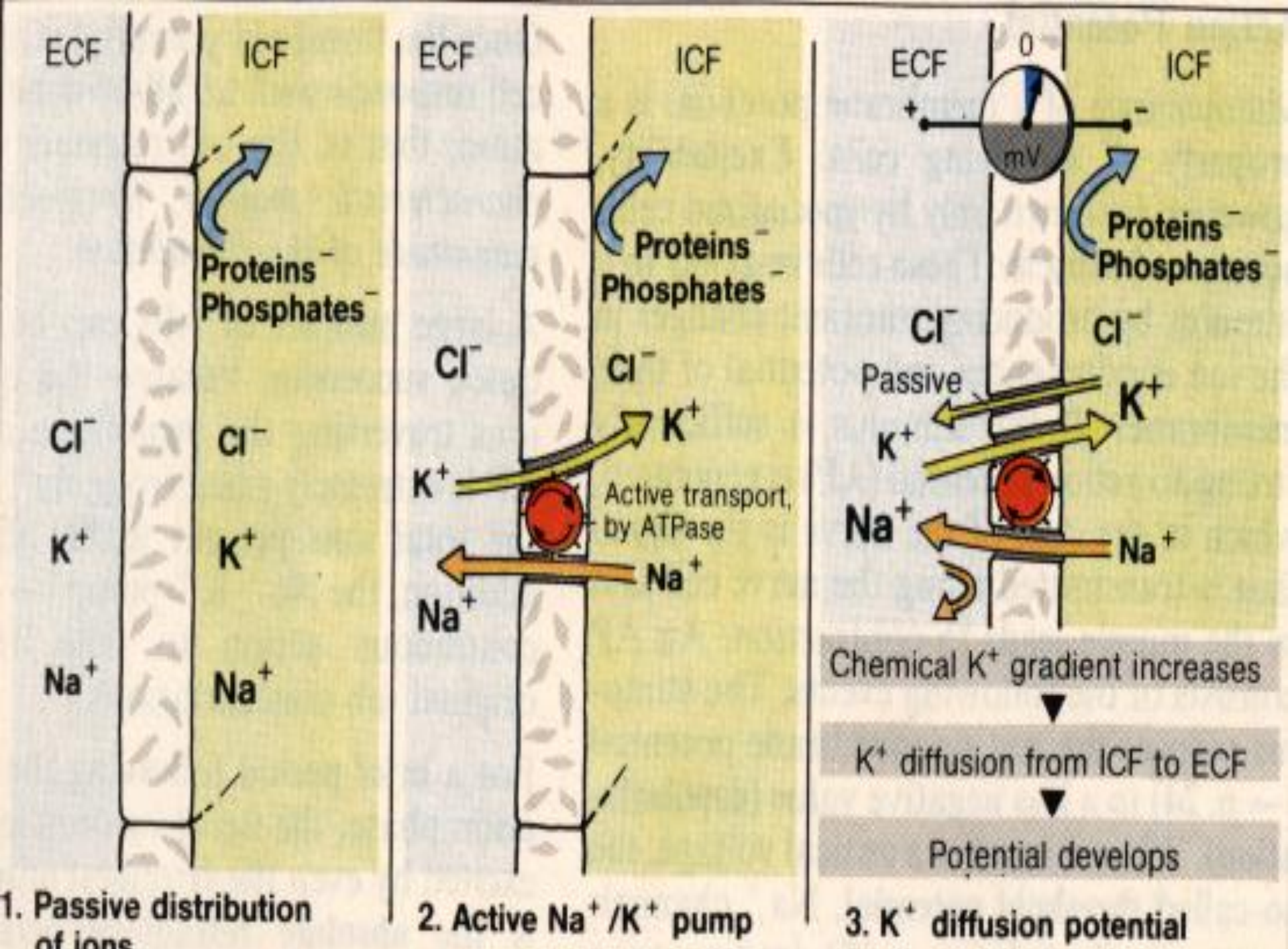
Channel gating



Ionic gradients: Extracellular space has more [Na+] and [Cl-], while intracellular space has more [K+]

	"Effective" concentration (mmol/kg H_2O)		Equilibrium potential
	Interstitium (ECF)	Cell (ICF)	
K^+	4.5	160	– 95 mV
Na^+	144	7	+ 80 mV
H^+	$4 \cdot 10^{-5}$ (pH 7.4)	10^{-4} (pH 7.0)	– 24 mV
Cl^-	114	7	– 80 mV
HCO_3^-	28	10	– 27 mV

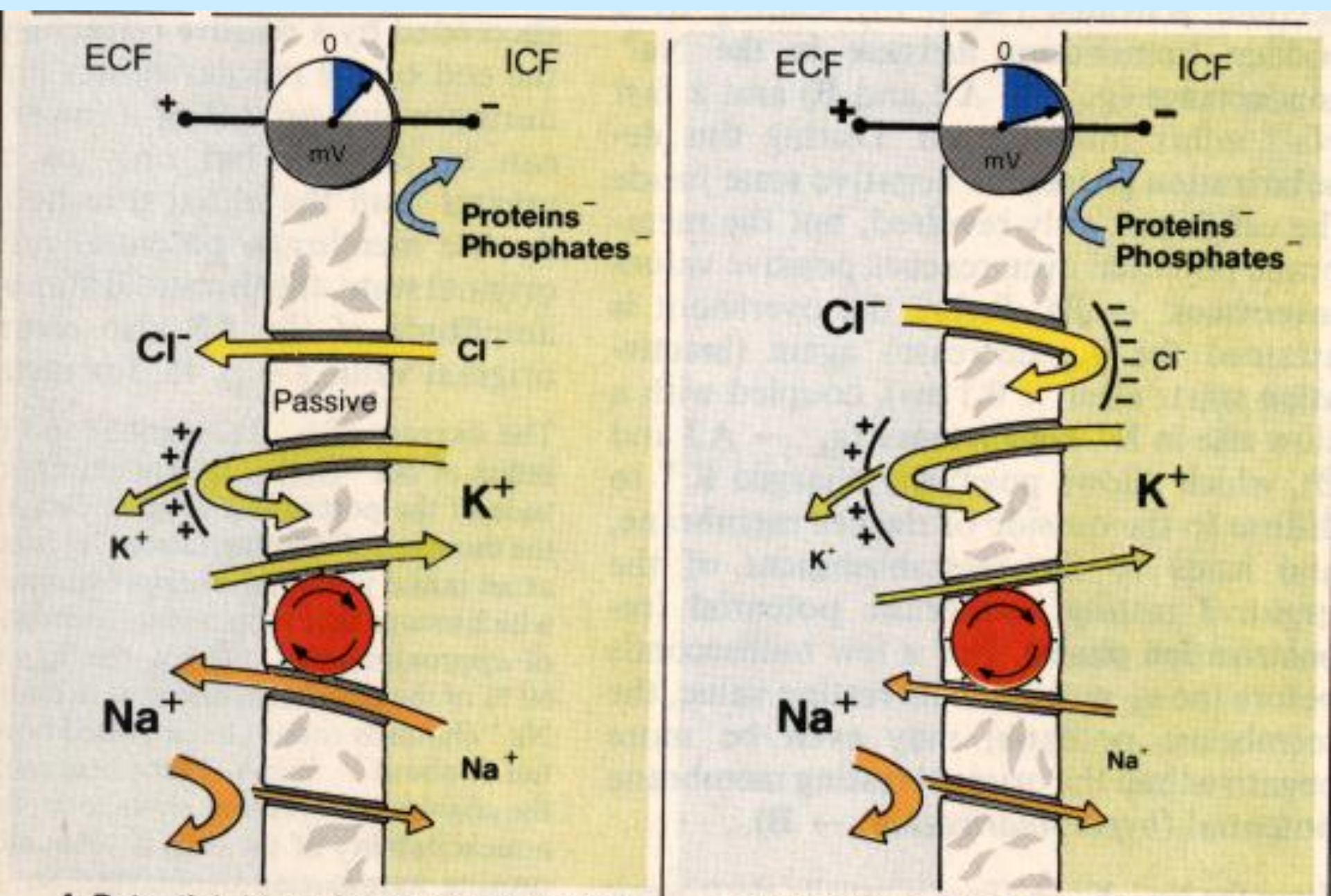
B. Typical "effective" concentrations and equilibrium potentials of important ions in skeletal muscle (37° C) (after Conway)



1. Passive distribution of ions

2. Active Na^+ /K^+ pump

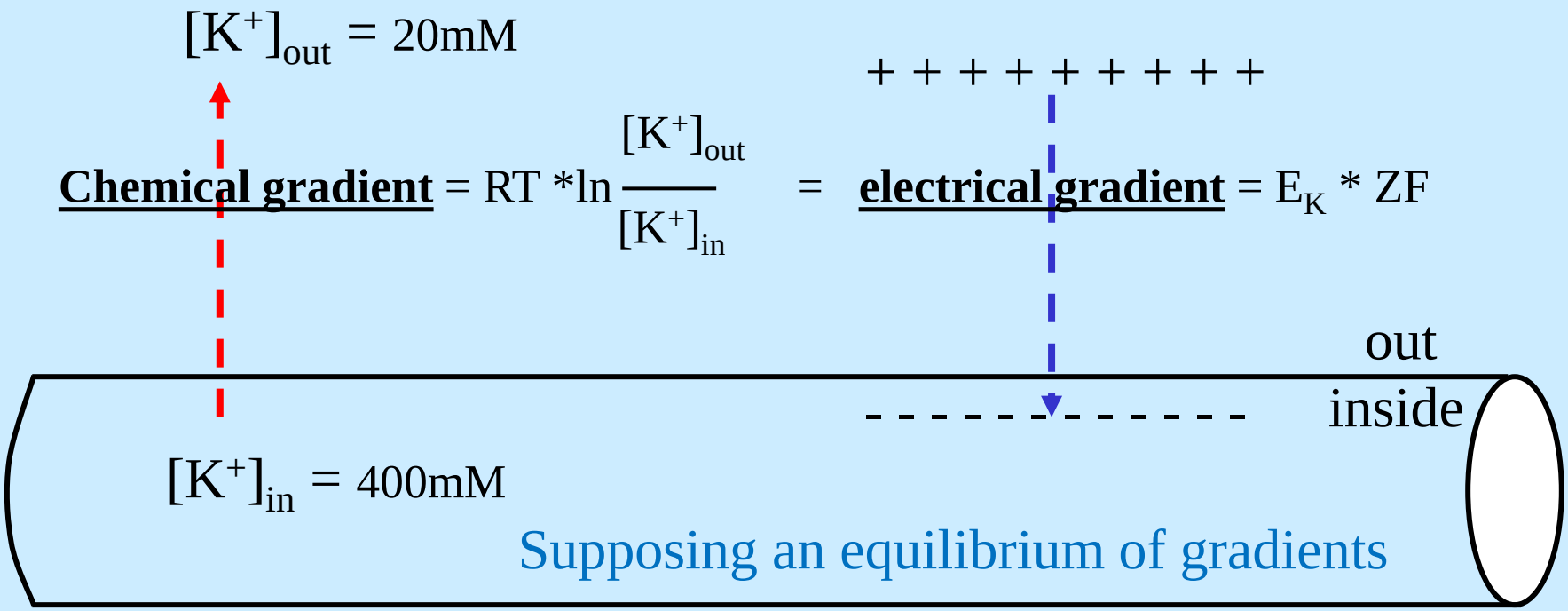
3. K^+ diffusion potential



4. Potential drives Cl^- from ICF to ECF

5. Final state: resting potential

A. Causes and consequences of the resting potential

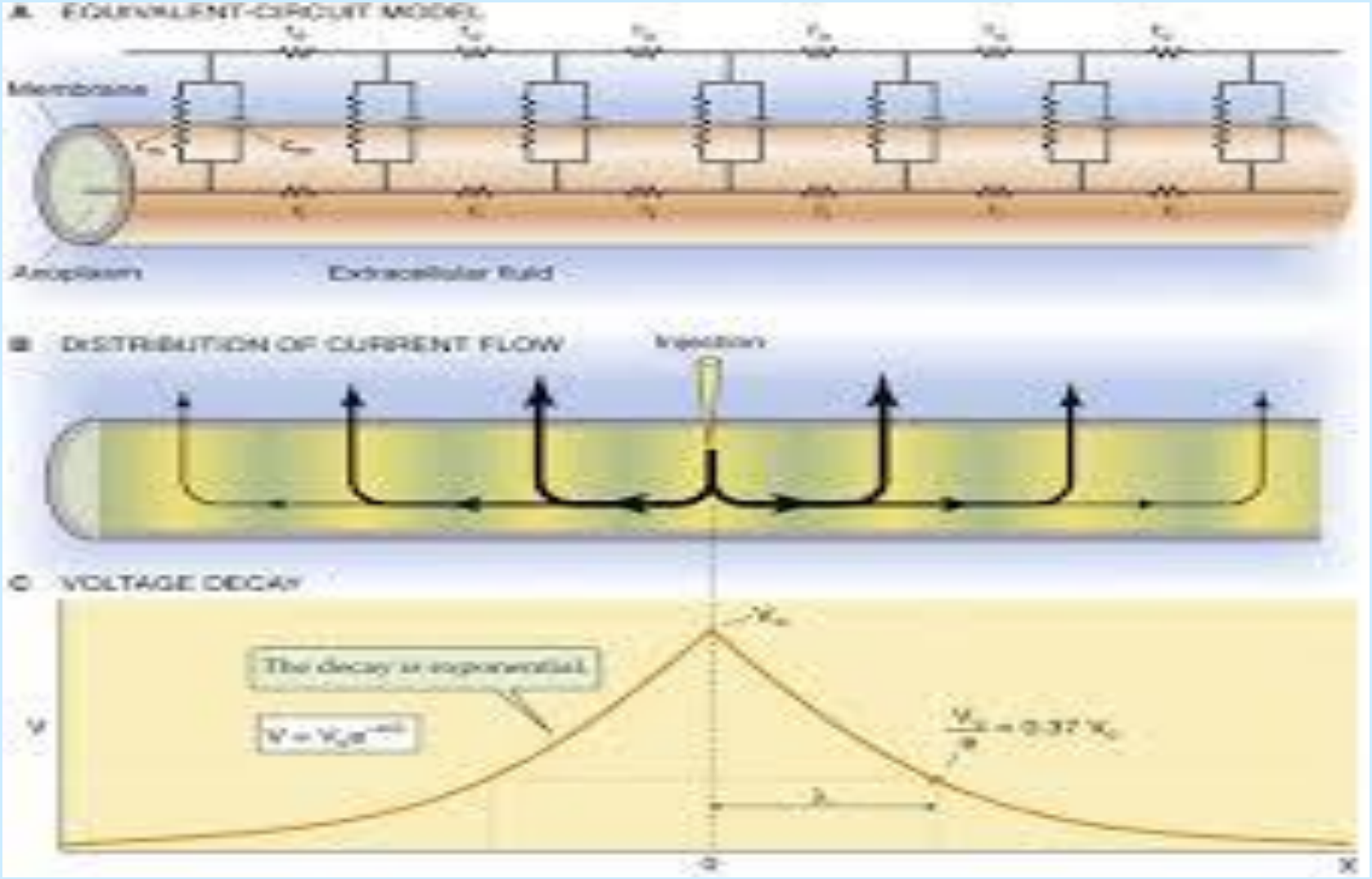


Using this thermodynamics relationship Nernst suggested an equation for measuring the equilibrium potential E_{ion} of an ion crossing a membrane

NERNST EQUATION: $E_{ion} = \frac{RT}{ZF} * \ln\frac{[K^+]_{out}}{[K^+]_{in}}$

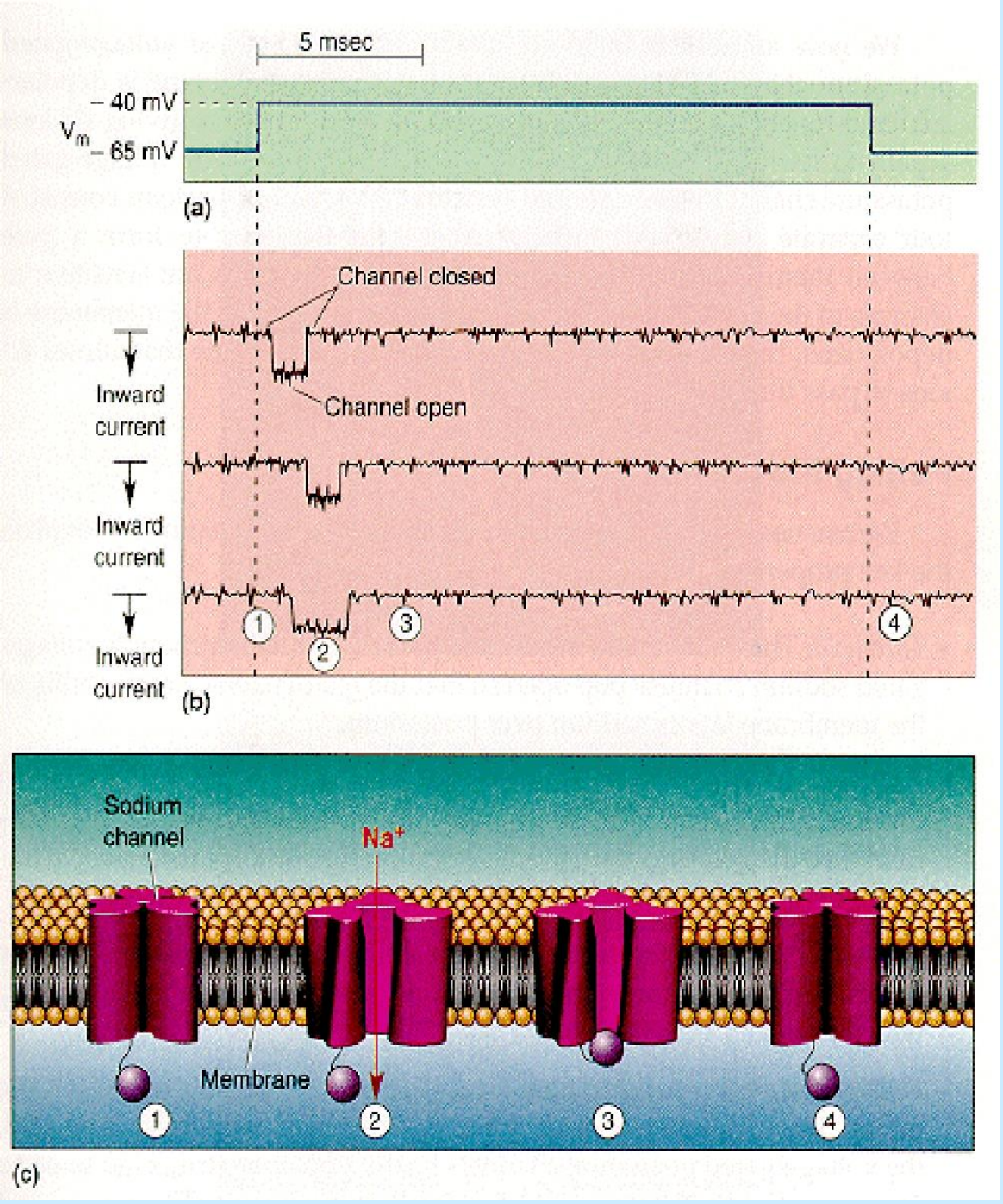
Where
R is the universal gas constant (8.314570 J K-1 mol-1)
T the temperature in Calvin
z the valence of the ion
F is the Faraday constant (96,485 Cmol-1)

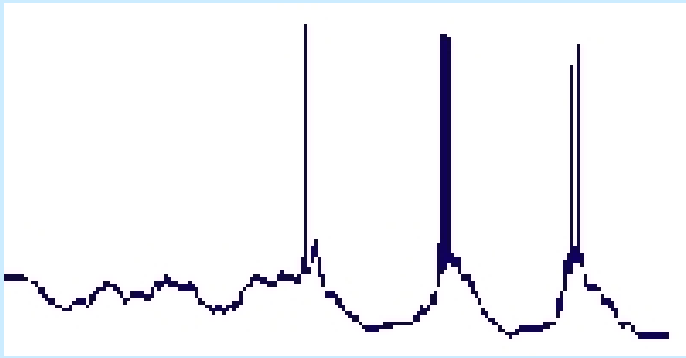
The membrane potential depends on the **ionic gradients** and the membrane **permeability**

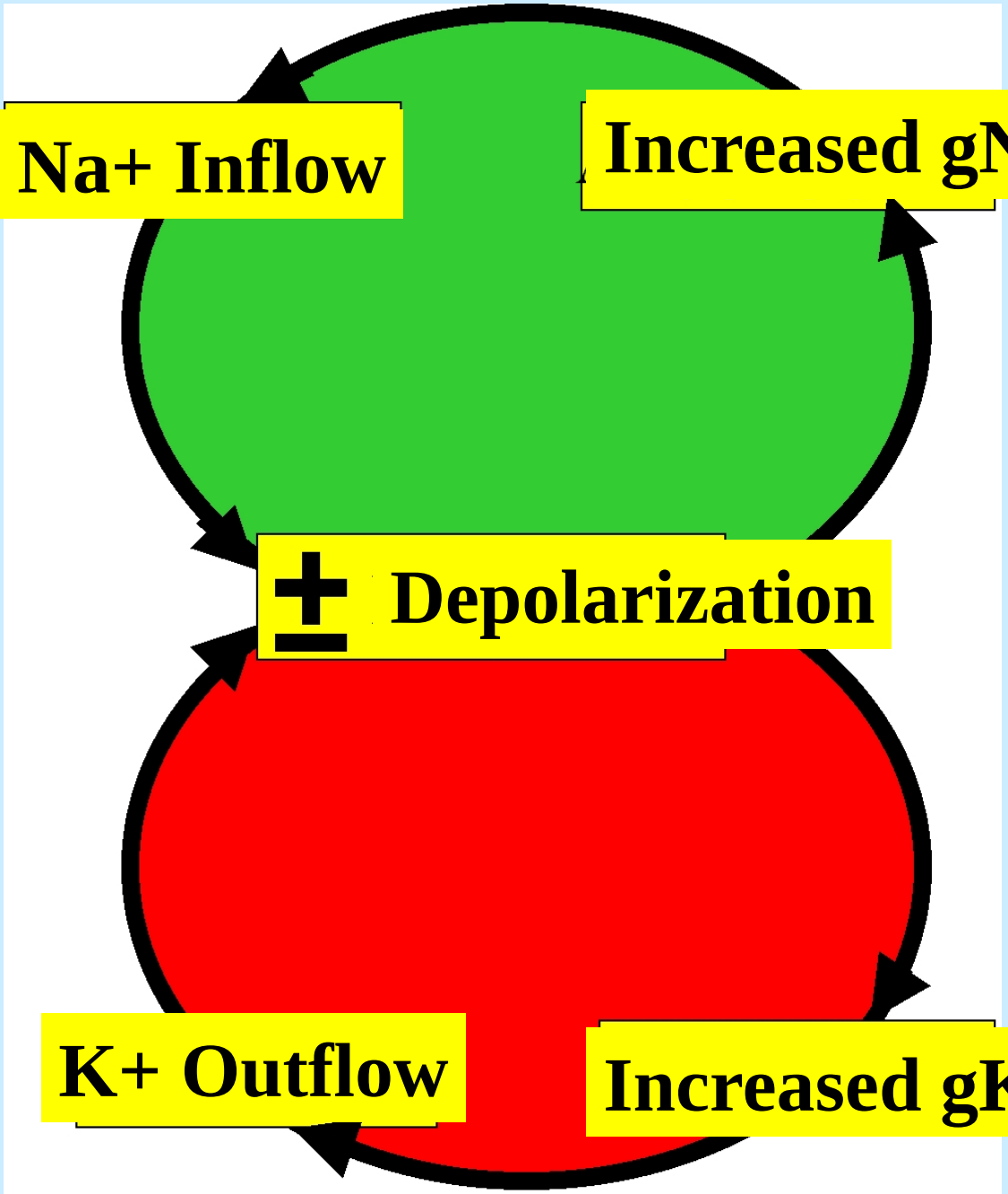


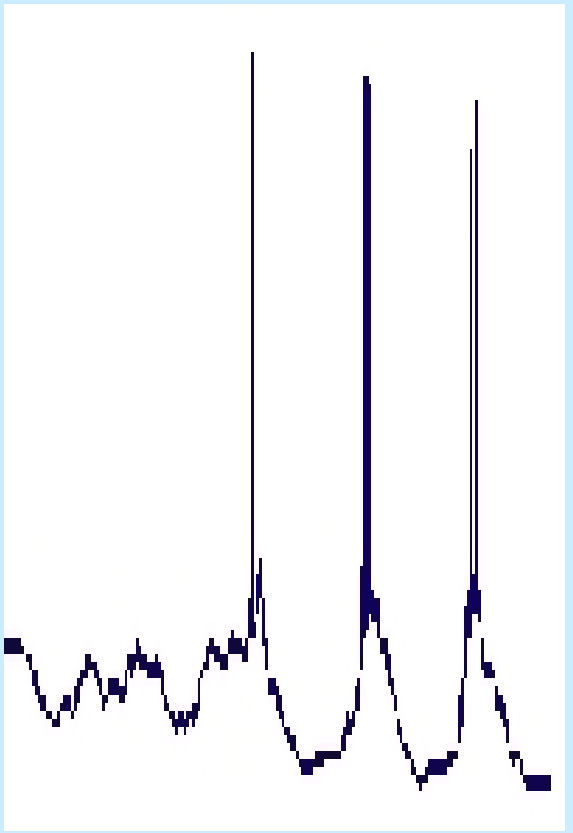
Changes of he membrane potential spread electrotonically with the potential gradually diminishing with distance from the point the change was made – **depending on what?**

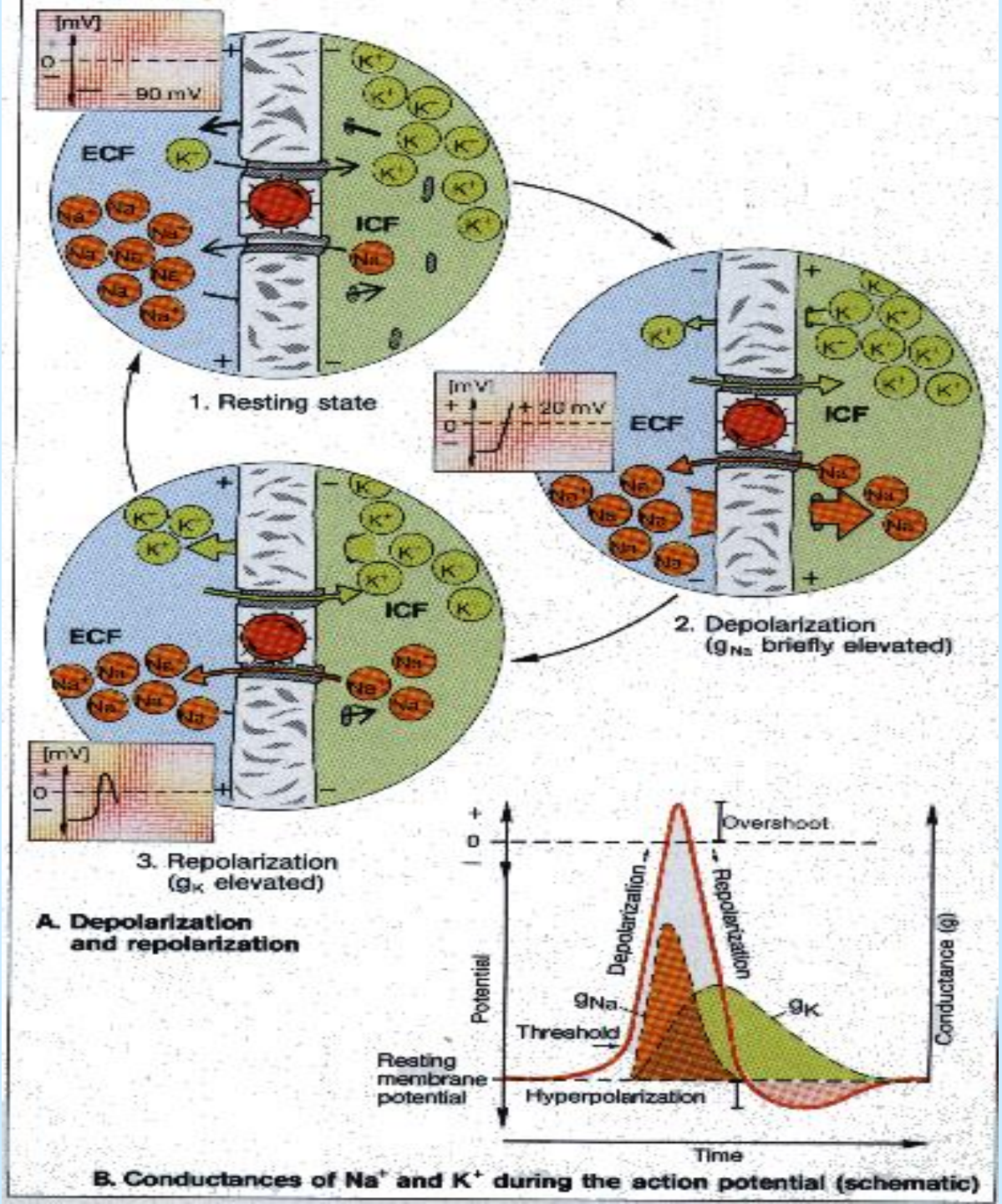
EXCITABILITY:
Upon suffuicient depolarization from RMP, neurons can generate **action potentials. This property is called excitability**

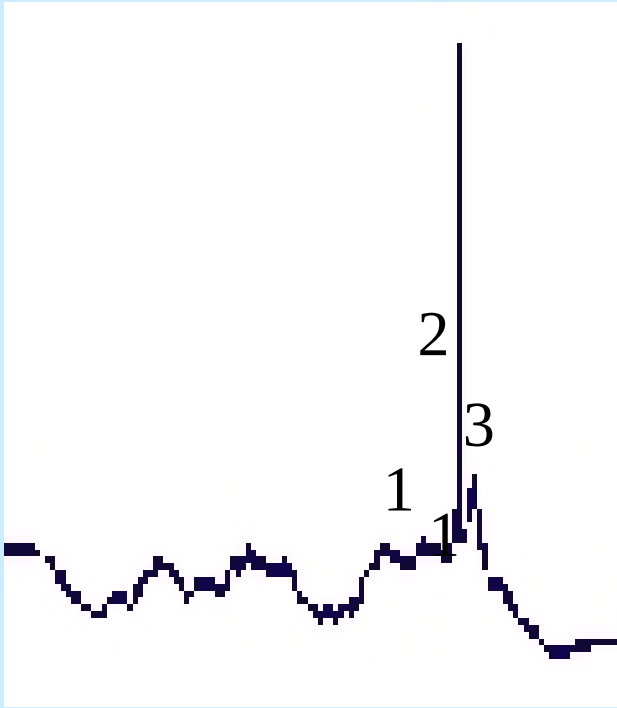

5 msec
– 40 mV
V_m
– 65 mV
(a)
Channel closed
Channel open
Inward current
Inward current
Inward current
1
2
3
4
(b)
Sodium channel
Na^+
Membrane
1
2
3
4
(c)

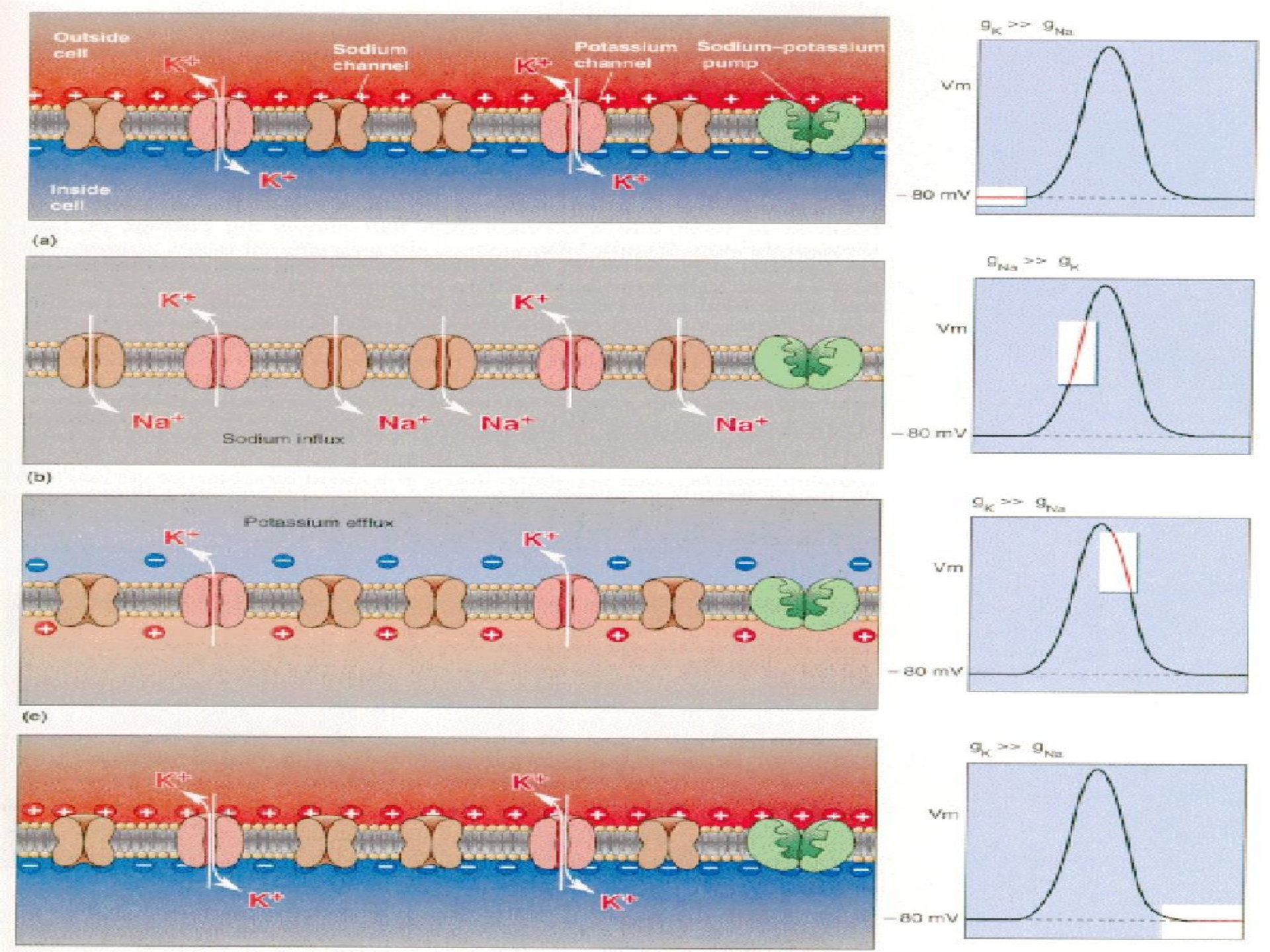


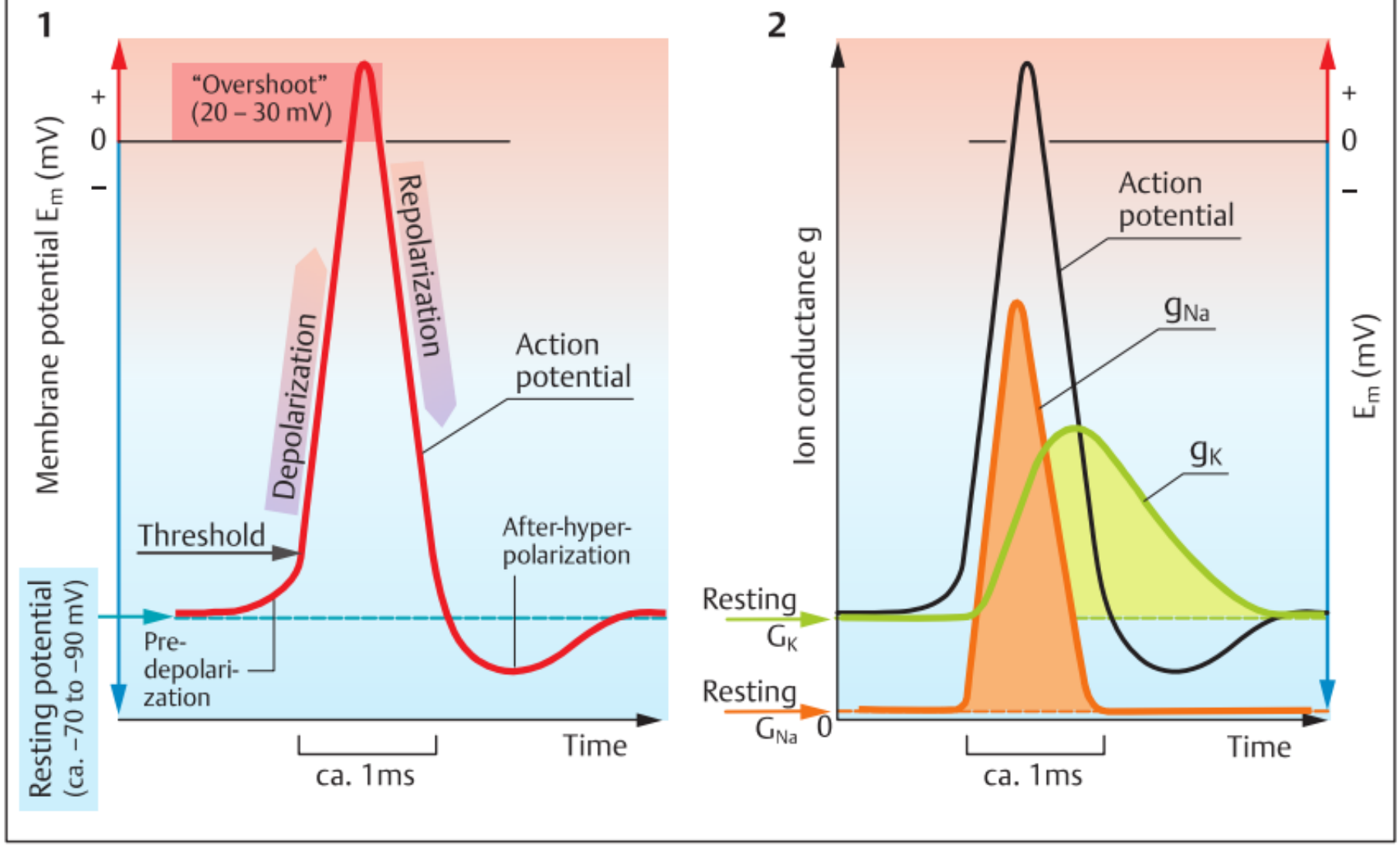

Na+ Inflow
Increased gNa+
± Depolarization
K+ Outflow
Increased gK+




[mV]
0
−90 mV
ECF
ICF
1. Resting state
[mV]
+ 20 mV
2. Depolarization
(g_{Na} briefly elevated)
3. Repolarization
(g_K elevated)
A. Depolarization and repolarization
Overshoot
Depolarization
Repolarization
Potential
g_{Na}
g_K
Threshold
Resting membrane potential
Hyperpolarization
Conductance (g)
Time
B. Conductances of Na^+ and K^+ during the action potential (schematic)


1
1
2
3


Outside cell
Sodium channel
Potassium channel
Sodium–potassium pump
Inside cell
K+
(a)
Na+
Sodium influx
(b)
Potassium efflux
(c)
Vm
−80 mV
gK >> gNa
gNa >> gK


A. Action potential (1) and ion conductivity (2) (nerve and skeletal muscle)
1
"Overshoot"
(20 – 30 mV)
+
0
–
Membrane potential E_m (mV)
Depolarization
Repolarization
Action potential
Threshold
After-hyper-polarization
Resting potential
(ca. –70 to –90 mV)
Pre-depolari-zation
Time
ca. 1ms
2
Ion conductance g
Action potential
g_{Na}
g_K
Resting G_K
Resting G_{Na}
0
+
0
–
E_m (mV)
Time
ca. 1ms

Action Potential

•Conducted change in the permeability of the cell membrane.

•**Threshold stimulus** - stimulus that is strong enough to initiate an impulse in a neuron.

•In response to a threshold stimulus, voltage-gated sodium ion channels open and **Na + rushes into** the cell.

•Influx of Na + results in reversal of the electrical charge at the point of stimulus to about 30 mV. Called **depolarizatio**n.

•Nerve is said to **fire** when stimulus is strong enough to depolarize the membrane to threshold level and generate a nerve impulse.

•Depolarizing a small area on the axon stimulates the adjacent area, which also contains voltage-gated sodium ion channels, to depolarize and an **action potential** is generated.

•**Nerve impulse** - train of action potentials.

Action Potential - Repolarization

•Shortly after depolarization, voltage-gated potassium ion channels open which accelerates the **outflow** of K + ions.
•Na + channels close and sodium ions are **pumped ou**t.
•Outflow of K+ may result in **hyperpolarization** to below -70 mV.
•Potassium ion channels eventually close and membrane is restored to resting potential.

Refractory Period

•Absolute: Brief period, 0.5 - 1 msec, after depolarization before an adequate stimulus can generate another action potential. Most nerve fibers are cable of generating about 300 impulses per second.
•Relative: several msec

All-or-None Principle

When the response is independent of stimulus size.

Minimum stimulus is necessary to initiate an action potential. Increase in the intensity of the stimulus does not increase the strength of the impulse. Like a gun. If don't pull the trigger hard enough, nothing happens. As soon as pull above the minimum amount, bullet will fire. Pulling the trigger harder will not make the gun fire harder. Applies primarily to action potentials in axons.

In contrast to: Graded response - occurs if only a small part of the membrane is affected. Not enough to cause action potential.

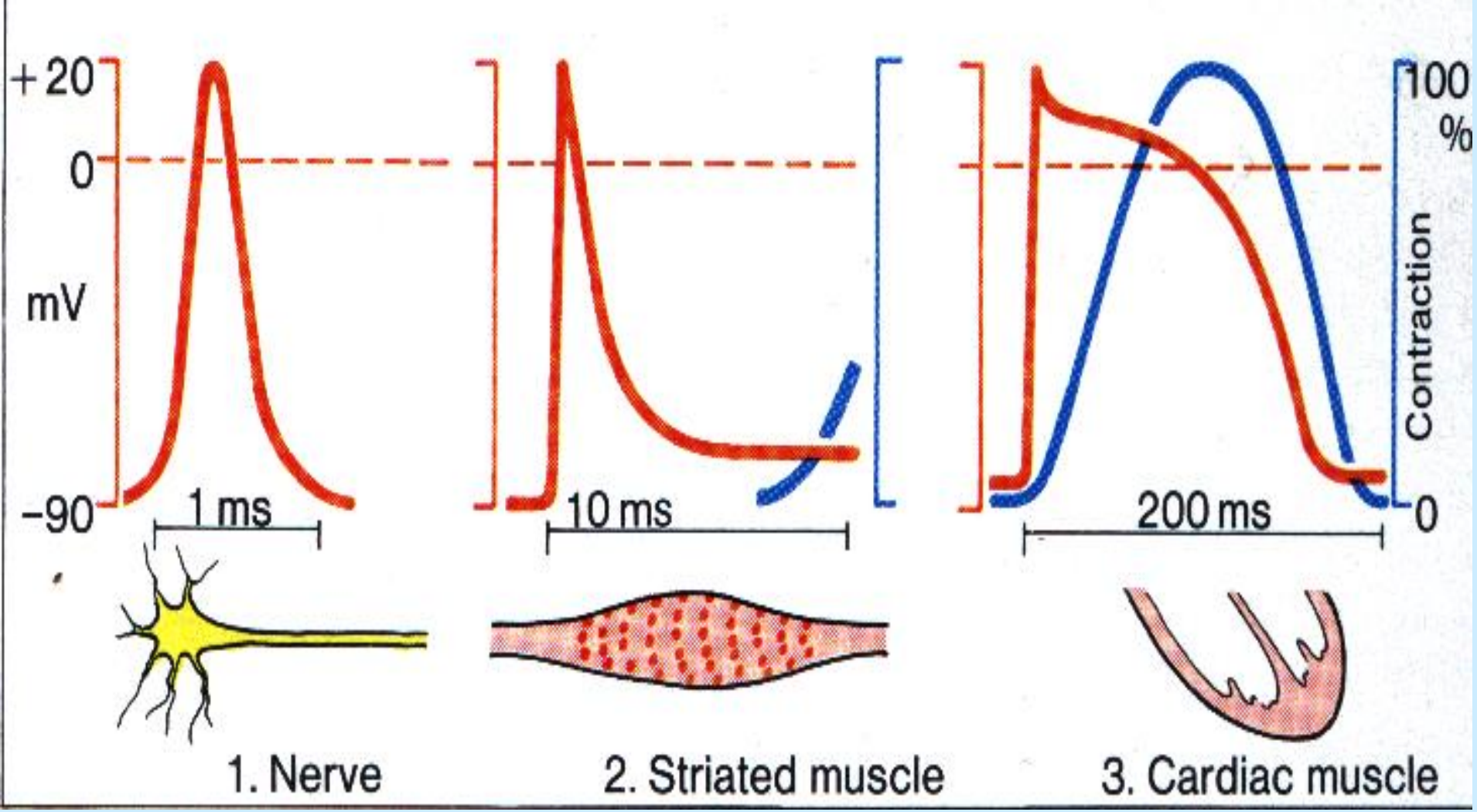
If all action potentials are alike….then how do we perceive Differences in Sensation?

i.e. Light touch versus strong shove or soft sound versus loud one.

Differences perceived when

.**Frequency** of the impulses (not their strength) is changed. Neurons can fire at different frequencies per second. The more frequent the impulses, the higher the level of excitation.

.**Number of neurons involved** - shove affects more neurons than does a light touch.



- **Excitability is the ability to sustain action potentials.**
- It differs in the 3 types of excitable cells. How?

PATHOPHYSIOLOGY OF THE NERVOUS SYSTEM

EXAMPLES OF MECHANISMS UNDERLYING SOME NEUROLOGICAL DISEASES

Pathophysiology is the physiology of abnormal states;

- it studies the functional changes that accompany a particular syndrome or disease;
- it describes the morphological and physiological changes occurring in disease and
- It tries to present the underlying mechanisms of disease.

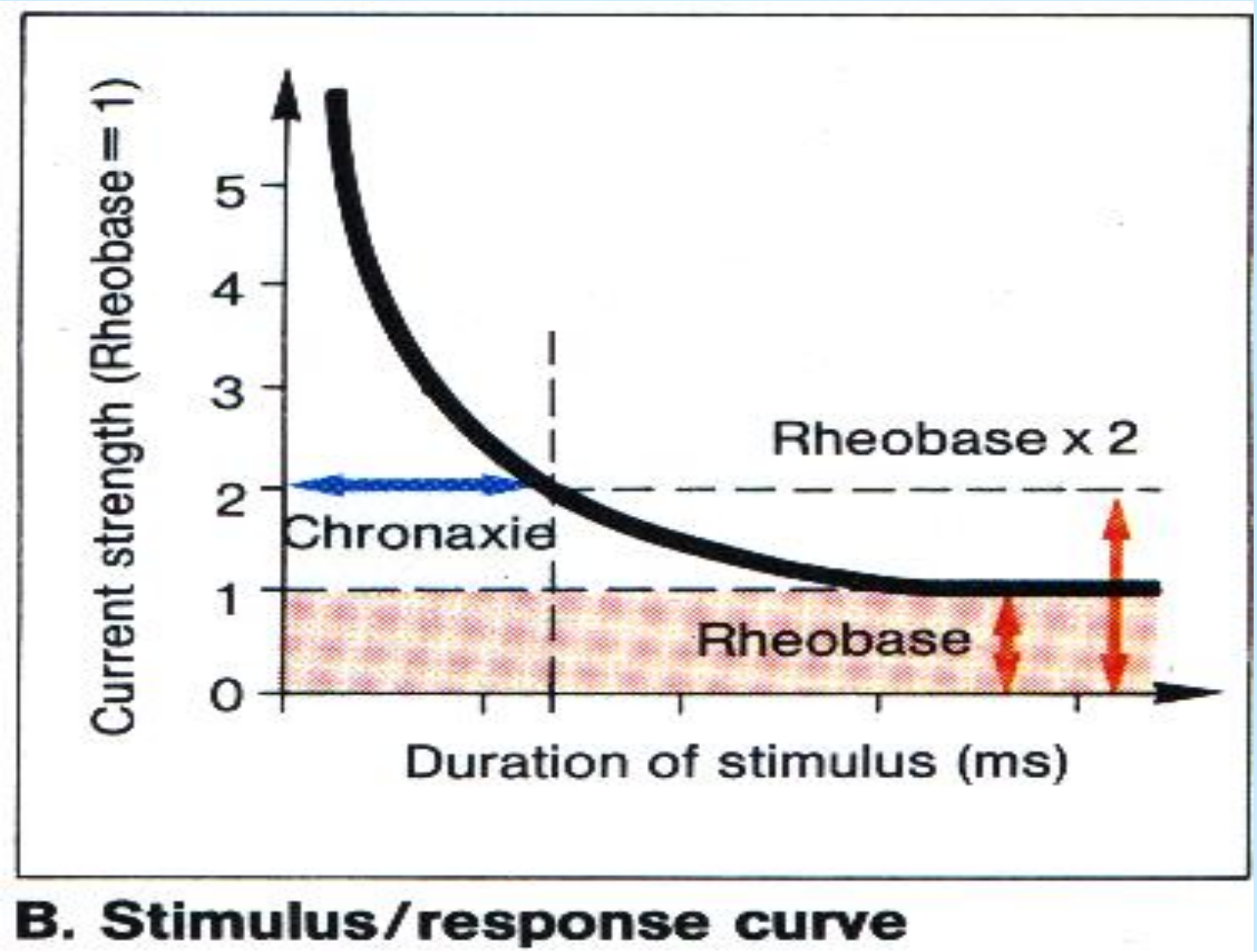
Speransky in 1934 had said: “Every disease is an exaggeration or a defect or a change of s specific physiological function”. A diagnosing physician therefore has first to identify which normal function has changed in each disease.

Examples will be given from diseases related to the specified normal functions as well as some examples of the related action of therapeutic drugs and poisons:

Neuronal and muscle excitability

- **Potassium** currents keep the membranes hyperpolarized at rest. Increase of extracellular [K+] as in renal failure or in Primary Hyperkalemic Paralysis decreases these currents and so causes **depolarization** of nerve and muscle membranes some of them going beyond excitation threshold (overdepolarization). As a result we see episodes of painful spontaneous contractures of muscle followed by paralysis. In heart the increase in ecitability has even more dramatic effects
- **Tetrodotoxin** is a specific blocker of voltage gated channels responsible for the action potential generation. It is contained in puffer fish and may therefore kill if this fish is not properly prepared

The excitability curve quantifies excitability for clinical evaluation



B. Stimulus/response curve

Axonal transport is important in pathology. Primary afferent neurons and motoneurons link the central nervous system with the periphery and thus form a protoplasmic bridge that crosses the blood-brain barrier. Certain viruses, such as the **rabies** and **polio viruses,** and toxins, such as **tetanus toxin,** can enter the central nervous system from the periphery if they are taken up and transported in the axons of these neurons.

Action potentials propagate on axons

Action potential propagation

Action potentials (to be useful as messages) have to **travel long distances with fidelity.**

Solution: AP propagation by **regeneration** on neighbouring parts of membrane after this is being electrotonically depolarized to threshold. → new AP. The power of an AP (100mV) ensures regeneration of identical AP in many small steps.

Second requirement: Message has to **travel fast**.

Solution: AP should depolarize more and further along the axon, so that fewer steps will be needed for the same distance. Given equal time for each AP, fewer steps make for higher speed.

This length of the step(how far the depolarization will still be above threshold) depends on

- **high r_m**
- **low C_m** and
- **low r_a**

This lengthening of the regeneration steps depends on

- **high r_m**
- **low C_m** and
- **low r_a**

Nature took two approaches:

(a)increase axon diameter, so that r_a decreases.

(b)when this solution reached space limits, it rapped axons with myelin so that r_m increased and on the same time C_m dropped. In this way we have saltatory propagation of AP from node to node.

Types of Conduction

Saltatory in minimal steps (therefore appearing as Continuous) - local current depolarizes adjacent portions of the membrane. When threshold is reached, action potential results. Process continues in a chain reaction. This happens in unmyelinated fibers.

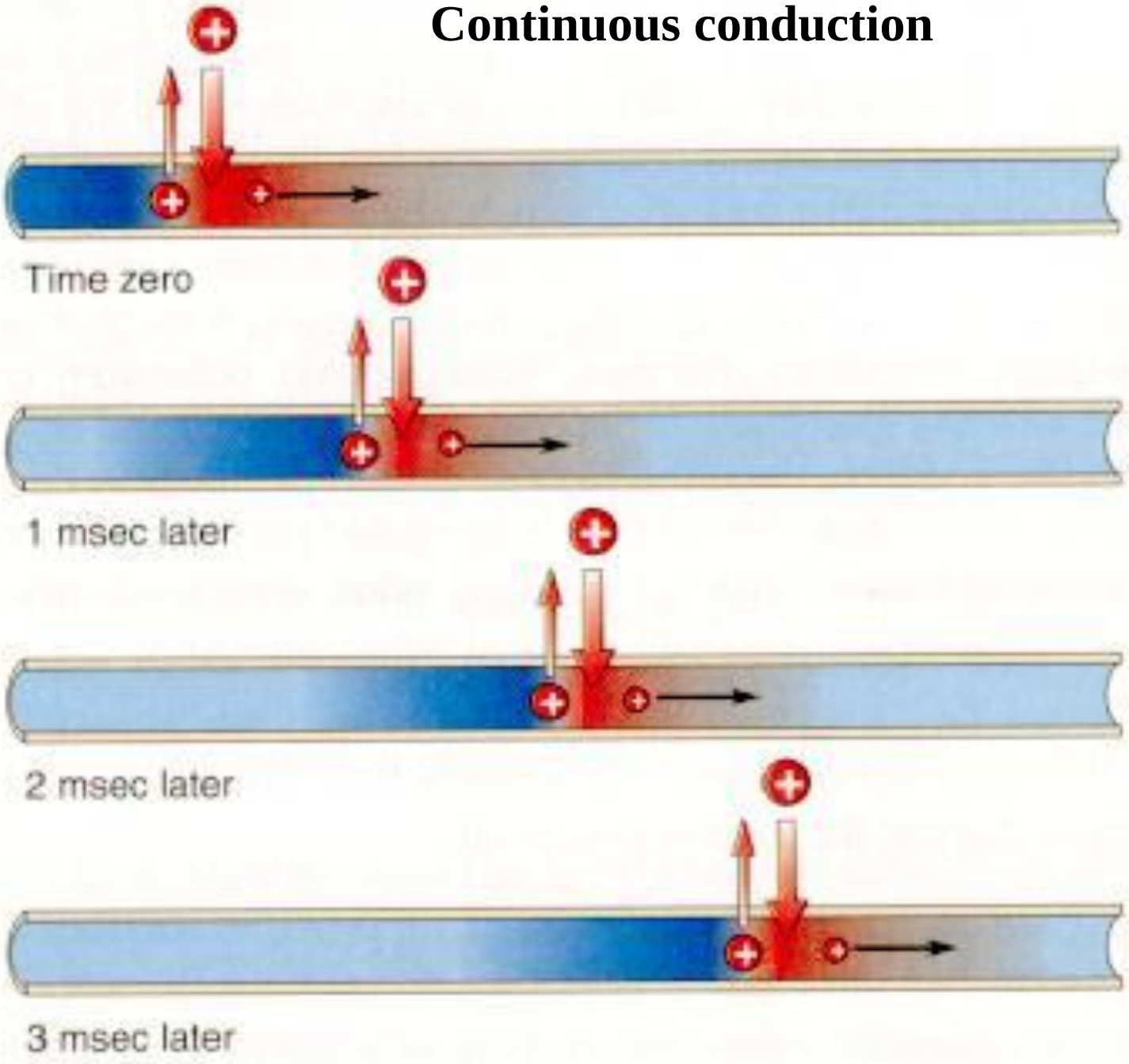
Saltatory in maximal steps- current loops are formed at Nodes of Ranvier due to insulation of myelin sheath. Action potential "jumps" from one node to the next where high concentration of voltage-gated channels are exposed to ECF. The longer the internode, the faster the speed of conduction. Requires less energy.

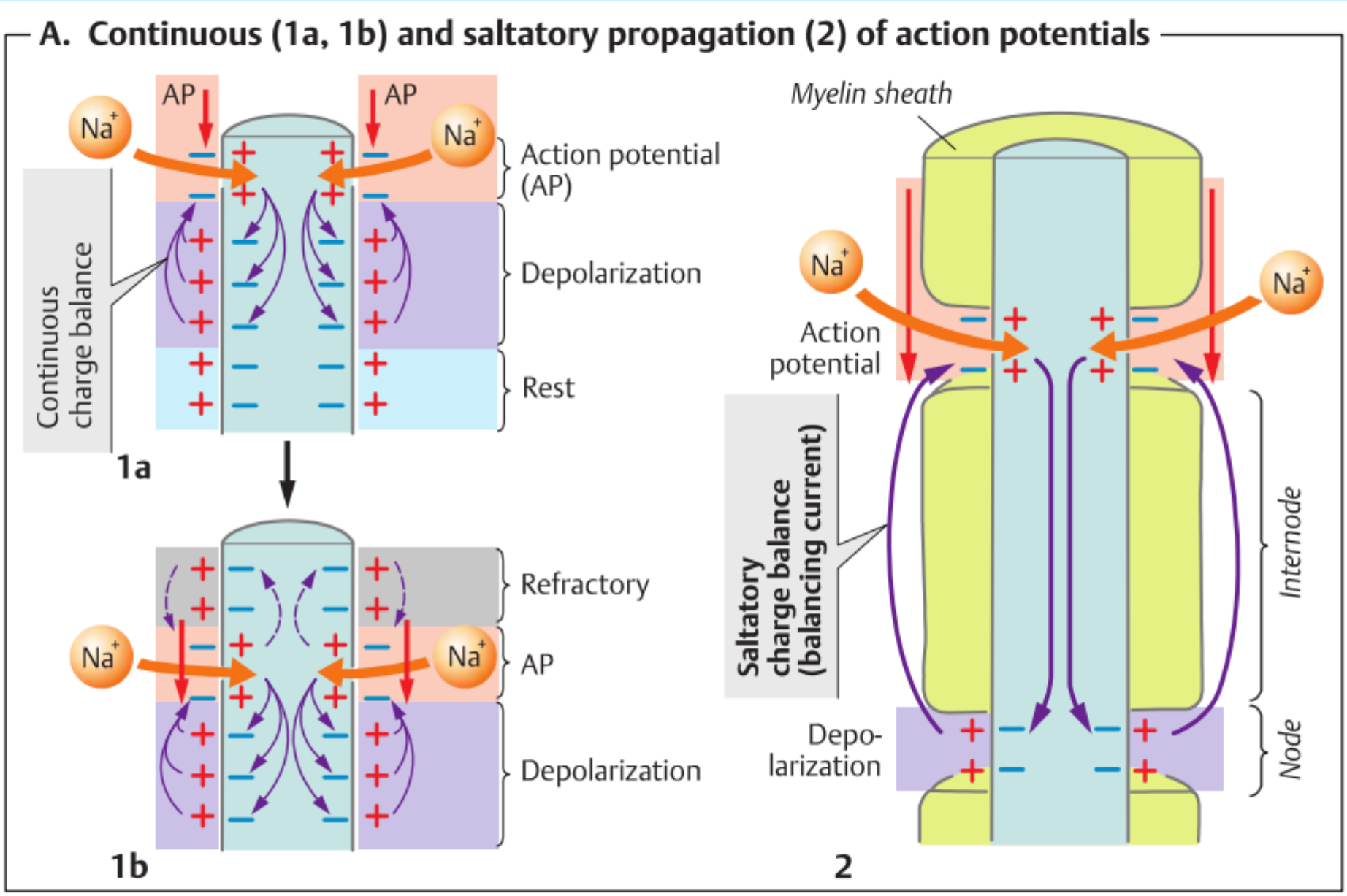
Speed of Impulse Conduction

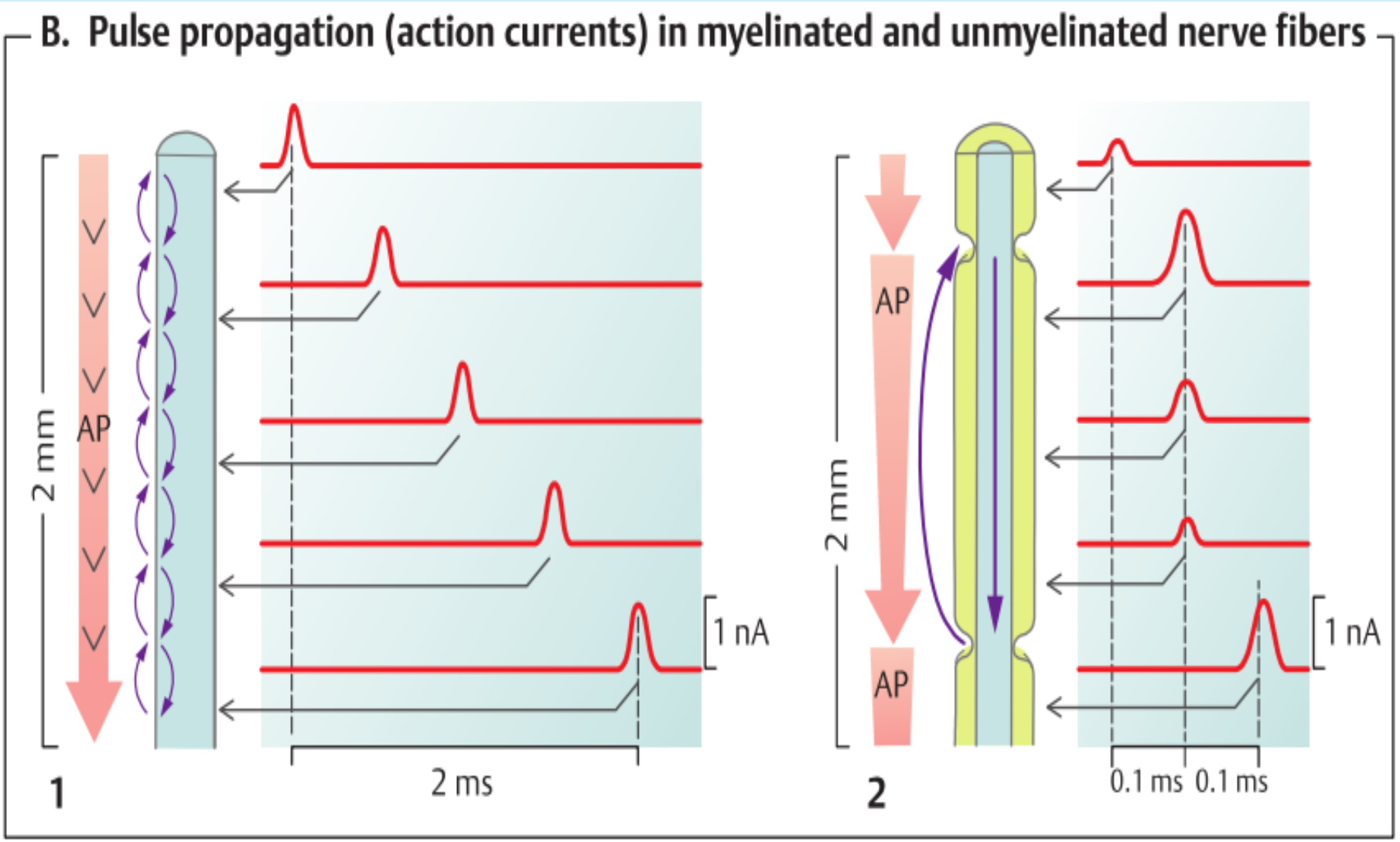
Large diameter fibers (5 to 20 μm) conduct impulses at speeds greater than smaller fibers.

Presence of myelin increases conduction velocity - up to 12 to 120 m/s versus 0.5 to 2 m/s for unmyelinated fibers.

Continuous conduction




A. Continuous (1a, 1b) and saltatory propagation (2) of action potentials
AP
AP
Na+
Na+
Action potential (AP)
Depolarization
Rest
Continuous charge balance
1a
Refractory
AP
Depolarization
1b
Myelin sheath
Action potential
Saltatory charge balance (balancing current)
Depo-larization
Internode
Node
2


B. Pulse propagation (action currents) in myelinated and unmyelinated nerve fibers
2 mm
AP
1 nA
2 ms
1
AP
AP
2 mm
1 nA
0.1 ms 0.1 ms
2

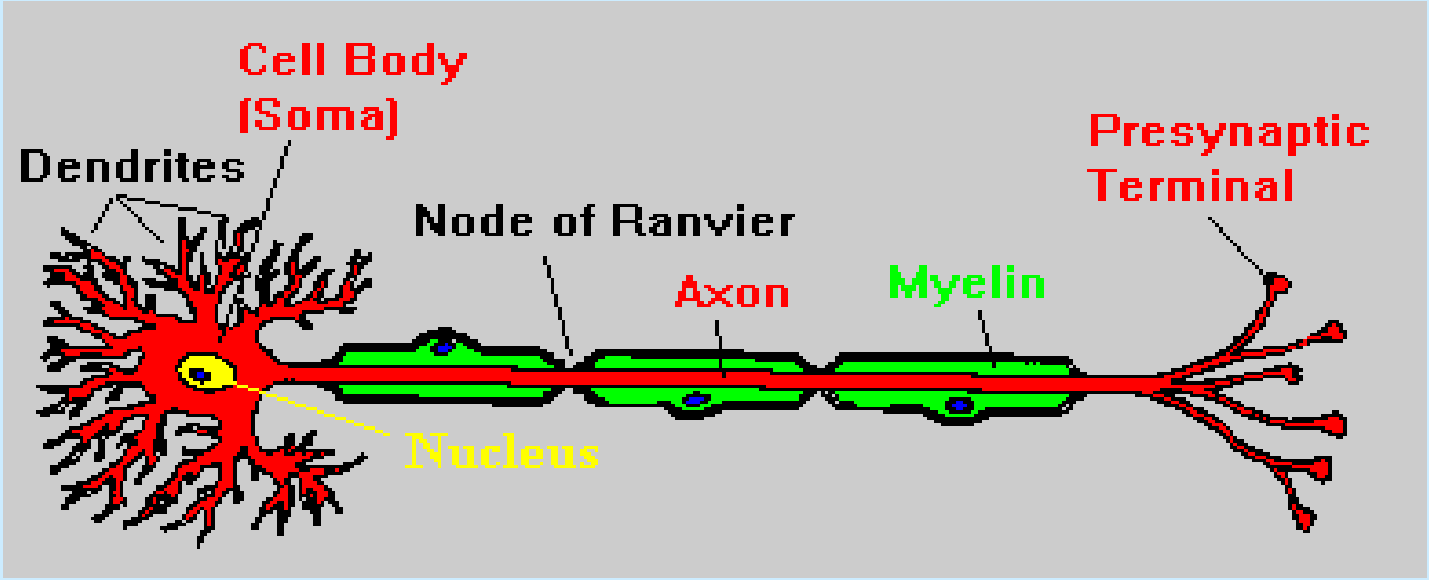
C. Classification of nerve fibers (in humans)

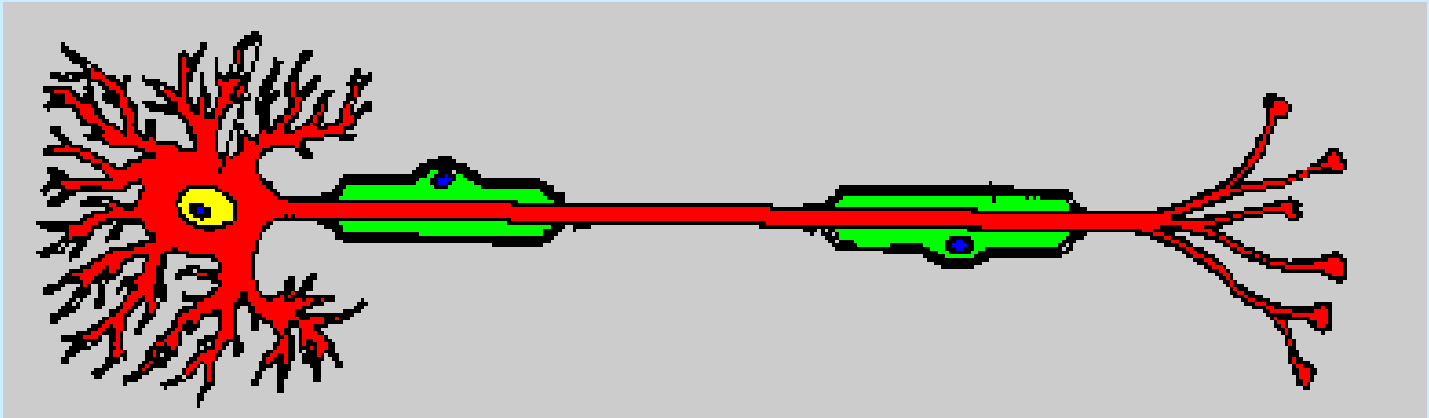
Fiber type	Function according to fiber type (Lloyd and Hunt types I – IV)	Diameter (µm)	Conduction rate (m/s)
Aα	Skeletal muscle efferent, afferents in muscle spindles (Ib) and tendon organs (Ib)	11 – 16	60 – 80
Aβ	Mechanoafferents of skin (II)	6 –11	30 – 60
Aγ	Muscle spindle efferents	1 – 6	2 – 30
Aδ	Skin afferents (temperature and "fast" pain) (III)		
B	Sympathetic preganglionic; visceral afferents	3	3 – 15
C	Skin afferents ("slow" pain) (IV); sympathetic postganglionic afferents	0.5 –1.5 (unmyelinated)	0.25 – 1.5

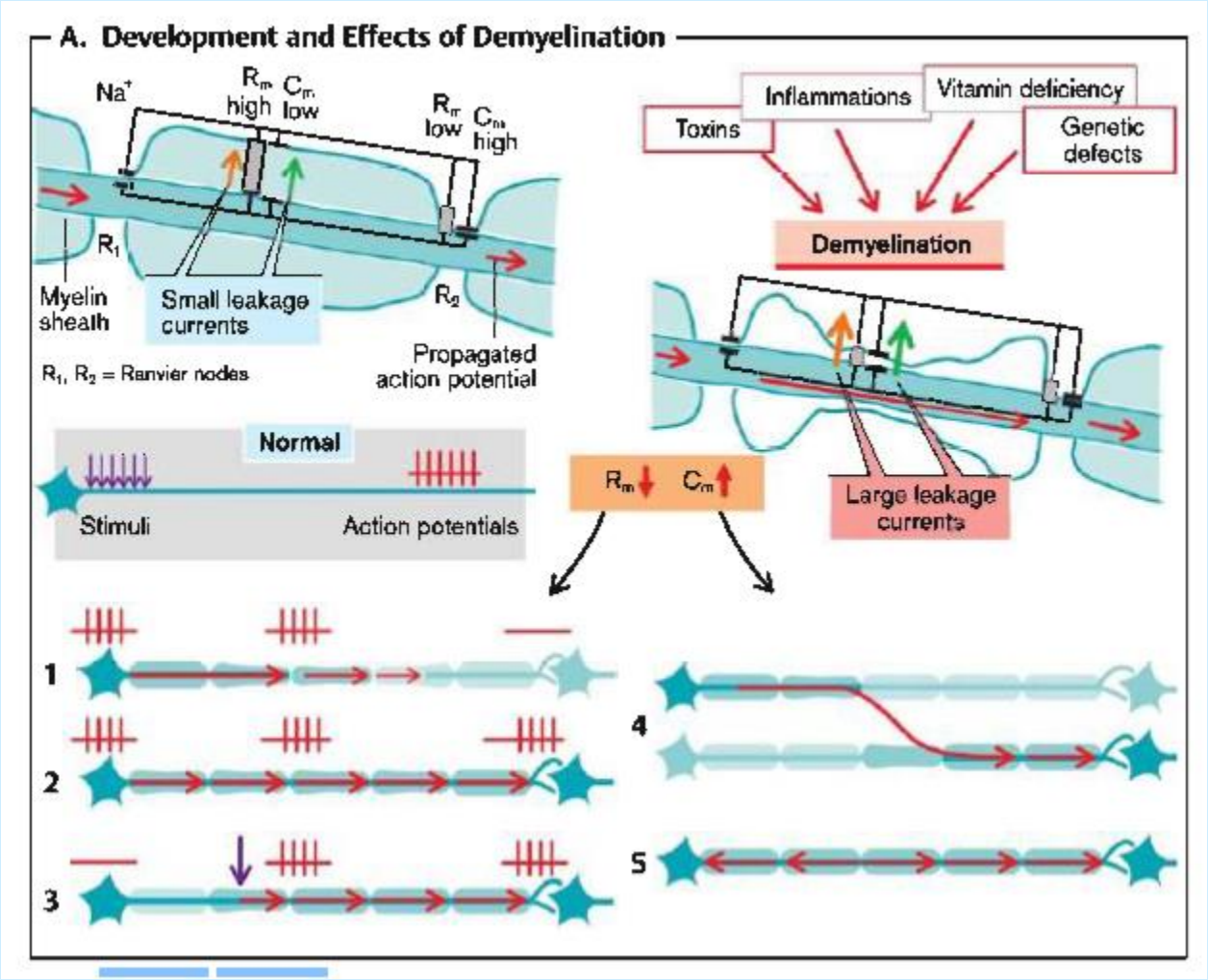
(After Erlanger and Gasser)

Note that the ratio between speed and diameter is about 6

Pathophysiology: In some diseases, known as **demyelinating disorders,** the myelin sheath deteriorates and may be lost over one or more inter-nodes of many axons without interruption of the axons. In such cases, conduction of nerve impulses may be slowed or blocked, and the function of the affected axons is therefore abnormal.






A. Development and Effects of Demyelination
Na+
Rm high Cm low
Rm low Cm high
R1
Myelin sheath
Small leakage currents
R2
Propagated action potential
R1, R2 = Ranvier nodes
Toxins
Inflammations
Vitamin deficiency
Genetic defects
Demyelination
Normal
Stimuli
Action potentials
Rm Cm
Large leakage currents
1
2
3
4
5

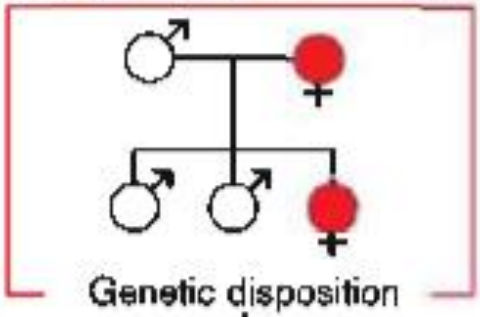
Pathophysiology -

Such demyelination occurs in the peripheral nervous system in the **Guillain-Barre syndrome** and in **diphtheria.** The neuropathy common in severe cases of **diabetes mellitus** is due to demyelination of peripheral axons.

When myelin is lost, the length constant, which is dramatically increased by myelination, becomes much shorter. Hence when the action potential is electrotonically conducted from one node of Ranvier to the next, it loses amplitude. If demyelination is sufficiently severe, the action potential may arrive at the next node of Ranvier with insufficient strength to fire an action potential. The axon will then fail to propagate action potentials.

An important demyelinating disease of the central nervous system is **multiple sclerosis,** where scattered progressive demyelination of axons in the CNS results in loss of motor control and sensory function.

B. Multiple Sclerosis



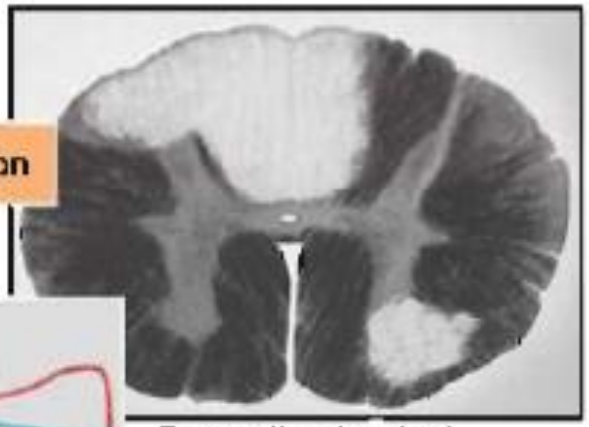
Genetic disposition

Autoimmune disease, possibly caused by viruses

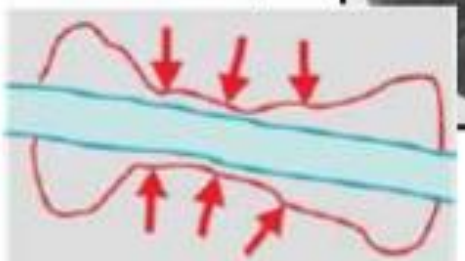
?

MHC
IL-2 rec.
IL-7 rec.

Inflammation



Demyelinating foci in spinal cord (after Netter)

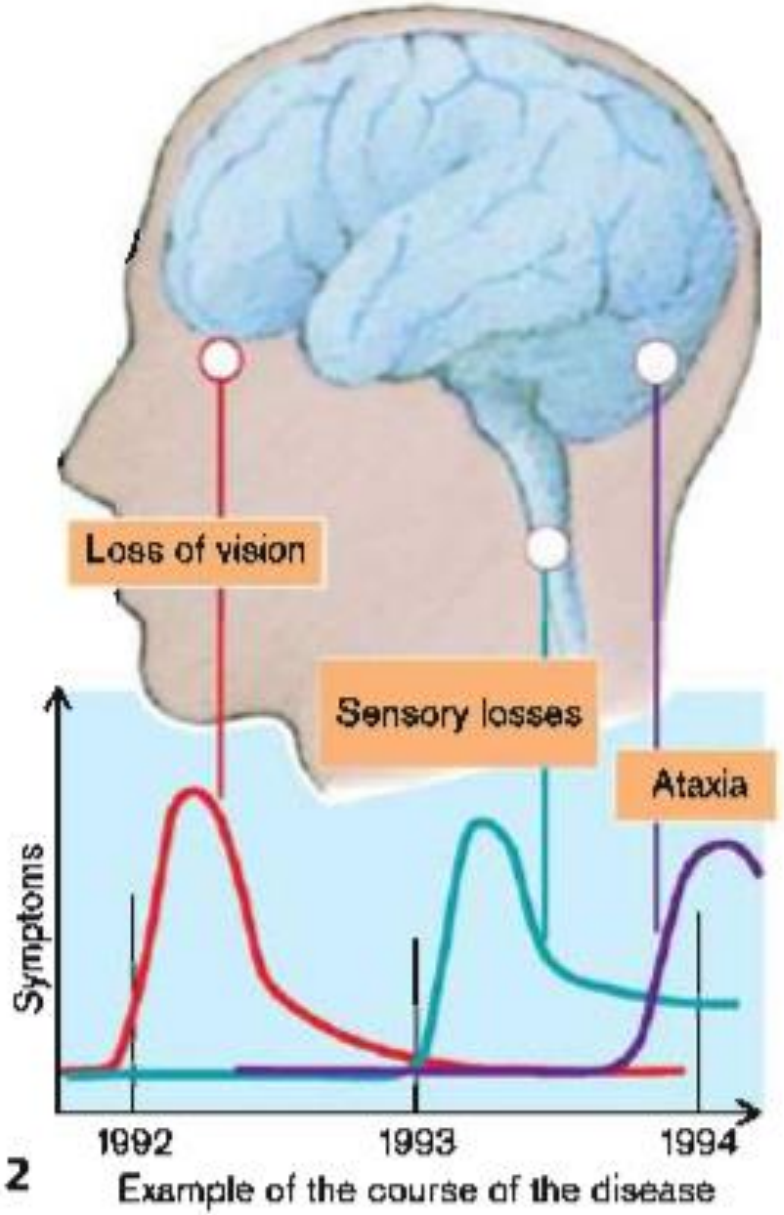


Demyelination in CNS

Multiple sclerosis

periodically recurrent neuronal losses

1



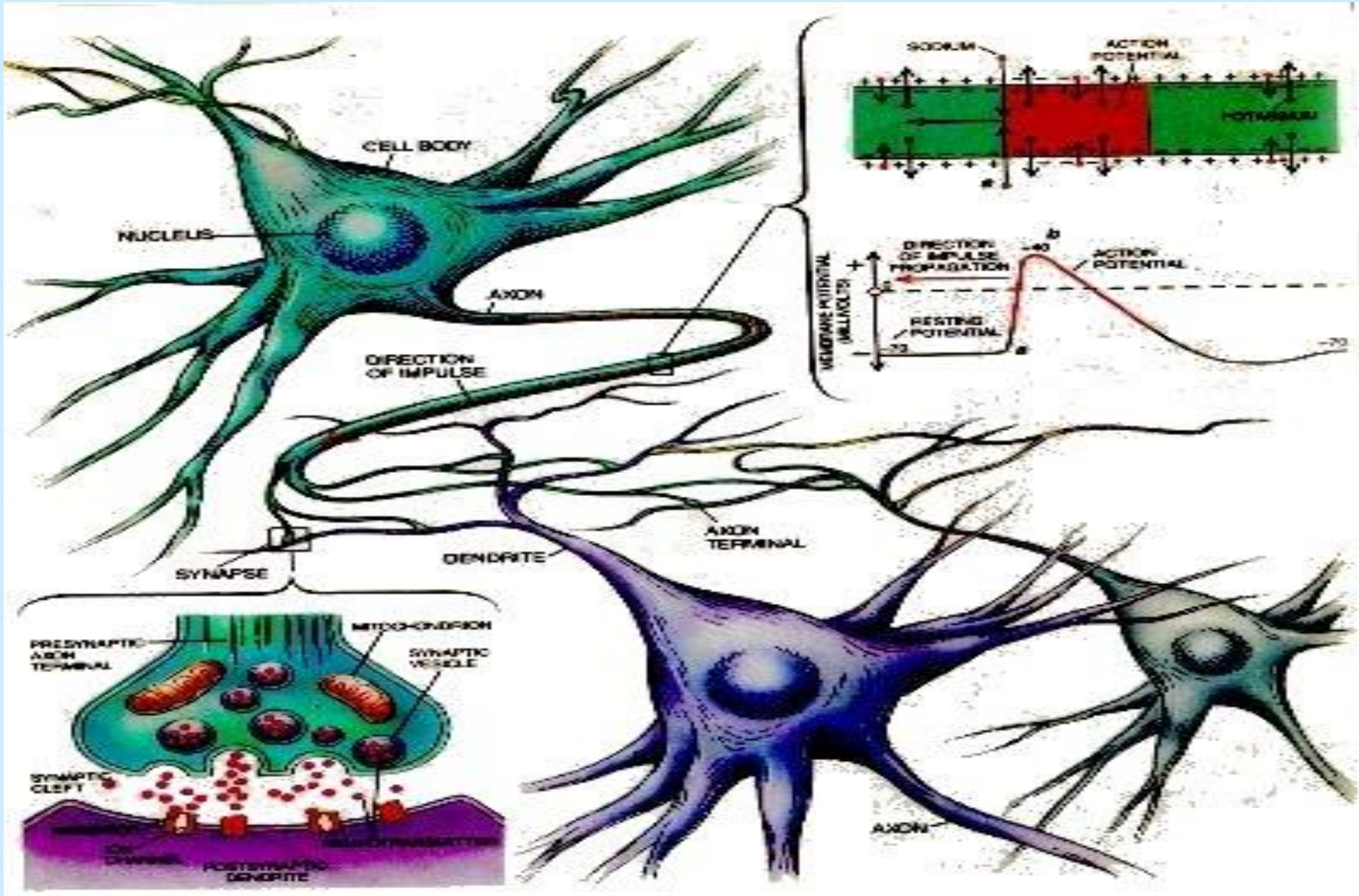
2 Example of the course of the disease

IN PRACTICE

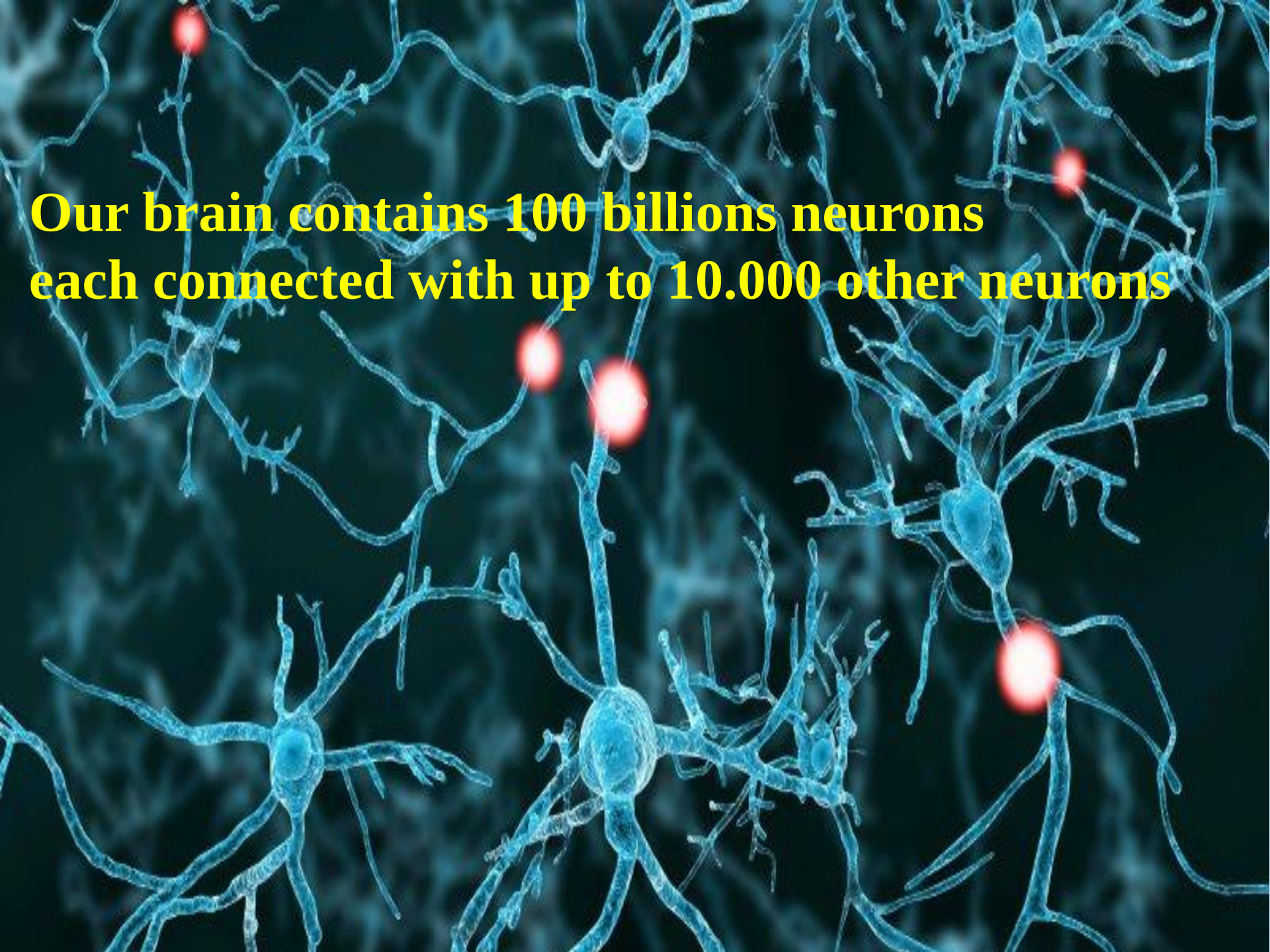
- How can we experimentally excite a neuron?
- How can we measure the conduction velocity of an axon or a nerve ?
- How fast can this be?
- What conditions may lead to accidental electrification? [low contact resistance with high voltage low frequency AC. ACDC only with stimulus ON and OFF.]
- What would be the main risk to our health? [ventricular fibrillation in heart]
- How does diathermy work? [with high frequency AC (>15 Hz)]

SYNAPTIC TRANSMISSION

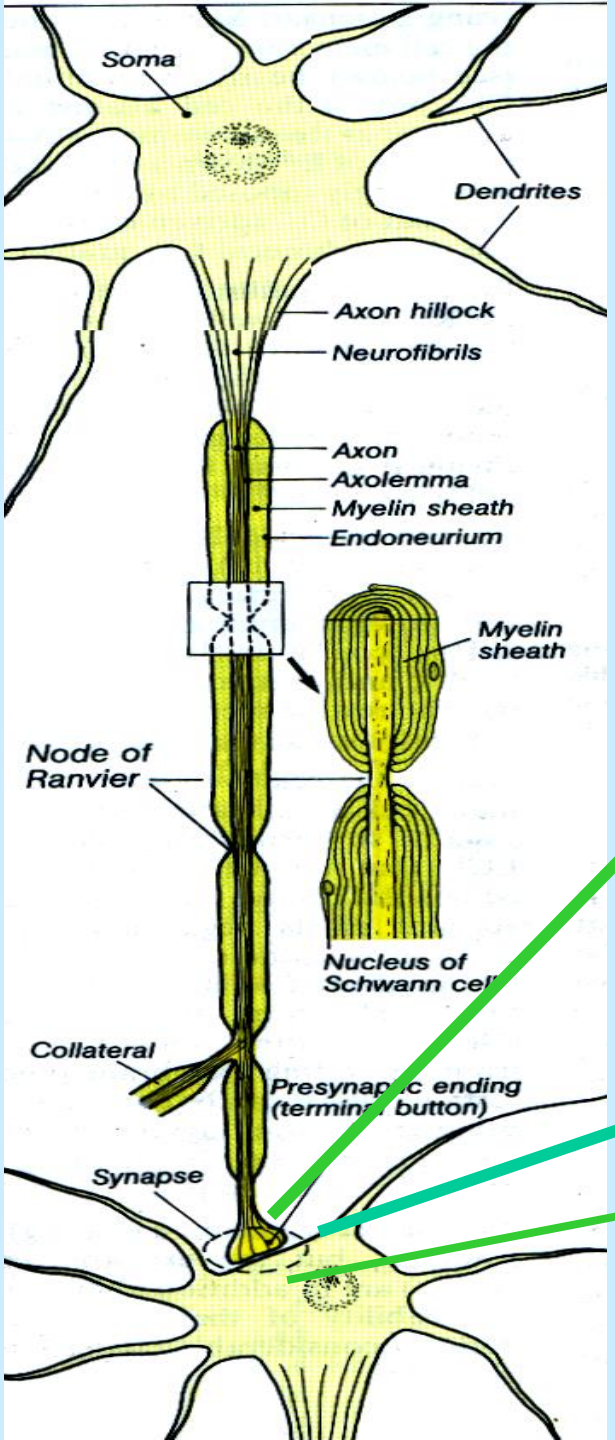
ACTION POTENTIAL CONDUCTION

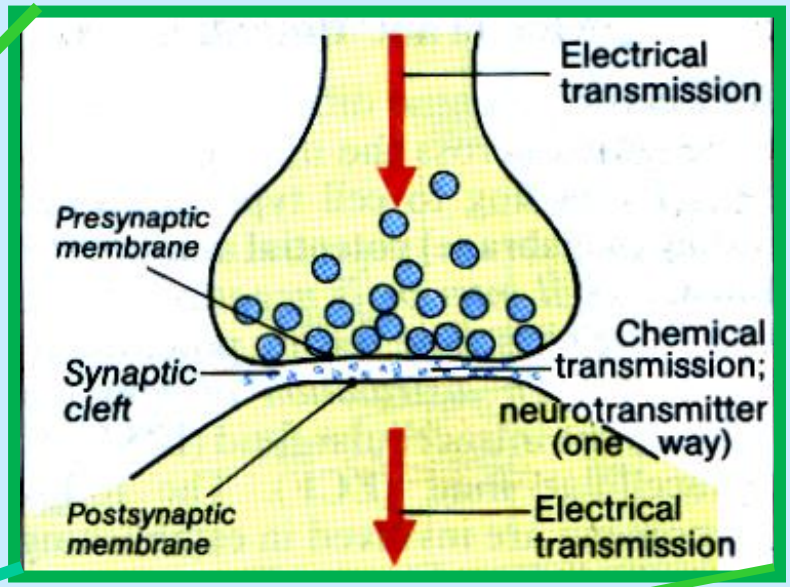


SYNAPTIC TRANSMISSION


Our brain contains 100 billions neurons
each connected with up to 10.000 other neurons

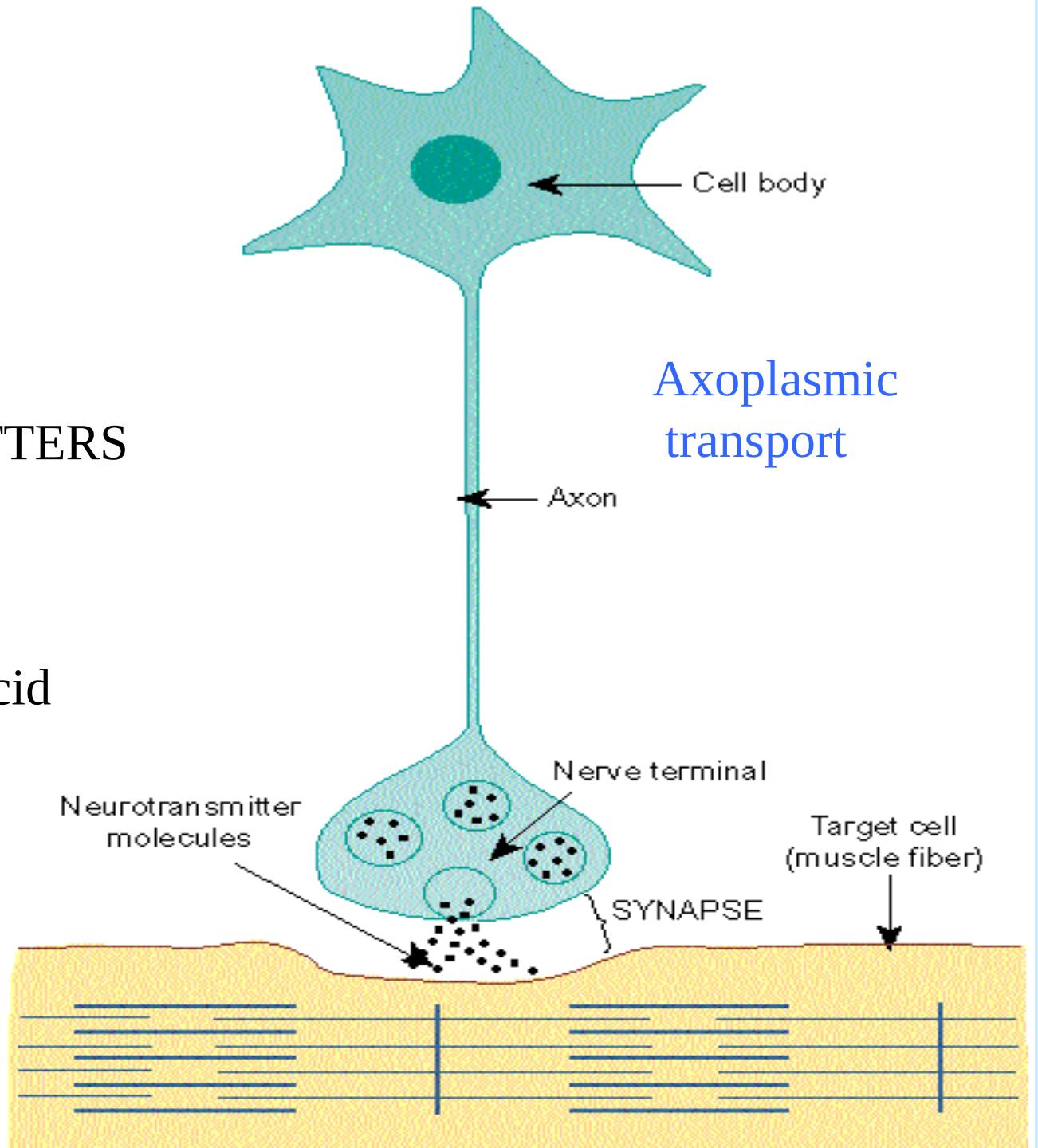
Synaptic transmission





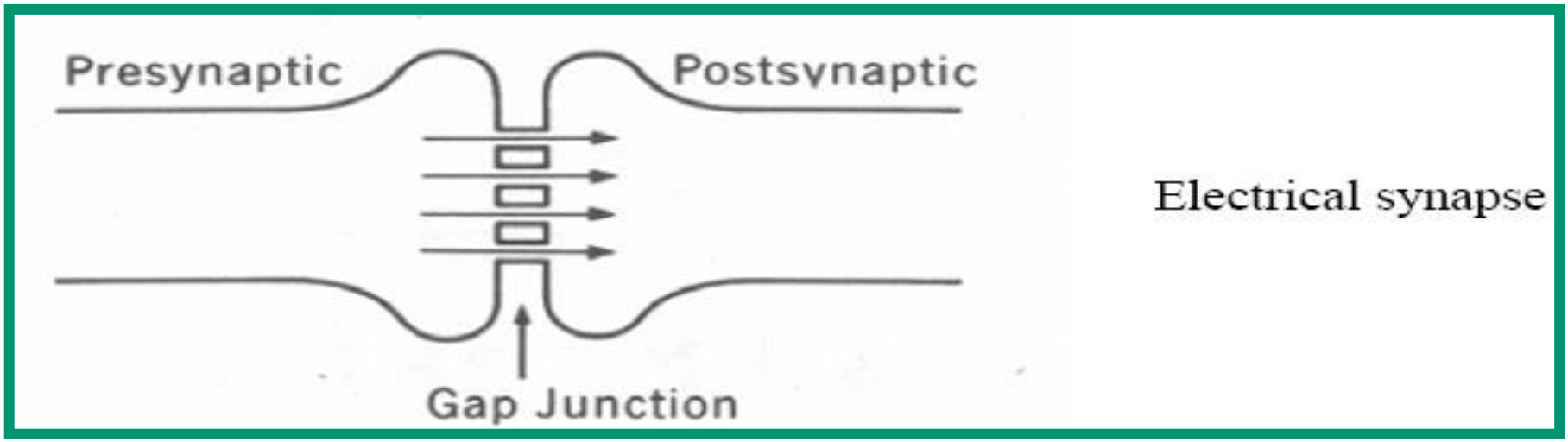
NEUROTRANSMITTERS

- Acetylcholine
- Norepinephrine
- dopamine
- γ-amino-butyric acid
- Glutamate
- Glycine
- Aspartate
- Substance P

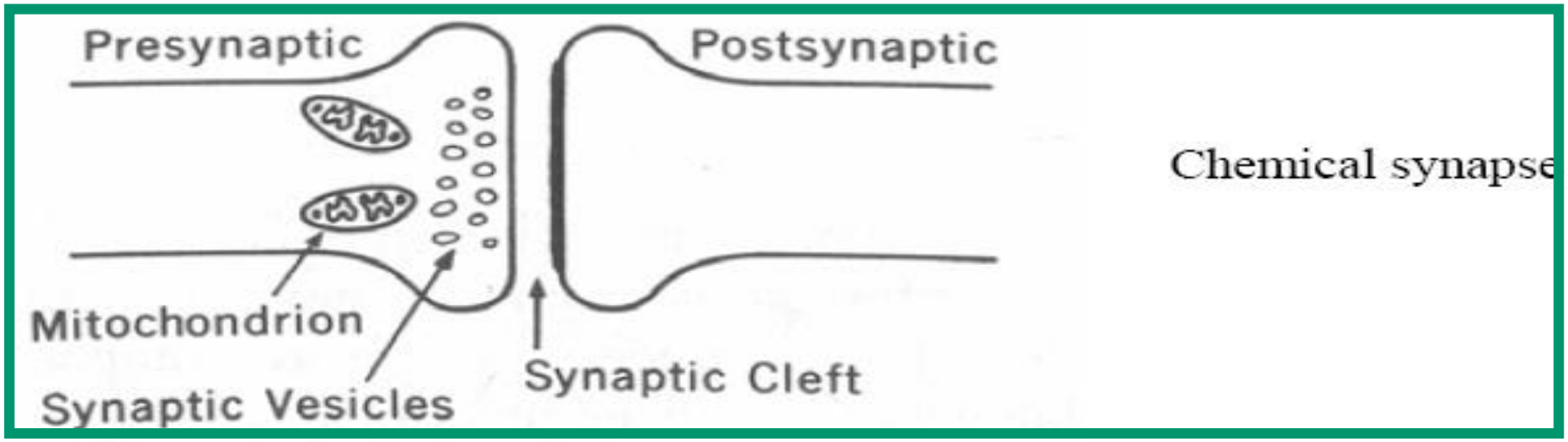


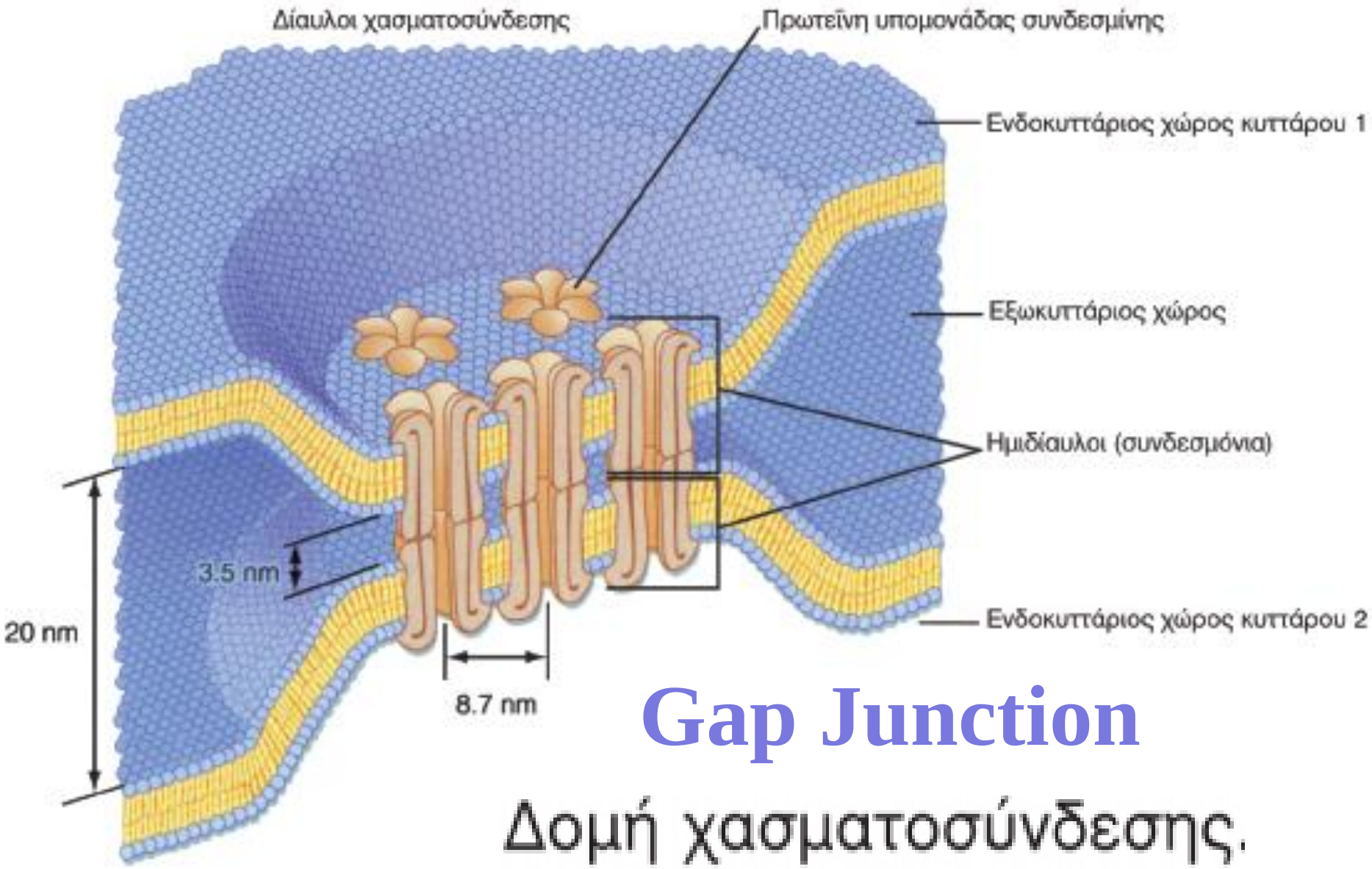
Synaptic transmission can be either electrical or (most often) chemical

A



B





Gap Junction

Δομή χασματοσύνδεσης.

Synaptic transmission – chemical ST

When action potential reaches the synaptic knob, it causes synaptic vesicles to release a **neurotransmitte**r.

Neurotransmitter diffuses across **synaptic cleft** (~25nm) at synapse **(neuroeffector junctio**n) and binds with receptors on post-synaptic membrane (another neuron, muscle cell, or gland cell).

Neurotransmitters are of 3 chemical types:

- small molecules: amines and aminocids:

ACh - released at **cholinergic synapse**s. Common inside and outside CNS. Include neuromuscular junction.

Norepinephrine (NE) - important in brain and in portions of autonomic nervous system. Also called **noradrenalin**e. **Adrenergic synapse**s.

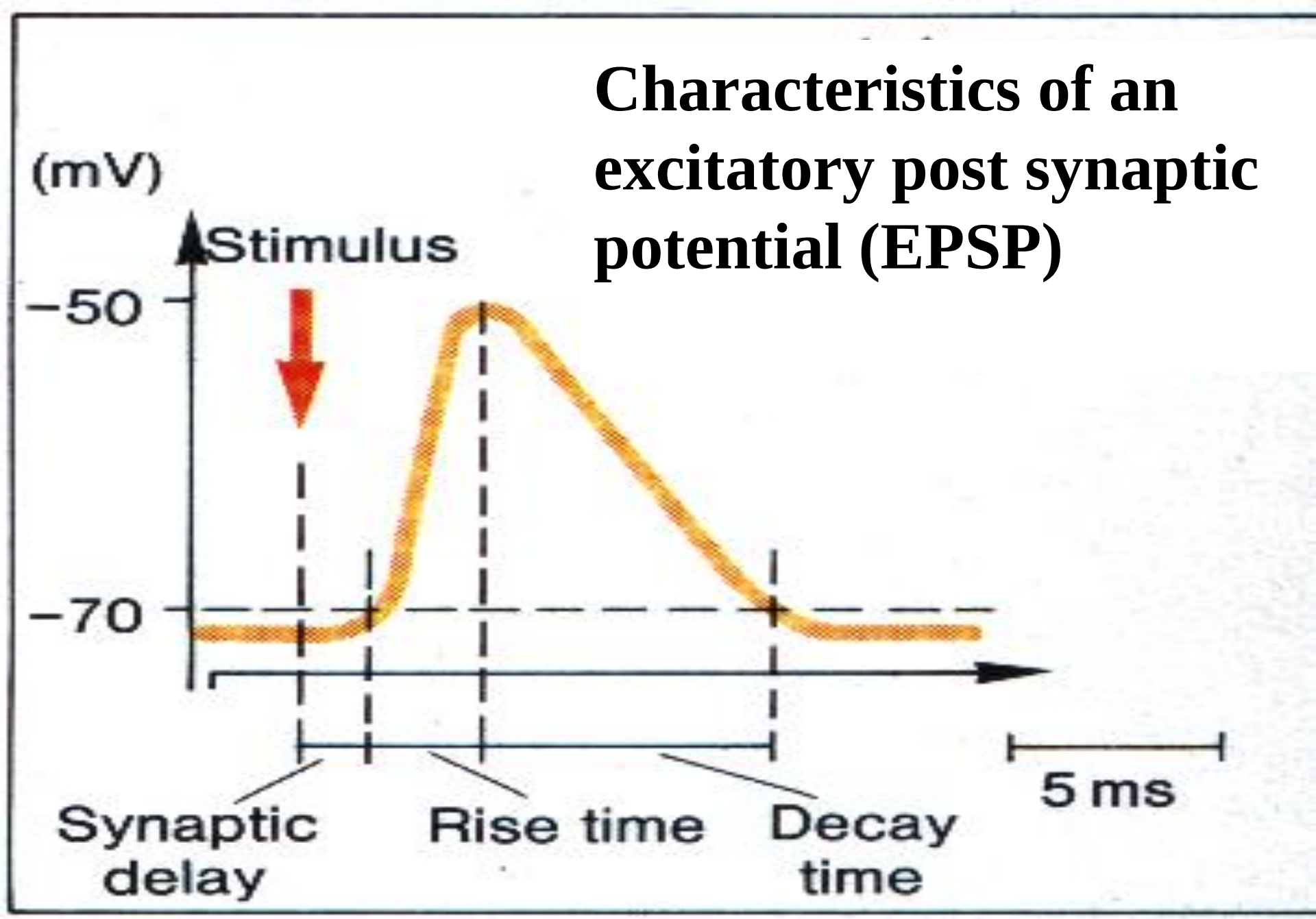
Others: **dopamin**e, **gamma aminobutyric acid (GABA**), **glycine** and **serotoni**n usually act as inhibitors. **Glutamate** and **aspartate** usually in excitatory synapses

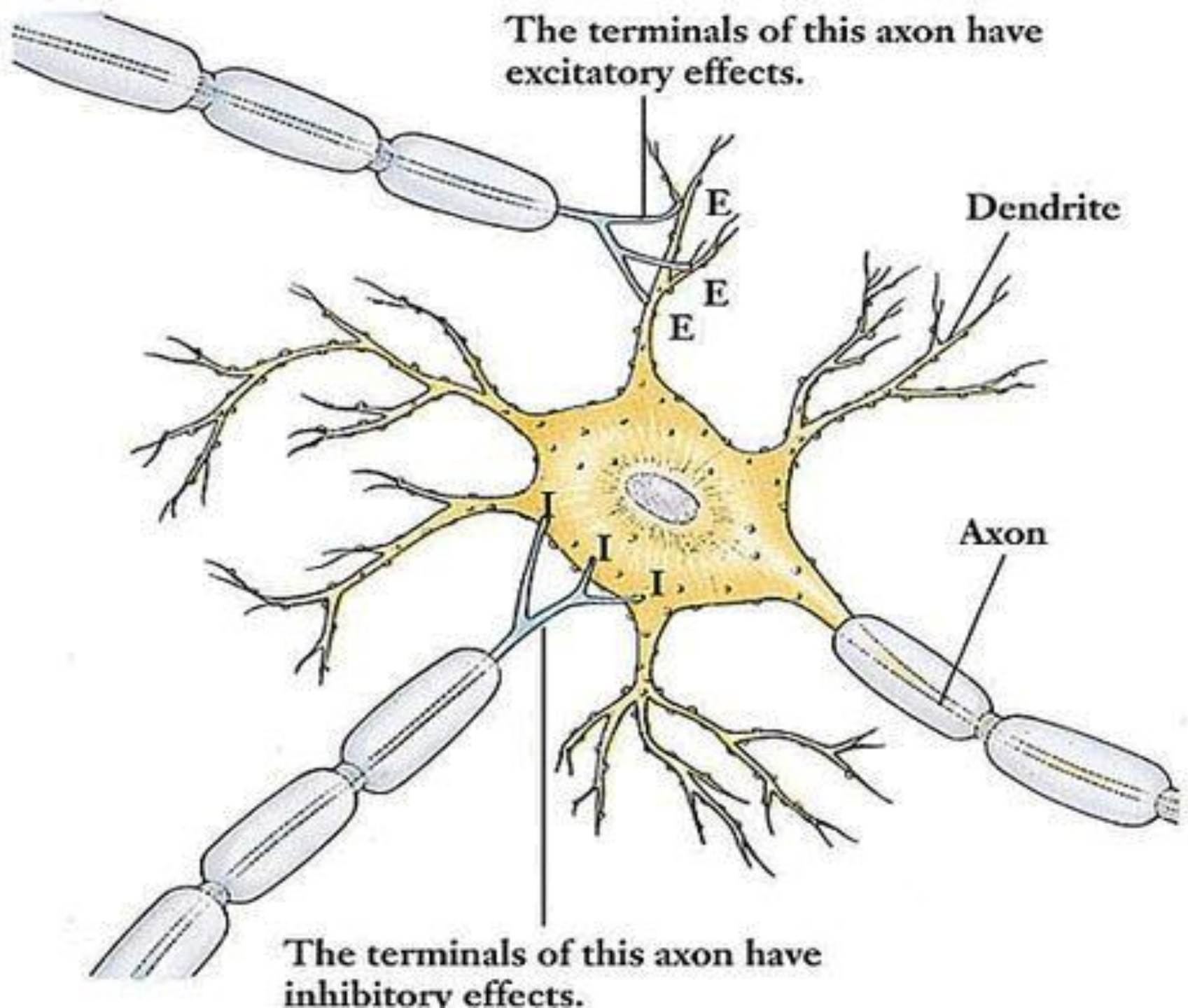
- Peptides
- Gases

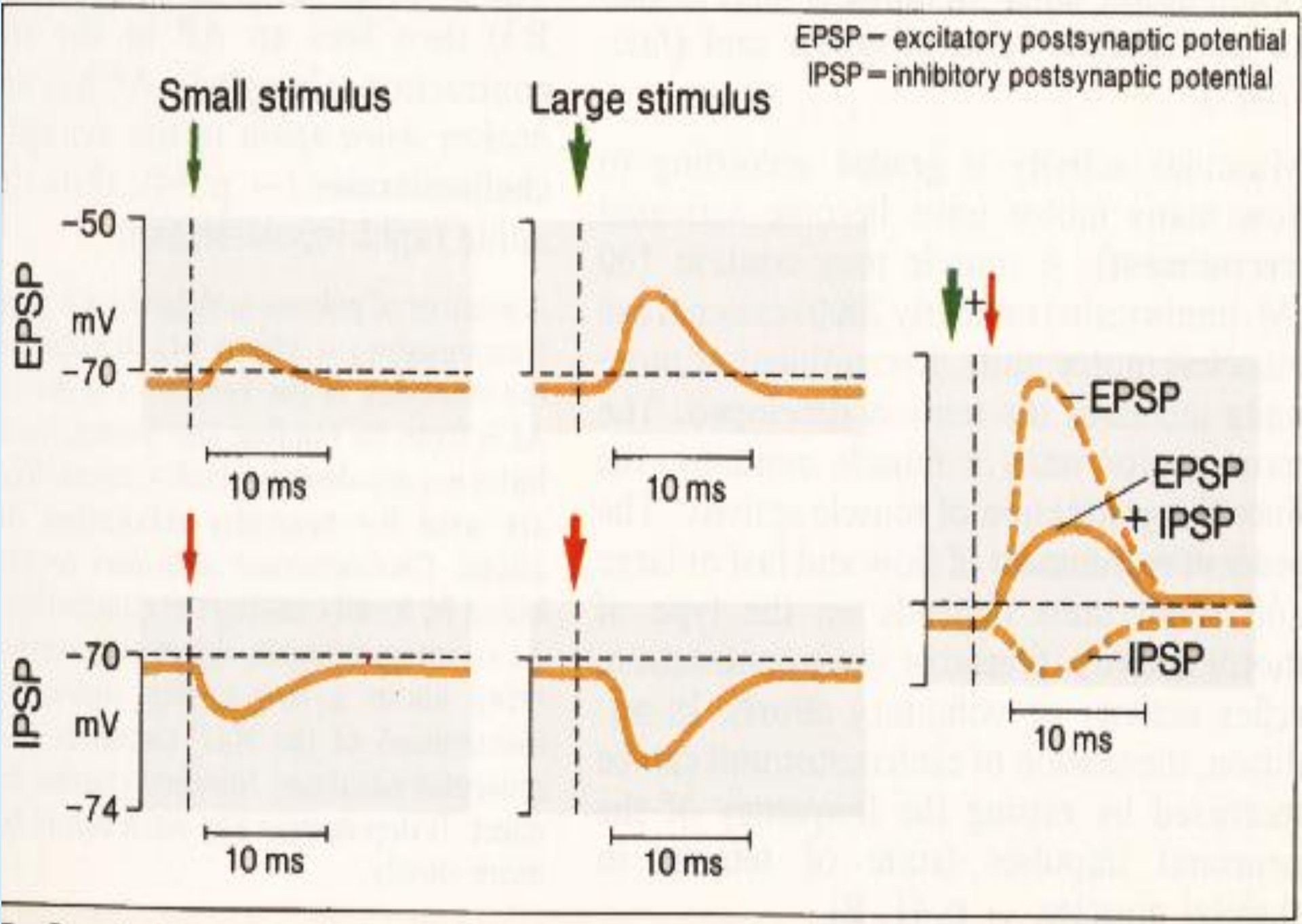
2 types of neurotransmitter receptors:

Ionotropic and metabolotropic

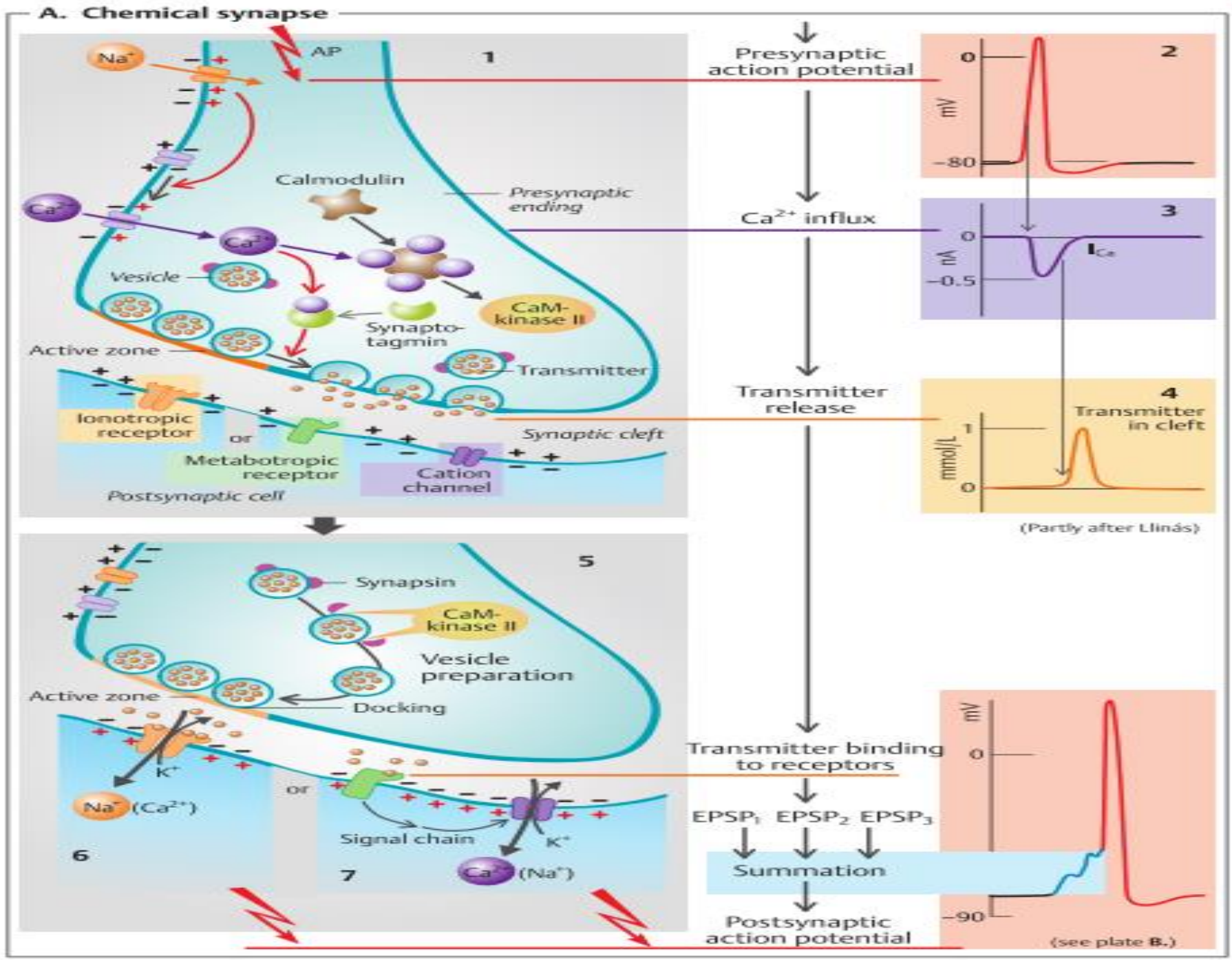
Characteristics of an excitatory post synaptic potential (EPSP)

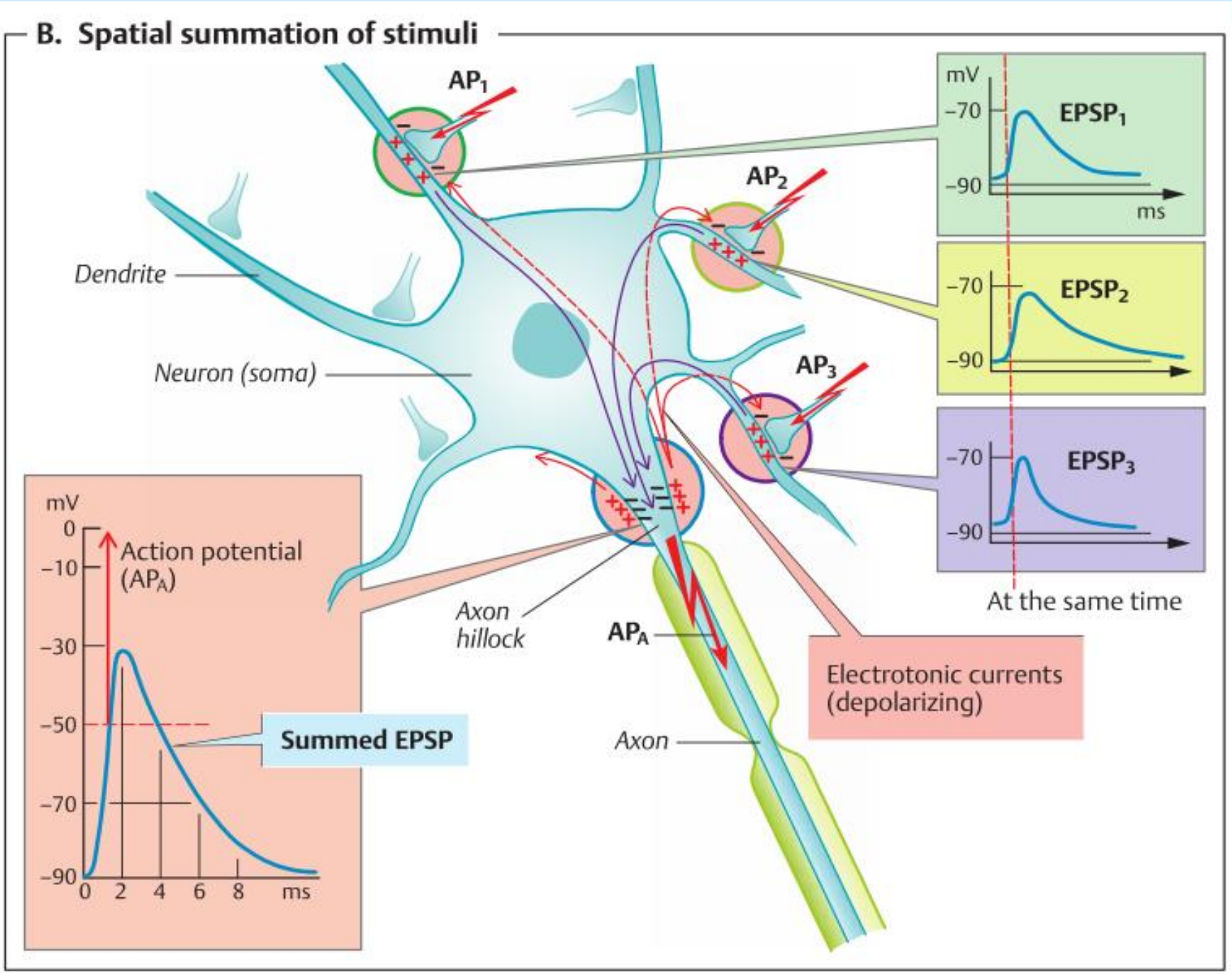



The terminals of this axon have excitatory effects.
E
E
E
Dendrite
I
I
I
Axon
The terminals of this axon have inhibitory effects.



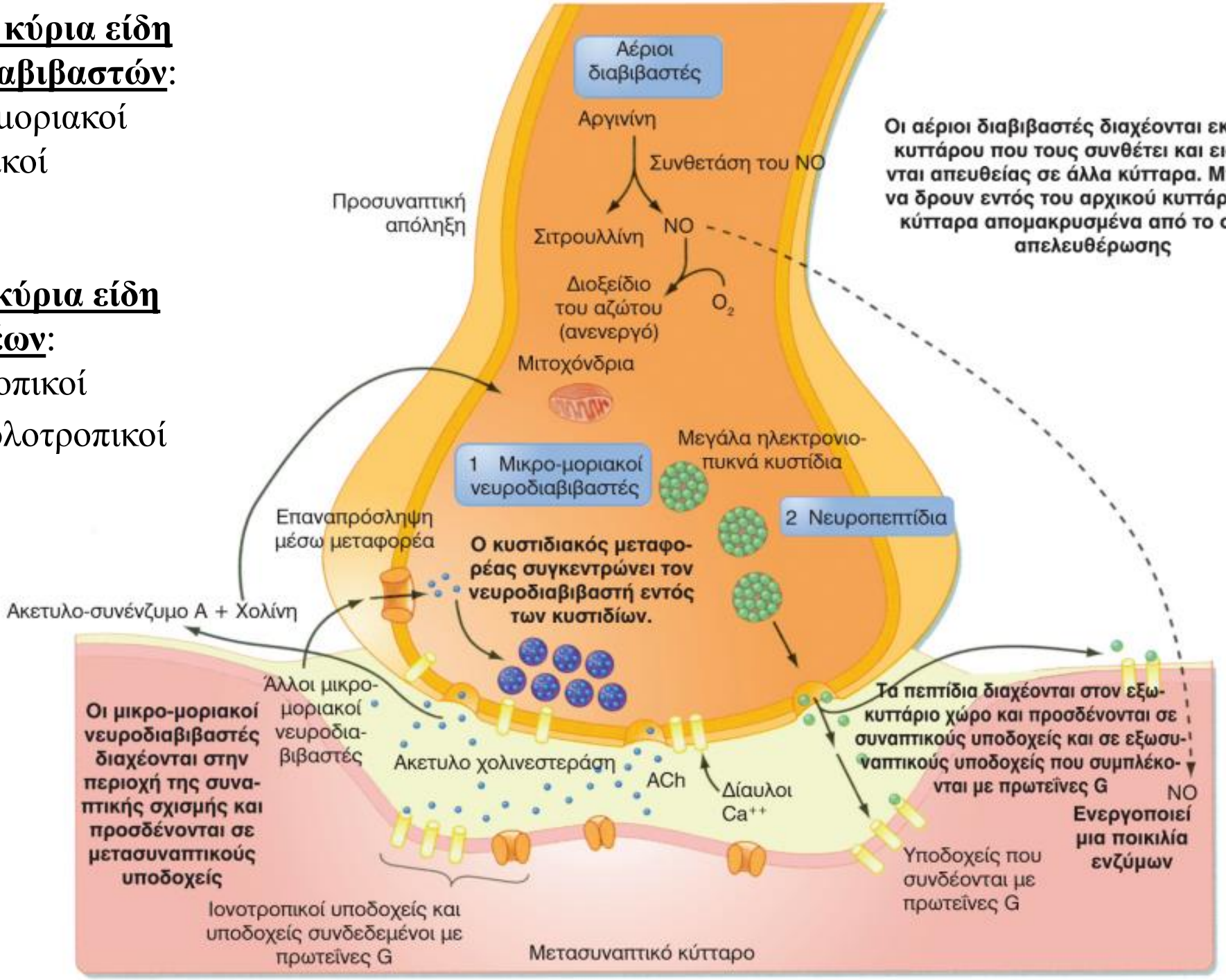
D. Graded response of EPSP and IPSP to stimuli


A. Chemical synapse
Na+
AP
1
Presynaptic action potential
2
0
mV
−80
Calmodulin
Presynaptic ending
Ca2+
Ca2+ influx
3
0
nA
−0.5
ICa
Vesicle
CaM-kinase II
Synapto-tagmin
Active zone
Transmitter
Transmitter release
4
Transmitter in cleft
mmol/L
1
0
Ionotropic receptor
or
Metabotropic receptor
Synaptic cleft
Cation channel
Postsynaptic cell
(Partly after Llinás)
5
Synapsin
CaM-kinase II
Vesicle preparation
Active zone
Docking
K+
Na+ (Ca2+)
or
Signal chain
K+
Ca2+ (Na+)
6
7
Transmitter binding to receptors
EPSP1 EPSP2 EPSP3
Summation
Postsynaptic action potential
mV
0
−90
(see plate B.)

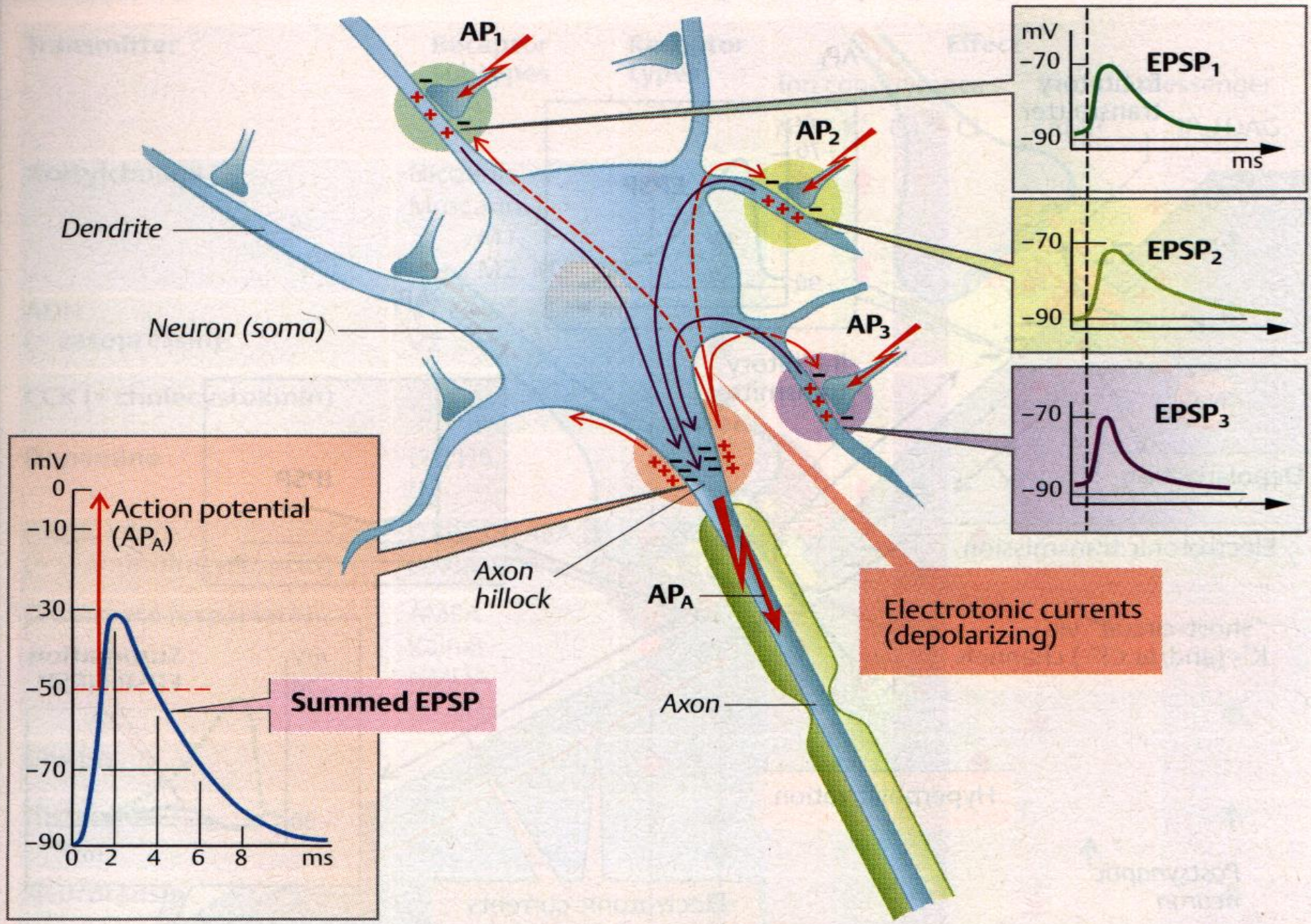

B. Spatial summation of stimuli
AP1
AP2
AP3
Dendrite
Neuron (soma)
Axon hillock
APA
Axon
mV
-70
-90
ms
EPSP1
EPSP2
EPSP3
At the same time
Electrotonic currents (depolarizing)
mV
0
-10
-30
-50
-70
-90
0 2 4 6 8 ms
Action potential (APA)
Summed EPSP

α κύρια είδη διαβιβαστών:
-μοριακοί
οικοί

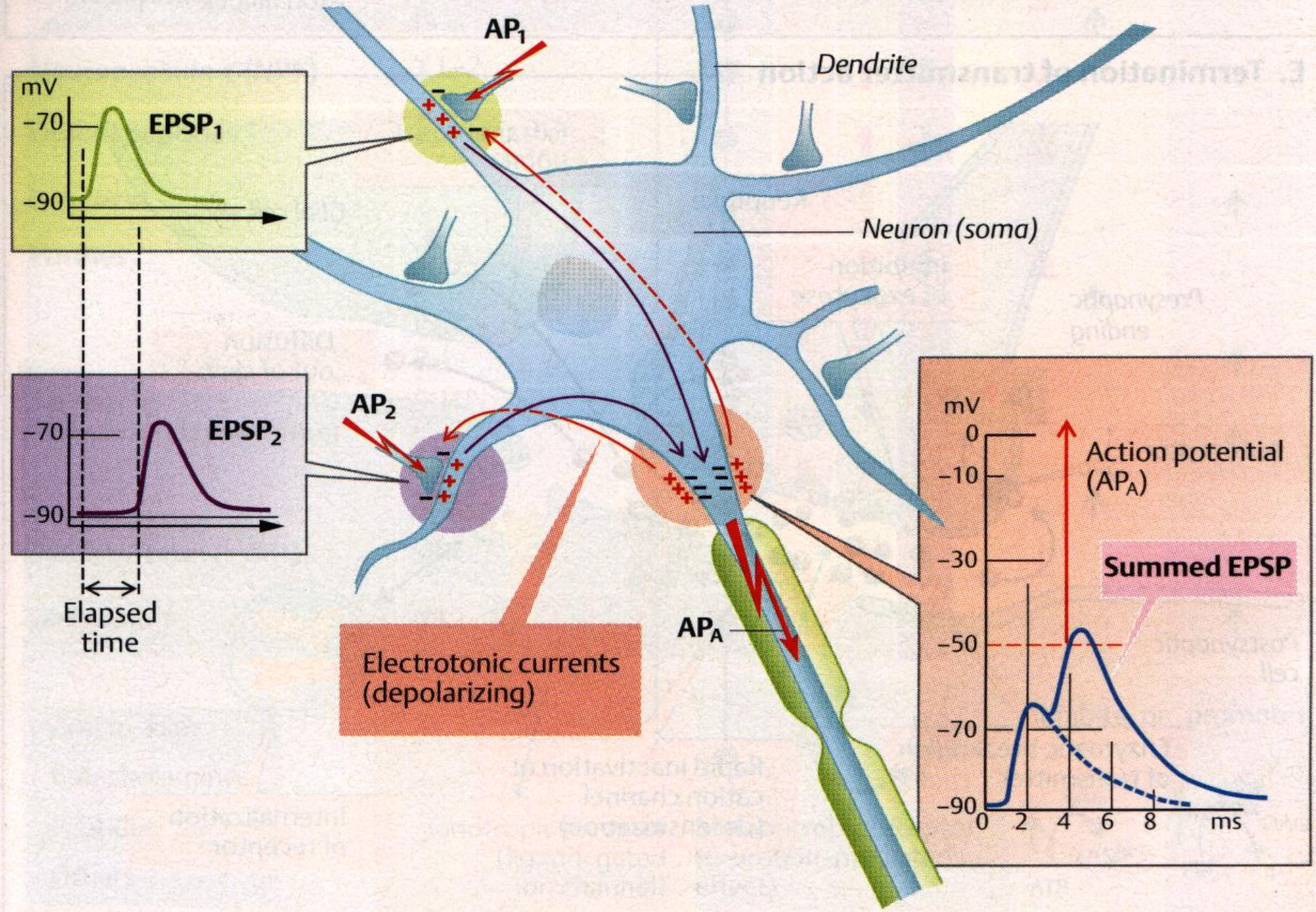
κύρια είδη έων:
οποικοί
ολοτροπικοί



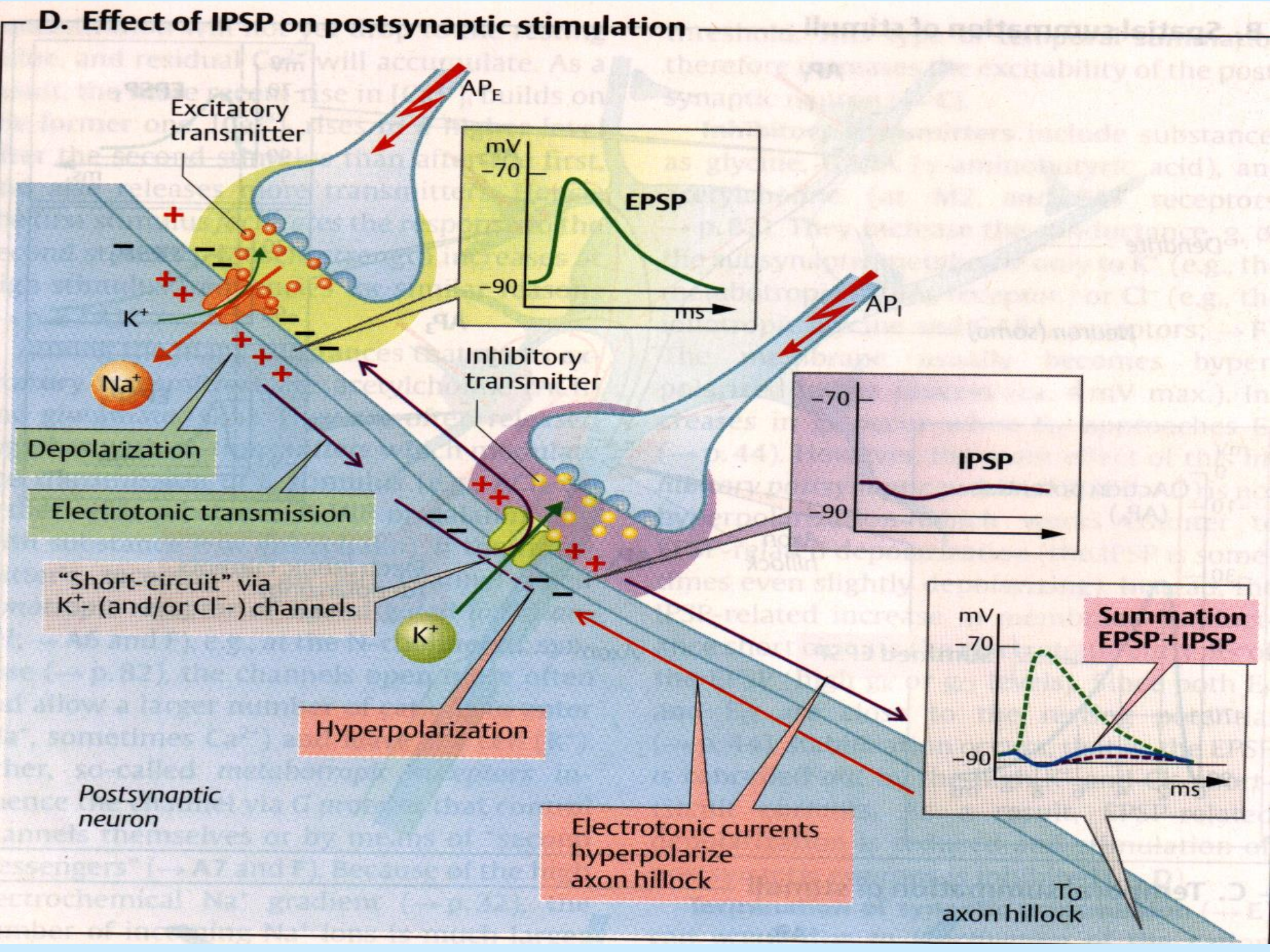
B. Spatial summation of stimuli



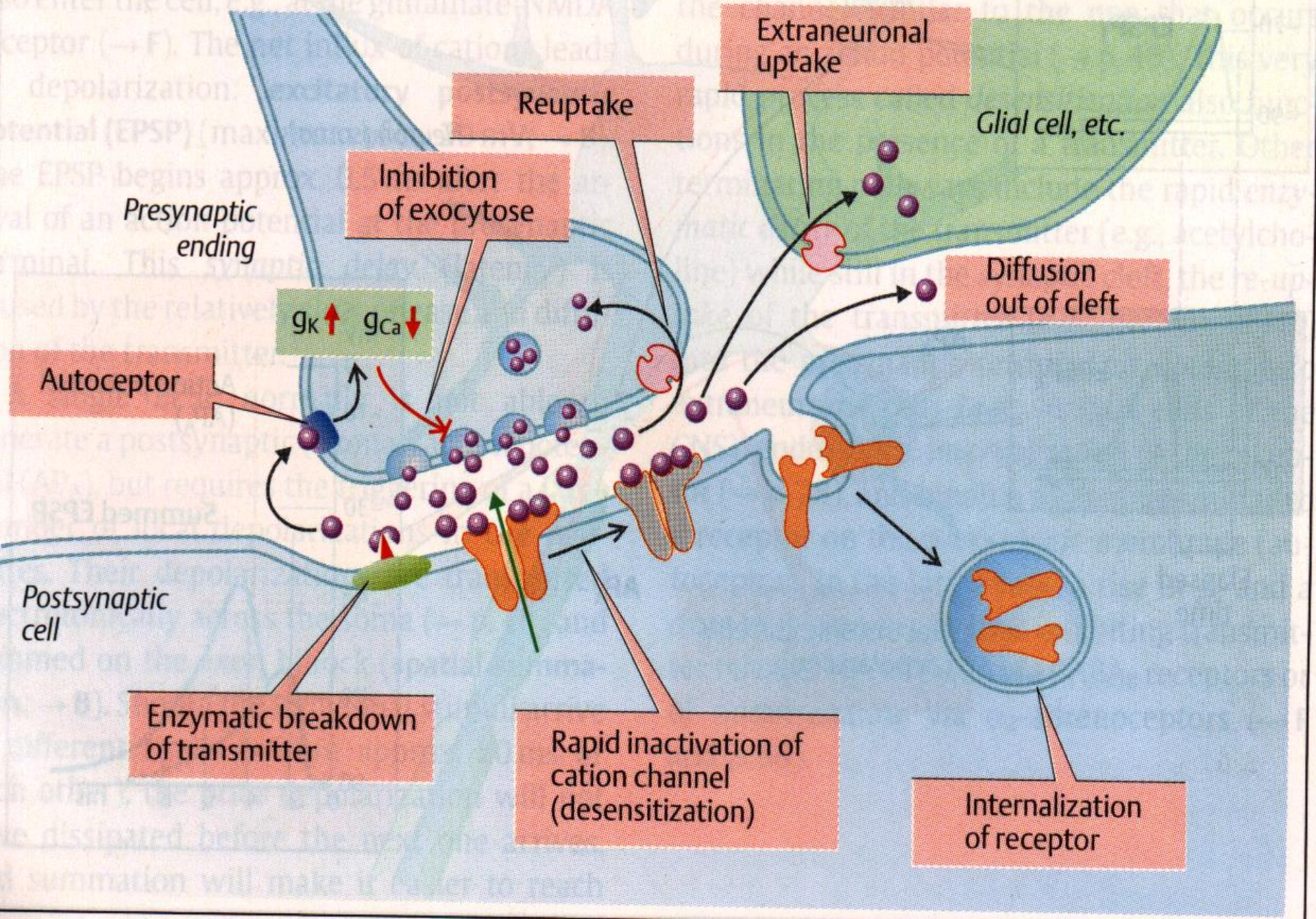
C. Temporal summation of stimuli



D. Effect of IPSP on postsynaptic stimulation



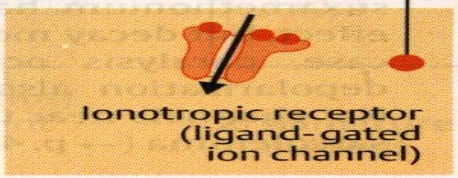
E. Termination of transmitter action

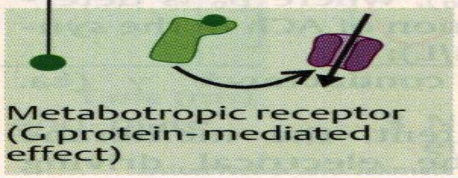


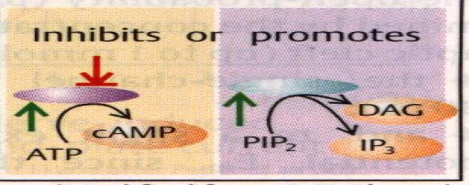
F. Neurotransmitters in the central nervous system

Transmitter	Receptor subtypes	Receptor types	Effect: Ion conductance Na^+	K^+	Ca^{2+}	Cl^-	Second messenger: cAMP	IP_3/DAG
Acetylcholine	Nicotinic		↑	↑	↑			
	Muscarinic: M1, M2, M3			↑			↓	↑
ADH (= vasopressin)	V1							↑
	V2						↑	
CCK (= cholecystokinin)	CCK_{A-B}							↑
Dopamine	D1, D5						↑	
	D2			↑	↓		↓	
GABA (= γ-aminobutyric acid)	$GABA_A$, $GABA_C$					↑		
	$GABA_B$			↑	↓		↓	
Glutamate (aspartate)	AMPA		↑	↑				
	Kainat		↑	↑				
	NMDA		↑	↑	↑			
	m-GLU						↓	↑
Glycine	—					↑		
Histamine	H_1							↑
	H_2						↑	
Neurotensin	—						↓	↑
Norepinephrine, epinephrine	$\alpha_{1(A-D)}$			↑				↑
	$\alpha_{2(A-C)}$			↑	↓		↓	
	β_{1-3}						↑	
Neuropeptide Y (NPY)	Y1–2			↑	↓		↓	
Opioid peptides	μ, δ, κ			↑	↓		↓	
Oxytocin	—							↑
Purines	P_1: A_1			↑	↓		↓	
	A_{2a}						↑	
	P_{2X}		↑	↑	↑			
	P_{2Y}							↑
Serotonin (5-hydroxytryptamine)	5-HT_1			↓			↓	
	5-HT_2							↑
	5-HT_3		↑	↑				
	5-HT_{4-7}						↑	
Somatostatin (= SIH)	SRIF			↑	↓		↓	
Tachykinin	NK 1–3							↑

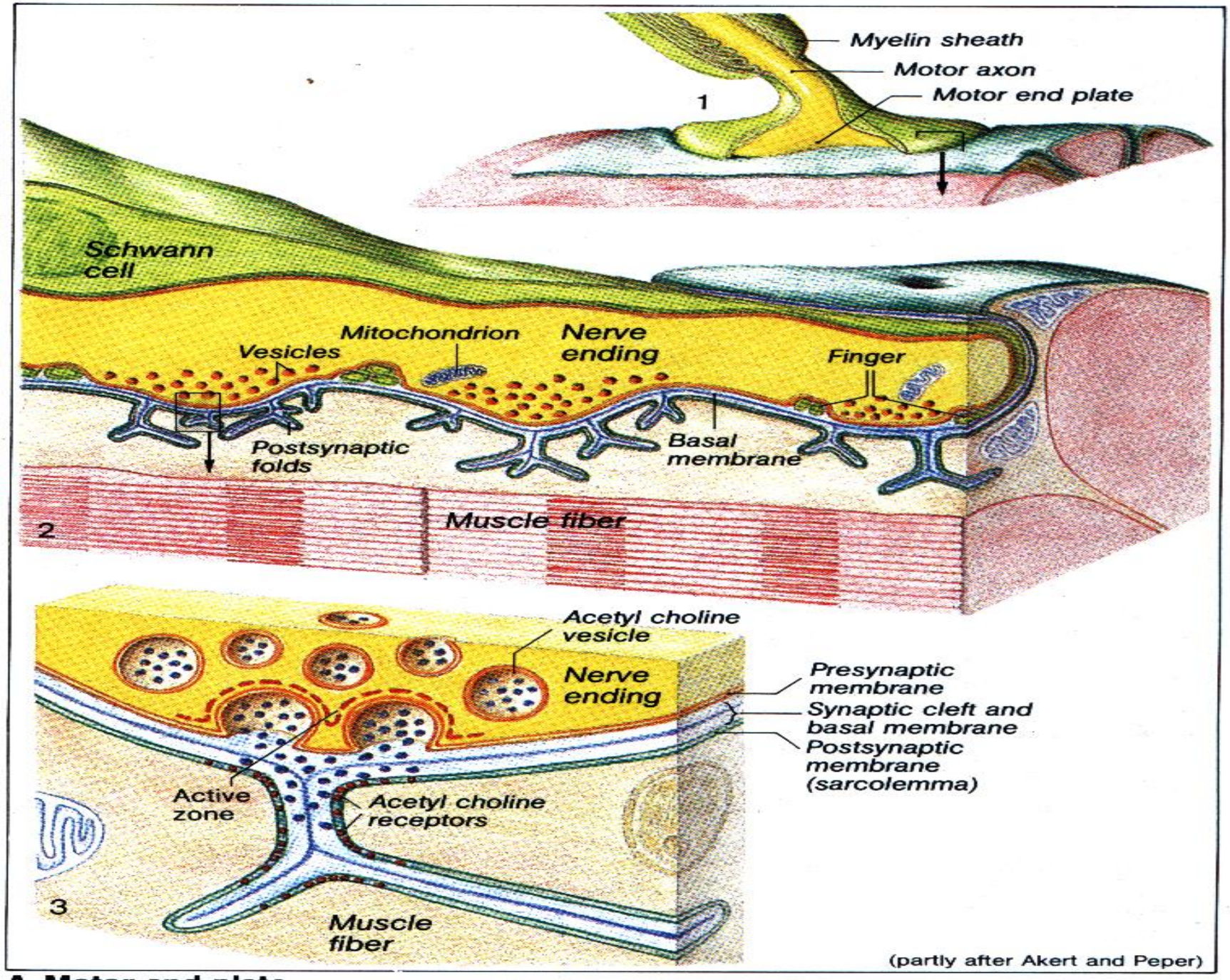
Amino acids
Catecholamines
Peptides
Others





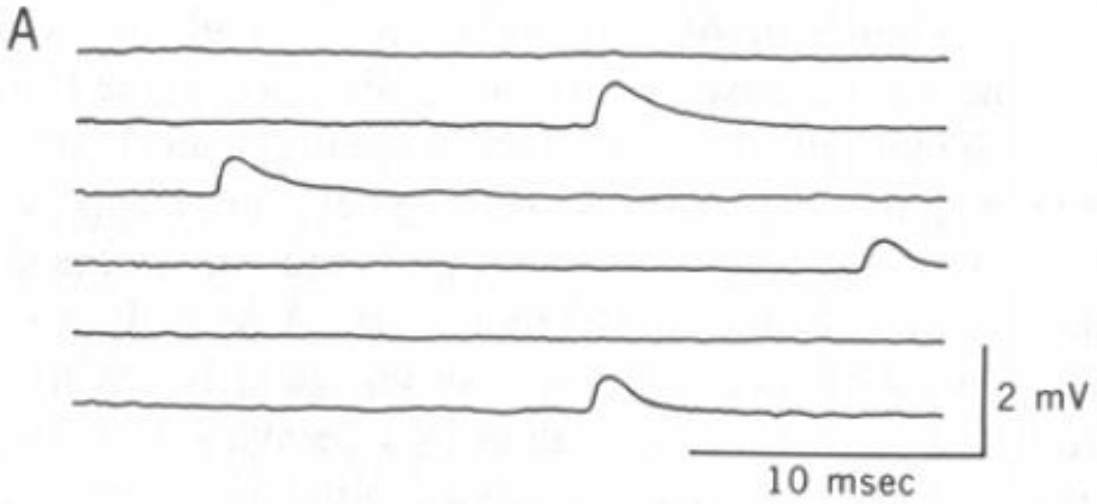


(Modified from F. E. Bloom)

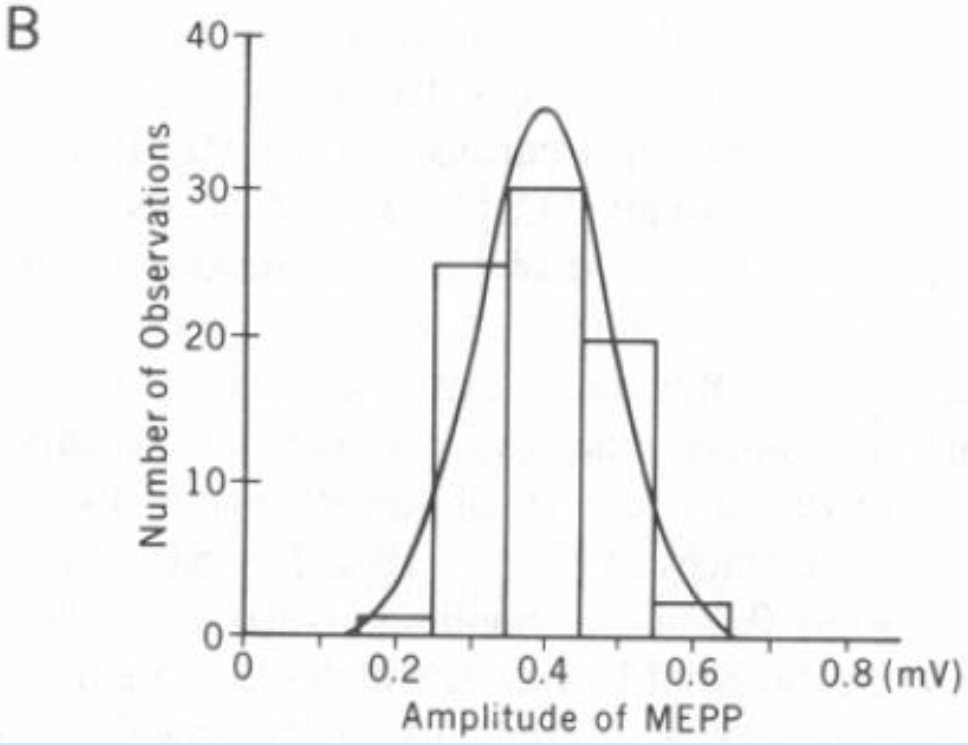


A. Motor end-plate

Quantal release of neurotransmitters

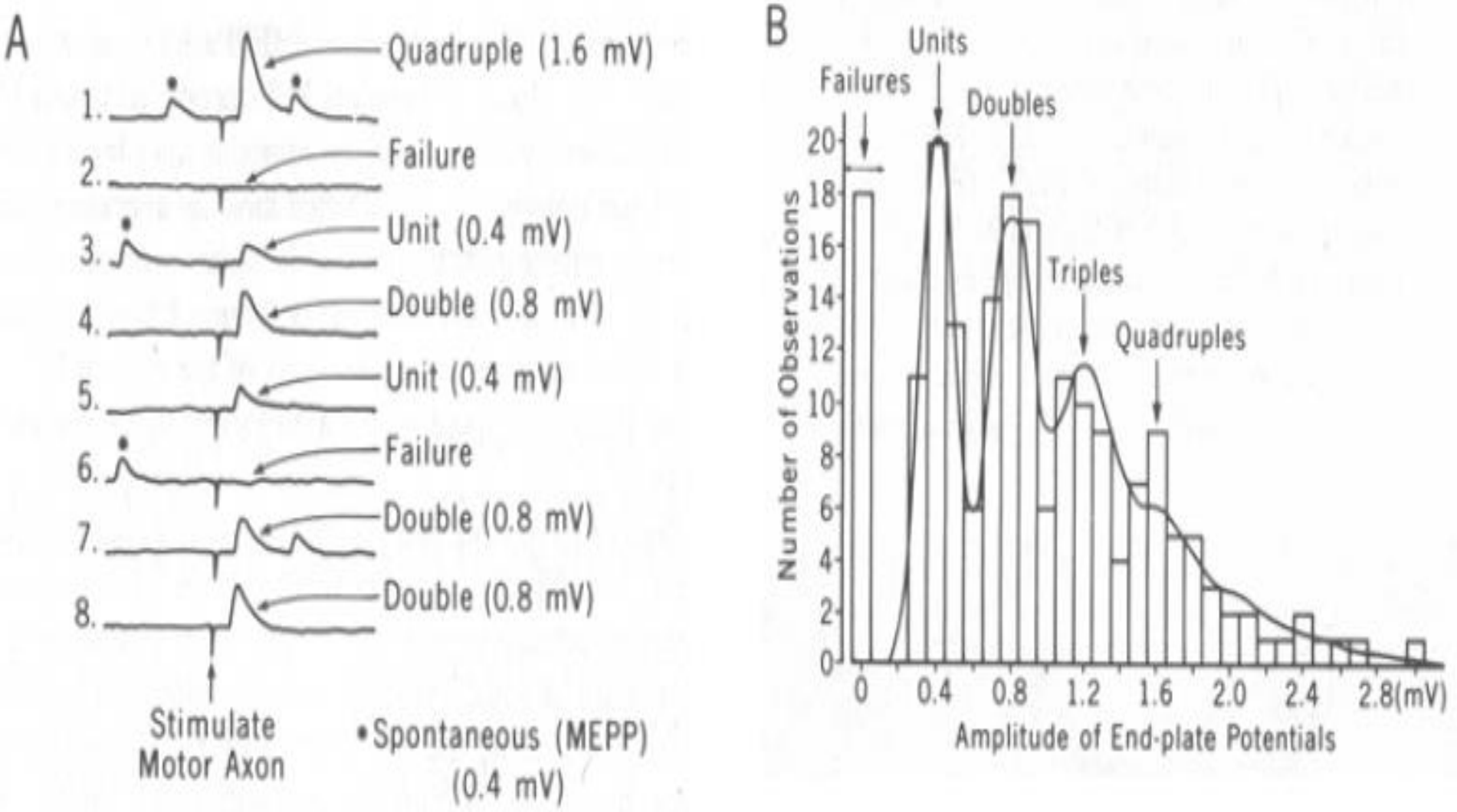


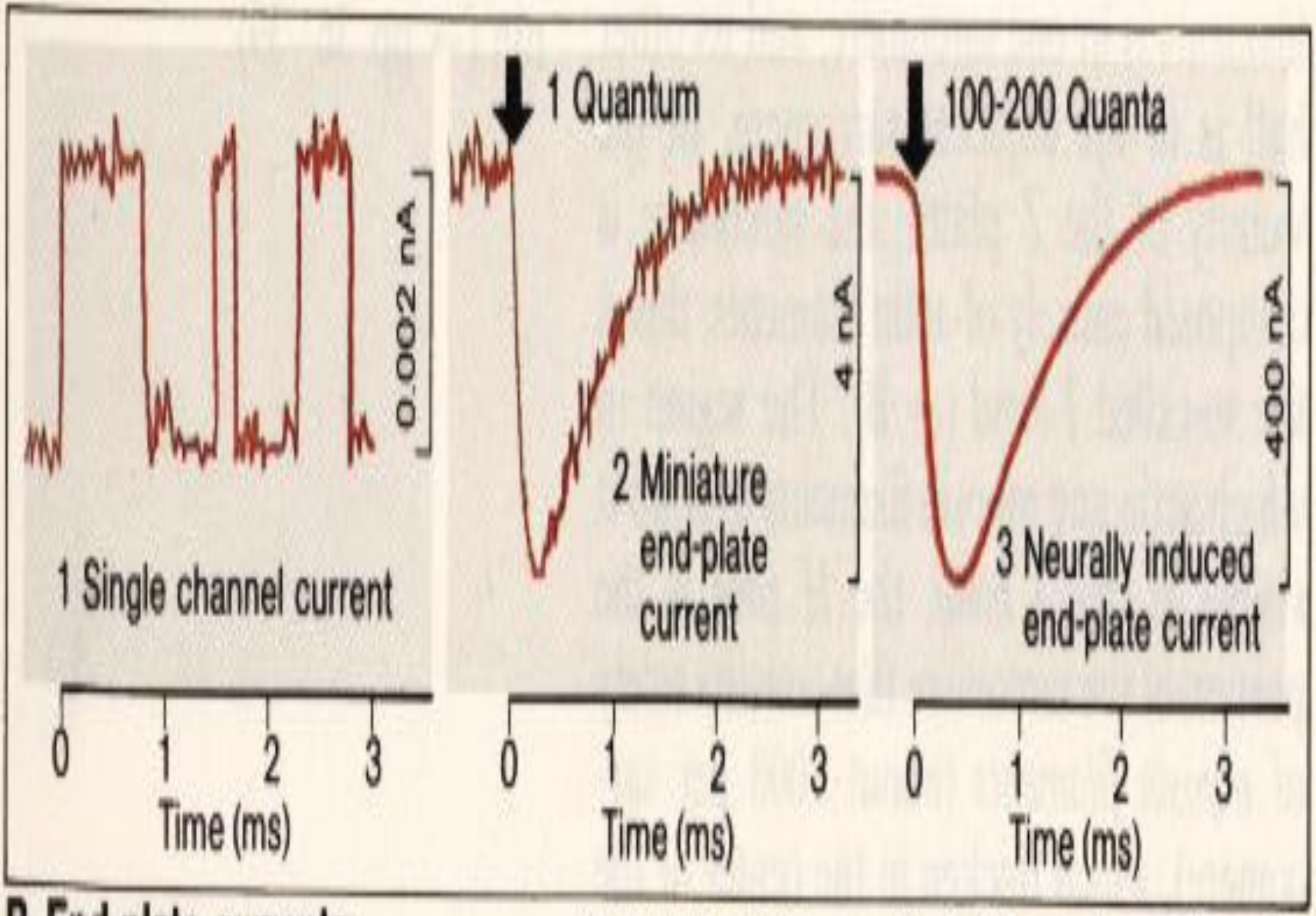
Spontaneous formation of miniature endplate potentials (MEPPs) due to spontaneous activity of nicotinic acetylcholine receptors (nAChR).



Average MEPP is 0.4mV and the result of a single exocytosis event.

Quantal release of neurotransmitters





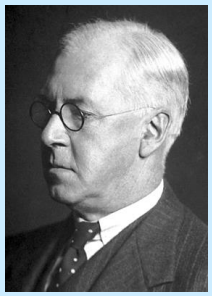
B. End-plate currents

(after Neher and Sakmann(1), after Peper and co-workers (2))

Nobel prices awarded for work on synaptic transmission

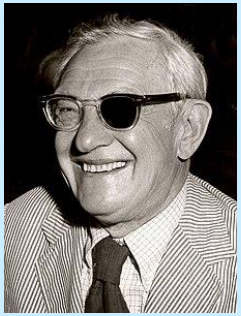
1906 – Camillo Golgi, Italy and Santiago Ramón y Cajal, Spain for their work on the parts of the nervous system.[6]

1932 – Sir Charles Scott Sherrington, United Kingdom, and Edgar Douglas Adrian, United Kingdom, for discoveries about neurons (nerve cells).[25]



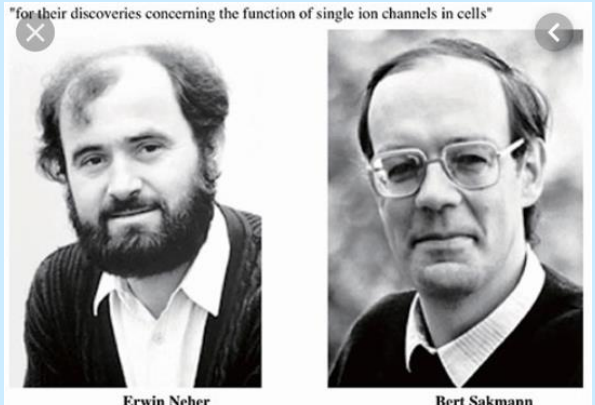
1936 – Sir Henry Hallett Dale, United Kingdom, and Otto Loewi, Austria for their discoveries about neurotransmitters and nerve impulses.[30]

1963 – Sir John Eccles, Australia, Alan Hodgkin, United Kingdom, and Andrew Huxley, United Kingdom, for their discoveries about nerve cell membrane.[54]

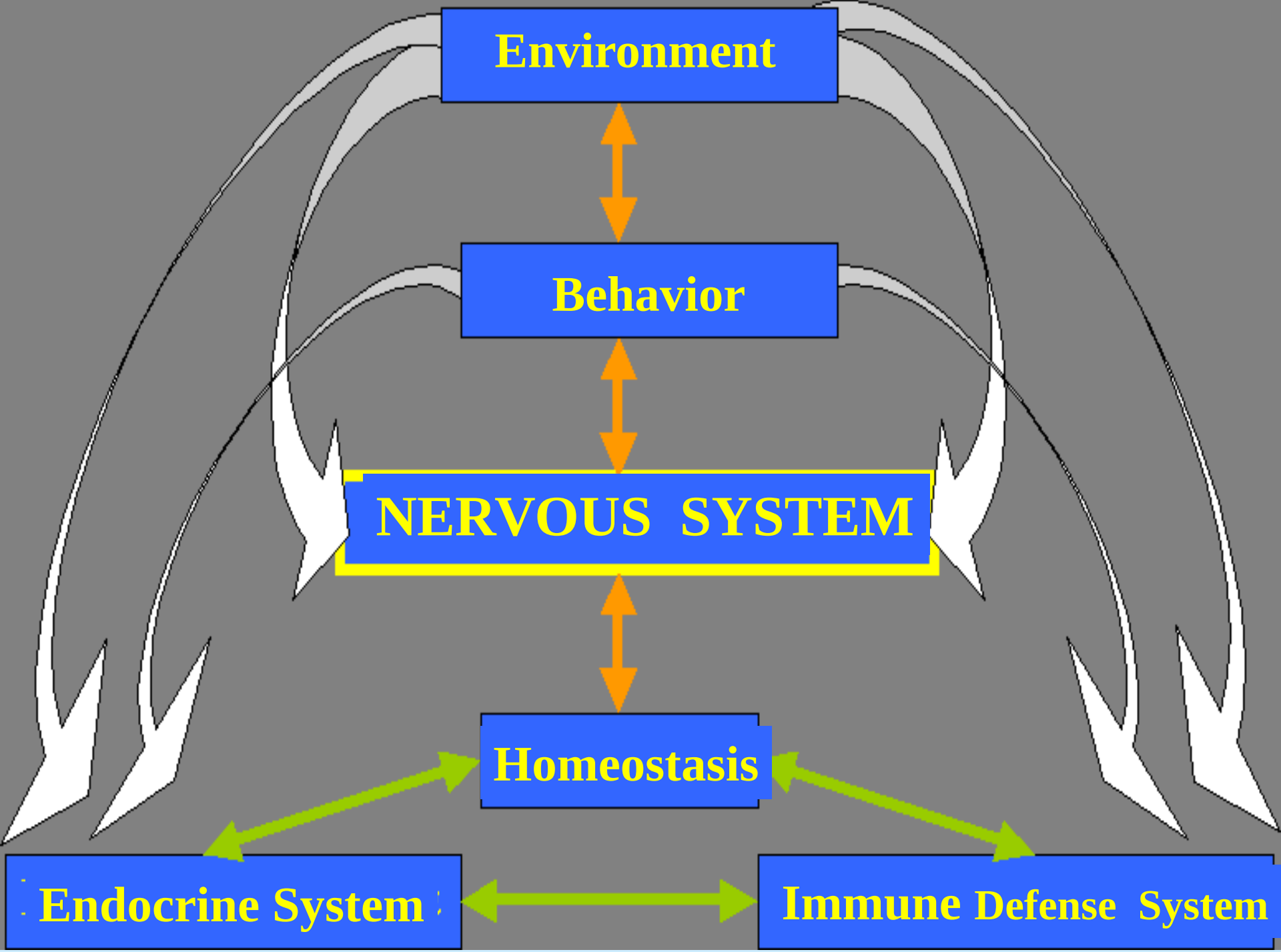


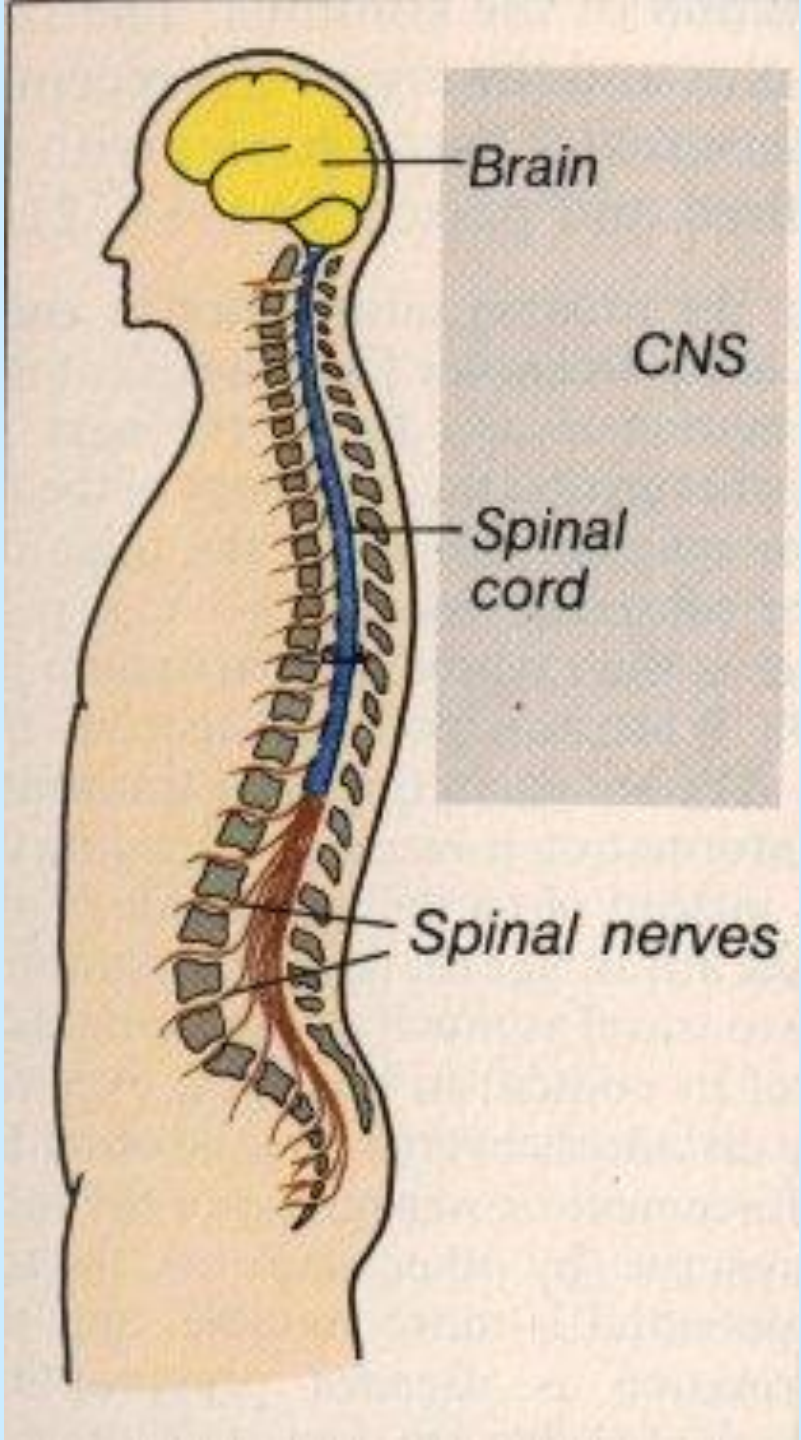
1970 – Julius Axelrod, Ulf von Euler, Sweden, and Sir Bernard Katz, United Kingdom, for finding out about transmittors in the nerve terminals and how they work[61]

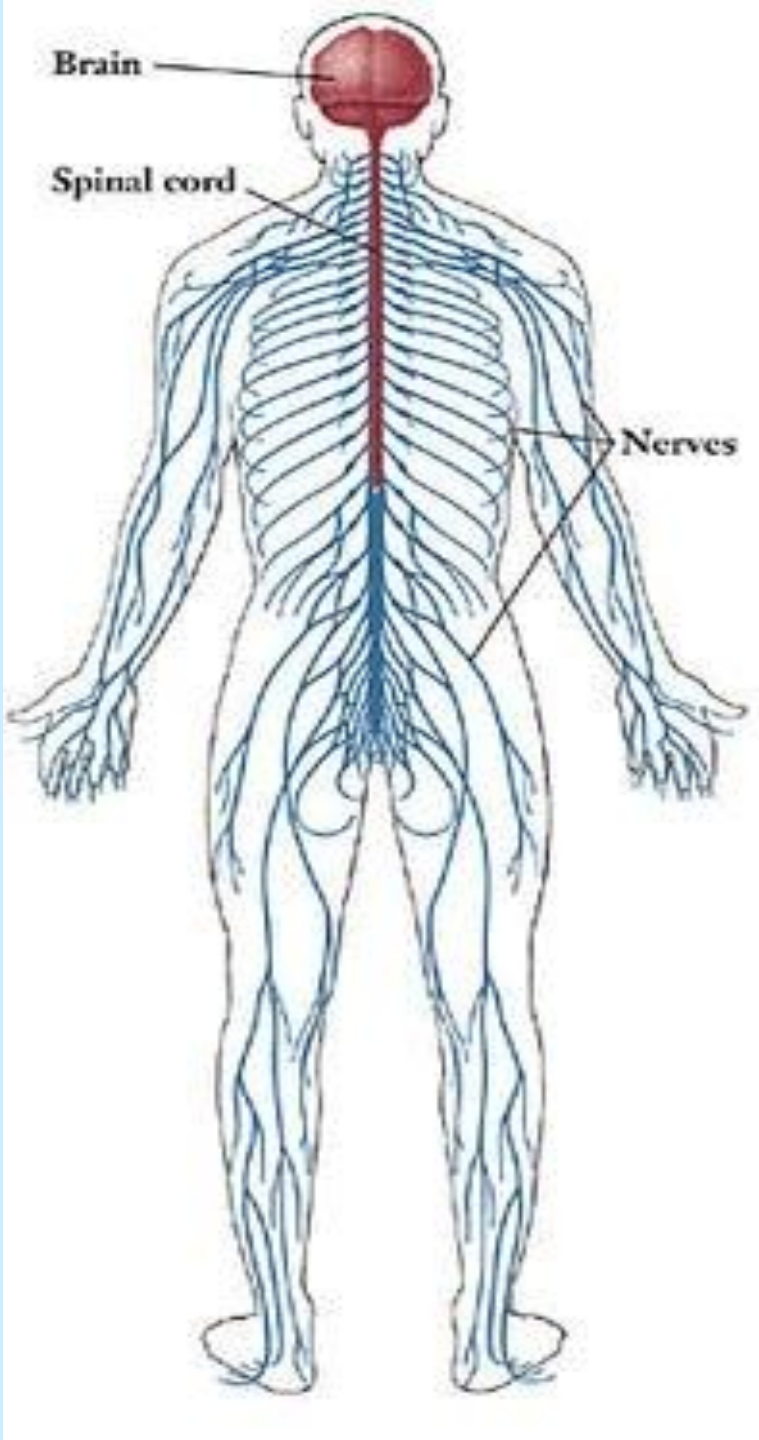
1991 – Erwin Neher and Bert Sakmann, Federal Republic of Germany, for finding what single ion channels do in cells.[62]



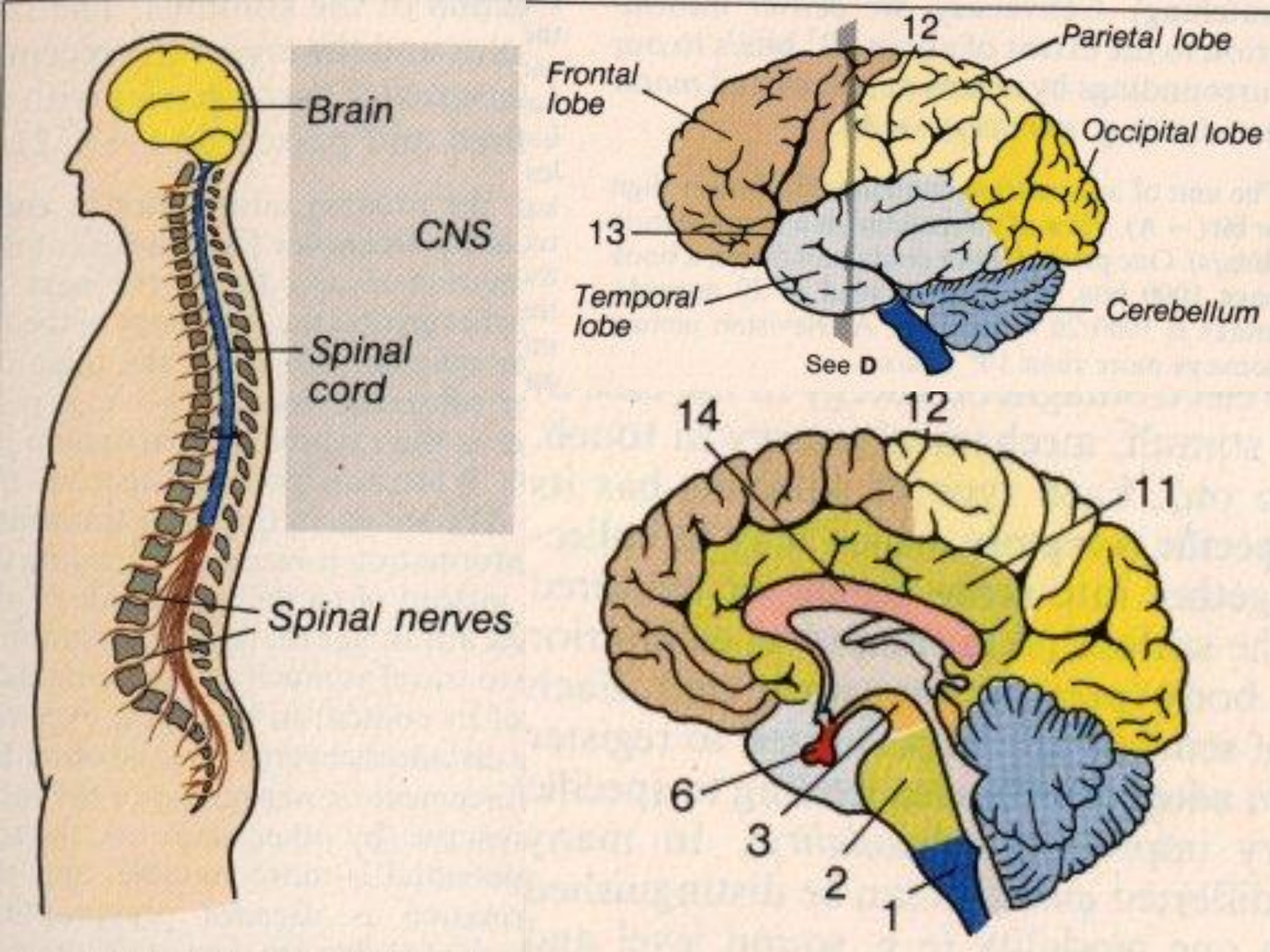
Organization of the Nervous System

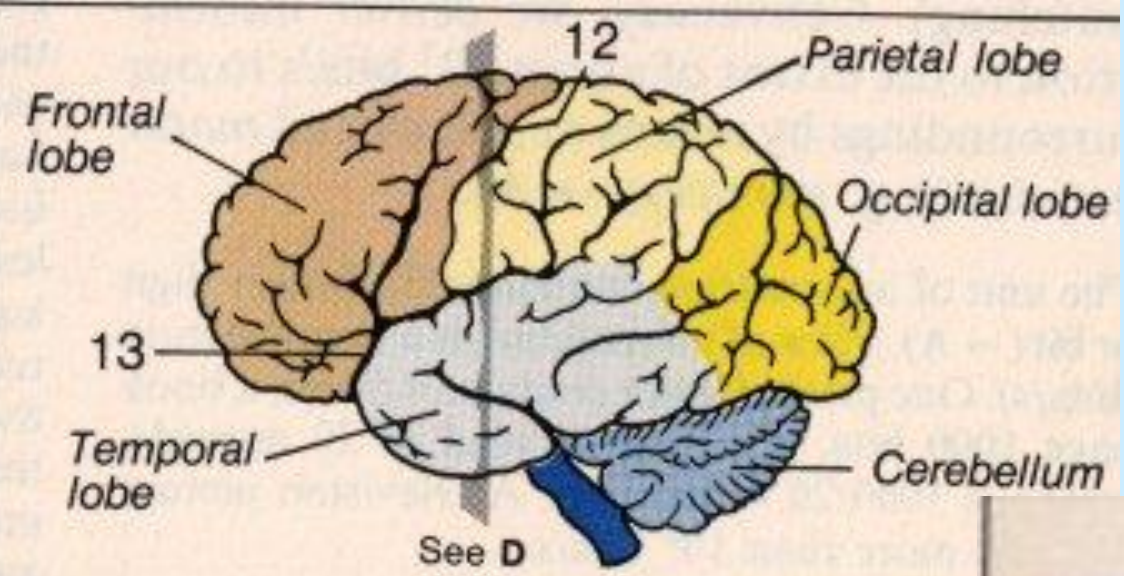

Environment
Behavior
NERVOUS SYSTEM
Homeostasis
Endocrine System
Immune Defense System


Brain
CNS
Spinal cord
Spinal nerves

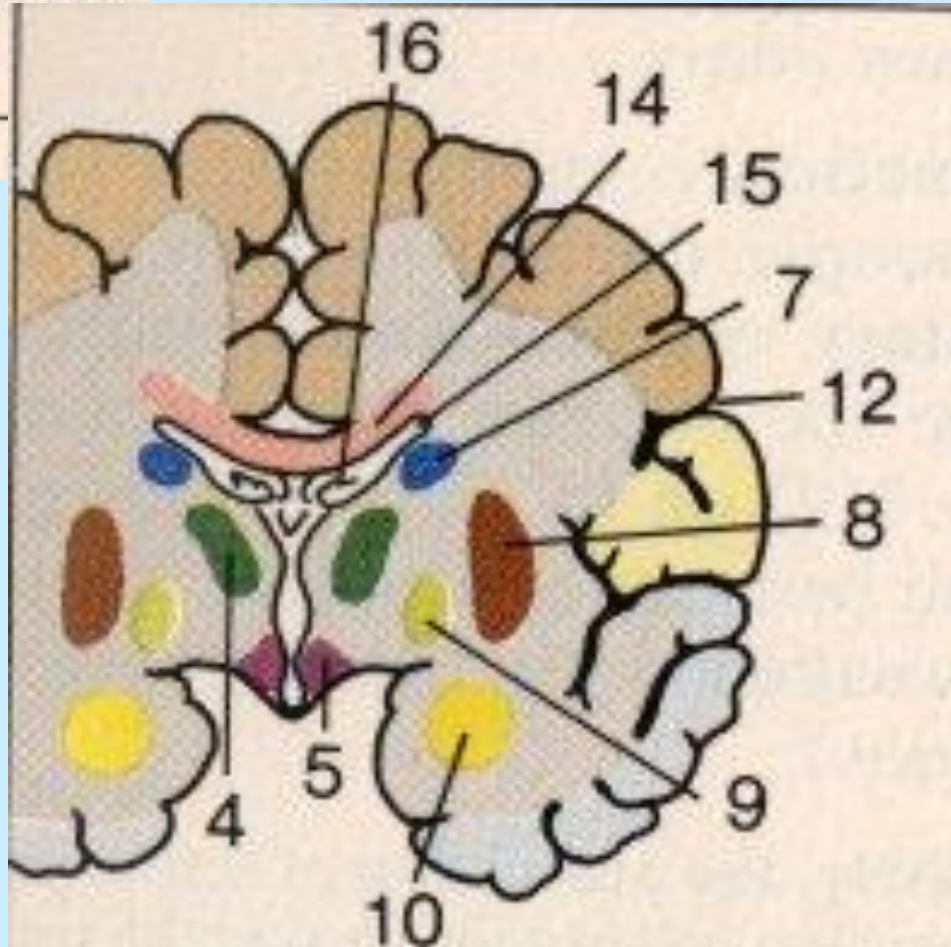

Brain
Spinal cord
Nerves

Central Nervous System


Brain
CNS
Spinal cord
Spinal nerves
12
Parietal lobe
Frontal lobe
Occipital lobe
13
Temporal lobe
Cerebellum
See D
14
12
11
6
3
2
1



C. Brain: lateral surface



Organization of the Nervous System

Divided on a gross anatomical basis into two systems but really is a single, unified communications network.

Central Nervous System - consists of **brain** and **spinal cor**d.

Peripheral Nervous System - consists of the nerve cells **(neuron**s) and their fibers that emerge from and go to the brain **(cranial nerve**s) and spinal cord **(spinal nerve**s). P N S is composed of the **afferent (sensor**y) **division** and the **efferent (moto**r) **divisio**n.

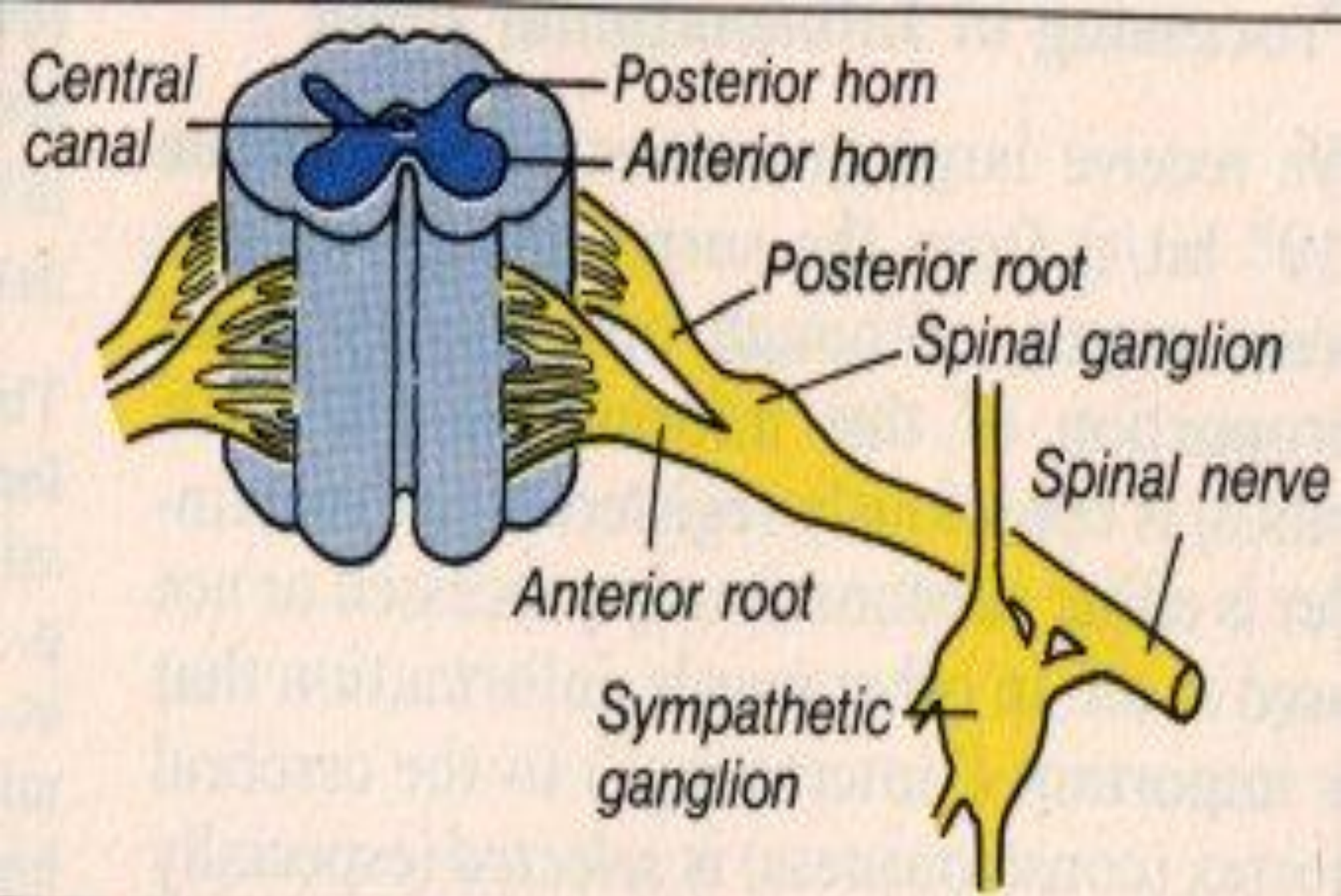
Somatic Nervous System - composed of

•**somatic afferent division** (which receives sensory information and conveys it to the spinal cord and brain via nerves) and the

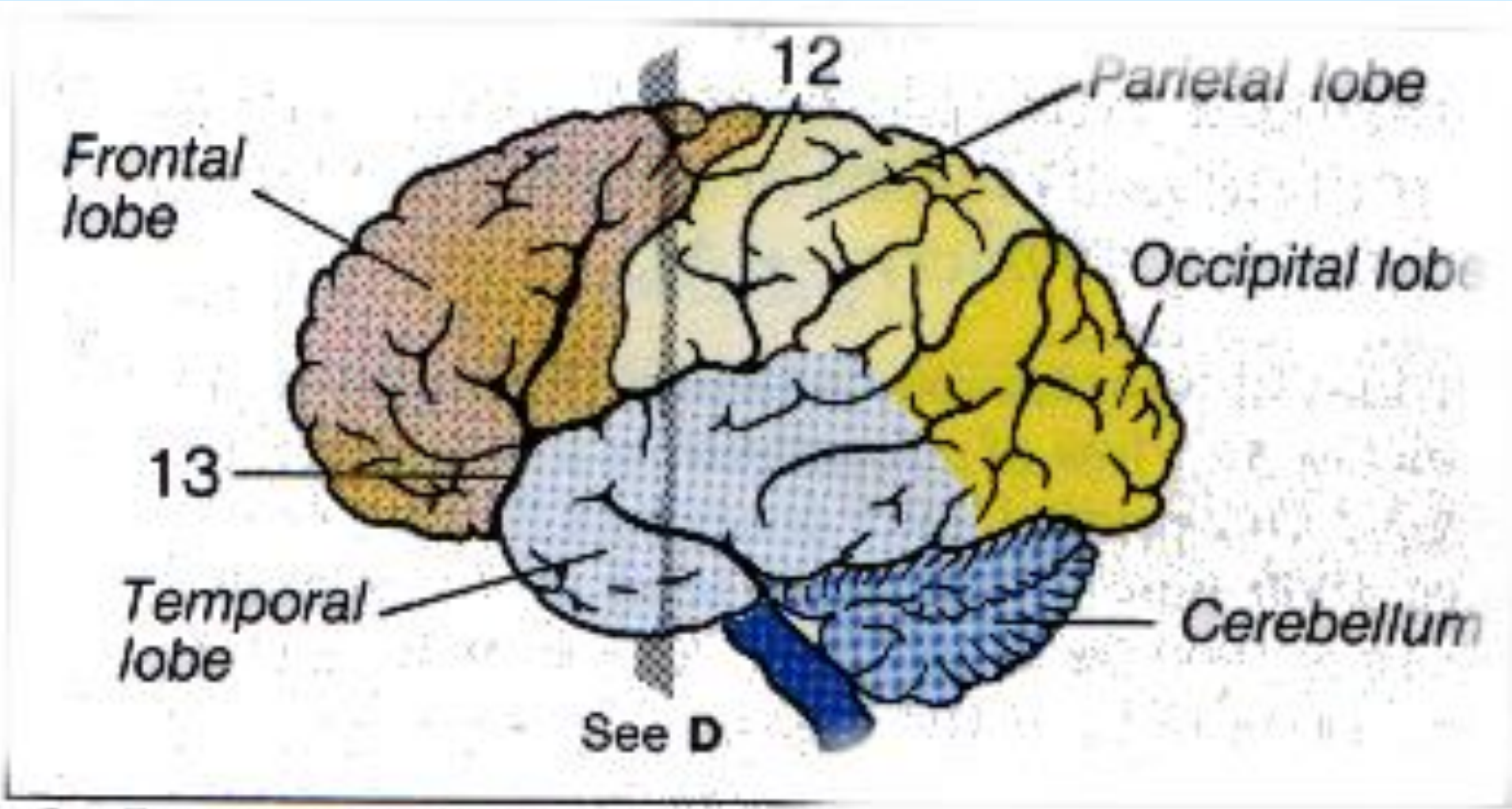
•**somatic efferent division** (which regulates the contractions of skeletal muscles via neuronal pathways that descend from the brain and spinal cord to lower motor neurons).

Autonomic (Visceral) Nervous System - composed of

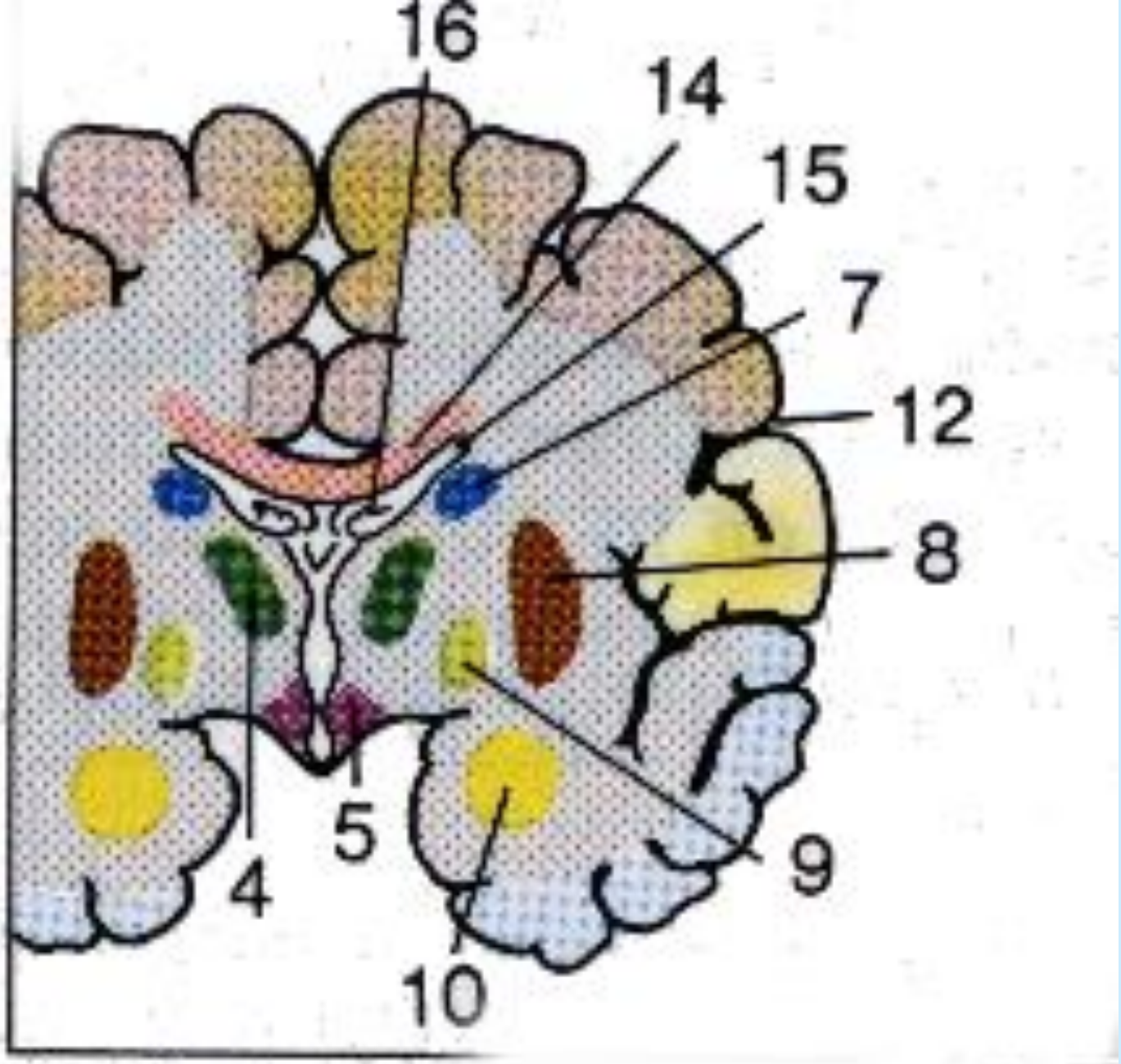
•**Afferent division** (which conveys sensory information from visceral organs) and the **efferent division** (which is involved in motor activities that influence smooth muscle, cardiac muscle, glands).



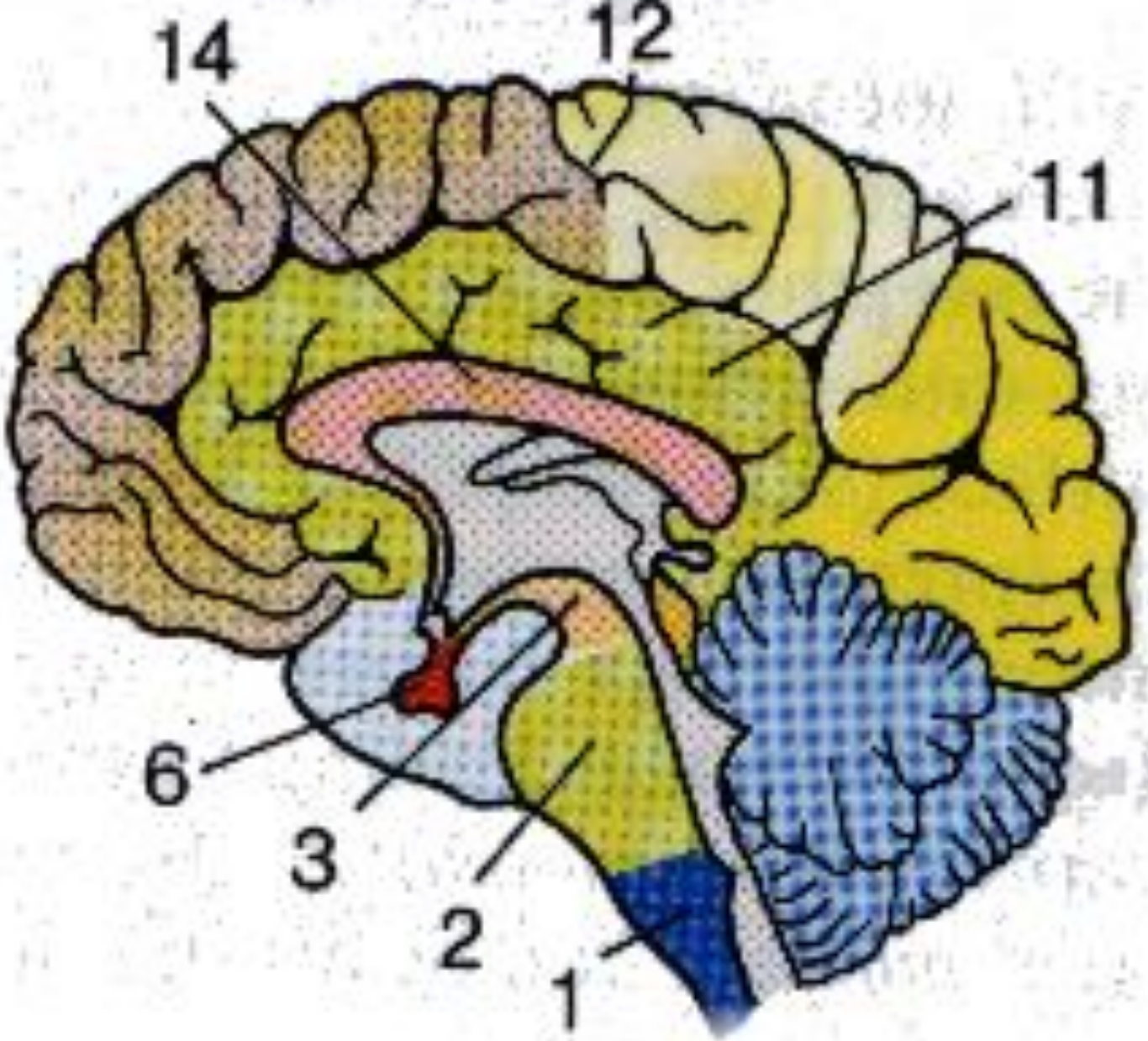
B. Section of spinal cord



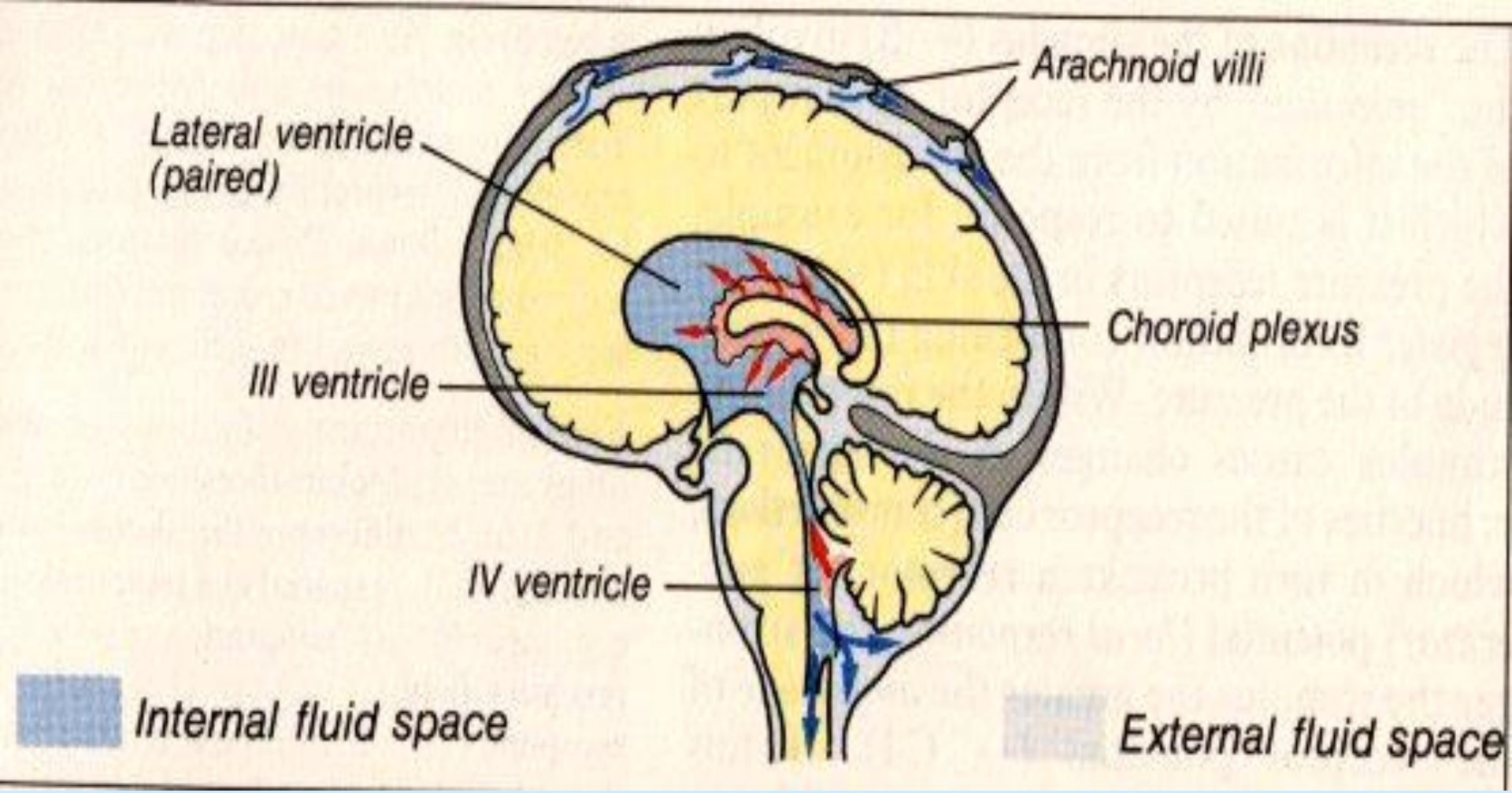
C. Brain: lateral surface



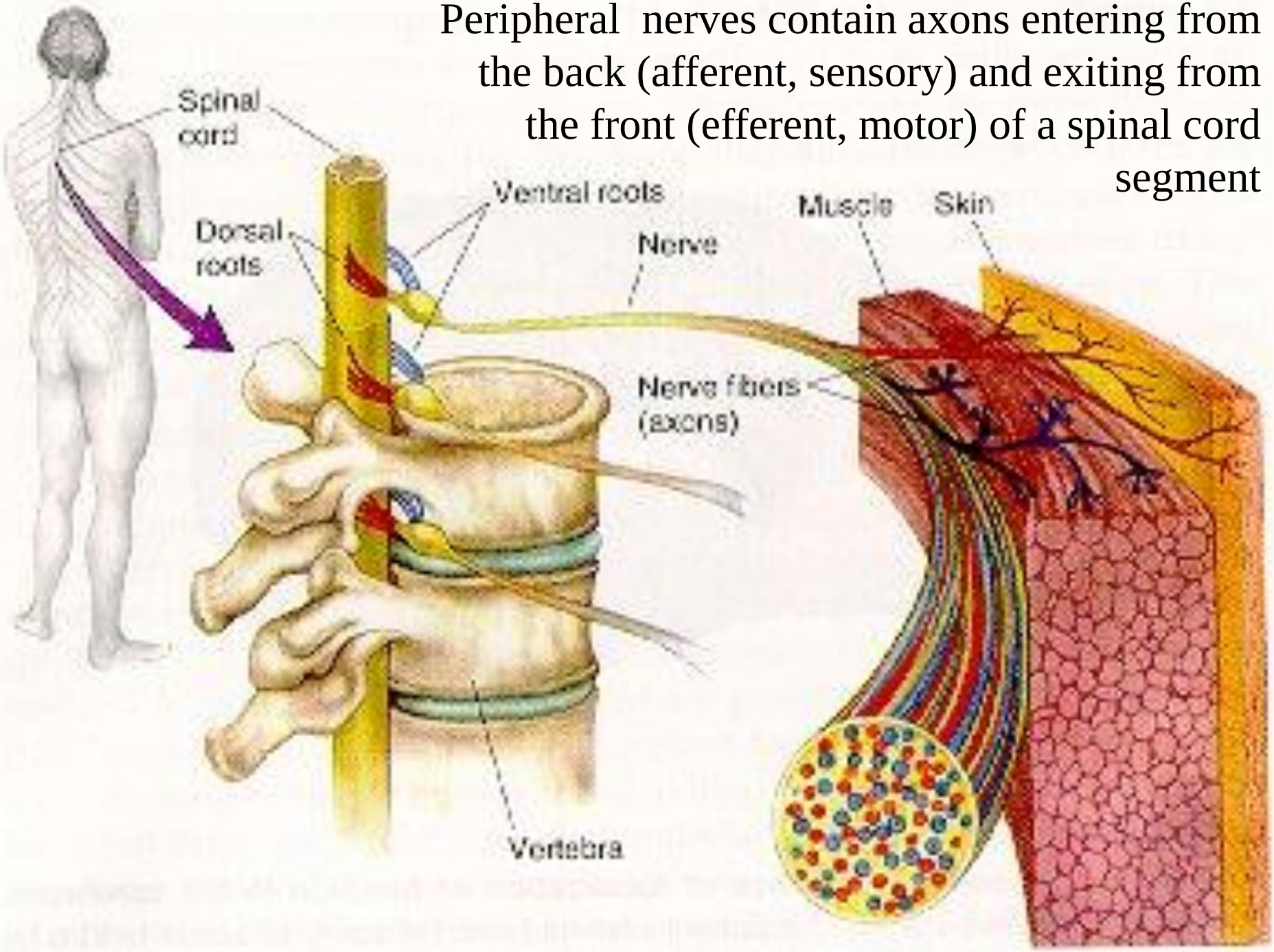
D. Brain: transverse section

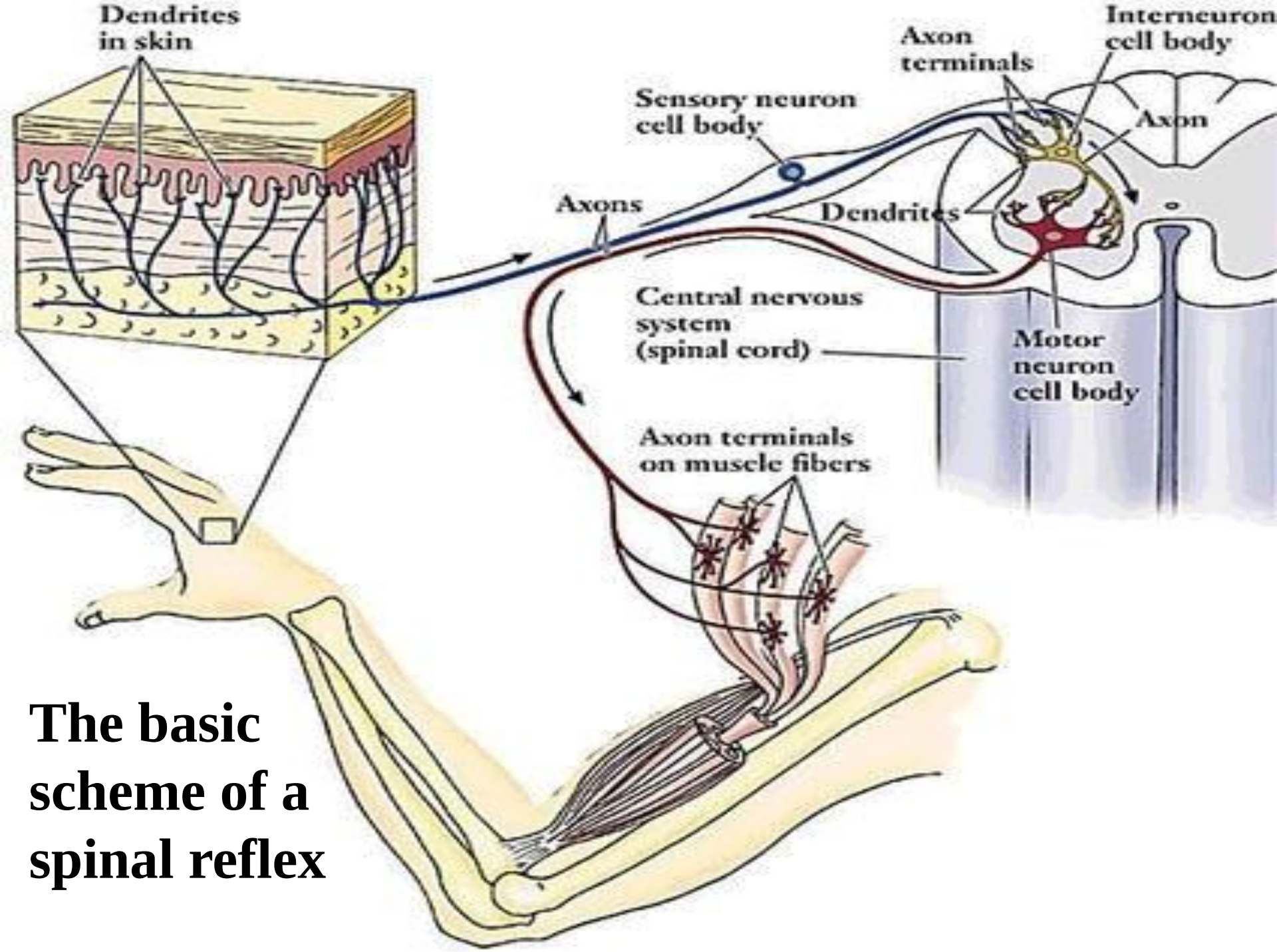


Brain: median saggital section


Arachnoid villi
Lateral ventricle (paired)
Choroid plexus
III ventricle
IV ventricle
Internal fluid space
External fluid space

Peripheral nerves contain axons entering from the back (afferent, sensory) and exiting from the front (efferent, motor) of a spinal cord segment





The basic scheme of a spinal reflex

Organization of the Nervous System

Divided on a gross anatomical basis into two systems but really is a single, unified communications network.

Central Nervous System - consists of **brain** and **spinal cor**d.

Peripheral Nervous System - consists of the nerve cells **(neuron**s) and their fibers that emerge from and go to the brain **(cranial nerve**s) and spinal cord **(spinal nerve**s).

Peripheral Nervous System

Composed of the **afferent (sensor**y) **division** and the **efferent (moto**r) **divisio**n.

Somatic Nervous System - composed of

- **somatic afferent division** (which receives sensory information and conveys it to the spinal cord and brain via nerves) and the
- **somatic efferent division** (which regulates the contractions of skeletal muscles via neuronal pathways that descend from the brain and spinal cord to lower motor neurons).

Autonomic (Visceral) Nervous System - composed of

- **afferent division** (which conveys sensory information from visceral organs) and the
- **efferent division** (which is involved in motor activities that influence smooth muscle, cardiac muscle, glands).

What is a nerve?

Simply a bundle of nerve fibers enclosed in a connective tissue sheath, like many telephone wires in a cable.

Tracts - anatomical term for bundles of nerve fibers and their myelin sheaths in the CNS.

Nerves - anatomical term for bundles of nerve fibers and their myelin sheaths in the PNS.

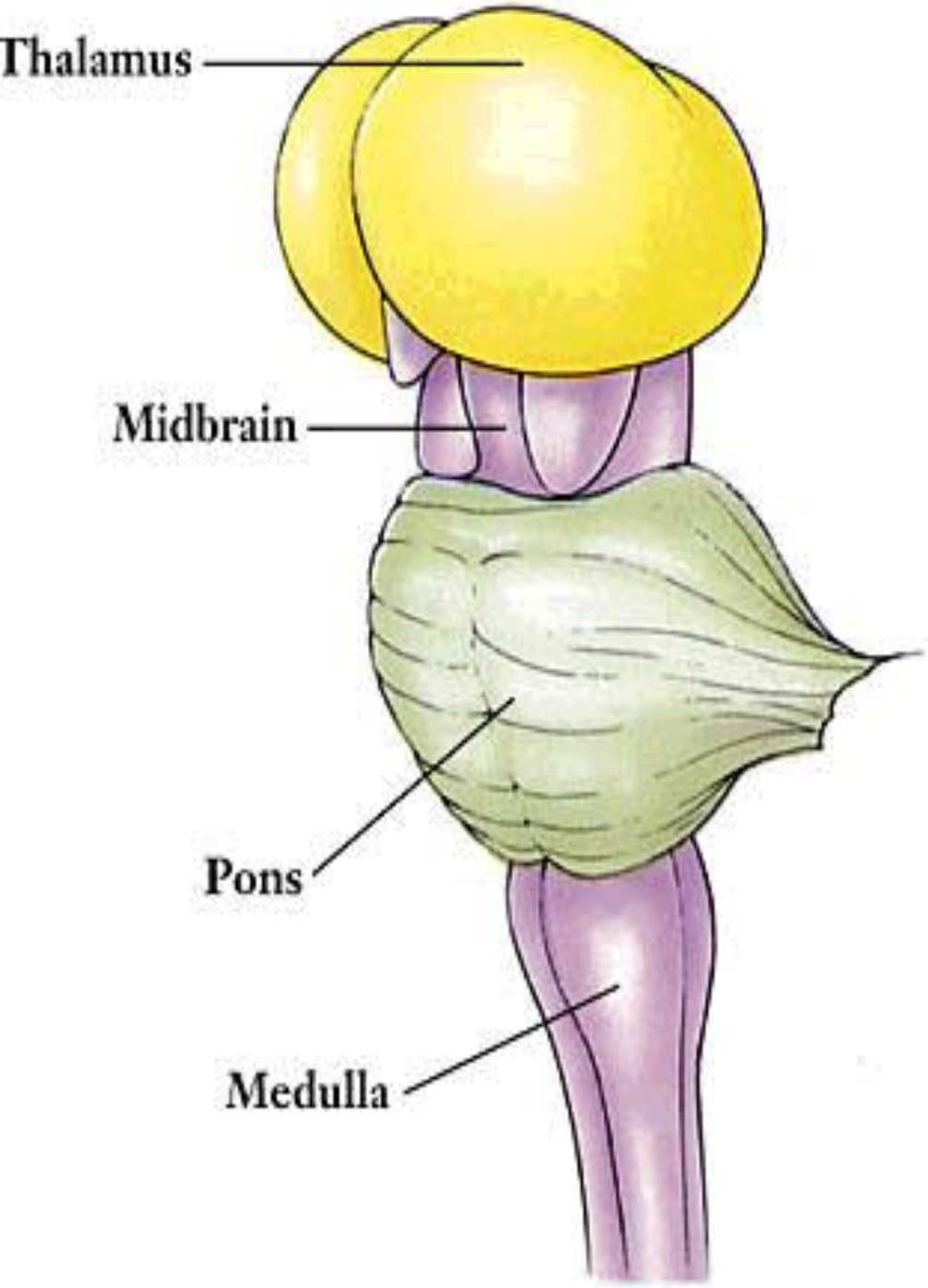
Types of PNS Neurons - Function

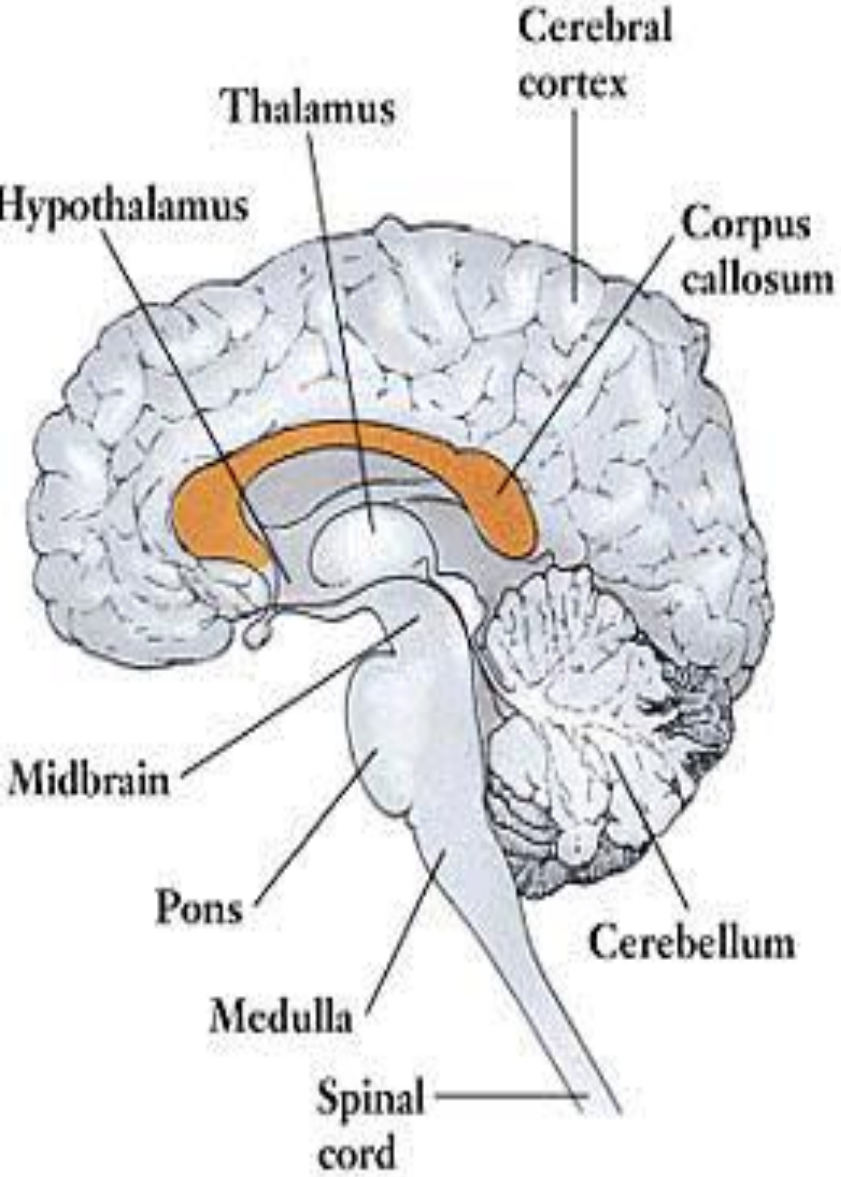
Based on direction in which they transmit nerve impulses.

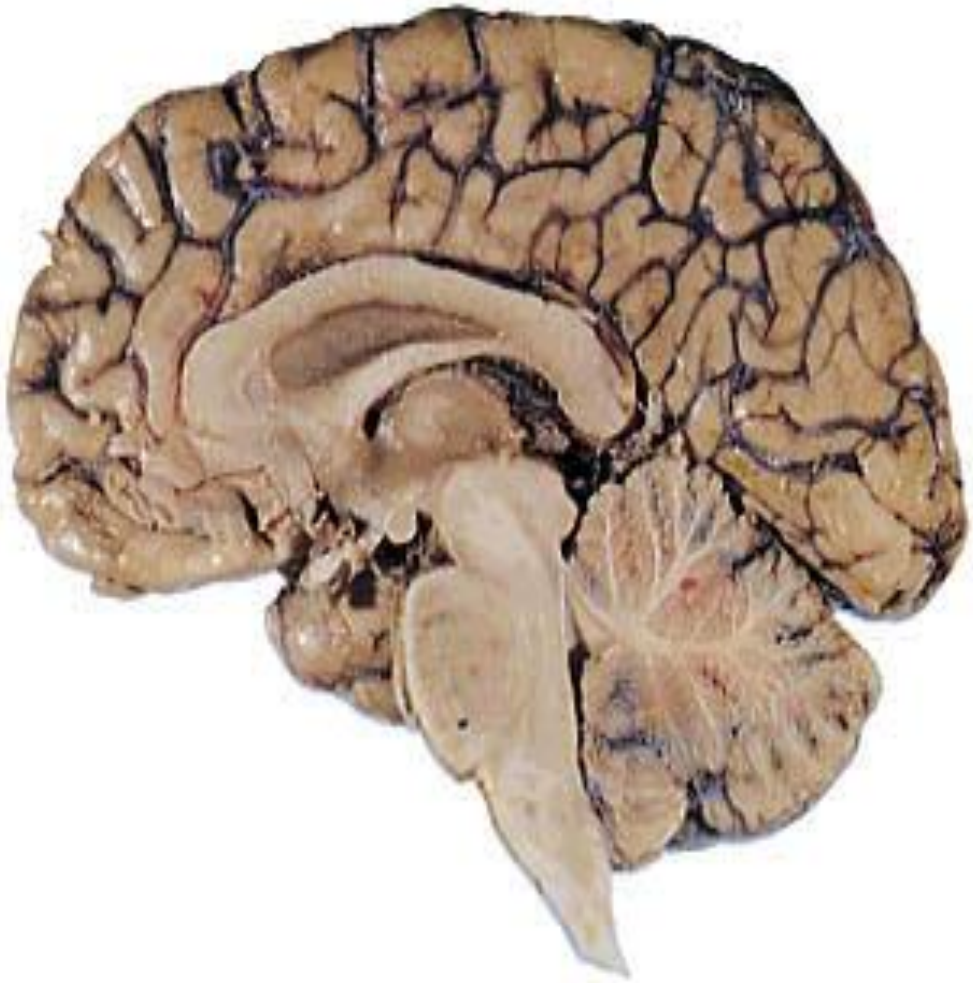
Afferent (sensory) neurons - convey information from sensory receptors in the skin, sense organs, muscles, joints, and viscera to the CNS. **Exteroceptors** (monitor external), **proprioceptors** (monitor position), **interoceptors** (monitor internal activities).

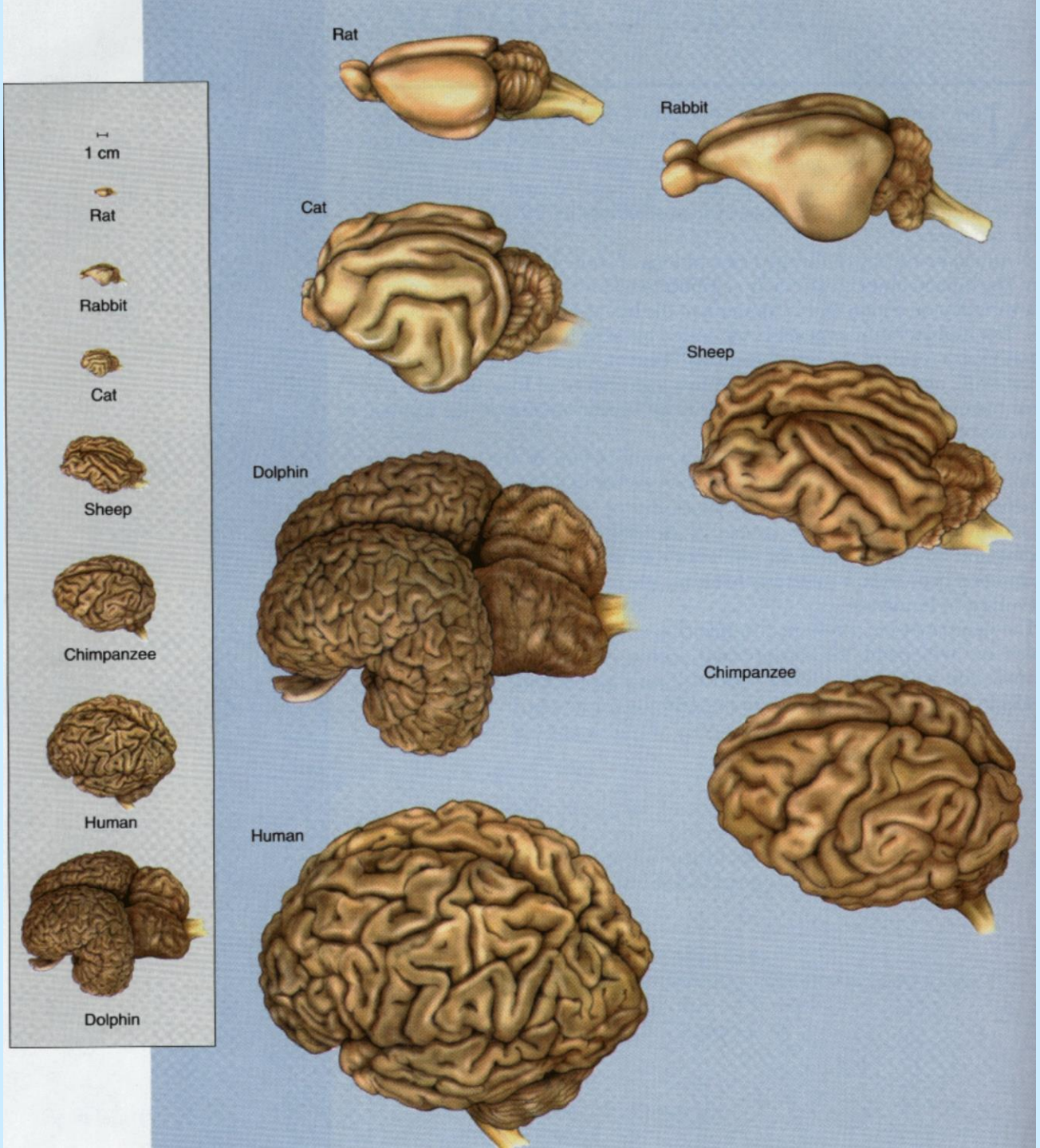
Efferent (motor) neurons - convey nerve impulses away from the CNS to the effectors (muscles and glands).

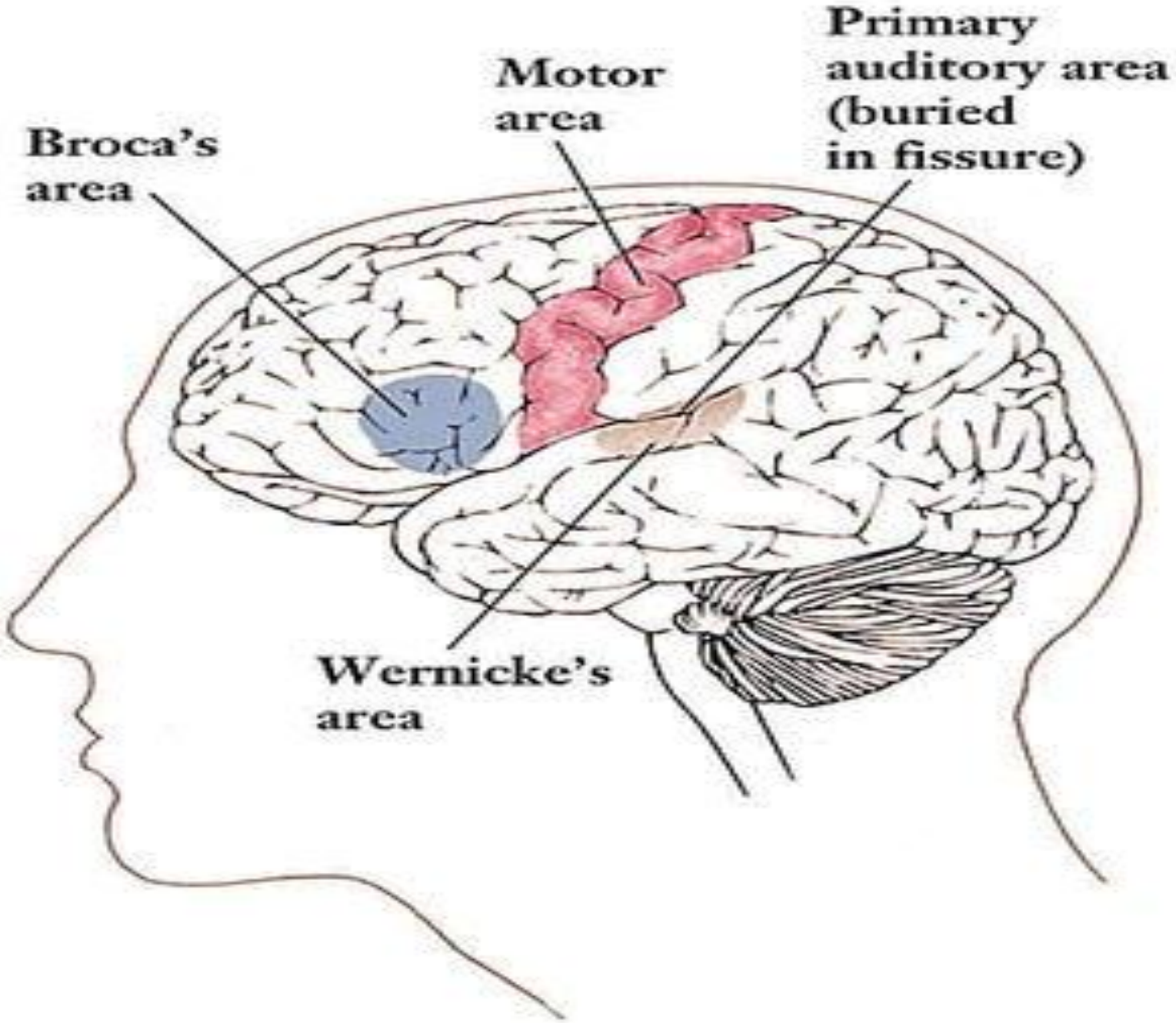
Interneurons - lie (1) between sensory and motor neurons in neural pathways and transmit signals through pathways of the CNS, where integration often occurs, and (2) in autonomic ganglia. About 90% of the neurons of the body are interneurons.


Thalamus
Midbrain
Pons
Medulla


Cerebral cortex
Thalamus
Hypothalamus
Corpus callosum
Midbrain
Pons
Cerebellum
Medulla
Spinal cord




1 cm
Rat
Rabbit
Cat
Sheep
Chimpanzee
Human
Dolphin
Rat
Rabbit
Cat
Sheep
Dolphin
Chimpanzee
Human


Primary
auditory area
(buried
in fissure)
Motor
area
Broca's
area
Wernicke's
area

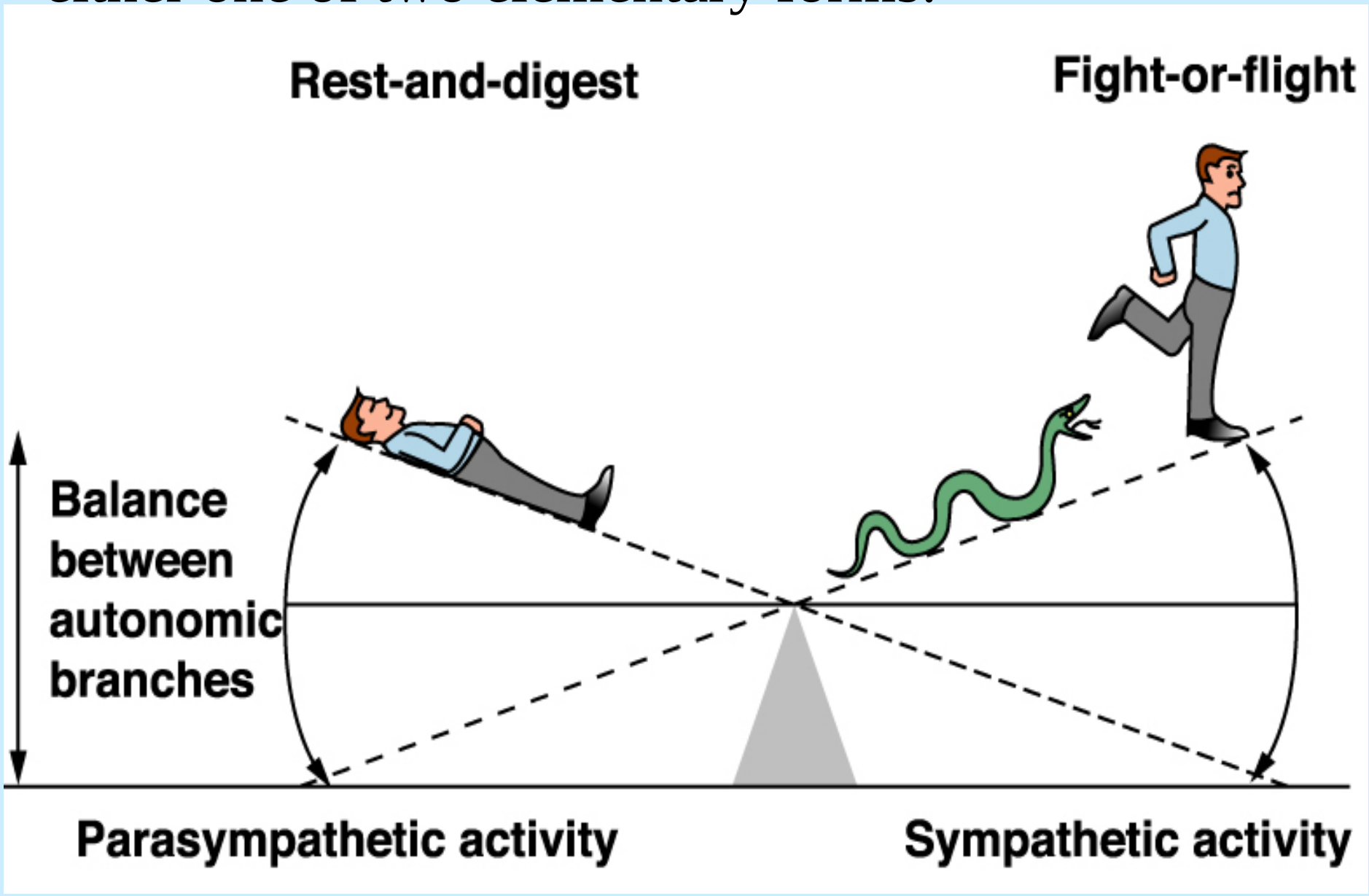
Our behavior may be categorized in several ways

Prominent appear to be the **four Fs** = the four basic drives or mind states that animals (including humans) are evolutionarily adapted to be good at:

- Fighting
- Fleeing
- Feeding
- reproduction ☺

In all four the hypothalamus, hormones and the autonomic nervous system are mainly involved

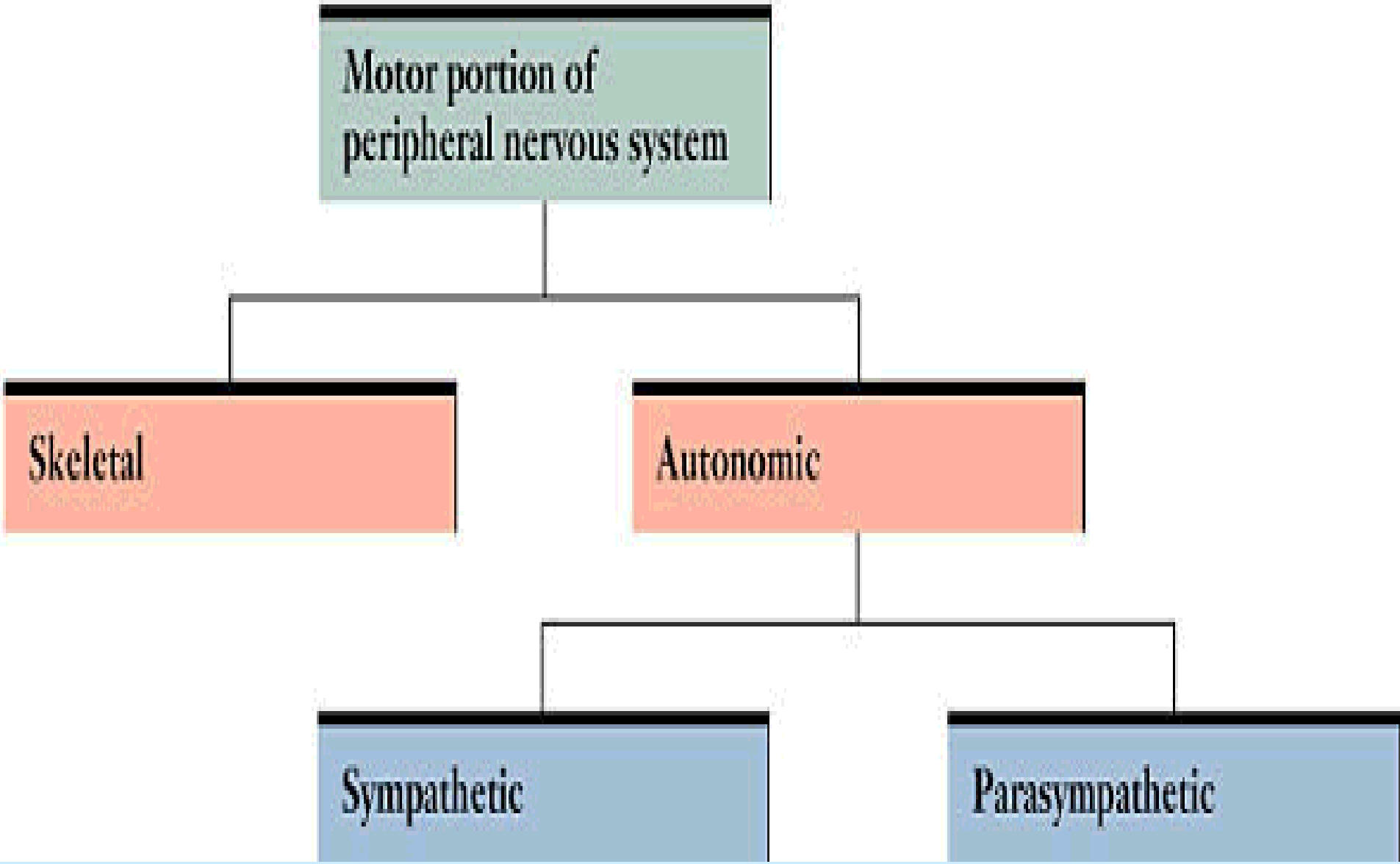
As a further generalization, Our behavior may take either one of two elementary forms:

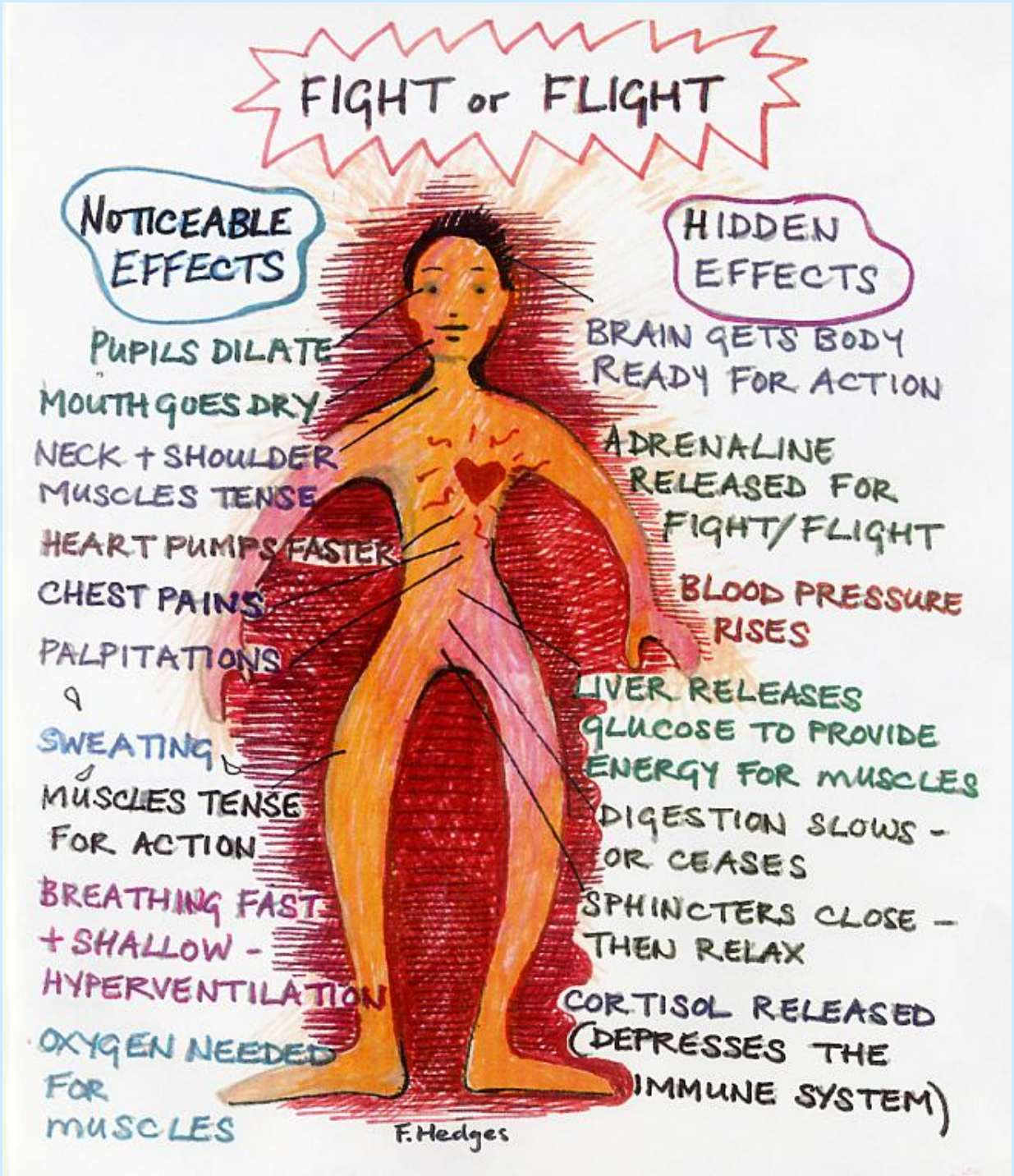



Dinner


FIGHT
—or—
FLIGHT
Swerdlow

Peripheral NS = afferent (sensory) + efferent (motor)



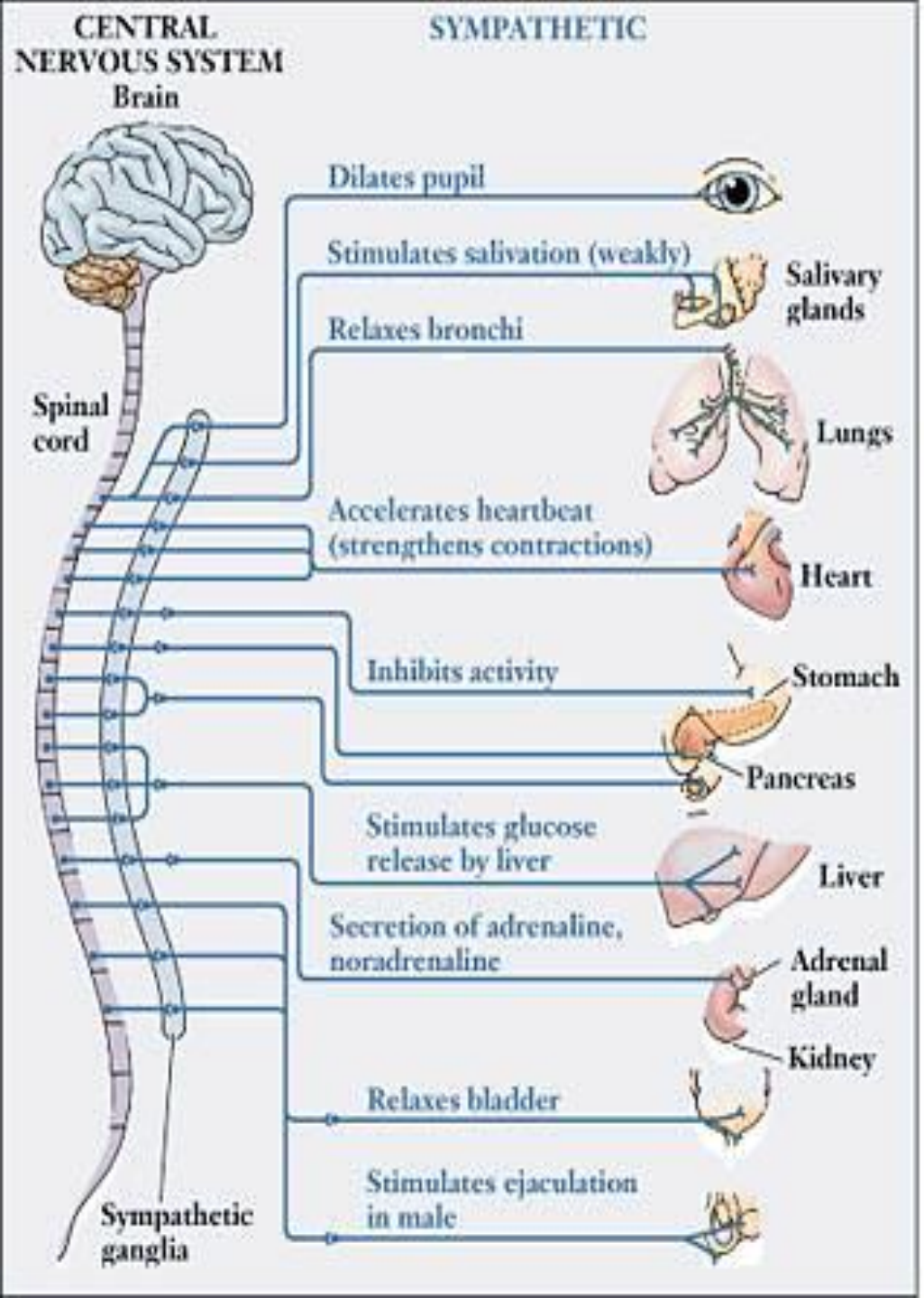

FIGHT or FLIGHT
NOTICEABLE EFFECTS
HIDDEN EFFECTS
PUPILS DILATE
MOUTH GOES DRY
NECK + SHOULDER MUSCLES TENSE
HEART PUMPS FASTER
CHEST PAINS
PALPITATIONS
SWEATING
MUSCLES TENSE FOR ACTION
BREATHING FAST + SHALLOW - HYPERVENTILATION
OXYGEN NEEDED FOR MUSCLES
BRAIN GETS BODY READY FOR ACTION
ADRENALINE RELEASED FOR FIGHT/FLIGHT
BLOOD PRESSURE RISES
LIVER RELEASES GLUCOSE TO PROVIDE ENERGY FOR MUSCLES
DIGESTION SLOWS - OR CEASES
SPHINCTERS CLOSE - THEN RELAX
CORTISOL RELEASED (DEPRESSES THE IMMUNE SYSTEM)
F. Hedges

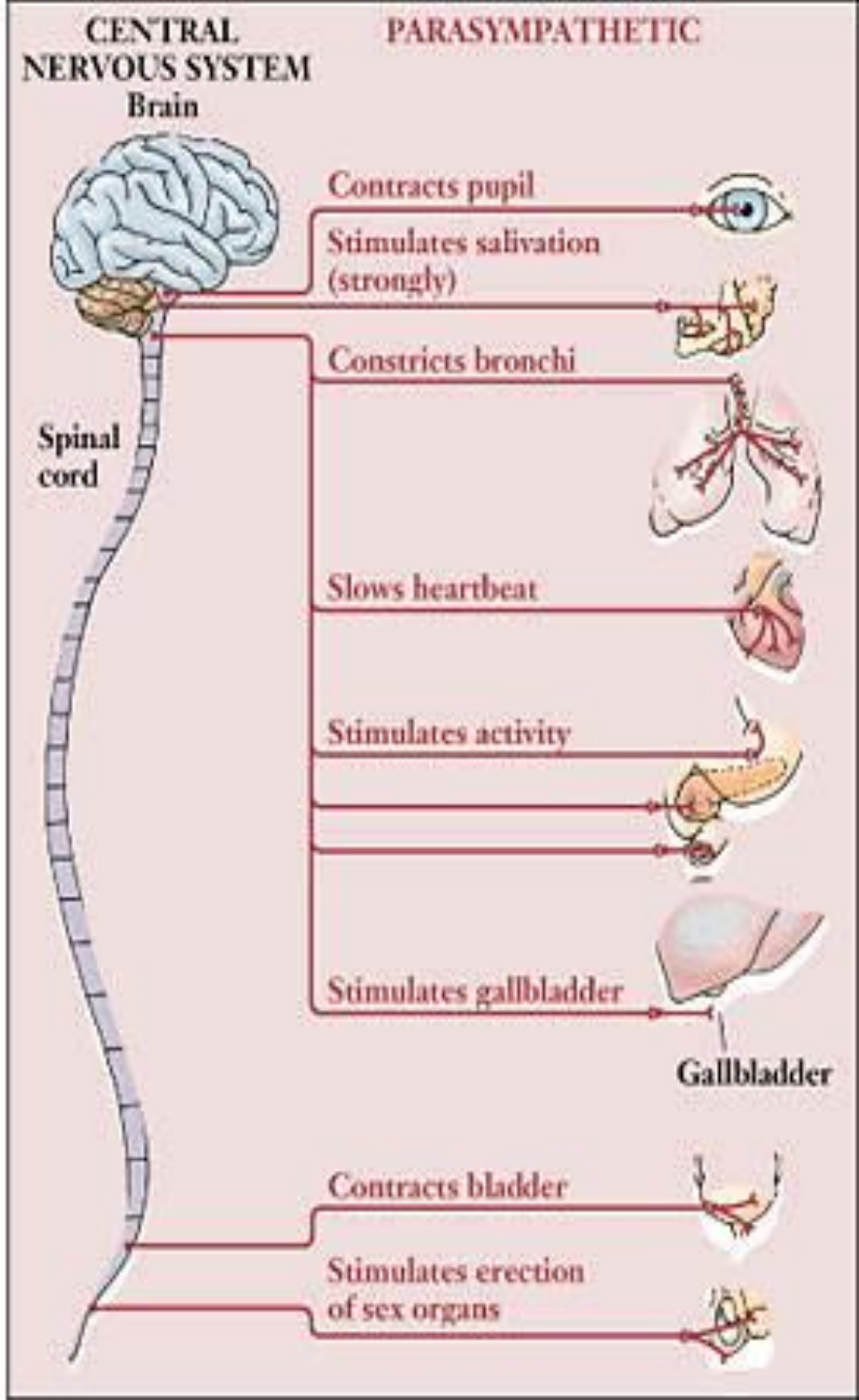
Autonomic (Visceral) Nervous System

- composed of
- **afferent division** (which conveys sensory information from visceral organs) and the
- **efferent division** (which is involved in motor activities that influence smooth muscle, cardiac muscle, glands).
- Concerned with involuntary regulation of smooth muscle, cardiac muscle, and glands.
- Utilizes two neurons between CNS and effectors while somatic nervous system uses one. Neurons synapse in **autonomic ganglia** that are outside the CNS. Can also contain **intrinsic neuron**s.

.**Preganglionic neuron** - first neuron. Cell body in brainstem or spinal cord and its **myelinated axon** courses through a cranial or spinal peripheral nerve. Cholinergic.

.**Postganglionic neuron** - cell body is in an autonomic ganglion and its **unmyelinated axon** courses through nerves and plexuses to a motor ending on cardiac muscle, smooth muscle, or a gland.


CENTRAL NERVOUS SYSTEM
Brain
SYMPATHETIC
Dilates pupil
Stimulates salivation (weakly)
Salivary glands
Relaxes bronchi
Spinal cord
Lungs
Accelerates heartbeat (strengthens contractions)
Heart
Inhibits activity
Stomach
Pancreas
Stimulates glucose release by liver
Liver
Secretion of adrenaline, noradrenaline
Adrenal gland
Kidney
Relaxes bladder
Stimulates ejaculation in male
Sympathetic ganglia


CENTRAL NERVOUS SYSTEM
Brain
PARASYMPATHETIC
Contracts pupil
Stimulates salivation (strongly)
Constricts bronchi
Spinal cord
Slows heartbeat
Stimulates activity
Stimulates gallbladder
Gallbladder
Contracts bladder
Stimulates erection of sex organs

Divisions of the ANS

Sympathetic division - preganglionic fibers from the thoracic and lumbar spinal segments (T1 to L2) synapse in ganglia near the spinal cord. Stimulate tissue metabolism, increase alertness, and generally prepares body to deal with emergencies. Most postganglionic fibers are adrenergic (norepinephrine) with excitatory effects.

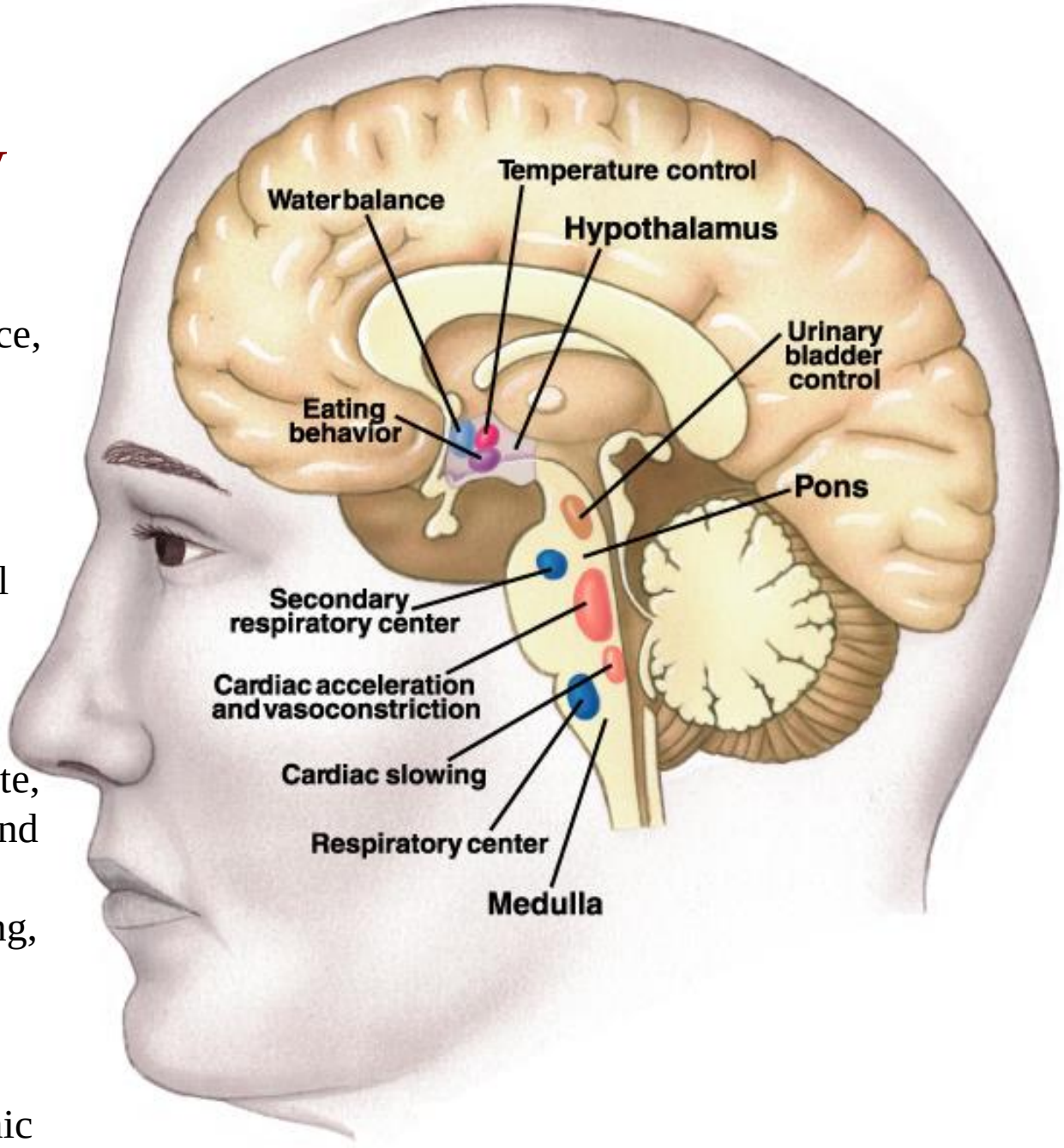
Parasympathetic division - preganglionic fibers originate in the brain and sacral spinal segments. Synapse with ganglia located inside visceral organs. Conserve energy and promote sedentary activities. Postganglionic fibers are cholinergic. Effects can be excitatory or inhibitory.

Homeostasis: The sympathetic and parasympathetic branches maintain homeostasis.

Most internal organs (except sweat glands and smooth muscles in most blood vessels) are innervated by both autonomic branches, which exhibit antagonistic control.

ANS Regulation by Brain

Hypothalamus – water balance, temperature control, eating behavior.
Midbrain – urinary bladder control, visual reflexes.
Pons – coordination of control of breathing, cardiac acceleration and vasoconstriction.
Medulla oblongata – heart rate, respiratory rate, constriction and dilation of blood vessels, swallowing, vomiting, sneezing, coughing.
Descending pathways from cerebral cortex and limbic system can influence autonomic output.



Sympathetic Division

Preganglionic neurons in the lateral gray horns of the spinal cord. Short axons enter ventral roots.

Ganglionic neurons located in **spinal chain ganglia** (either side of vertebral column; neurons that control effectors in the body wall and inside thoracic cavity) and **collateral ganglia** (unpaired, anterior to vertebral column; control tissues and organs in abdominopelvic cavity).

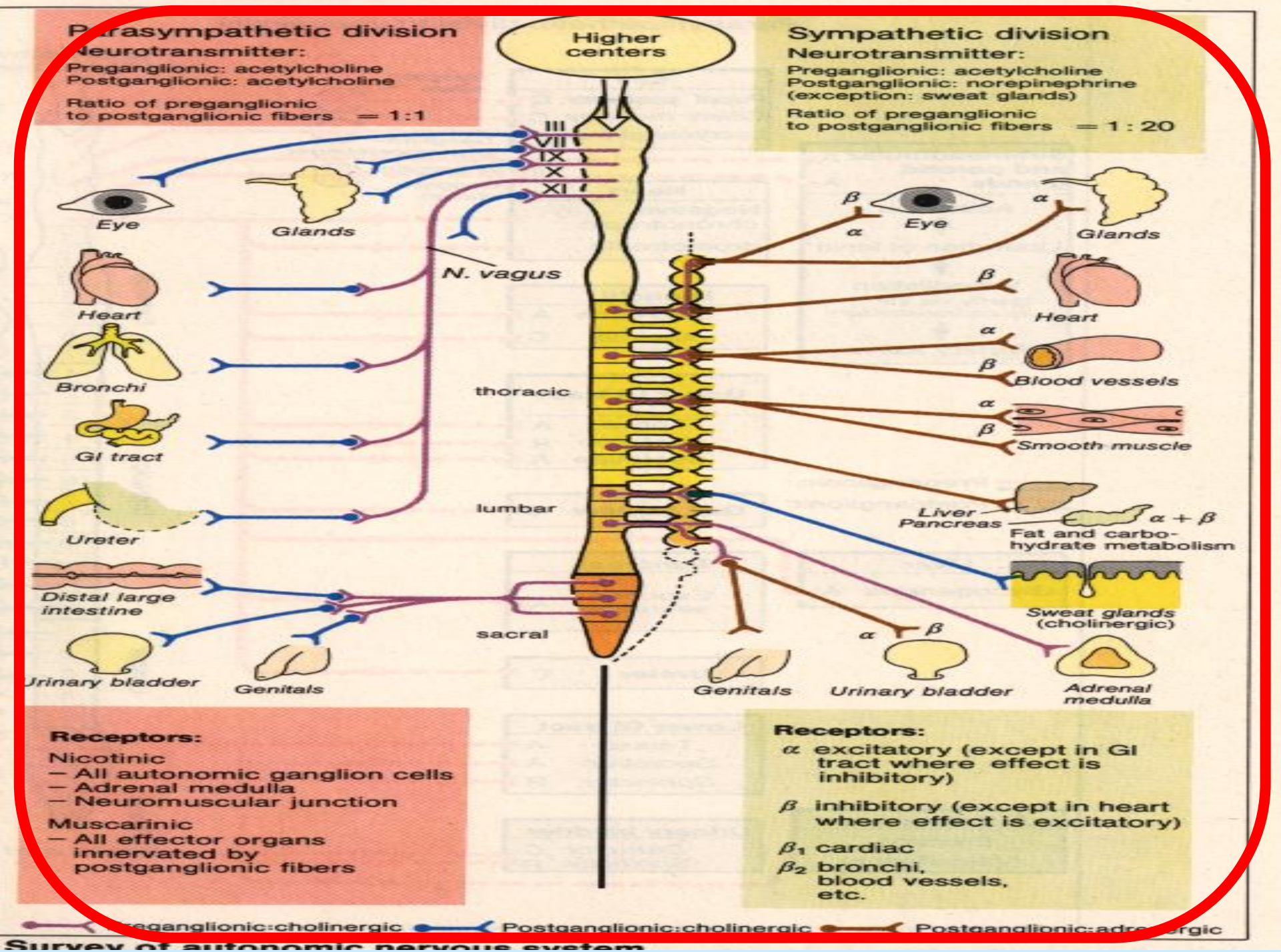
Adrenal medulla - specialized neurons in modified ganglion inside adrenal gland. Have no axons and release norepinephrine and epinephrine into general circulation.

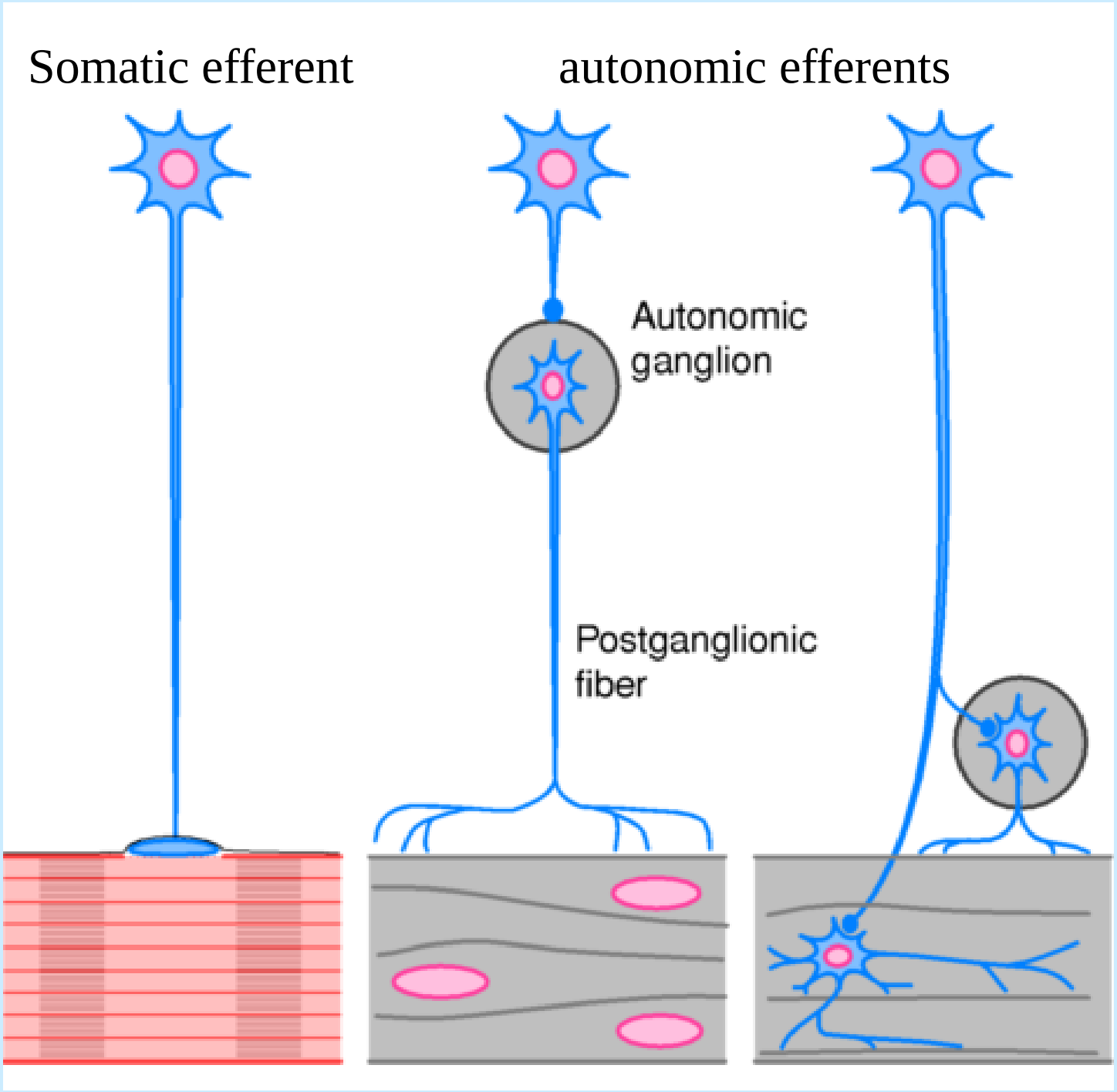
Parasympathetic Division

Preganglionic neurons in lateral gray horns of S2 to S4 and in brainstem.

Ganglionic neurons in peripheral ganglia located within or adjacent to target organs.

Dual innervation - some organs innervated by both divisions. Opposing effects.


Parasympathetic division
Neurotransmitter:
Preganglionic: acetylcholine
Postganglionic: acetylcholine
Ratio of preganglionic to postganglionic fibers = 1:1
Higher centers
Sympathetic division
Neurotransmitter:
Preganglionic: acetylcholine
Postganglionic: norepinephrine (exception: sweat glands)
Ratio of preganglionic to postganglionic fibers = 1 : 20
III
VII
IX
X
XI
Eye
Glands
N. vagus
Heart
Bronchi
GI tract
Ureter
Distal large intestine
Urinary bladder
Genitals
thoracic
lumbar
sacral
β
α
Eye
Glands
Heart
Blood vessels
Smooth muscle
Liver
Pancreas
α + β
Fat and carbohydrate metabolism
Sweat glands (cholinergic)
Adrenal medulla
Genitals
Urinary bladder
Receptors:
Nicotinic
— All autonomic ganglion cells
— Adrenal medulla
— Neuromuscular junction
Muscarinic
— All effector organs innervated by postganglionic fibers
Receptors:
α excitatory (except in GI tract where effect is inhibitory)
β inhibitory (except in heart where effect is excitatory)
β1 cardiac
β2 bronchi, blood vessels, etc.
Postganglionic:cholinergic
Postganglionic:cholinergic
Survey of autonomic nervous system


Somatic efferent
autonomic efferents
Autonomic ganglion
Postganglionic fiber

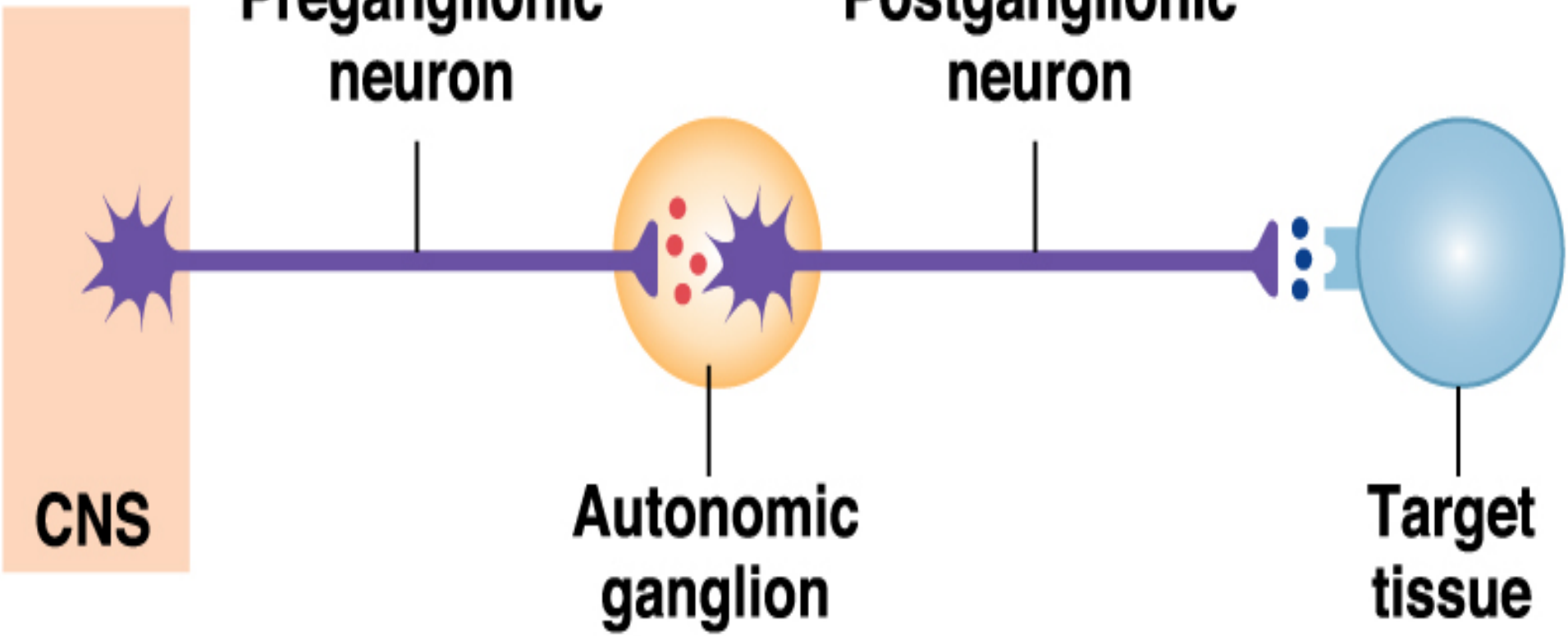
Autonomic Synapses

All autonomic **preganglionic neurons** are **cholinergi**c, i.e. release acetylcholine onto cholinergic **nicotinic** receptors. (Nicotine is agonist.)

Most **sympathetic postganglionic neurons** are **adrenergi**c, i.e. release norepinephrine.

Most **parasympathetic postganglionic neurons** are **cholinergi**c, i.e. release acetylcholine onto cholinergic **muscarinic** receptors. (Muscarine is agonist).

Autonomic pathway



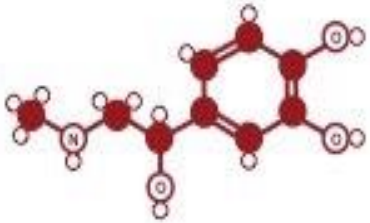
NEUROTRANSMITTERS

- Acetyl-choline
- Nor-epinephrine (or nor-adrenaline)
- Dopamine
- Serotonine (or 5-HT)
- GABA (or γ-aminobutyric acid)
- Glutamate

NEUTOMODULATORS

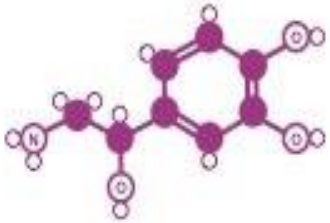
- adenosine

ADRENALINE



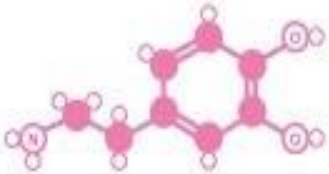
Fight or flight neurotransmitter

NORADRENALINE



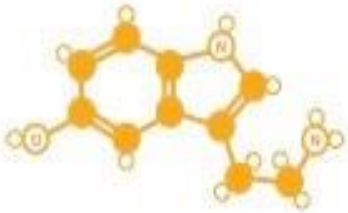
Concentration neurotransmitter

DOPAMINE



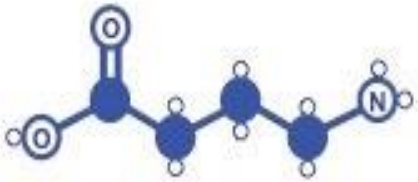
Pleasure neurotransmitter

SEROTONIN



Mood neurotransmitter

GABA



Calming neurotransmitter

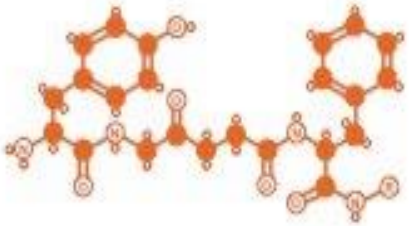
ACETYLCHOLINE

Learning neurotransmitter

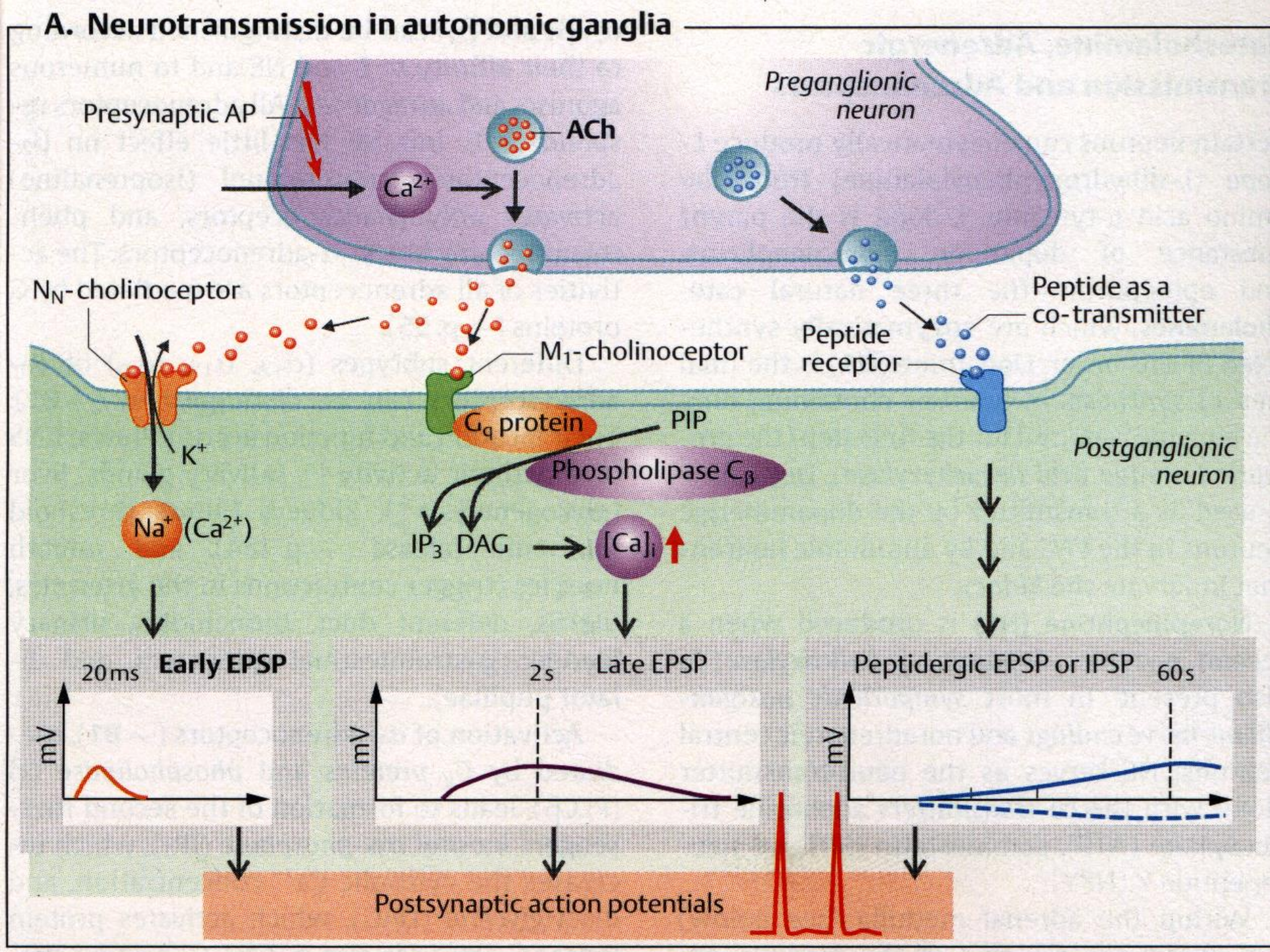
GLUTAMATE

Memory neurotransmitter

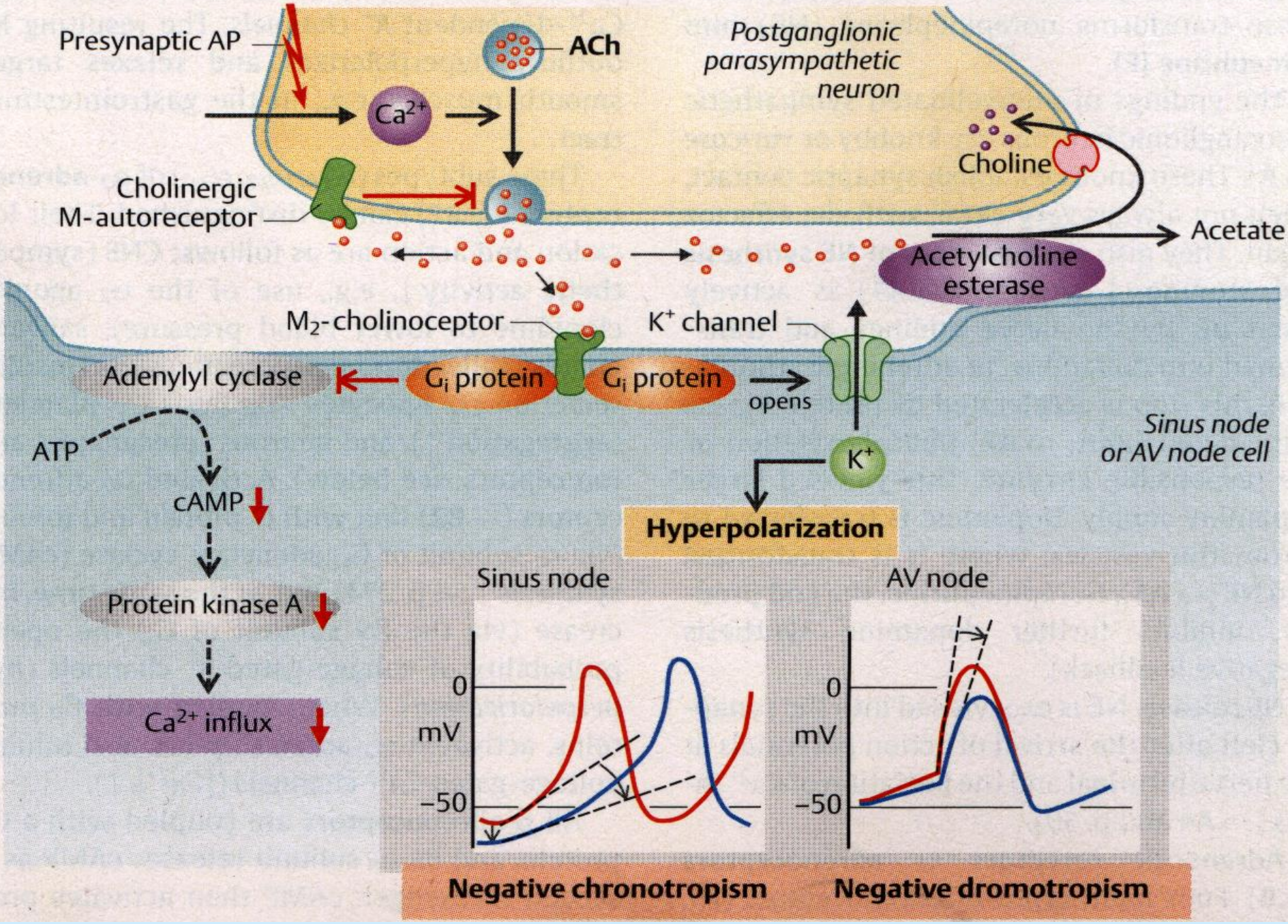
ENDORPHINS

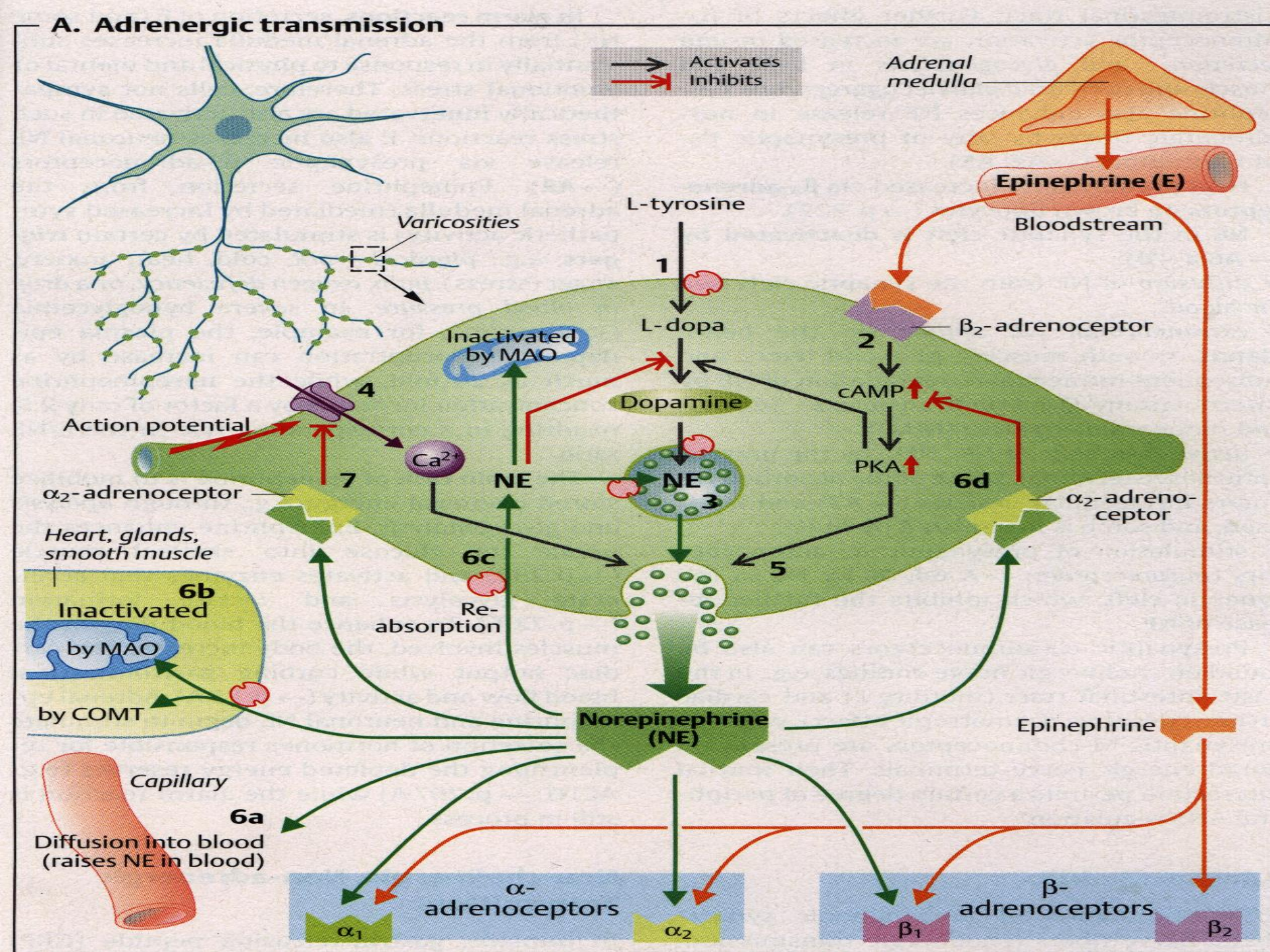


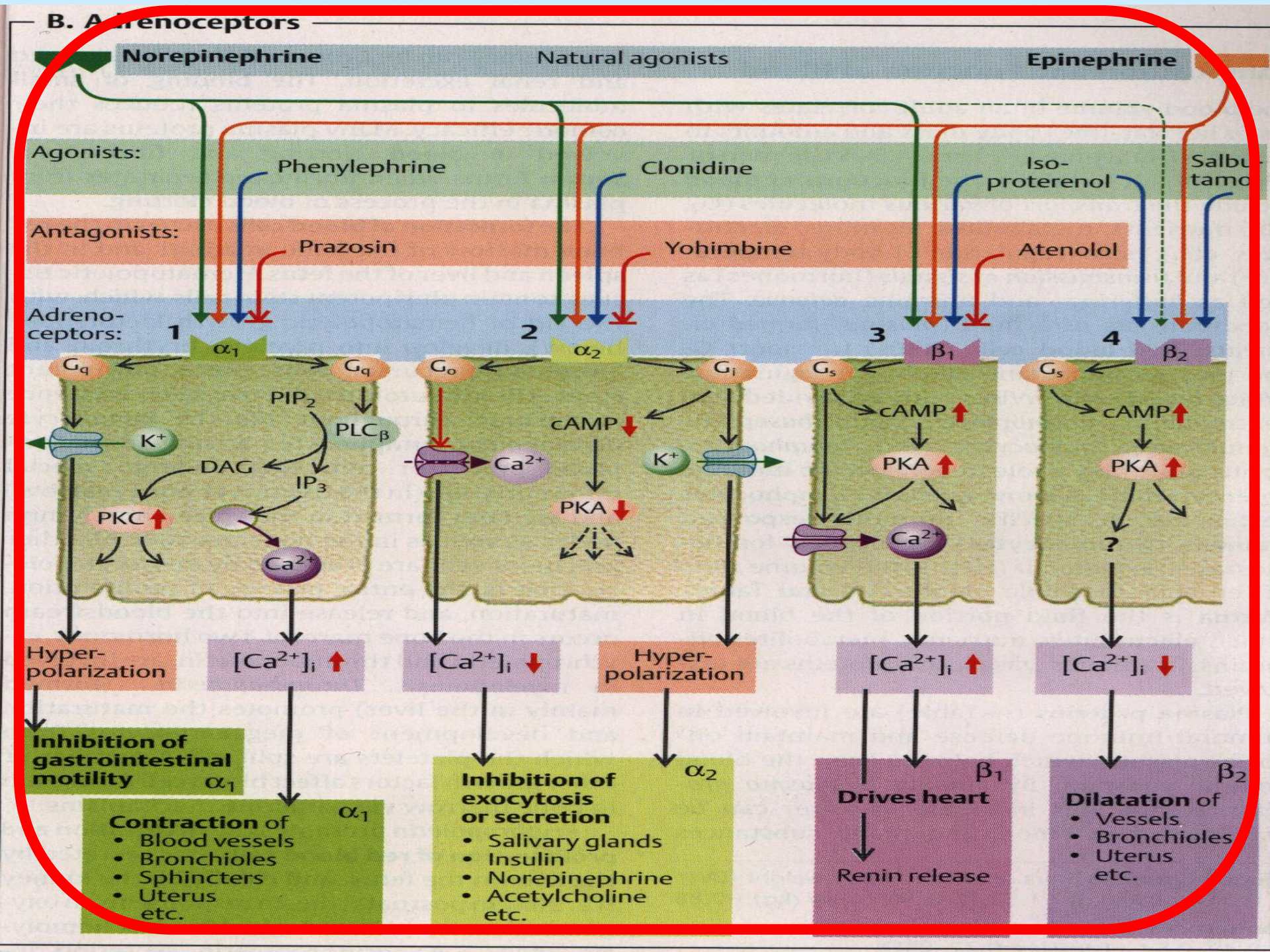
Euphoria neurotransmitter


A. Neurotransmission in autonomic ganglia
Presynaptic AP
ACh
Ca2+
Preganglionic neuron
NN-cholinoceptor
M1-cholinoceptor
Peptide as a co-transmitter
Peptide receptor
Gq protein
PIP
Phospholipase Cβ
K+
Na+ (Ca2+)
IP3 DAG
[Ca]i
Postganglionic neuron
20 ms
Early EPSP
2 s
Late EPSP
Peptidergic EPSP or IPSP
60 s
mV
Postsynaptic action potentials

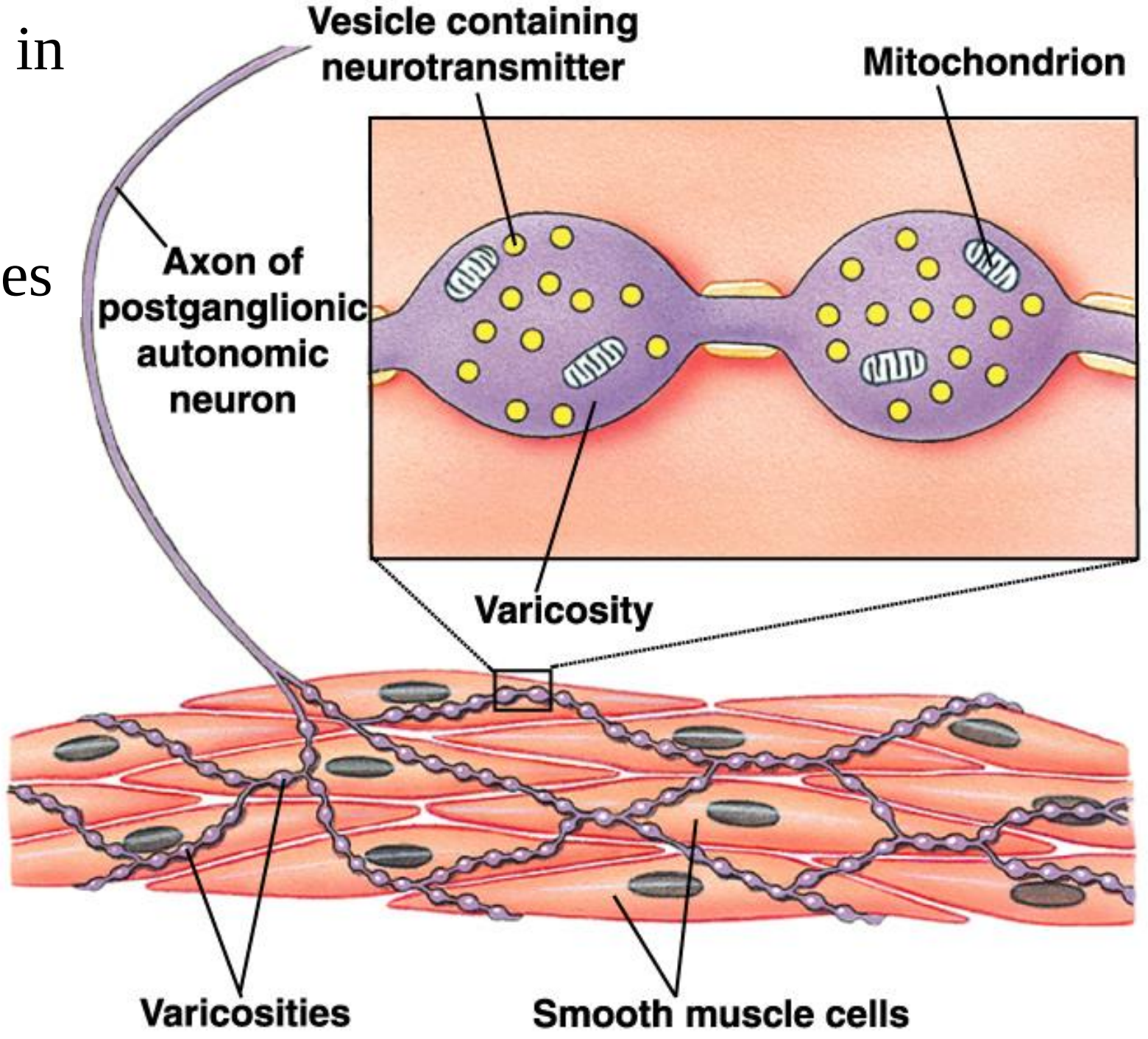
B. Cholinergic transmission in the heart

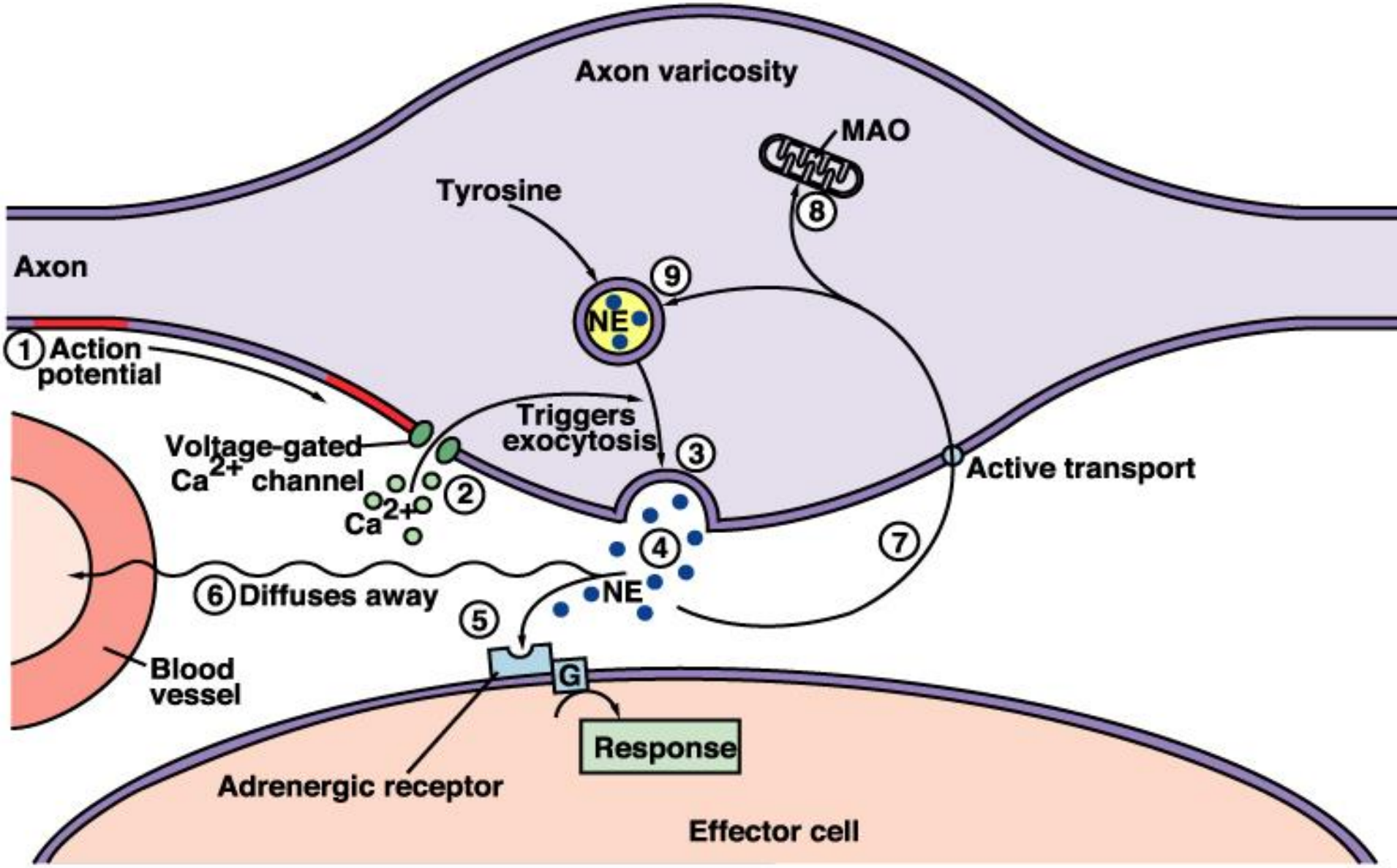



A. Adrenergic transmission
Activates
Inhibits
Adrenal medulla
Epinephrine (E)
Bloodstream
L-tyrosine
Varicosities
1
L-dopa
β2-adrenoceptor
2
cAMP
Inactivated by MAO
Dopamine
4
Action potential
Ca2+
NE
NE
3
PKA
6d
α2-adrenoceptor
7
α2-adreno-ceptor
Heart, glands, smooth muscle
6c
5
6b
Inactivated
by MAO
by COMT
Re-absorption
Norepinephrine (NE)
Epinephrine
Capillary
6a
Diffusion into blood (raises NE in blood)
α-adrenoceptors
α1
α2
β-adrenoceptors
β1
β2


B. Adrenoceptors
Norepinephrine
Natural agonists
Epinephrine
Agonists:
Phenylephrine
Clonidine
Iso-proterenol
Salbu-tamo
Antagonists:
Prazosin
Yohimbine
Atenolol
Adreno-ceptors:
1
α1
2
α2
3
β1
4
β2
Gq
Gq
Go
Gi
Gs
Gs
PIP2
PLCβ
K+
DAG
IP3
PKC
Ca2+
cAMP
PKA
K+
Ca2+
cAMP
PKA
Ca2+
cAMP
PKA
?
Hyper-polarization
[Ca2+]i
[Ca2+]i
Hyper-polarization
[Ca2+]i
[Ca2+]i
Inhibition of gastrointestinal motility
α1
Contraction of
• Blood vessels
• Bronchioles
• Sphincters
• Uterus
etc.
α1
Inhibition of exocytosis or secretion
• Salivary glands
• Insulin
• Norepinephrine
• Acetylcholine
etc.
α2
β1
Drives heart
Renin release
β2
Dilatation of
• Vessels
• Bronchioles
• Uterus
etc.

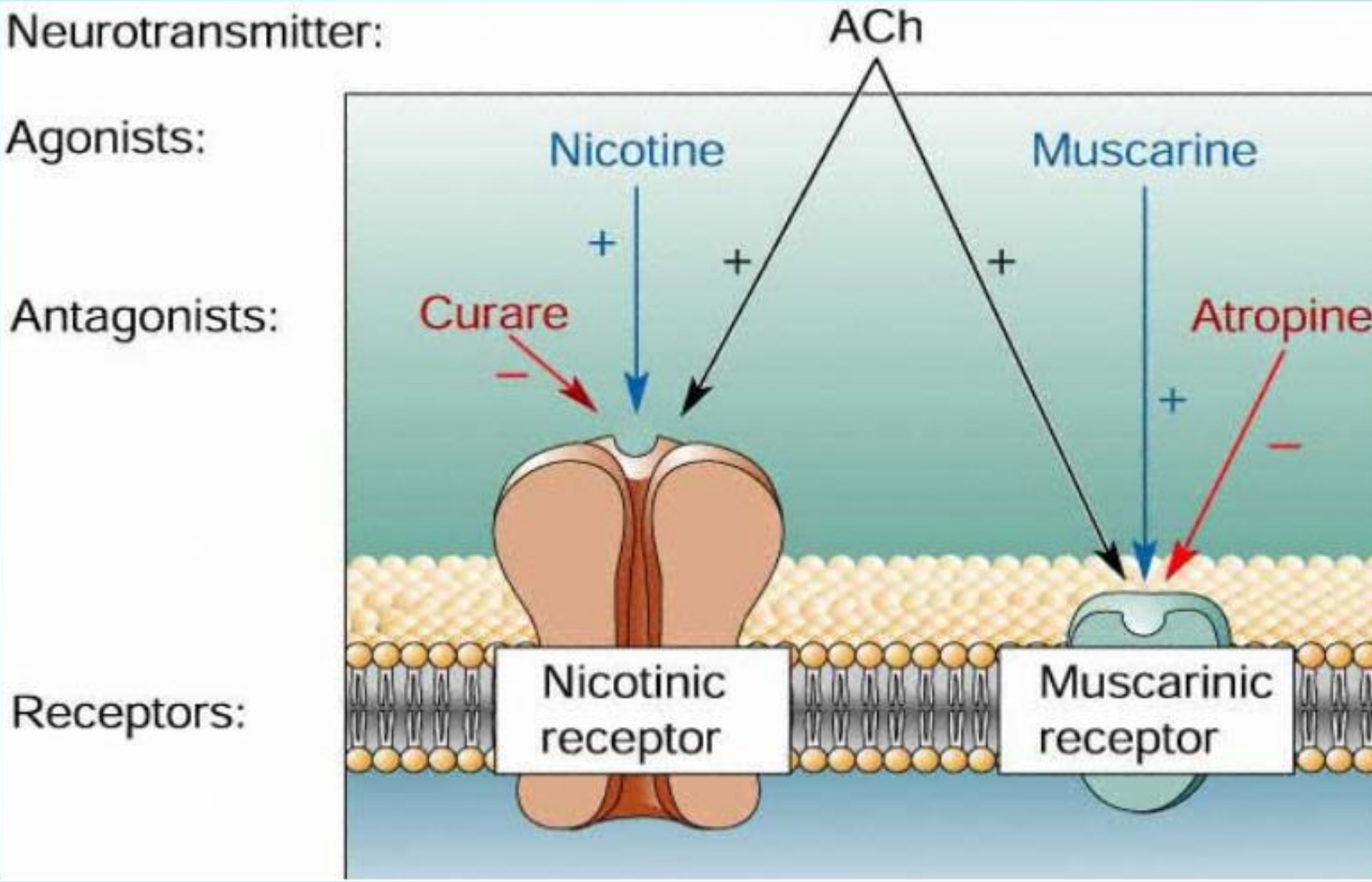
Synapses in ANS display varicosities





Release of norepinephrine at a varicosity of a sympathetic neuron

Acetyl-choline



DRUGS

Most drugs - sold both over and under the counter – work in synaptic transmission.

.**Cocaine** – blocks reuptake of norepinephrine.

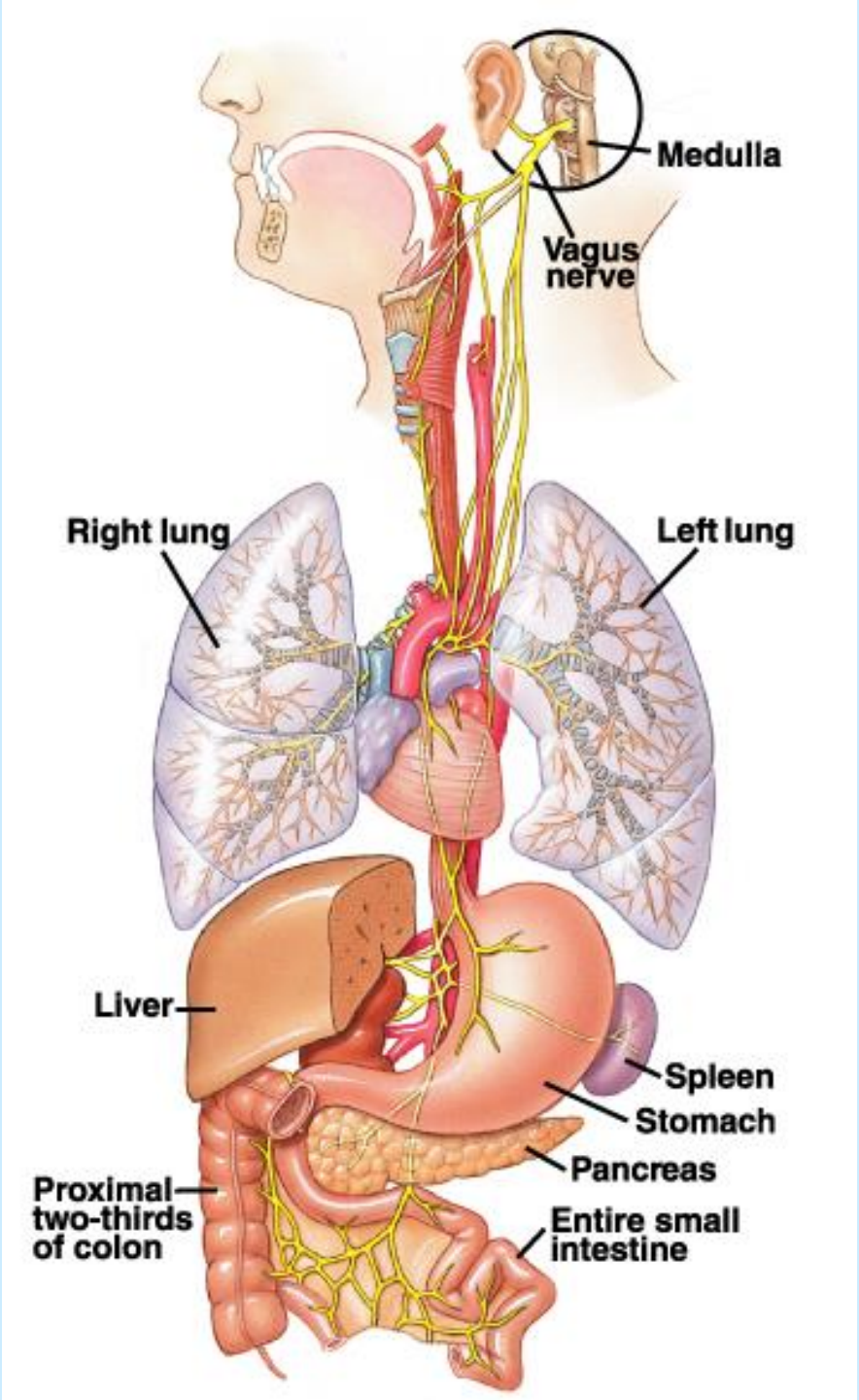
.**Neostigmine** – inhibits cholinesterase and prolongs life of ACh. Used to treat myasthenia gravis.

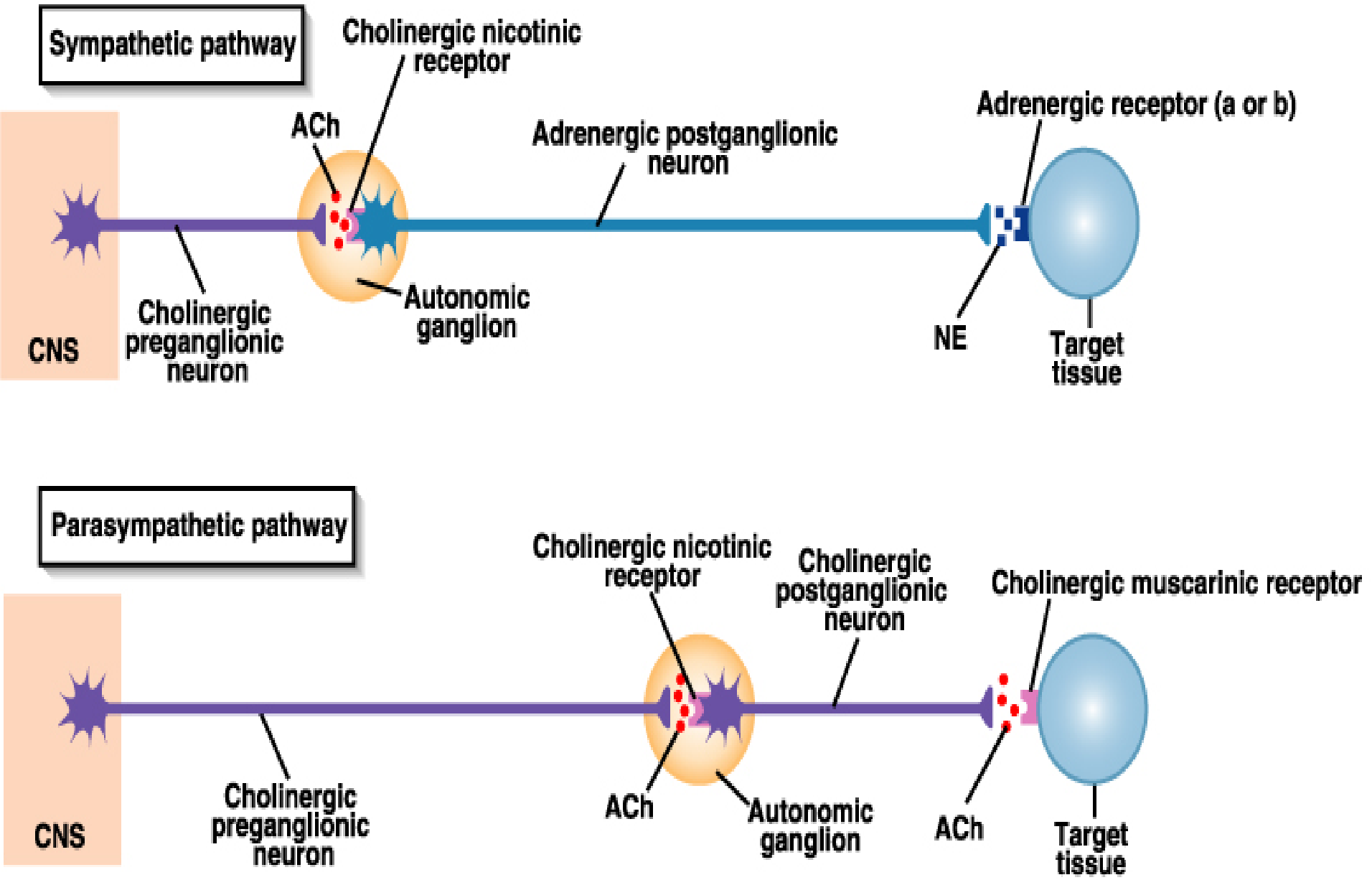
Botulin toxin Blocks Ach reuptake

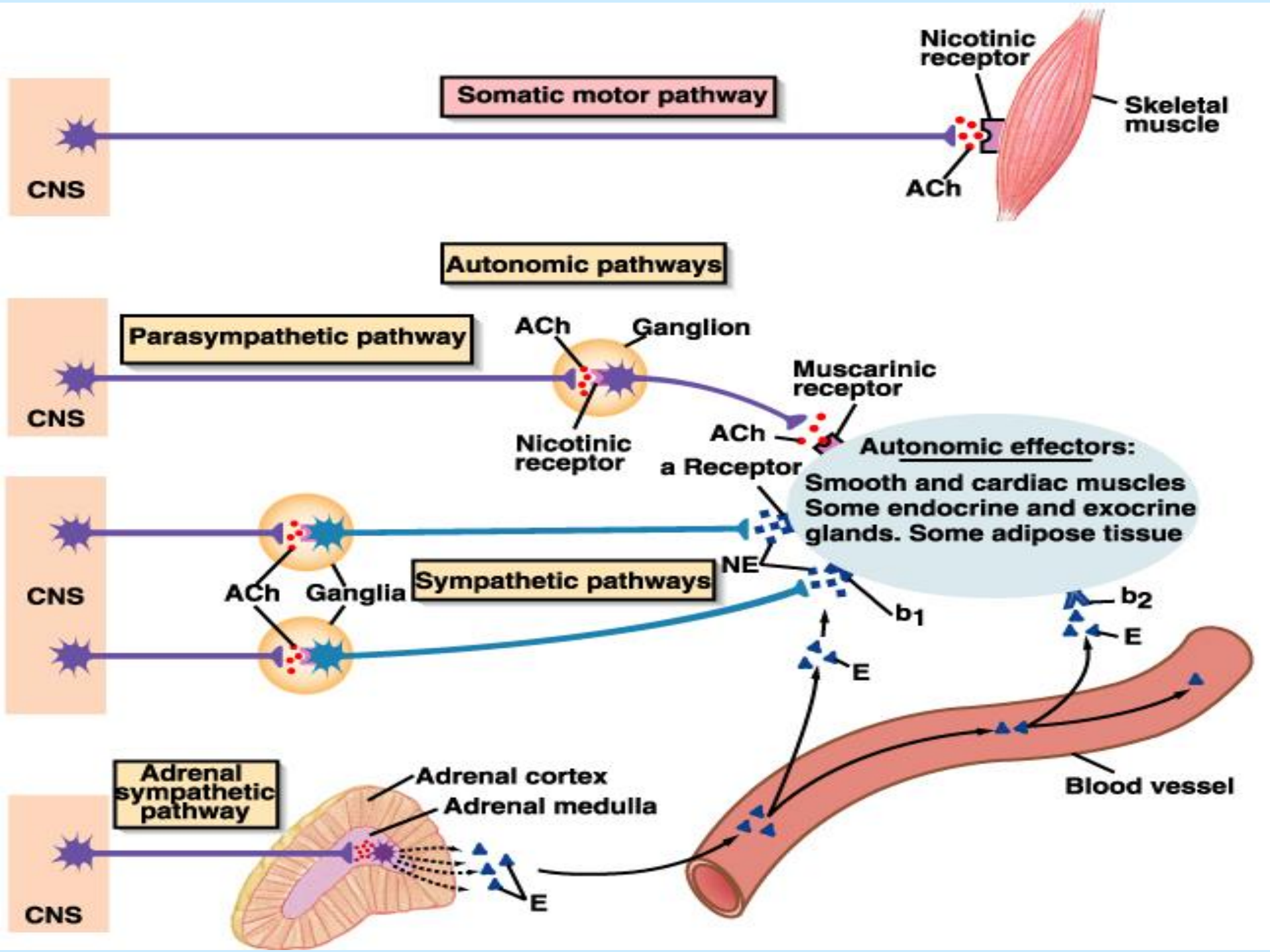
.Older **antidepressant** drugs (tricyclics and Mono Amine Oxidase inhibitors) acted on NE transport and metabolism and could have side effects related to their actions in the ANS.

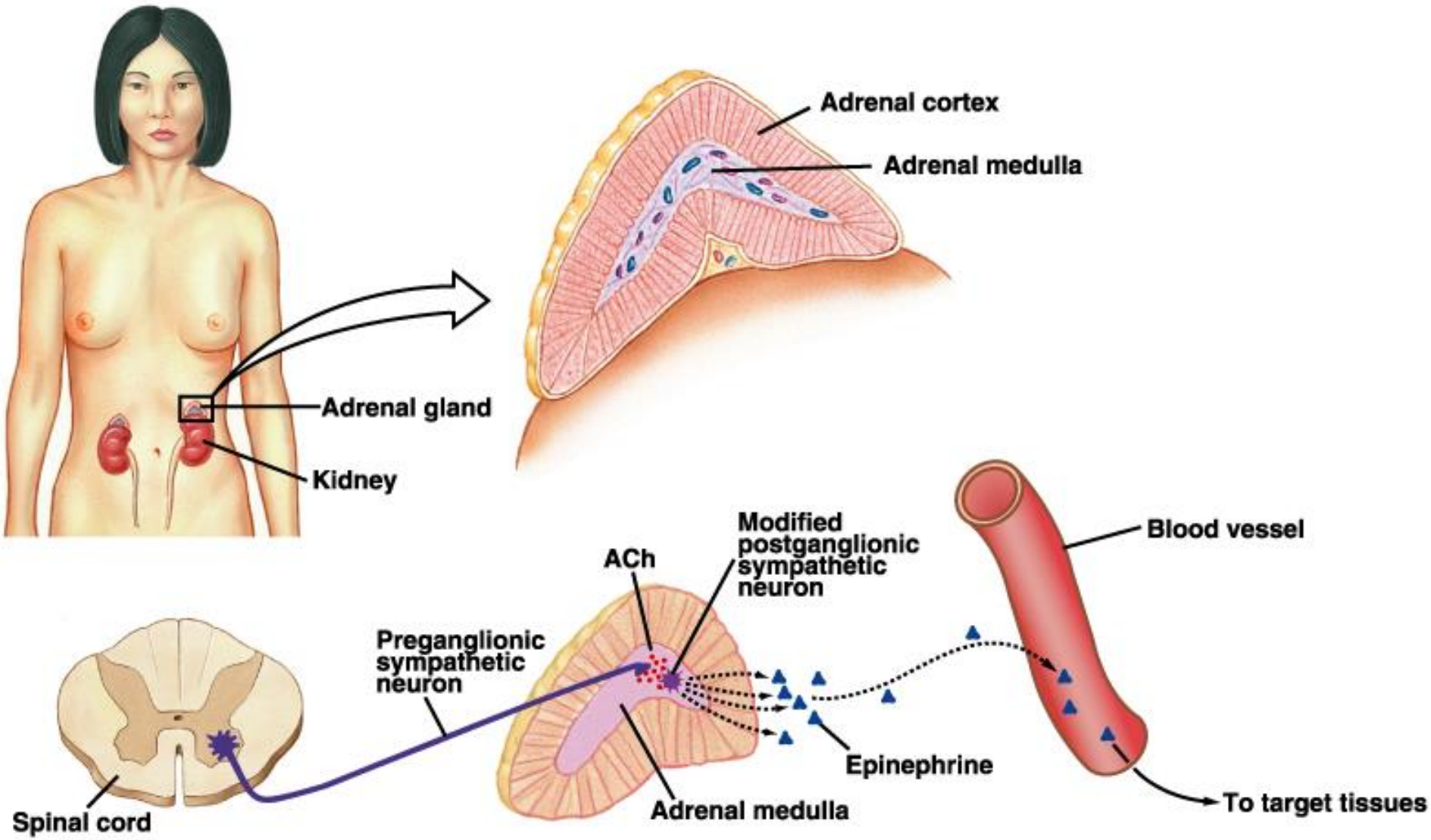
Currently used antidepressants mainly block the reuptake of serotonine, which elevates the mood

The major parasympathetic tract:
the **vagus nerve (X)**



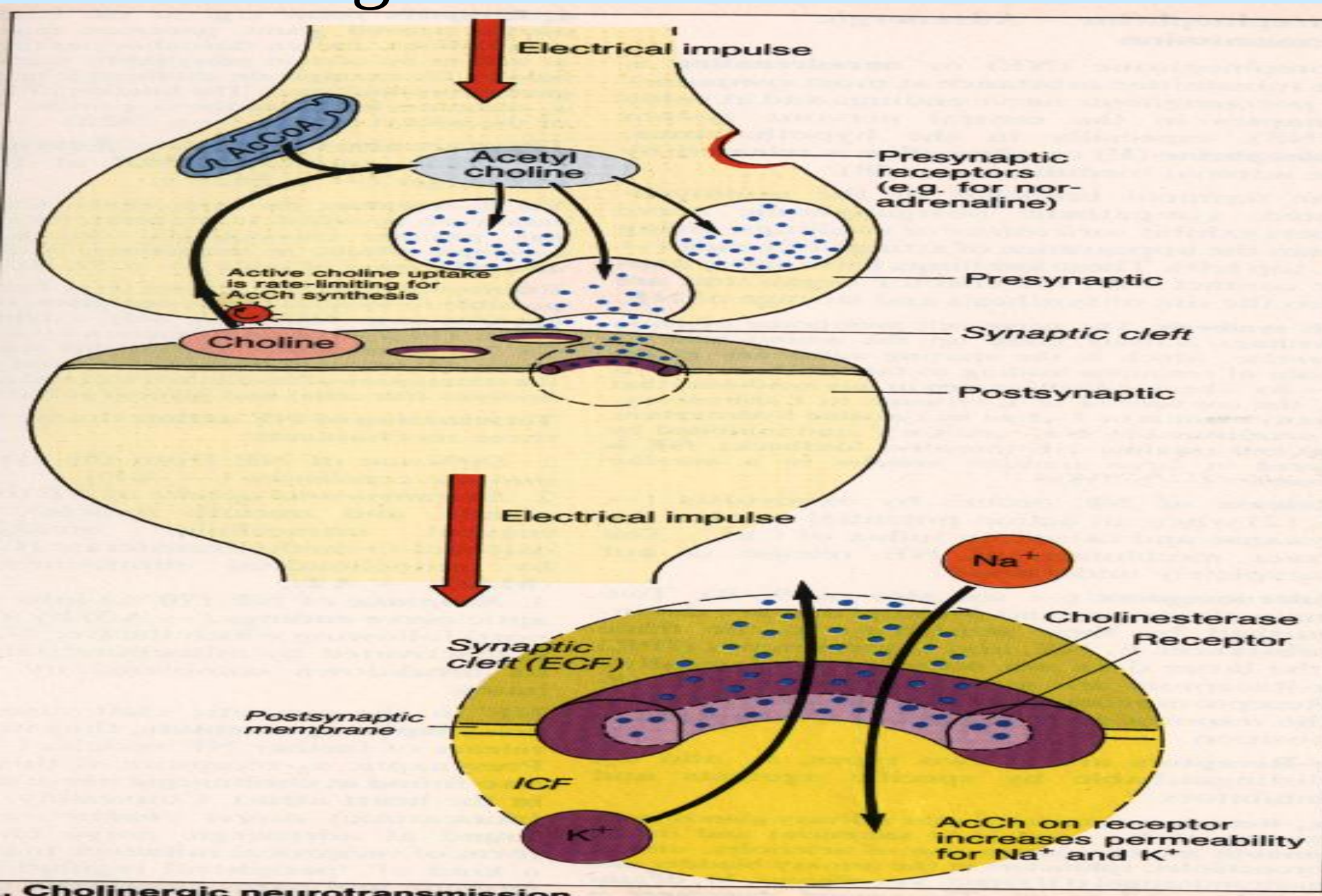

Sympathetic pathway
Cholinergic nicotinic receptor
ACh
Adrenergic postganglionic neuron
Adrenergic receptor (a or b)
CNS
Cholinergic preganglionic neuron
Autonomic ganglion
NE
Target tissue
Parasympathetic pathway
Cholinergic nicotinic receptor
Cholinergic postganglionic neuron
Cholinergic muscarinic receptor
CNS
Cholinergic preganglionic neuron
ACh
Autonomic ganglion
ACh
Target tissue


Somatic motor pathway
CNS
Nicotinic receptor
Skeletal muscle
ACh
Autonomic pathways
Parasympathetic pathway
CNS
ACh
Ganglion
Nicotinic receptor
Muscarinic receptor
ACh
a Receptor
Autonomic effectors:
Smooth and cardiac muscles
Some endocrine and exocrine glands. Some adipose tissue
CNS
ACh
Ganglia
Sympathetic pathways
NE
b1
E
b2
E
Blood vessel
Adrenal sympathetic pathway
CNS
Adrenal cortex
Adrenal medulla
E

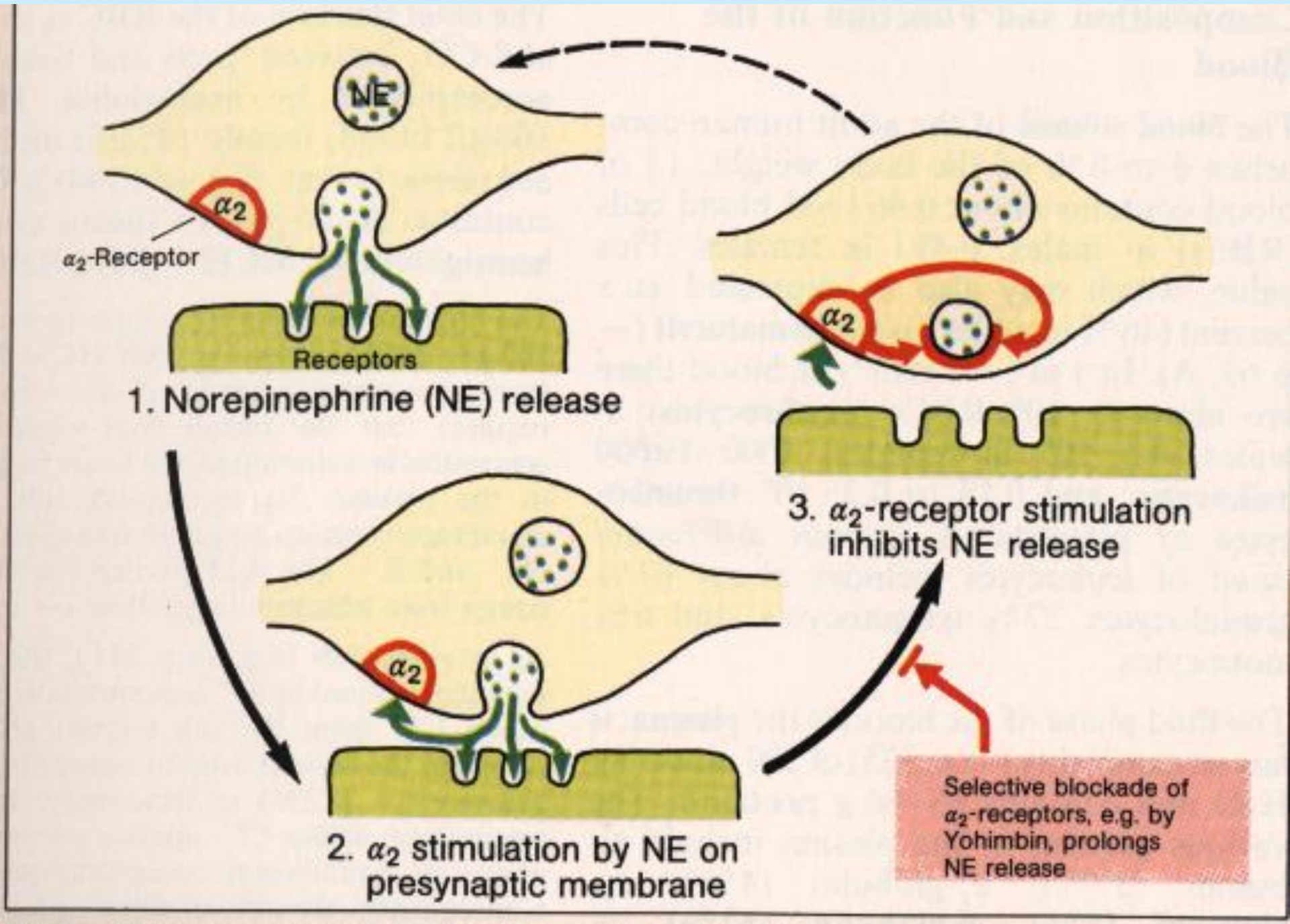


The adrenal medulla is a modified sympathetic ganglion whose postganglionic neurons have no axons, but secrete norepinephrine into the blood as a neurohormone

Cholinergic neurotransmission



Cholinergic neurotransmission



A. Feedback control of NE release via presynaptic α_2-receptors

Pathophysiology:

the study of mechanisms leading to a disease

Pathophysiology of Synaptic transmission - 1

- The importance of the influx of Ca^{++} into the nerve terminal to initiate the release of transmitter is illustrated by a disease, known as **Lambent-Eaton syndrome,** in which there are circulating antibodies against the type of voltage-gated Ca^{++} channels present in nerve terminals. Patients with this disorder experience muscular weakness and diminished stretch reflexes.
- General **anesthetics** prolong the open time of γ-amino-butyric acid (GABA) receptor chloride channels, and thus prolong the inhibition of the postsynaptic neurons at GABA-ergic synapses. GABA receptors may be the principal targets of general anesthetics.
- Deficits in pathways involving acetylcholine **(cholinergic pathways)** in the brain have been implicated in some forms of **senile dementia** (such as **Alzheimer's disease).** Treatment with long-lasting anticholinergic drugs that penetrate the blood-brain barrier may improve cognitive function in some individuals suffering from dementia.

Pathophysiology of Synaptic transmission - 2

- Neurons that contain high levels of dopamine are prominent in the midbrain regions known as the **substantia nigra** and the **ventral tegmentum.** Some of the axons of these terminate in the **corpus striatum,** where they participate in controlling complex movements. The degeneration of dopaminergic synapses in the corpus striatum occurs in **Parkinson's disease** and may be a major cause of the muscular tremors and rigidity that characterize this disease. Treatment of some Parkinson's patients with l-dopa, a precursor of dopamine, improves motor control.
- Patients with a disorder called **myasthenia gravis** are unable to maintain prolonged contraction of skeletal muscle. These individuals have circulating antibodies against the acetylcholine receptor protein.
- So-called **a-toxins** in cobra venoms are responsible for paralyzing the snakes' prey. a-toxins bind to the acetylcholine binding site on the acetylcholine receptor protein and prevent acetylcholine from acting. Poison arrows whose tips are dipped in **curare,** an a-toxin extracted from certain plants, are used by some South American Indians to paralyze their prey.

Pathophysiology of the Autonomic Nervous system - 1

Autonomic dysfunction may result from diseases that affect primarily either

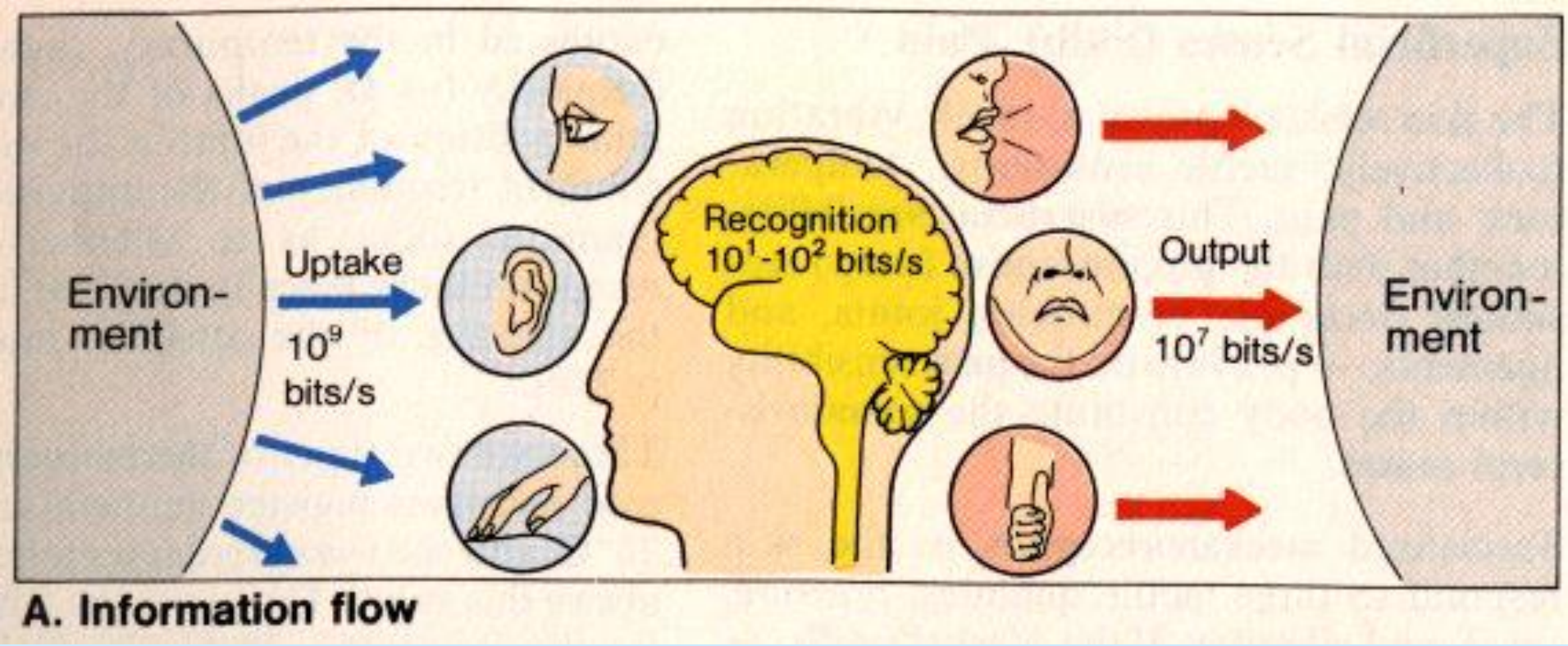
• the central nervous system (degeneration of the intermediolateral cell columns (progressive autonomic failure) or disease or damage to descending pathways that synapse on the intermediolateral column cells (spinal cord lesions, cerebrovascular disease, brainstem tumors, multiple sclerosis)

• Or the peripheral autonomic nervous system (damaged in isolation in the acute and subacute autonomic neuropathies or in association with a generalized peripheral neuropathy. The peripheral neuropathies most likely to cause severe autonomic disturbance are those in which small myelinated and unmyelinated fibers are damaged in the baroreflex afferents, the vagal efferents to the heart, and the sympathetic efferent pathways to the mesenteric vascular bed. Acute demyelination of the sympathetic and parasympathetic nerves in the Guillain-Barre syndrome may also cause acute autonomic dysfunction. Although autonomic disturbances may occur in other types of peripheral neuropathy, they are rarely clinically important.)

Pathophysiology of the Autonomic Nervous system - 2

Interruption of the sympathetic supply to the head (or of descending pathways from the hypothalamus that control sympathetic activity) results in **Horner'S syndrome,** which consists of

- a **partial ptosis** (drooping of the eyelid caused by paralysis of the superior tarsal muscle of the eyelid; it is a smooth muscle),
- **pupillary constriction** (because the unopposed parasympathetic supply of the iris is intact),
- **anhydrosis of the face** (caused by interruption of the innervation of the sweat glands of the face, and
- **enophthalmos** (retraction of the globe of the eye because of the interruption of the innervation of the smooth muscle of the orbit).



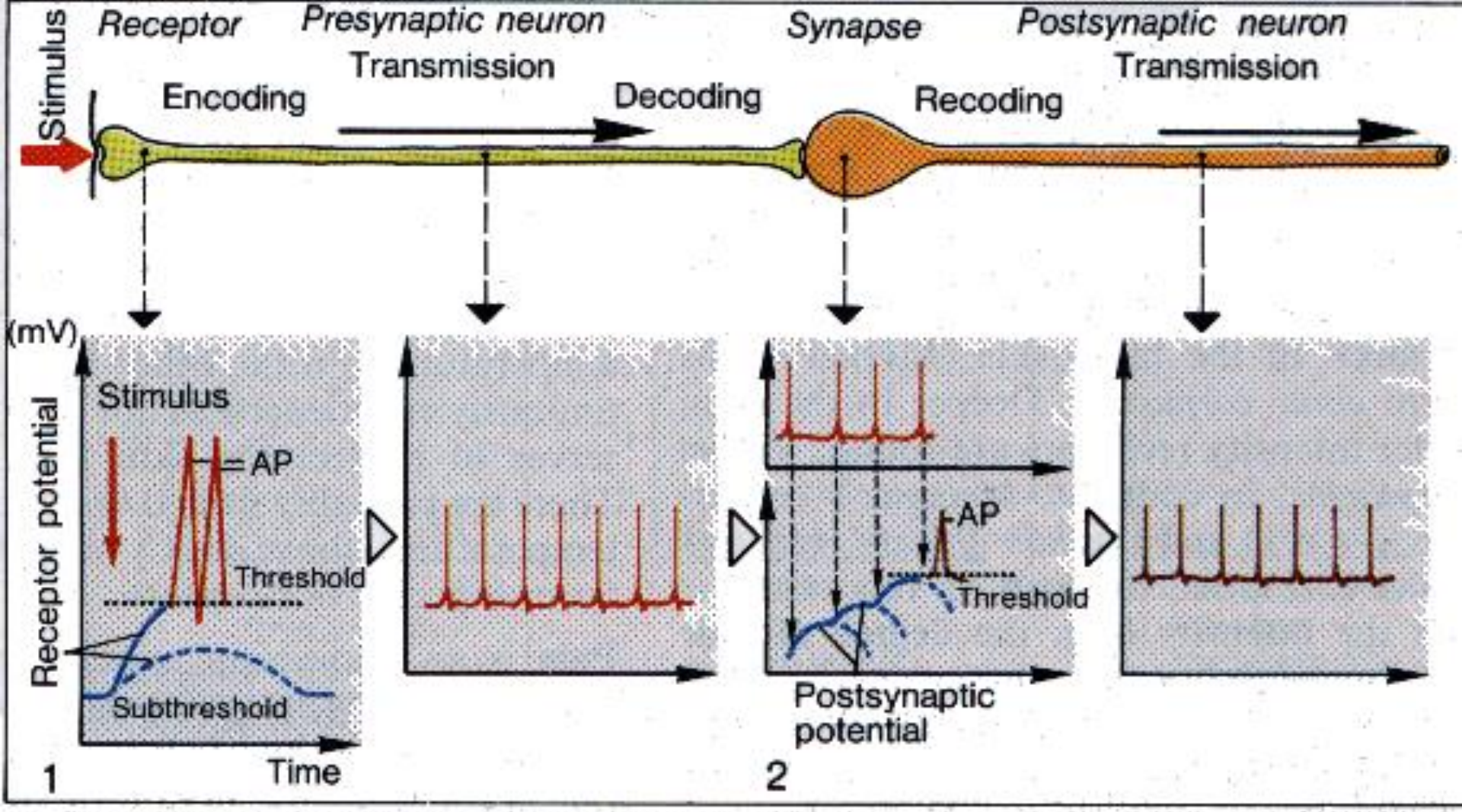
A. Information flow

Ο εγκέφαλος δέχεται, επεξεργάζεται και στέλνει μεγάλο πλήθος πληροφοριών.

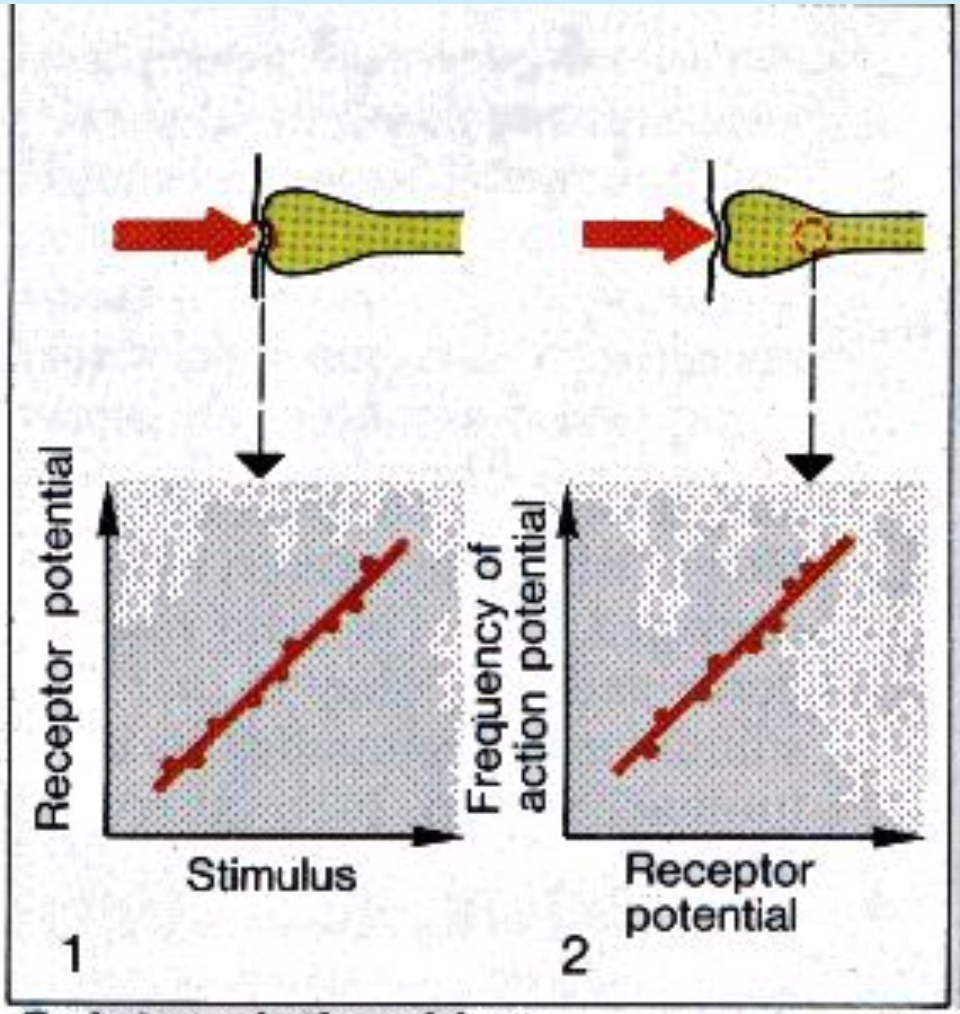
Η μετάδοση πληροφοριών από νευρώνα σε νευρώνα σχετικά με τους ΗΥ πιο αργή αλλά αποτελεσματικότερη στην επίλυση προβλημάτων.

Οι πληροφορίες μεταδίδονται με ΔΕ, τα οποία είναι «όλον ή ουδέν».

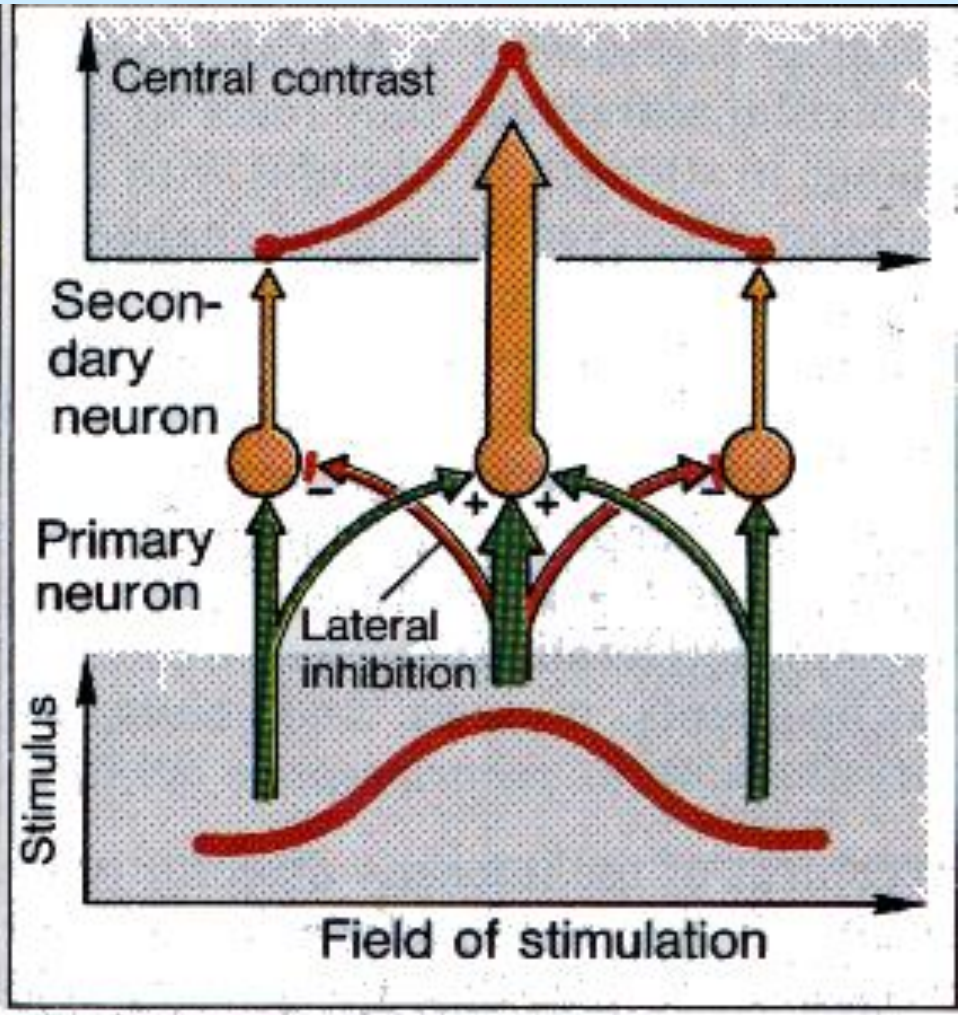
Πώς τότε κωδικοποιούνται τα μηνύματα;



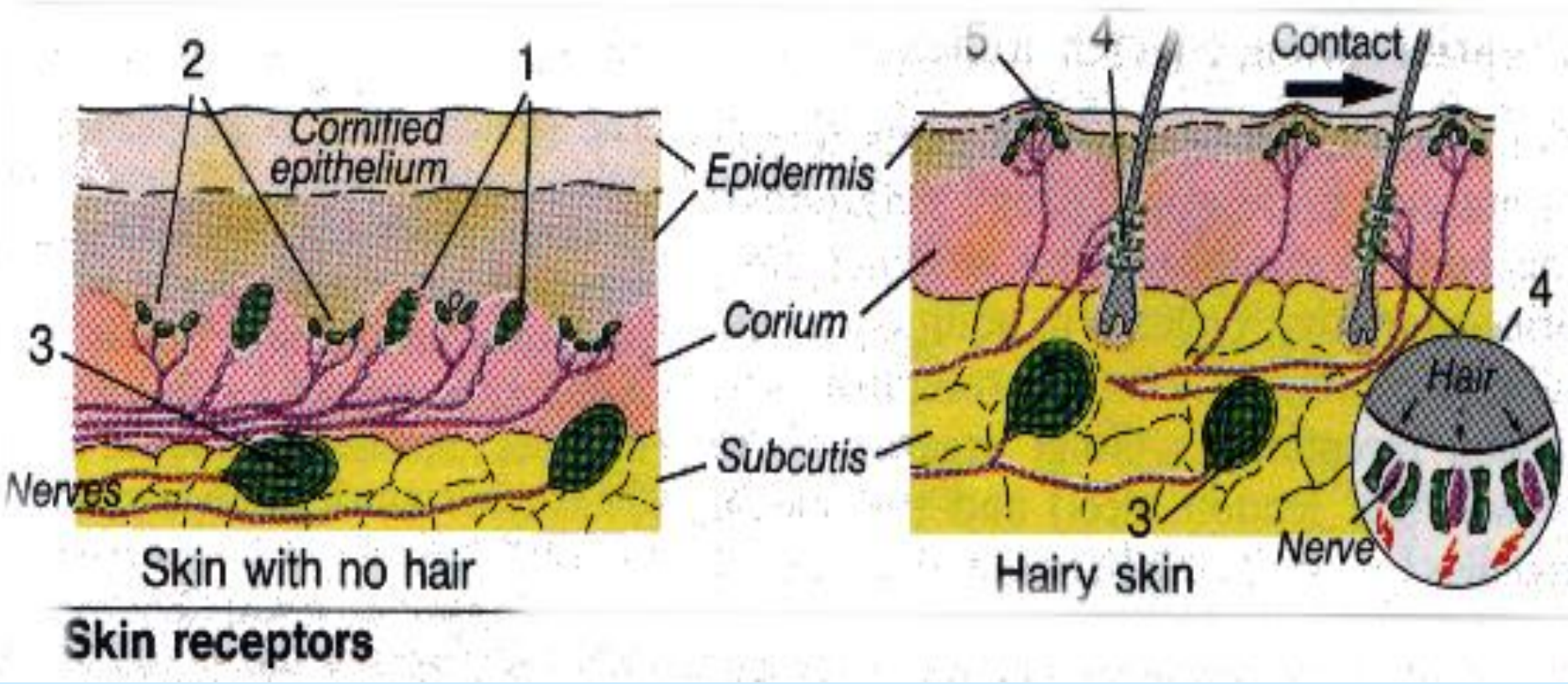
B. Processing of information; encoding



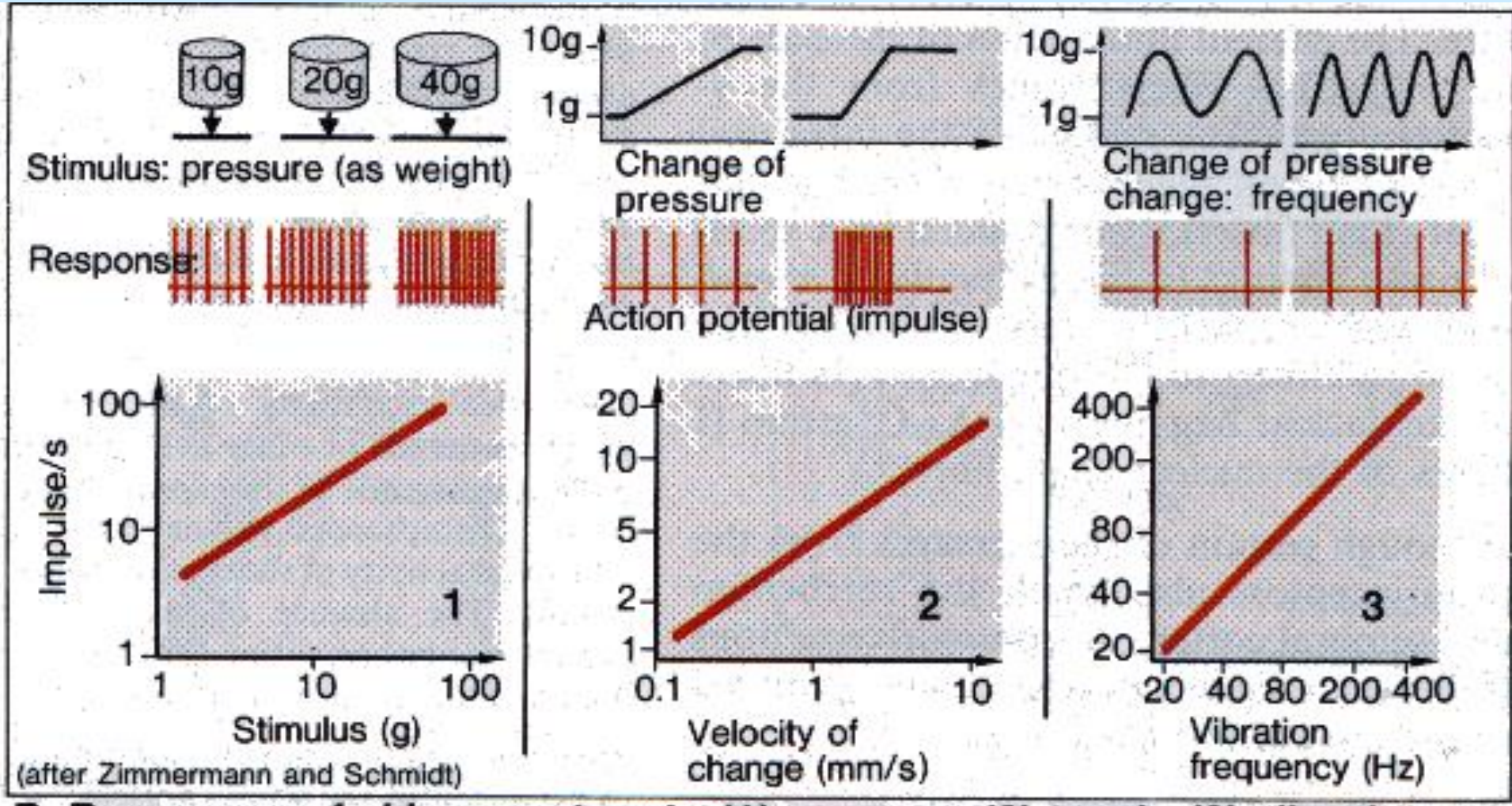
C. Interrelationships: stimulus, potentials



D. Contrast enhancement

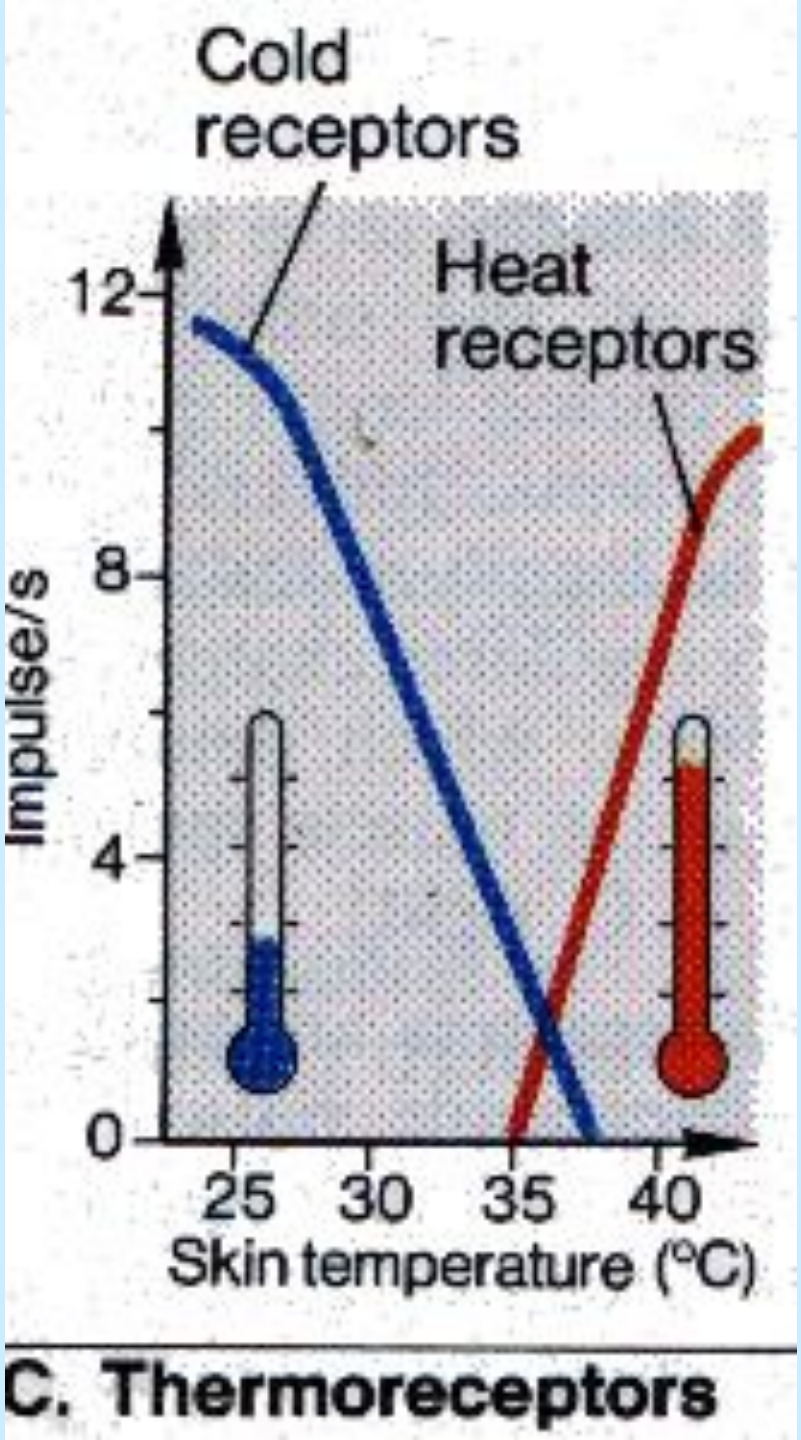


Skin receptors



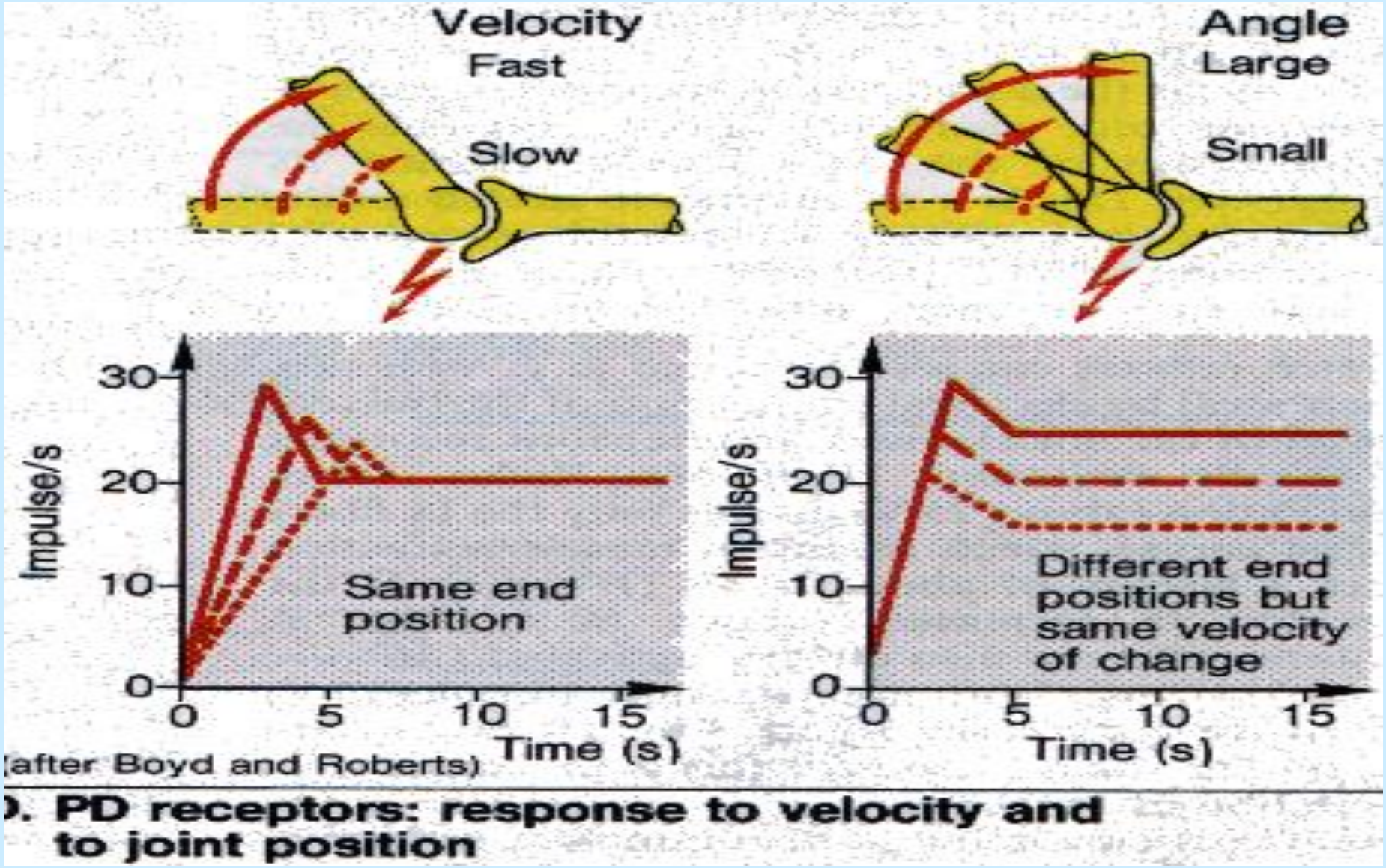
B. Responses of skin receptors to (1) pressure, (2) touch, (3) vibration

Ποια ιδιότητα των αισθητικών υποδοχέων αναδεικνύει η σύγκριση;

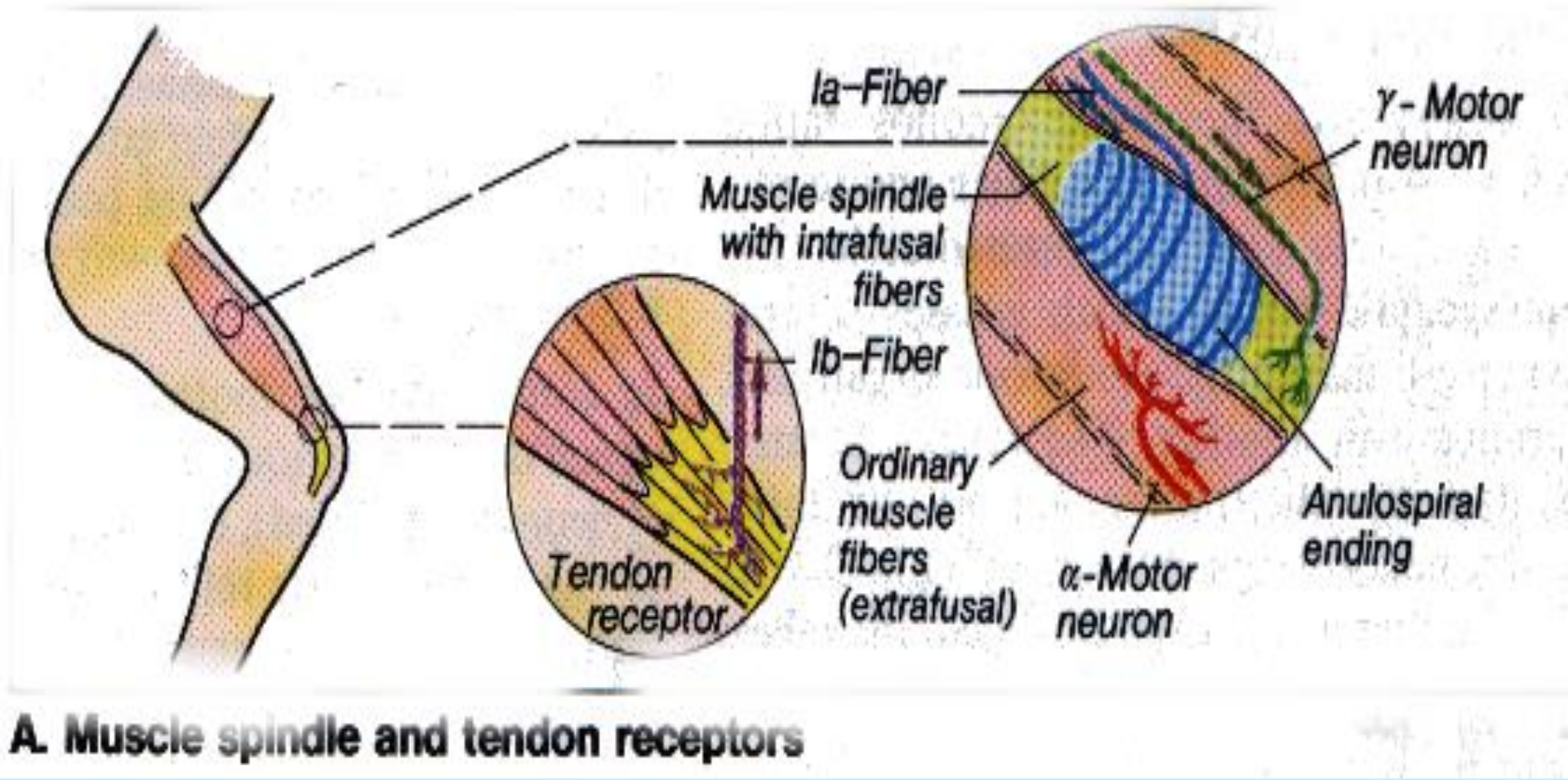


C. Thermoreceptors

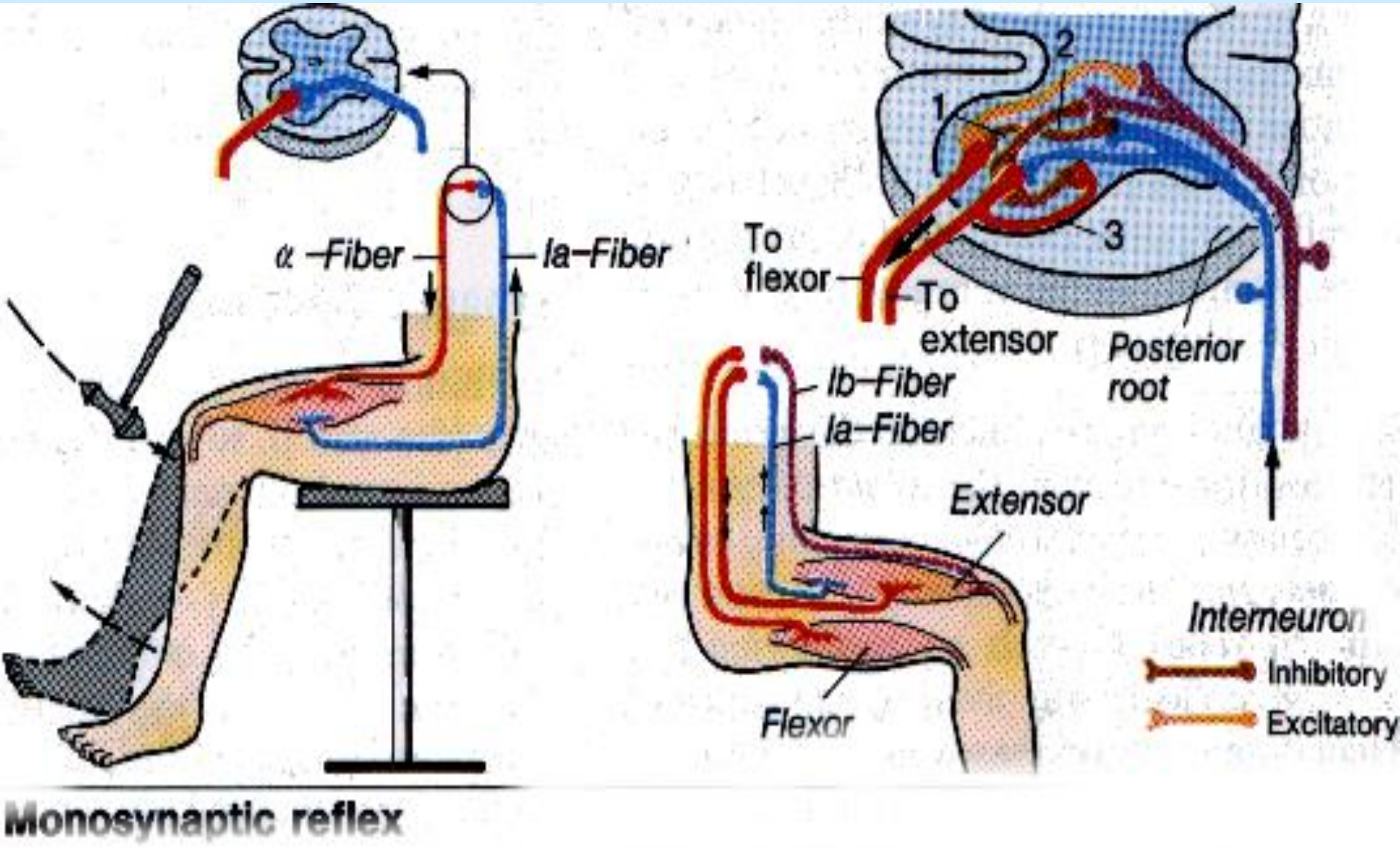
… δύο είναι καλύτερα από ένα…



Ιδιοδεκτικοί υποδοχείς μικτής ευαισθησίας: και αναλογικοί (Proportional, τονικοί), και διαφορικοί (Differential, φασικοί)



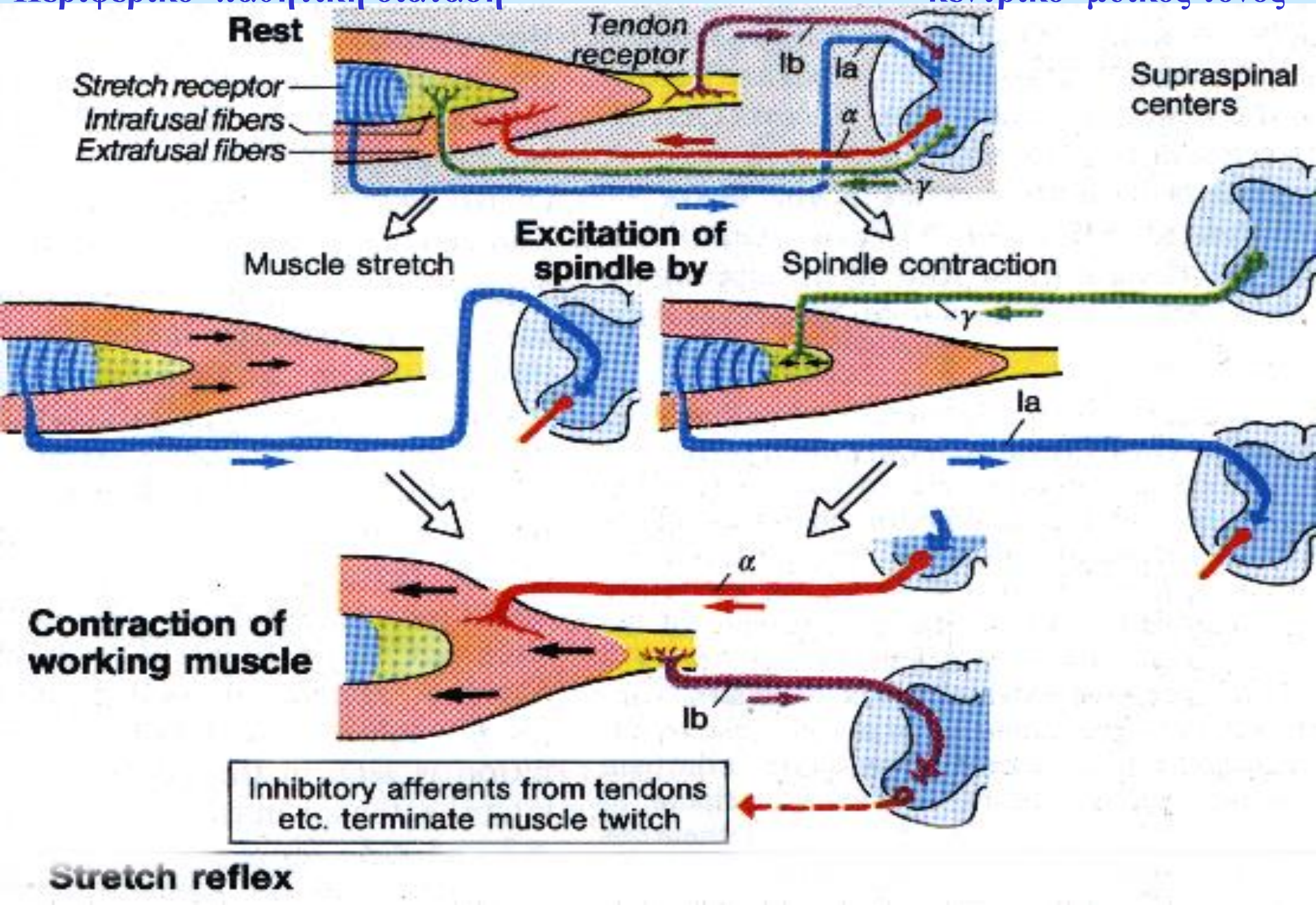
Μυϊκές άτρακτοι και τενόντια όργανα

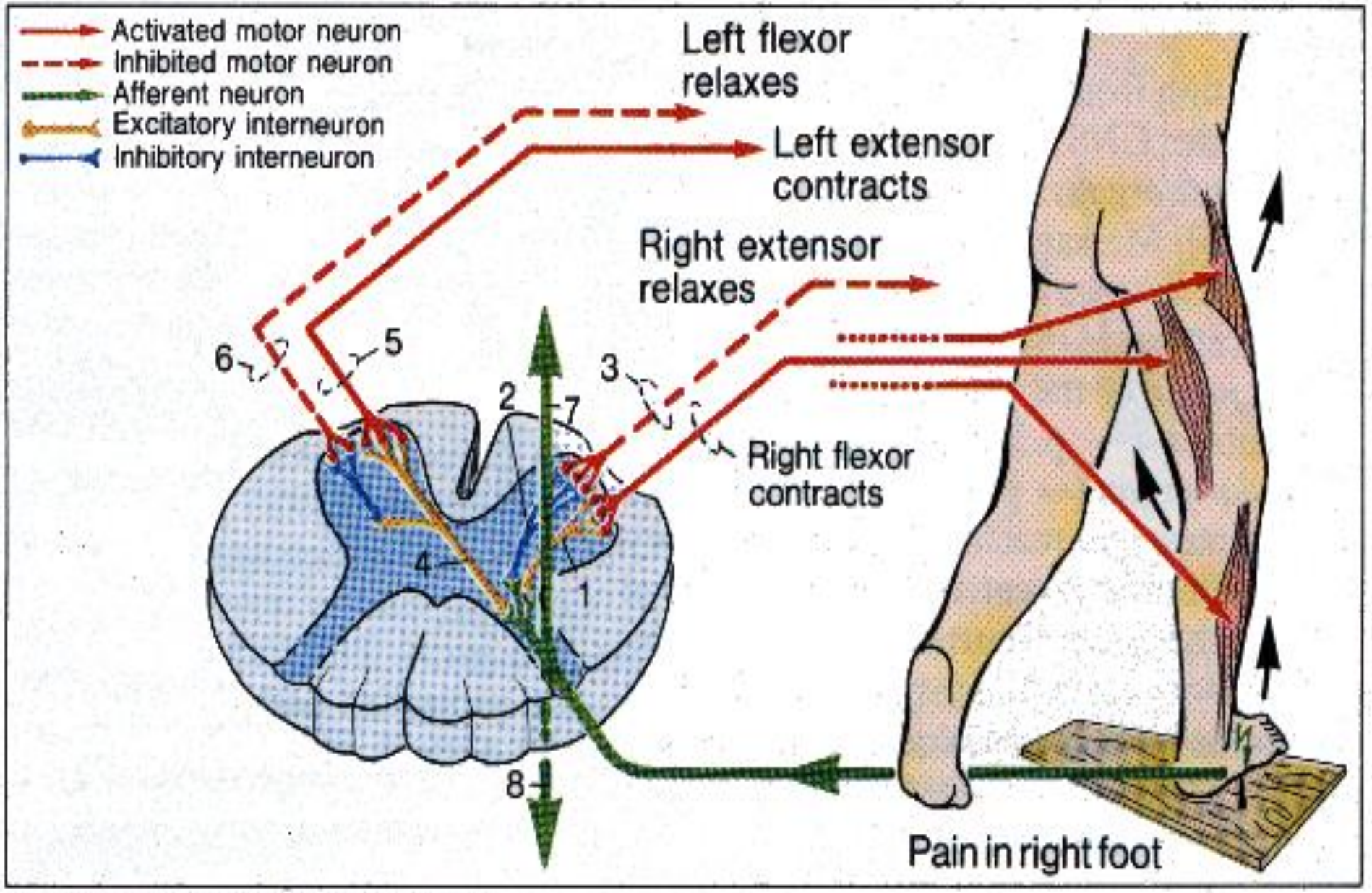


Το μυοτατικό μονοσυναπτικό αντανακλαστικό

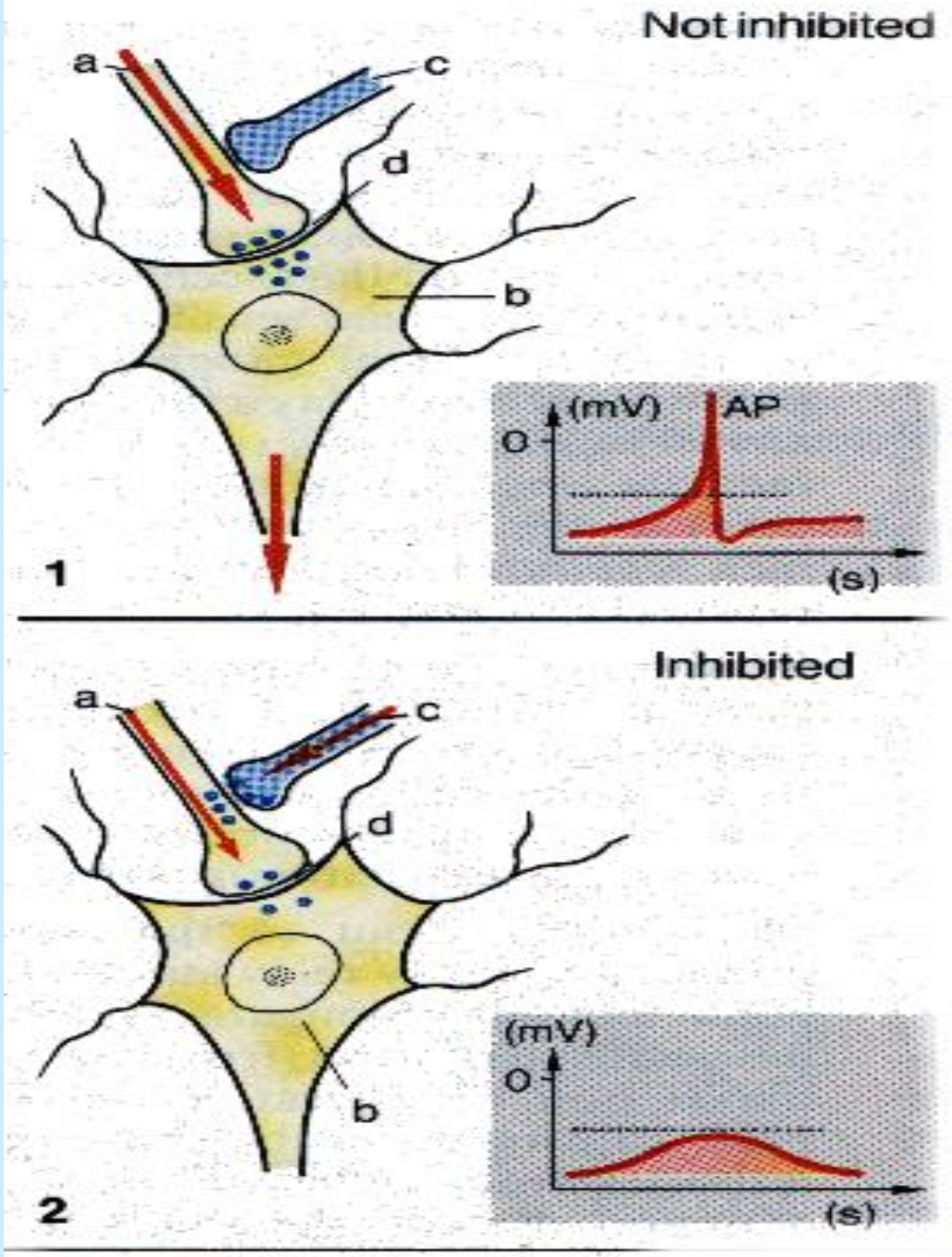
ΜΥΟΤΑΤΙΚΟ ΑΝΤΑΝΑΚΛΑΣΤΙΚΟ εκκλυόμενο από ερέθισμα:

Περιφερικό- παθητική διάταση **κεντρικό- μυϊκός τόνος**

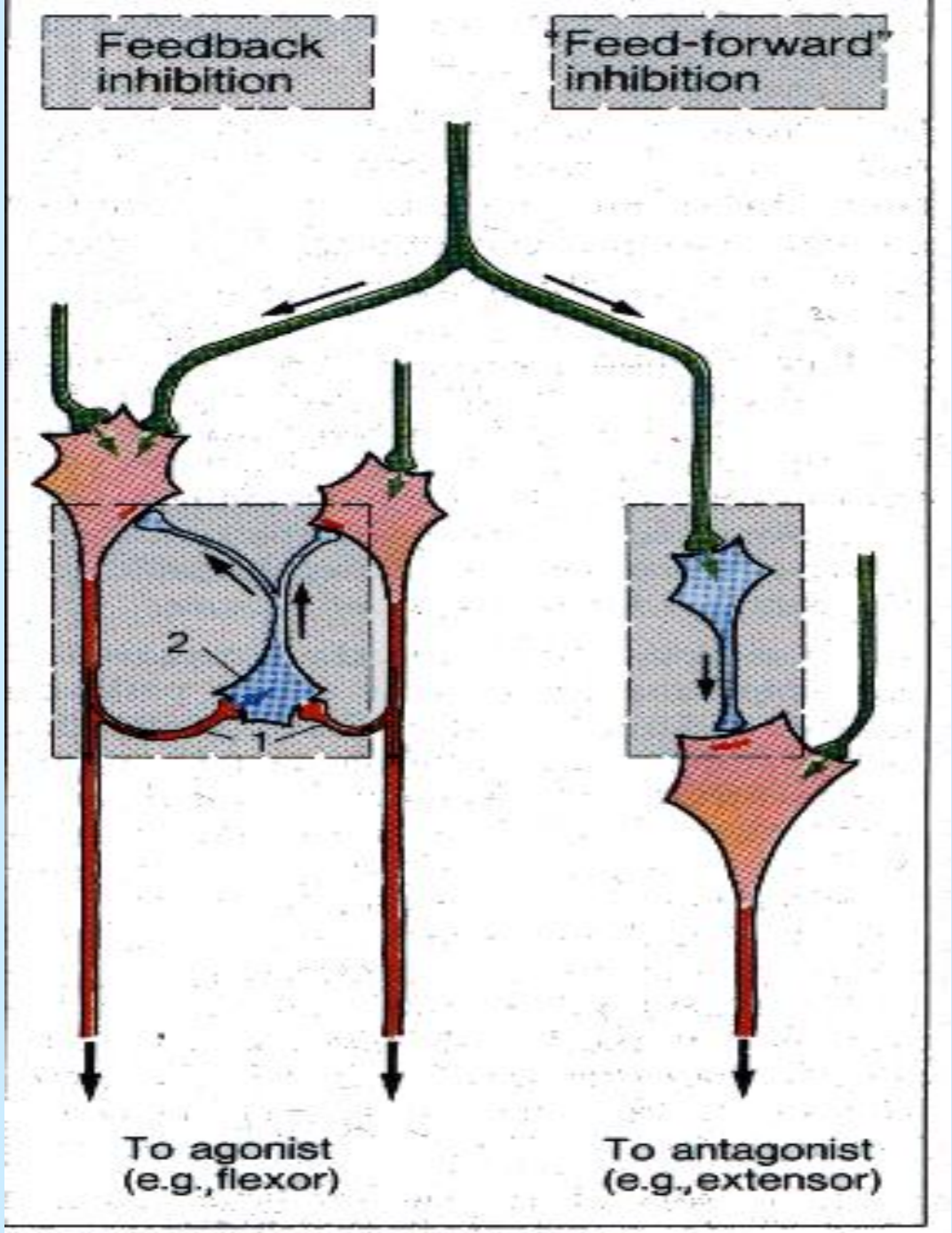




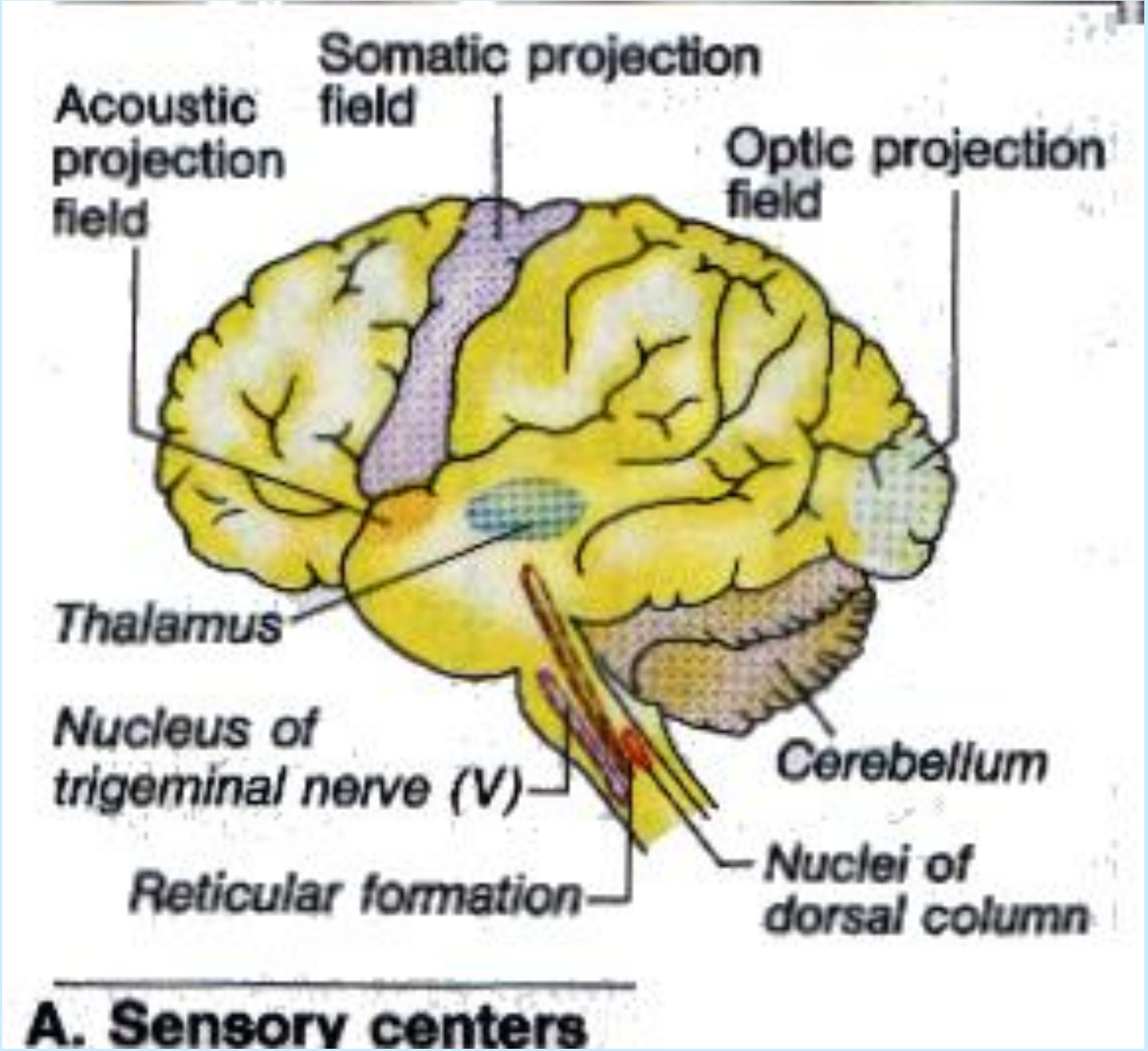
A. Polysynaptic flexor reflex



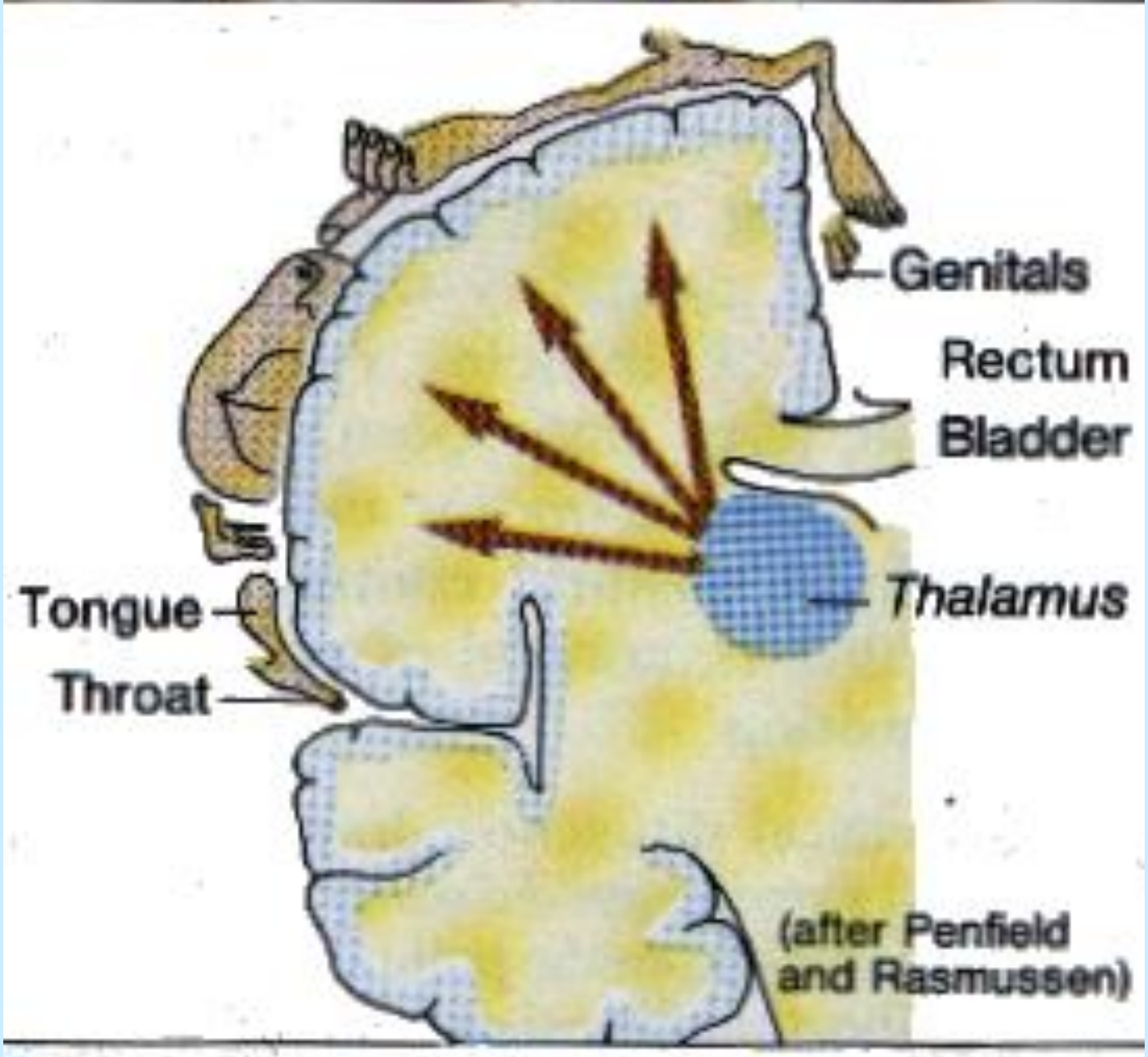
Presynaptic inhibition



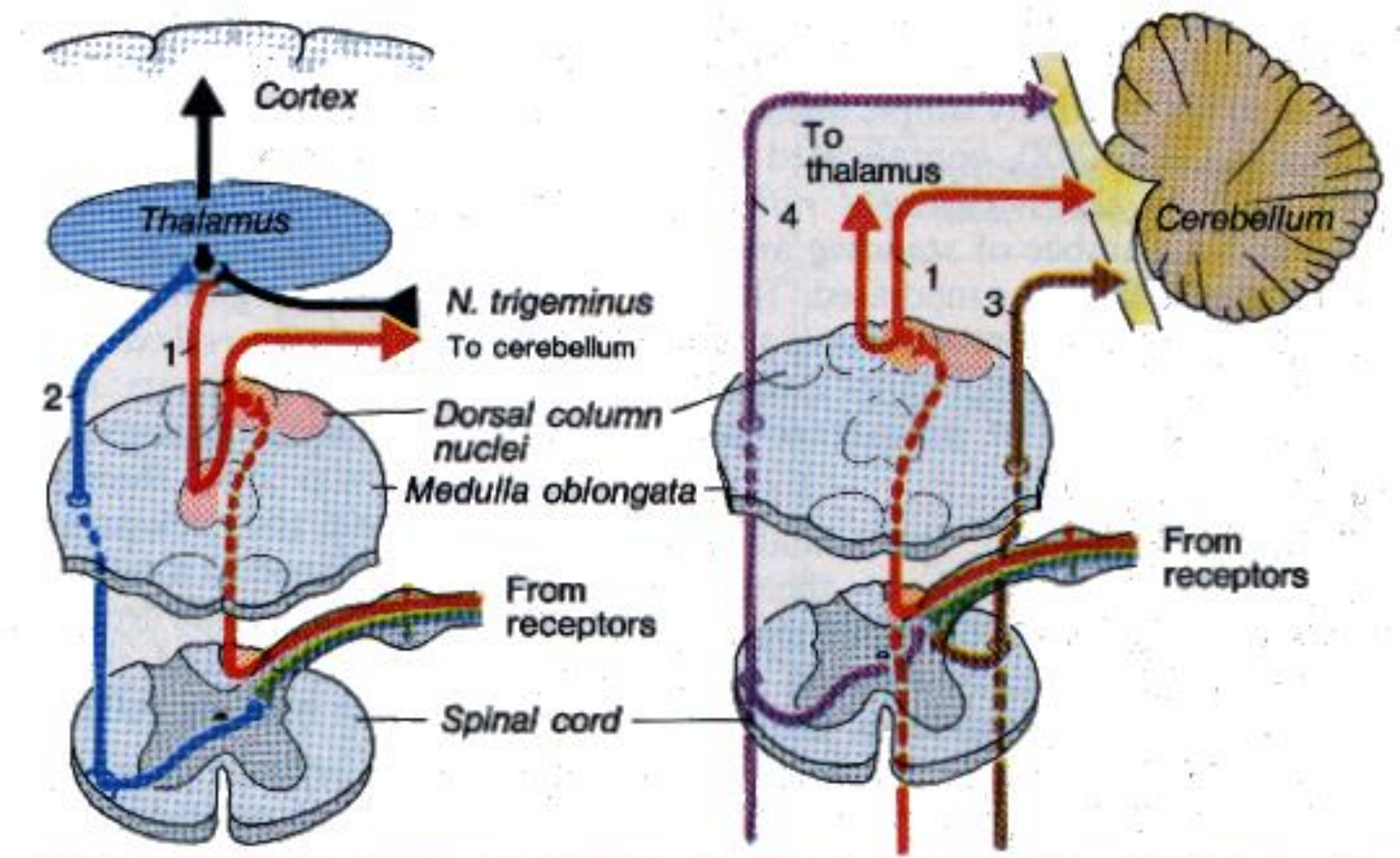
C. Postsynaptic inhibition



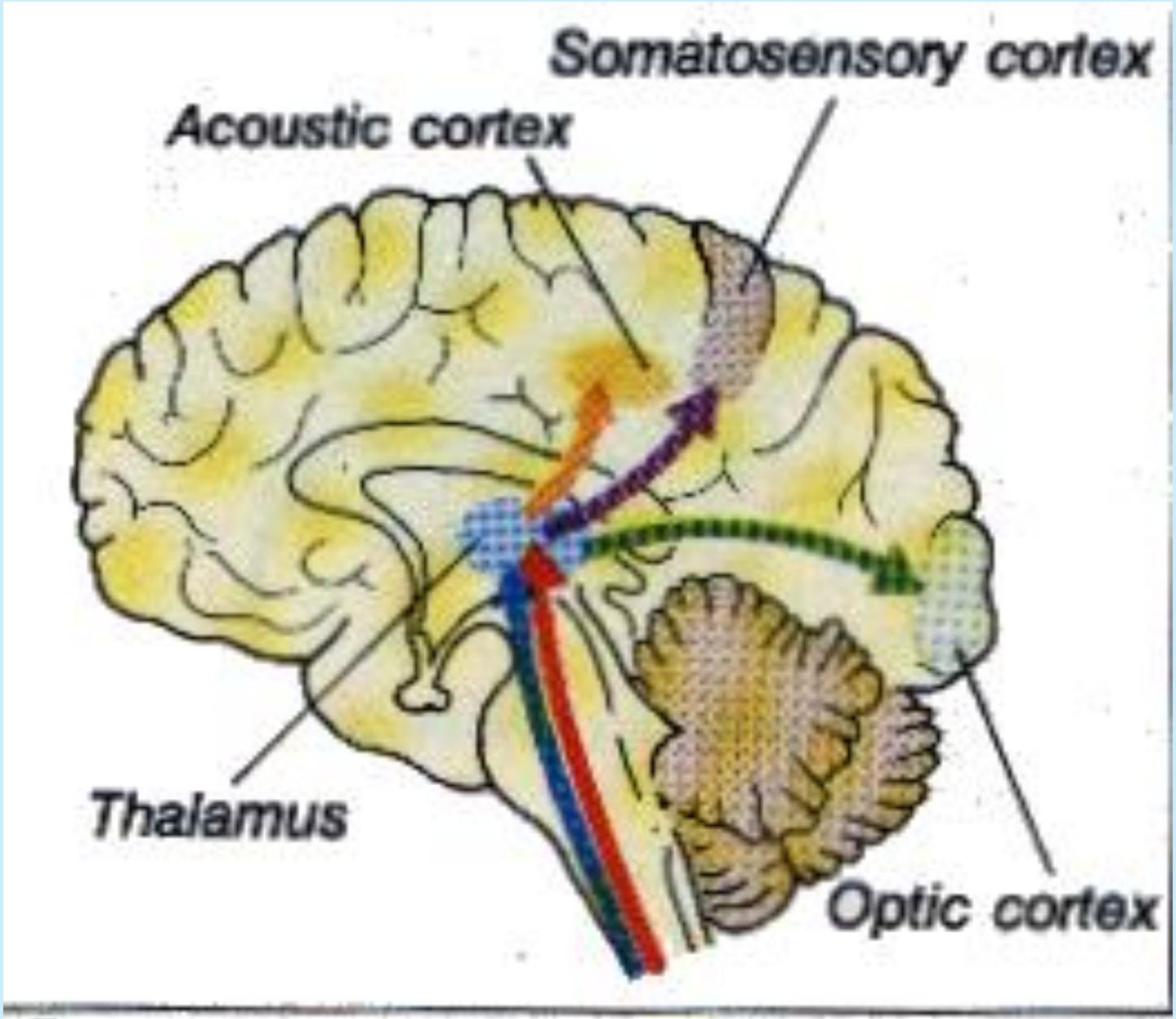
A. Sensory centers



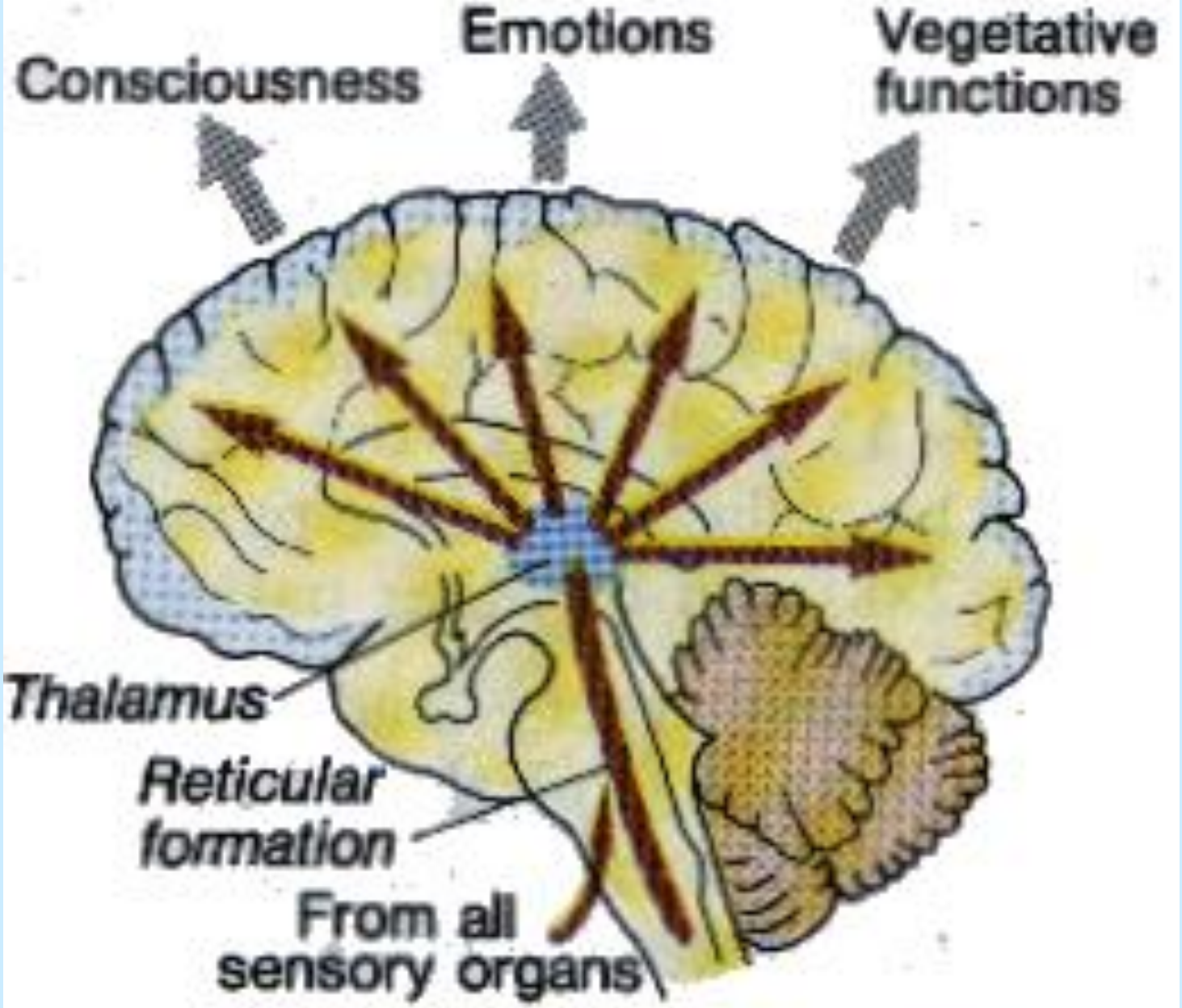
B. Somatotopic representation in somatosensory cortex



Spinal afferent pathways



Specific projection pathways to cortex

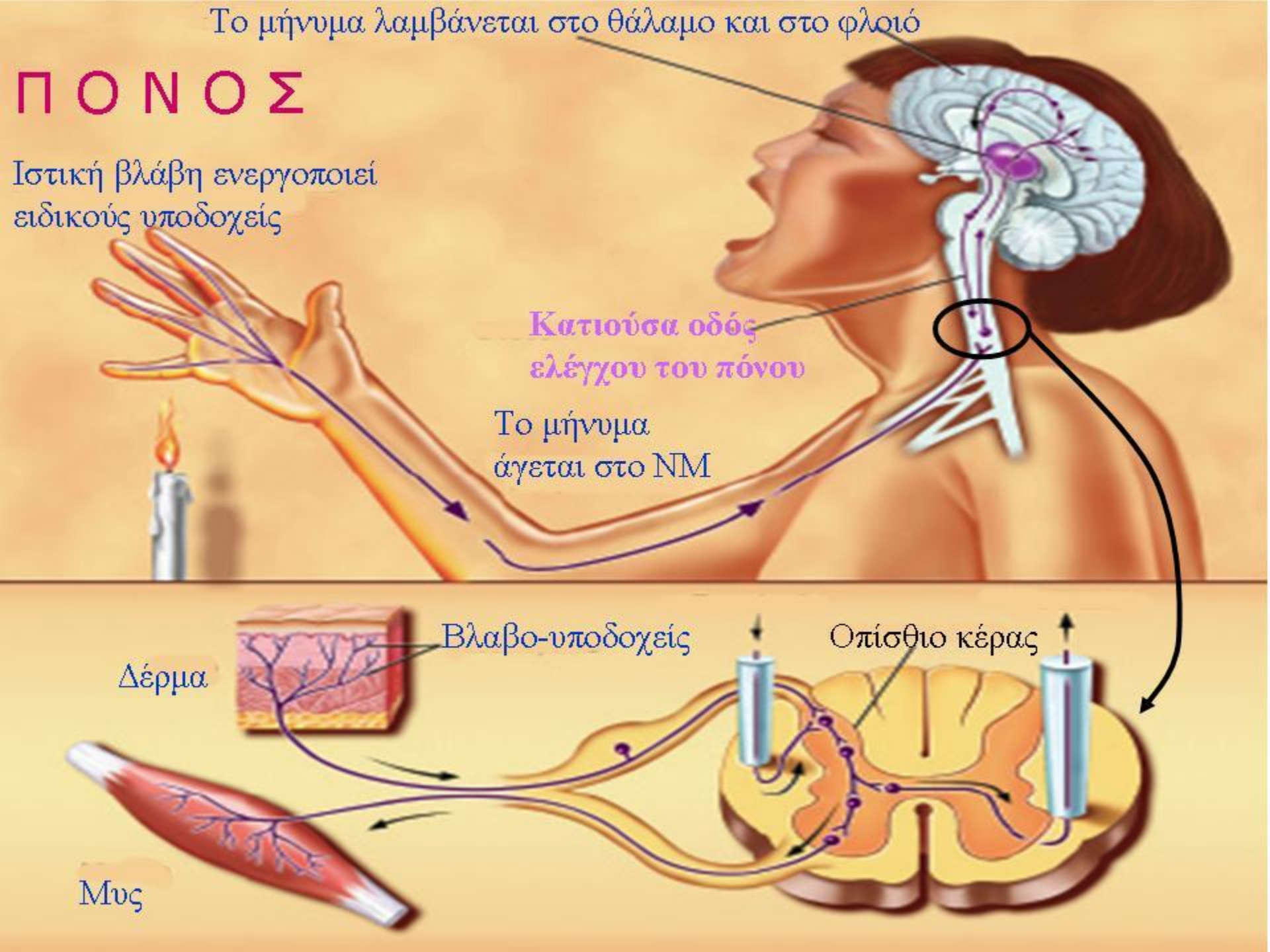


Nonspecific (reticular) paths to cortex

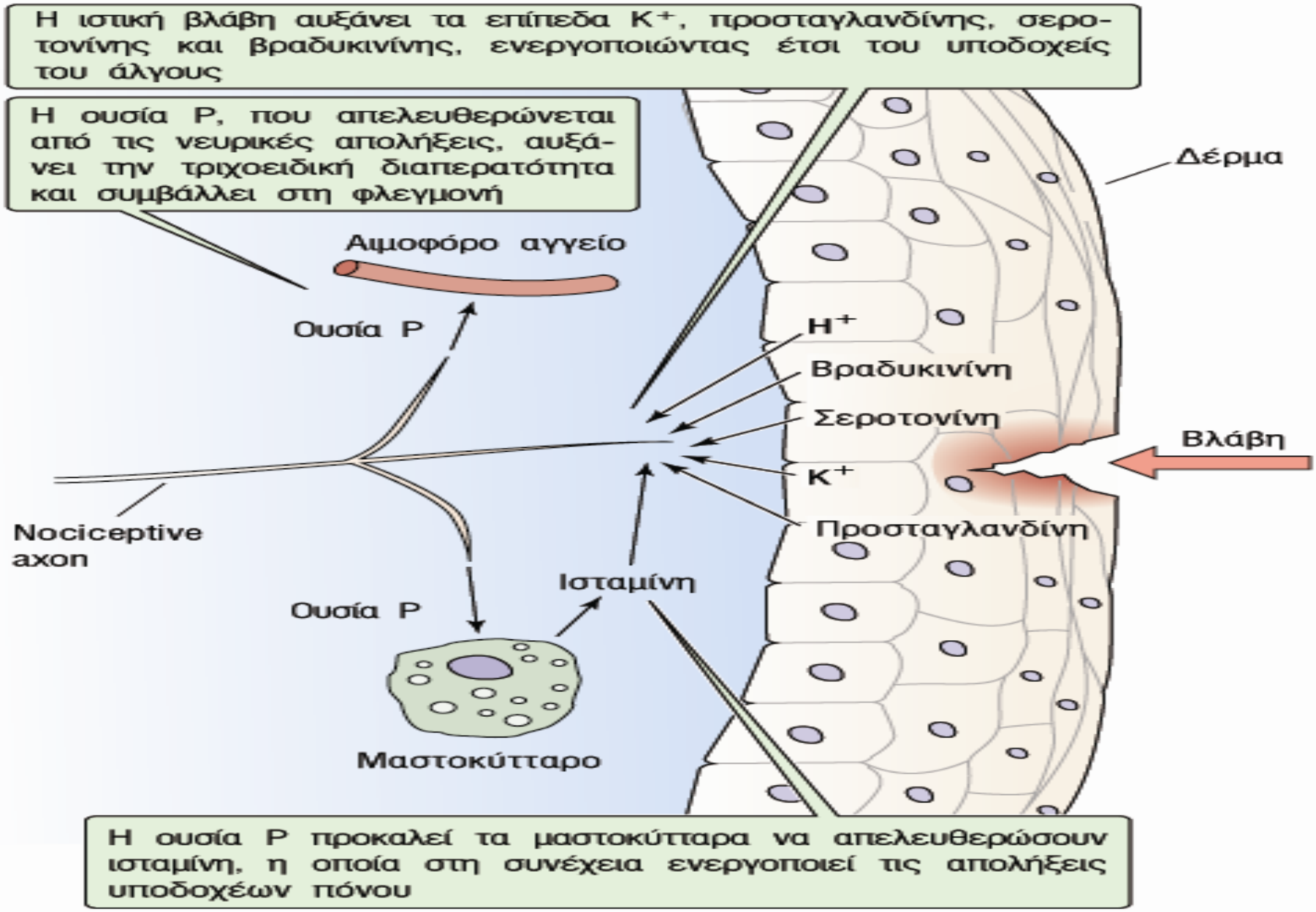
ΡΟΛΟΣ ΤΟΥ ΠΟΝΟΥ

Σηματοδοτεί τελεσθείσα ή απειλούμενη βλάβη ιστών, με σκοπό:

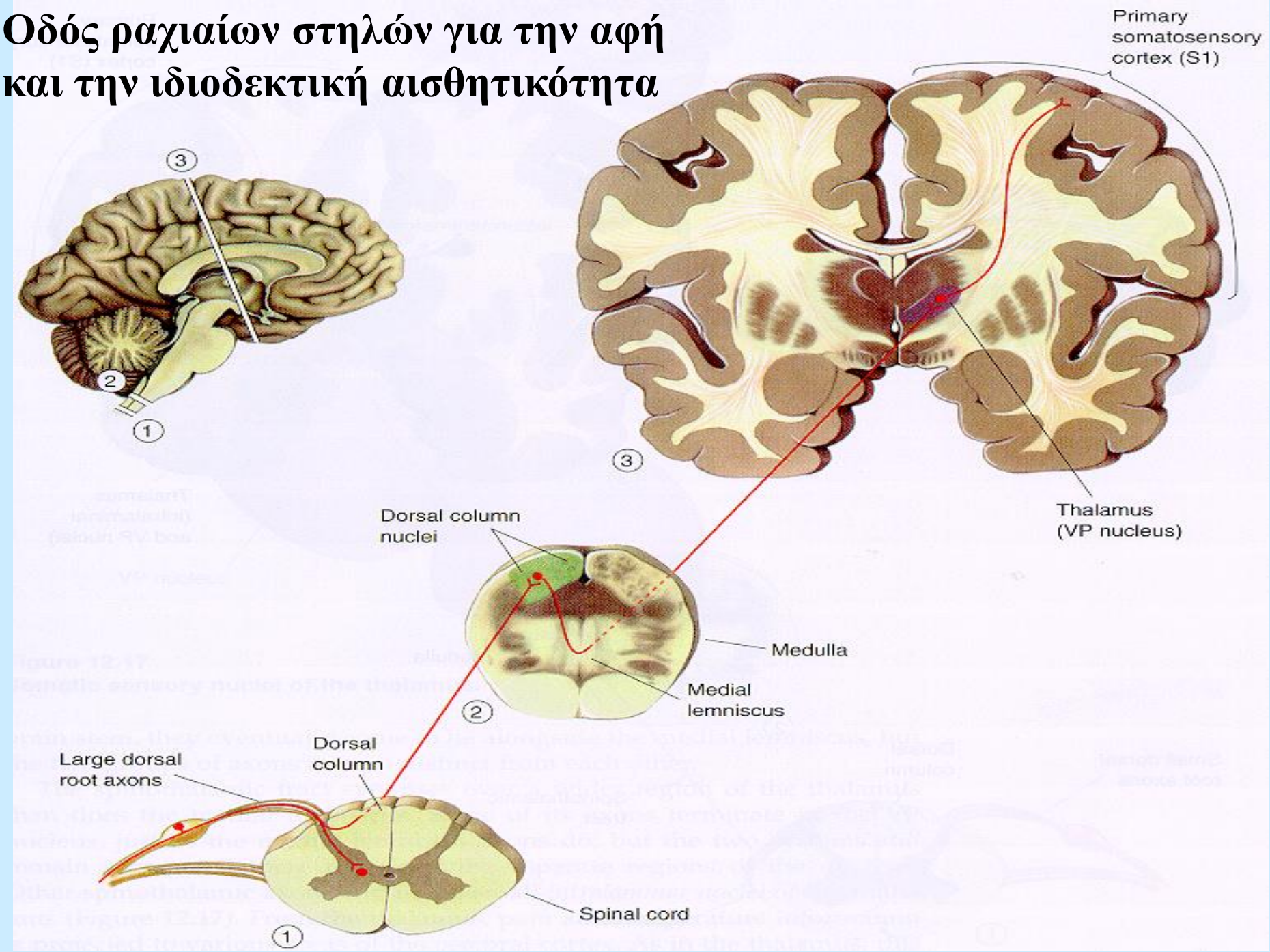
- **Απόσυρση** από το ερέθισμα
- **Προσοχή** στη βλάβη και αντιμετώπιση του κινδύνου
- **Μάθηση** αποφυγής παρόμοιων ερεθισμάτων
- **Προσαρμογή** συμπεριφοράς: επιβάλλεται αναστολή της δραστηριότητας, καθώς η ανάπαυση επιτρέπει την επούλωση της όποιας βλάβης του ιστού.


Το μήνυμα λαμβάνεται στο θάλαμο και στο φλοιό
Π Ο Ν Ο Σ
Ιστική βλάβη ενεργοποιεί ειδικούς υποδοχείς
Κατιούσα οδός ελέγχου του πόνου
Το μήνυμα άγεται στο ΝΜ
Δέρμα
Βλαβο-υποδοχείς
Οπίσθιο κέρας
Μυς

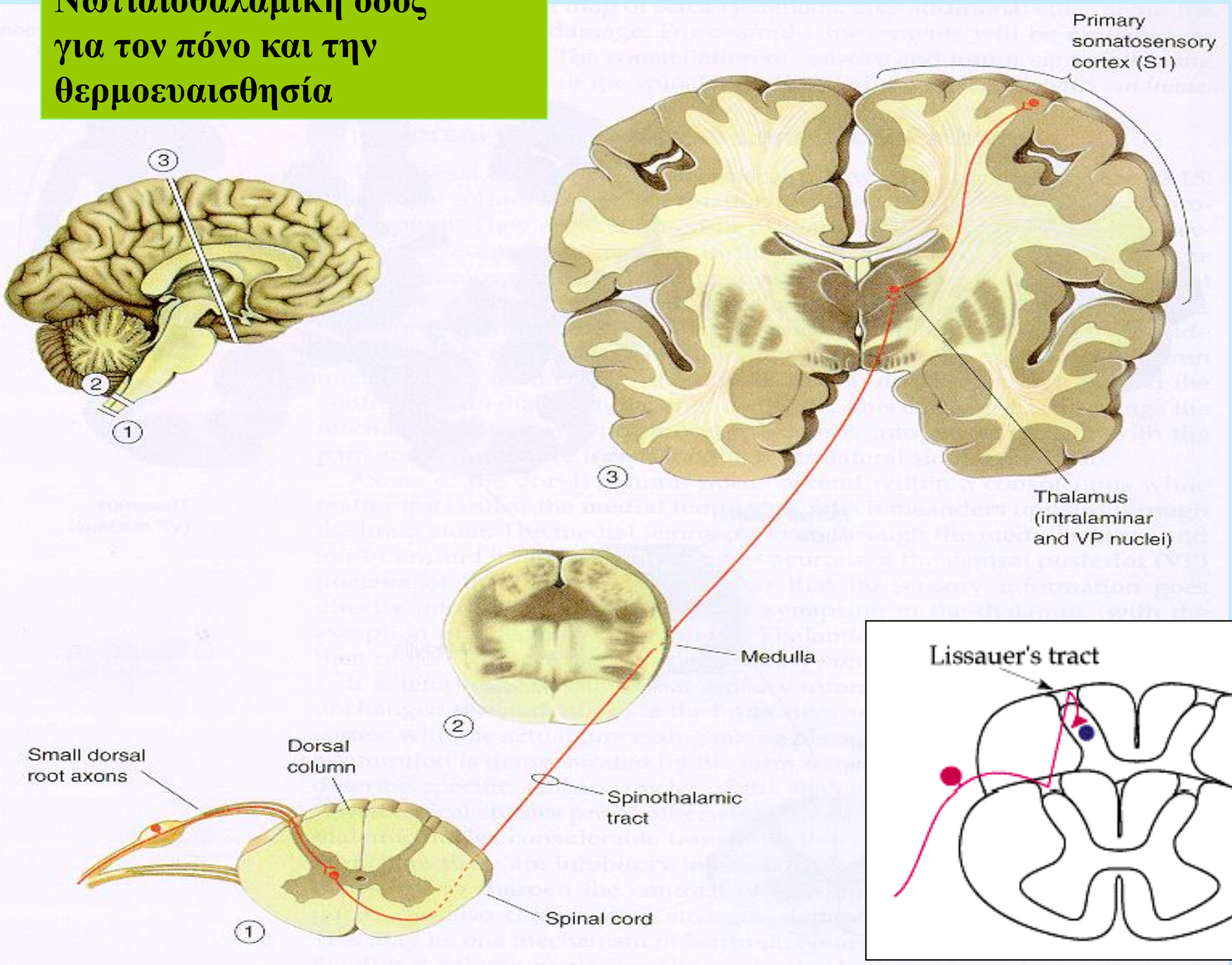
ΜΗΧΑΝΙΣΜΟΙ ΠΟΝΟΥ: ΕΝΕΡΓΟΠΟΙΗΣΗ ΚΑΙ ΕΥΑΙΣΘΗΤΟΠΟΙΗΣΗ ΠΕΡΙΦΕΡΙΚΩΝ ΒΛΑΒΟΔΕΚΤΙΚΩΝ ΥΠΟΔΟΧΕΩΝ



Οδός ραχιαίων στηλών για την αφή και την ιδιοδεκτική αισθητικότητα



Νωτιαιοθαλαμική οδός για τον πόνο και την θερμοευαισθησία



ΤΥΠΟΙ (ΠΟΙΟΤΗΤΕΣ) ΤΟΥ ΠΟΝΟΥ

- **Διαξιφιστικός πόνος**
  - **οξύς**
  - **Σύντομης διάρκειας, εντοπισμένος με ακρίβεια στο δέρμα**
  - **Προκαλεί άμεση αντίδραση**
- **Αμβλύς πόνος**
  - **χρόνιος**
  - **Μπορεί να συνοδεύεται από εφίδρωση, ταχυκαρδία κτλ**
- Διπλός πόνος
  - Ταχύς οξύς που ακολουθείται από επιδιαρκούντα αμβλύ πόνο
- Αλλοι:
  - Διατιτραίνων, καυστικός, φαγούρα ...

τα δύο κύρια είδη πόνου

Σωματοαισθητικός φλοιός (SI)
[**εντόπιση πόνου**]

φλοιός
[**εγρήγορση, πολύ αδρά εντόπιση**]

Κοιλιοβασικοί π. Θαλάμου
[**αίσθηση πόνου**]

δικτυωτός σχηματισμός + ε-π.π.θ.

2-ταγής αισθ. ν. 2-3 νευροτ. ψηλότερα
Χιασμός. Ανοδος με προσθιο- πλάγιο Ν-Θ δεμ.

2-ταγής αισθ. ν. 2-3 νευροτ. ψηλότερα
Χιασμός. Ανοδος με προσθιο- πλάγιο Ν-Θ δεμ

Οπίσθιο κέρας ΝΜ πέταλα I και V

Οπίσθιο κέρας ΝΜ πέταλα II και III

Ίνες Αδ (III) 6-30 M/sec

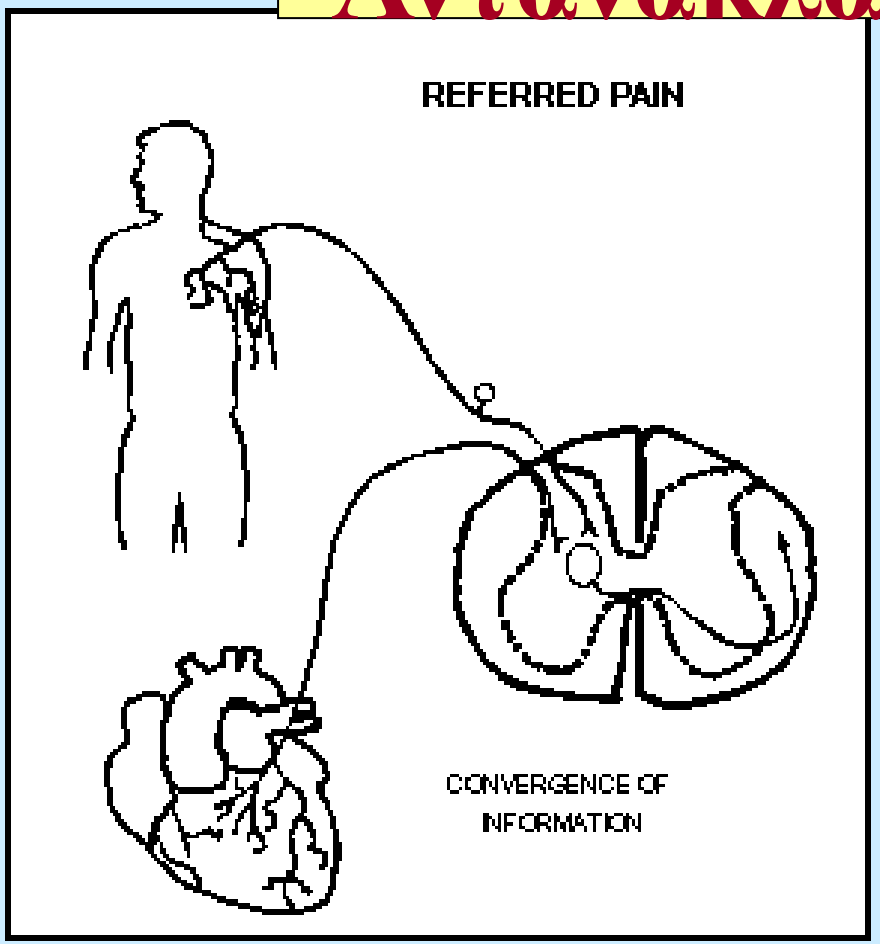
ίνες C (IV) 0.5-2 M/sec

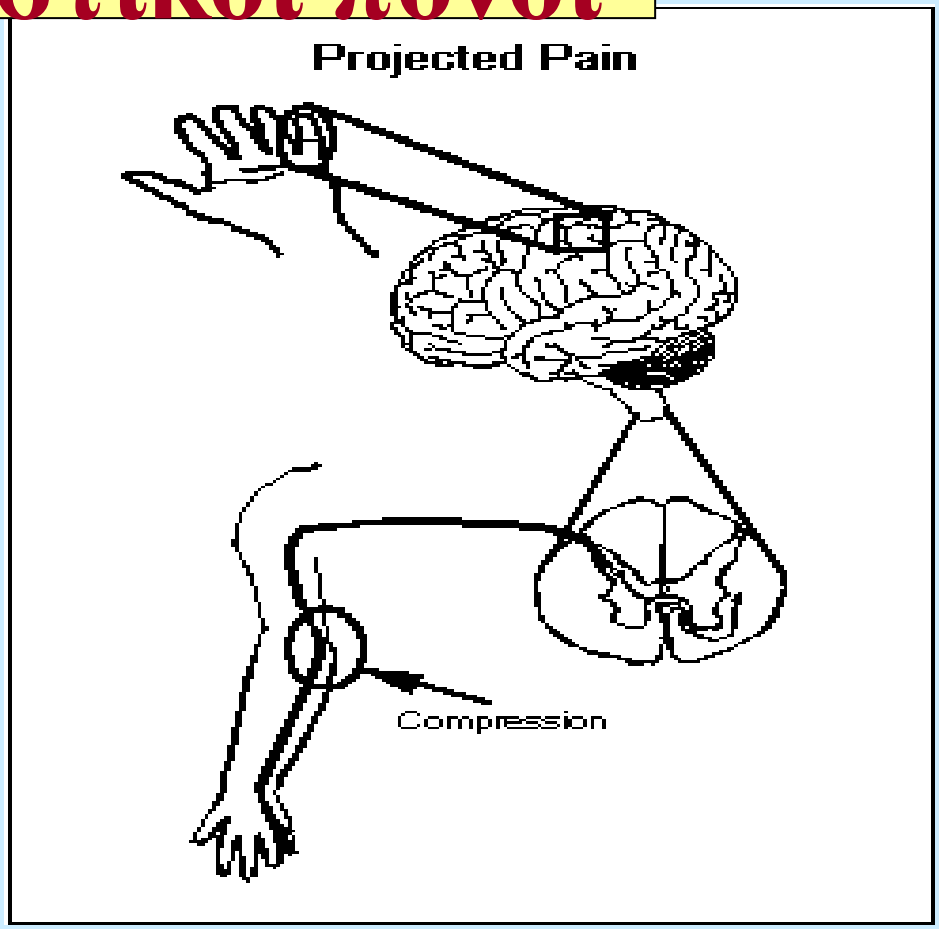
Διαξιφιστικός πόνος (ταχύς) **Αμβλύς/Καυστικός (βραδύς)**

Μόνο στο δέρμα

Δέρμα, αρθρώσεις, εν τω βάθει ιστοί και σπλάχνα

Αντανακλαστικοί πόνοι





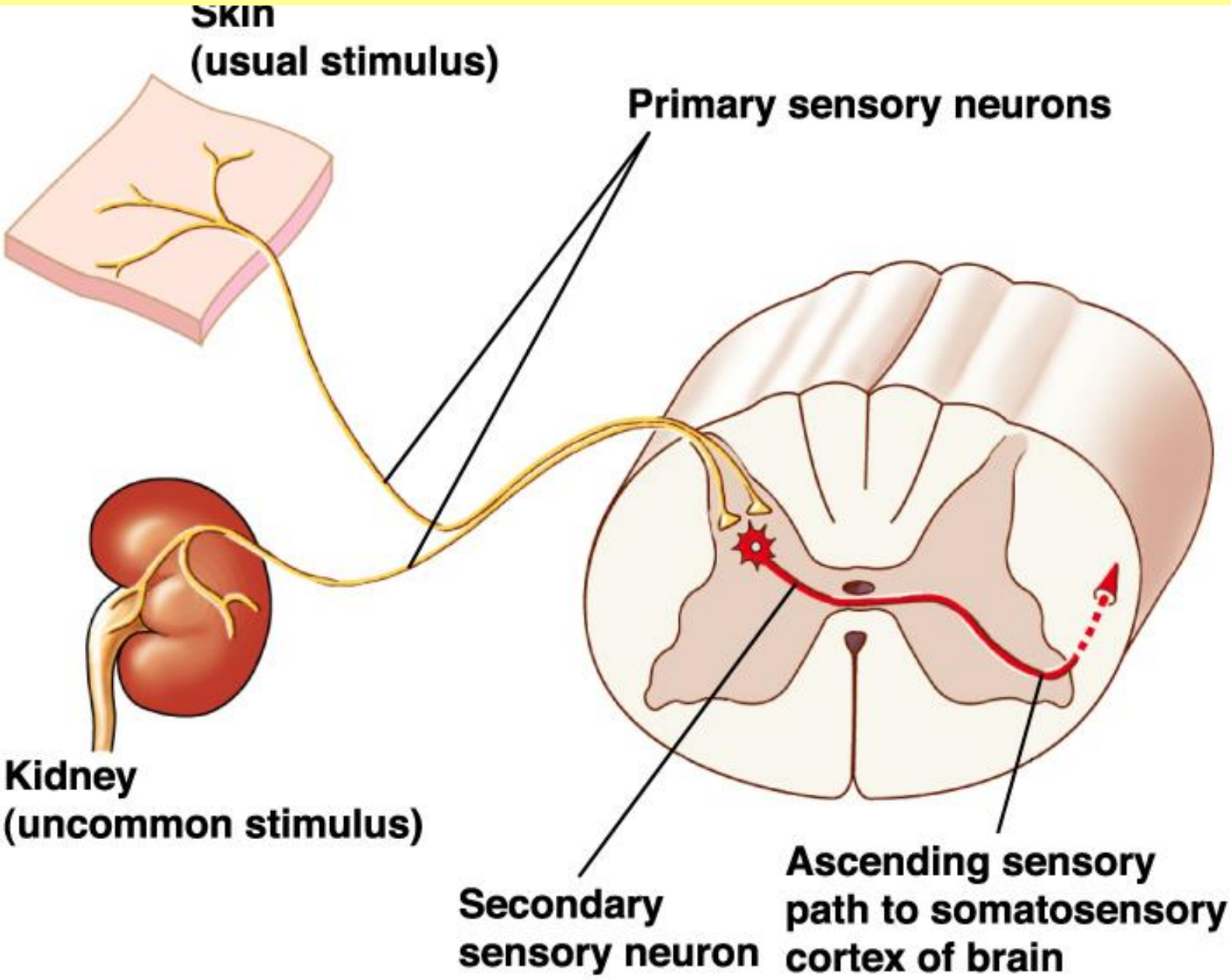
Αναφερόμενος αντανακλαστικός πόνος

- προέρχεται από εσωτερικά όργανα, π.χ. στηθάγχη
- συνειδητοποιείται σε άλλες περιοχές του σώματος

Προβαλλόμενος αντανακλαστικός πόνος.

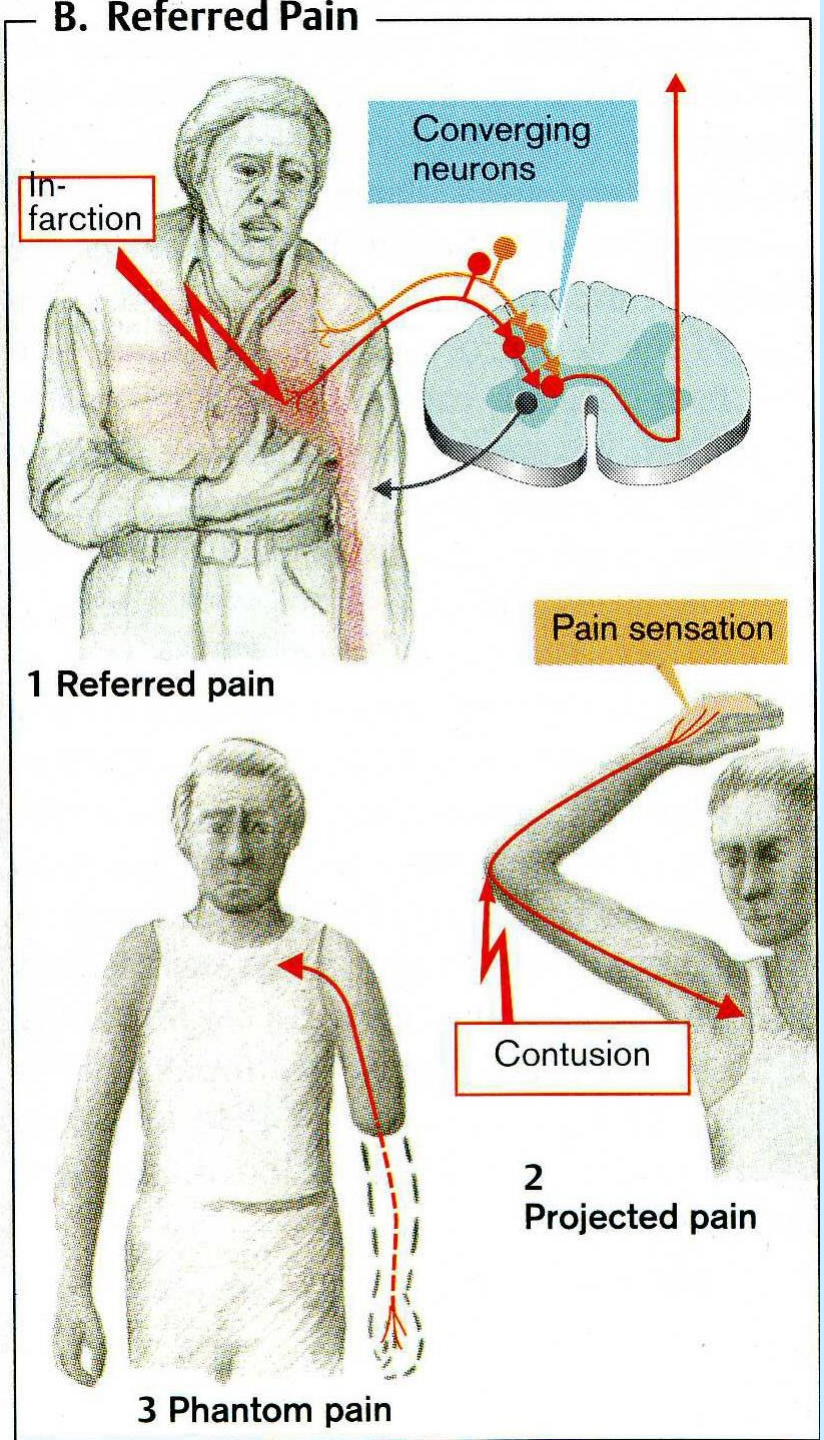
- προέρχεται από μηχανικό ή άλλο ερεθισμό κατά την πορεία πρωτοταγών αισθητικών ινών σε ένα νεύρο
- συνειδητοποιείται ως αίσθηση στις περιοχές και στους αισθητικούς τύπους που εξυπηρετούν αυτές οι ίνες

Προτεινόμενη εξήγηση του αναφερόμενου πόνου



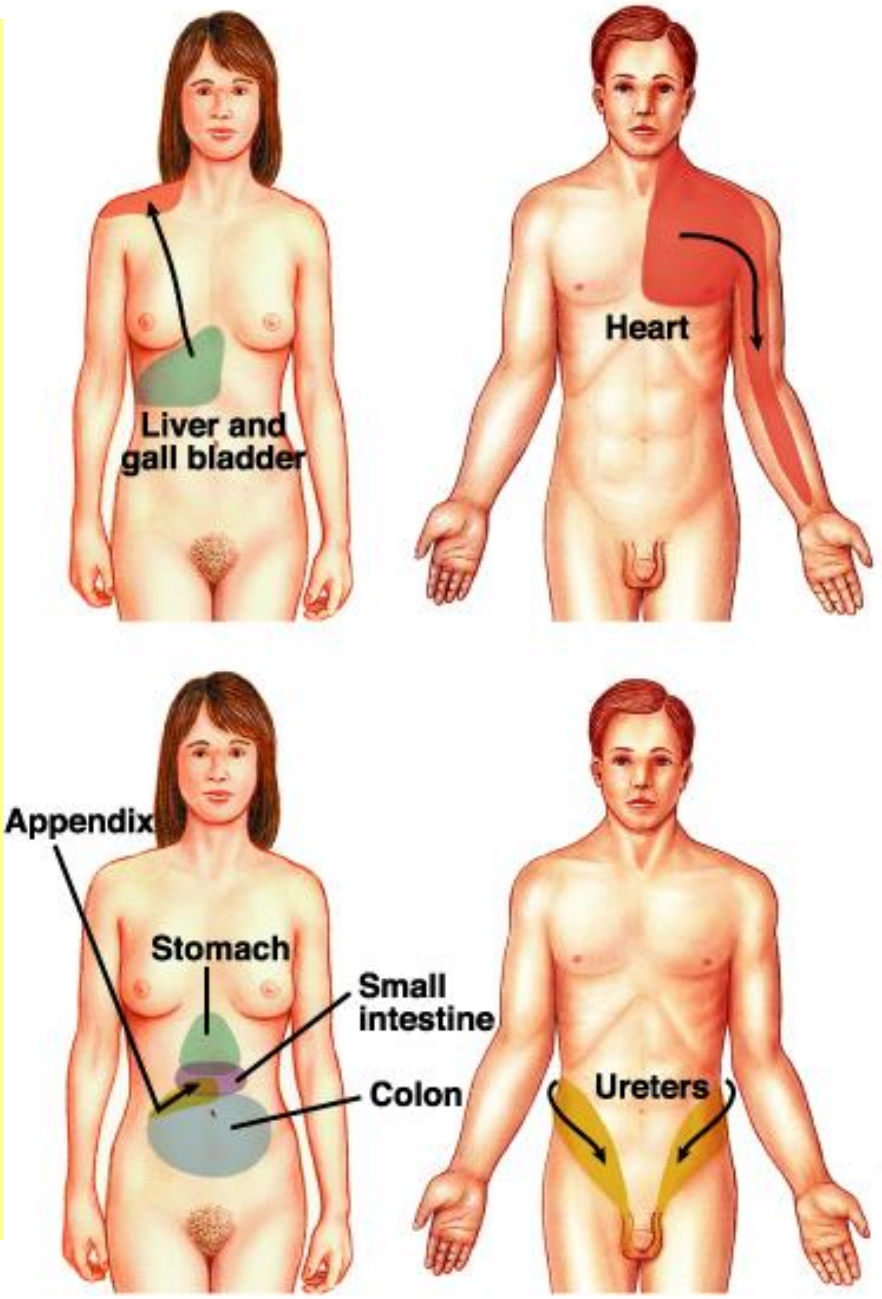
Αντανακλαστικοί πόνοι

1. Αναφερόμενος πόνος
2. Προβαλλόμενος πόνος
3. Πόνος μέλους φάντασμα



Αναφερόμενος πόνος

Βλαβοδεκτικά ερεθίσματα από τα σπλάχνα συνειδητοποιούνται (εσφαλμένα) ως πόνος εντοπιζόμενος σε συγκεκριμένες δερματικές περιοχές (που φαίνονται άσχετες, αλλά ανήκουν στο ίδιο νευροτόμιο, όπου εισέρχονται και οι βλαβοδεκτικές ίνες από τα σπλάχνα – βλ. παρακάτω)

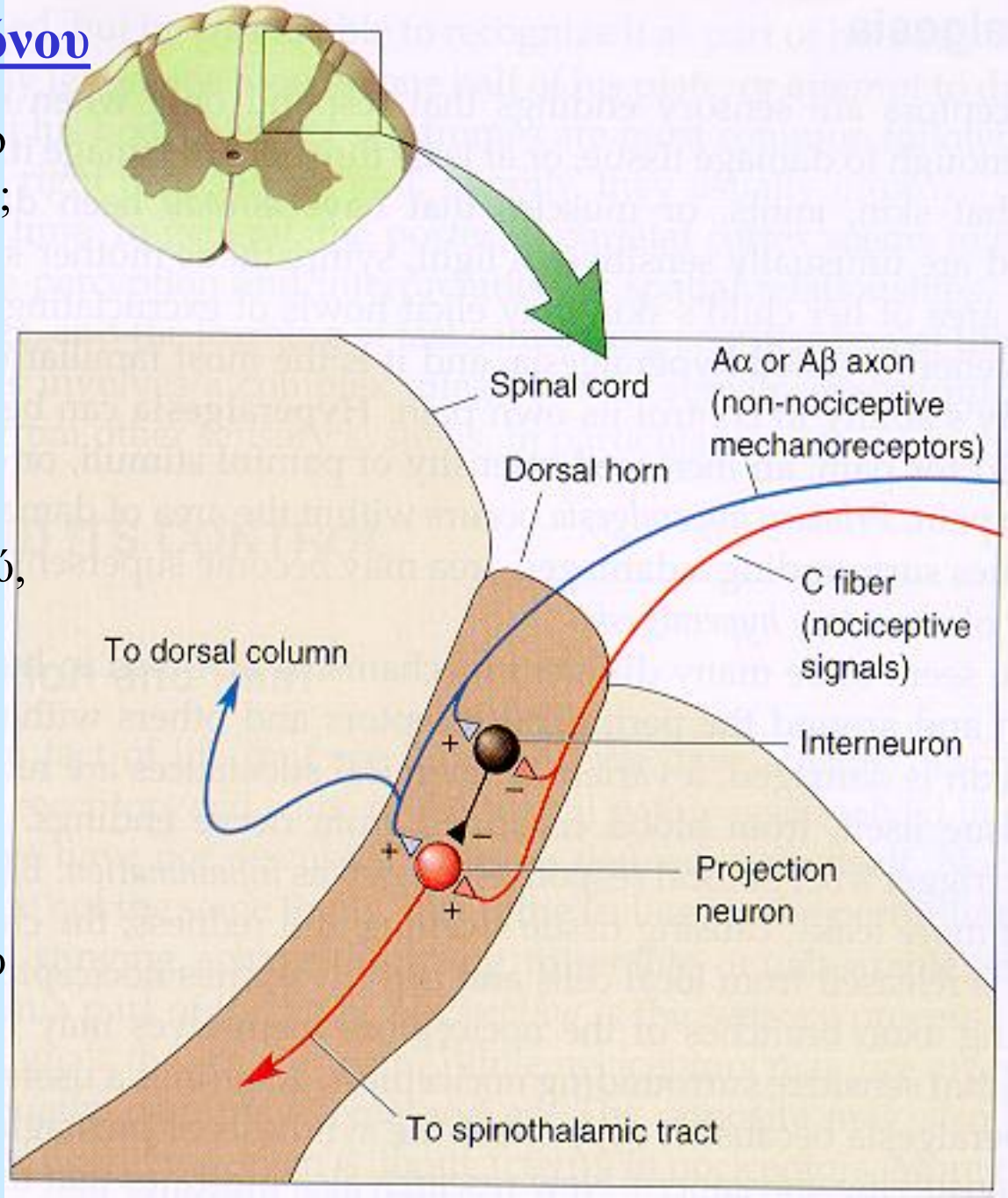


Η θεωρεία των Melzack και Wall περί Πύλης Εισόδου του Πόνου

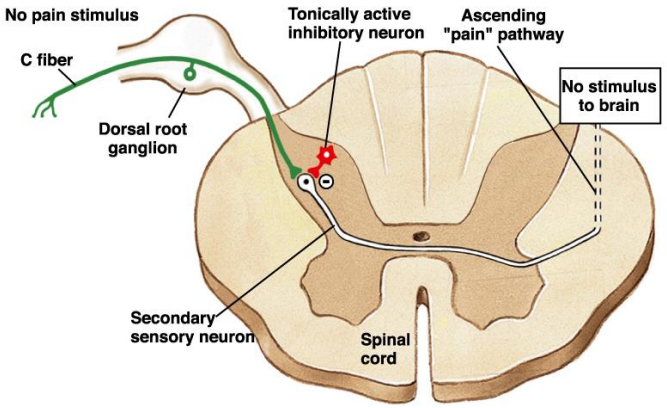
Γιατί η τριβή ένός άκρου γύρω από τη πληγή ανακουφίζει από το πόνο;

Τα **βλαβοδεκτικά σήματα** τροποποιούνται από οδούς της **αφής.**

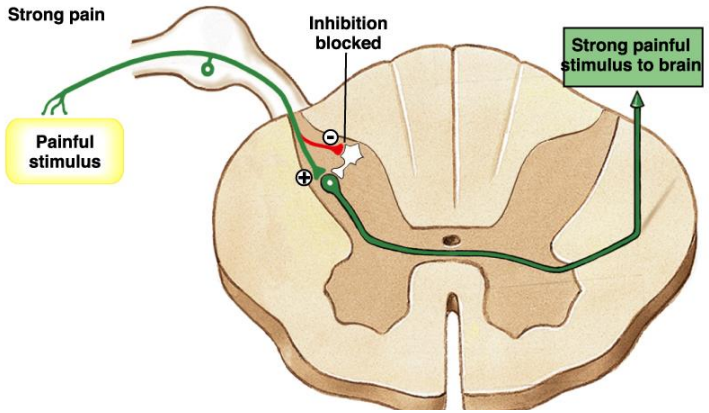
Ενας **διάμεσος νευρώνας** στο οπίσθιο κέρας του νωτιαίου μυελού, ο οποιος αναστέλλεται από τις **βλαβοδεκτικές ίνες C** και διεγείρεται της ίνες **Αβ της αφής,** ελέγχει την πύλη εισόδου των βλαβοδεκτικών σημάτων αναστέλλοντας μέσω **οποιοειδών** τον **2ταγή νευρώνα** → μείωση του πόνου.



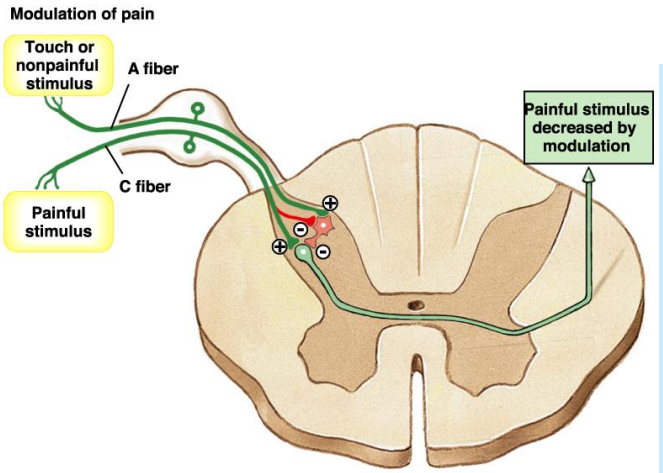
Απουσία ισχυρού (υπερ-ουδικού) βλαβοδεκτικού ερεθίσματος δεν προωθείται κανένα κεντρομόλο μήνυμα. Η πύλη είναι κλειστή λόγω αναστολής του δευτεροταγούς νευρώνα από διάμεσο νευρώνα



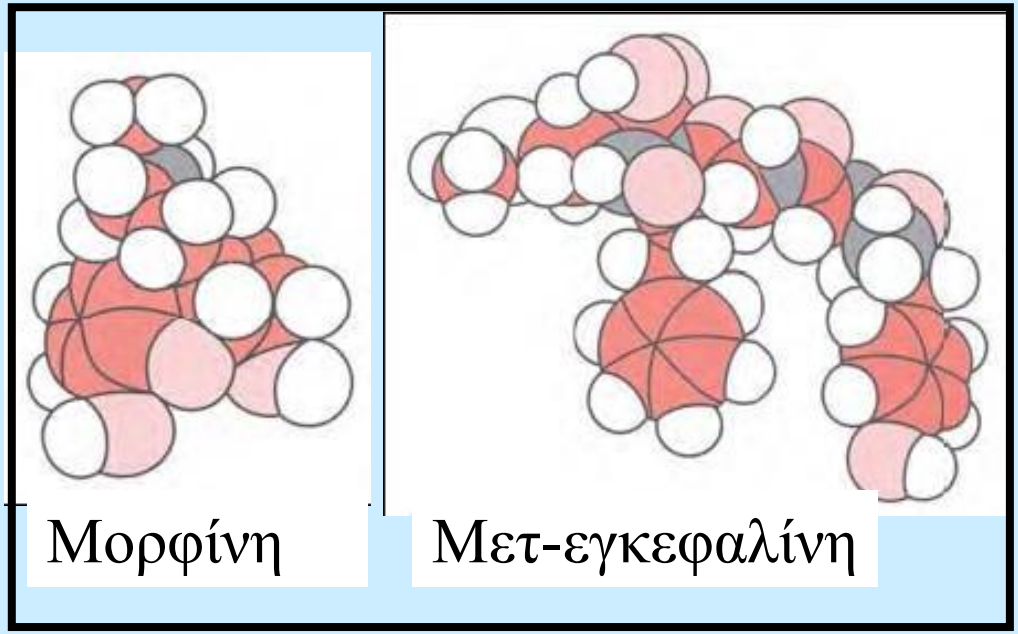
Ενα ισχυρό βλαβοδεκτικό ερέθισμα αναστέλλει τον διάμεσο νευρώνα και έτσι (με δυσανατολή) ανοίγει η πύλη και προωθείται το κεντρομόλο μήνυμα



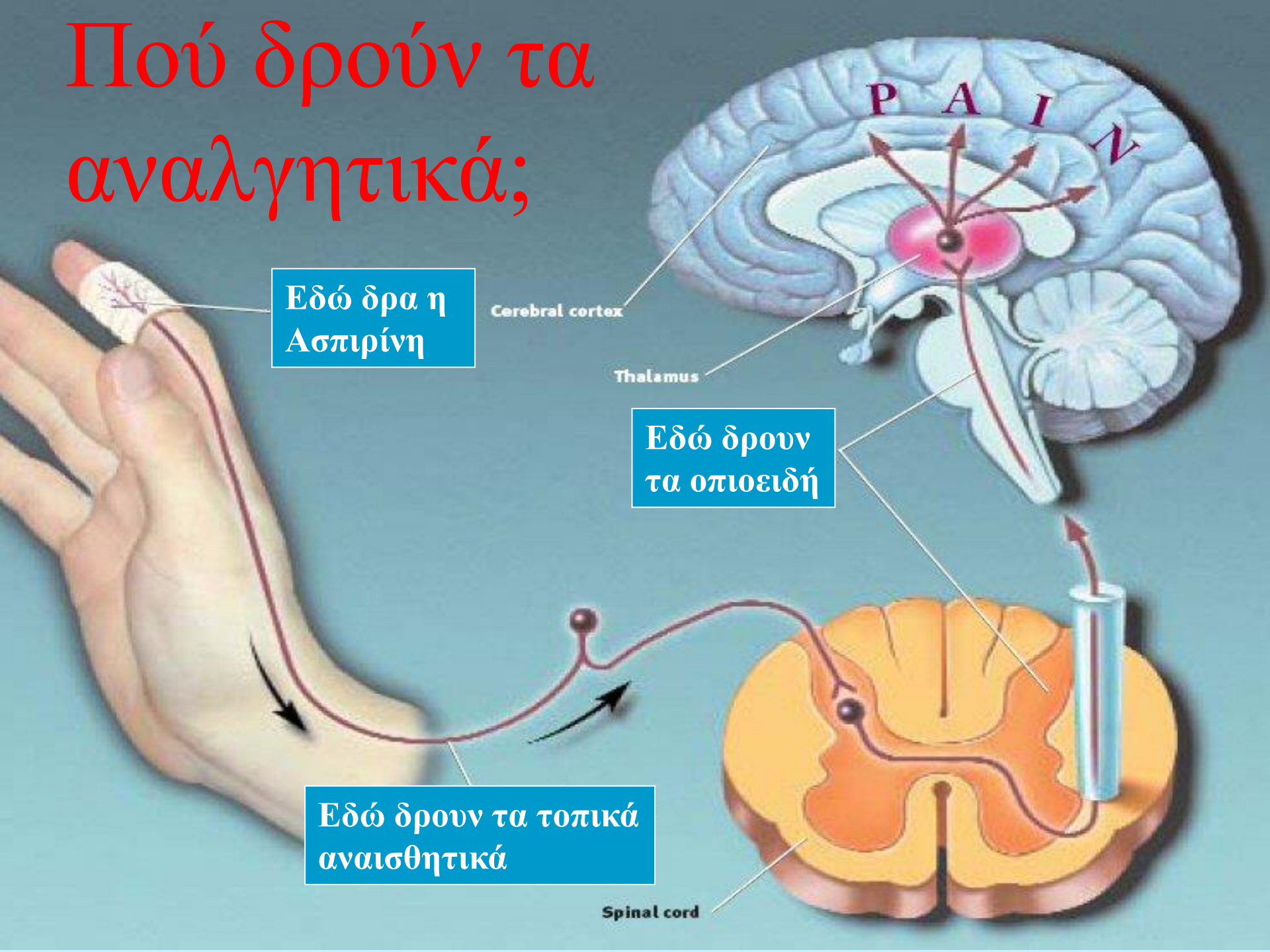
Η ισορροπία της πύλης μπορεί να τροποποιηθεί από μηνύματα των πρωτοταγών νευρώνων της αφής ή άλλα μη-βλαβοδεκτικά μηνύματα τα οποία διεγείρουν τον διάμεσο νευρώνα και έτσι επαναφέρουν την ανασταλτική του δράση στον δευτεροταγή βλαβοδεκτικό νευρώνα

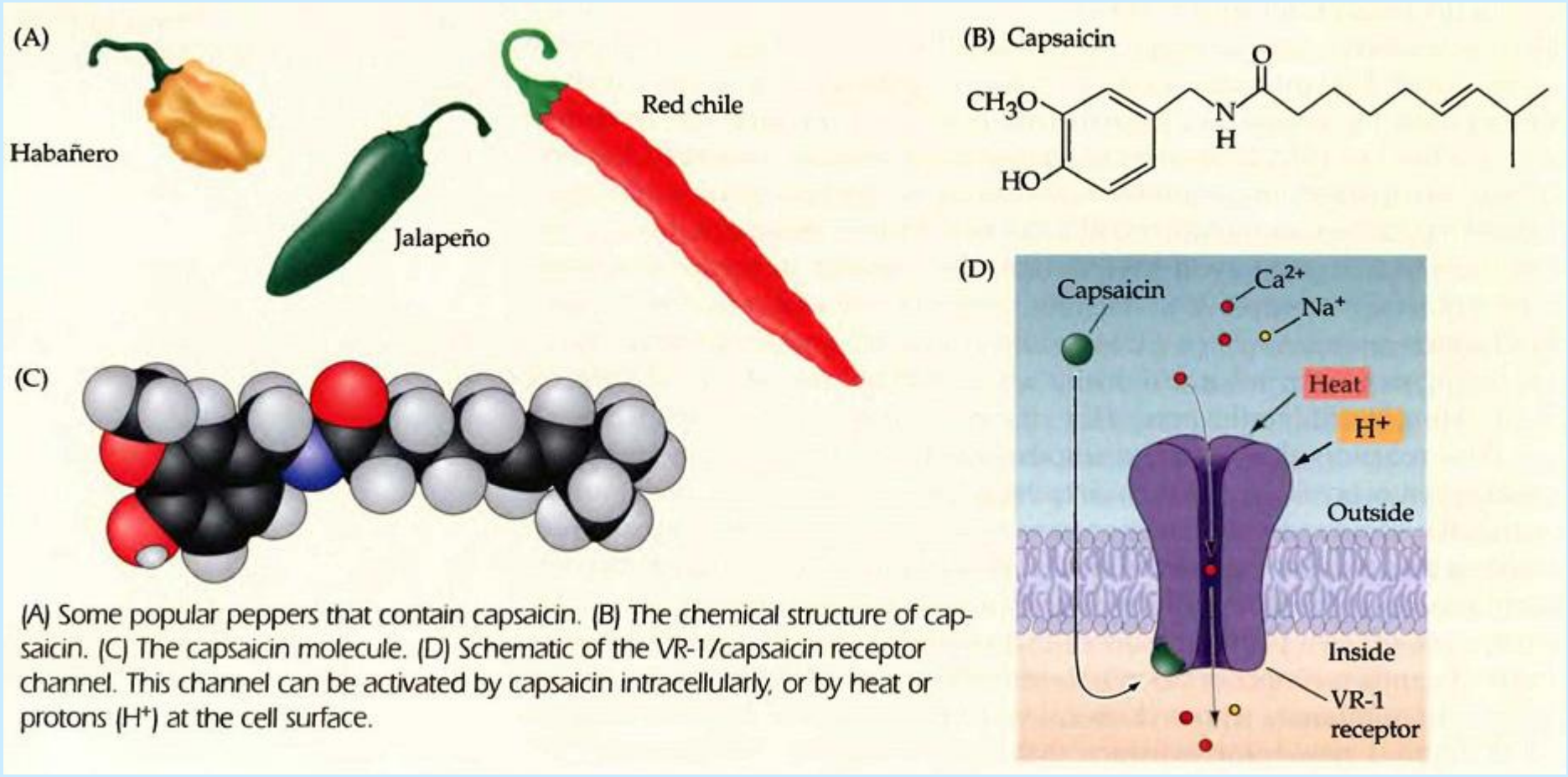


Στις διαδικασίες της αναστολής του πόνου εμπλέκεται ένας αριθμός χημικών διαβιβαστών, όπως τα ενδογενή οπιοειδή, π.χ. **μετεγκεφαλίνη**. Η μορφίνη, ισχυρό αναλγητικό φάρμακο, δρα στους ίδιους υποδοχείς, στους οποίους δρουν κάποια από τα ενδογενή οπιοειδή.



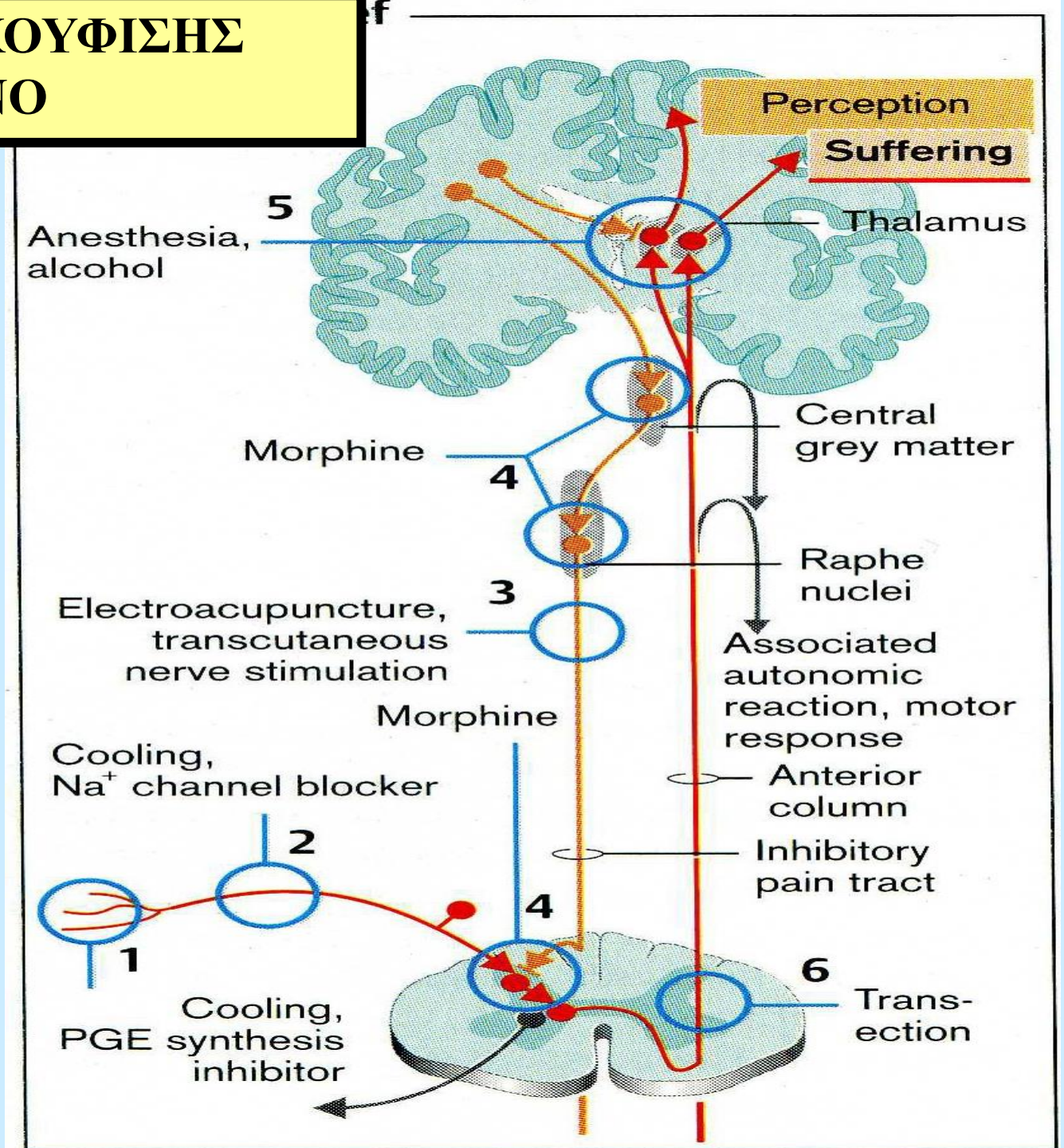
Πού δρούν τα αναλγητικά;



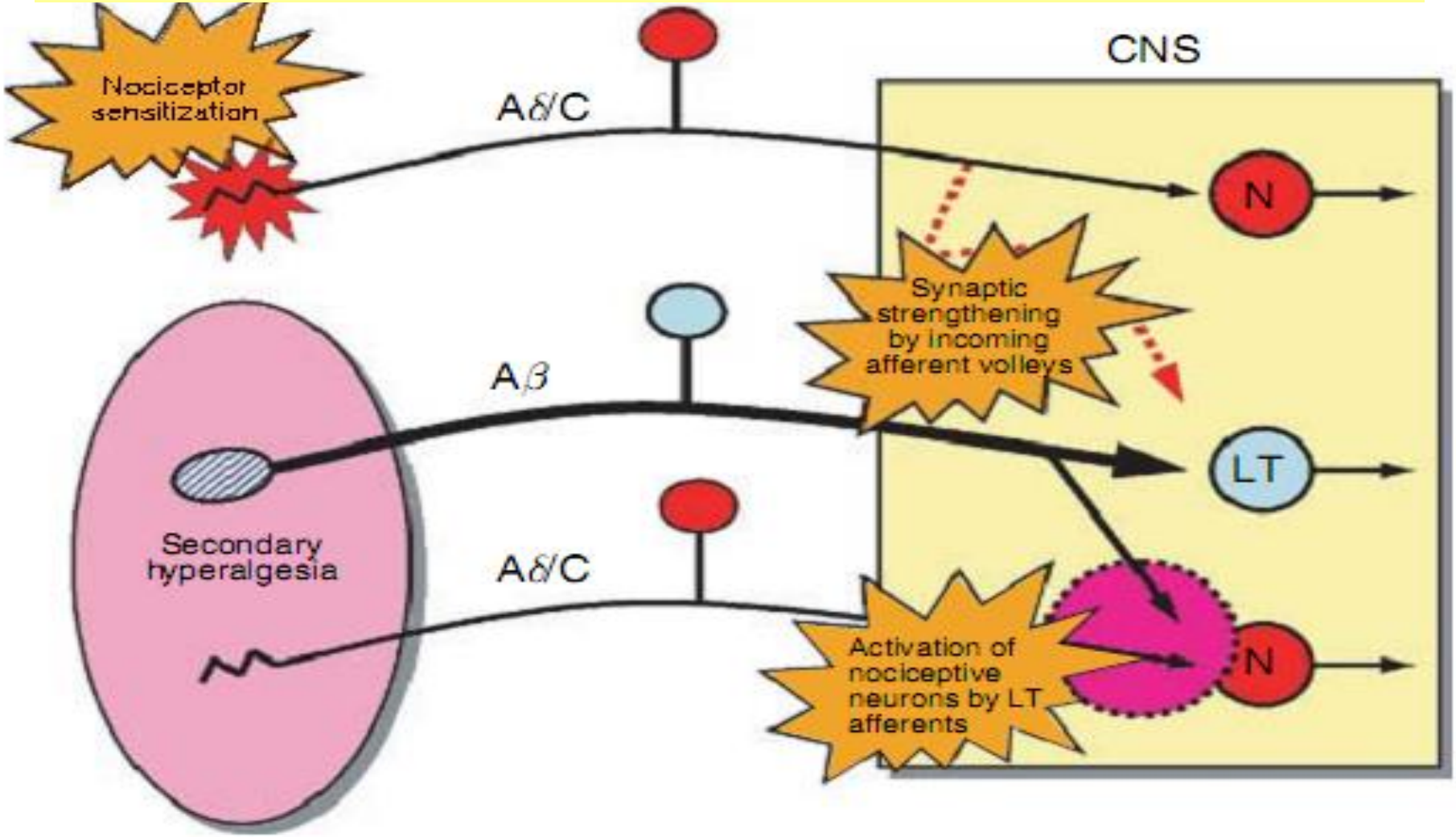


(A) Some popular peppers that contain capsaicin. (B) The chemical structure of capsaicin. (C) The capsaicin molecule. (D) Schematic of the VR-1/capsaicin receptor channel. This channel can be activated by capsaicin intracellularly, or by heat or protons (H^+) at the cell surface.

ΤΡΟΠΟΙ ΑΝΑΚΟΥΦΙΣΗΣ ΑΠΌ ΤΟΝ ΠΟΝΟ



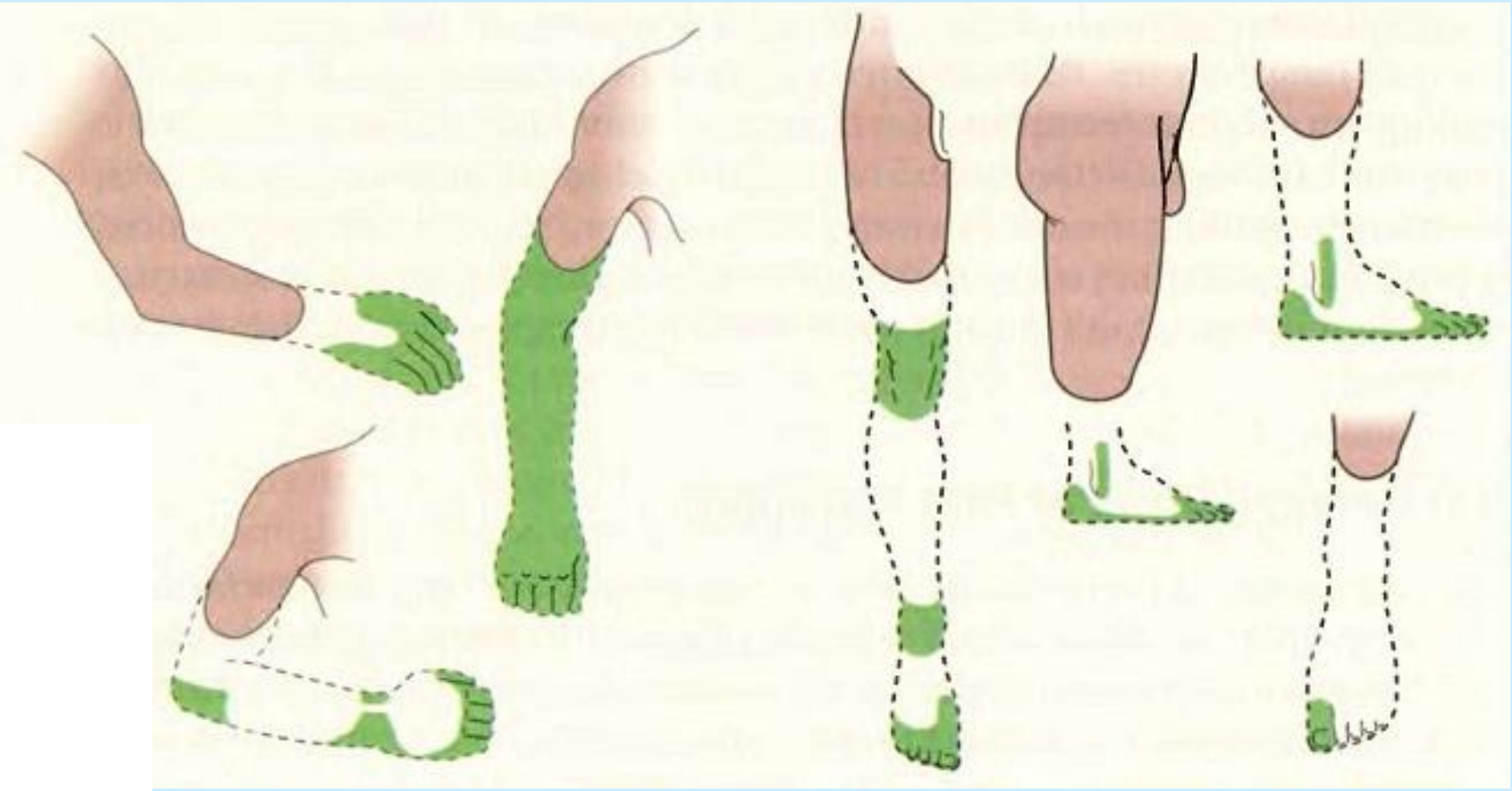
ΥΠΕΡΑΛΓΗΣΙΑ: Πρωτογενής και δευτερογενής



Προηγούνται σήματα από βλαβοδεκτικούς υποδοχείς. Η επίδρασή τους ενισχύεται συναπτικά στο ΝΜ από προσαγωγούς Αβ ίνες του συστήματος χαμηλού ουδού. ➔

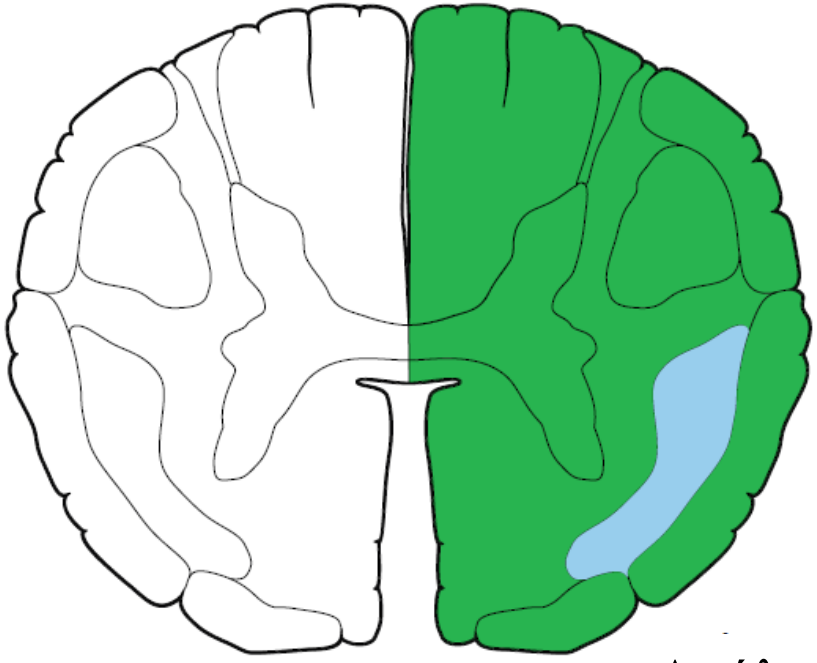
Μειώνεται ο ουδός των δευτεροταγών ινών του πόνου

ΠΟΝΟΣ ΑΠΌ «ΜΕΛΟΣ ΦΑΝΤΑΣΜΑ»: Περιφερικοι και κεντρικοί μηχανισμοί

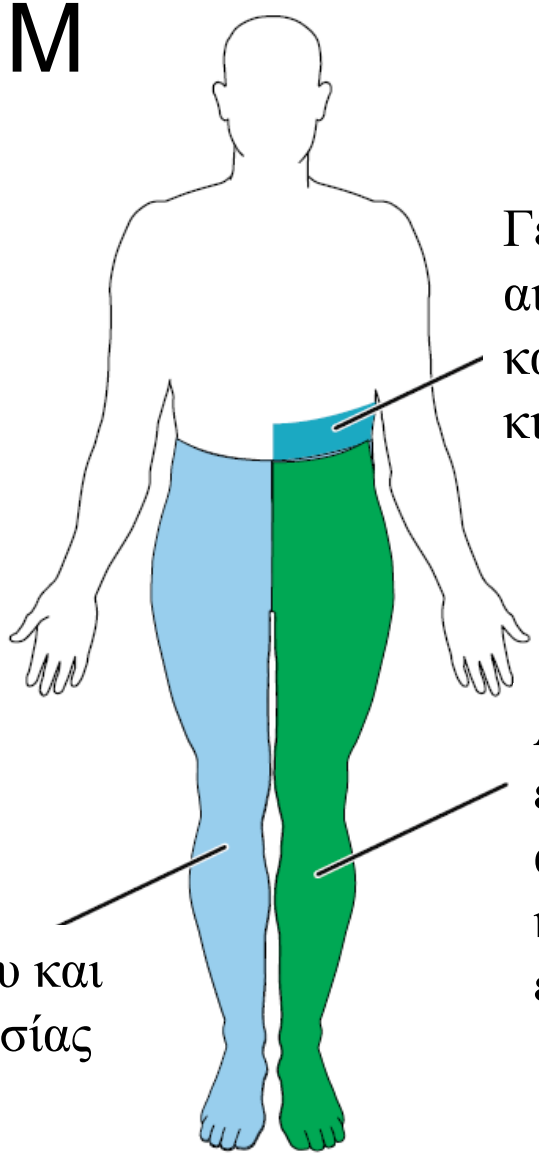


Σύνδρομο Brown-Séquard
Οριζόντια ημιδιατομή ΝΜ

Δεξιά - Αριστερά



Πρόσθια όψη

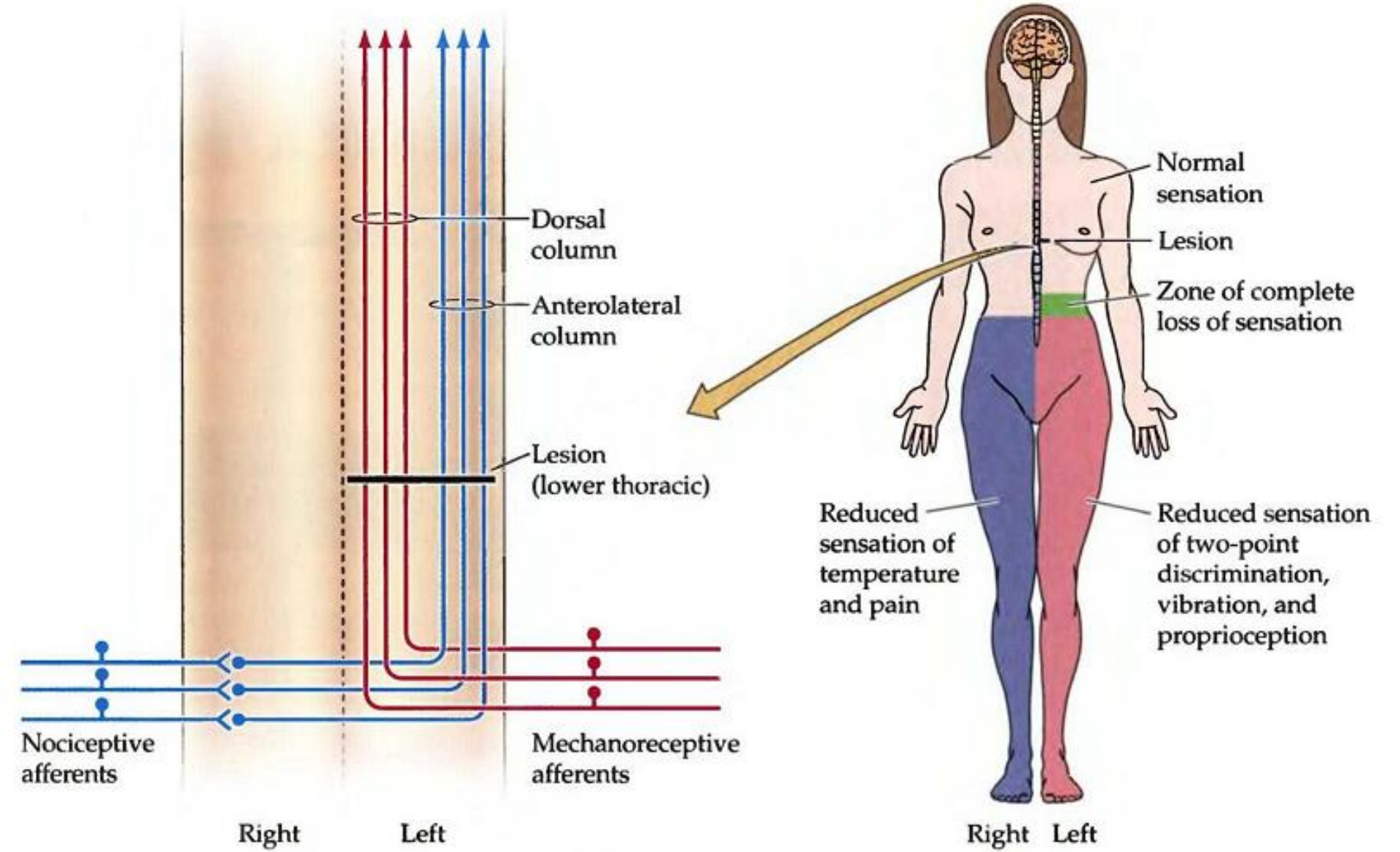


Γενική απώλεια αισθητικότητας και κινητικότητας

Απώλεια επικριτικής αφής και κινητικού ελέγχου

Απώλεια πόνου και θερμοευαισθησίας

Σύνδρομο Brawn-Sequard (εγκάρσια ημιδιατομή του ΝΜ



Ερεθισμός μέσου νεύρου

δεξιά αριστερά

e

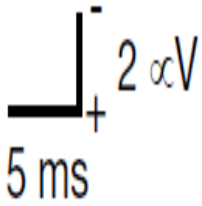
Καταγραφή

σε αριστερό κρόταφο

σε δεξιό κρόταφο

σε αριστερό τράχηλο

σε δεξιό τράχηλο



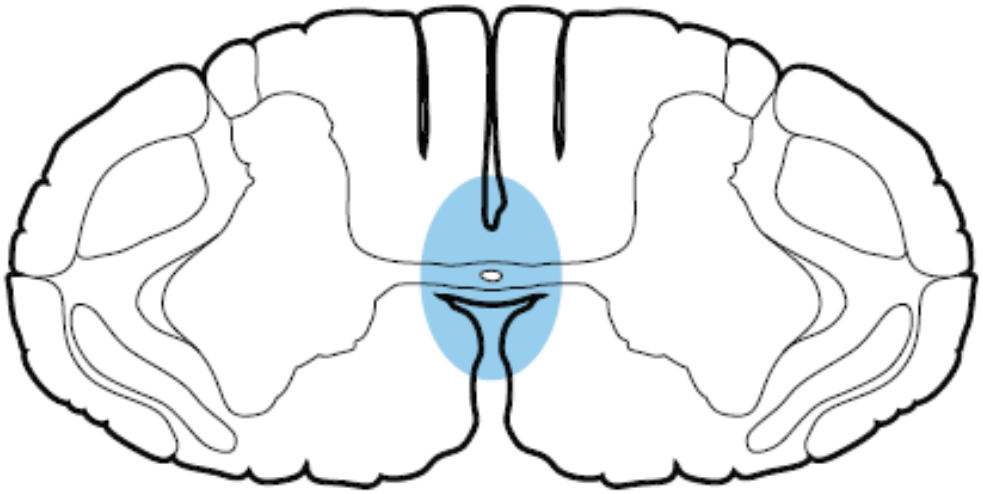
Πολλαπλή σκλήρυνση:

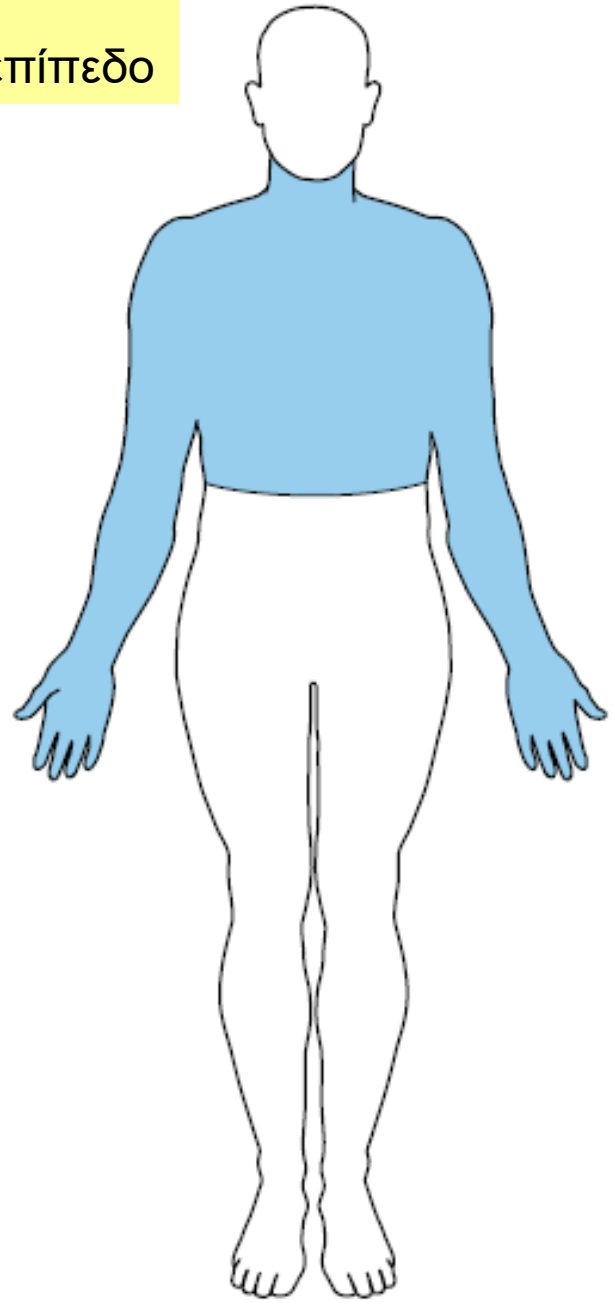
Αισθητικά προκλητά δυναμικά.

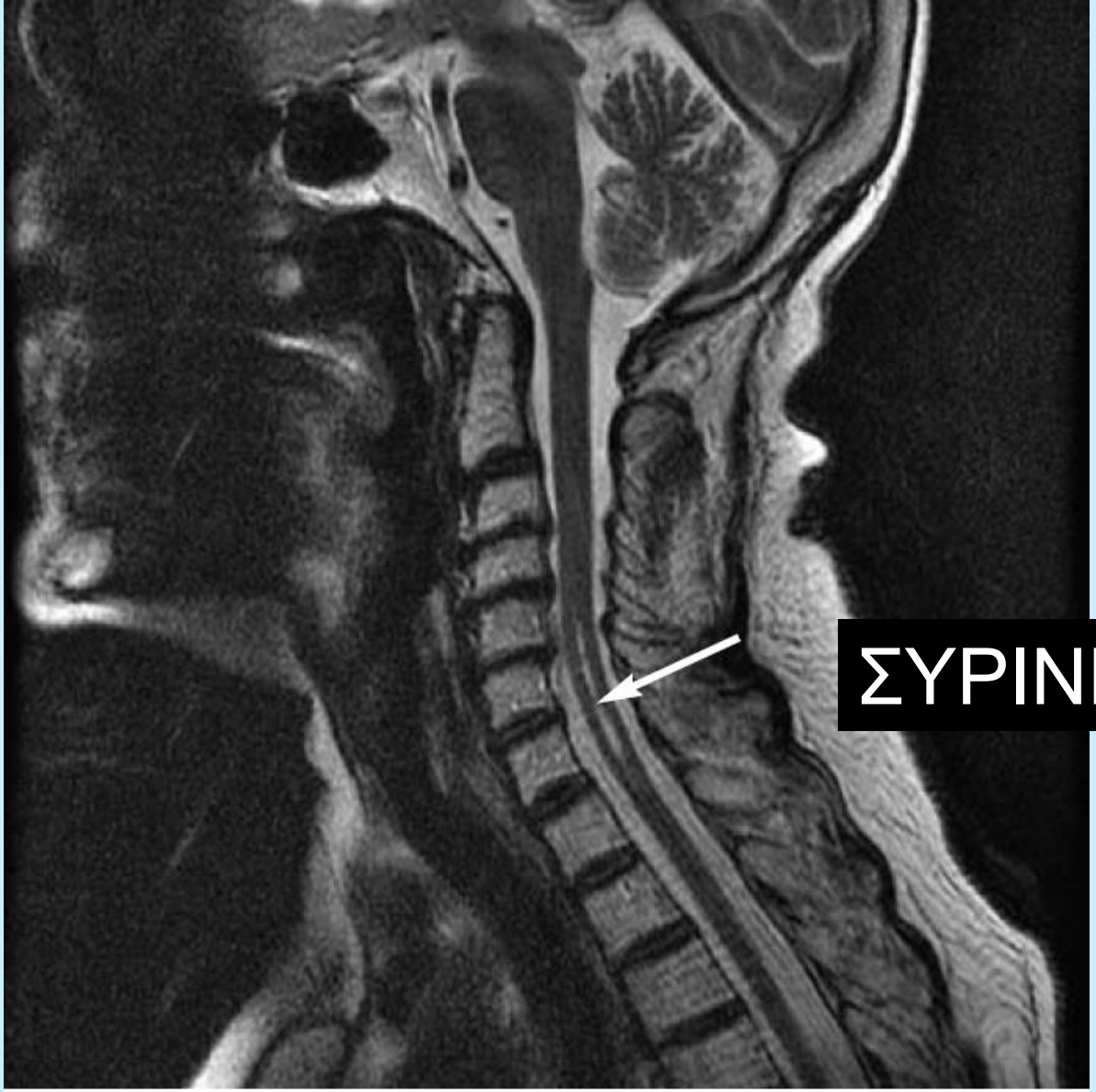
Πού μπορεί να εντοπίζεται η απομυελωτική βλάβη;

ΣΥΝΔΡΟΜΟ ΣΥΝΔΕΣΜΟΥ:

Αμφοτερόπλερη αισθητική απώλεια ανάλογα με το επίπεδο



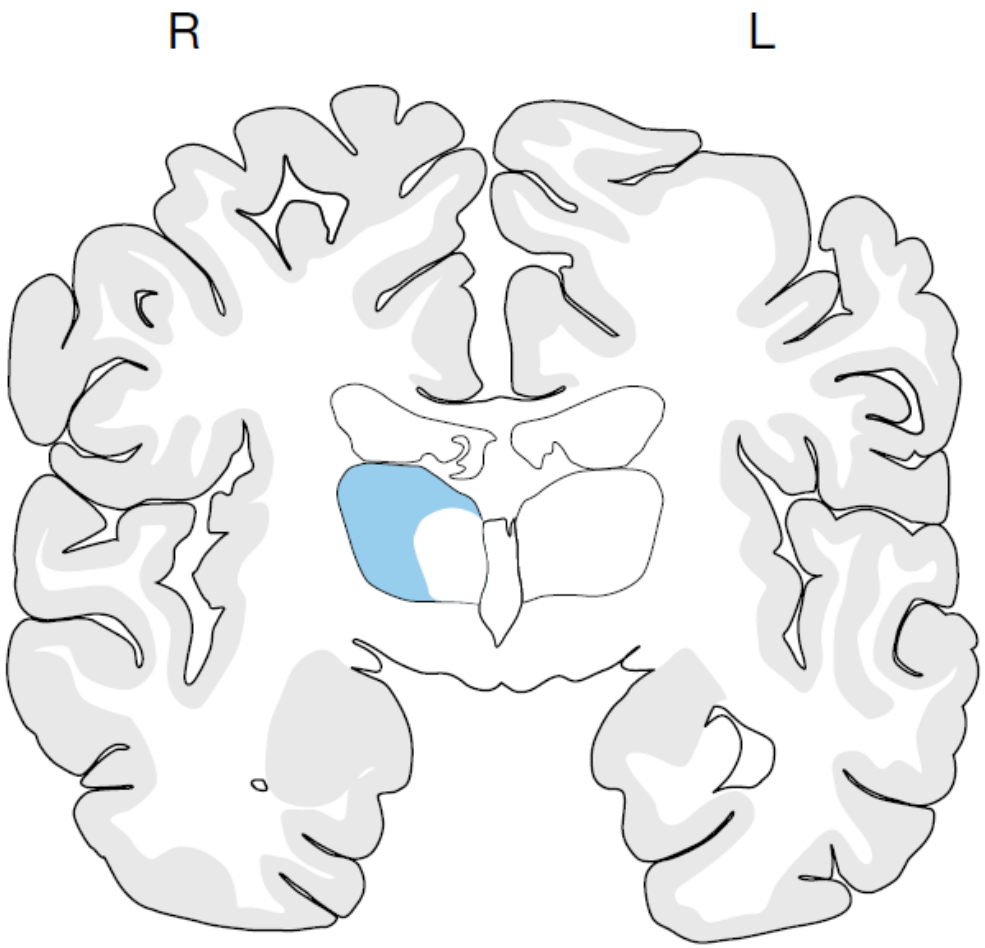


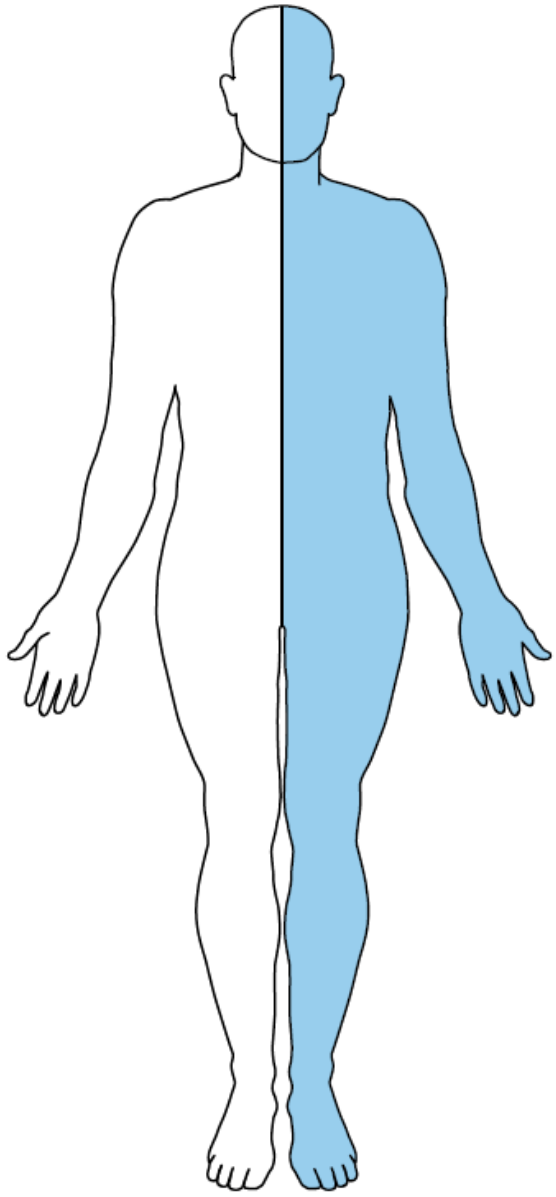


Η συριγγομυελία μπορεί να προκαλέσει απώλεια της ικανότητας αίσθησης ακραίων τιμών ψυχρού και θερμού, ιδιαίτερα στα χέρια και γενικά οδηγεί σε απώλεια αίσθησης πόνου και θερμοκρασίας με κατανομή δίκην χιτώνα, κατά μήκος της ράχης και των βραχιόνων

Θαλαμικό σύνδρομο:

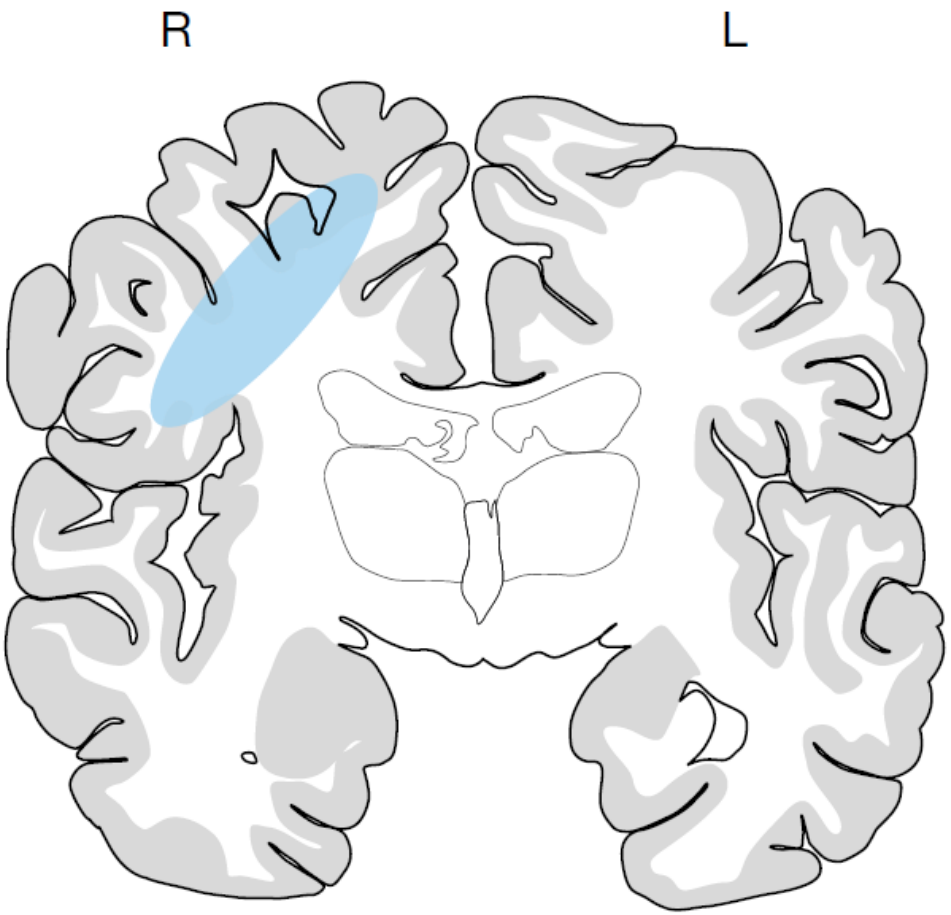
Απώλεια αισθητικών λειτουργιών ετερόπλευρα της βλάβης.

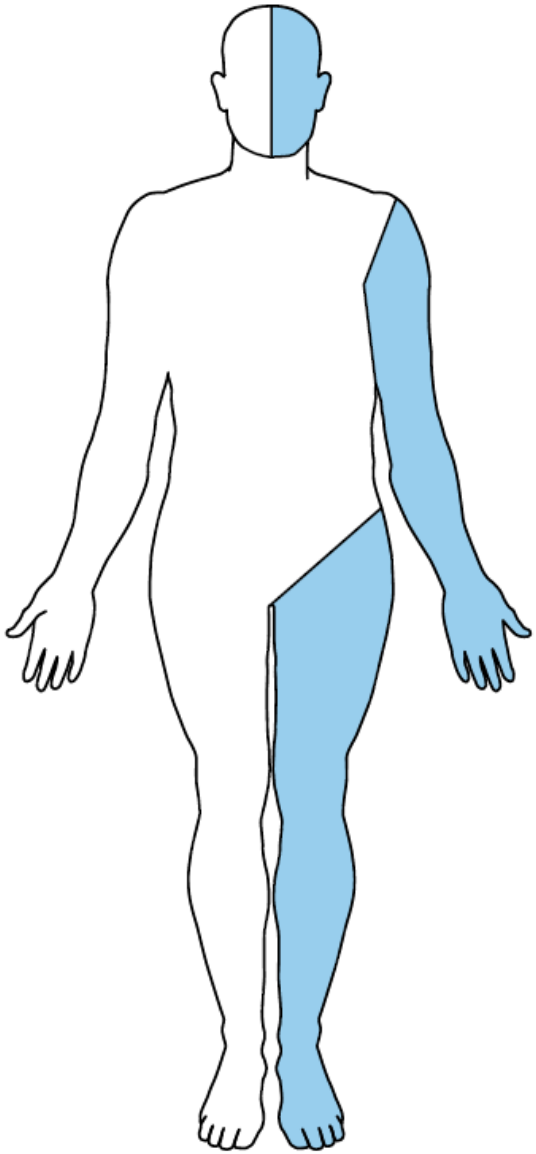


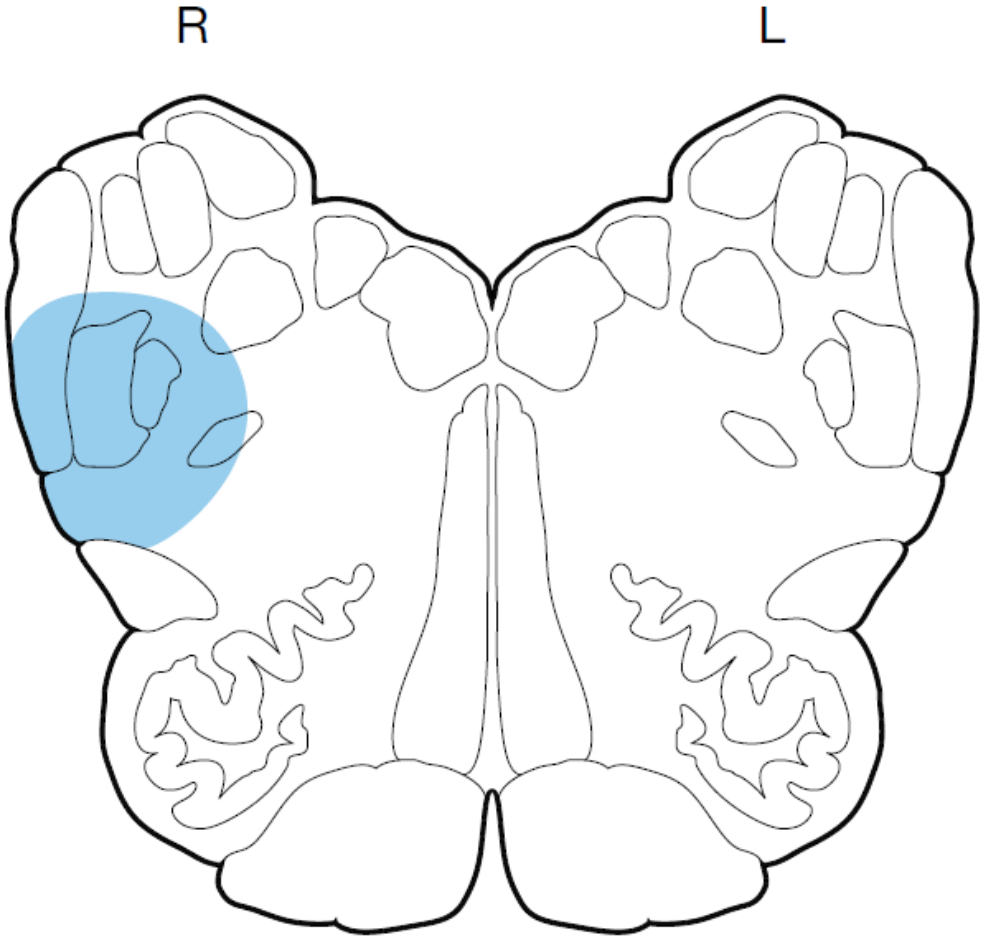


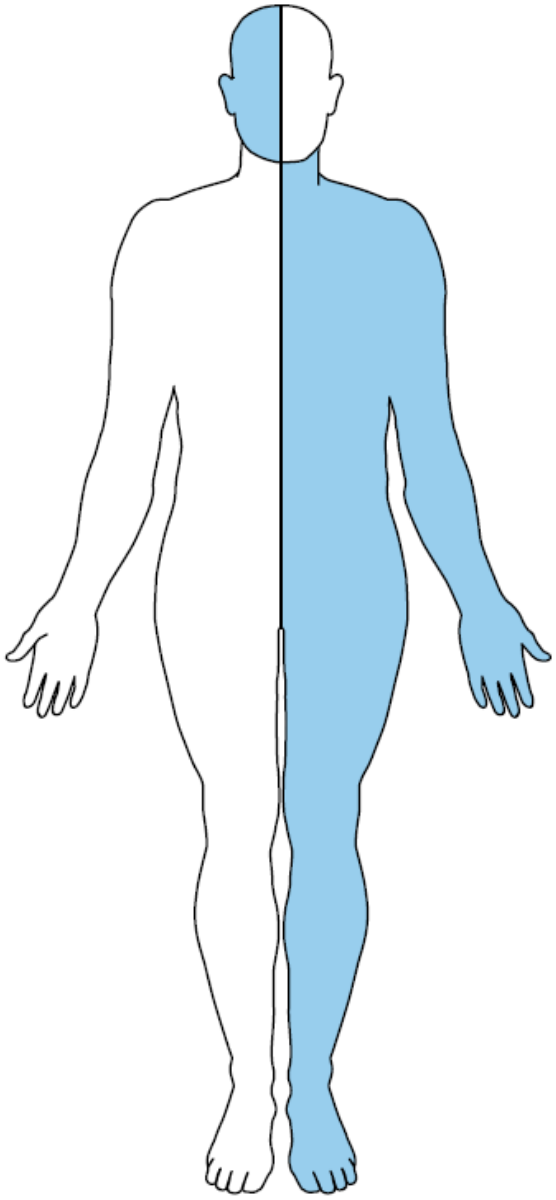
Υπερθαλαμικό σύνδρομο:

Απώλεια φλοιϊκών αισθητικών λειτουργιών ετερόπλευρα της βλάβης



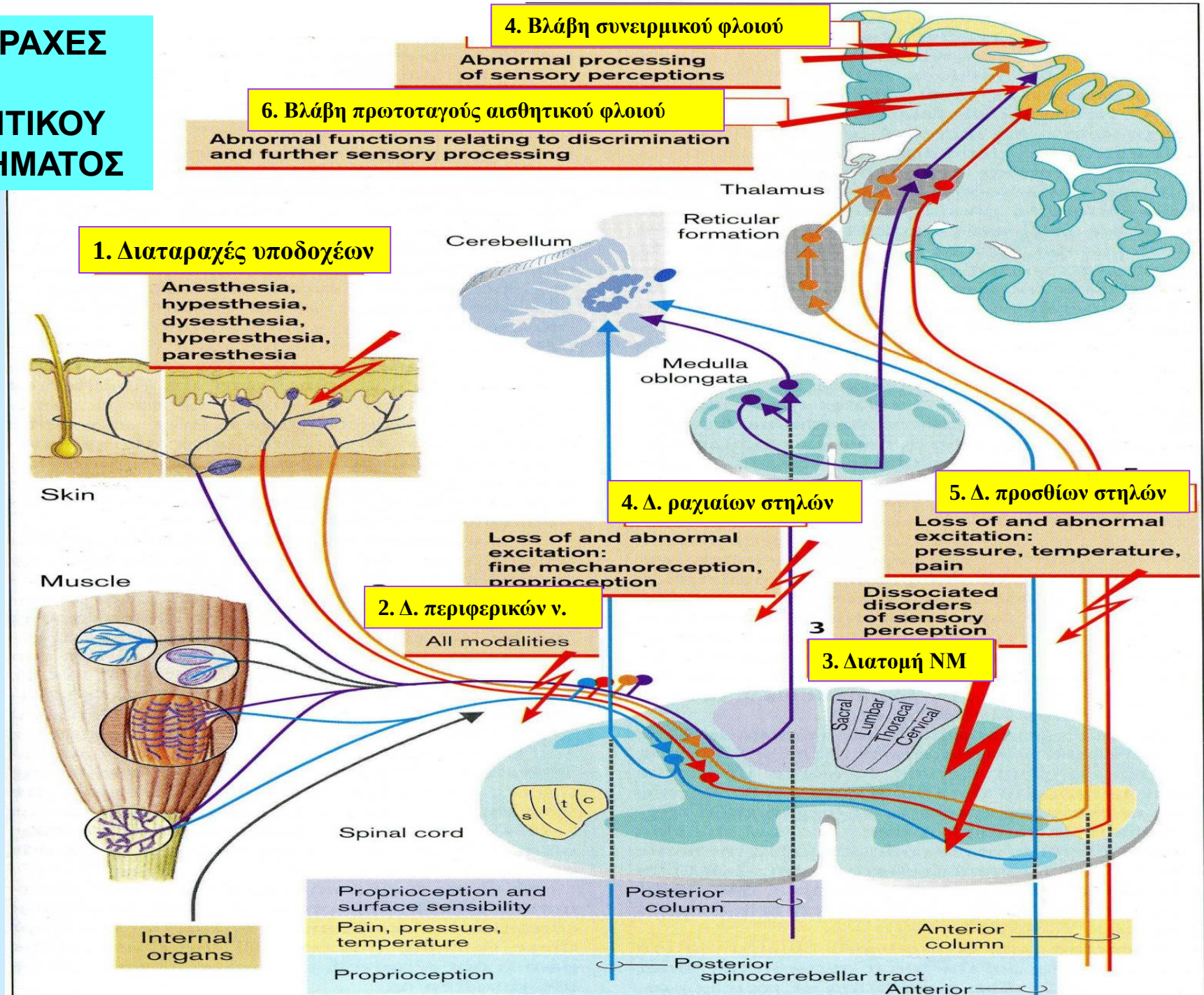


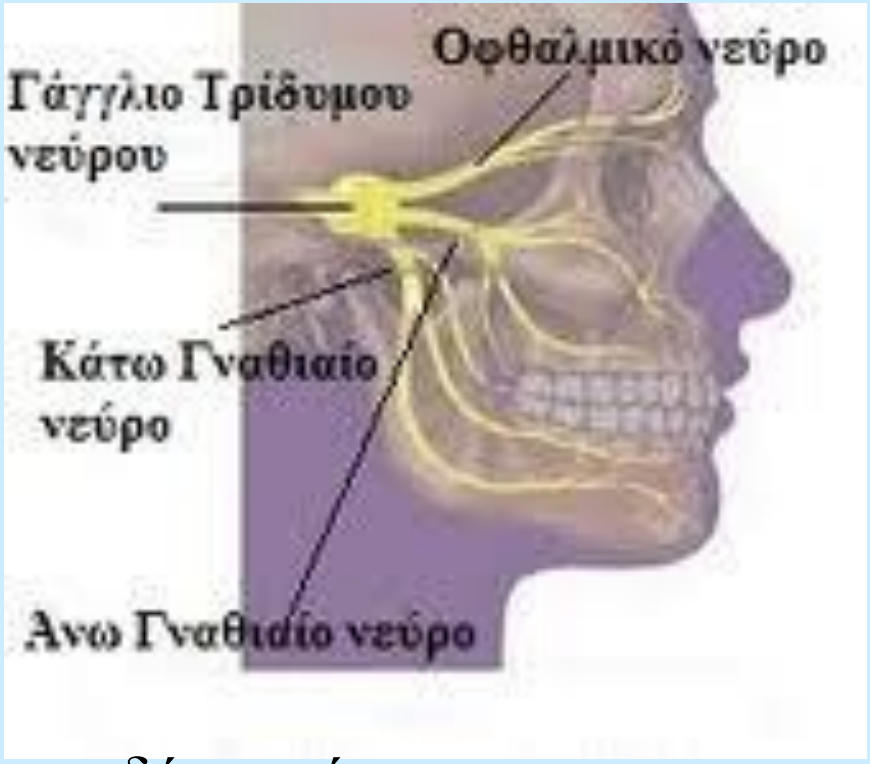




Βλάβη στο επίπεδο του οπισθίου βόθρου

ΔΙΑΤΑΡΑΧΕΣ ΤΟΥ ΑΙΣΘΗΤΙΚΟΥ ΣΥΣΤΗΜΑΤΟΣ





Η νευραλγία του τριδύμου είναι …

Α. σπλαχνικός πόνος

Β. αναφερόμενος αντανακλαστικός πόνος

Γ. προβαλλόμενος αντανακλαστικός πόνος

Δ. ημιπληγία

Ε. αλλοδυνία

Ζ. προσωπαγνωσία

Pathophysiology: Pain - 1

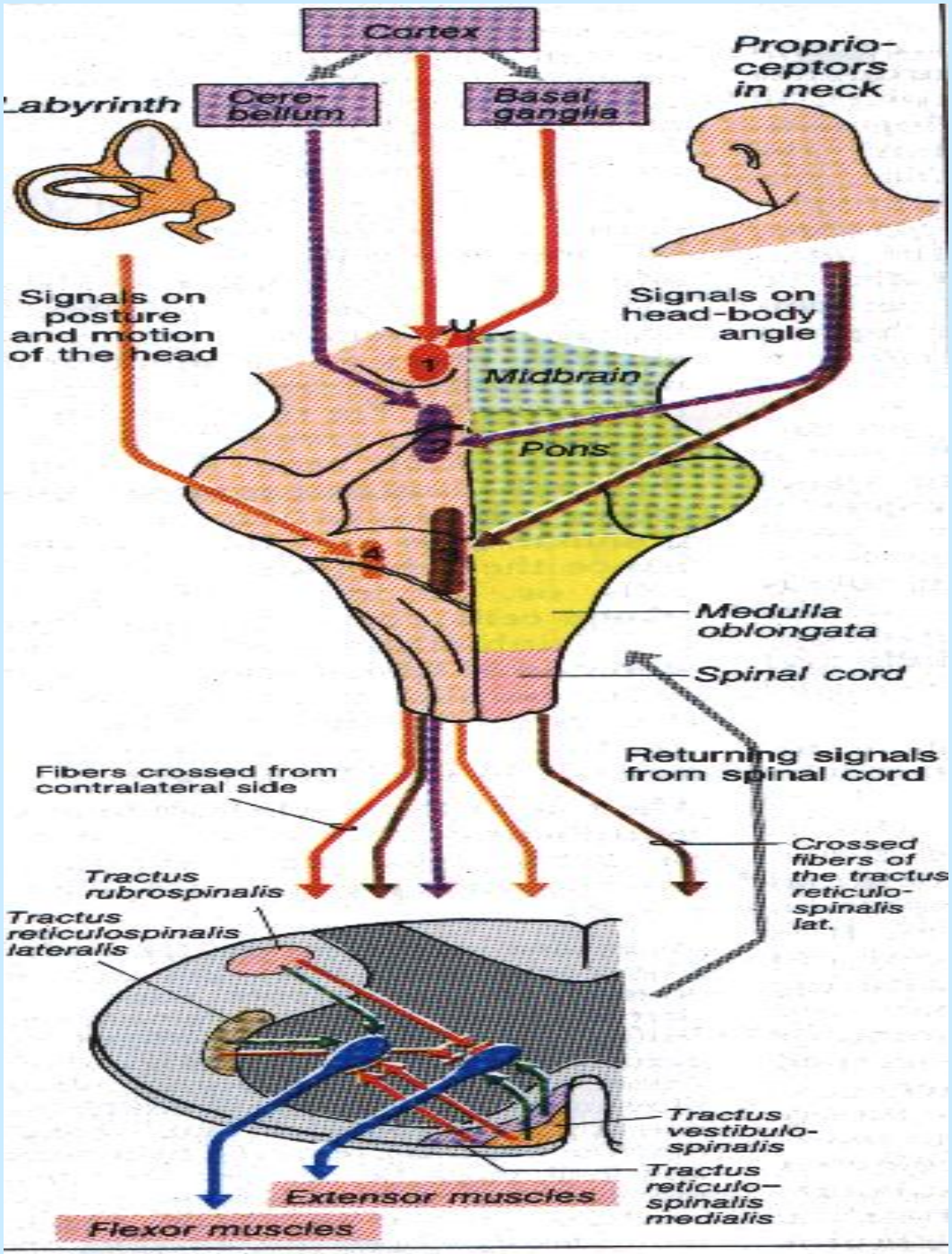
- **Pain** is a perception (not objective sensation) of tissue damage **(nociception).** It can therefor vary according to the prevailing body state, memories, training etc.
- Nociceptive afferents synapse in the dorsal horn and cross at the level they enter the spinal cord and ascend via spinothalamic track. Therefor a spinal cord damage on the left side will produce analgesia on the contralateral side of the body innervated by the lower than the damage spinal cord segments (the same for temperature sensation, while discriminatory touch and proprioception will be affected ipsi-laterally, **crossed sensory defect**).
- **Arthritis** is a common painful condition caused by inflammation of one or more joints. The nociceptors become sensitized by the release of a number of chemical substances from nerve endings, mast cells, and blood elements. These substances include the neuropeptides, substance P and calcitonin gene-related peptide, histamine, bradykinin, serotonin, and prostaglandins. The sensitized nerve endings cause the joint to develop **hyperalgesia,** a condition in which the threshold for pain is lowered and the amount of pain produced by a given stimulus is increased. The joint also becomes swollen. This is caused by **neurogenic edema,** which is the collection of edema fluid that follows an increase in capillary permeability caused by the release of neuropeptides from joint nociceptors. These peptides also cause **vasodilation,** which increases the temperature of the joint. Arthritic pain is often treated successfully with substances, such as acetylsalicylic acid, that block the synthesis of prostaglandins.

Pathophysiology: Pain - 2

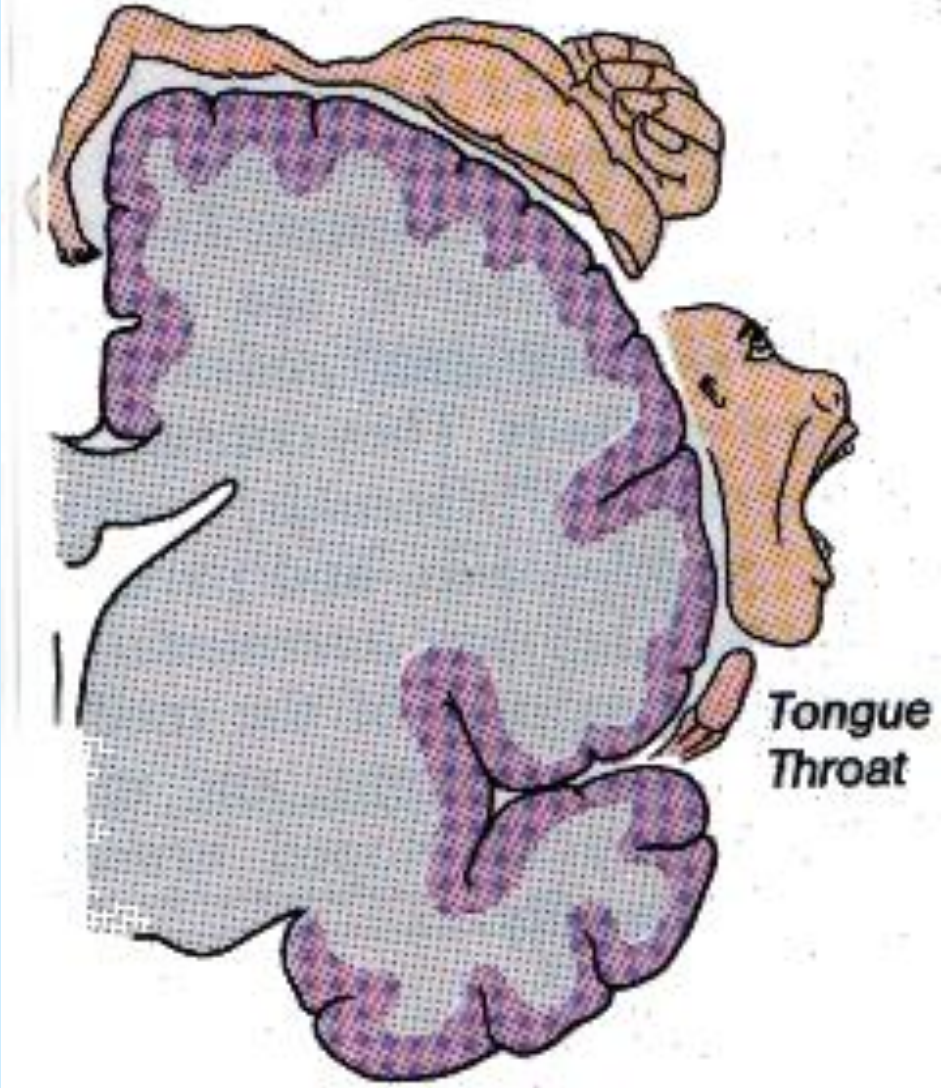
- **Allodynia** is a pathological state where activation of mechanoreceptors causes pain. It is prominent in **central pain,** which can result from damage to the central nervous system. For example, a central pain syndrome called **thalamic pain** may be caused by a lesion involving the VPL nucleus. The pain is typically burning in quality, although it can be sharp. Pain is often evoked by very weak stimulation, such as contact of the clothing with the skin.
- There exist several therapeutically powerful **analgesics** (pain relievers. **Aspirin** works at the periphery: the activation of nociceptors (it stops the production of prostaglandins which sensitize nociceptors. **Local anaesthetics** stop the conduction in nociceptive primary afferents Paracetamol and other compounds work in the CNS. Opiates and endogenous opioids work on same central receptors in several brain areas including the central gray matter and the posterior horn of spinal cord, where they help "close" the "pain gate". The latter can be also achieved by stimulation of primary sensory afferents and of descending pathways from the grey matter to the posterior horn. Opiates exert their analgesic effect by binding to specific opiate receptors. The binding of opiates to their receptors is stereospecifically inhibited by a morphine derivative called **naloxone.** It is medically very important to recognize that we all have a system of **endogenous analgesia** activated in times of emergency.
-

Pathophysiology: Pain - 3

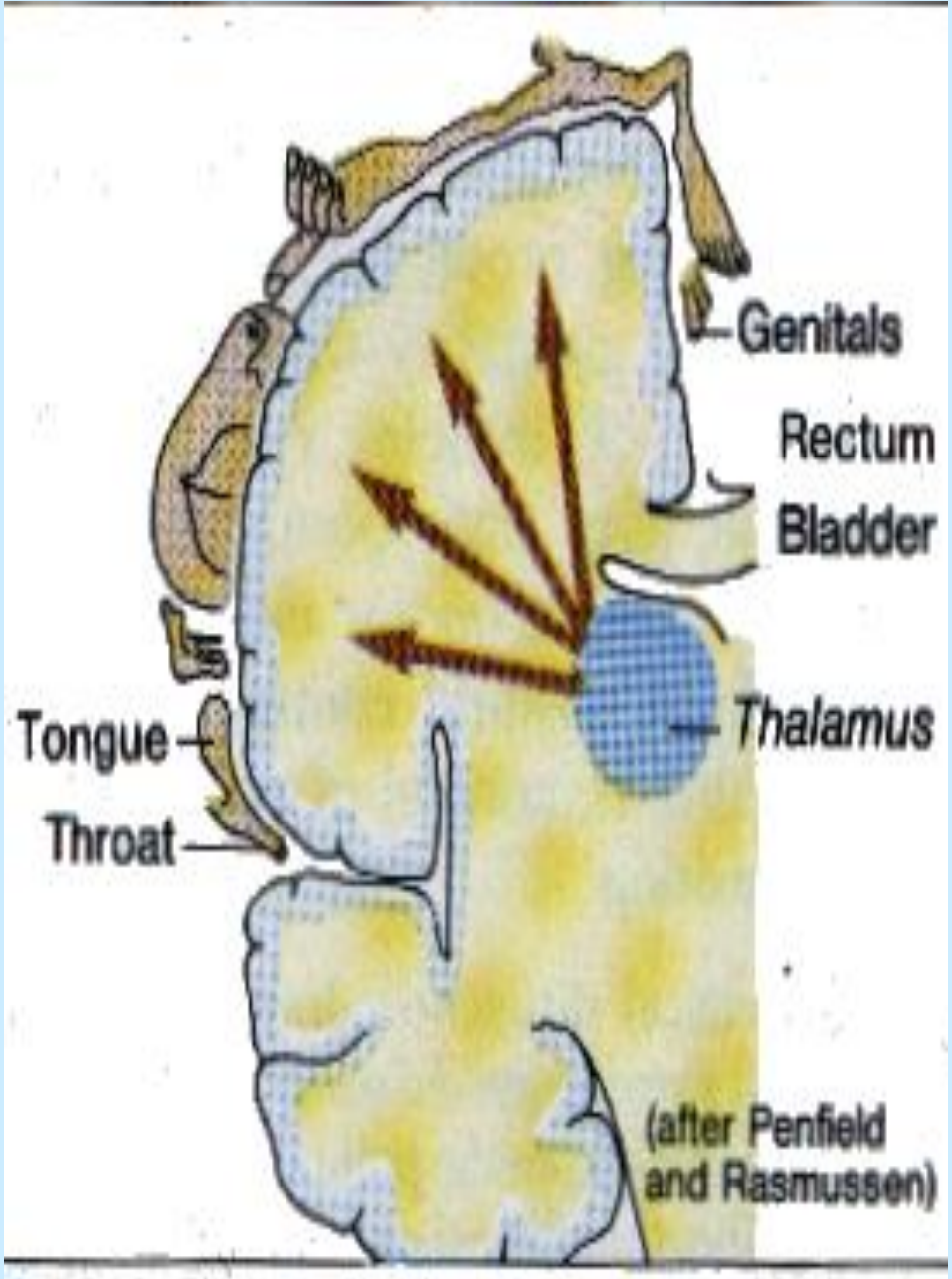
- Visceral nociception is not accurately perceived in terms of location, because we do not possess an image of our interior organs. However we are informed about internal organs tissue damage via **referred pain** i.e. pain referred to specific body surface. For example, angina pectoris is due to ischaemia of myocardium, but may be felt in the inner aspect of the left arm; appendicitis is due to infection of the gut but is usually felt on the abdominal surface. The mix up is due to the fact that visceral afferents branch in the spinal cord and synapse also with secondary sensory neurons of touch, which are located on the same spinal segment. The latter lead to a conscious perception of surface located pain, while the normal nociceptive paths serve only for unconscious reflexes
- **Projected pain** results when the injury affects the course of a nerve and the sensation projects to the body area it normally innervates i.e. when we accidentally hit our elbow, mechanical pressure on our ulvar nerve may be projected as pain of the small fingers



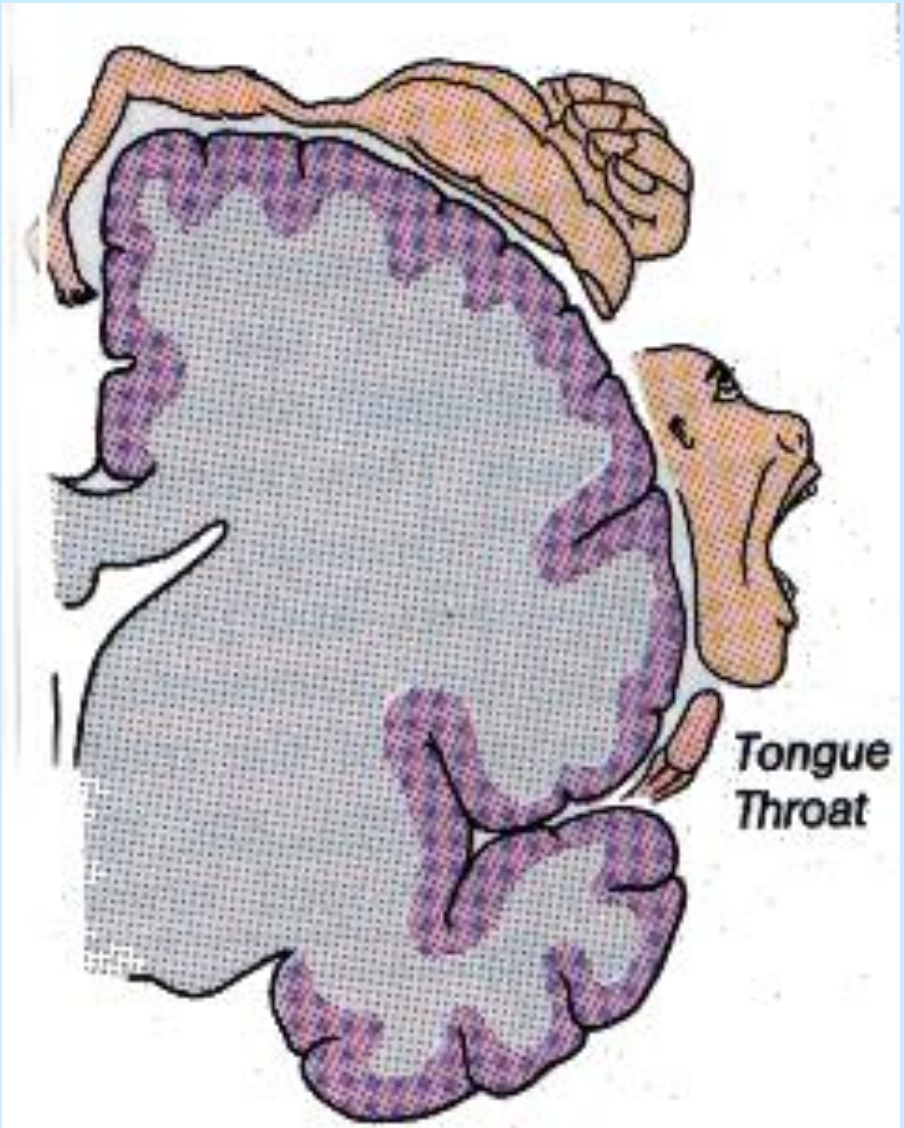
A. Postural control



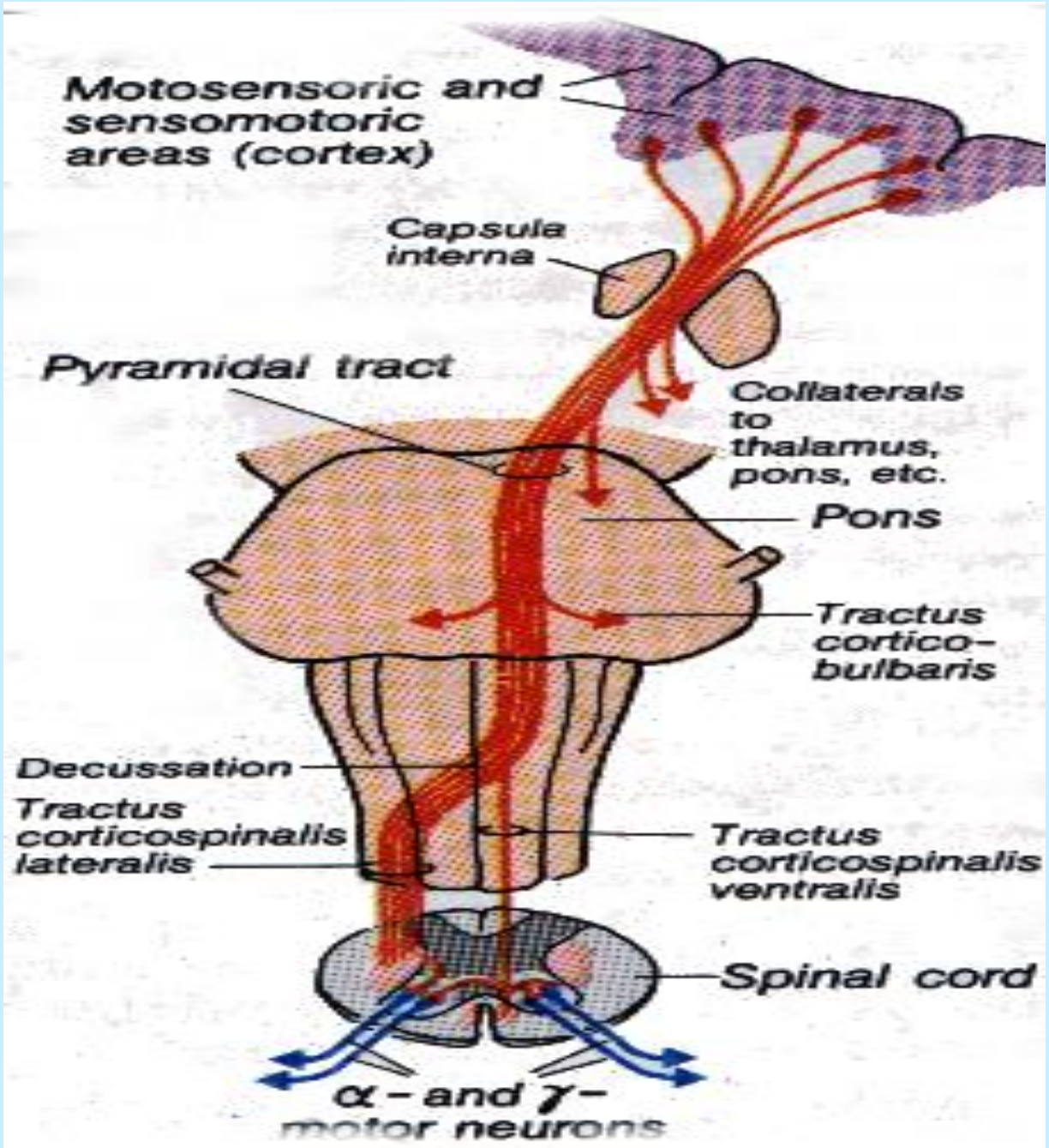
Somatotopic representation in motor cortex



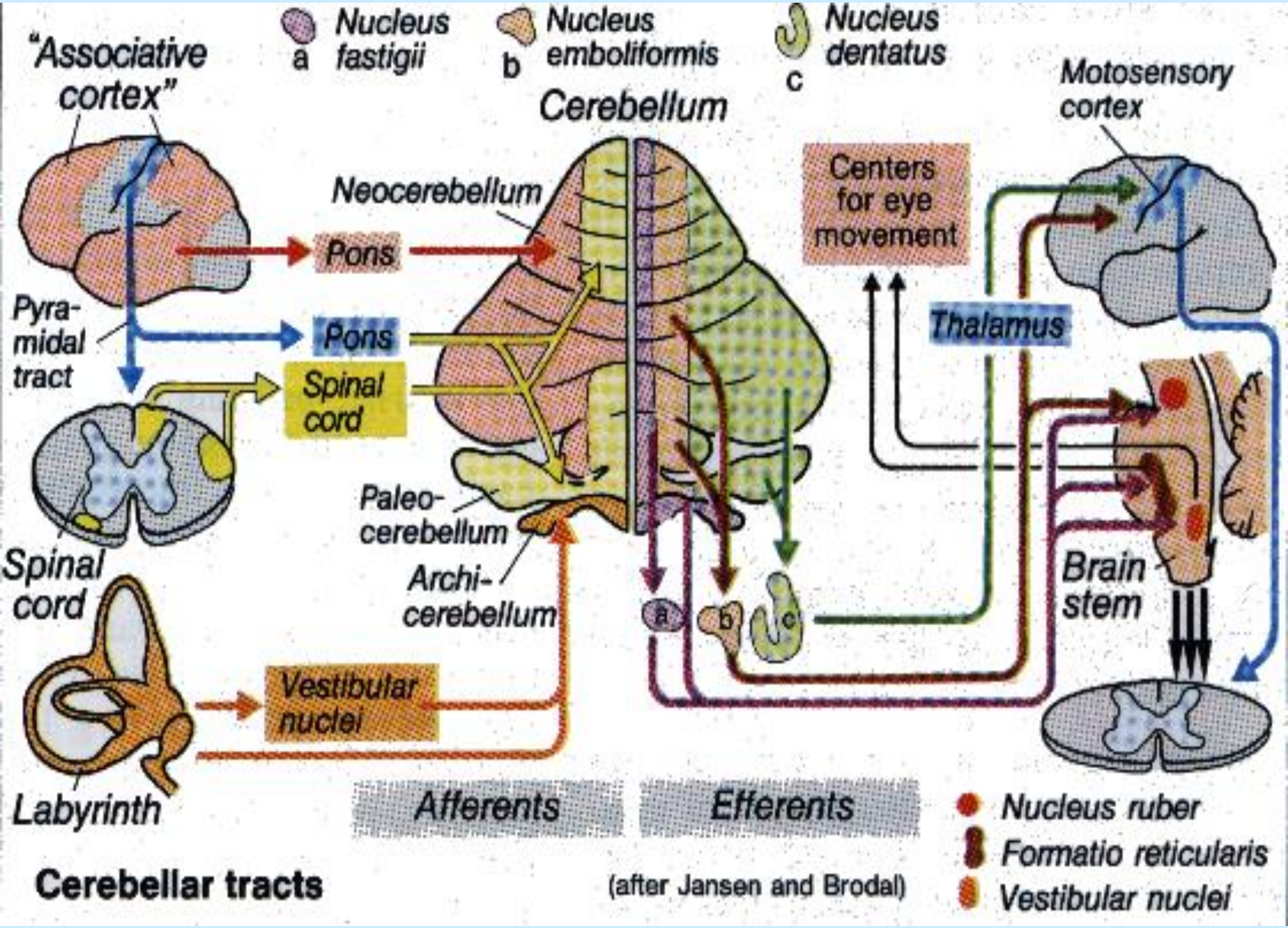
B. Somatotopic representation in somatosensory cortex



Somatotopic representation in motor cortex



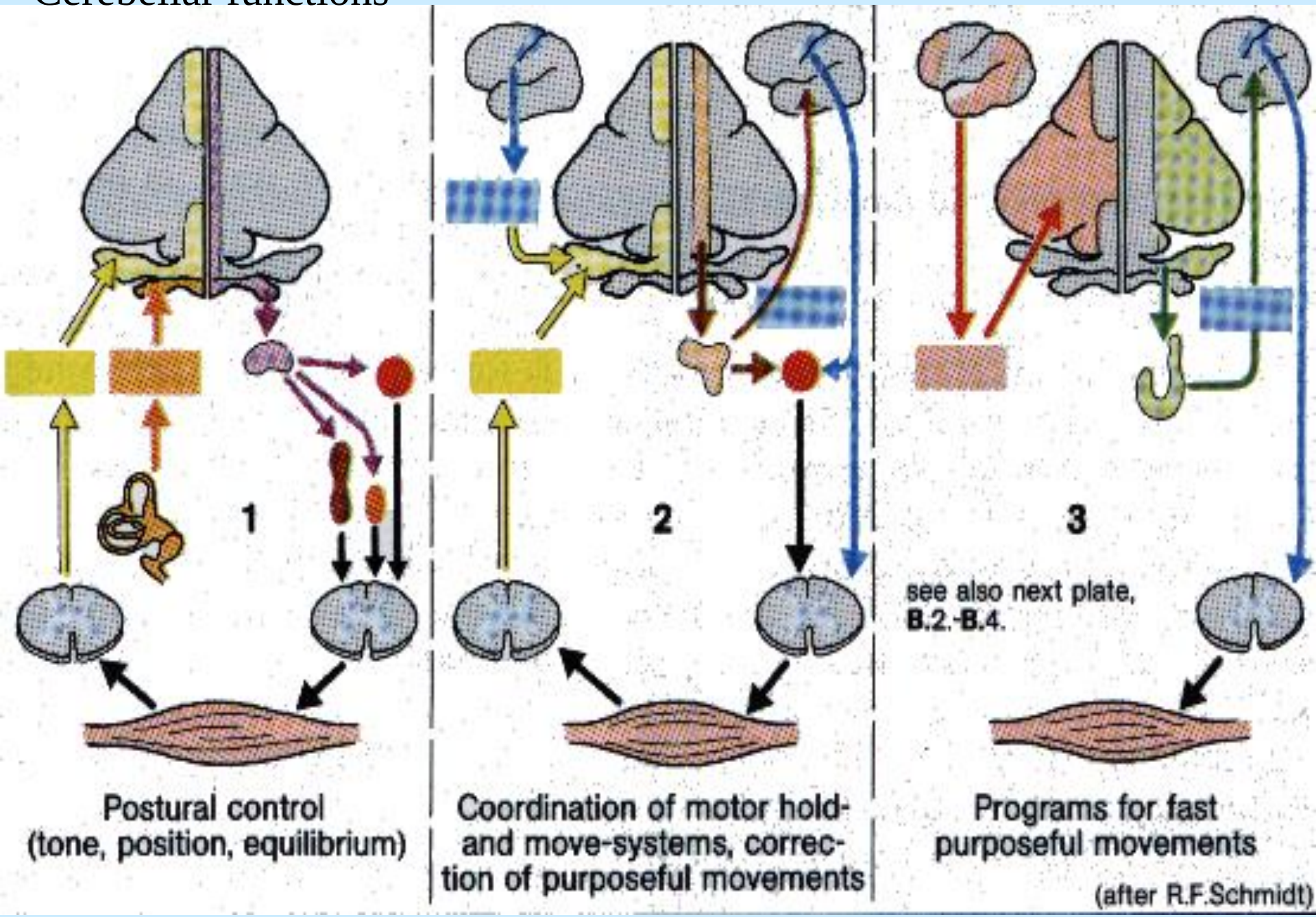
Pyramidal tract

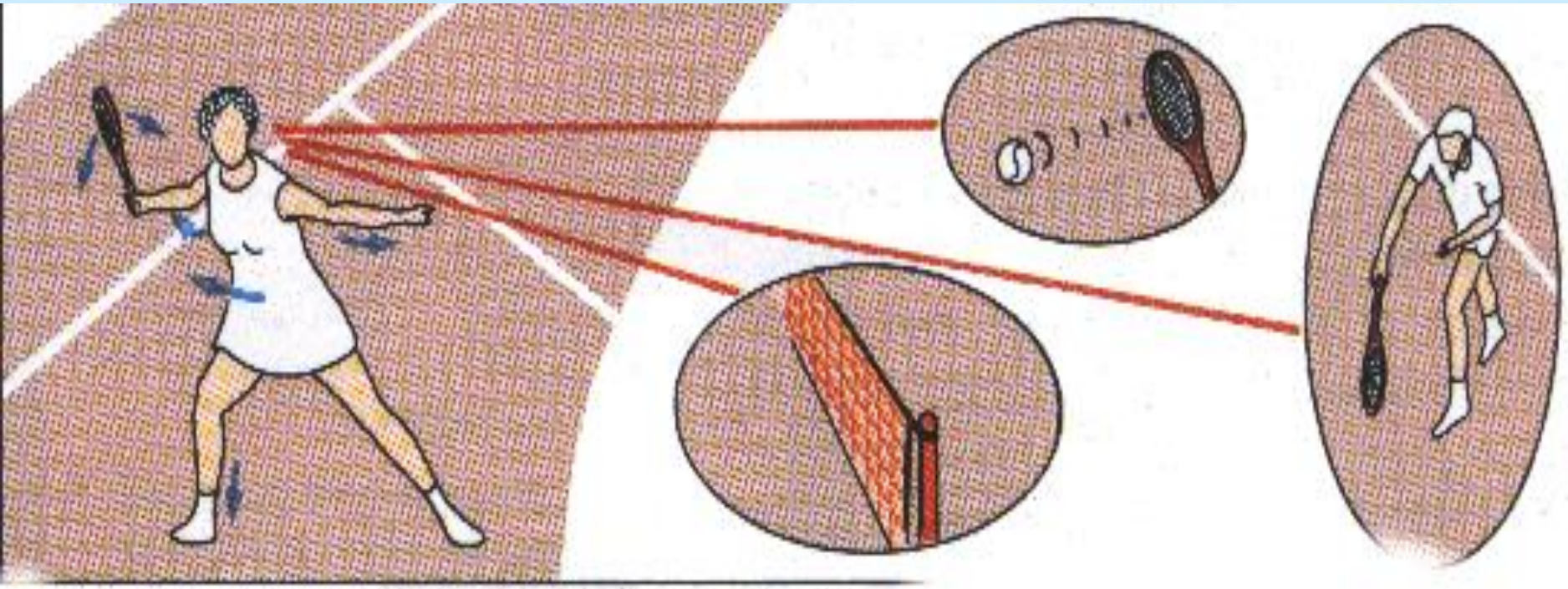


Cerebellar tracts

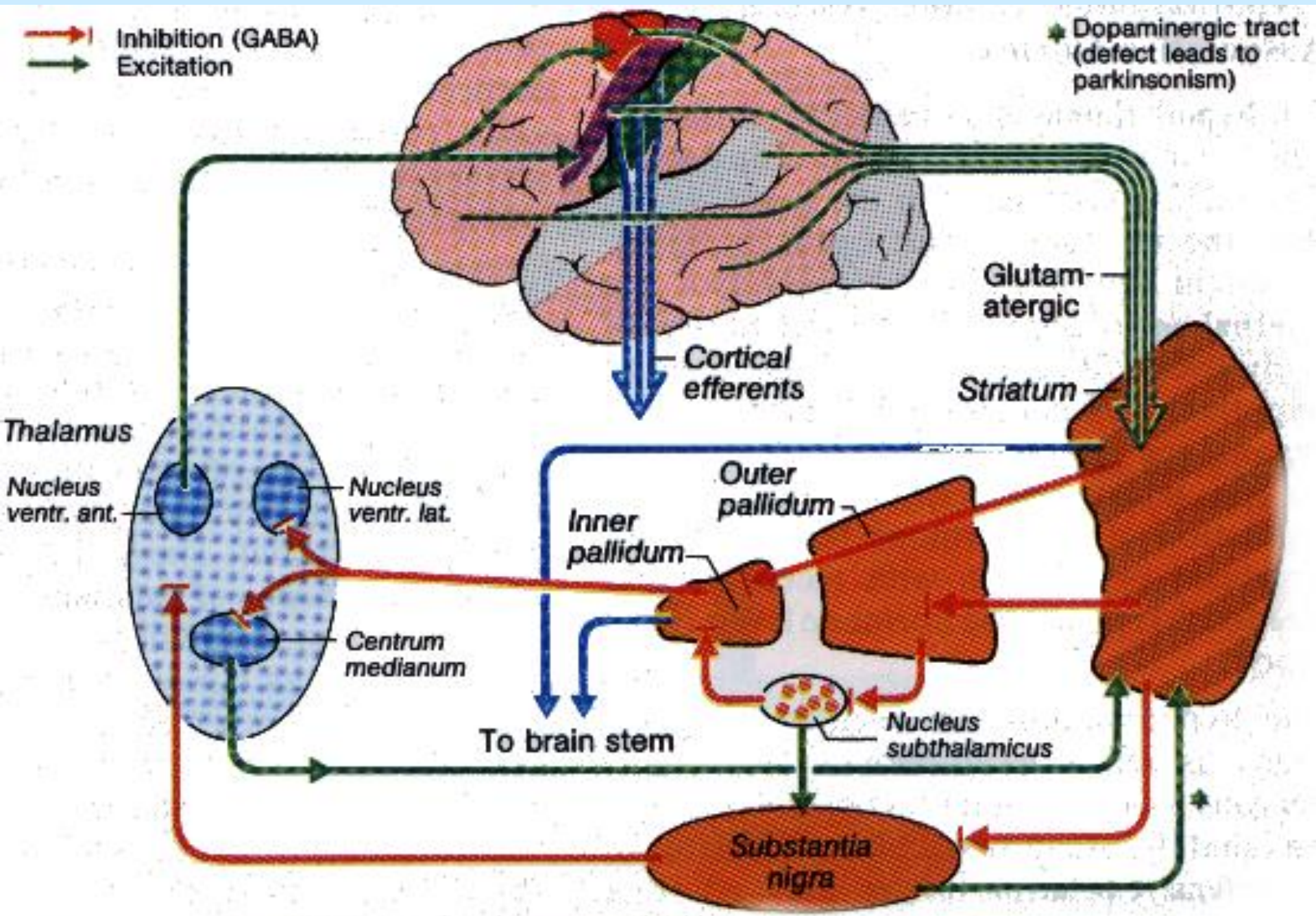
(after Jansen and Brodal)

Cerebellar functions

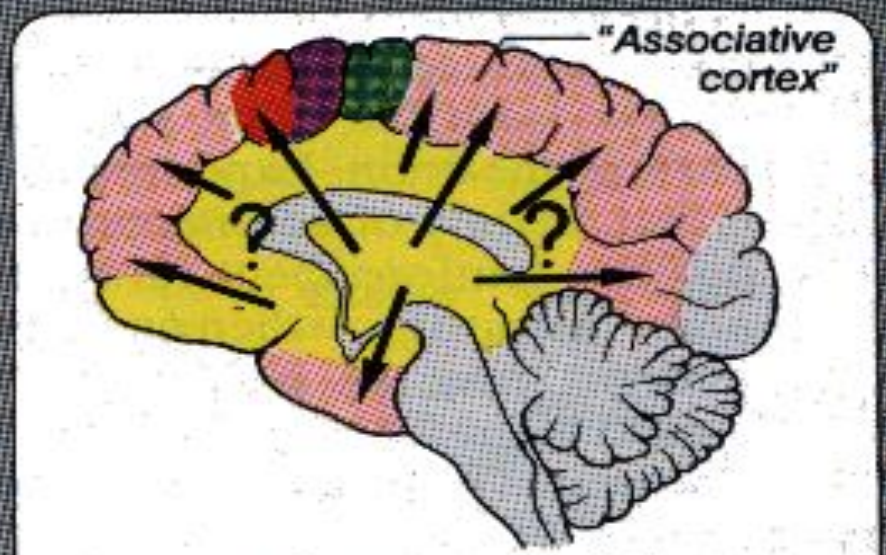




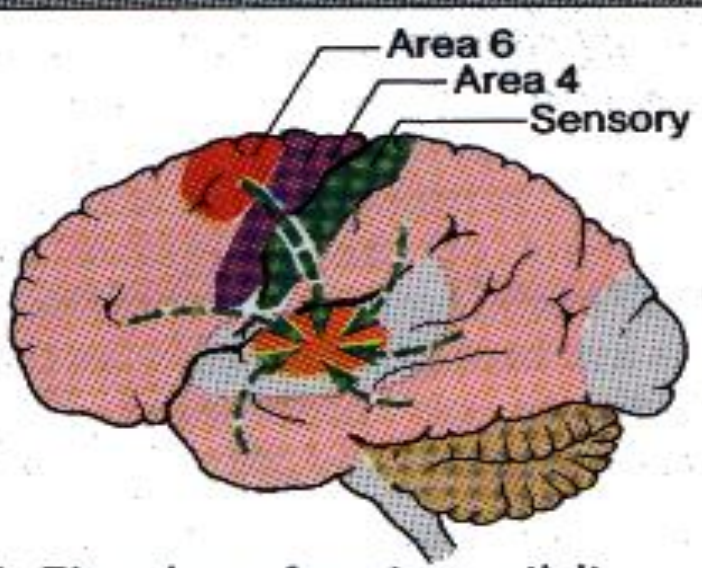
Motor hold and motor move integration



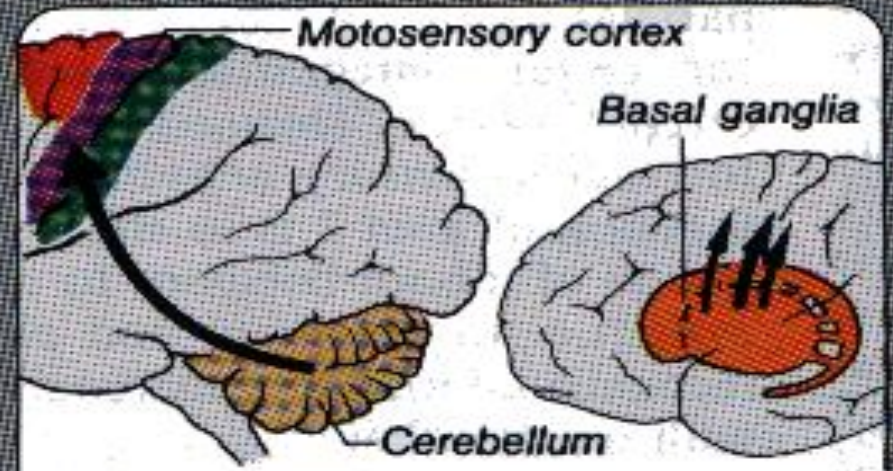
Basal ganglia: afferents and efferents



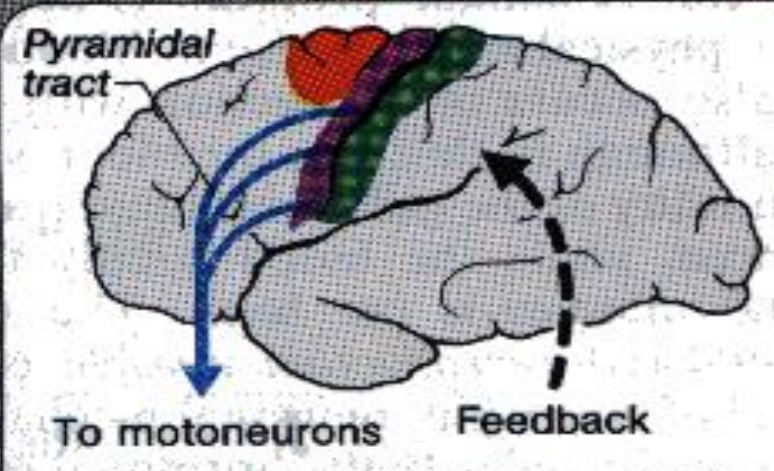
1. Impetus for motor activity
(limbic system, cortex, hypothalamus?)



2. Planning of motor activity
(associative cortex)

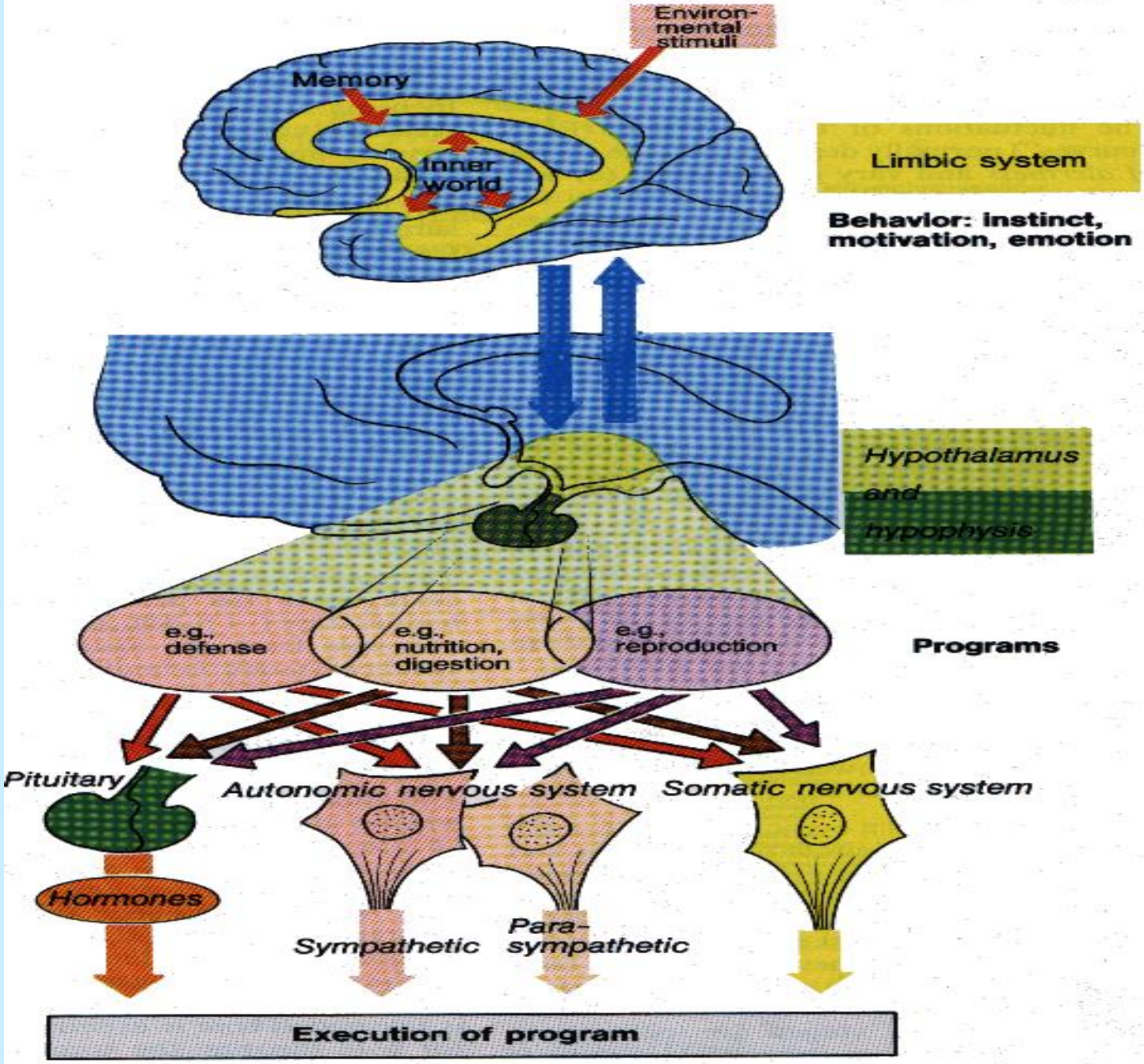


3. Recalling of programs
(cerebellum, basal ganglia)

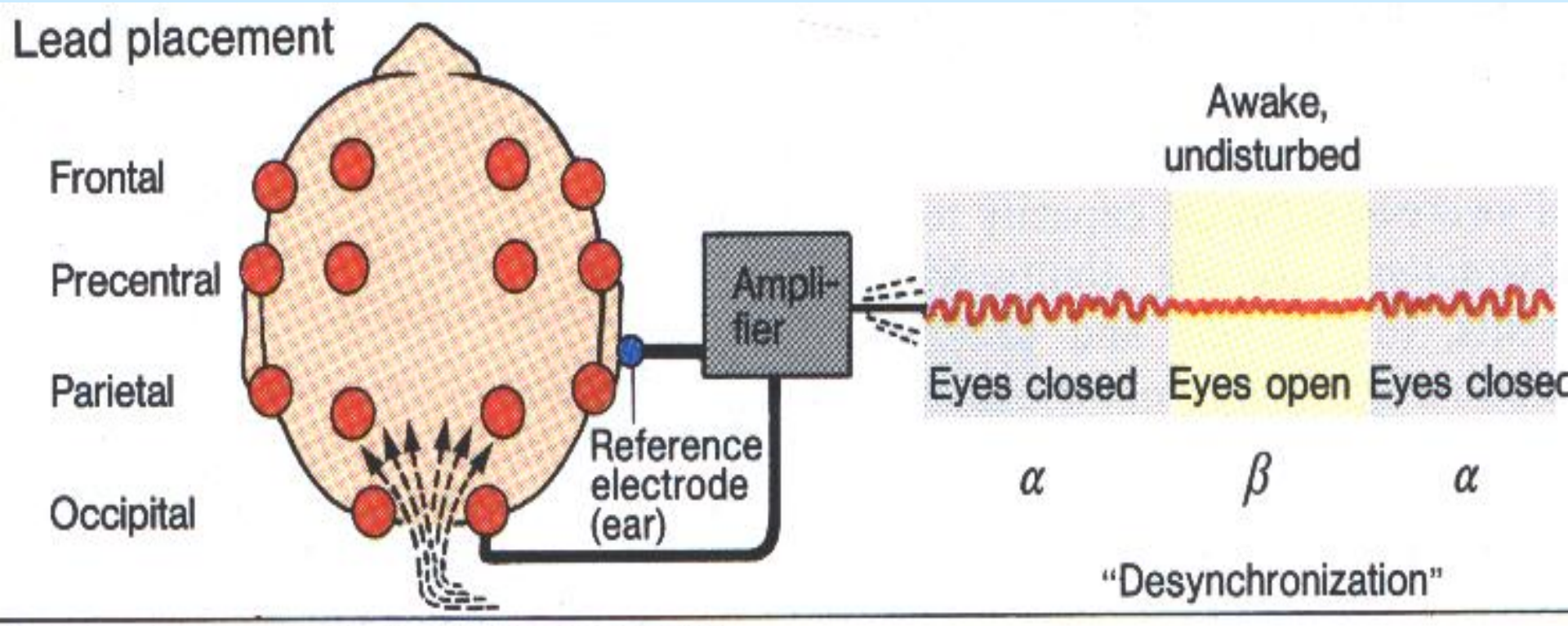


4. Execution of motor activitiy
(motosensory cortex)

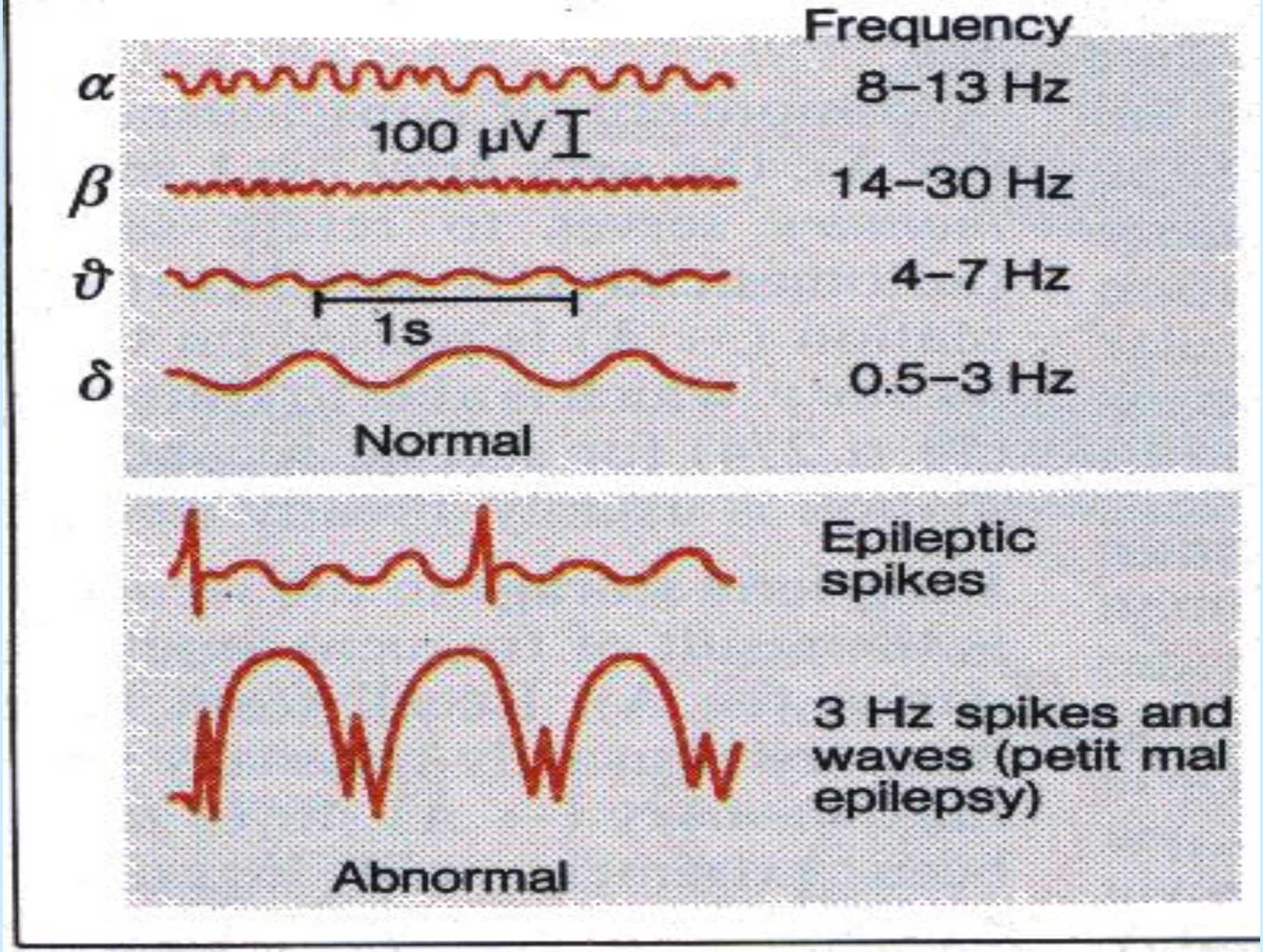
From Impetus to execution of motor activity



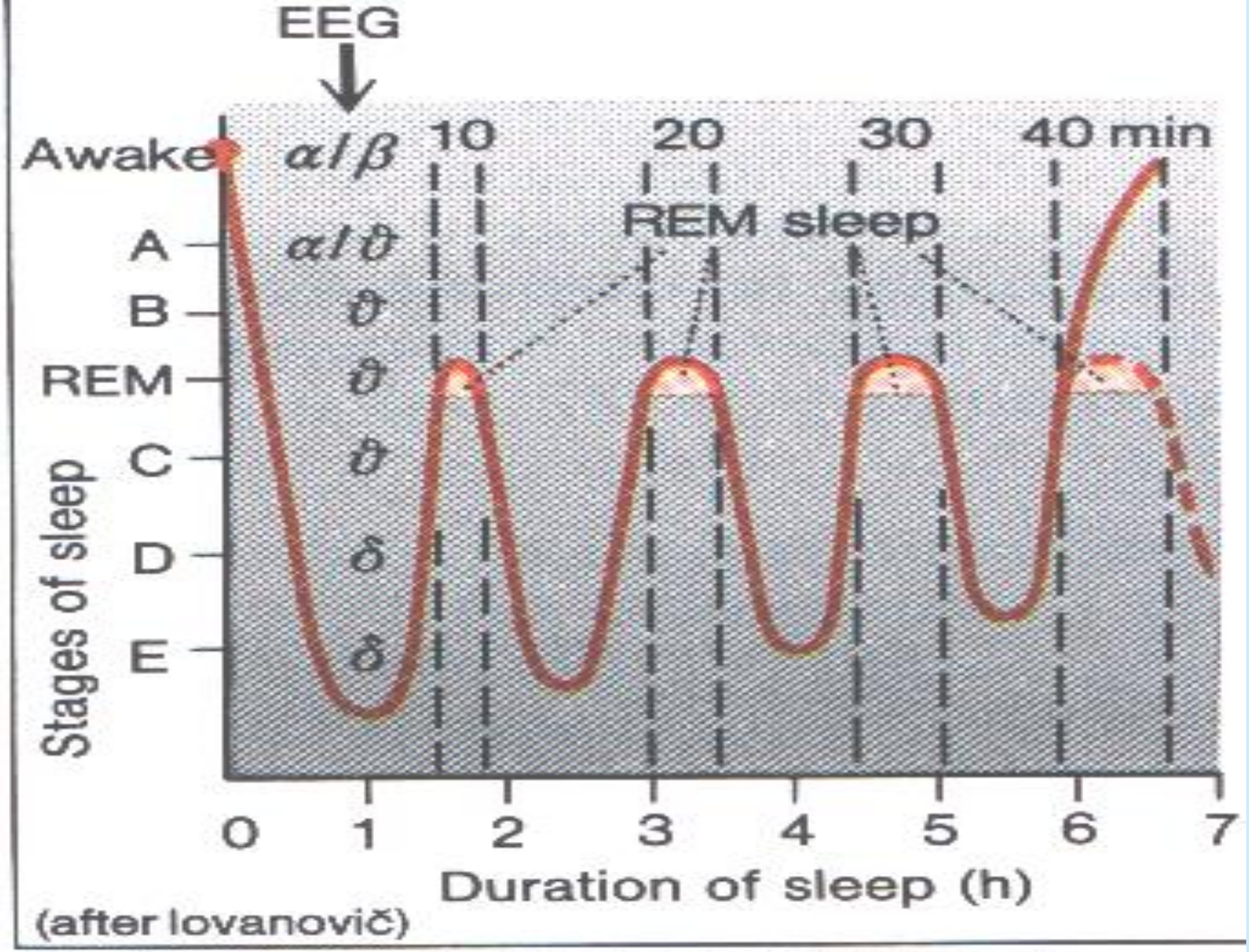
Limbic system and hypothalamus



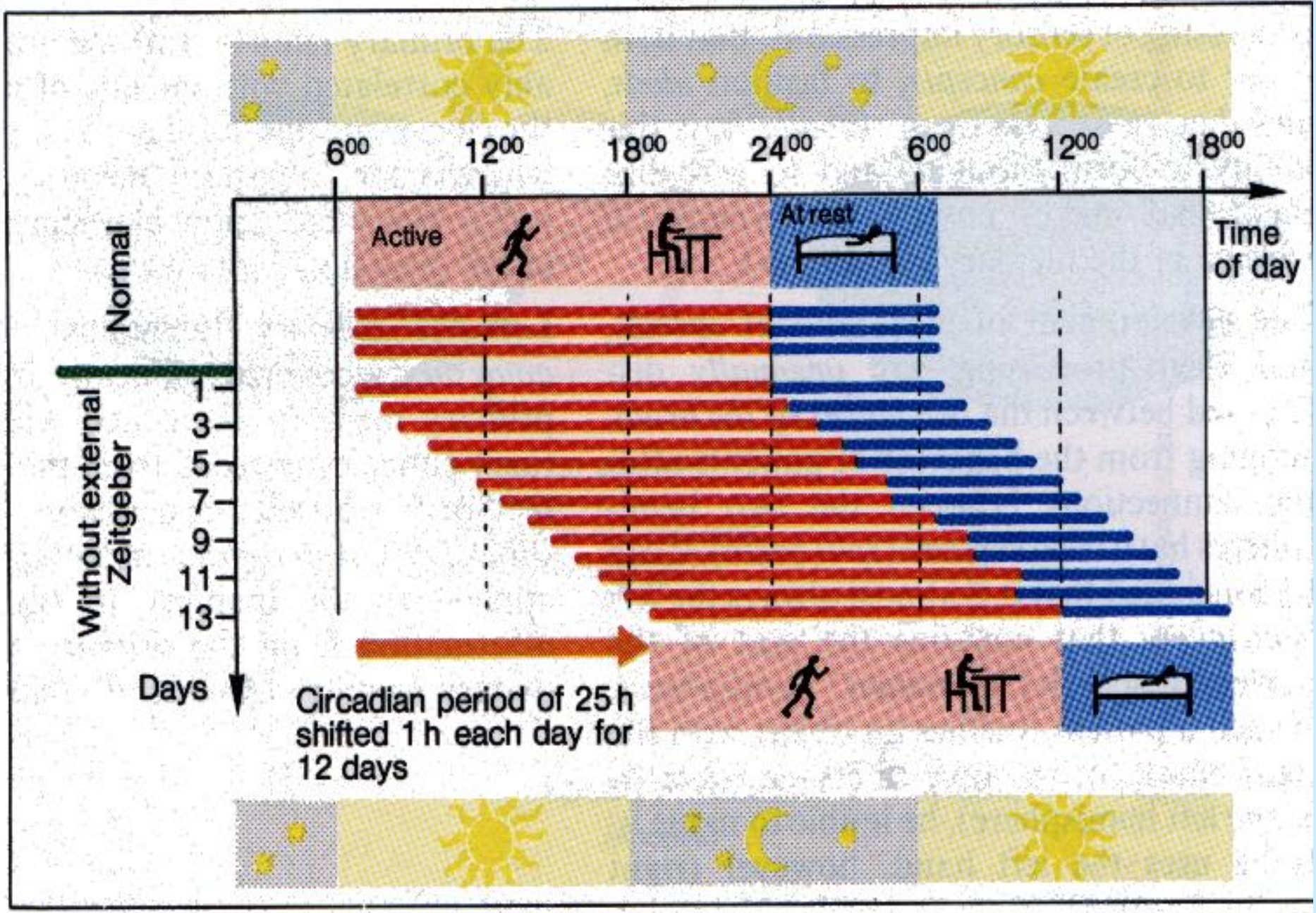
A. Electroencephalography (EEG)


Frequency
α
8–13 Hz
100 μV
β
14–30 Hz
ϑ
4–7 Hz
1s
δ
0.5–3 Hz
Normal
Epileptic spikes
3 Hz spikes and waves (petit mal epilepsy)
Abnormal

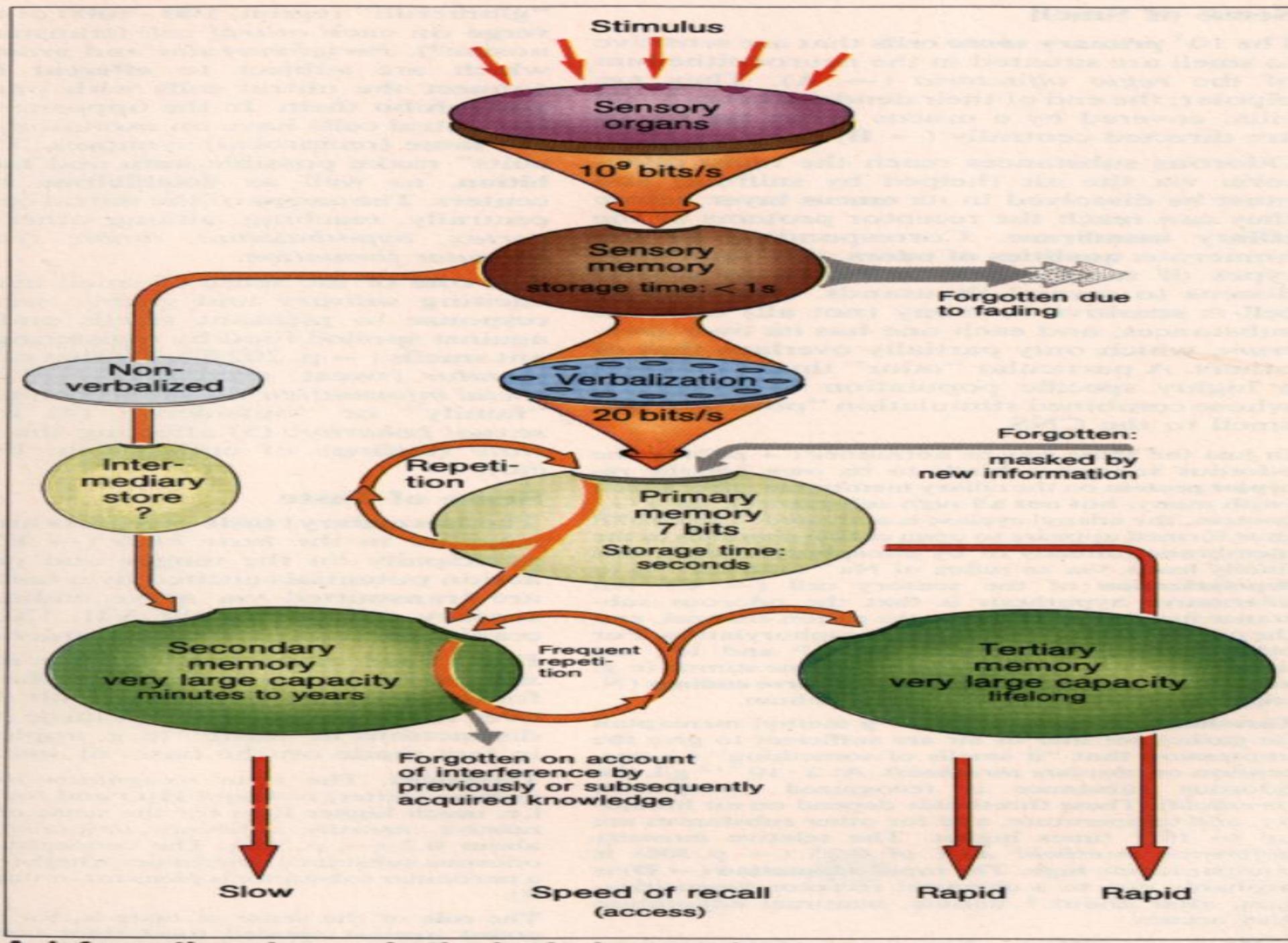
B. EEG waves



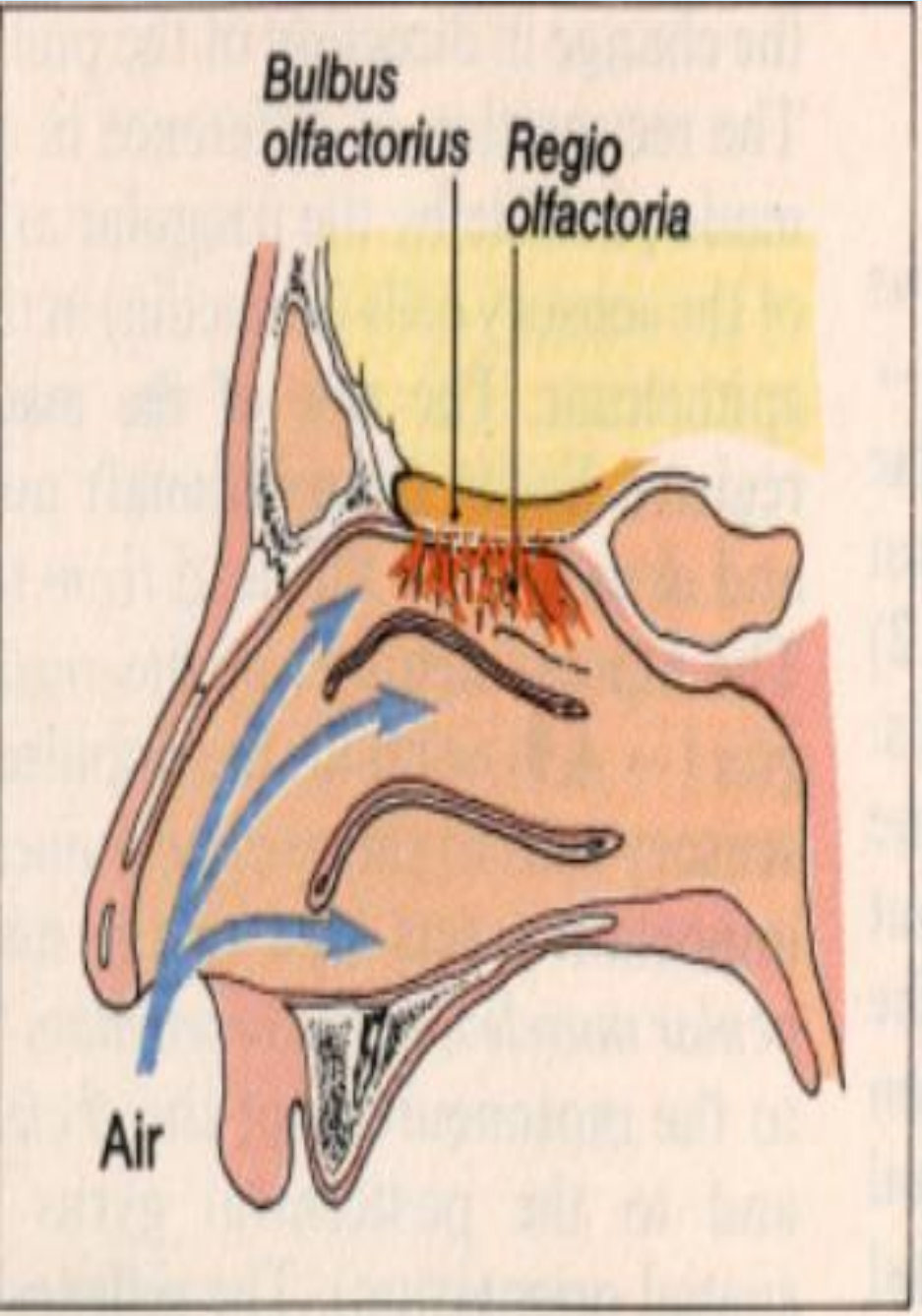
C. Stages of sleep, REM sleep



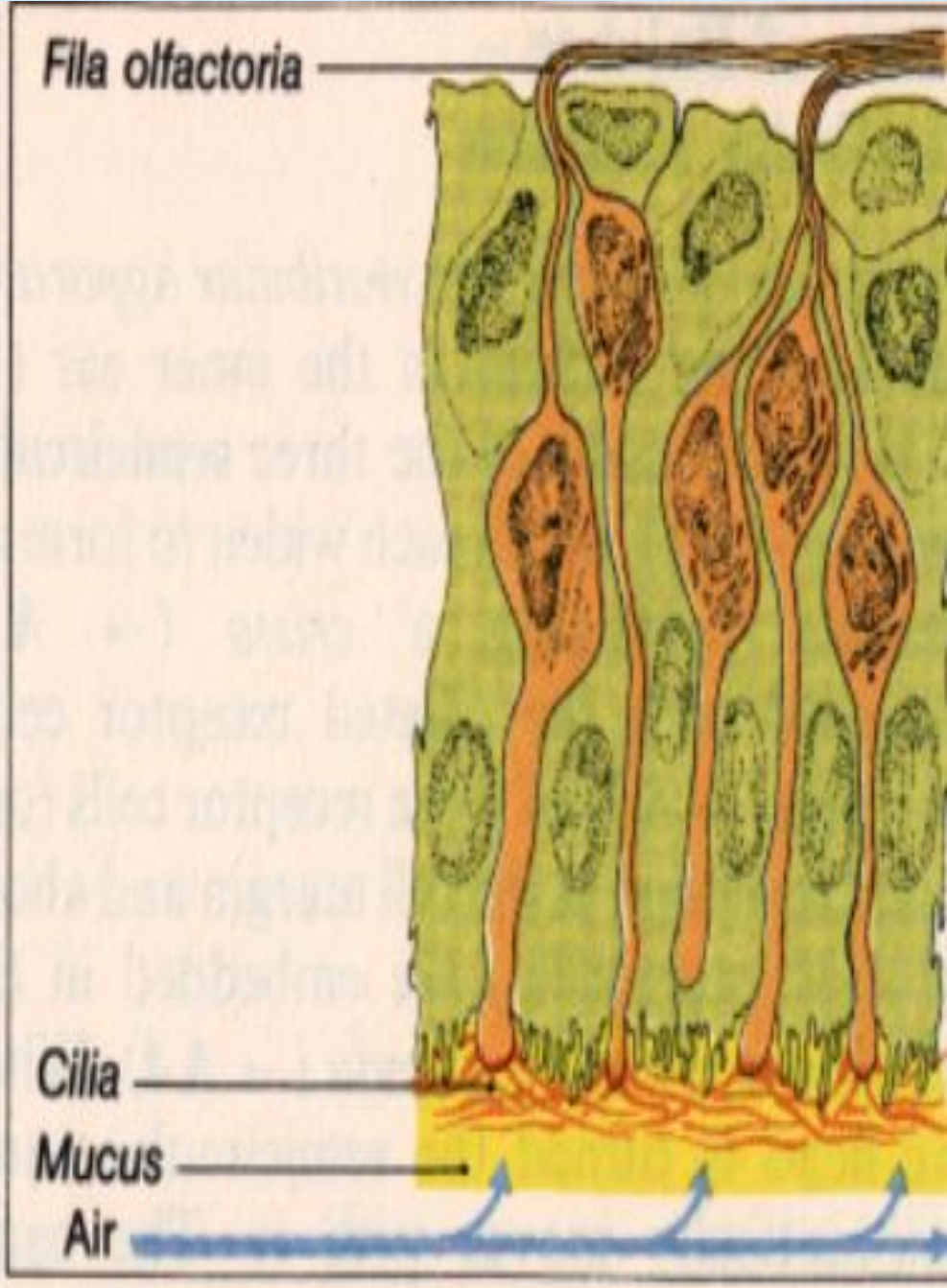
D. Circadian periods (after Aschoff)



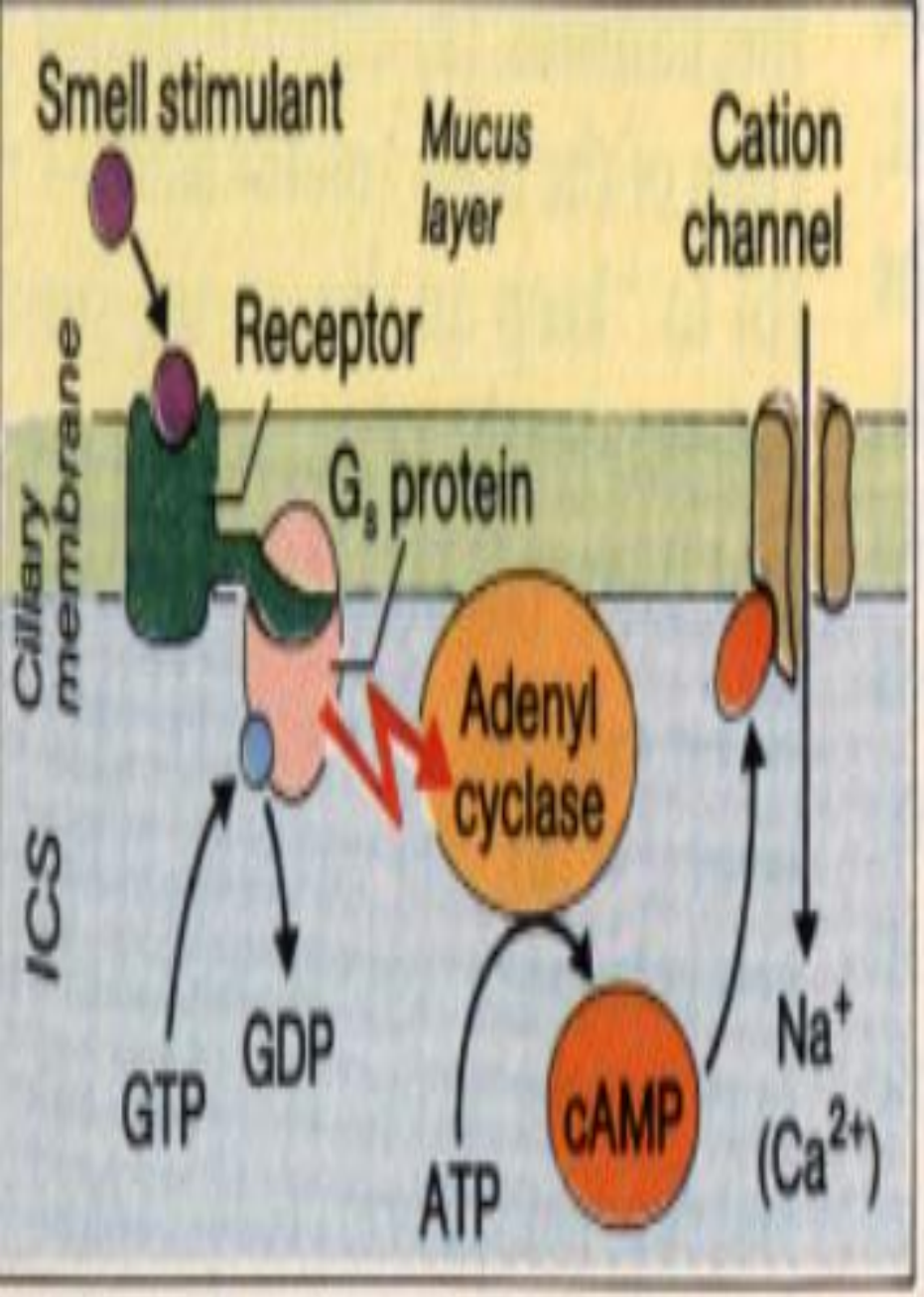
A. Information storage in the brain (memory)

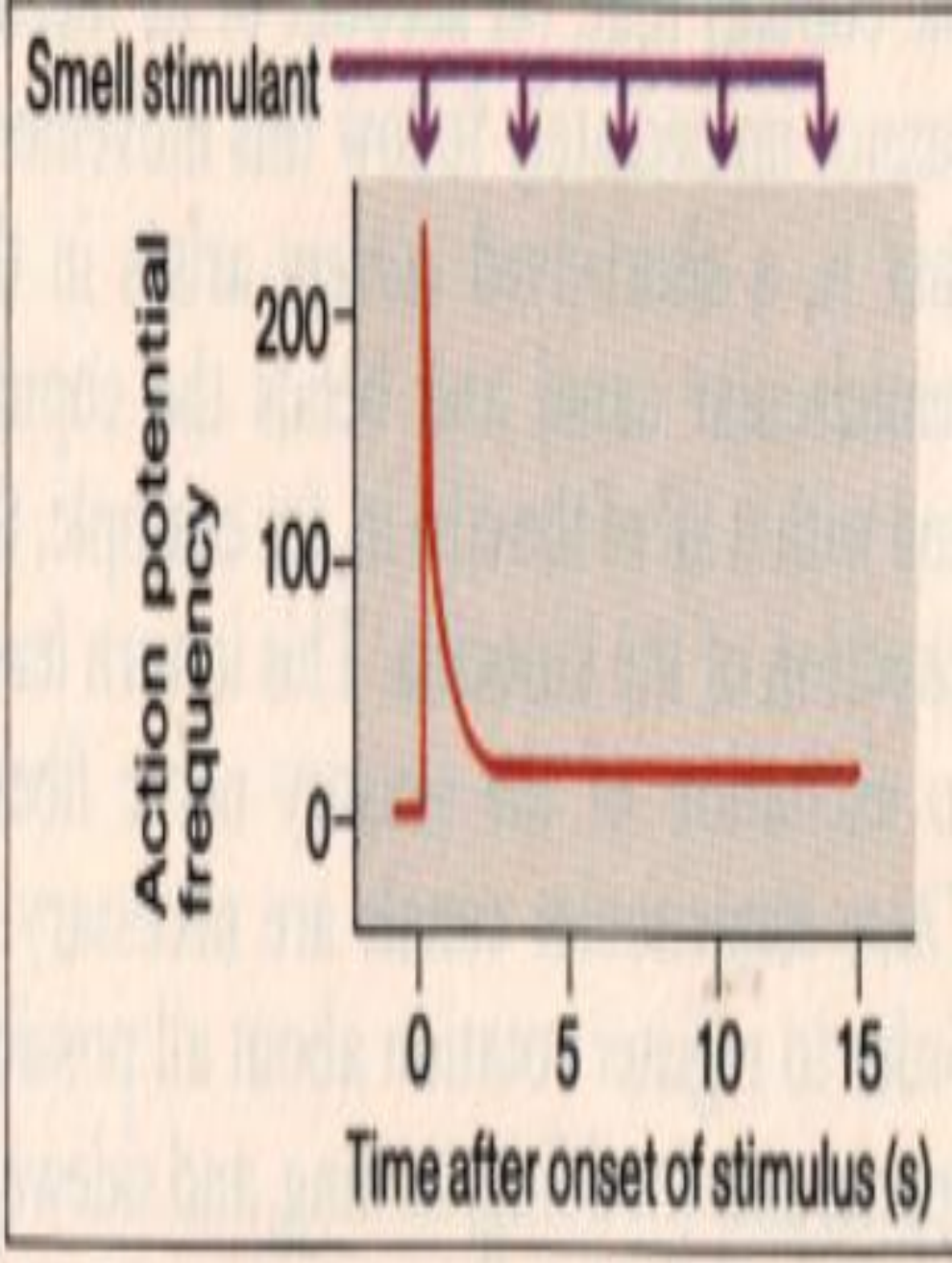


A. Nasal cavity: organ of smell

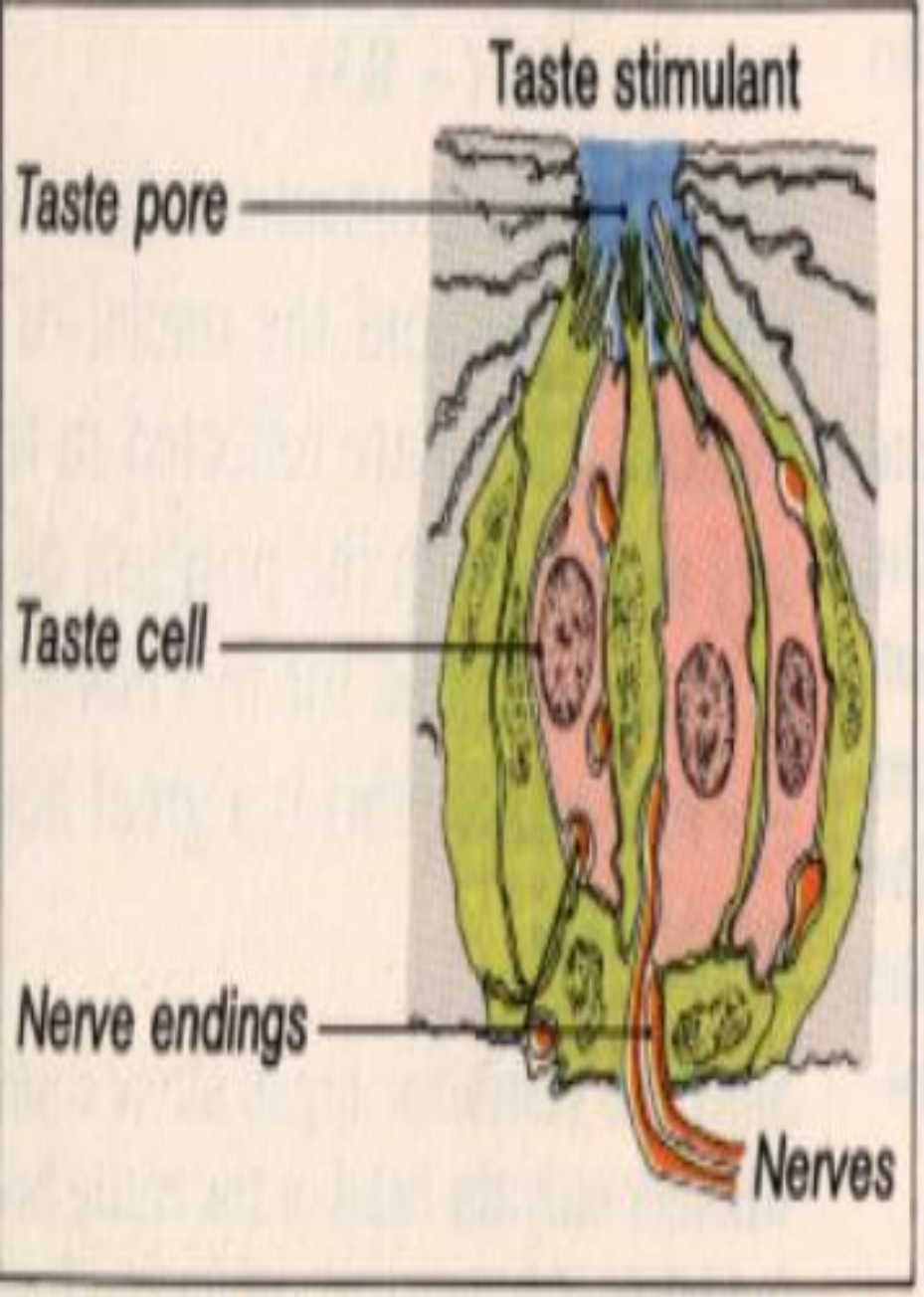


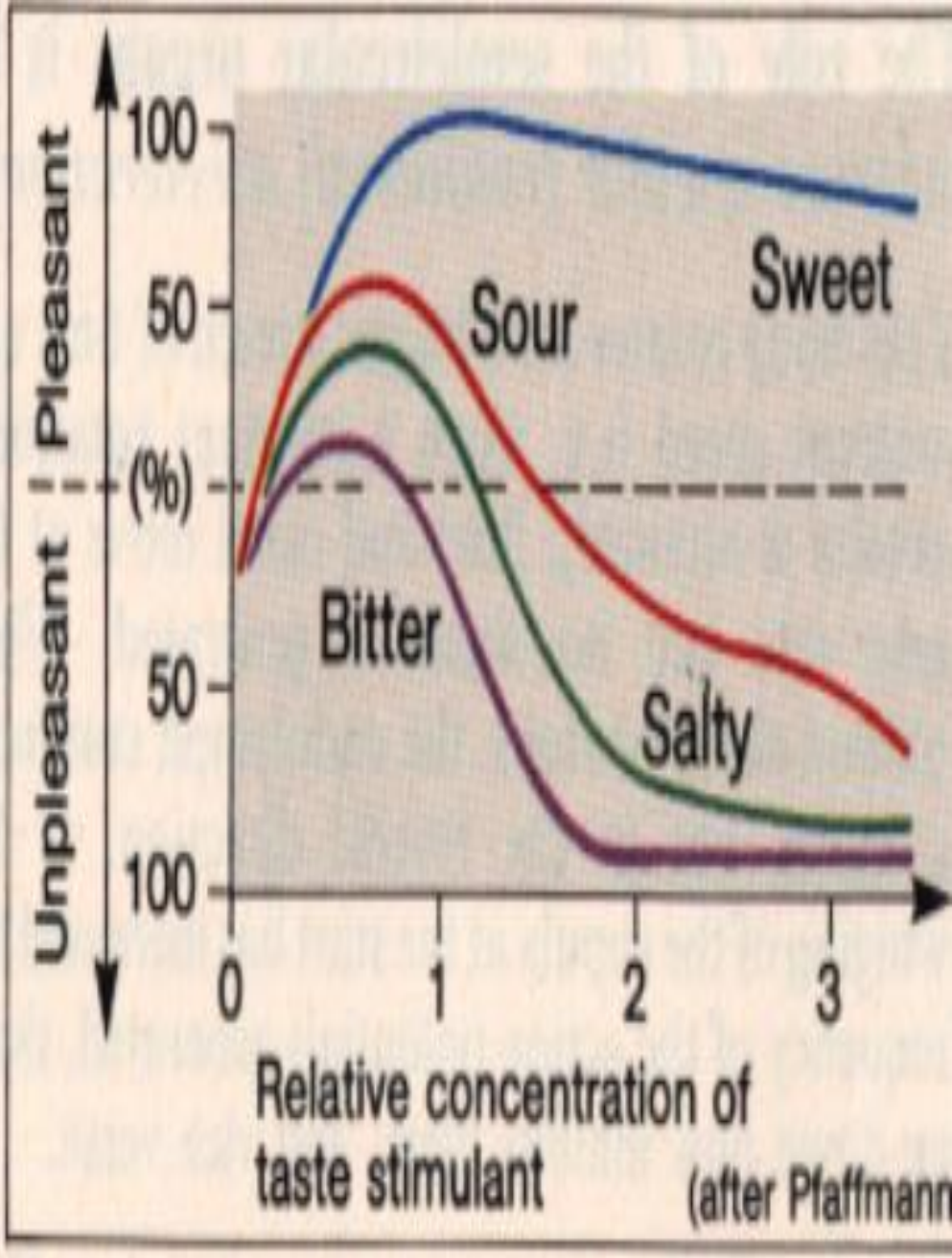
B. Olfactory epthelium (after Andre



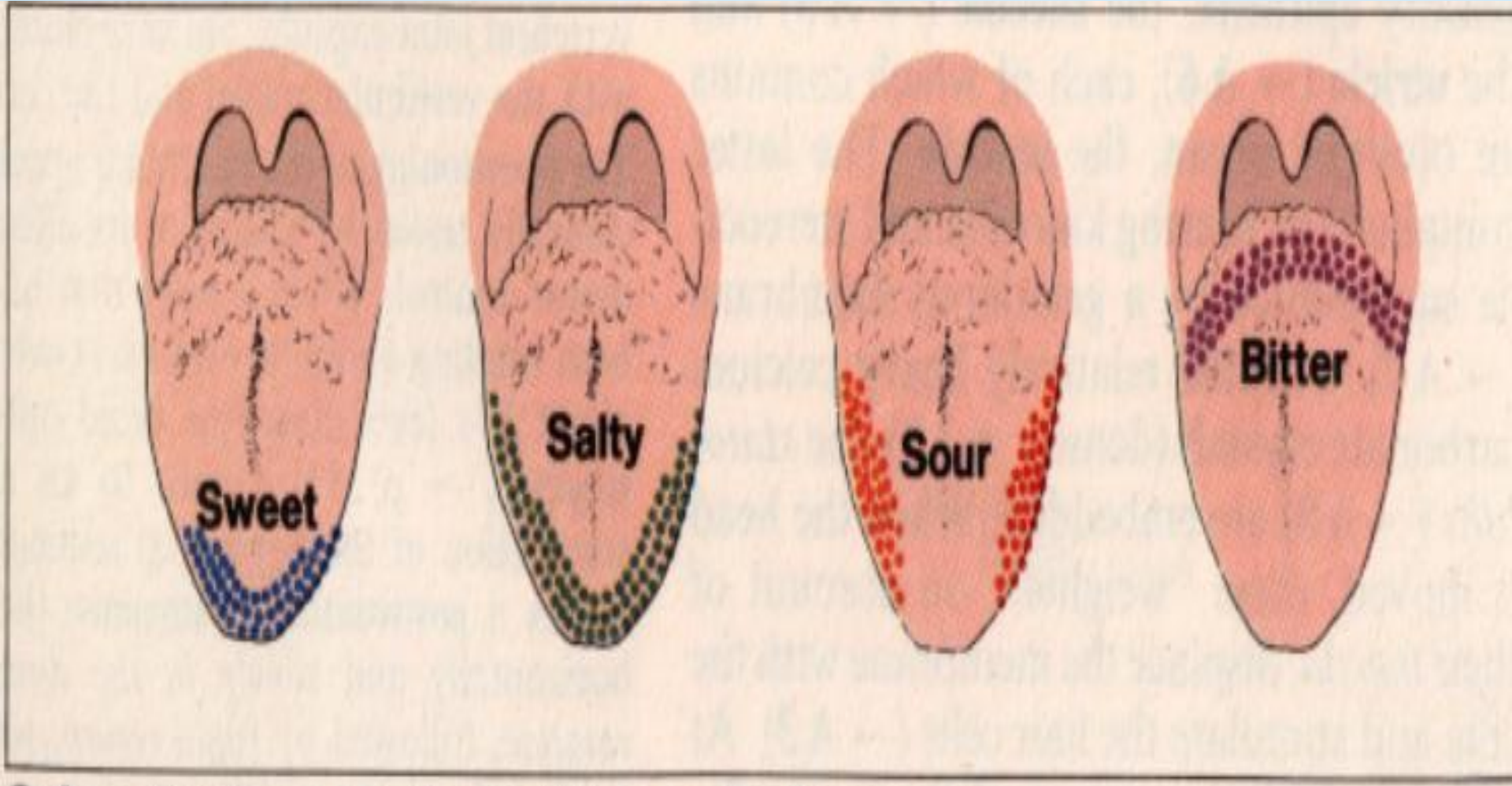


C. Transduction of olfactory stimulus D. Adaptation to smell



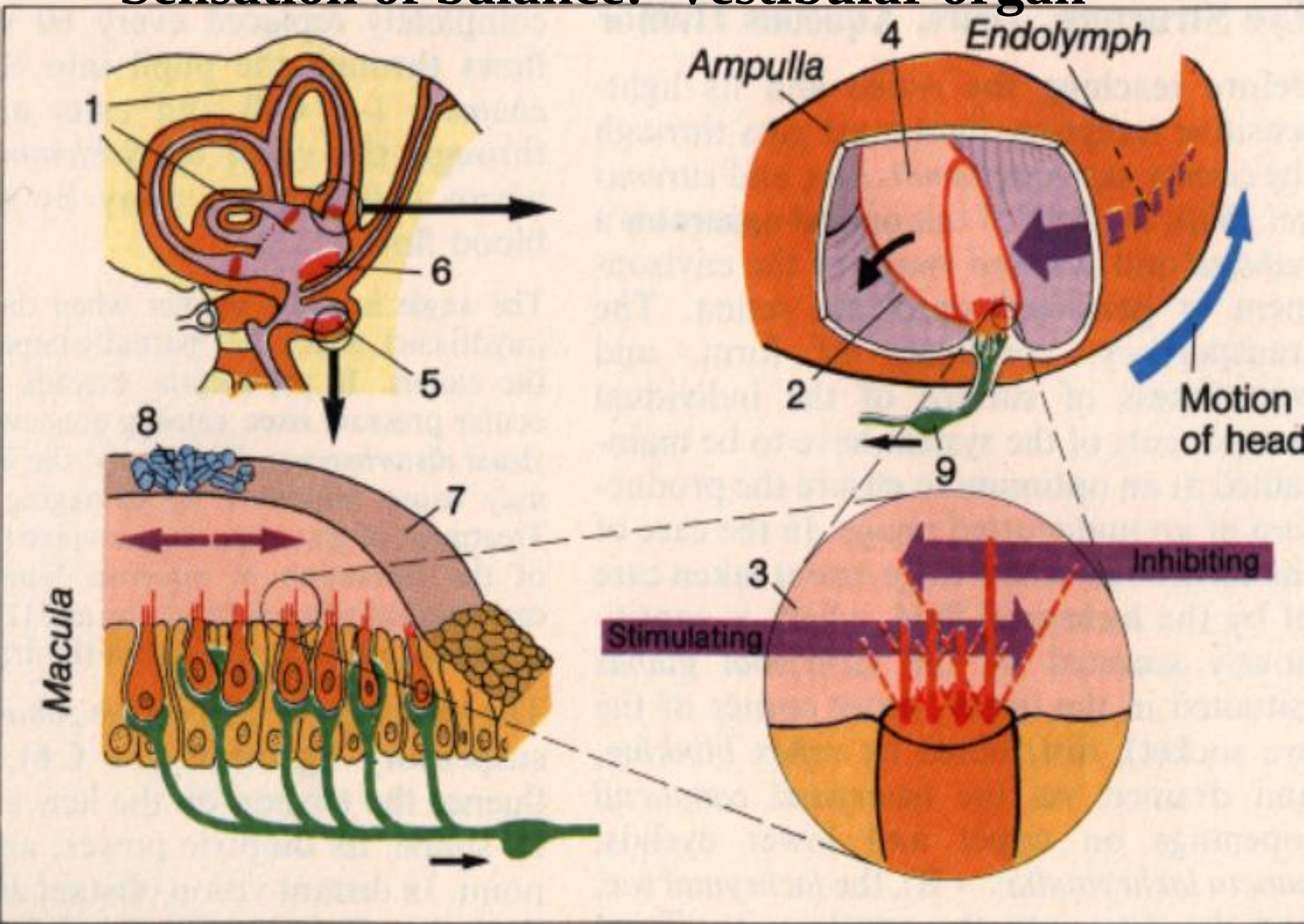


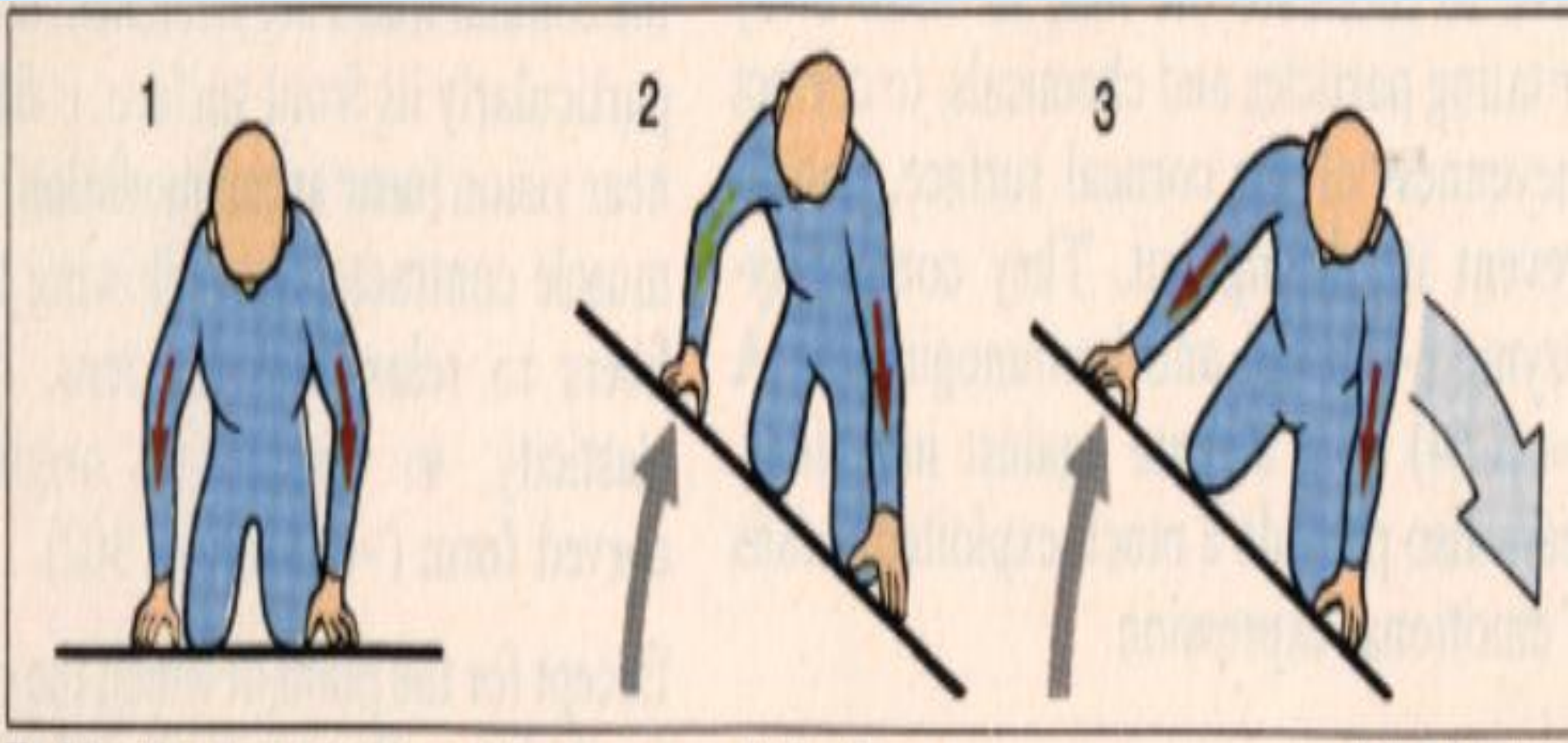
E. Taste buds (after Andres) **F. Evaluation of taste stimuli**



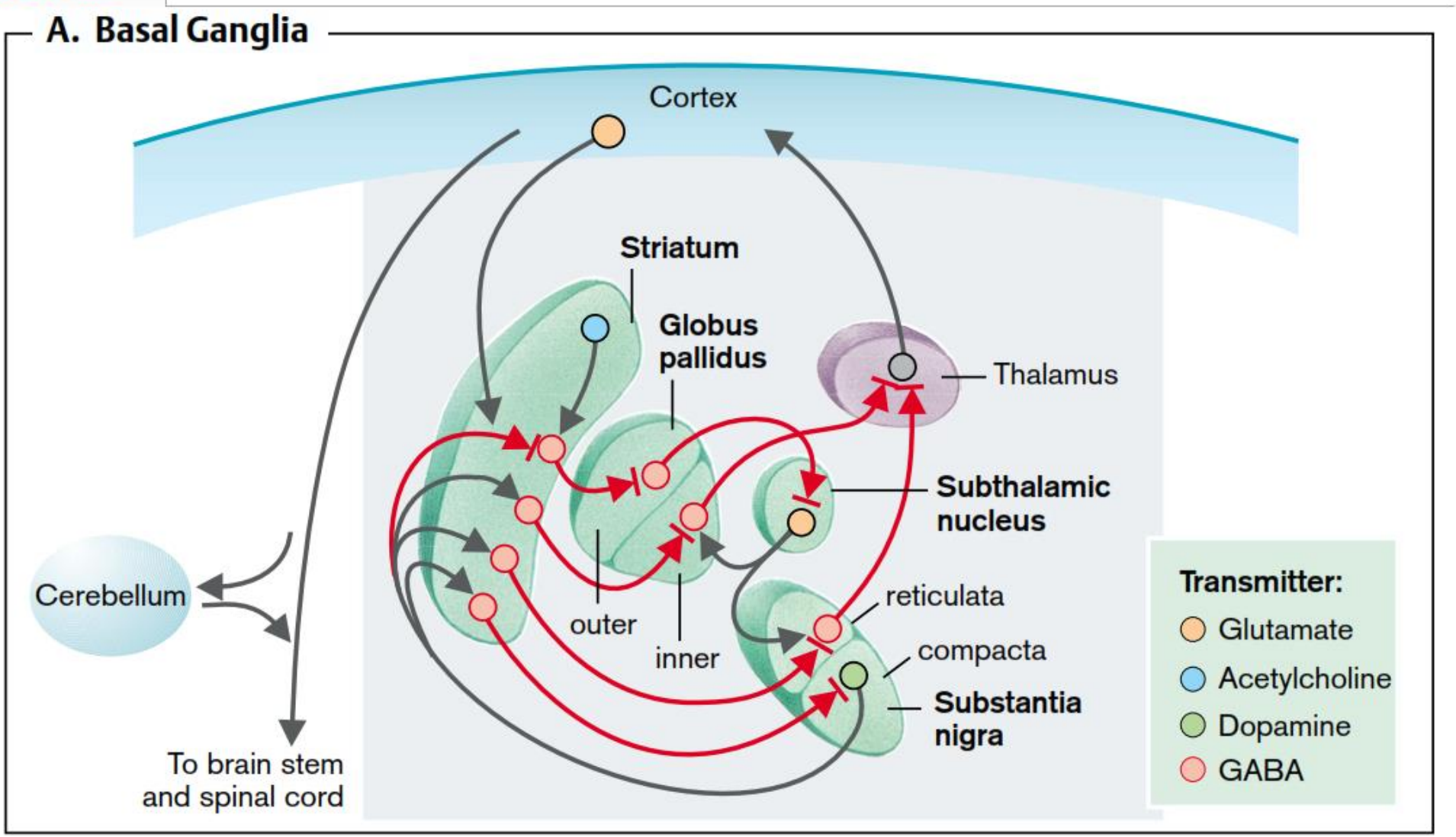
G. Localization of taste qualities on the tongue

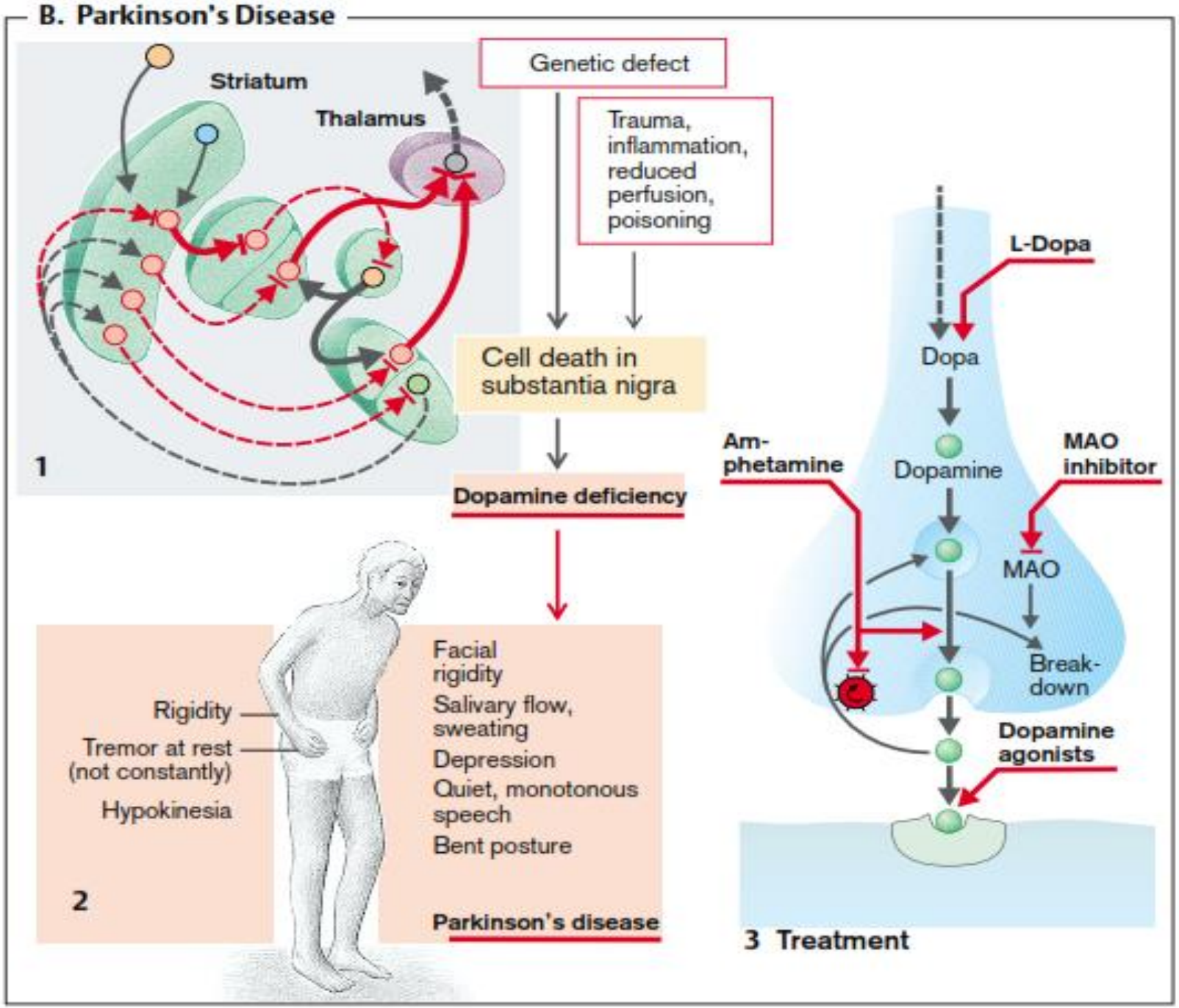
Sensation of balance: Vestibular organ

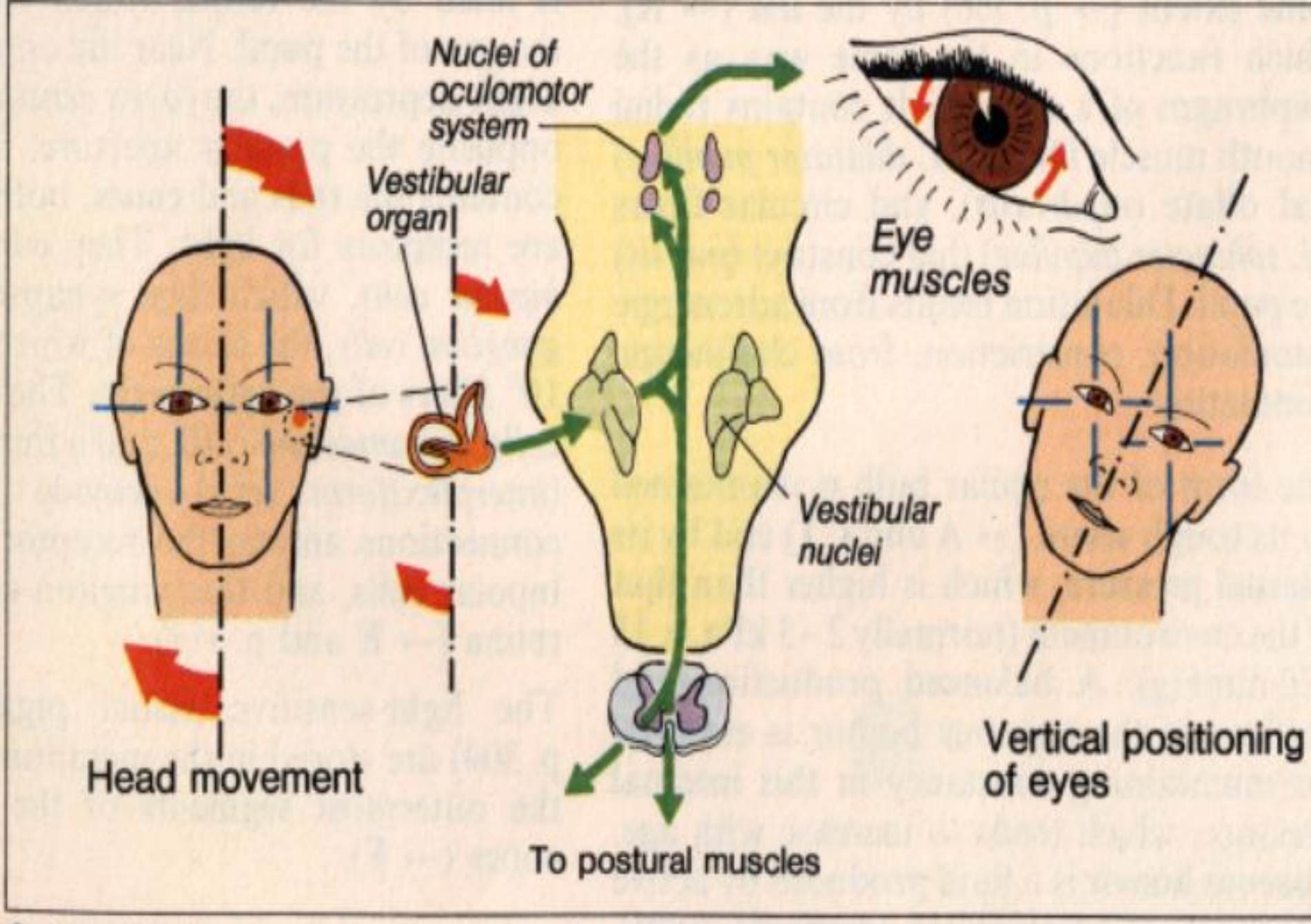




B. Vestibular organ: effect on equilibration (after Kornhub

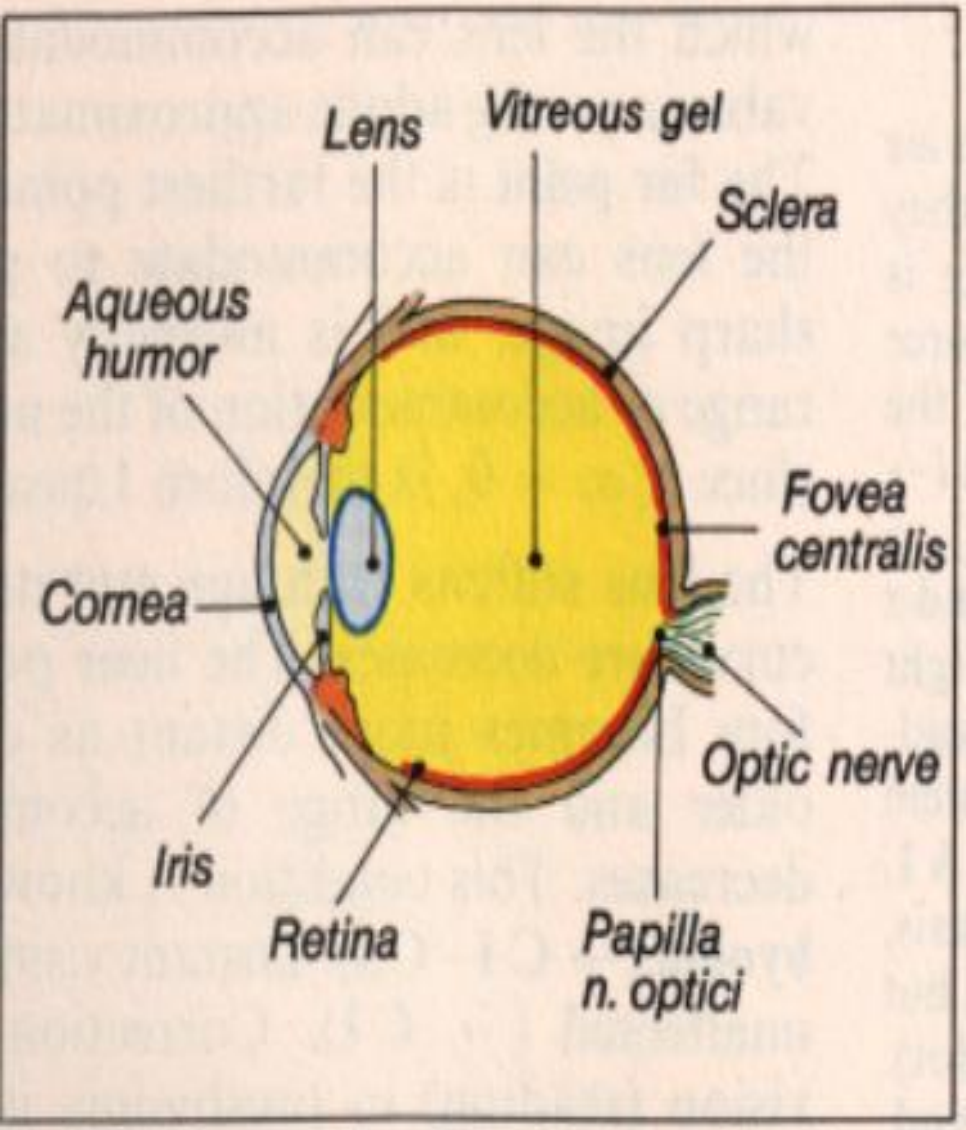

A. Basal Ganglia
Cortex
Striatum
Globus pallidus
Thalamus
Subthalamic nucleus
Cerebellum
outer
inner
reticulata
compacta
Substantia nigra
To brain stem and spinal cord
Transmitter:
Glutamate
Acetylcholine
Dopamine
GABA


B. Parkinson's Disease
Striatum
Thalamus
1
Genetic defect
Trauma, inflammation, reduced perfusion, poisoning
Cell death in substantia nigra
Dopamine deficiency
Rigidity
Tremor at rest (not constantly)
Hypokinesia
2
Facial rigidity
Salivary flow, sweating
Depression
Quiet, monotonous speech
Bent posture
Parkinson's disease
L-Dopa
Dopa
Dopamine
Am-phetamine
MAO inhibitor
MAO
Break-down
Dopamine agonists
3 Treatment

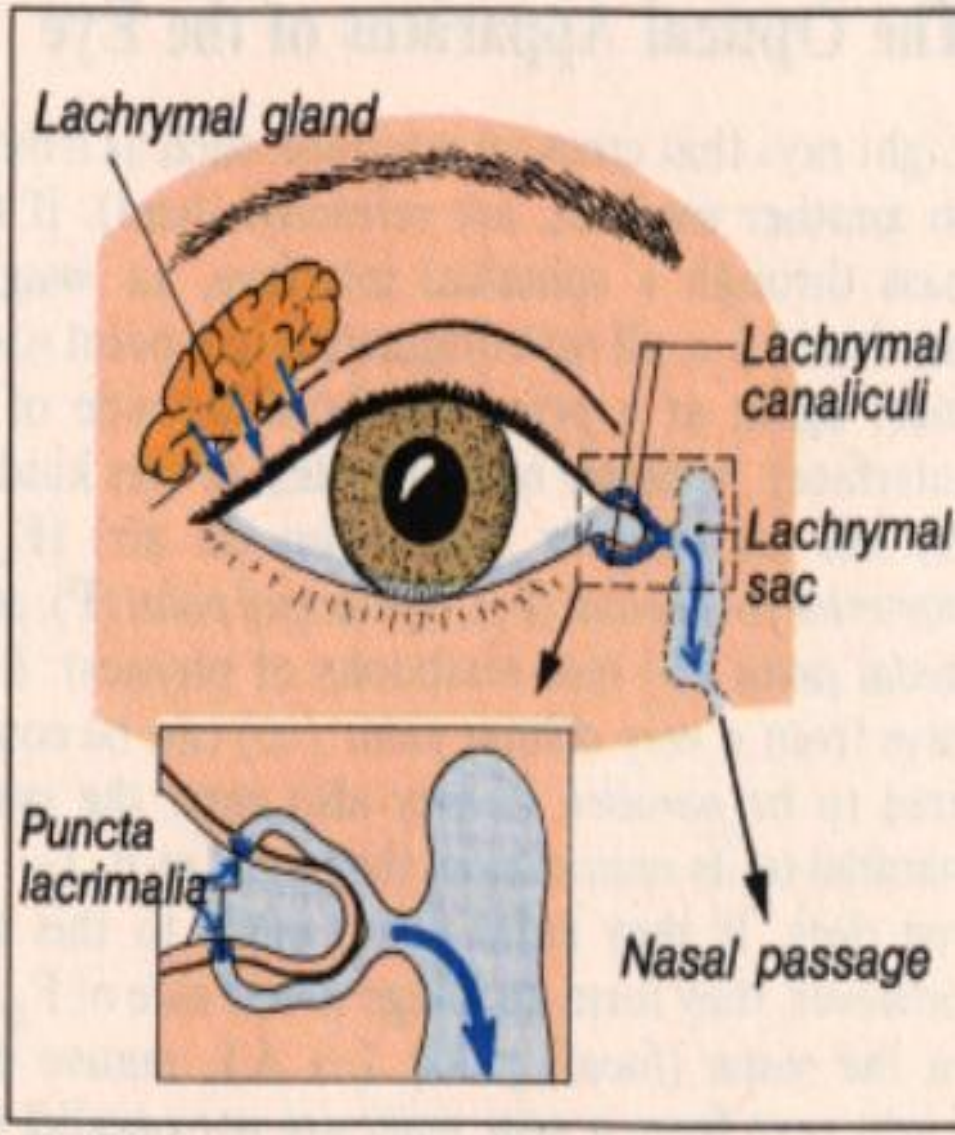


C. Vestibular organ: effect on eye movement

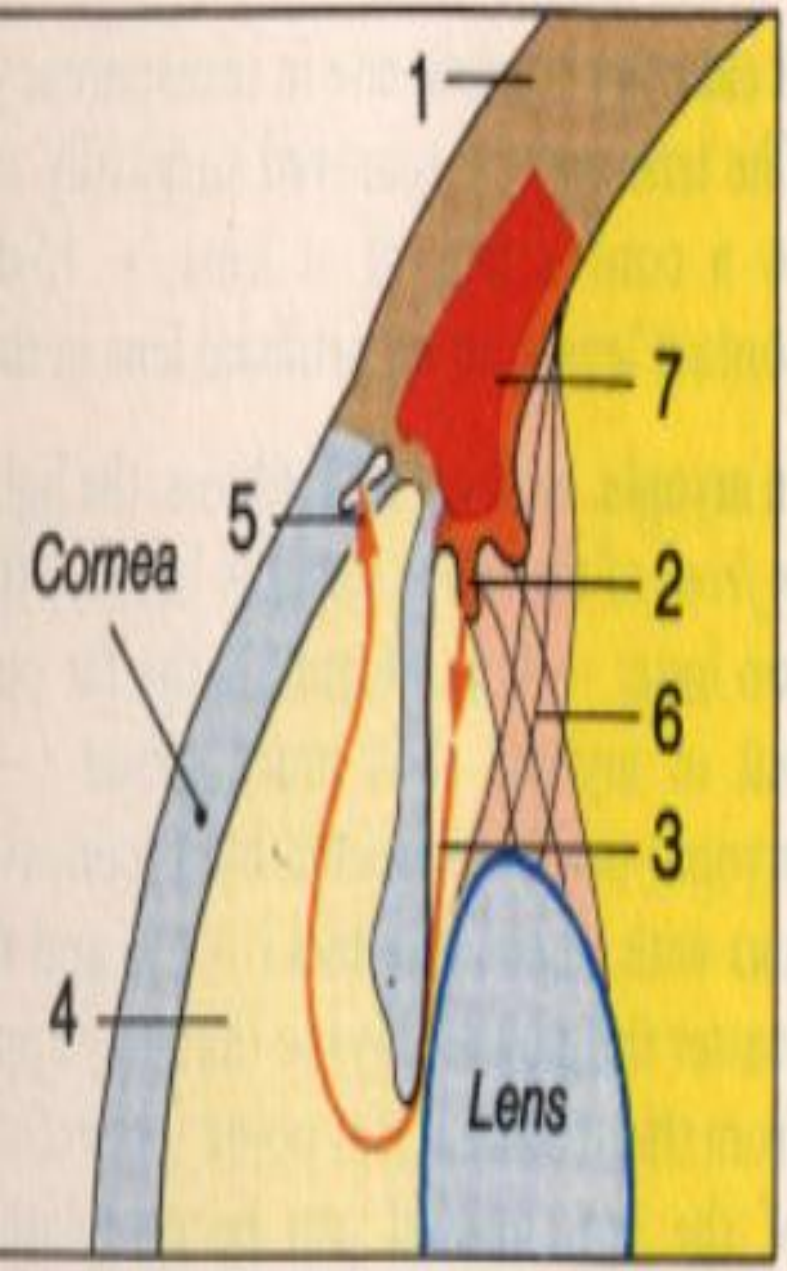
vision



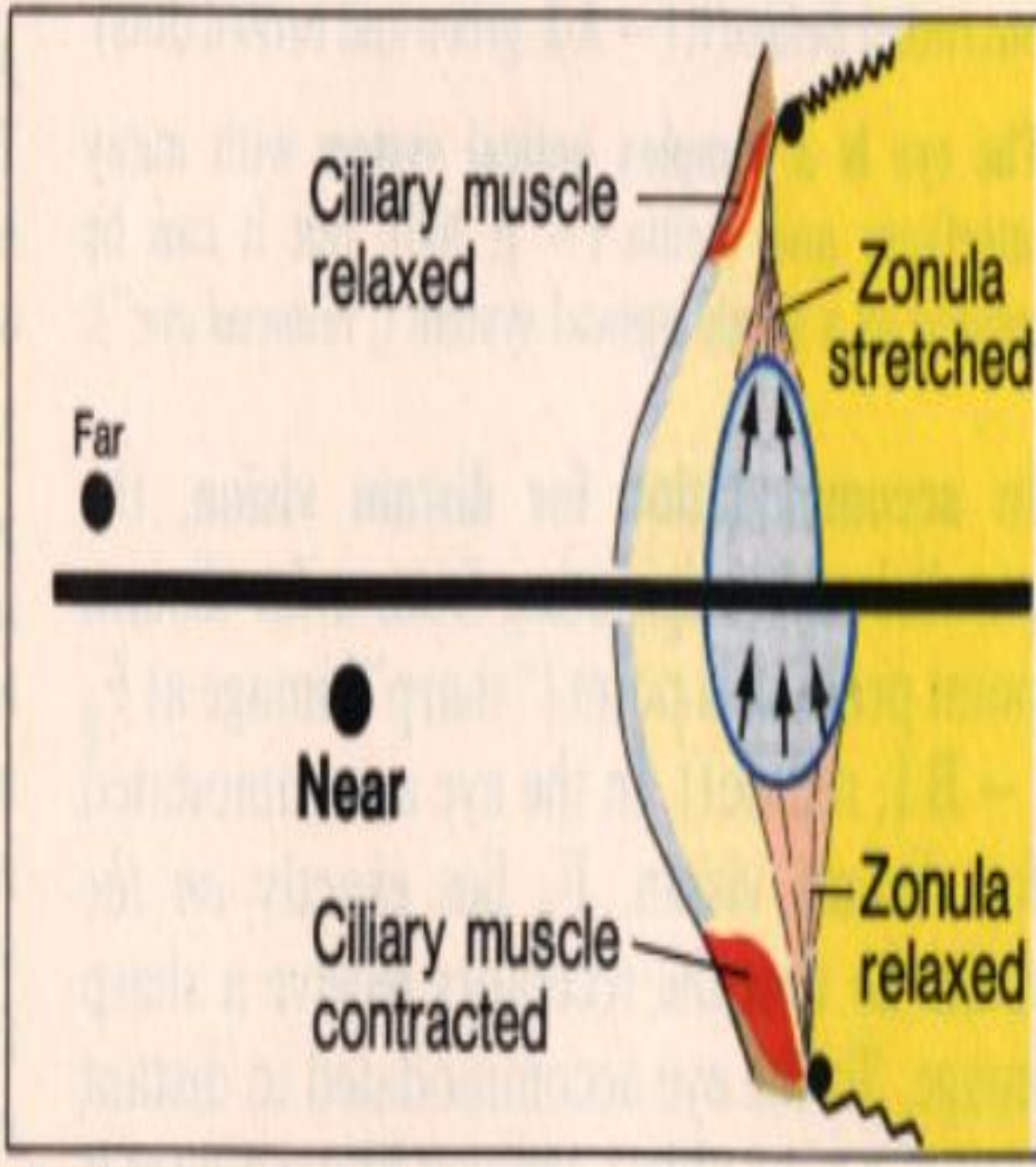
A. Right eye (horizontal section)



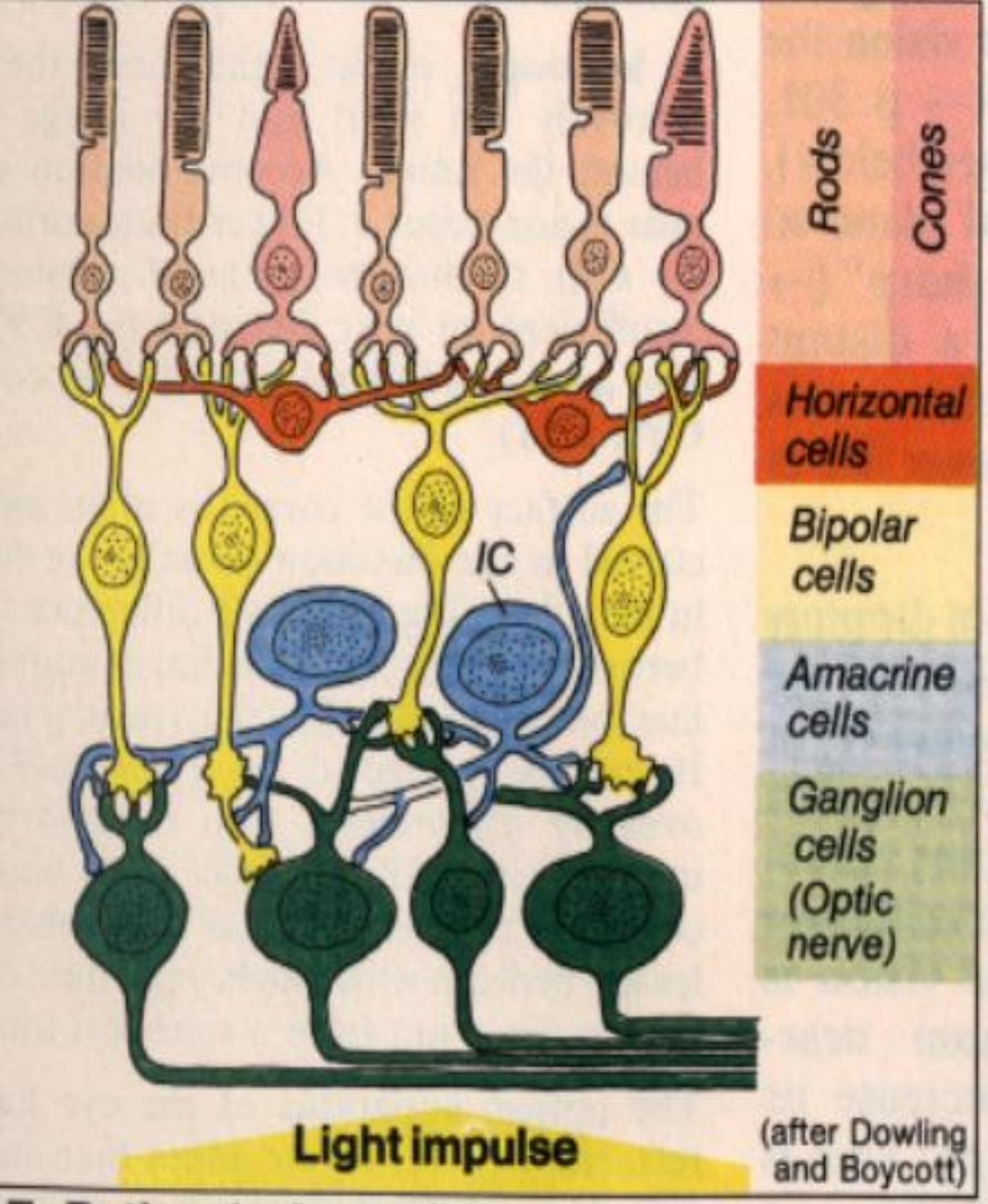
B. Right eye: tear flow



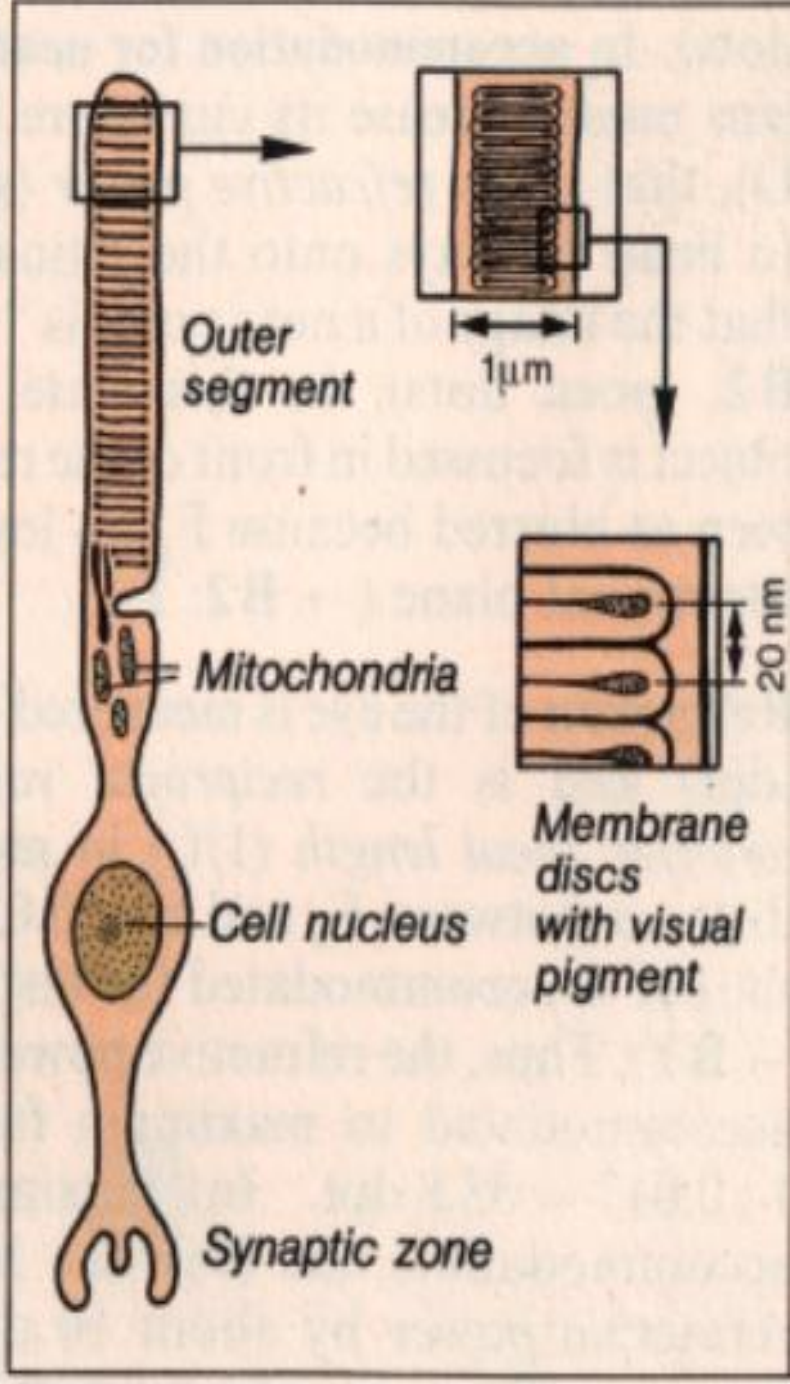
C. Aqueous humor



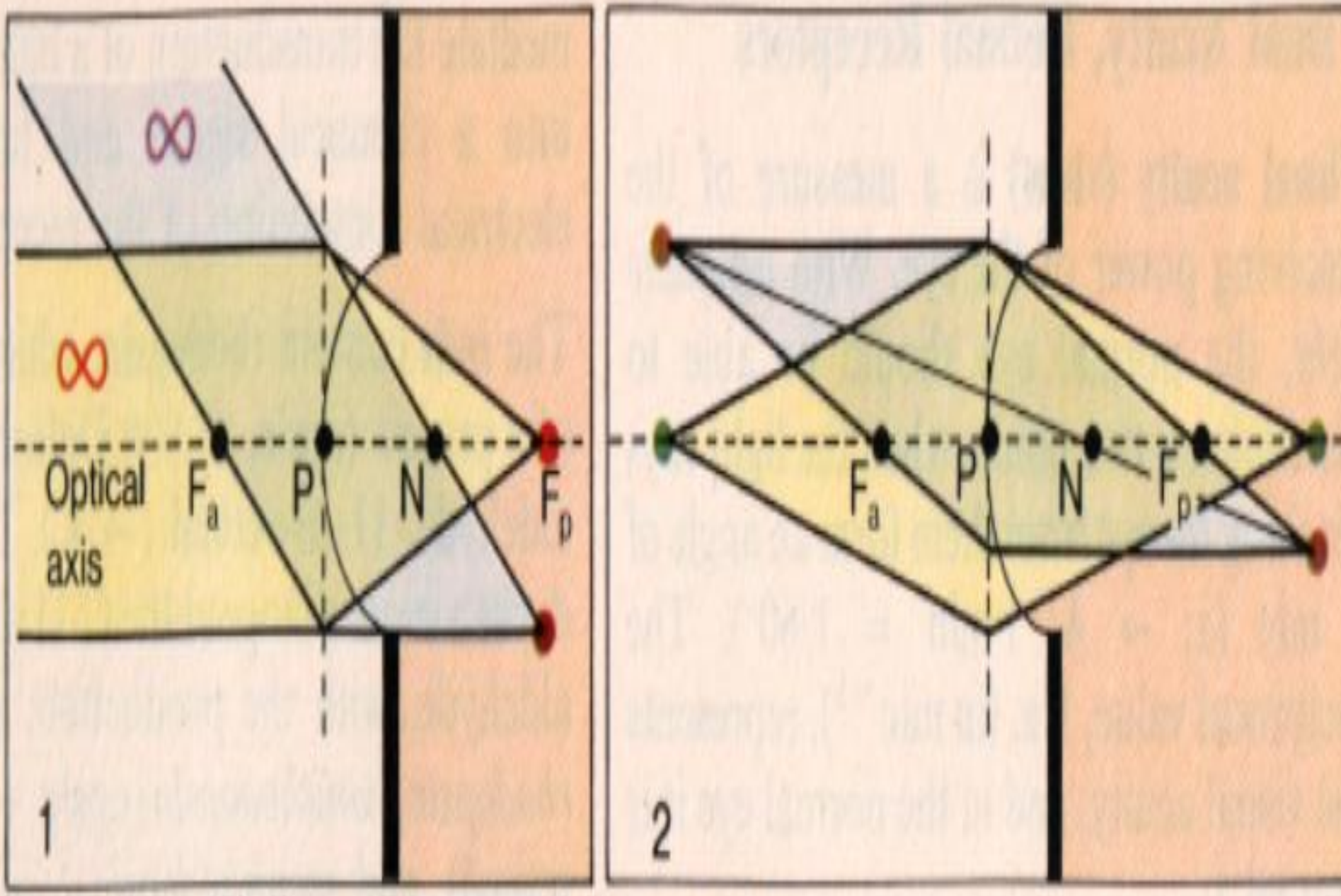
D. Accommodation



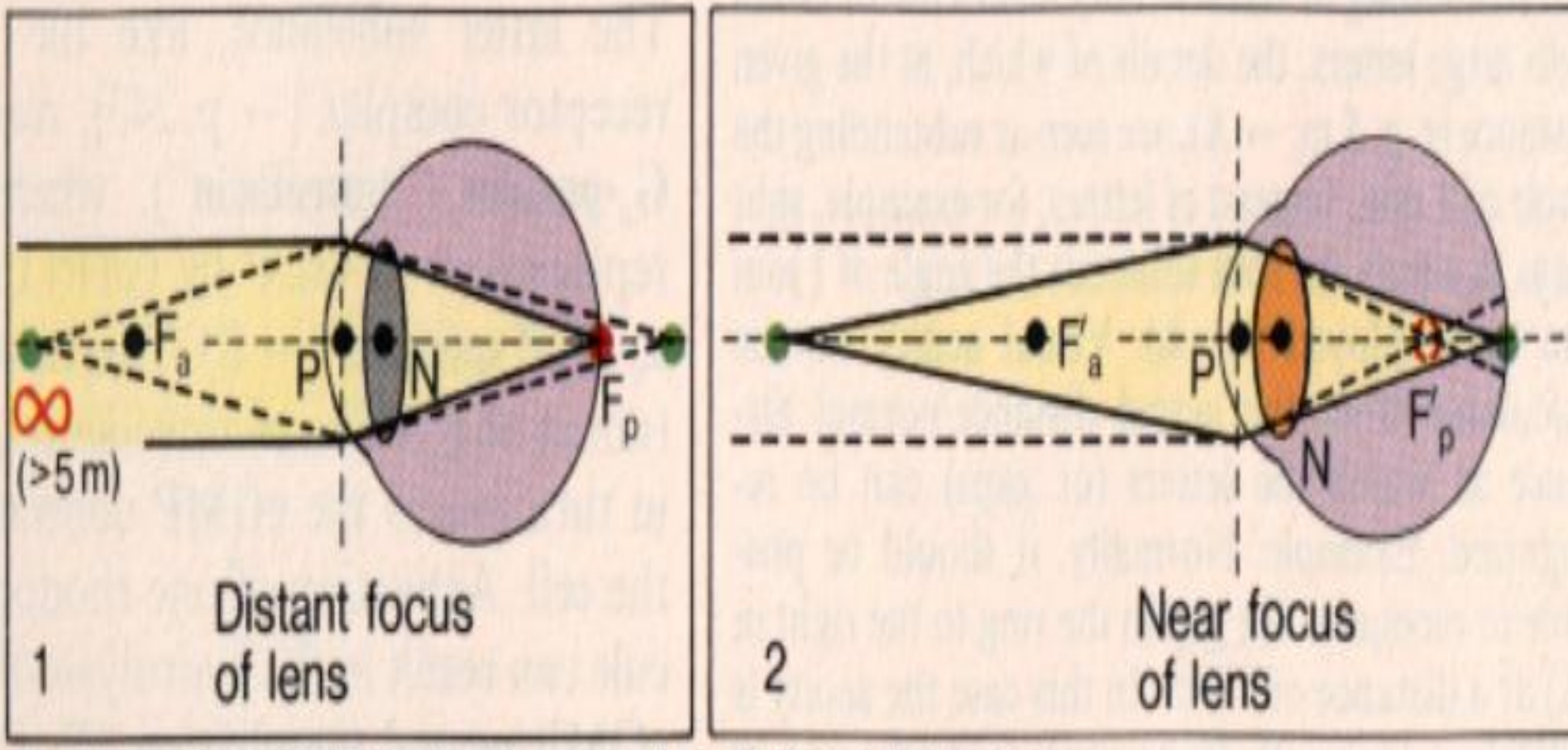
E. Retina (schematic)



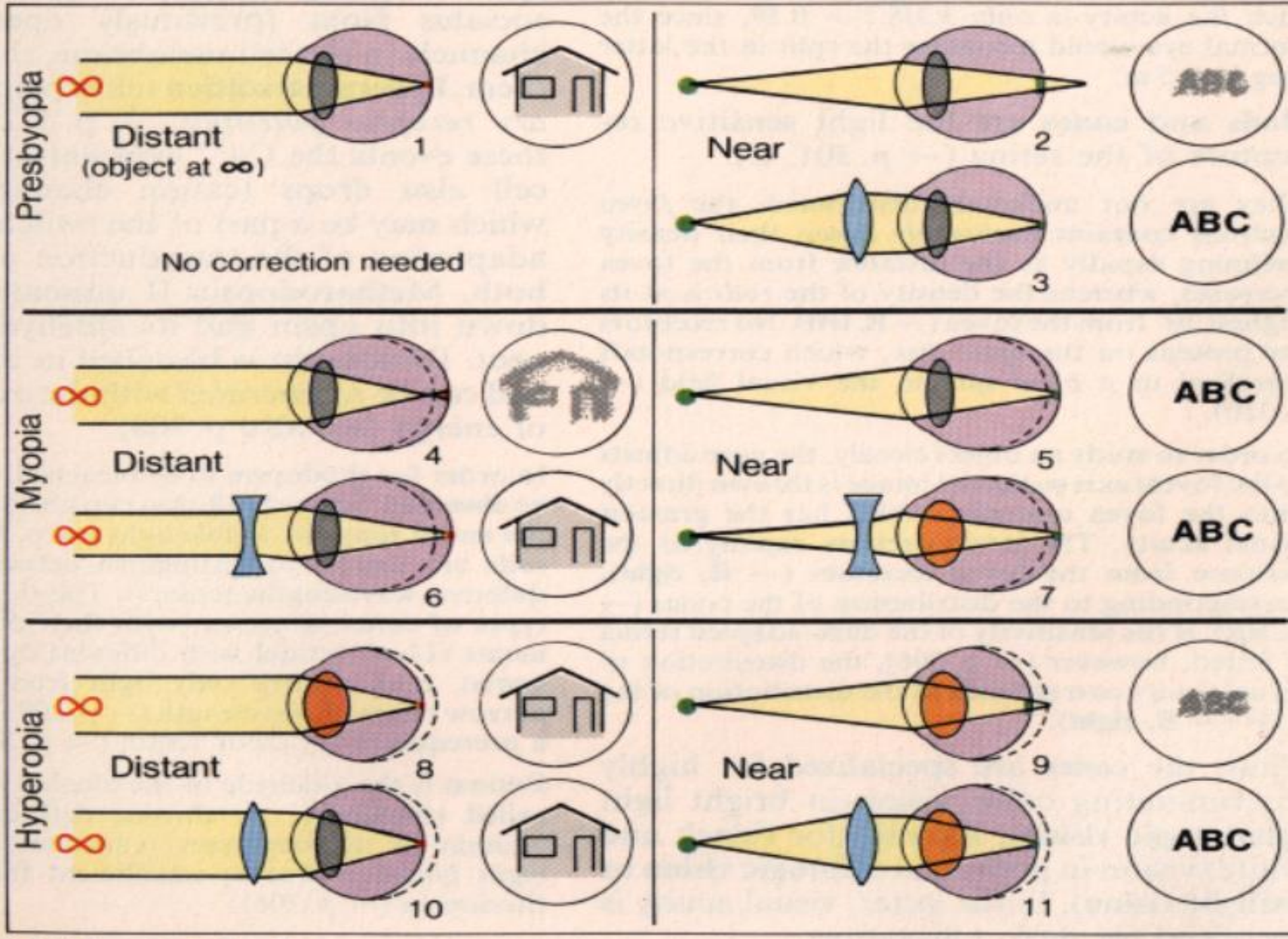
F. Rods



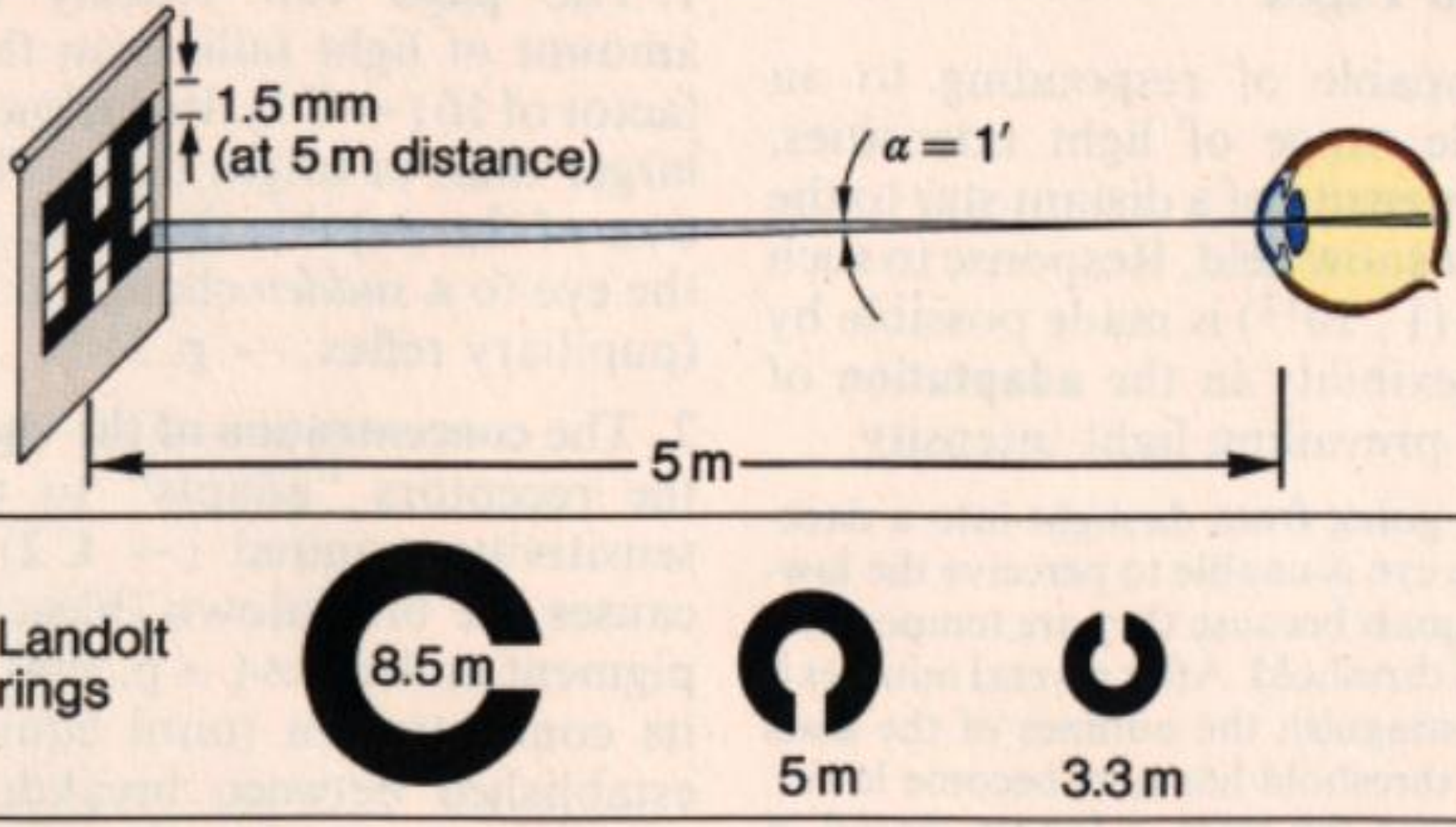
A. Optics: (1) distant, (2) near light source



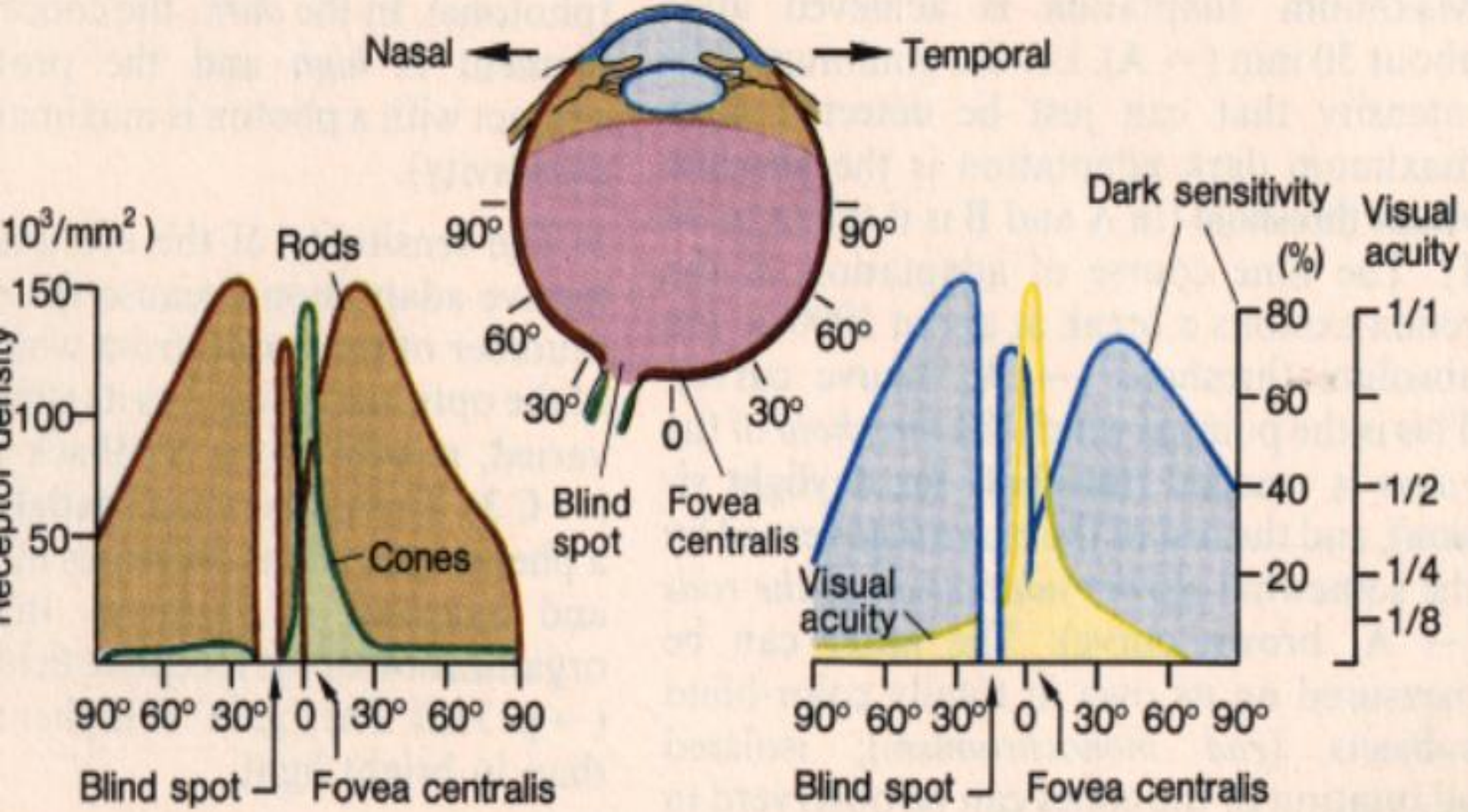
B. Accommodation in the eye (1) distant, (2) near



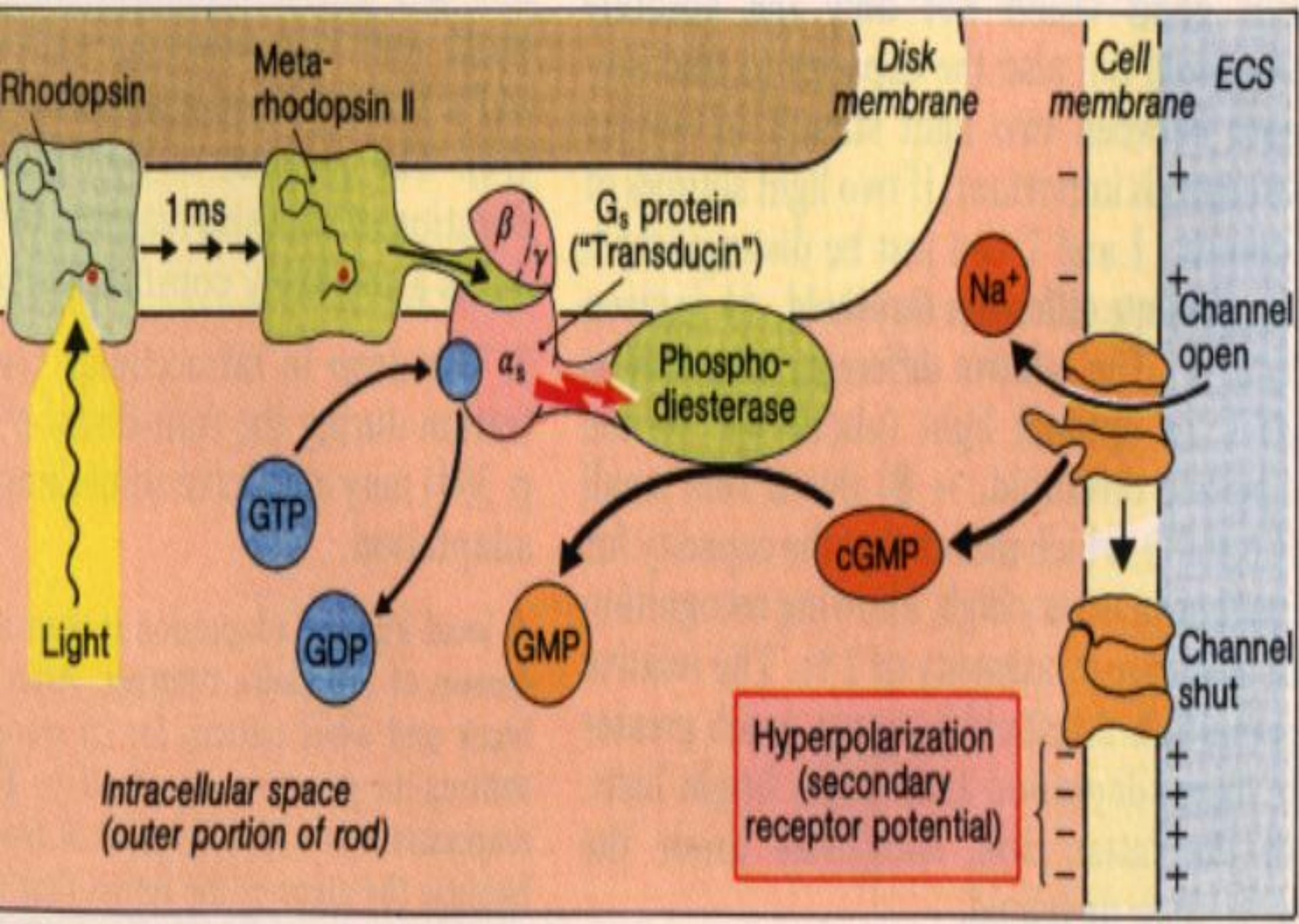
C. Visual defects



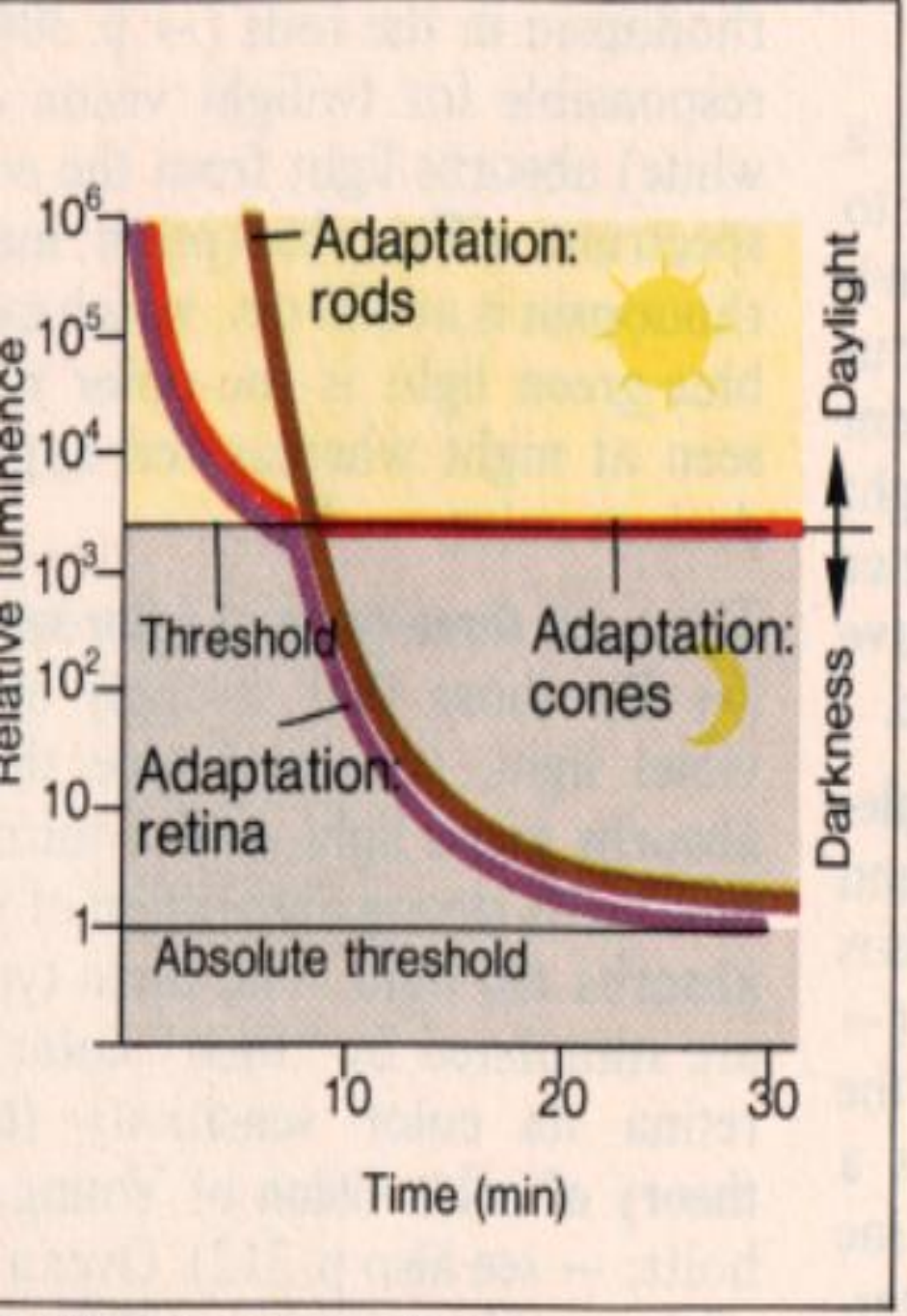
A. Visual acuity



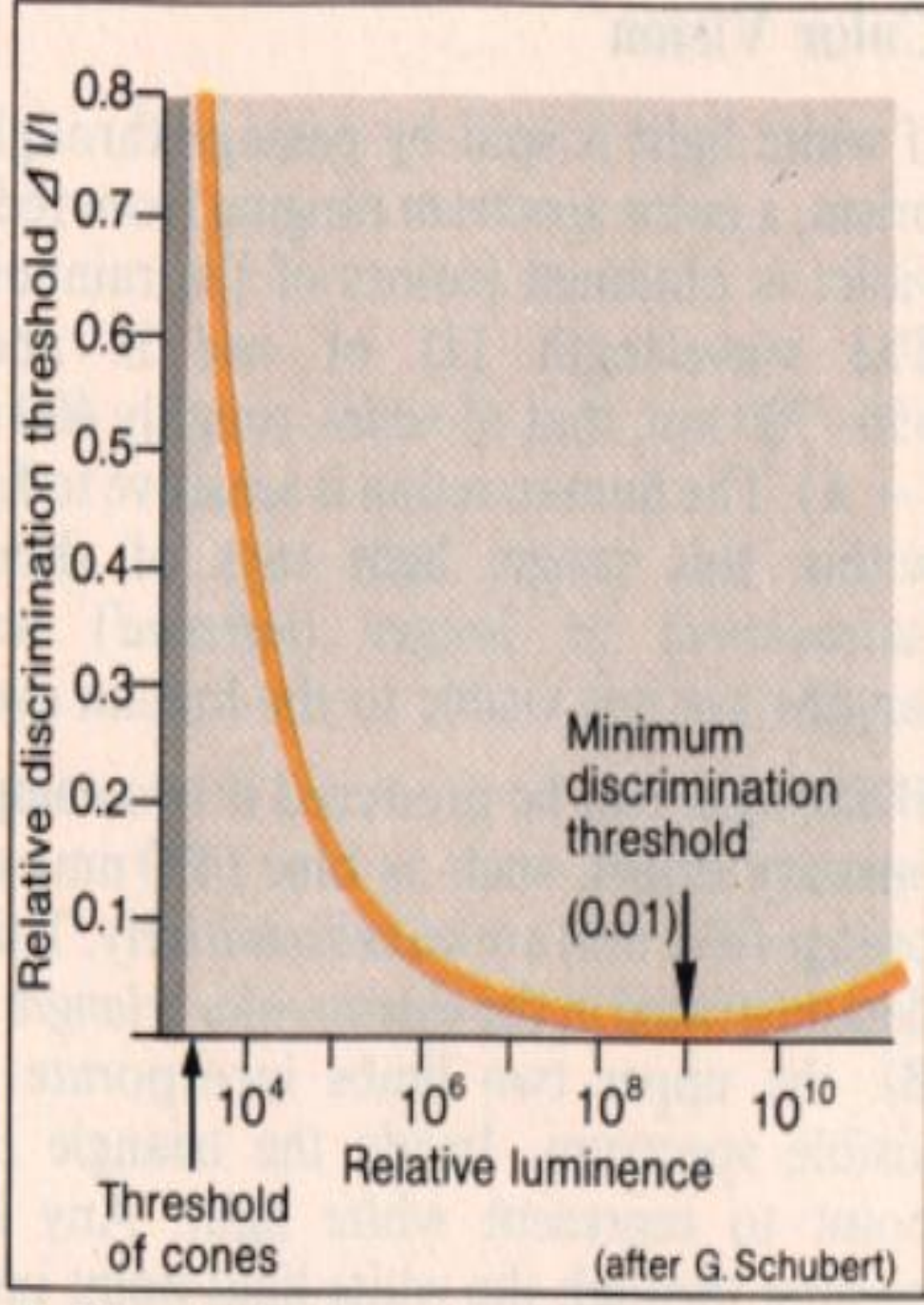
3. Retina: distribution of rods, cones, dark sensitivity and visual acuity



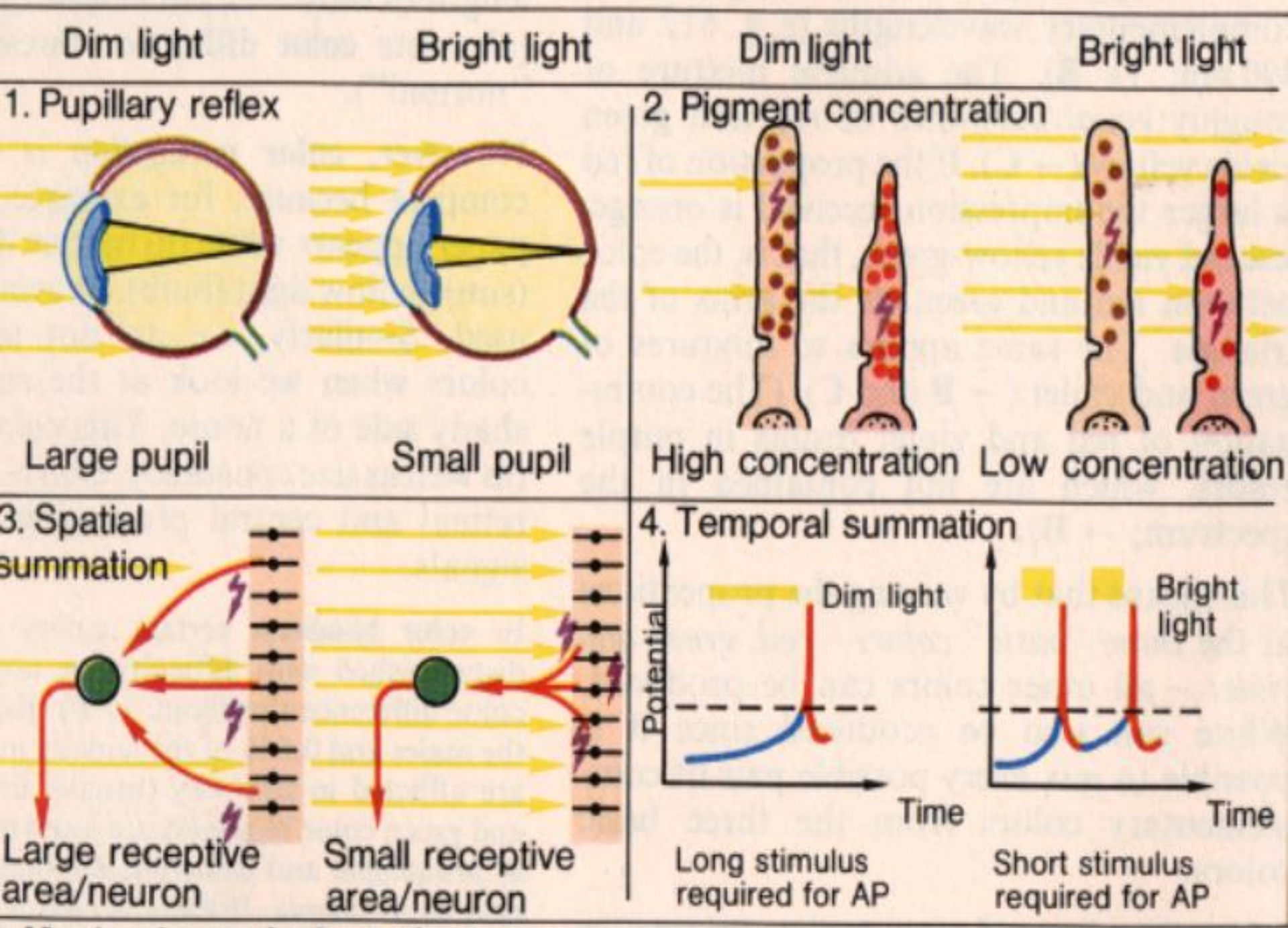
. Transduction process in the rods



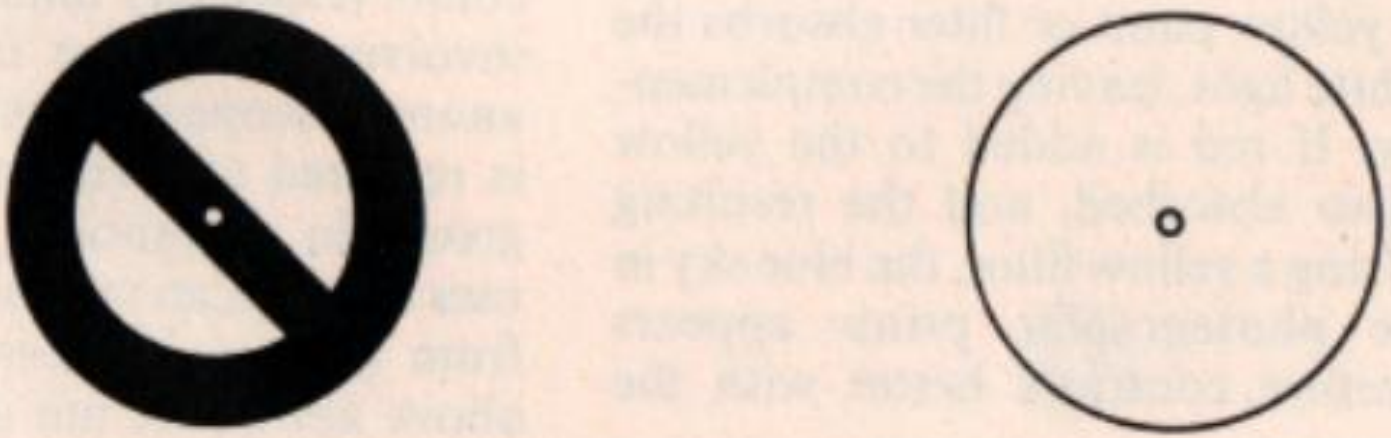
A. Visual adaptation



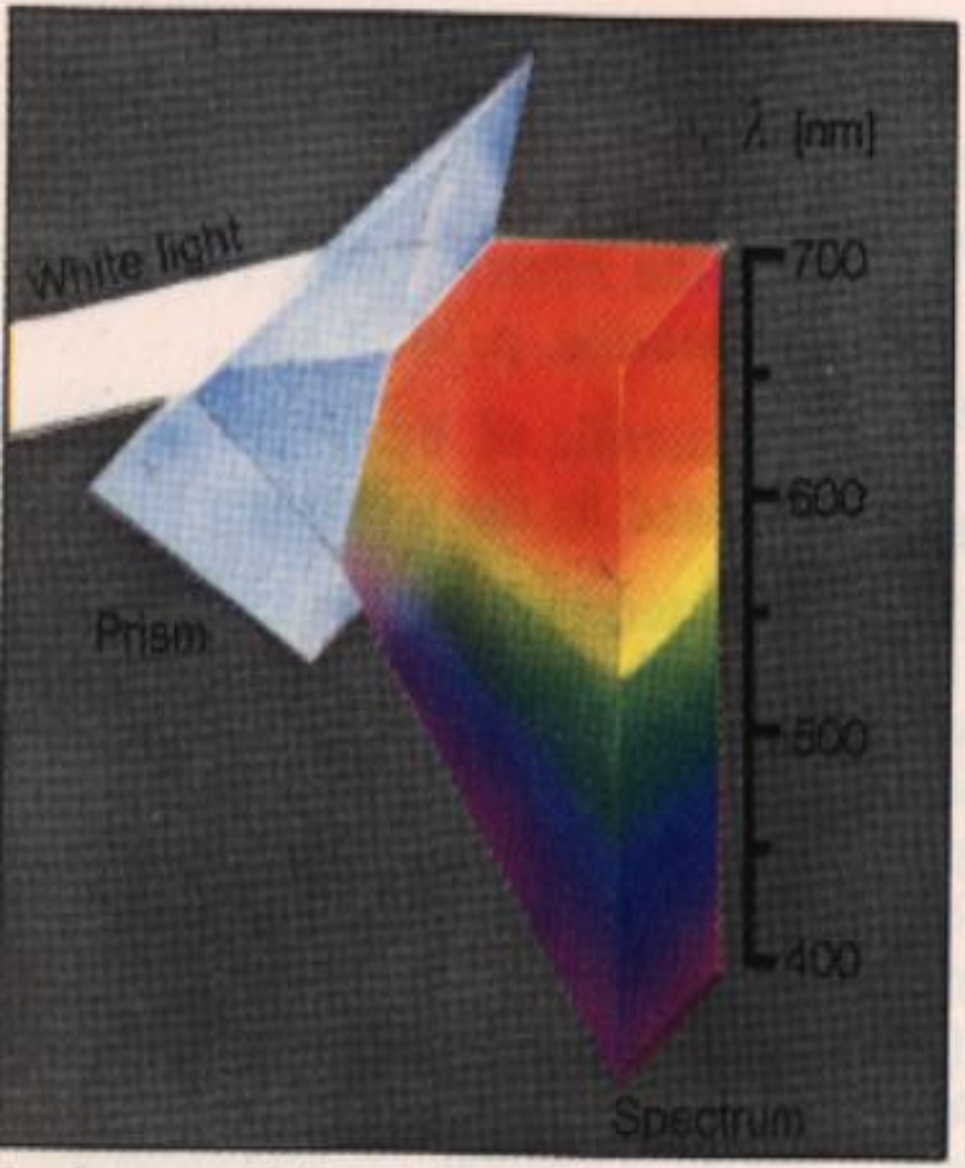
B. Discrimination threshold



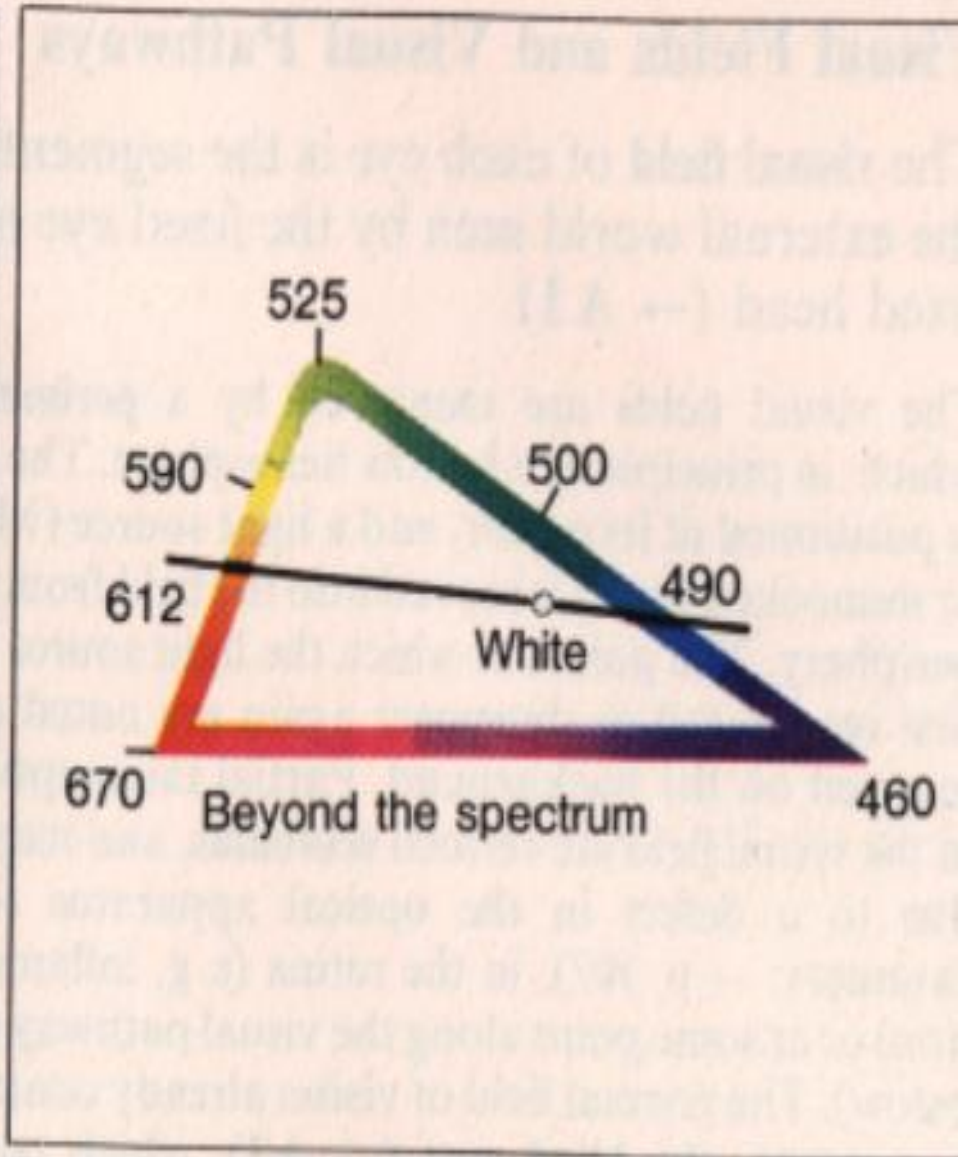
. Mechanisms of adaptation



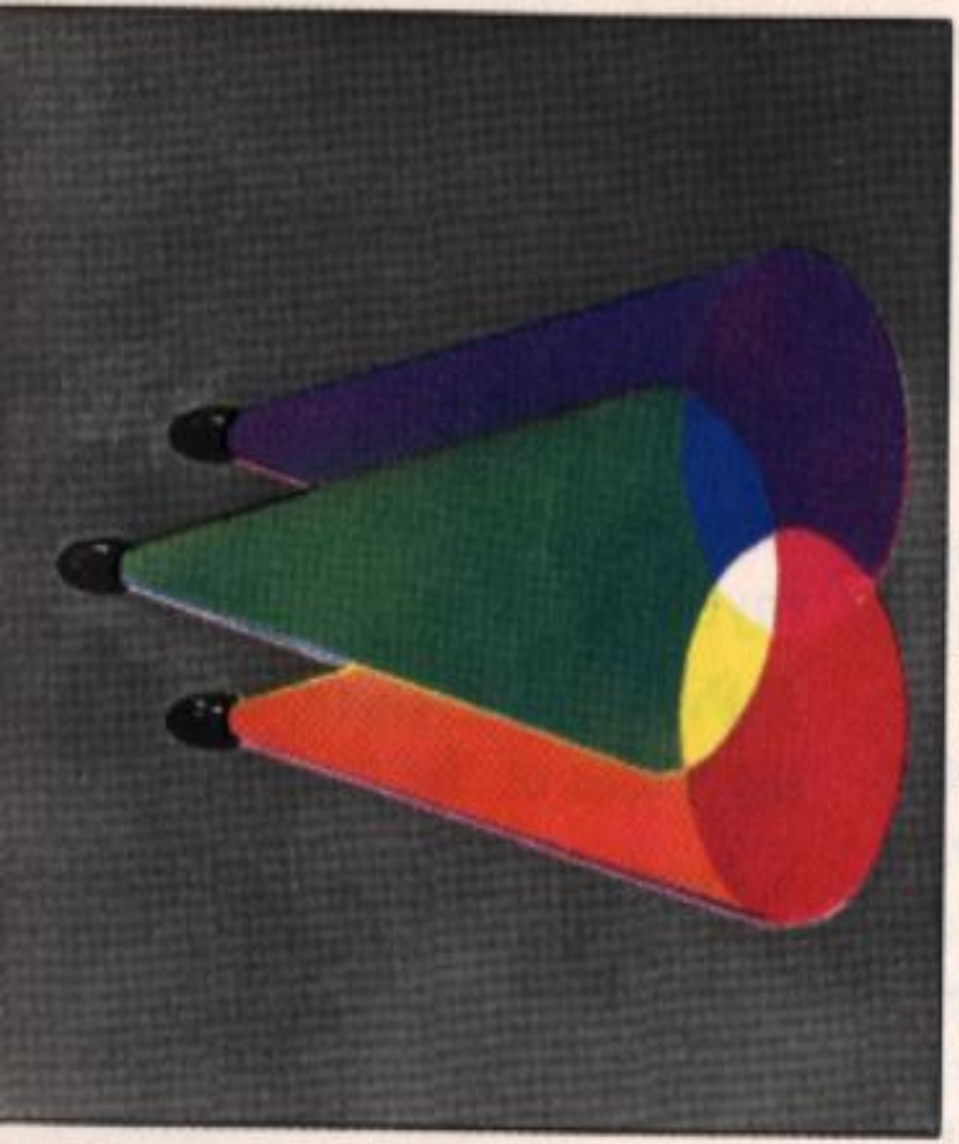
. **Successive contrast ("local adaptation")** (see text)



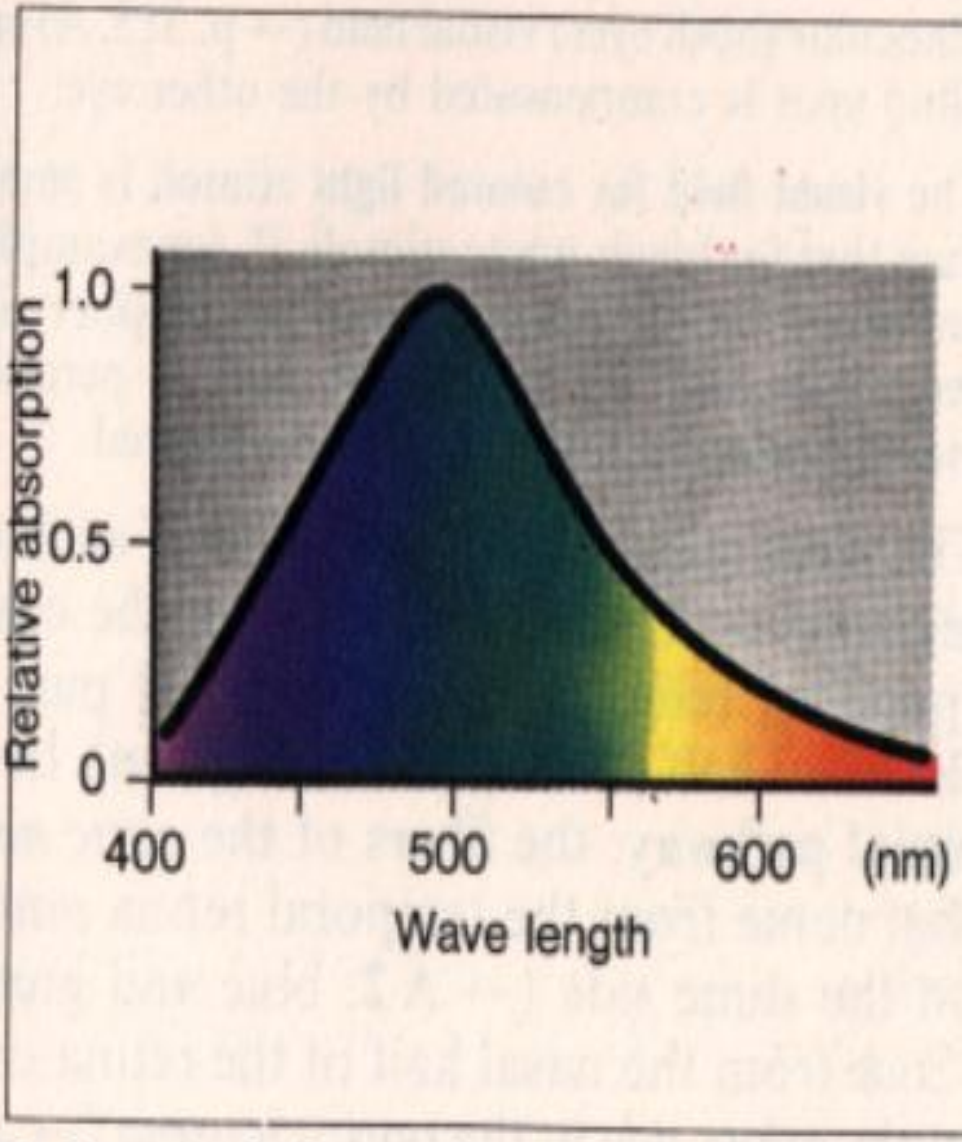
A. Composition of white light



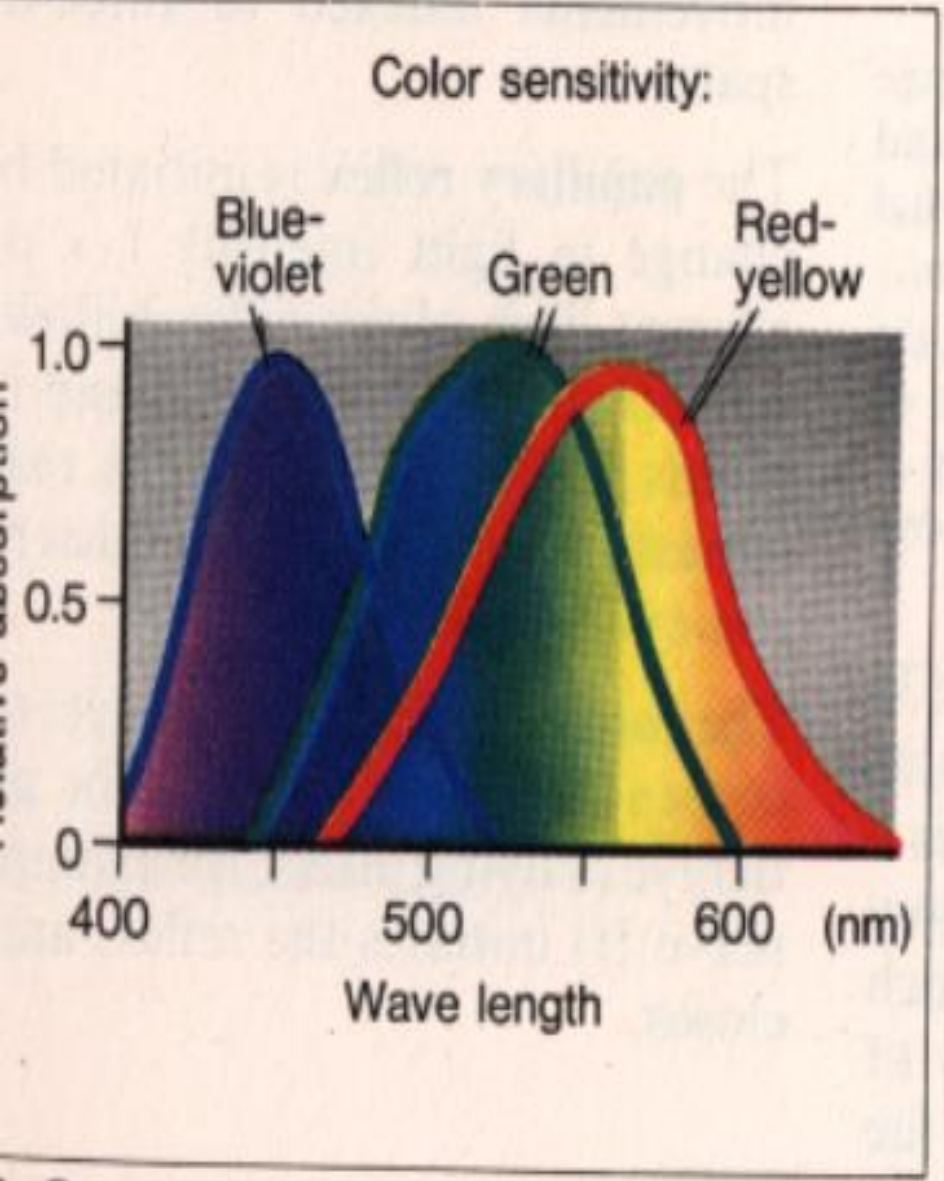
B. Color triangle (after Kries)

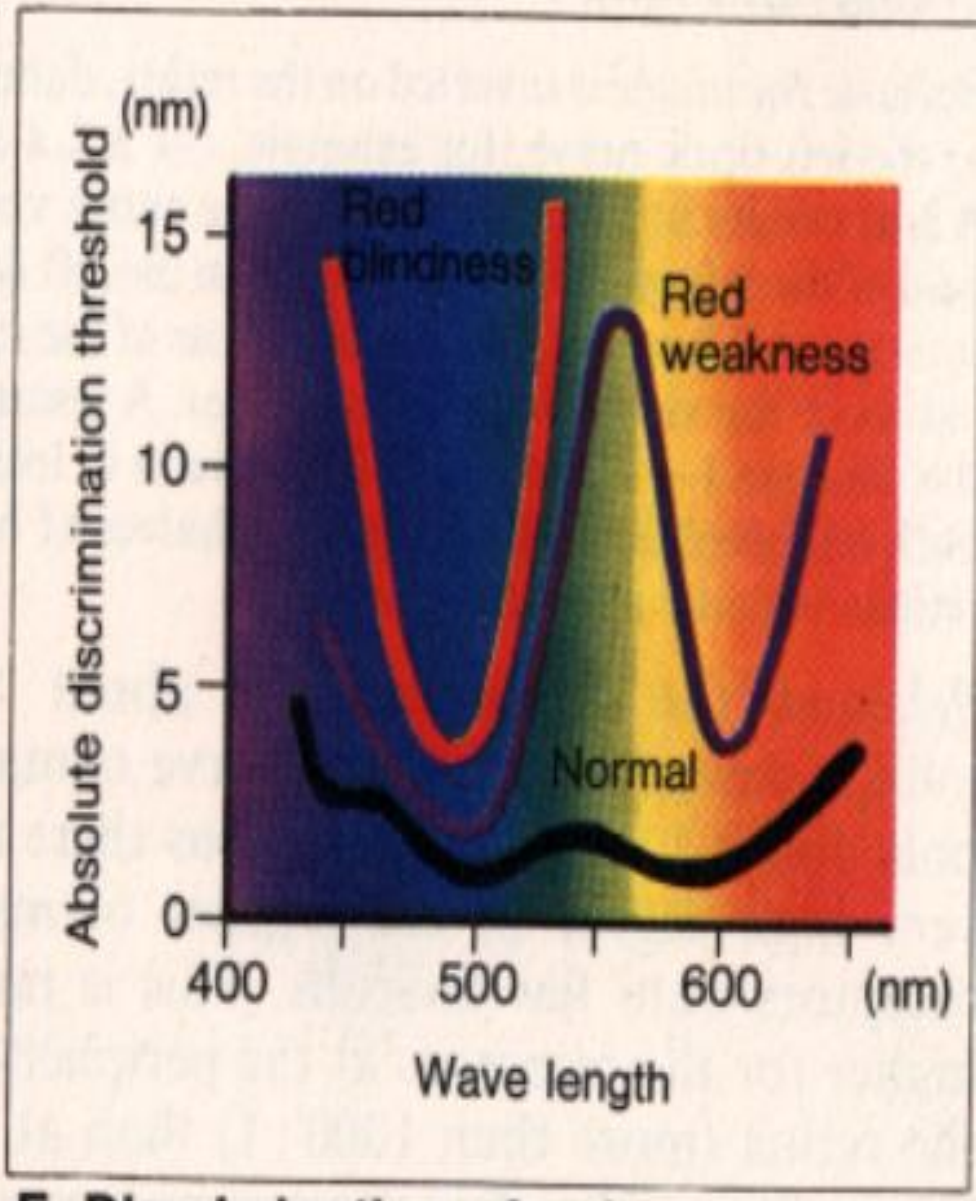


C. Additive color mixing

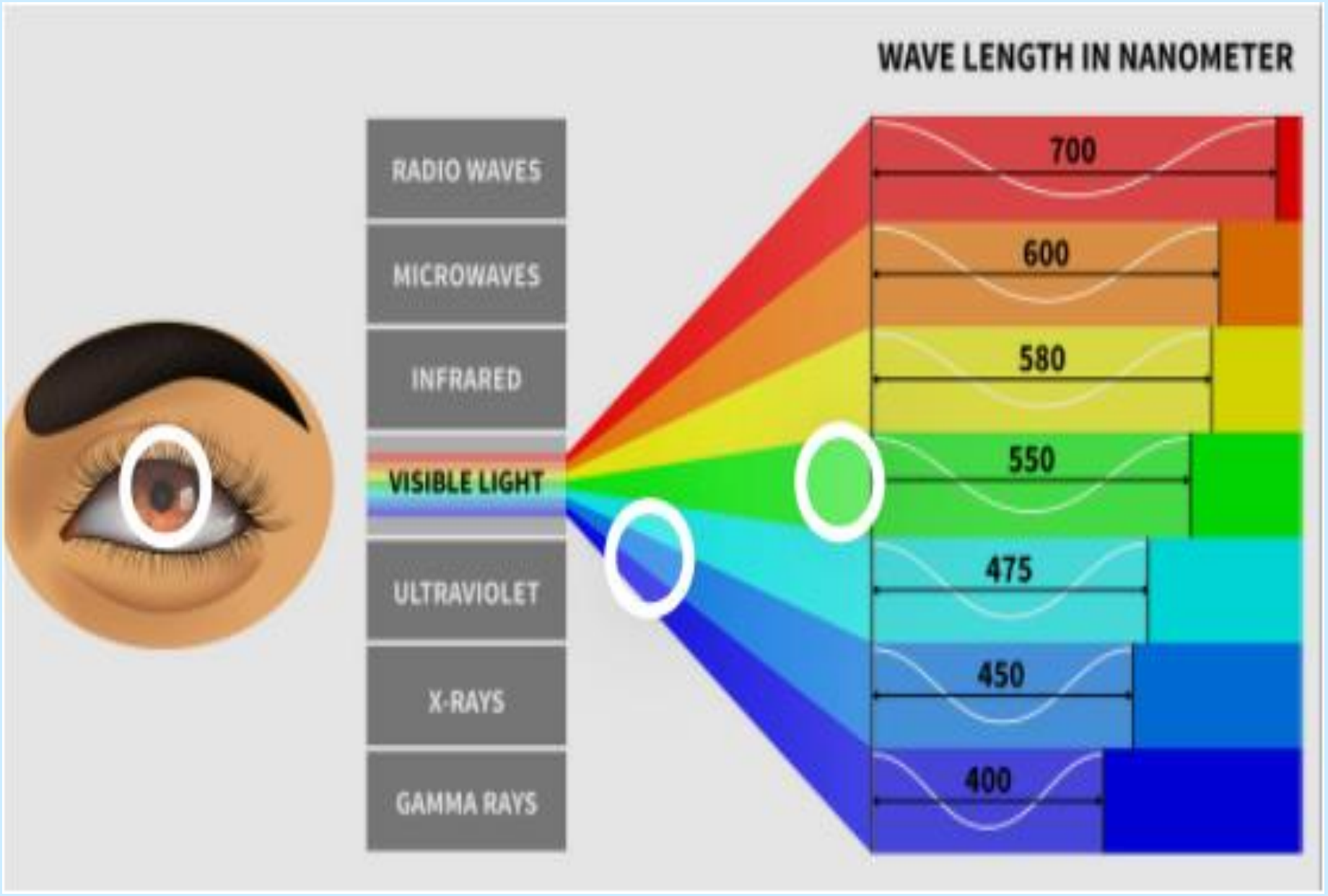


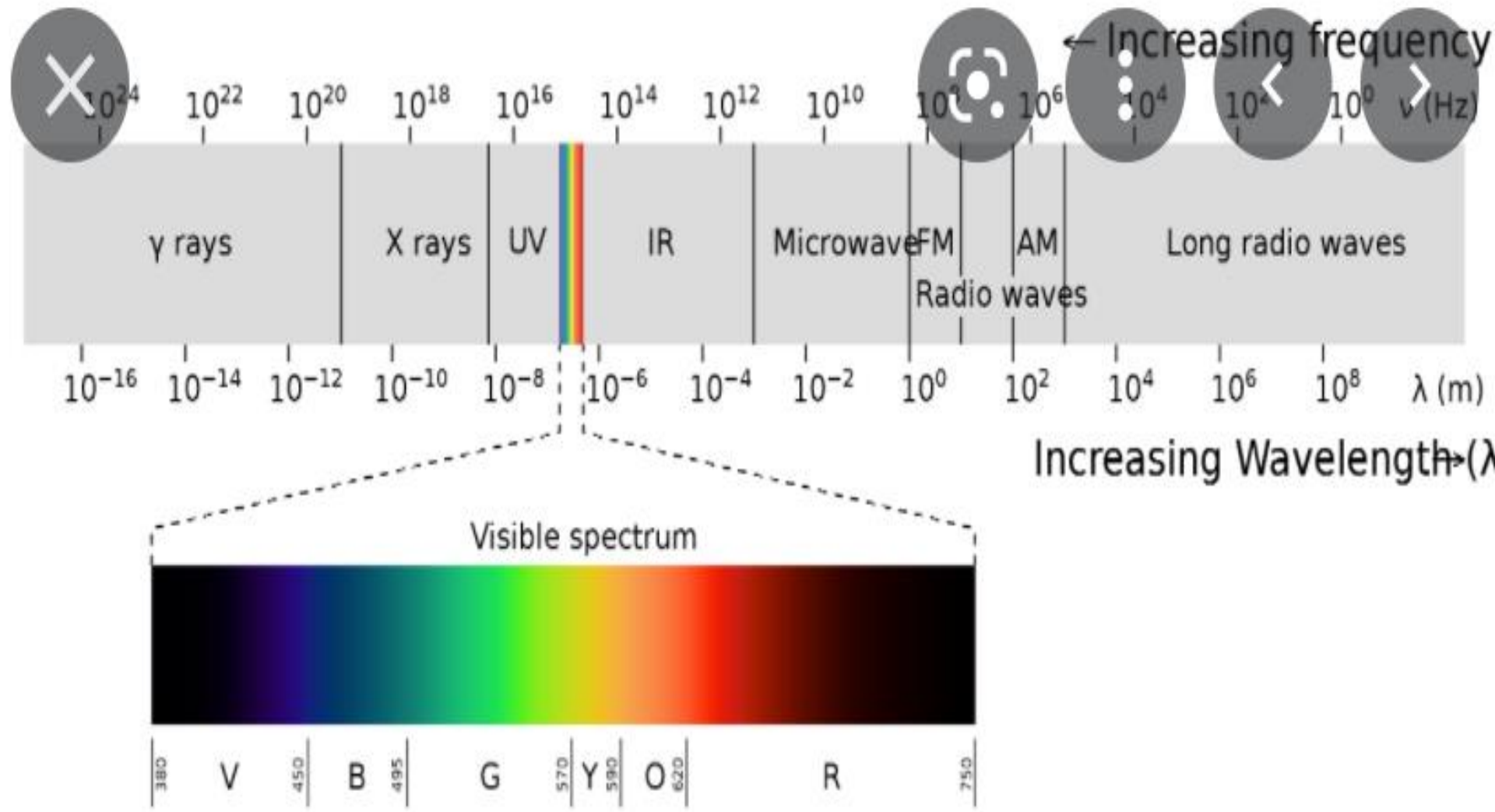
D. Spectral absorption curve: rhodopsin

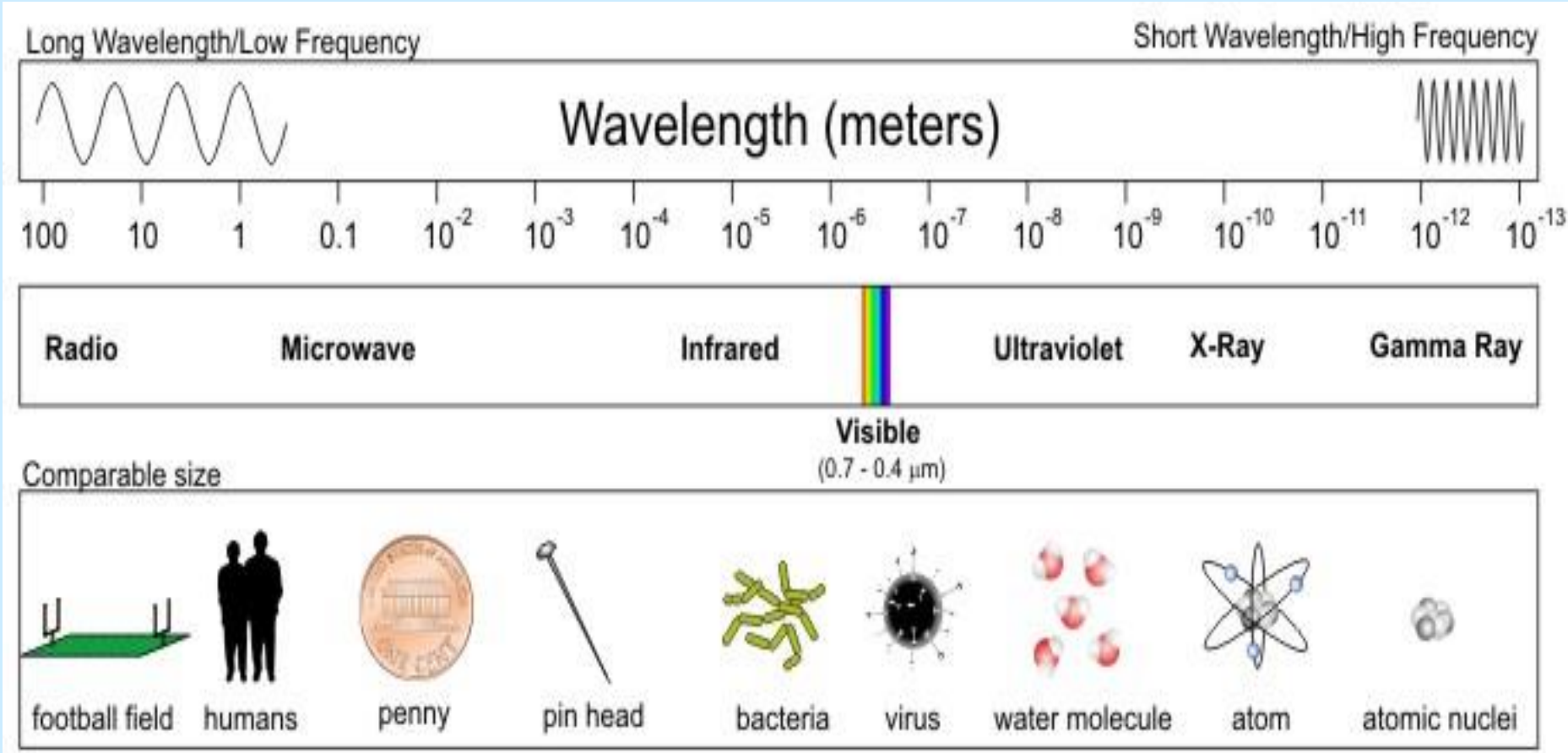


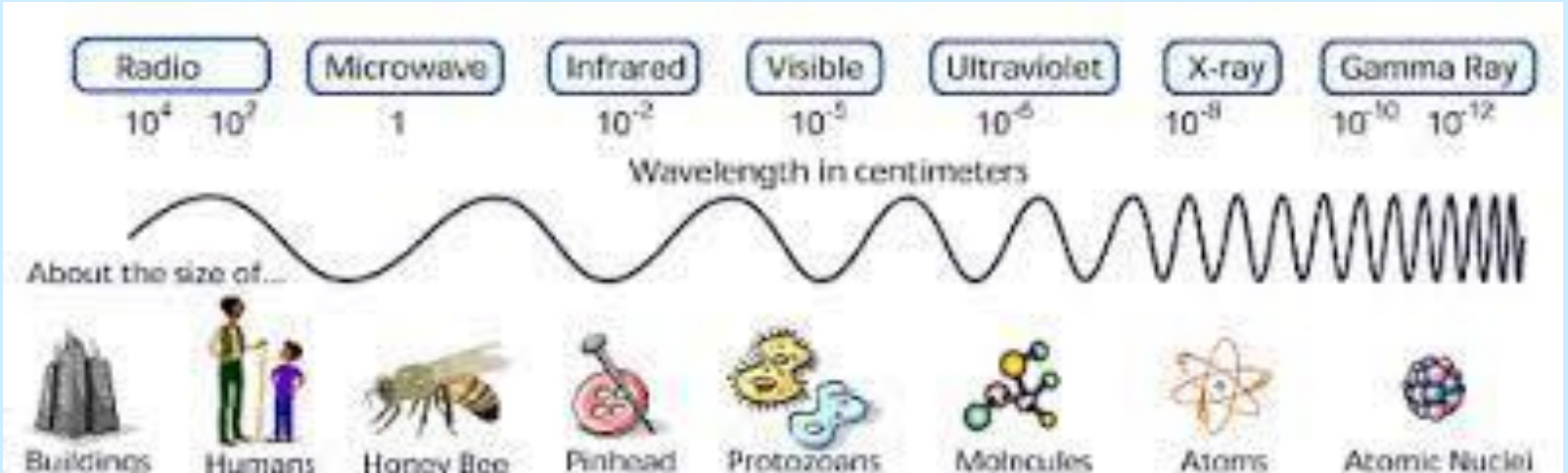


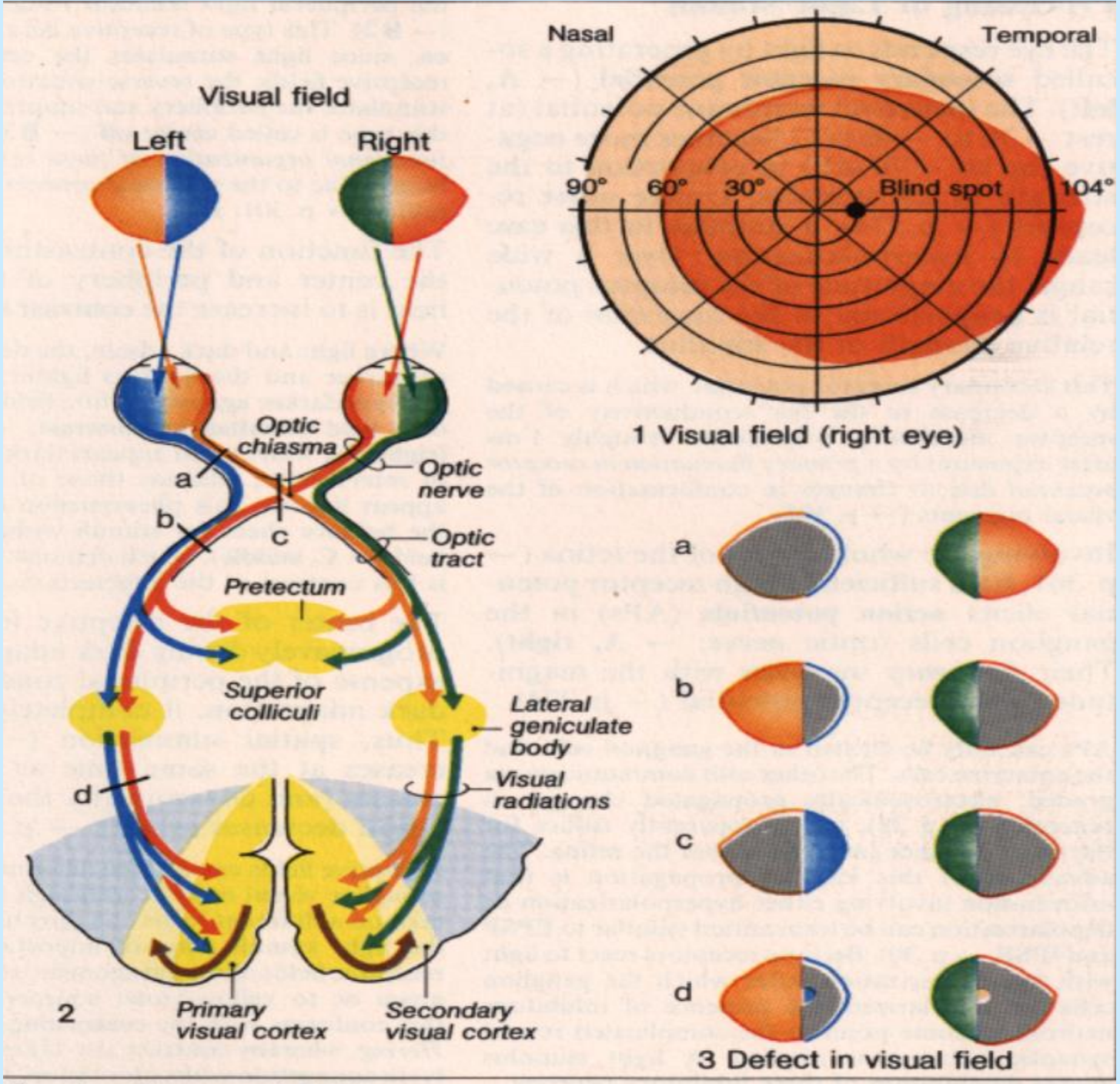
E. Spectral curves of cone pigments F. Discrimination of color


WAVE LENGTH IN NANOMETER
RADIO WAVES
MICROWAVES
INFRARED
VISIBLE LIGHT
ULTRAVIOLET
X-RAYS
GAMMA RAYS
700
600
580
550
475
450
400

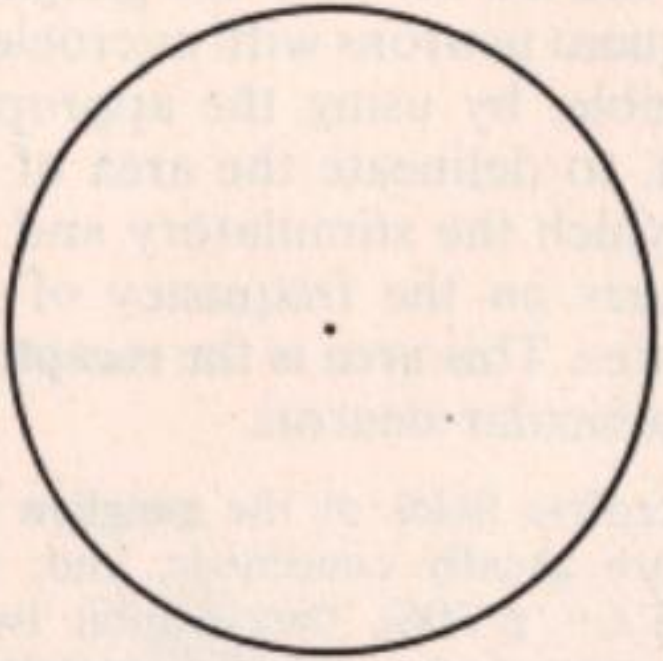

← Increasing frequency
10^{24} 10^{22} 10^{20} 10^{18} 10^{16} 10^{14} 10^{12} 10^{10} 10^{8} 10^{6} 10^{4} 10^{2} 10^{0} ν (Hz)
γ rays
X rays
UV
IR
Microwave
FM
AM
Radio waves
Long radio waves
10^{-16} 10^{-14} 10^{-12} 10^{-10} 10^{-8} 10^{-6} 10^{-4} 10^{-2} 10^{0} 10^{2} 10^{4} 10^{6} 10^{8} λ (m)
Increasing Wavelength →(λ
Visible spectrum
380 V 450 B 495 G 570 Y 590 O 620 R 750


Long Wavelength/Low Frequency
Short Wavelength/High Frequency
Wavelength (meters)
100 10 1 0.1 10^{-2} 10^{-3} 10^{-4} 10^{-5} 10^{-6} 10^{-7} 10^{-8} 10^{-9} 10^{-10} 10^{-11} 10^{-12} 10^{-13}
Radio
Microwave
Infrared
Visible
(0.7 - 0.4 μm)
Ultraviolet
X-Ray
Gamma Ray
Comparable size
football field
humans
penny
pin head
bacteria
virus
water molecule
atom
atomic nuclei

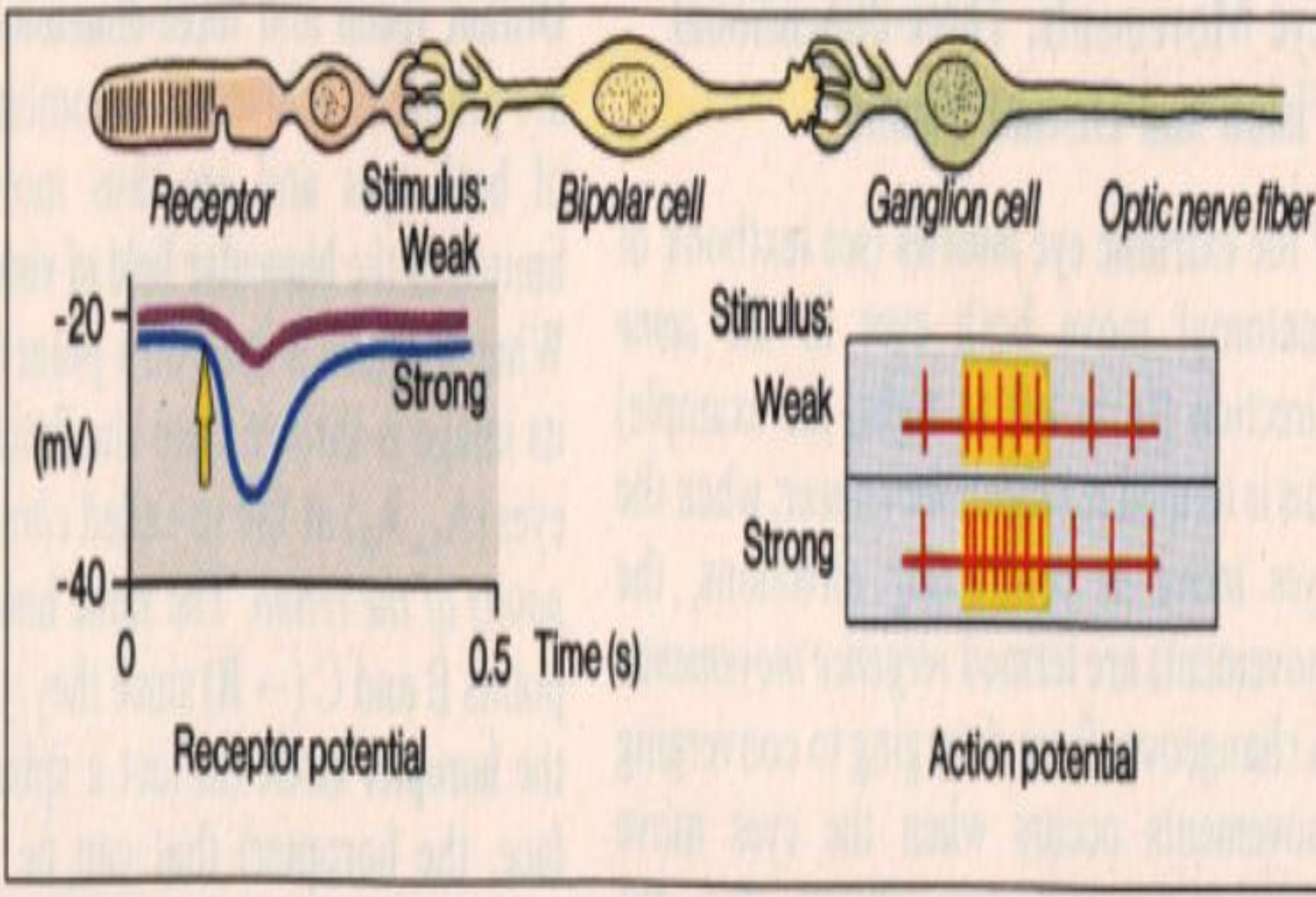

Radio
Microwave
Infrared
Visible
Ultraviolet
X-ray
Gamma Ray
10^{4} 10^{3}
1
10^{-2}
10^{-5}
10^{-6}
10^{-8}
10^{-10} 10^{-12}
Wavelength in centimeters
About the size of...
Buildings
Humans
Honey Bee
Pinhead
Protozoans
Molecules
Atoms
Atomic Nuclei



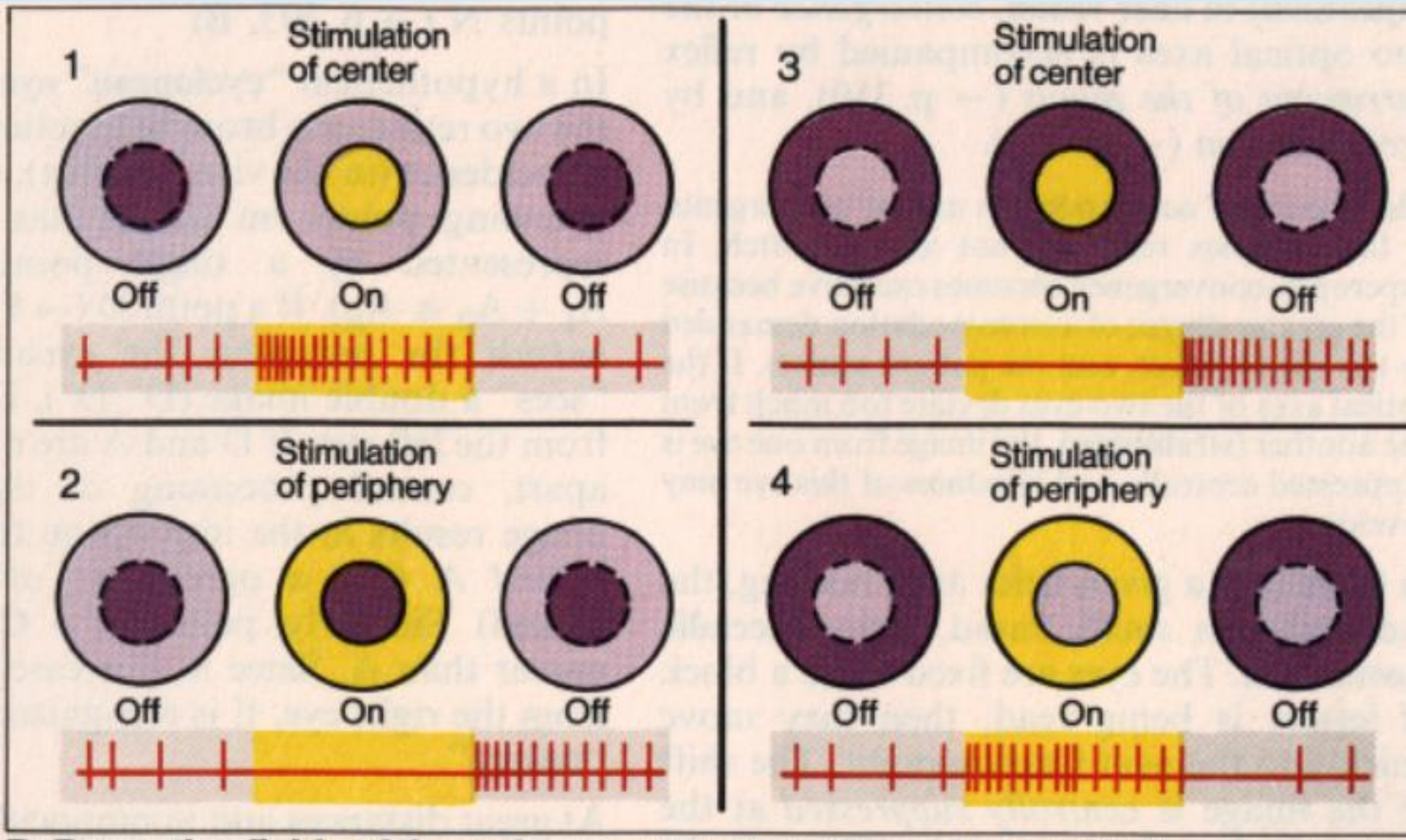
Visual pathway and field



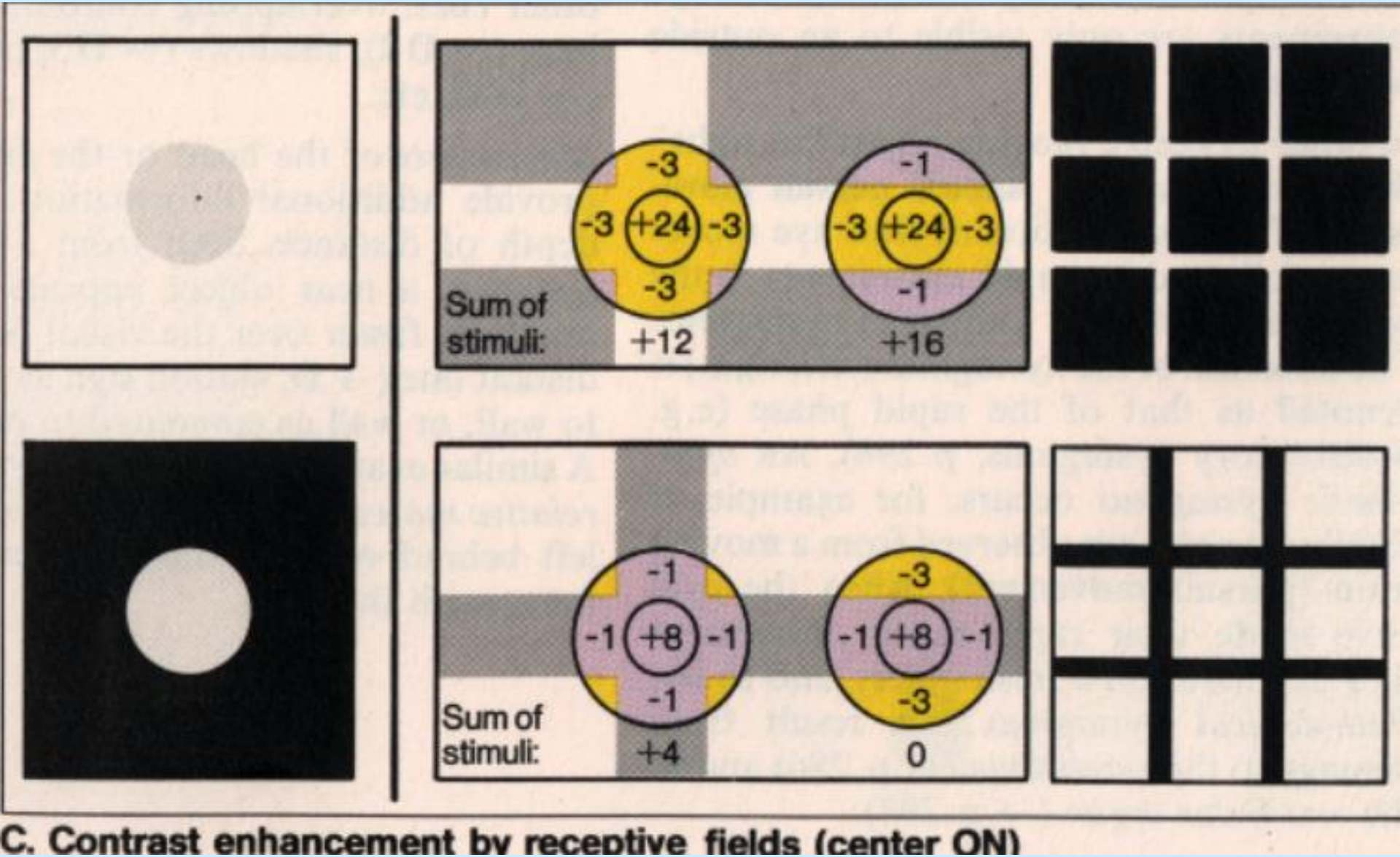
Successive contrast, color (see text, next page)



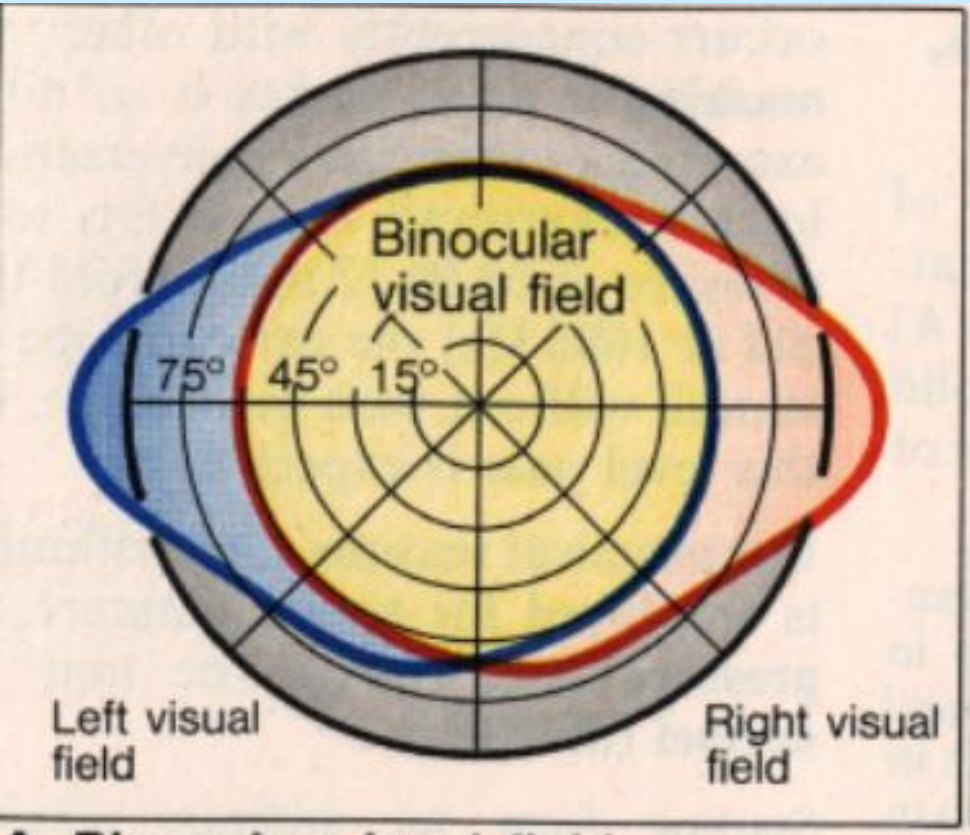
A. Receptor potential (1st and 2nd neuron) and action potentials of the retin



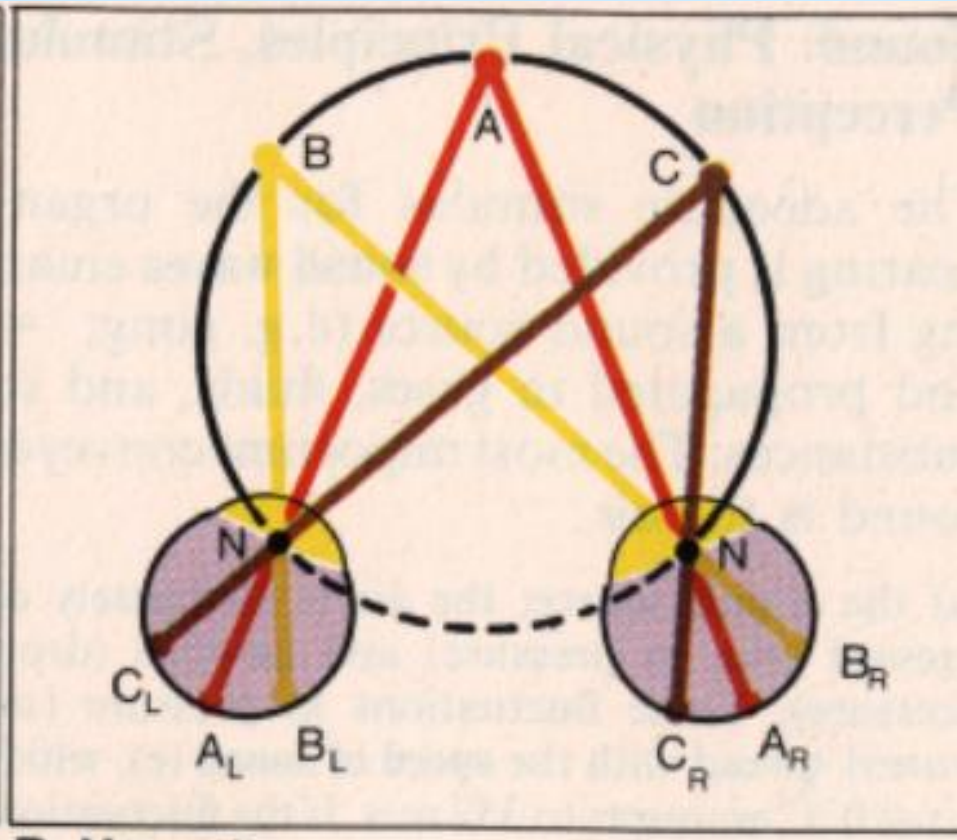
B. Receptive fields of the retina: center ON (1,2), center OFF (3,4)



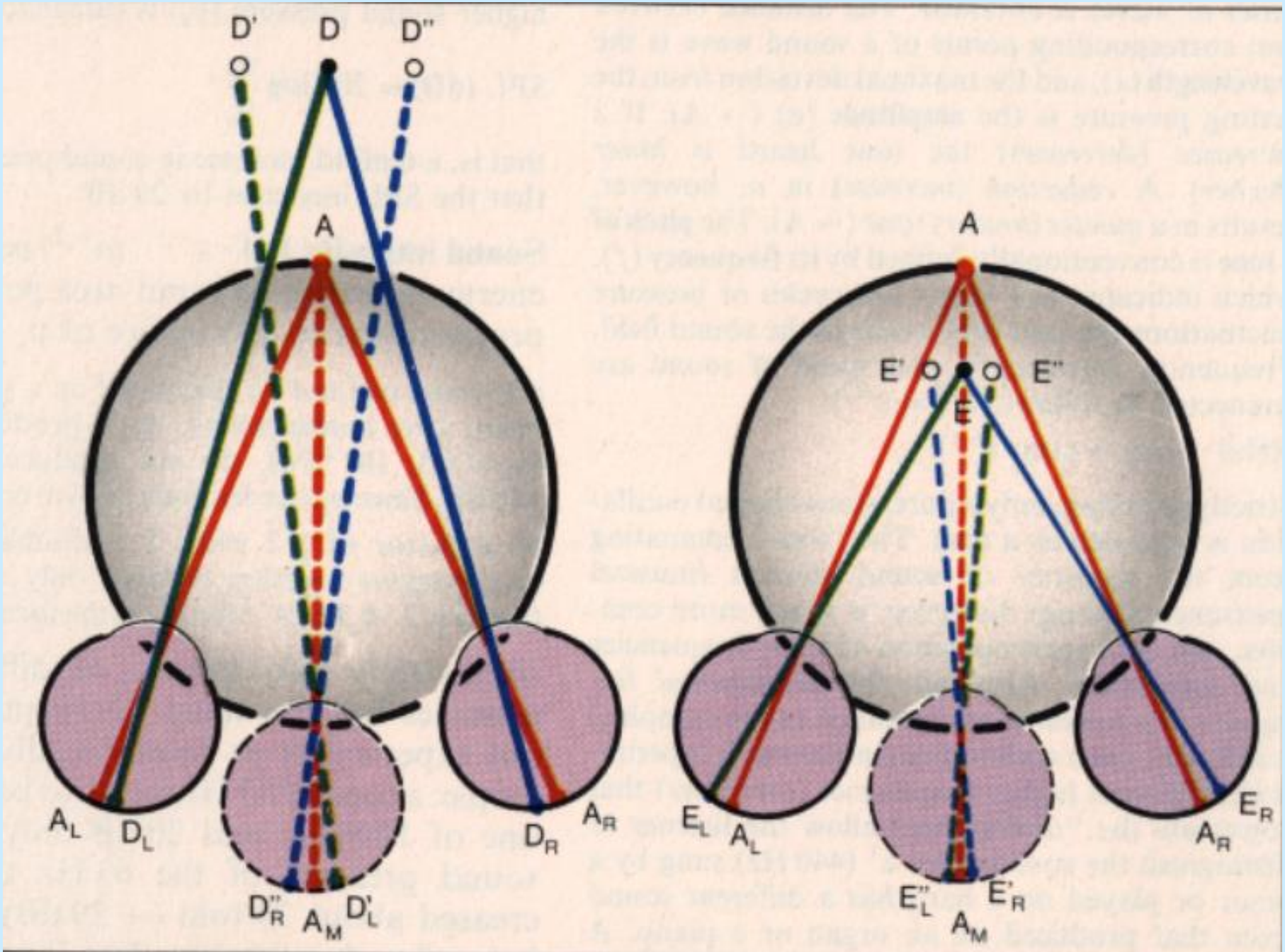
C. Contrast enhancement by receptive fields (center ON)



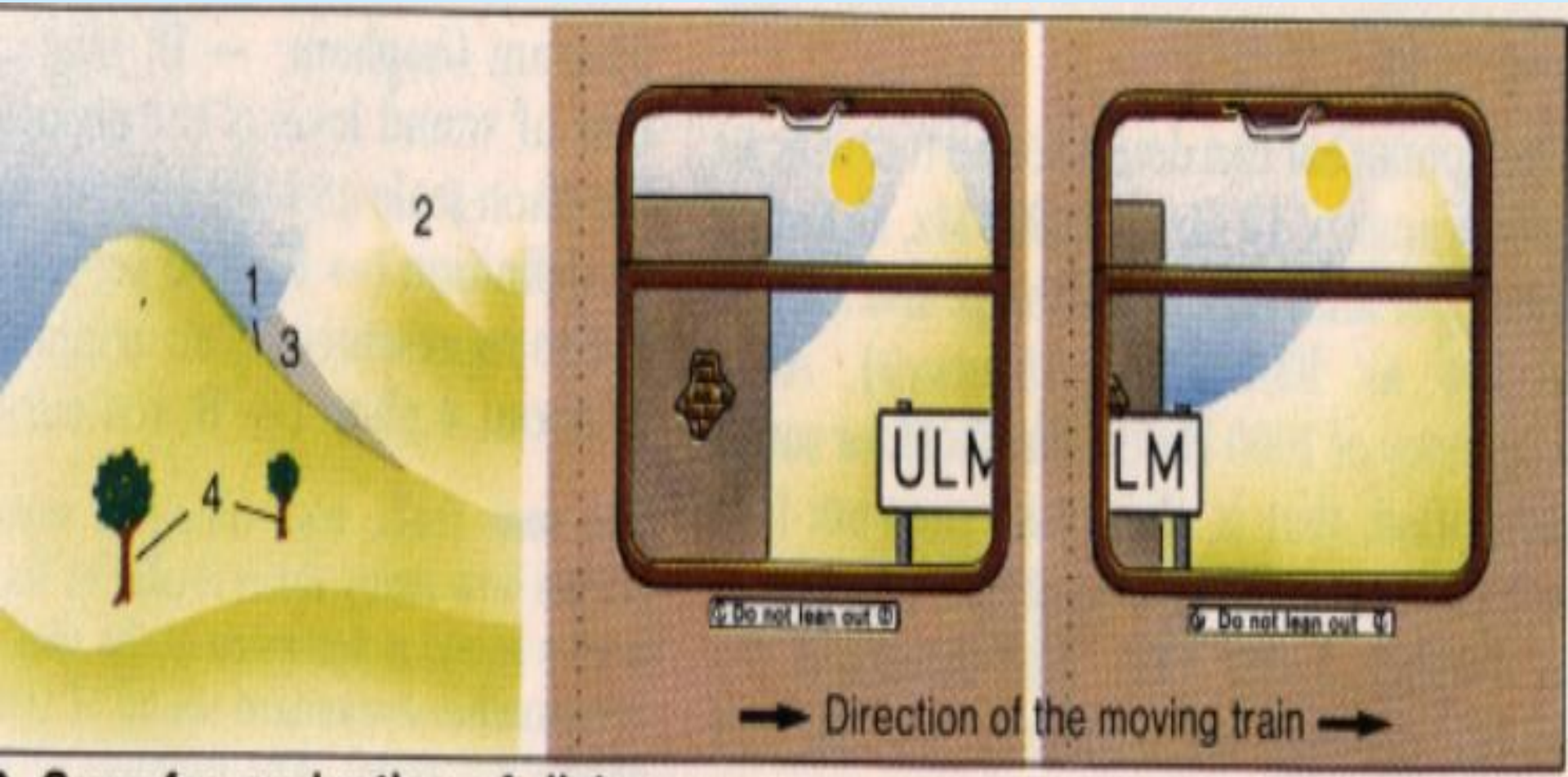
A. Binocular visual field



B. Horopter



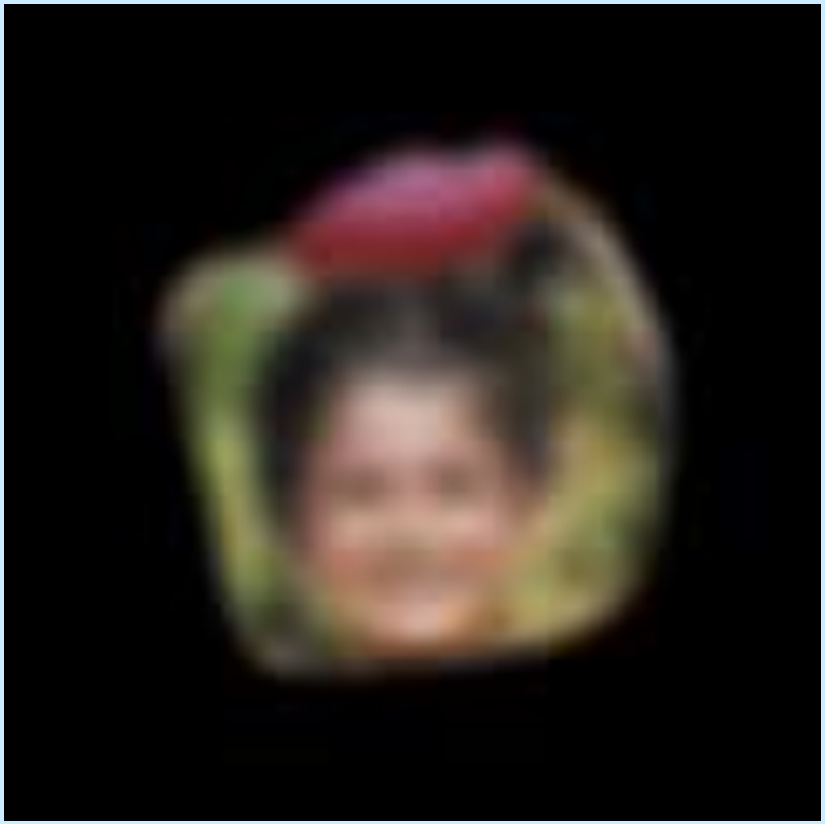
C. Binocular visualization (stereoscopic)



D. Cues for evaluation of distance

Retinitis Pigmentosa is an inherited degenerative disease of the retina at the back of the eye. The degeneration of the photoreceptor cells diminishes a patient's ability to see in dim light and can also diminish their peripheral vision with time eventually leading to blindness. The symptoms of RP most commonly appear in young adults. RP is one of the most common inherited causes of blindness in people between the ages of 20 and 60 affecting 1.6 million people worldwide.

Age-related macular degeneration is the main cause of blindness in elderly people (30% in the over seventies, i.e. over 25 million people worldwide).
The denegeration of the macula (the central portion of the retina) causes loss of vision in the center of the visual field. The macula is used for reading, driving, recognizing faces or color and usually for fine work.

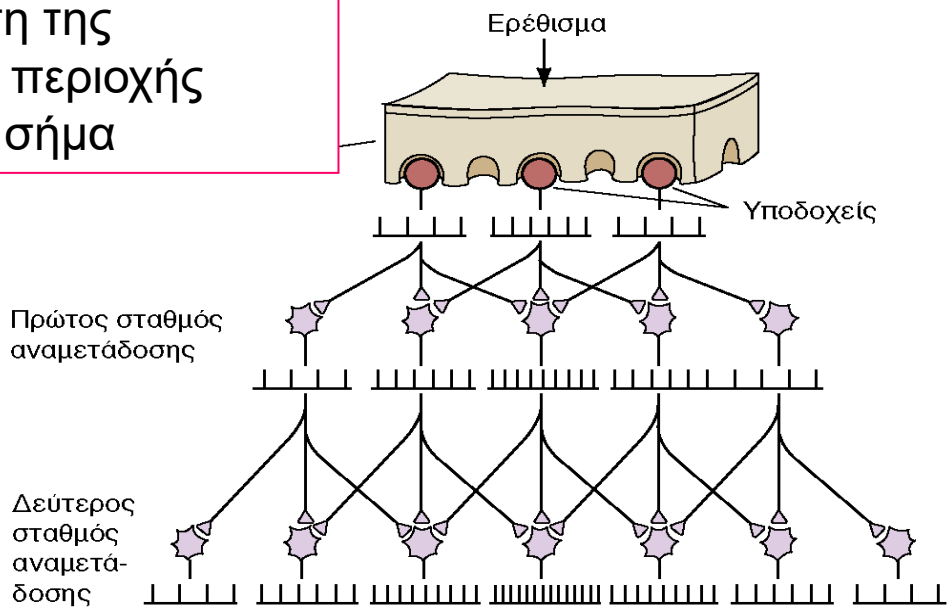


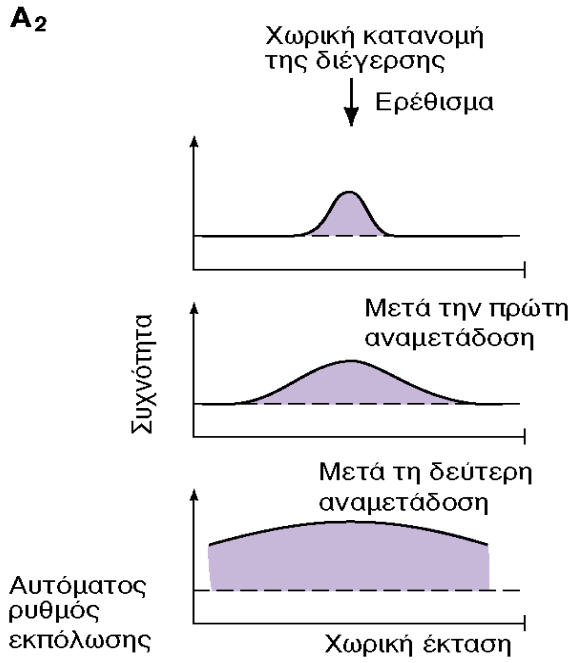
Diabetic Retinopathy (DR) is damage to the retina caused by the microvascular changes that occur due to diabetes.

DR is the leading cause of blindness in people aged between 40 and 60 in the U.S. where it affects 4.5 million of the 7 million known diabetic patients. Ninety percent of the patients with type I diabetes and 60% with type II develop DR after 20 years

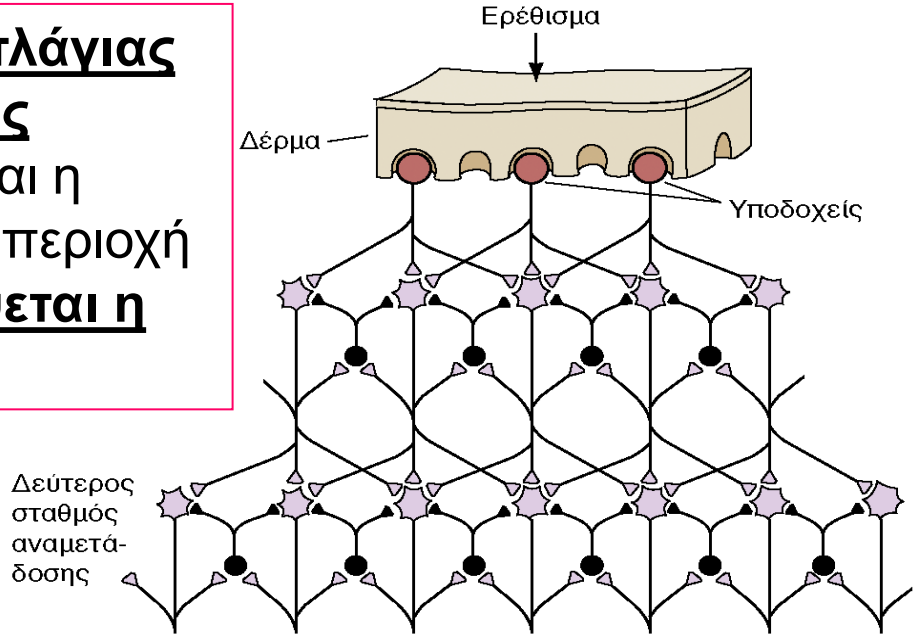
Glaucoma is a group of eye diseases that gradually steals sight without warning and often without symptoms. Vision loss is caused by damage to the optic nerve. Increase of intraocular pressure is a risk factor, but other factors must also be involved

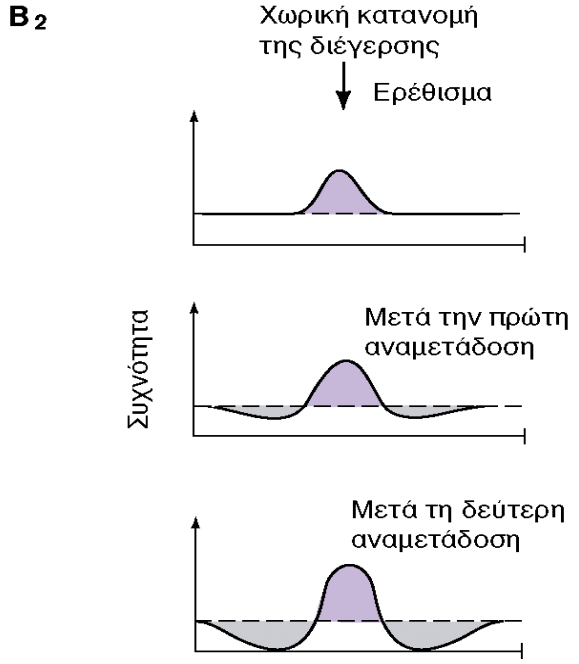
1. Επέκταση της διεγερτικής περιοχής ενισχύει το σήμα





2. Μέσω **πλάγιας αναστολής** περιορίζεται η διεγερτική περιοχή και **ενισχύεται η αντίθεση**





Αποτελέσματα πλάγιας αναστολής => ενίσχυση αντίθεσης

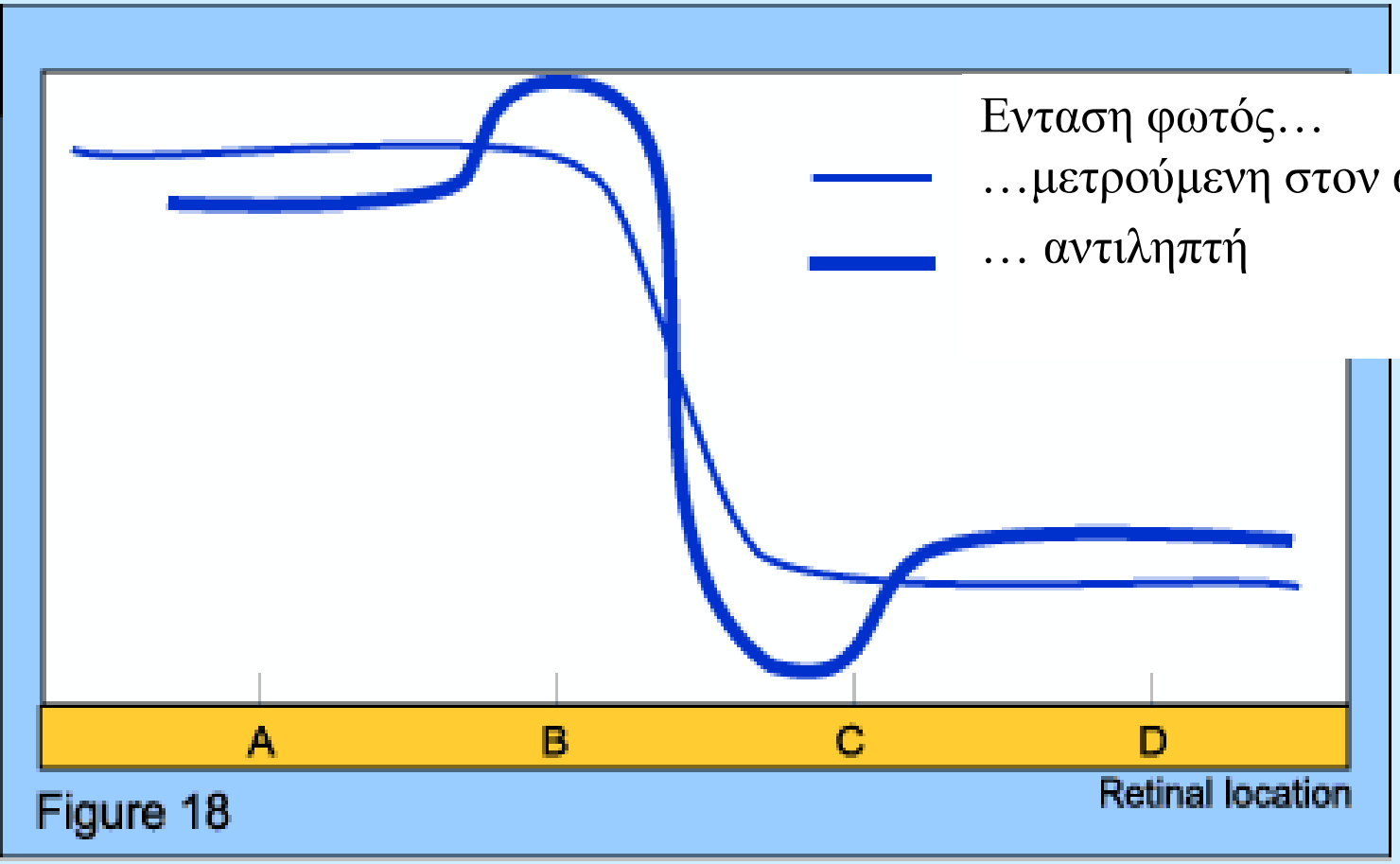
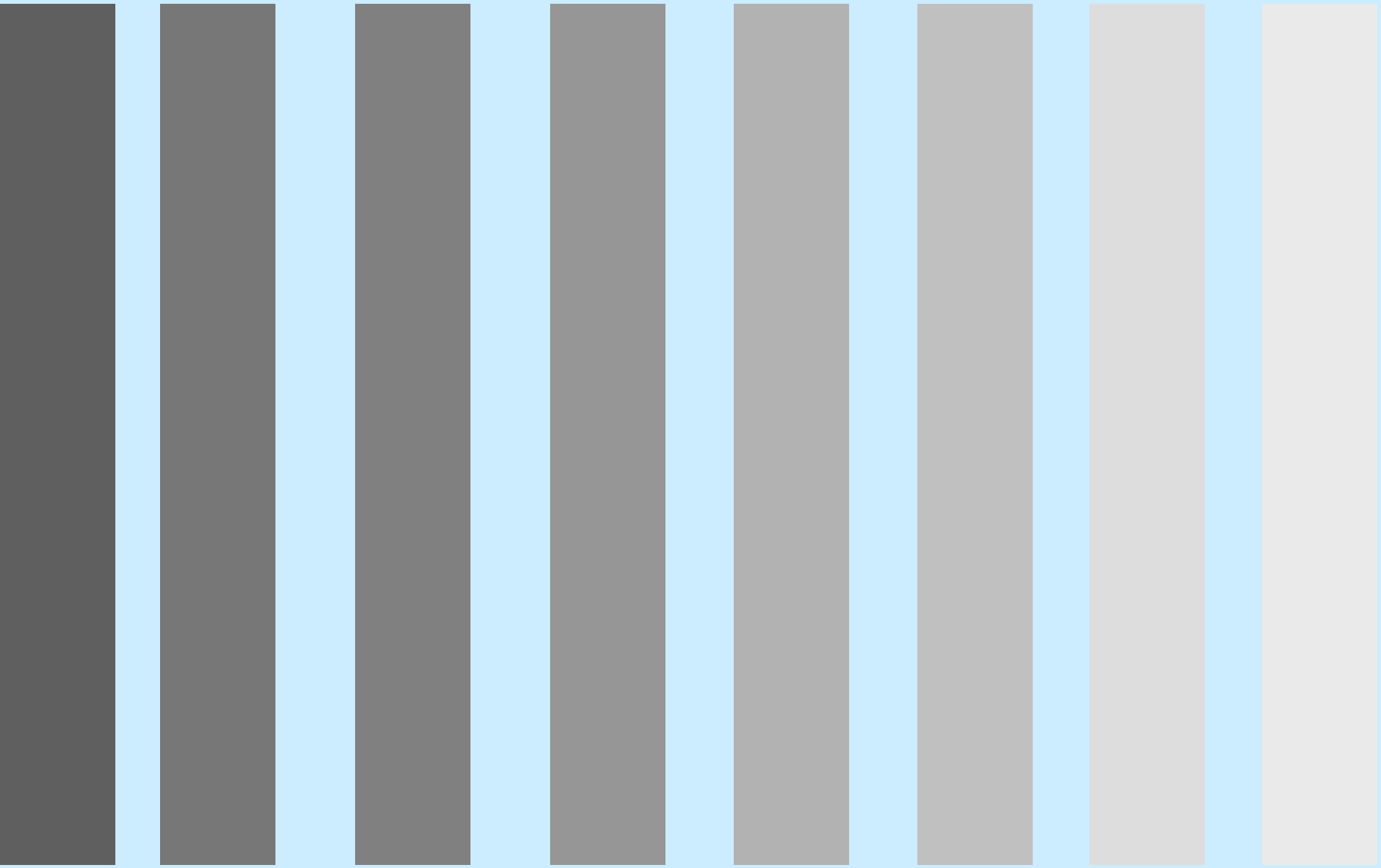
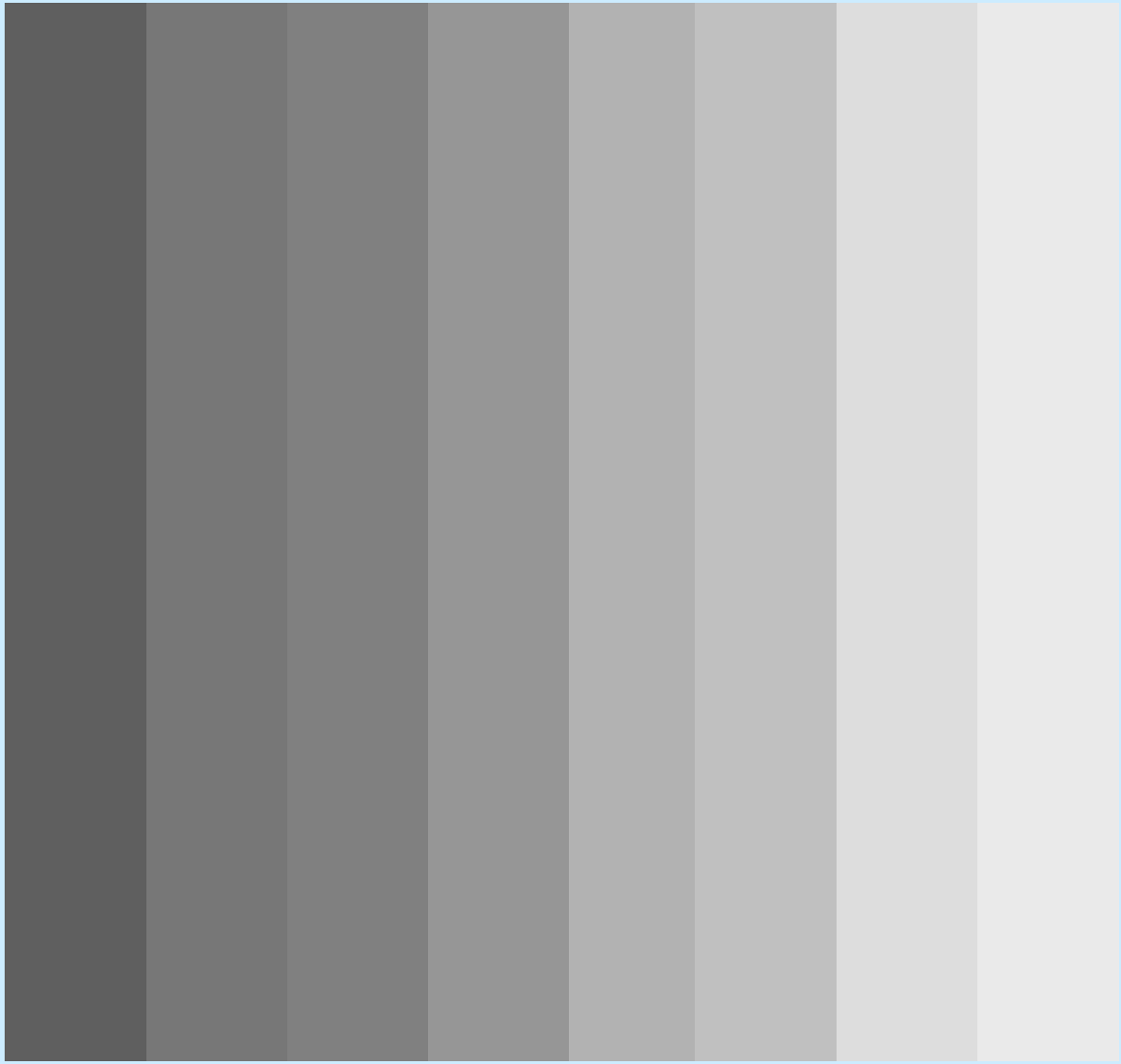


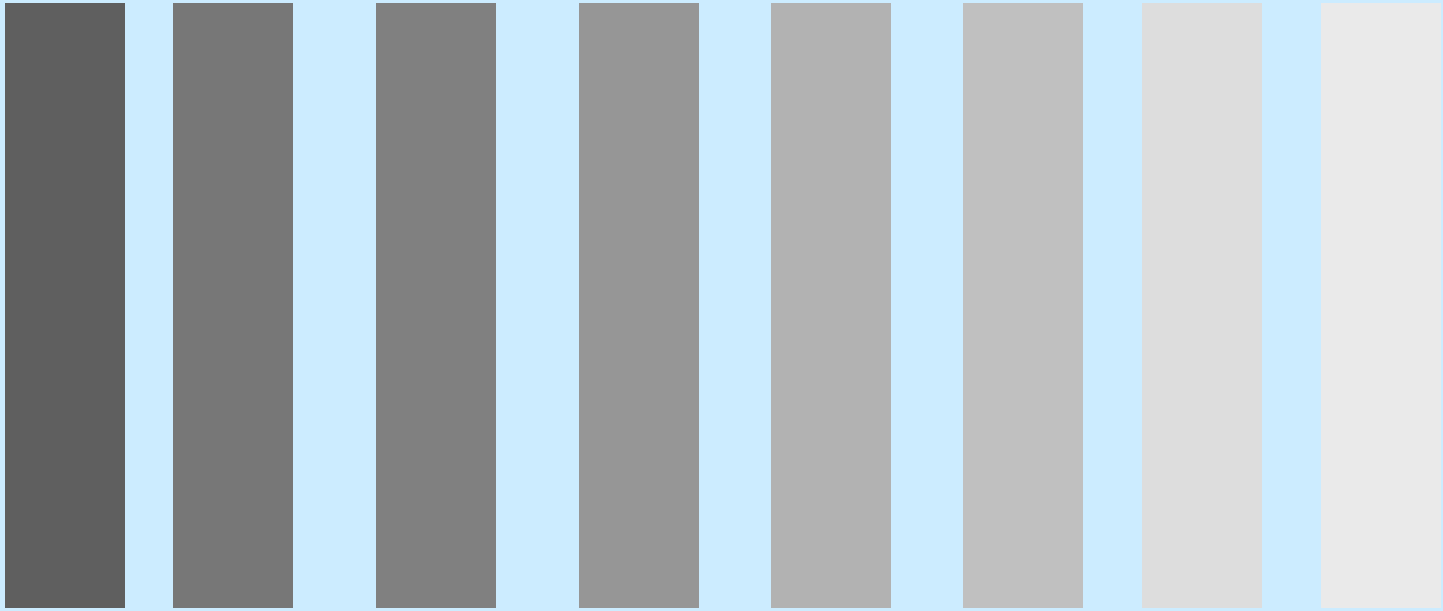
Figure 18

http://www.pc.rhul.ac.uk/staff/J.Zanker/PS1061/L2/PS1061_2.htm

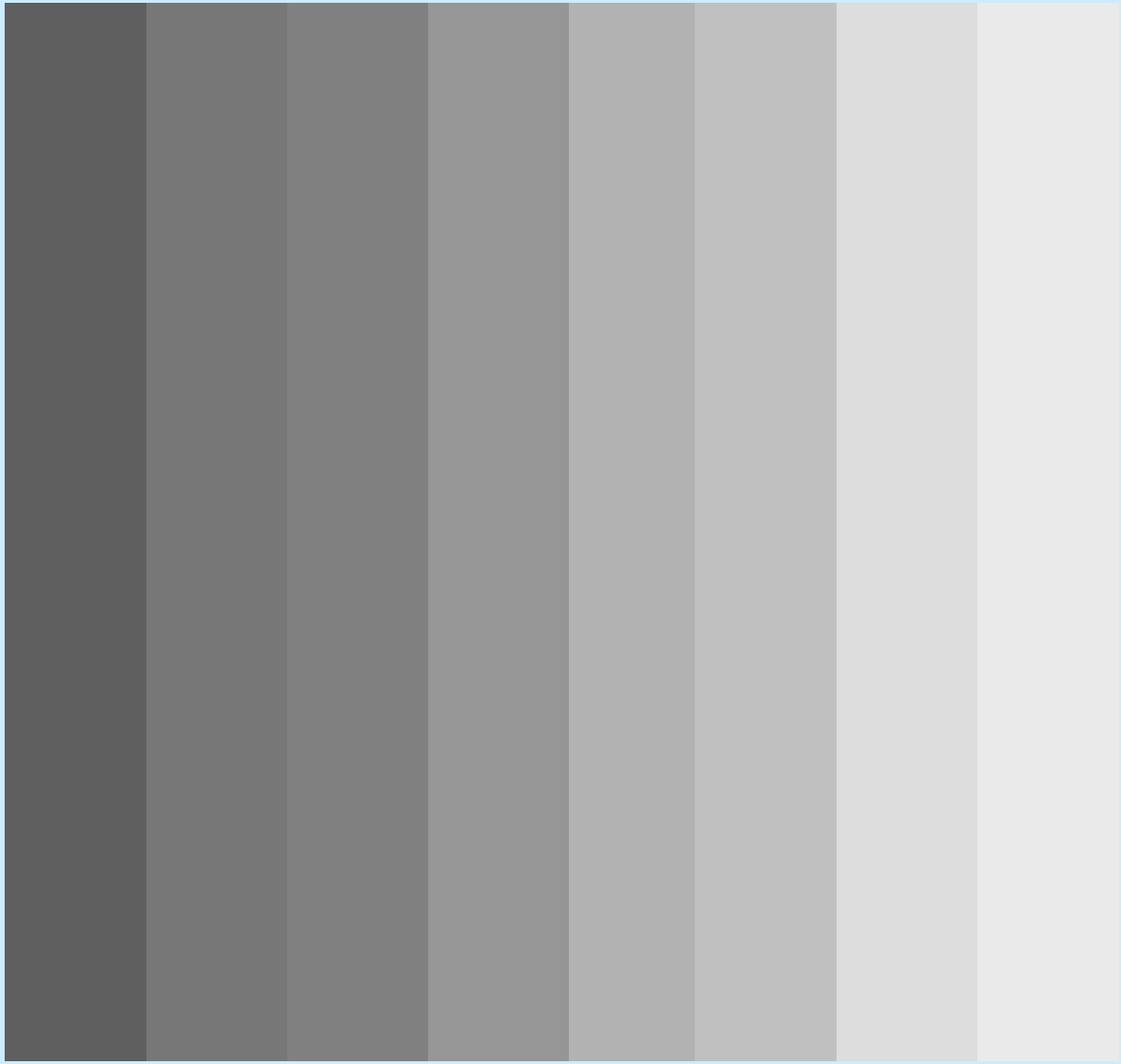


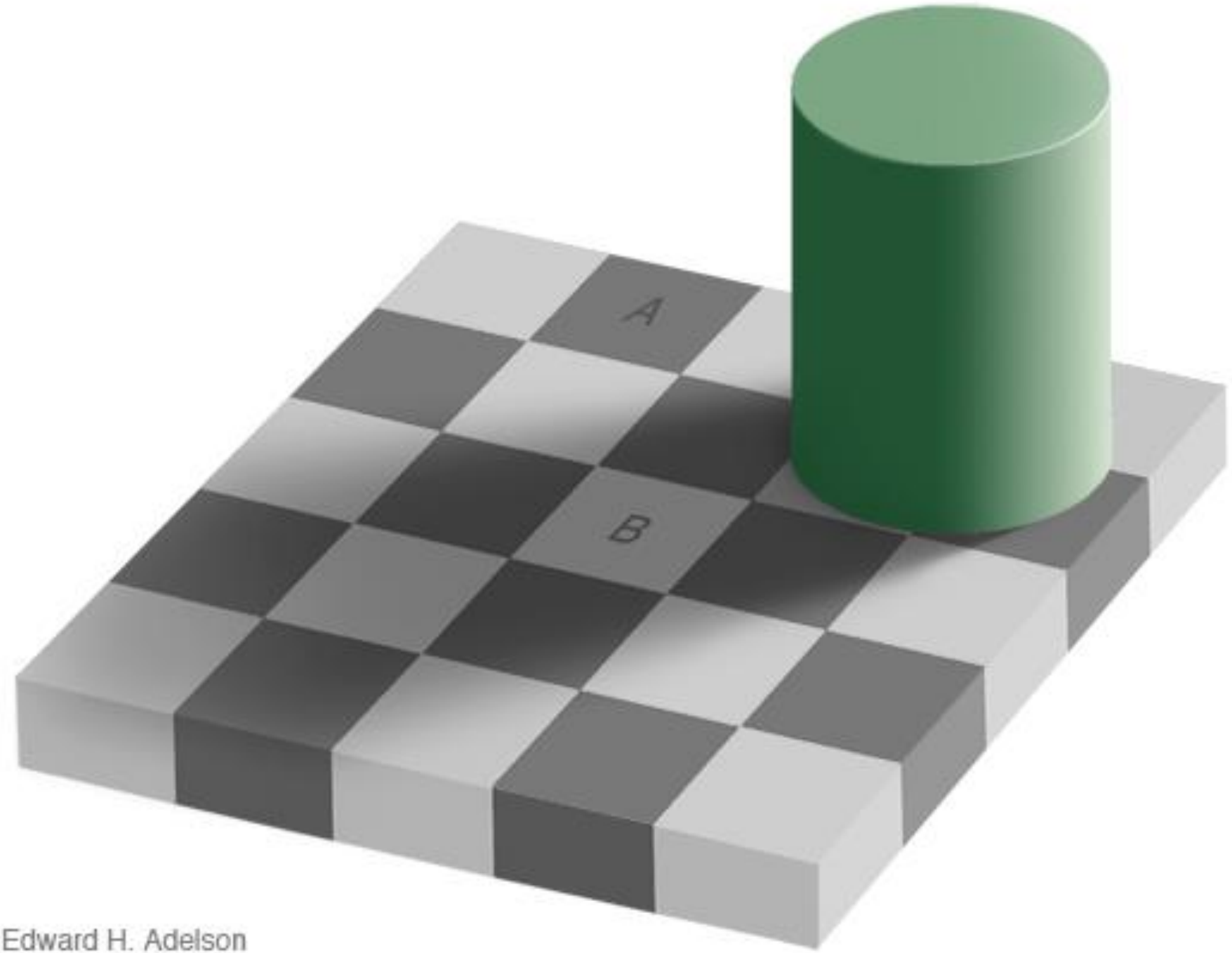


A

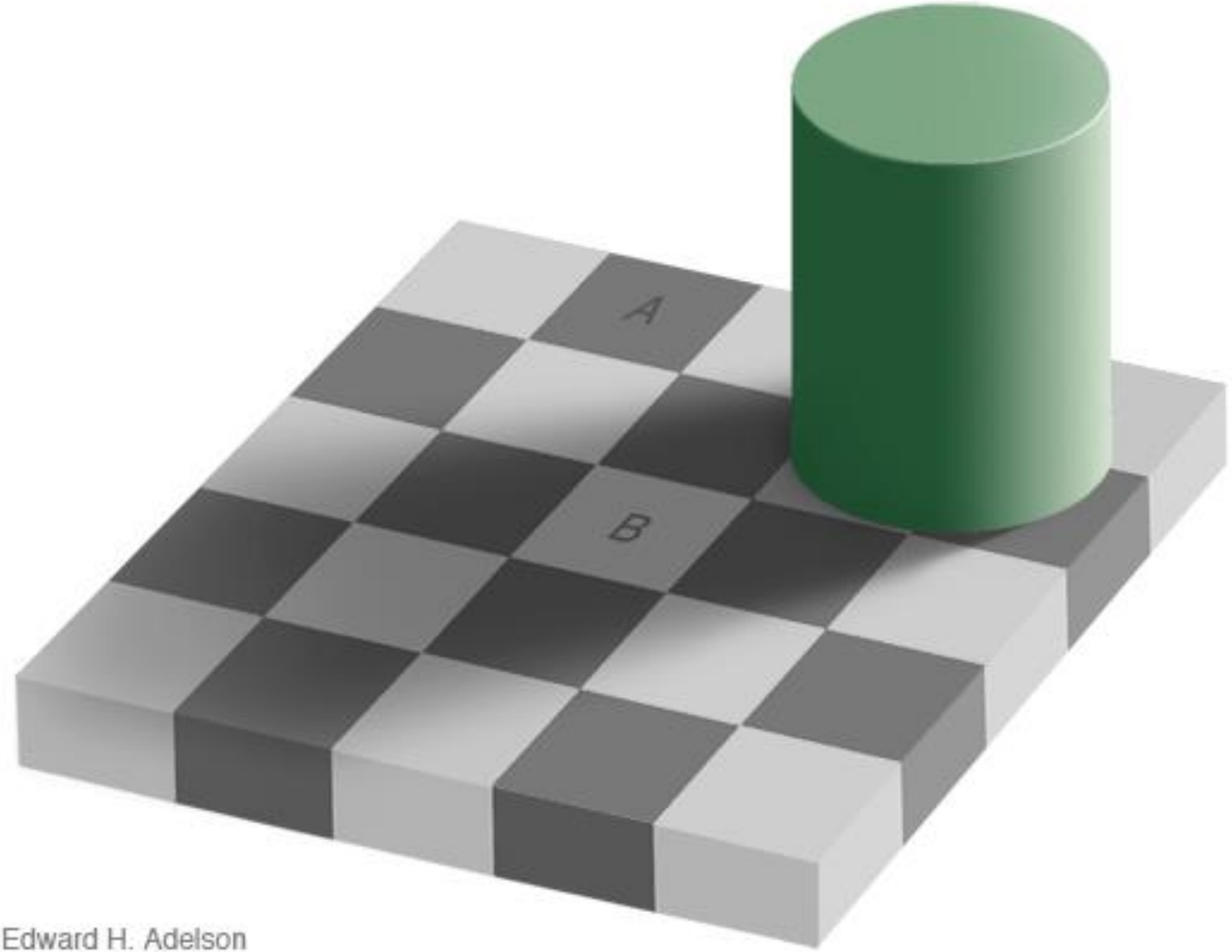


B

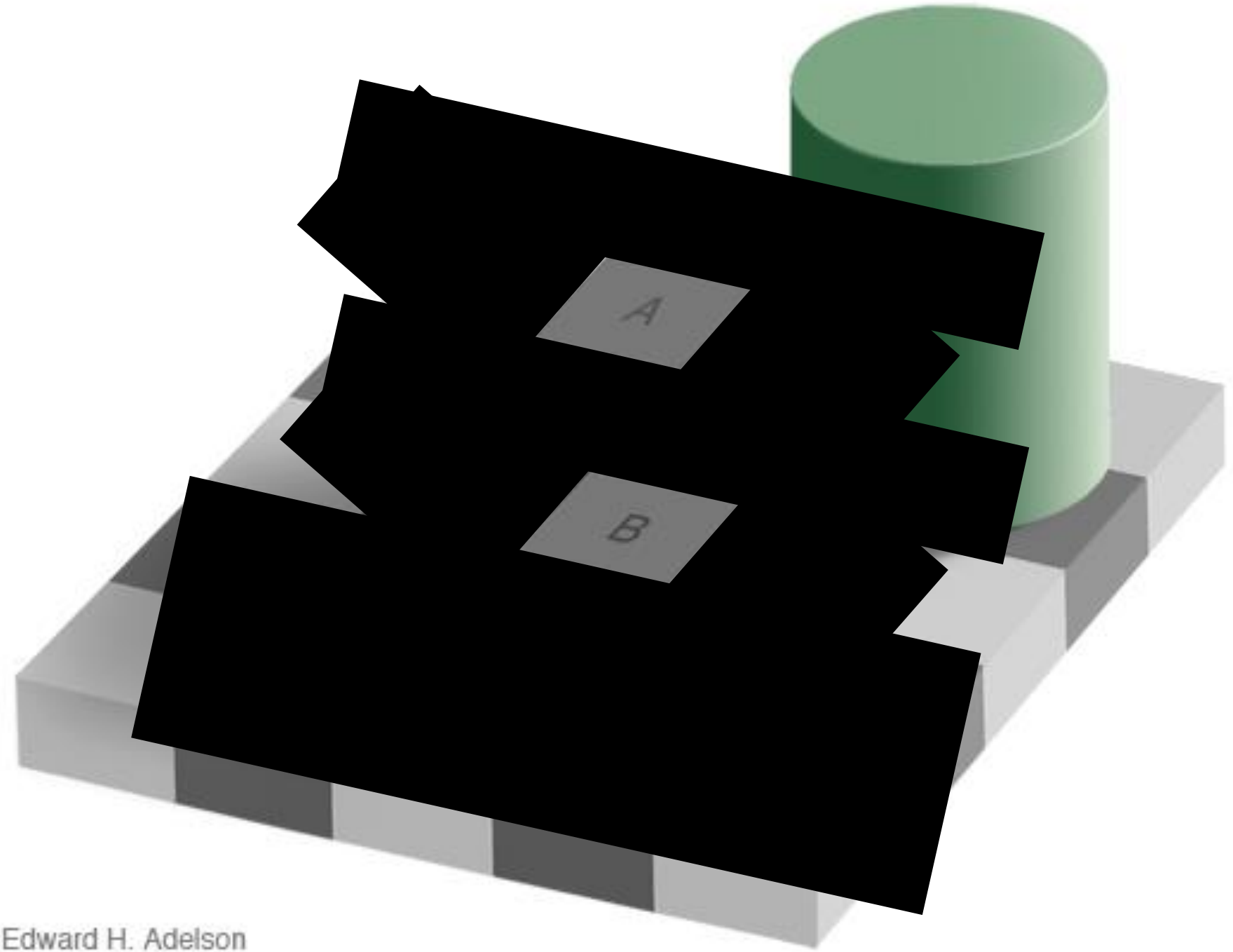




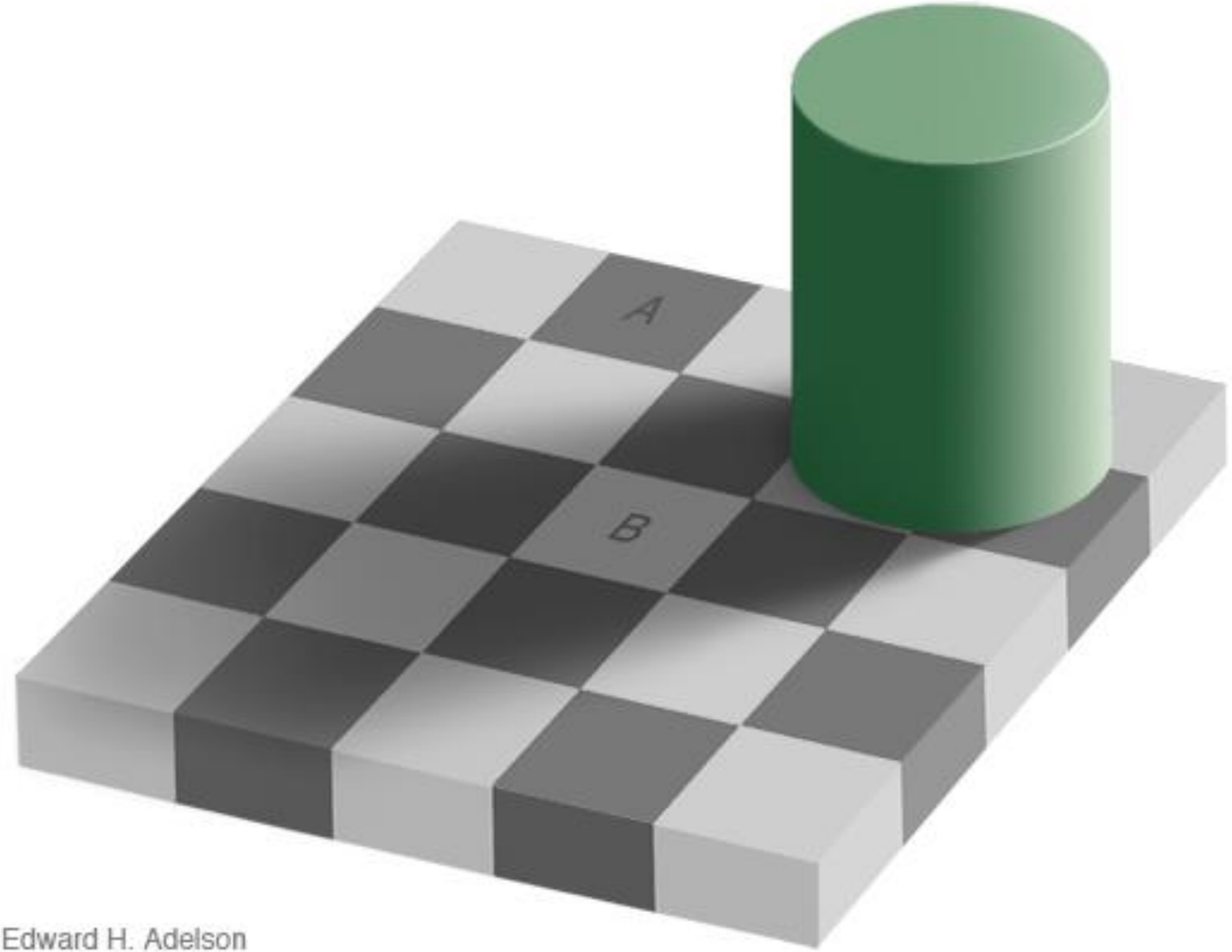
Edward H. Adelson



Edward H. Adelson

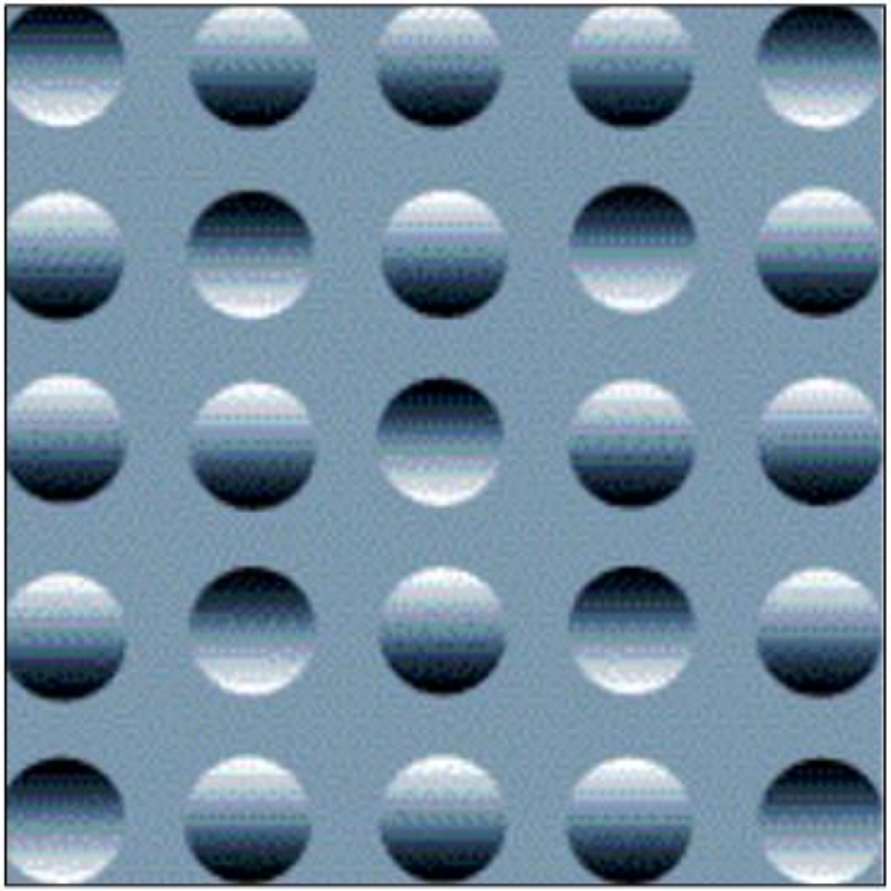


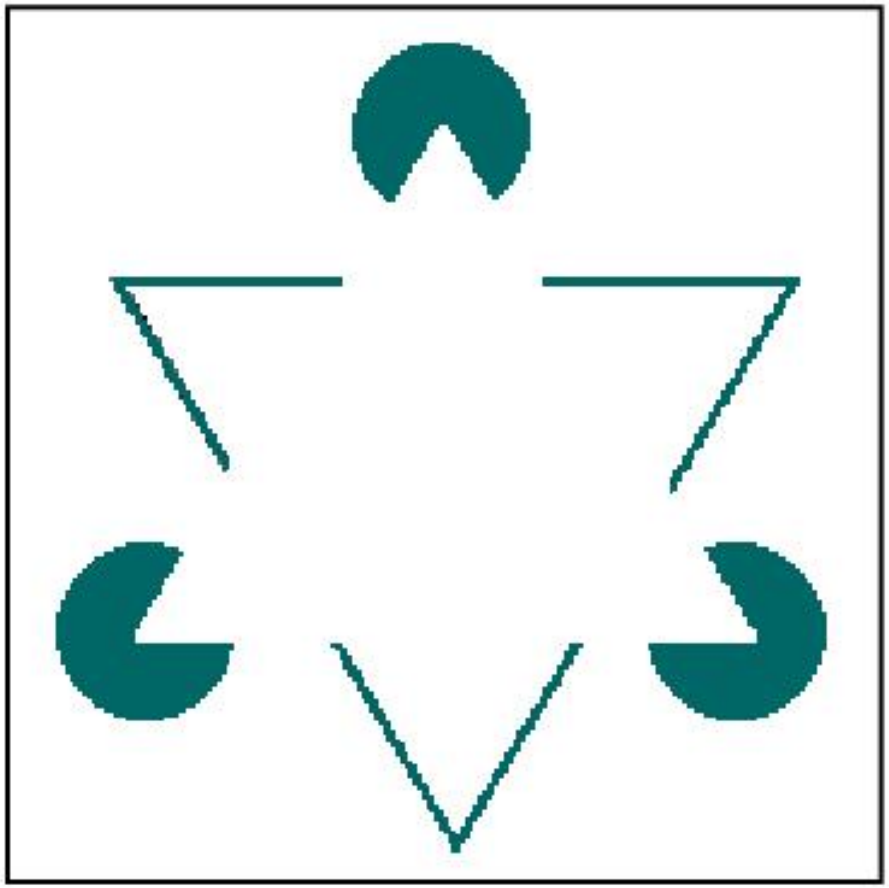
Edward H. Adelson



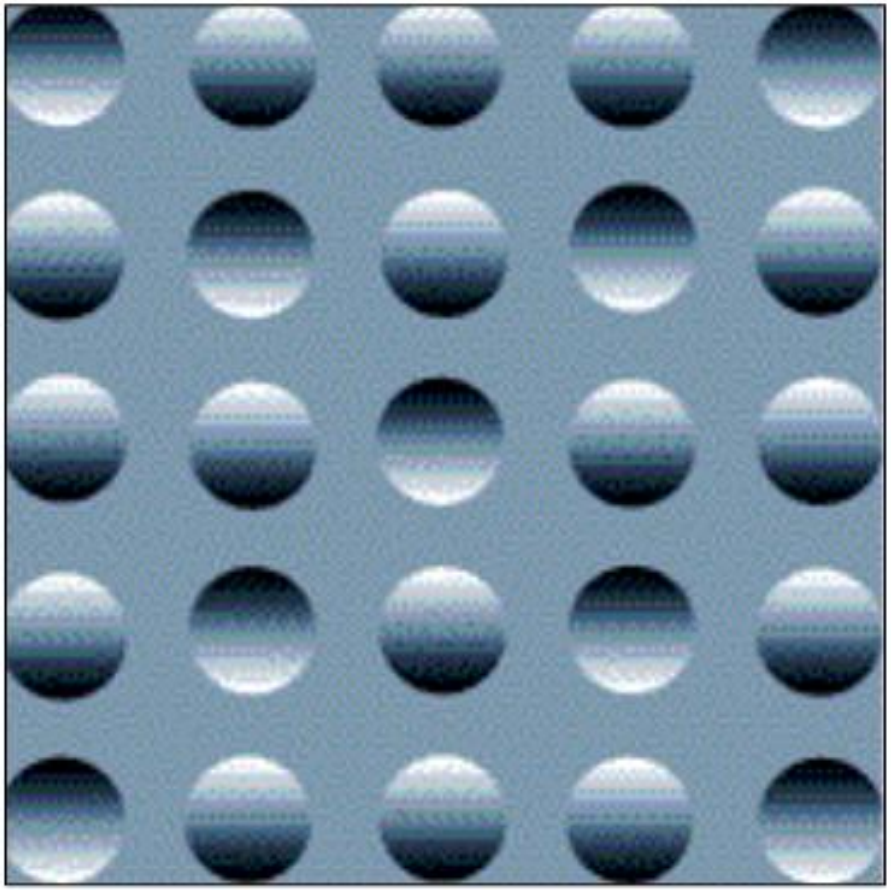
Edward H. Adelson

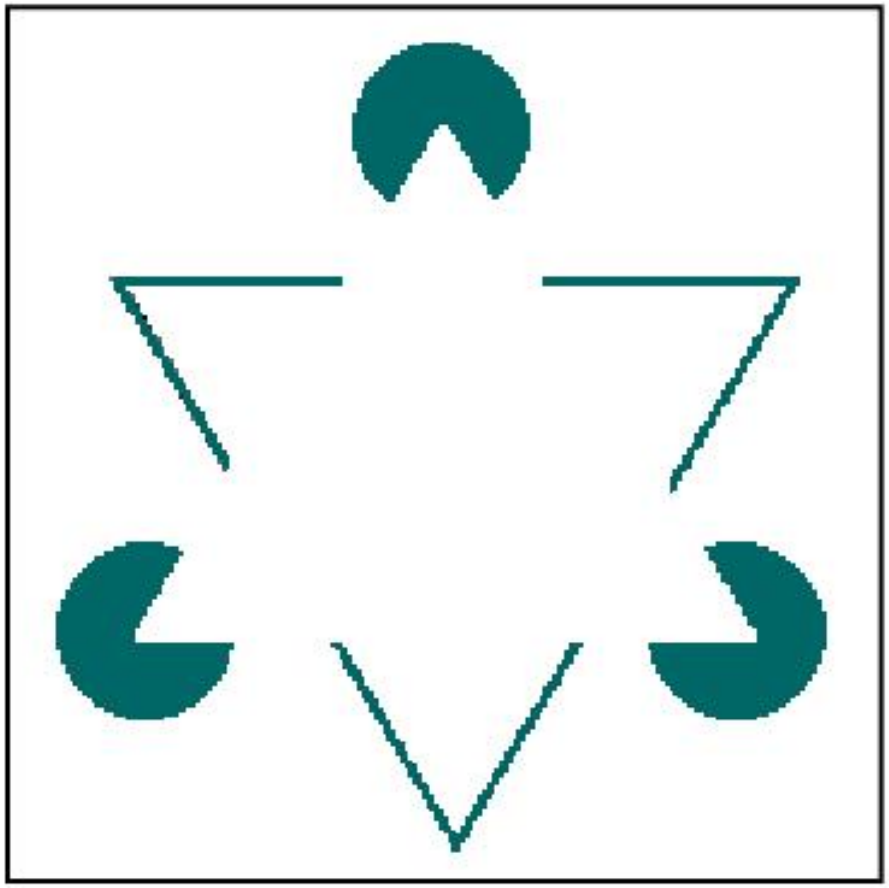
Illusions Reveal Some of the Brain's Assumptions

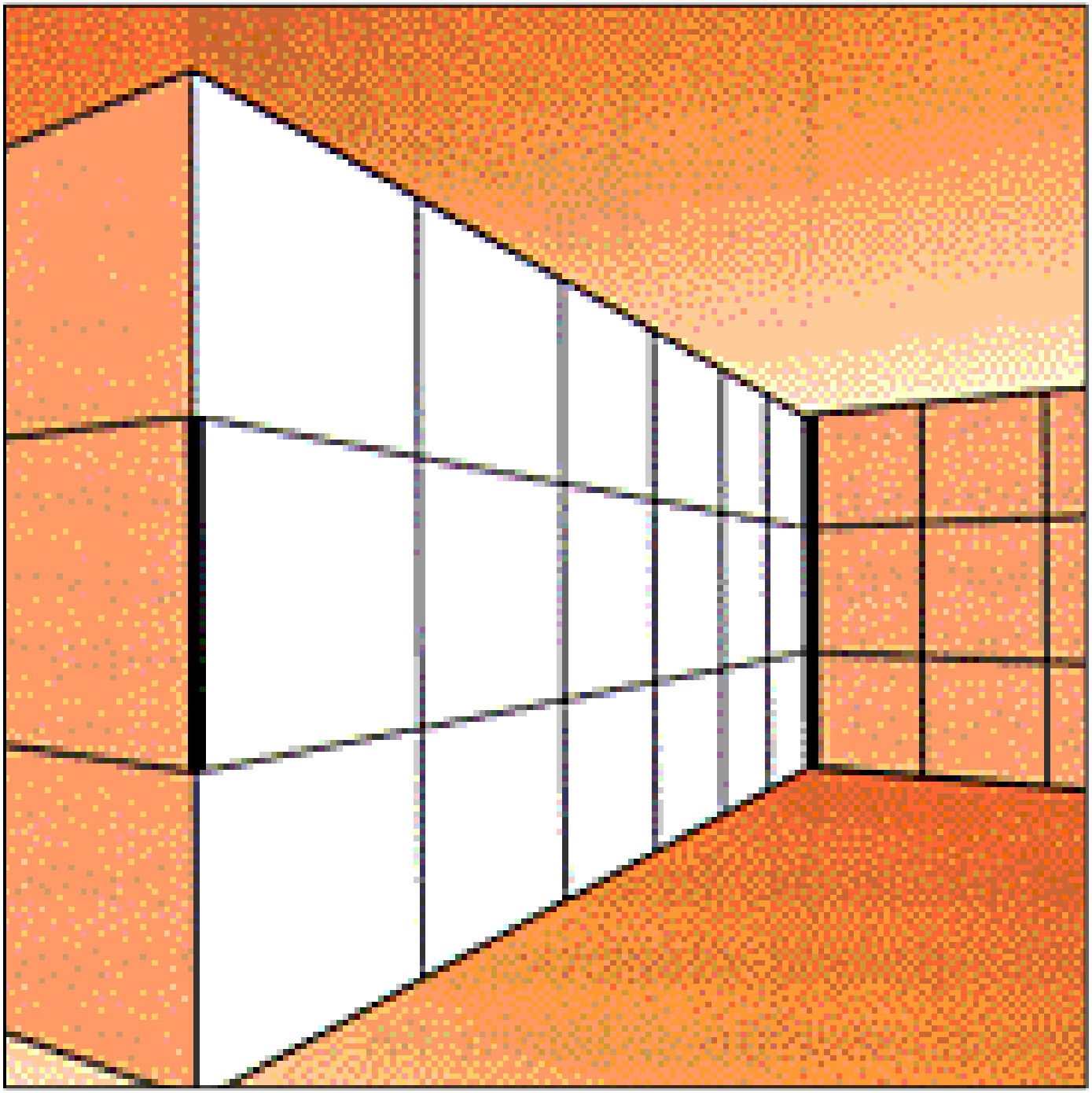




Illusions Reveal Some of the Brain's Assumptions







Pathophysiology of Brain as an organ

- Obstruction of the circulation of cerebro-spinal-fluid (CSF) leads to increased CSF pressure and hydrocephalus. In **hydrocephalus** the ventricles become distended. In young children, the intracranial volume may be increased because the sutures are not closed and the head can enlarge. However, if the increase continues, brain substance may be lost. In adults, an increase in the ventricular size compromises the flow of blood and causes the loss of brain tissue. (1)

REFERENCES

1. Berne RM and Levy MN Principles of Physiology, 2nd ed. Mosby 1996 (yellow boxes)

2. Despopoulos A and Silbernagl S, Color Atlas of Physiology, Thieme, 3d ed. 1986

3. Silbernagel, S., Lang, F.: Color Atlas of Pathophysiology. Stuttgart, Thieme 2000, pp. 406.

Pathophysiology: Motor control –1

- **Neurogenic paralysis**: A-motoneurons (α-MN) may be destroyed in the course of different diseases, resulting in muscle weakness or even paralysis of the muscles innervated by these α-MN, like in **poliomyelitis** caused by polio virus, or in **amyotrophic lateral sclerosis** (ALS). As α-MN die, they discharge erratically causing muscle **fasciculations** (visible contractions of muscle units). Afterα-Mn have died, the denervated muscles **atrophy** and develop **fibrilations** (spontaneous contractions of individual muscle fibers seen only with electromyography). Some of the denervated muscle fibers become innervated by collaterals from α-MN, which are still healthy and thus the size of some motor units is increased. This becomes a myographic characteristic differentiating neurogenic paralysis from **myogenic paralysis**, where the recorded potentials from motor unit are smaller (fewer muscle fibers alive per α-MN) and irregular.

Pathophysiology: Motor control – 2

➢ When muscles are stretched, increased activity in muscle **spindle** afferents excite α-MN monosynaptically and thus the muscle contracts (stretch reflex, negative feedback on muscle length). The force of contraction is sensed by the **tendon organs**, which disynaptically inhibit the same α-MN and the contraction stops (negative feedback on muscle force). The **stretch reflexes** are used routinely in the neurological examination. A reflex hammer is commonly employed to elicit phasic stretch reflexes. The limb to be examined is placed in a position that allows relaxation of the joint operated on by the muscles tested: The tendon of each muscle tested is struck briskly with the reflex hammer; and the 'subsequent contraction of the muscle is observed (or felt). Responses on the two sides are compared. The muscles that are often tested include the biceps brachii, the quadriceps, and the triceps surae. When stretch reflexes appear to be reduced, it is sometimes possible to enhance them by the **Jendrassik maneuver**, in which the subject hooks the fingers of the two hands and pulls the hands apart against resistance. Tonic stretch reflexes are examined by flexing and extending joints. In pathological conditions, the stretch reflexes may be either diminished or hyperactive. Causes of decreased stretch reflexes include interruption of peripheral nerves or spinal roots and motoneuron disease. Increased stretch reflexes care seen in diseases that affect the descending motor pathways, such as cerebrovascular accidents (strokes) that interrupt the internal capsule.

Pathophysiology: Motor control –3

- **Spinal cord injury** is unfortunately a relatively common occurrence and generally affects young adults. Frequent causes are automobile and motorcycle accidents and gunshot wounds. Incomplete transections are more frequent than complete ones and disastrous. When spinal injuries affect the upper cervical spinal cord, they are often fatal because of interruption of the respiratory control system that descends from the brainstem to the phrenic motor nucleus. A lesion below the phrenic nucleus may result in paralysis of all four extremities **(quadriplegia),** whereas a lesion of the thoracic spinal cord causes **paraplegia,** which is paralysis of the lower extremities.

Pathophysiology: Motor control – 4

- A misalignment of the two visual axes can cause double vision, or **diplopia.** Such misalignment, or **strabismus** (cross-eyed), can result from weakness of the muscles of one eye, causing its visual axis to differ from that of the other eye. Over time the misaligned eye may lose visual acuity, a condition called **amblyopia.**
- Damage to the frontal eye field, such as by a stroke that affects one frontal lobe, can result in tonic conjugate **deviation of the eyes** toward the damaged side (a stroke victim may look toward the side of the stroke). This is presumably because of the activity of the intact frontal eye field in the contralateral hemisphere. Electrical stimulation of the frontal eye field on the side causes forced conjugate deviation of the eyes toward the opposite side. A similar movement can occur during the onset of an epileptic seizure that originates in the frontal lobe. Tonic conjugate deviation of the eyes can also occur following damage to the horizontal gaze center in the pons. The eyes in this case would deviate toward the side opposite that which is damaged. This condition can be distinguished from that caused by frontal lobe damage by the distribution of paralysis of the extremities and by cranial nerve signs.

Pathophysiology: Motor control –5

- A **lesion of the posterior parietal cortex** will cause deficits in visually guided movements. Humans may develop a **neglect syndrome** (especially if the lesion is in the non-dominant hemisphere for speech, in which a patient will be unable to recognize objects placed in the contralateral hand and unable to 'draw three-dimensional objects accurately: In fact, the patient may deny that the contralateral limbs even belong to him.
- When the corticospinal and corticobulbar tracts are completely interrupted, the distal muscles of the contralateral upper and lower extremities and muscles of the contralateral lower face and tongue are paralyzed (**hemiplegia**). Unless the lesion is restricted to these tracts, the deficit is a **spastic paralysis**. Spasticity usually accompanies hemiplegia produced by a lesion of the internal capsule or at other levels of the nervous system, because the cortico-reticulo-spinal pathway is interrupted along with the pyramidal tract. Spasticity is also present in spinal cord injuries when transection at an upper cervical level causes paralysis of all four extremities **(quadriplegia)** or transection below the cervical enlargement causes paralysis of both lower extremities **(paraplegia).** Spastic paralysis is associated with an increase in muscle tone and increased phasic stretch reflexes. The latter may lead to **clonus,** such as in the ankle, in response to a brisk passive movement. Interruption of the cortico-spinal tract at any level causes an important release response, **Babinski's sign**.

Pathophysiology: Motor control –6

➢ Lesions of the neocerebellum affect chiefly the distal limbs. The deficits include:

• **delayed initiation** of movements,

• **ataxia of the limbs** (incoordination), and reduced muscle tone. The limb ataxia results in **asynergy** (lack of synergy in movements),

• **dysmetria** (inaccurate movements),

• **intention tremor** (oscillations at the end of a movement), and

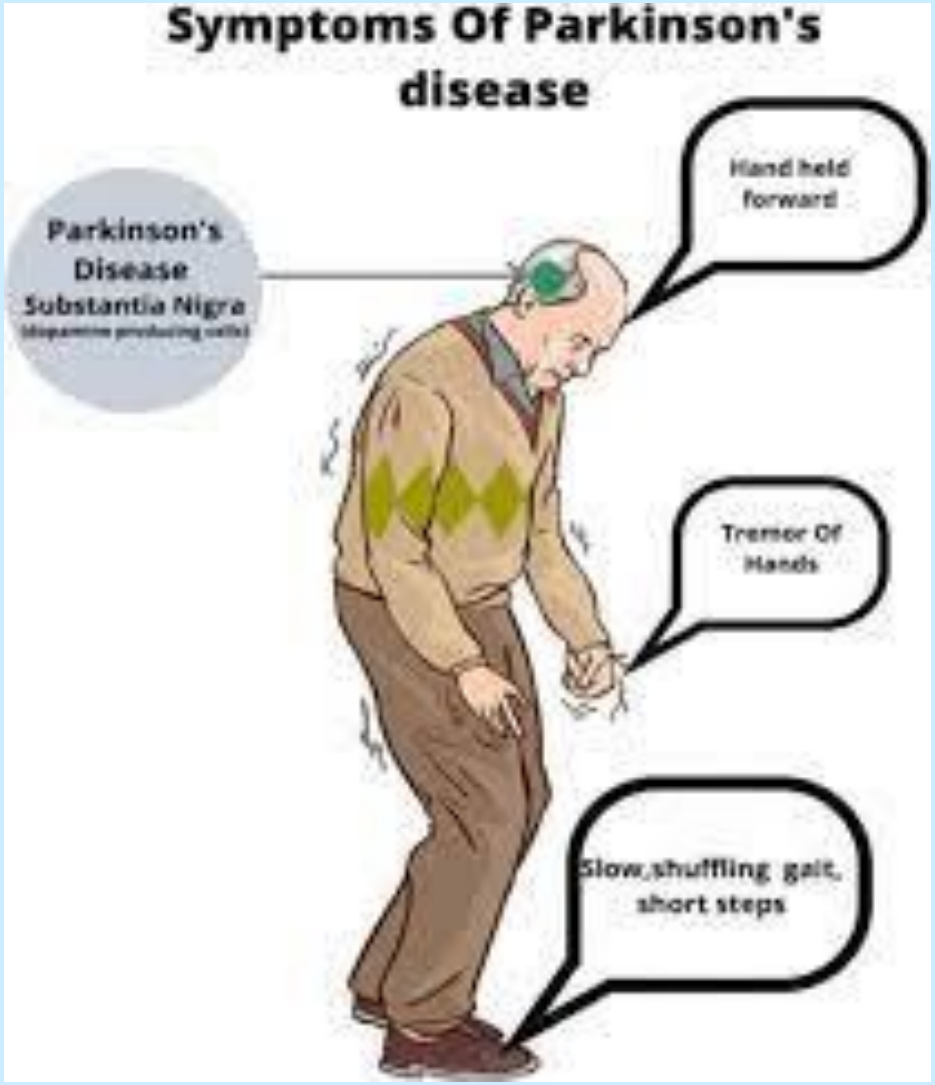
• **dysdiadochokinesia** (irregular performance of pronation and supination movements of the forearm).

• Reduced muscle tone leads to **pendular phasic stretch reflexes** in the lower extremity.

• Bilateral lesions of the neocerebellum may result in **dysarthria** (slow, slurred speech; synonymous with scanning speech).

These classical neocerebellar signs are often seen in **multiple sclerosis.**

Parkinson's disease is a brain disorder that causes unintended or uncontrollable movements, such as shaking, stiffness, and difficulty with balance and coordination. Symptoms usually begin gradually and worsen over time. As the disease progresses, people may have difficulty walking and talking.

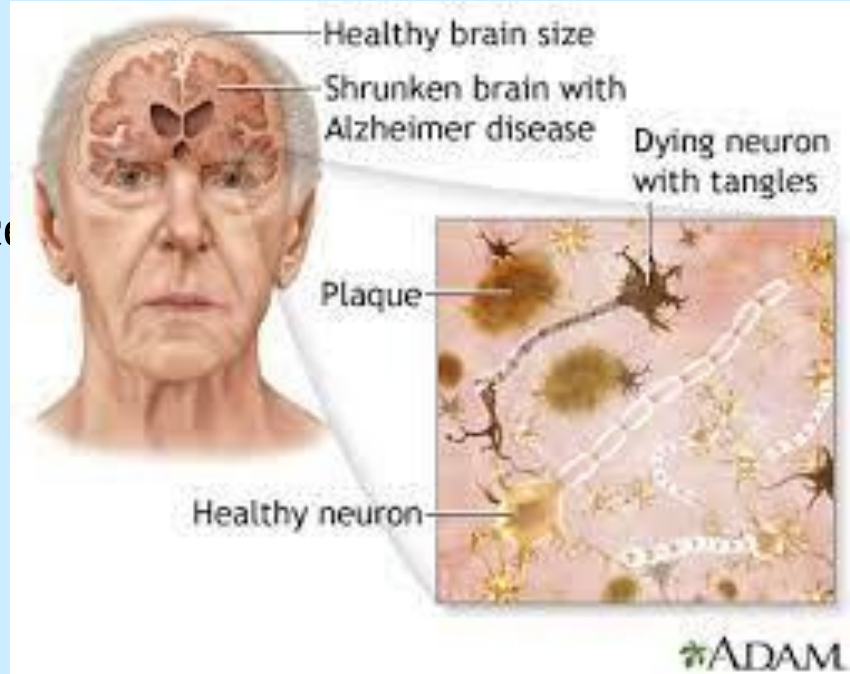


Huntington's disease is a rare, inherited disease that causes the progressive breakdown (degeneration) of nerve cells in the brain. Huntington's disease has a wide impact on a person's functional abilities and usually results in movement, thinking (cognitive) and psychiatric disorders.

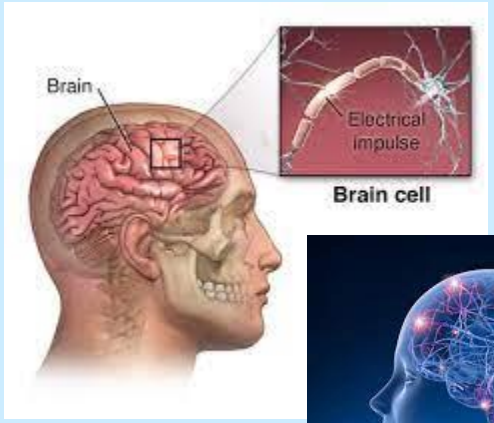
Signs of Mild **Alzheimer's disease**

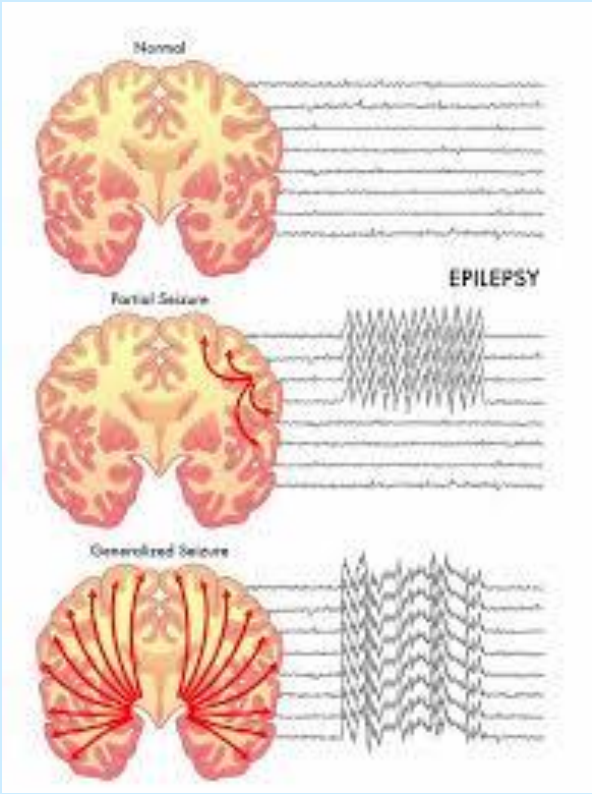
A person may seem healthy but has more and more trouble making sense of the world around them. The realization that something is wrong often comes gradually to the person and their family. Typically progresses in several stages: preclinical, mild, moderate, and severe. Problems can include:

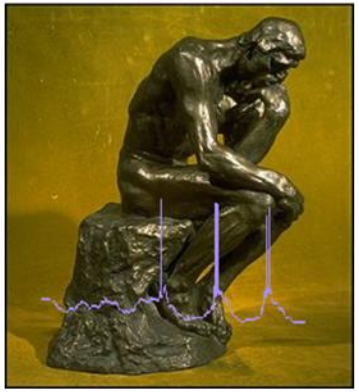
- Memory loss that disrupts daily life
- Poor judgment, leading to bad decisions
- Loss of spontaneity and sense of initiative
- Losing track of dates or knowing current location
- Taking longer to complete normal daily tasks
- Repeating questions or forgetting recently learned information
- Trouble handling money and paying bills
- Challenges in planning or solving problems
- Wandering and getting lost
- Losing things or misplacing them in odd plac
- Difficulty completing tasks such as bathing
- Mood and personality changes
- Increased anxiety and/or aggression



Epilepsy is a common condition that affects the brain and causes frequent seizures, which are bursts of electrical activity in the brain that temporarily affect how it works. They can cause a wide range of symptoms depending on the brain location of hypersynchronous activity and what was the physiological role oof the affected brain area. Epilepsy can start at any age, but usually starts either in childhood or in people over 60. It is incurable but its symptoms can be ameliorated by drugs or surgery in about 75% of cases.



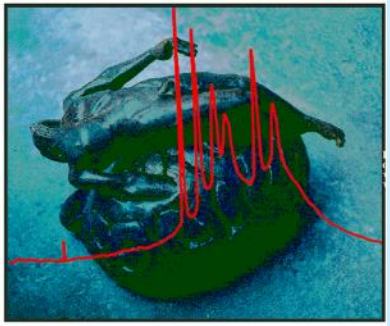




Φυσιολογία

- Υπέρμετρη
- Υπερσύγχρονη
- Διεγερσιμότητα

Νευρώνων



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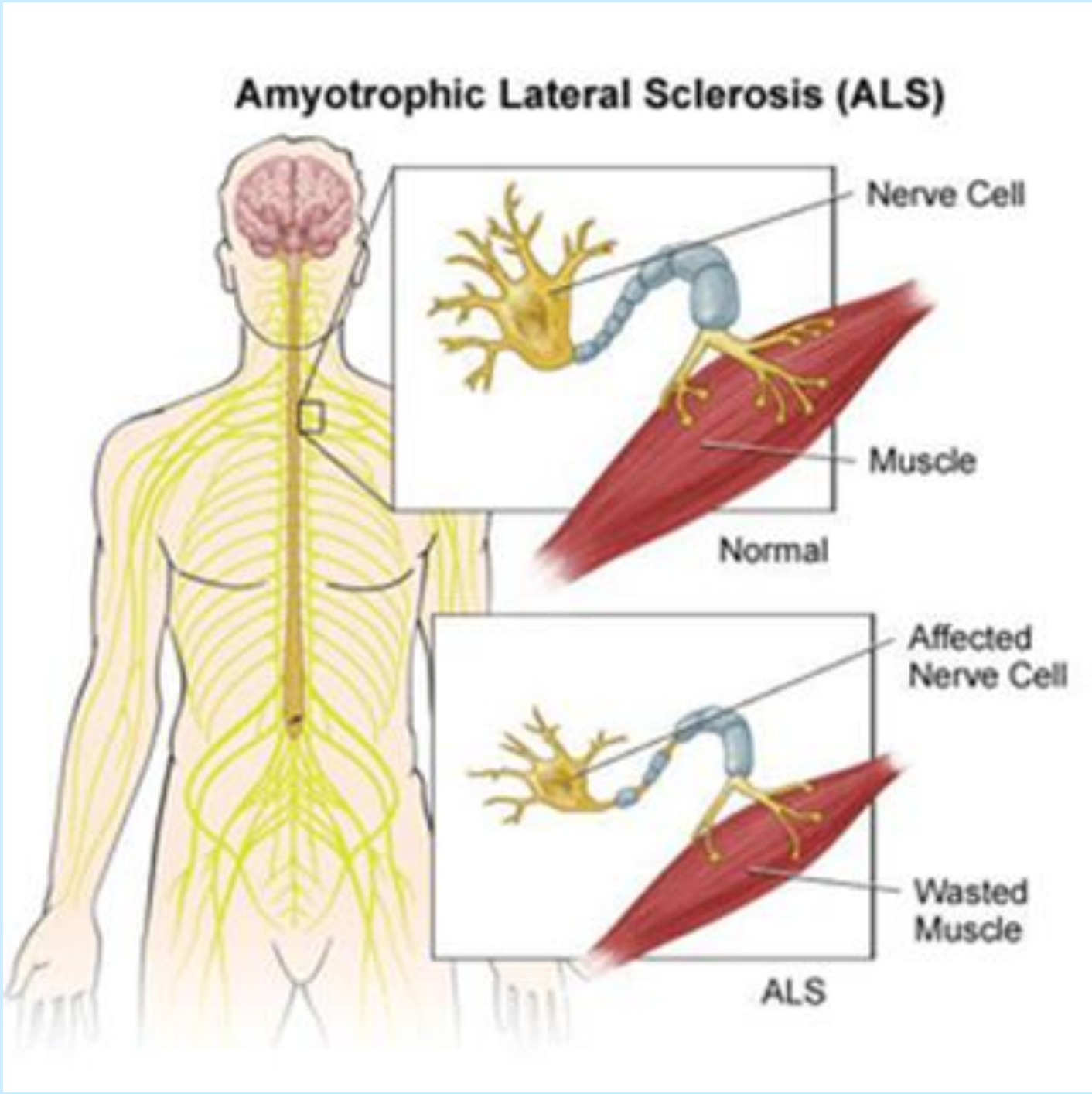
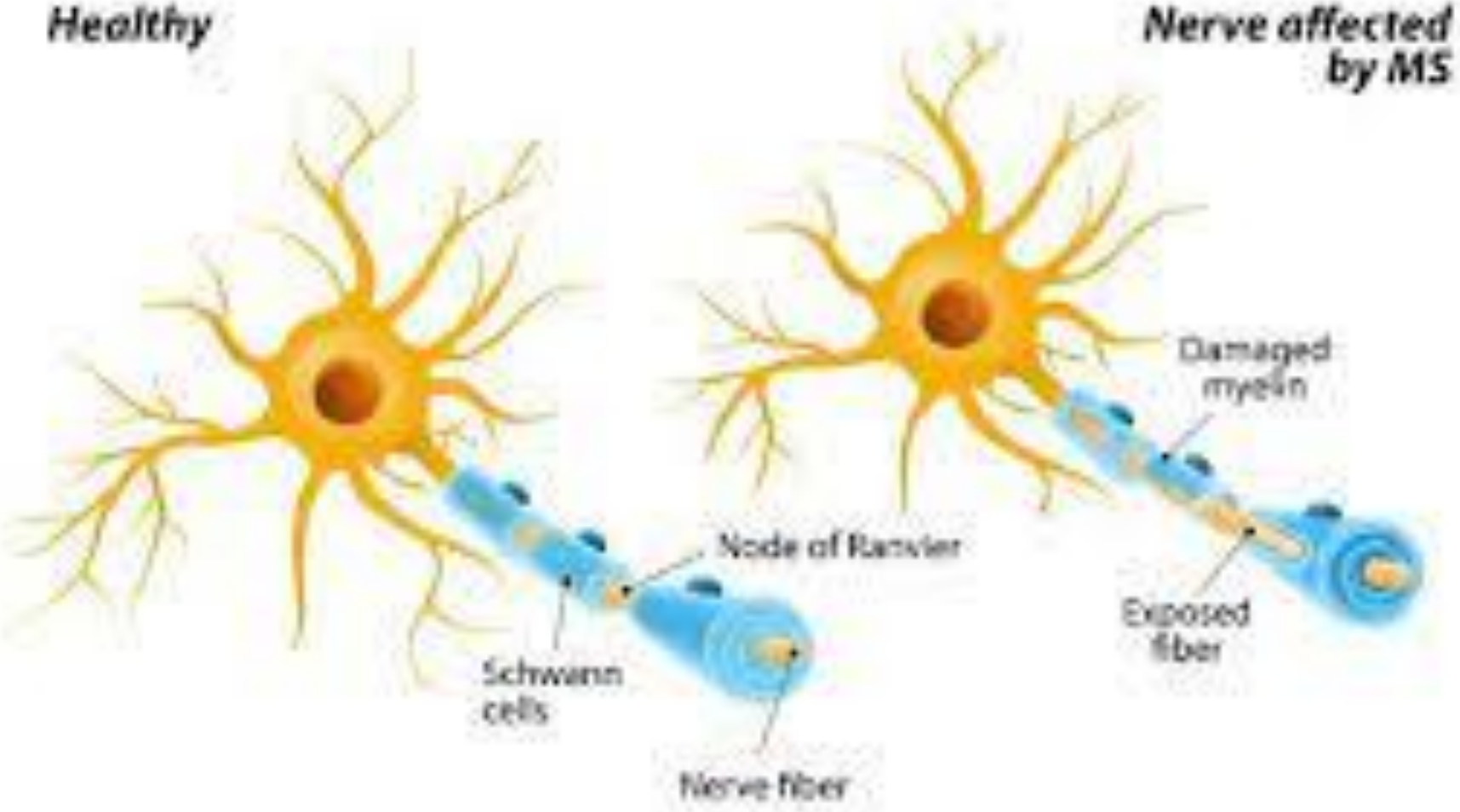
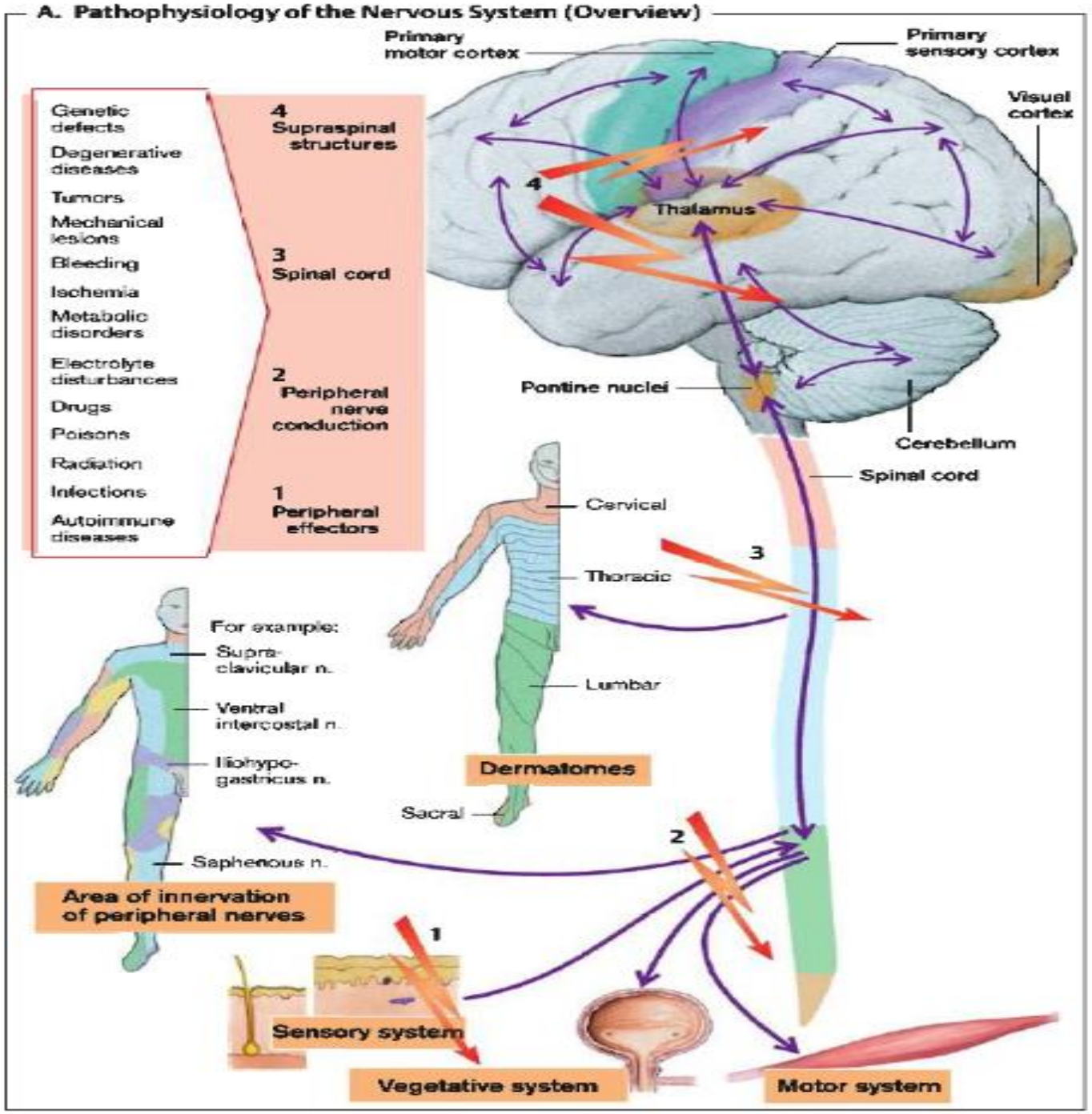

Amyotrophic Lateral Sclerosis (ALS)
Nerve Cell
Muscle
Normal
Affected
Nerve Cell
Wasted
Muscle
ALS

MULTIPLE SCLEROSIS




A. Pathophysiology of the Nervous System (Overview)
Primary motor cortex
Primary sensory cortex
Visual cortex
Thalamus
Pontine nuclei
Cerebellum
Spinal cord
Genetic defects
Degenerative diseases
Tumors
Mechanical lesions
Bleeding
Ischemia
Metabolic disorders
Electrolyte disturbances
Drugs
Poisons
Radiation
Infections
Autoimmune diseases
4 Supraspinal structures
3 Spinal cord
2 Peripheral nerve conduction
1 Peripheral effectors
Cervical
Thoracic
Lumbar
Sacral
Dermatomes
For example:
Supra-clavicular n.
Ventral intercostal n.
Iliohypo-gastricus n.
Saphenous n.
Area of innervation of peripheral nerves
Sensory system
Vegetative system
Motor system

Emerging pathophysiological concepts

- Autoimmune processes
- Degenerative processes
- Environmental toxicities
- Global epidemics

… and trends

- Costly advanced biotechnology
- Genetic & personalized treatment for the elite
- Bio(med) ethics


End