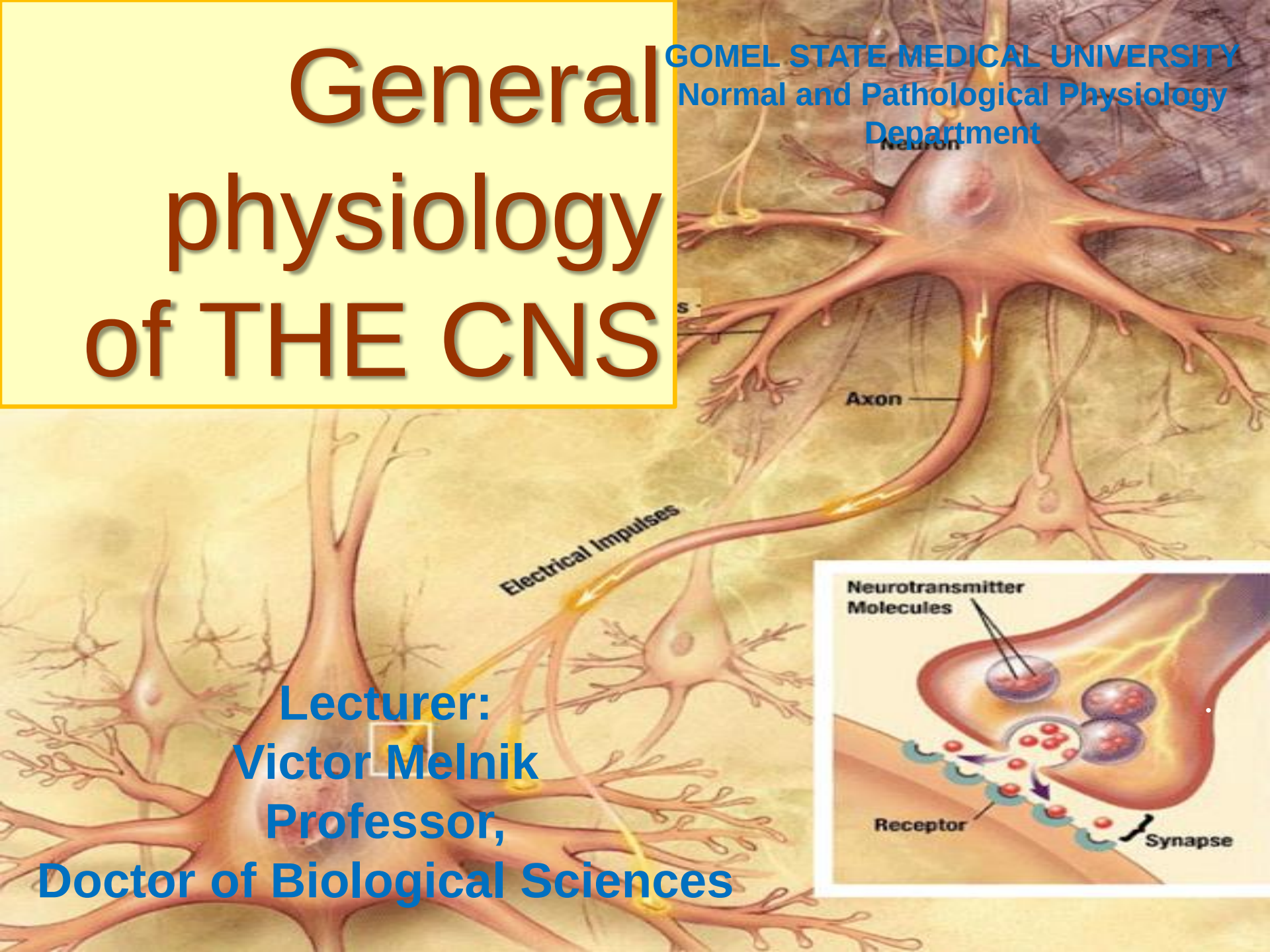
General physiology of THE CNS

GOMEL STATE MEDICAL UNIVERSITY
Normal and Pathological Physiology Department



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Lecture plan:

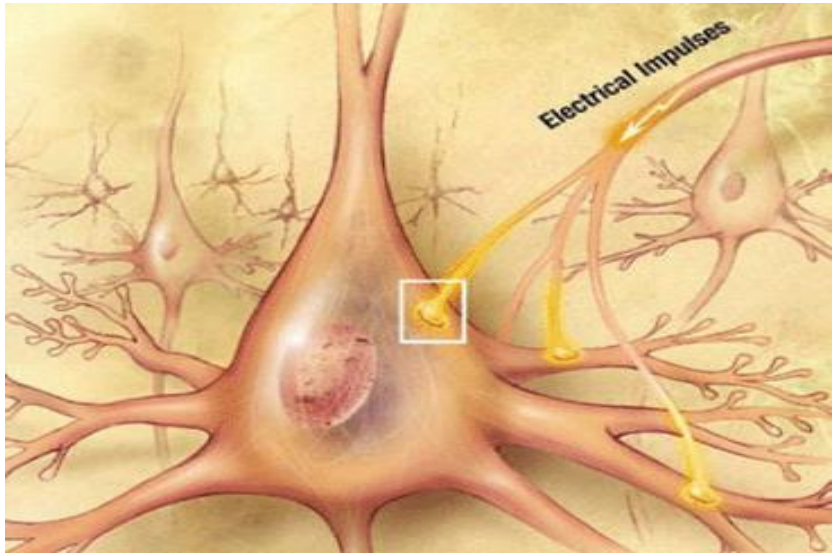
1. **Reflex activity of the nervous system.**
2. **Properties of the nerve centers. Main principles of excitation transmission in nerve centers.**
3. **Inhibition in the CNS. Inhibition mechanisms.**
4. **Coordination of reflexes. Dominant.**

1. Reflex activity of the nervous system

The central nervous system (CNS) is responsible for coordinated activity of all the organs and systems, as well as for the organism`s adaptation to environmental changes and formation of goal-seeking behaviour.

Functions of CNS

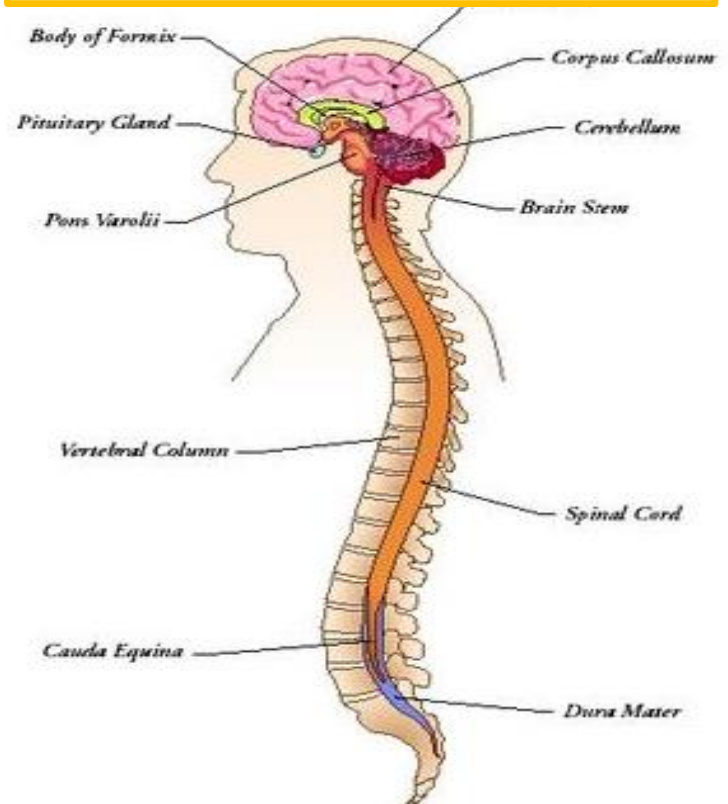
- **Sensory**
- **Integrative**
- **Control & regulation**
- **Informational**
- **Behavioral**



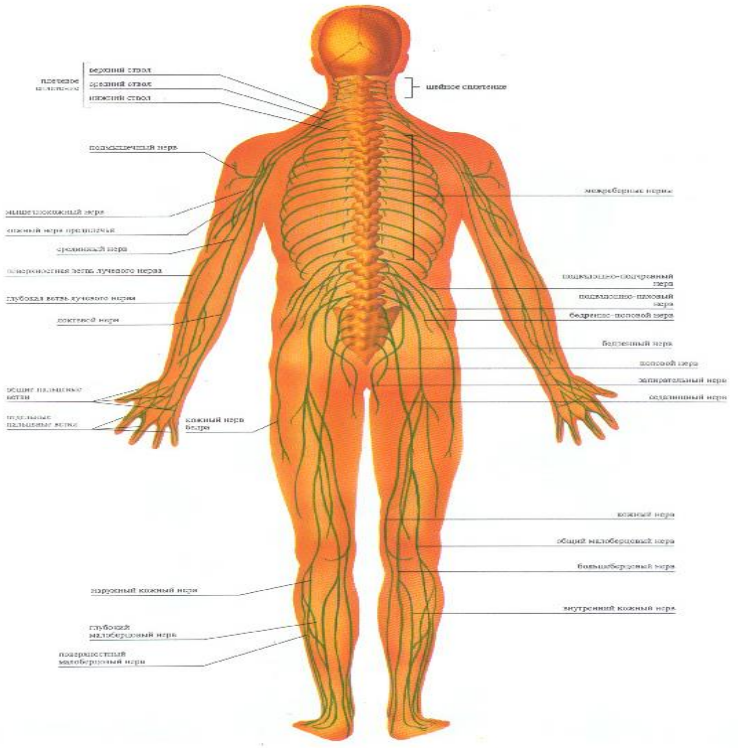
The human nervous system is divided **structurally** into **central** (the brain and spinal cord) and **peripheral** (nerve fibers, nerve plexuses, nerve terminations).

Structural division of the nervous system

Central nervous system (CNS)



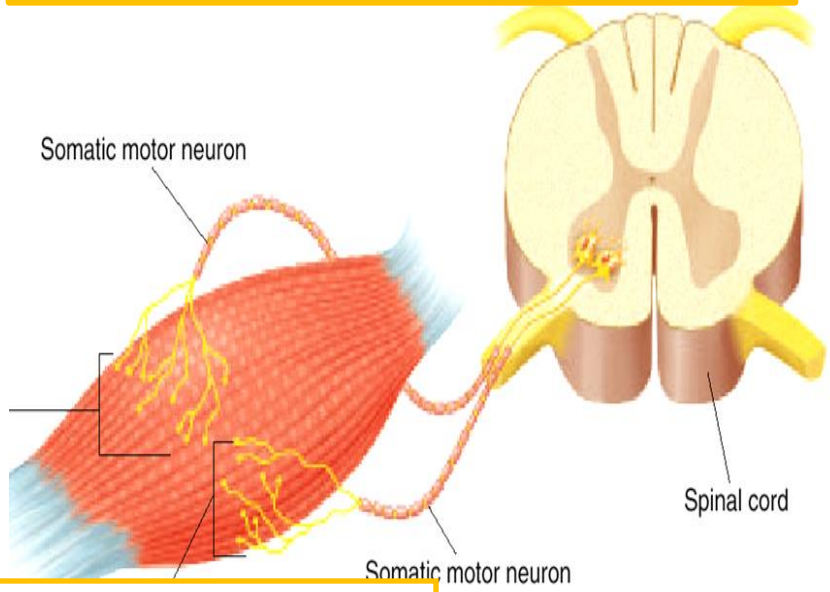
Peripheral nervous system



By its **functions**, the nervous system is divided into **somatic** and **vegetative (autonomic).**

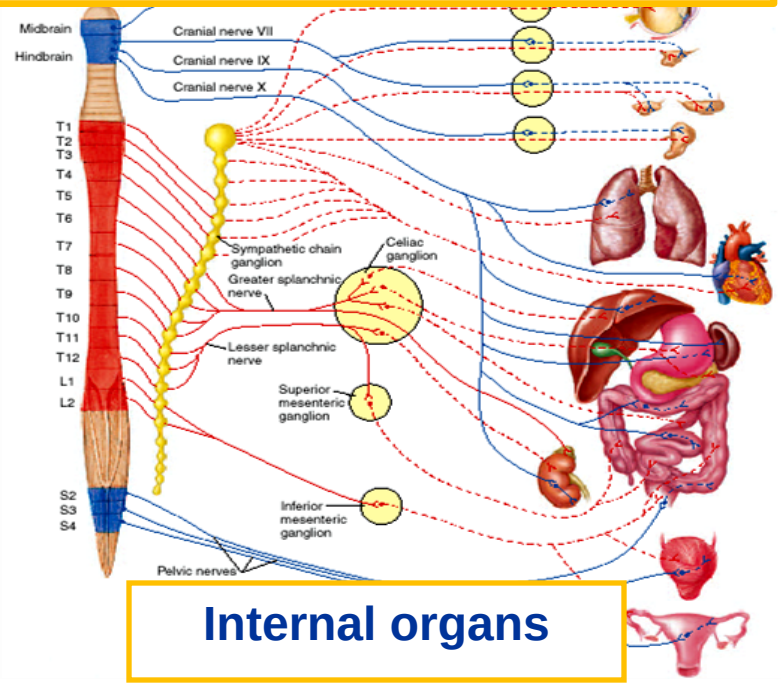
Functional division of the nervous system

Somatic nervous system



Skeletal muscle

Autonomic nervous system



Internal organs

The somatic nervous system:

— provides voluntary regulation;

— regulates the work of skeletal muscles;

— transmits sensory information from the external environment;

— its centers are located in the cortex of the cerebrum.

The vegetative (autonomic) nervous system (sympathetic, parasympathetic, and metasympathetic):

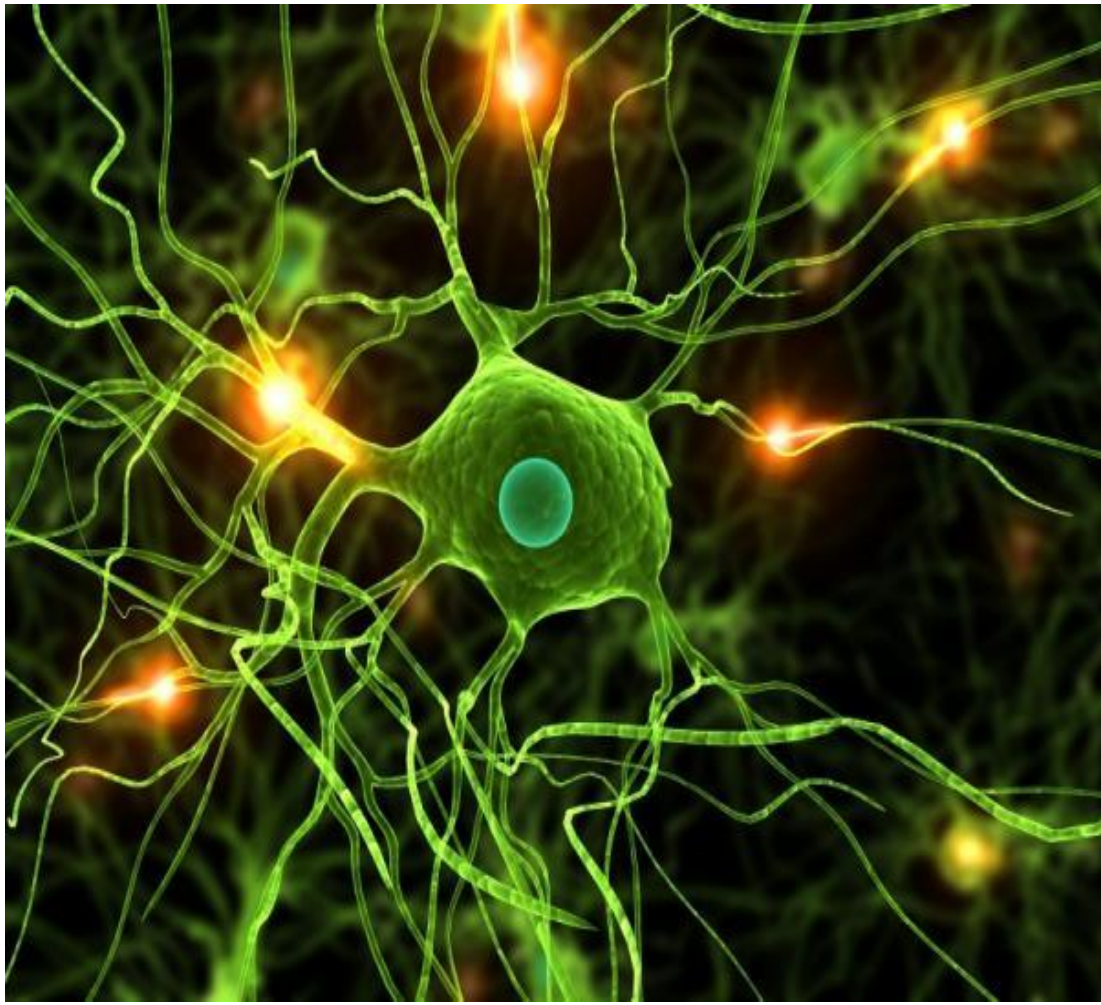
— provides involuntary regulation;

— regulates the work of the internal organs, glands, heart, and blood vessels;

— the main vegetative centers are located in the hypothalamus.

Neuron is the structural and functional unit of CNS

The nervous system consists of nervous cells (neurons), which process information, and glia, which provide neurons with mechanical and metabolic support.



Up to 10^{11} – 10^{12} neurons form the central nervous system

Neurons form chains and nerve centers, which compound the functional systems of the brain.

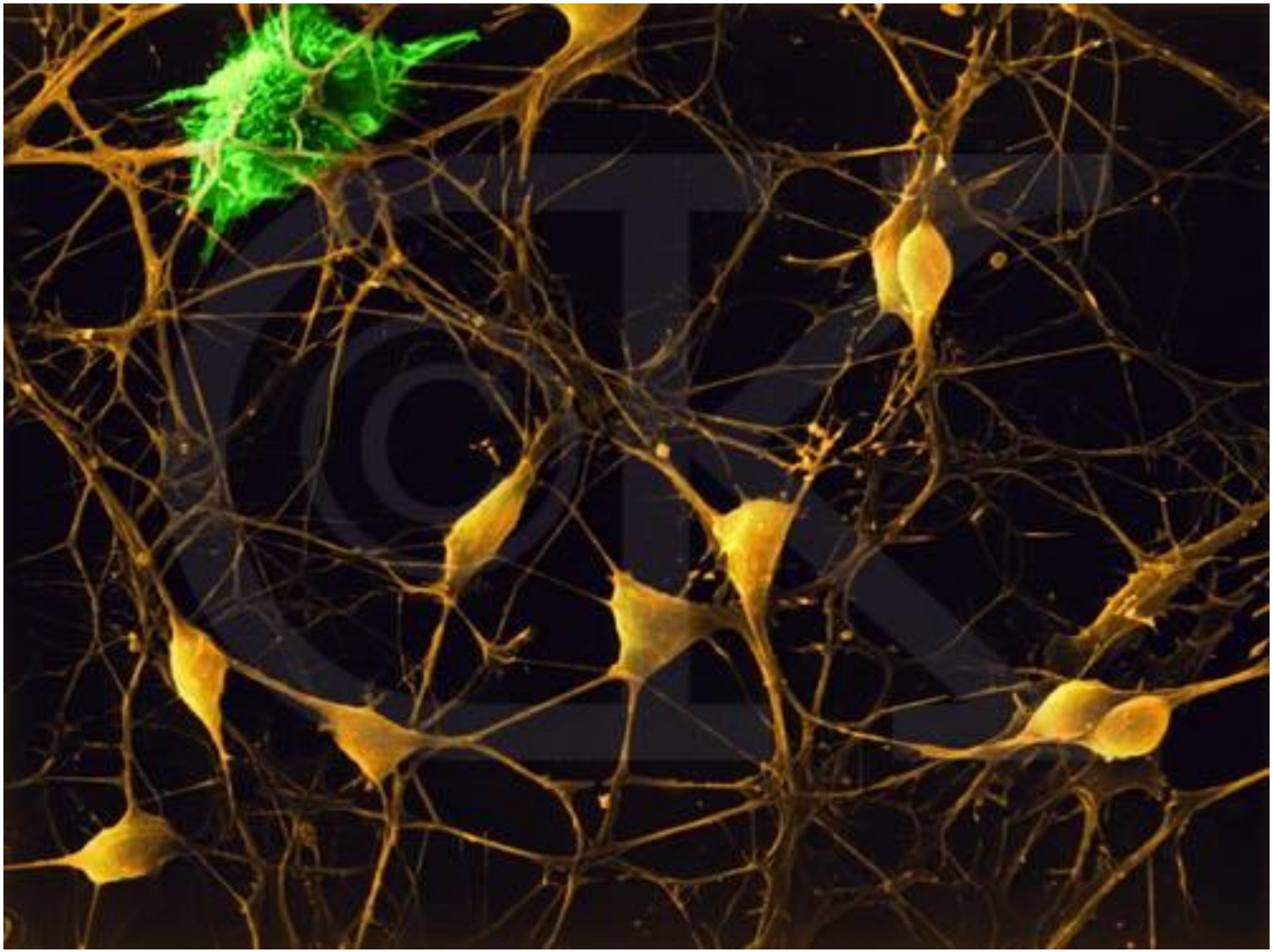


Figure — Neural networks

The main components of the nervous cell are:

— cell body (soma);

— dendrites;

— axon;

— presynaptic axon terminal.

Each of these parts performs a certain function. The **soma** contains organelles requisite for normal neuronal activity. The cell body of the neuron usually gives rise to multiple dendrites and to one axon.

In most neurons the **dendrites** have many branches and their entire surface significantly exceeds the surface of the cell body. The dendrites are the main structures which receive signals from body tissues or other neurons and pass them into the cell body.

The **axon** is a special cellular extension that arises from the cell body at a site called the axon hillock. The main function of the axon is to conduct signals to other nerve cells or innervated organs. The presynaptic axon terminal contains vesicles with the mediator, which, when released into the synaptic cleft, either excites or inhibits the postsynaptic membrane. Also, the membrane of the presynaptic terminal contains many calcium channels, and their activation provides an influx of calcium ions into the axon terminal.

Neurons differ by the size of the cell body, length, number of dendrites, and the length of the axon (Figure).

By their localization and functions, neurons are divided into:

1. Afferent (sensory) — which transmit signals from receptors to nerve centers.

2. Interneurons — which do not go outside the CNS boundaries and provide connections between different afferent and efferent neurons.

3. Efferent (motor) – which transmit information to muscles or executing organs.

By the number of neuronal processes, neurons are divided into:

— unipolar;

— pseudounipolar;

— bipolar;

— multipolar.

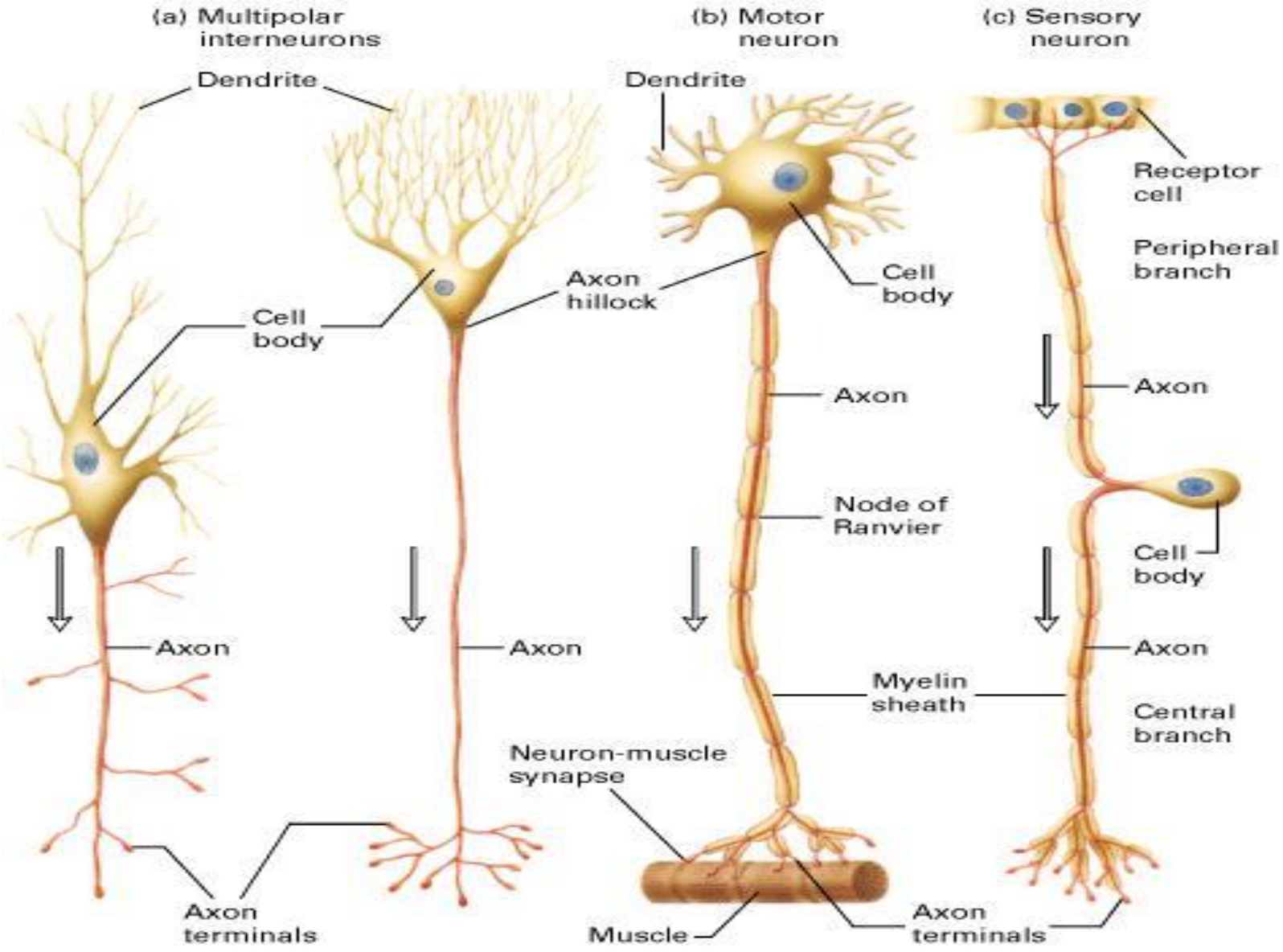


Figure — Types of neurons

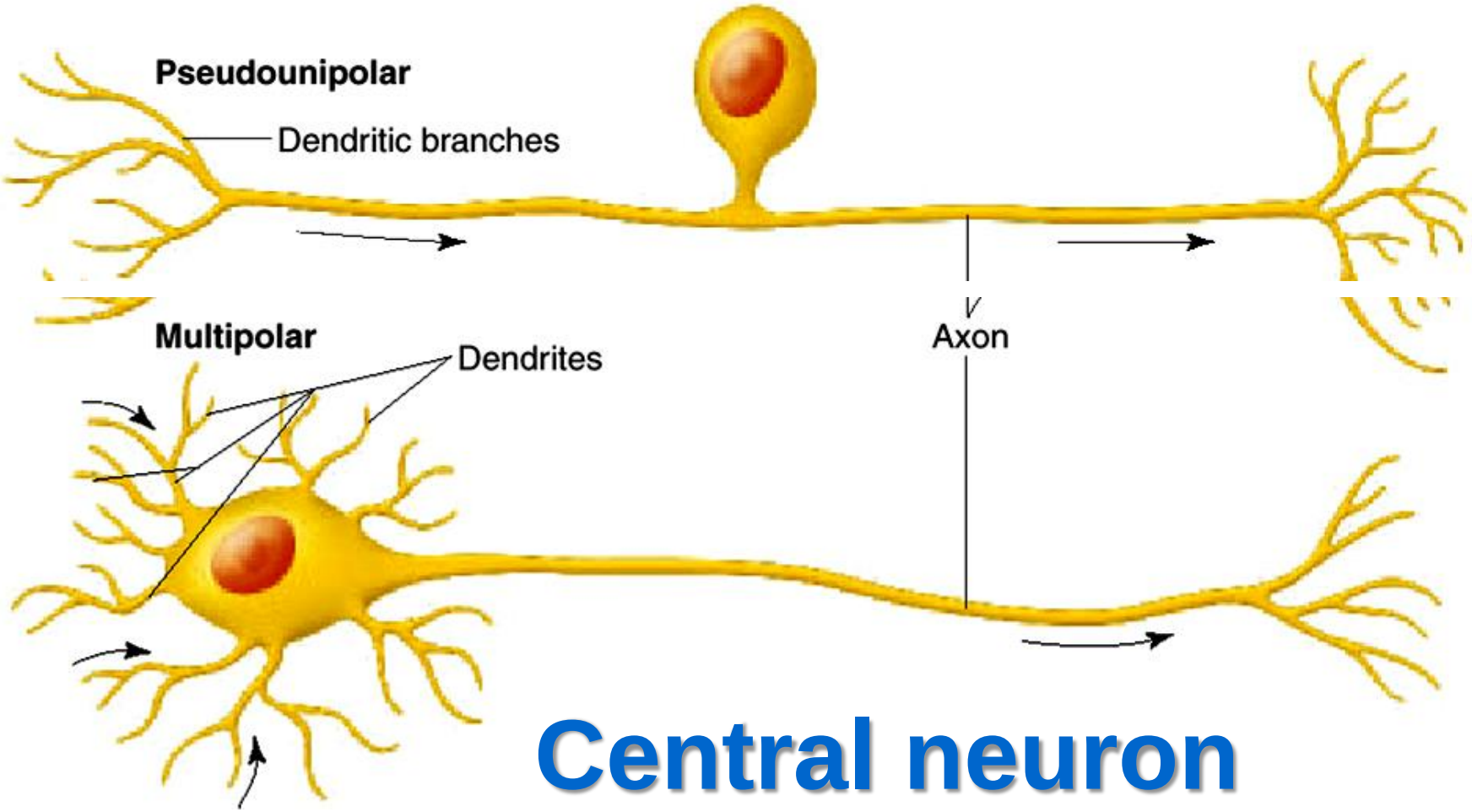
Unipolar neurons have only one process extending from the cell body. In humans they are located only in the mesencephalic nucleus of the trigeminal nerve and provide the proprioreceptive sensitivity of masticatory muscles.

Pseudounipolar neurons have two processors: one processor conducts signals from receptors and the other — to the CNS. These cells are located in the sensory ganglia and provide reception of sensory information (tactile, temperature, etc.).

Bipolar neurons are located mainly in the peripheral parts of the visual, acoustical, and olfactory systems. Their dendrites are connected with receptors, and axons – with the neurons of the next levels of the sensory system.

Multipolar neurons have several dendrites and one axon. There are about 60 different structural variations of multipolar neurons. Most neurons are multipolar.

Afferent neuron



Central neuron

Figure — Types of neurons

The main function of the nervous system is performed by **nervous cells**. They are only **10%,** and the **majority** are of the ***glia cells*** (astrocytes, microglia, astrodendroglia, oligodendrocyte, Schwann cells). Astrocytes are located between the blood vessels and neuron bodies. Their processes contact capillaries and are components of the hematoencephalic barrier.

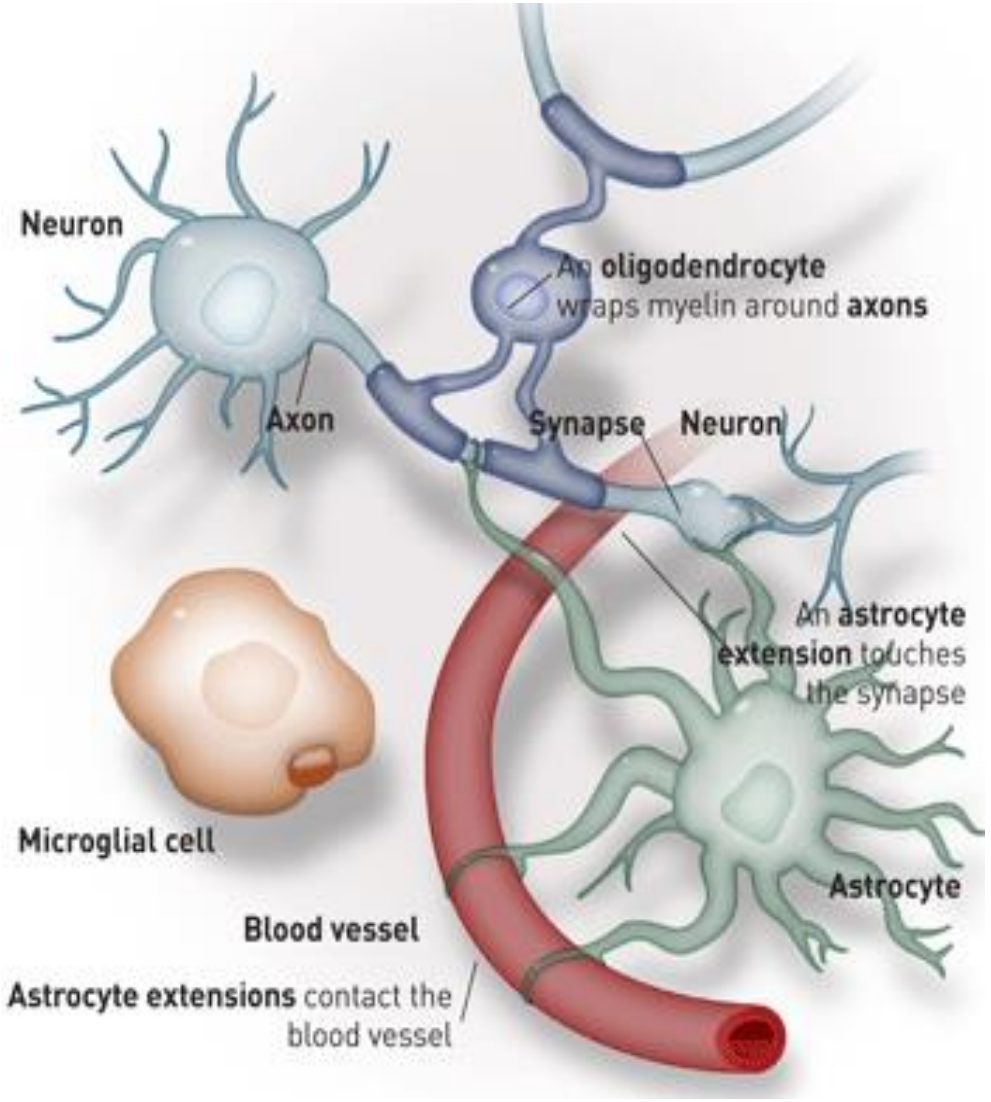


Figure — Neuroglia cells

Neuroglia cells functions:

- **Support function.**
- **Trophic function.**
- **Protective and reparative.**
- **Formation of myelin sheath (isolation).**
- **Growth factors production for nerves.**
- **Participation in blood-brain barrier formation.**
- **Regulation of brain extracellular fluid ionic composition (removal of K^+ excess).**
- **Replacement of brain tissue defects due to proliferation.**

Temporary blood deficiency of the brain results in a loss of consciousness, as the **brain is very *sensitive to any oxygen or glucose deprivation*.** The brain consumes **20% of oxygen** from the total volume in the organism.

The brain metabolism

- **High level of aerobic metabolism.**
- **Glucose is the main substrate.**
- **Intensive exchange of nucleic acids.**
- **Special mechanisms of blood supply regulation.**

The main specific manifestation of the CNS activity is a reflex.

***The reflex* is a natural reaction of an organism to internal or environmental changes with the participation of the CNS.** The value of reflexes and their mechanisms were studied by I. M. Setchenov and I. P. Pavlov.

The classification of reflexes:

I. ***By biological signs:***

1. **Food.**
2. **Defense.**
3. **Sexual.**
4. **Orientation.**
5. **Motor.**
6. **Parent, etc.**

II. ***By the location of receptors:***

1. **Extero (from the skin surface).**
2. **Viscero (from the internal organs).**
3. **Proprio (from muscles).**
4. **Intero (from the blood vessels), i.e. the reflex chains originate from them.**

III. ***By the participation of the CNS parts:***

1. **Spinal (the centers are located in the spinal cord).**
2. **Bulbar (the centers are located in the medulla oblongata) .**
3. **Mesencephalic (the centers are located in the midbrain).**
4. **Cortical, etc.**

IV. *By the character of responses:*

1. Motor (the response is a muscle contraction).

2. Secretory (the response is the secretion of the glands).

3. Vasomotor (the response is the change of the vascular tone).

V. *By the adaptation value:*

1. Unconditioned.

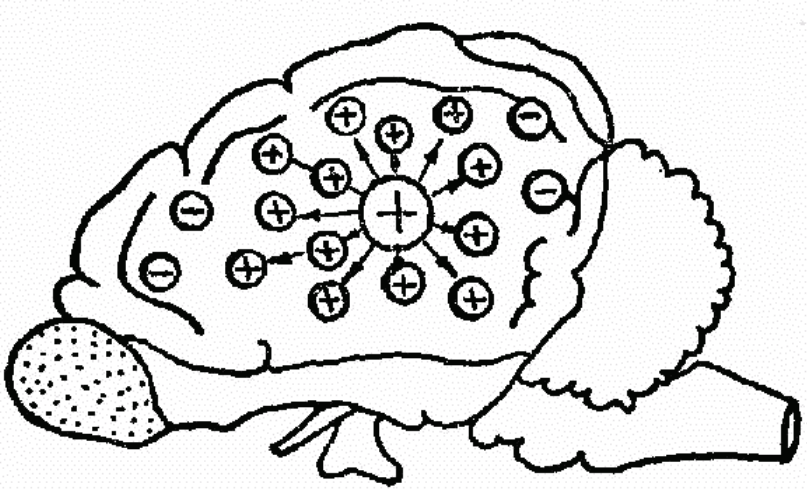
2. Conditioned.

Unconditioned reflexes (instincts) are congenital (specific) reactions of the nervous system. They are carried out by relatively constant nerve pathways in response to adequate stimuli. The inferior parts of the CNS (excluding the cortex) participate in the formation of unconditioned reflexes.

Conditioned reflexes are acquired during ontogenesis. The reaction is carried out by temporary reflex pathways in response to any stimulus. They are formed on the basis of unconditioned reflexes.

The pathway along which signals go from receptors to the executing organ through the CNS (i.e. the pathway through which the reflex action occurs) is called the ***reflex arc.***

A set of neurons necessary for the regulation of the functions or execution of a certain reflex is called the **nerve center** (NC), **e.g., respiratory, digestive, etc**.



2. Properties of the nerve centers. Main principles of excitation transmission in nerve centers.

The nerve center possesses a ***number of properties***. Basically, they depend on the features of *synapses* and structure of neural networks.

1. Summation of excitation is the combination of two or several sub-threshold stimuli which induce a response. A separate stimulus is not enough to induce a response. **There are 2 kinds of summation:**

a) ***Temporal summation***. If several sub-threshold signals enter a single presynaptic terminal in turns over a short period of time (successively). The total amount of neurotransmitter released may exceed the threshold value of the postsynaptic neuron. The higher the frequency of the action potential, the more quickly the threshold may be exceeded (Figure).

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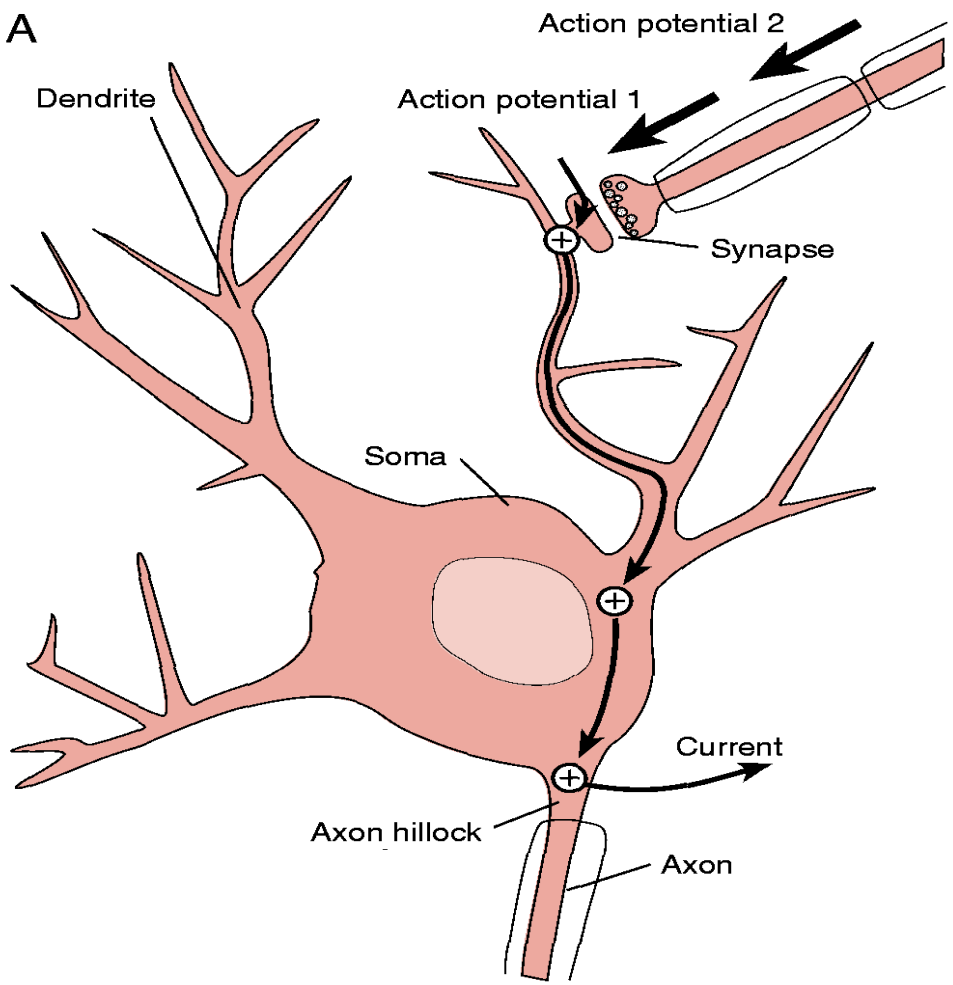


Figure – Temporal summation

b) ***Spatial summation.*** If two or more sub-threshold stimuli act simultaneously on different presynaptic terminals which form synapses on one neuron, and together release enough mediator to exceed the threshold of the postsynaptic neuron. For example, neuron A and neuron B may individually release insufficient neurotransmitter but when these quantities are combined, the threshold may be exceeded and an action potential generated (Figure).

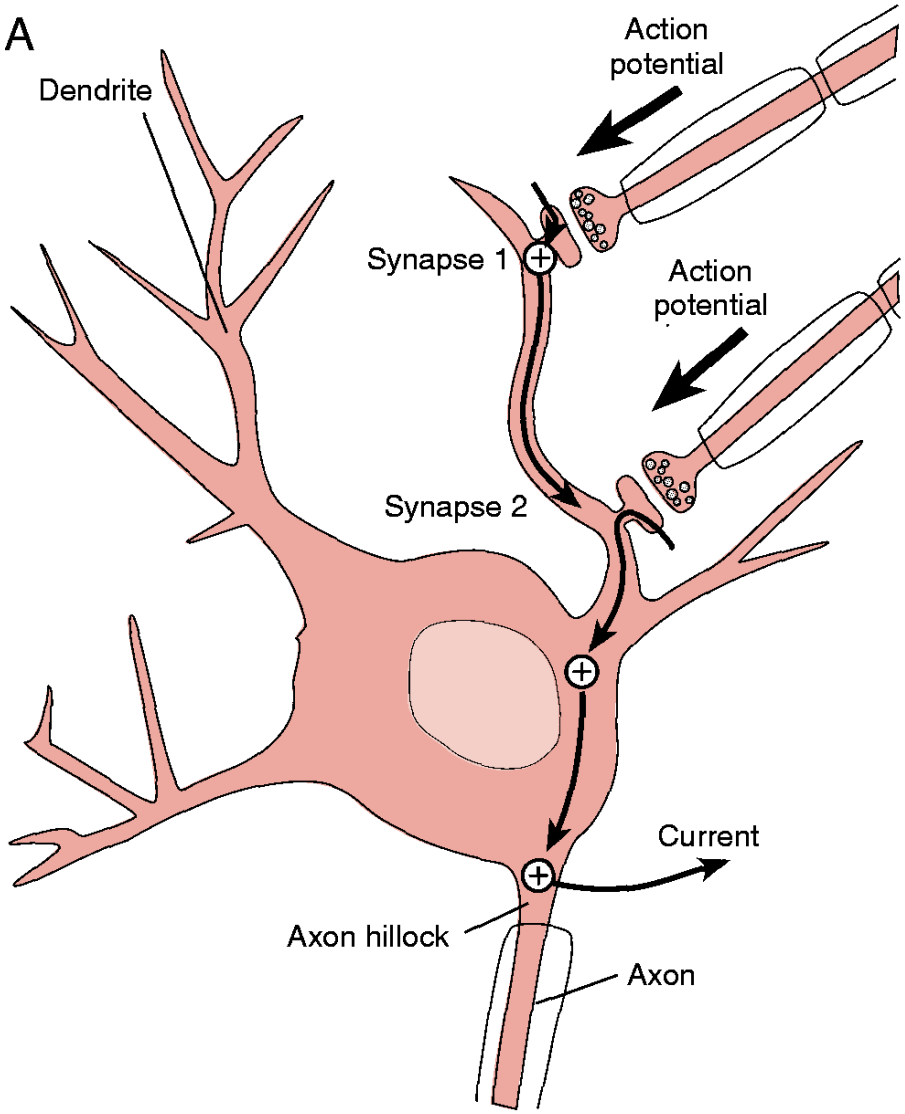


Figure – Spatial summation

2. Transformation of excitation rhythms. The frequency of signals coming into the nerve center is not equal to the frequency of signals coming out of the nerve center (Figure). It is explained by the fact that the postsynaptic potential appears to be very long or depends on the fluctuation of the afterpotentials of the membrane. If the negative afterpotential achieves the critical level, it is capable to induce a new AP.

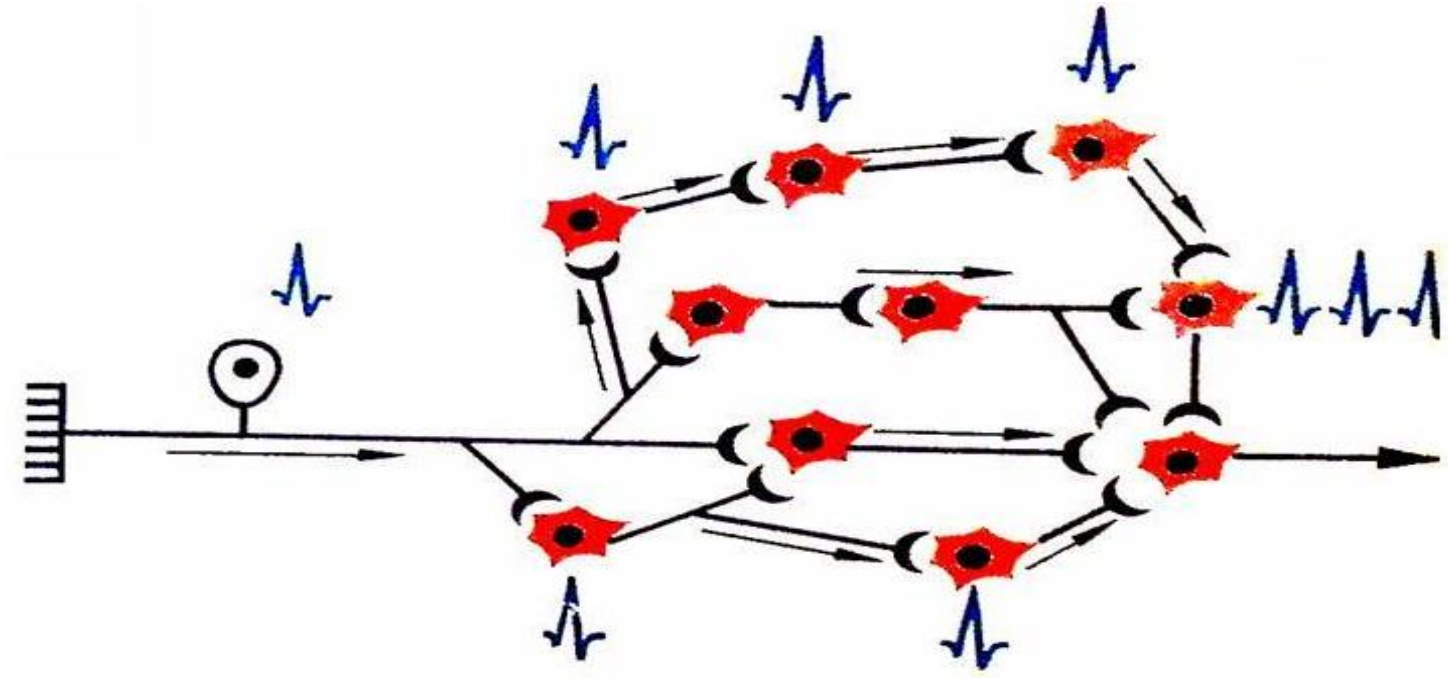


Figure – Transformation of excitation rhythms

3. Posttetanic potentiation. A temporary increase of the excitability of the nerve center and the strength of the reaction after rhythmic stimulation is called posttetanic potentiation. Low frequency stimulation of afferent nerves causes reflex reactions of certain intensiveness (force). If this nerve is imposed to rhythmic stimulation of high frequency (300–400 stimuli per second), then the following low frequency rhythmic stimulation will increase the reaction (Figure).

It is explained by the fact that due to the previous excitation, the ions of Ca^{++} are accumulated inside the presynaptic terminal, which raises the efficiency of the work of the synapse. In a frequent excitation rate each subsequent potential induces secretion of a greater amount of the mediator quanta, which promotes the increase of the postsynaptic potential amplitude.

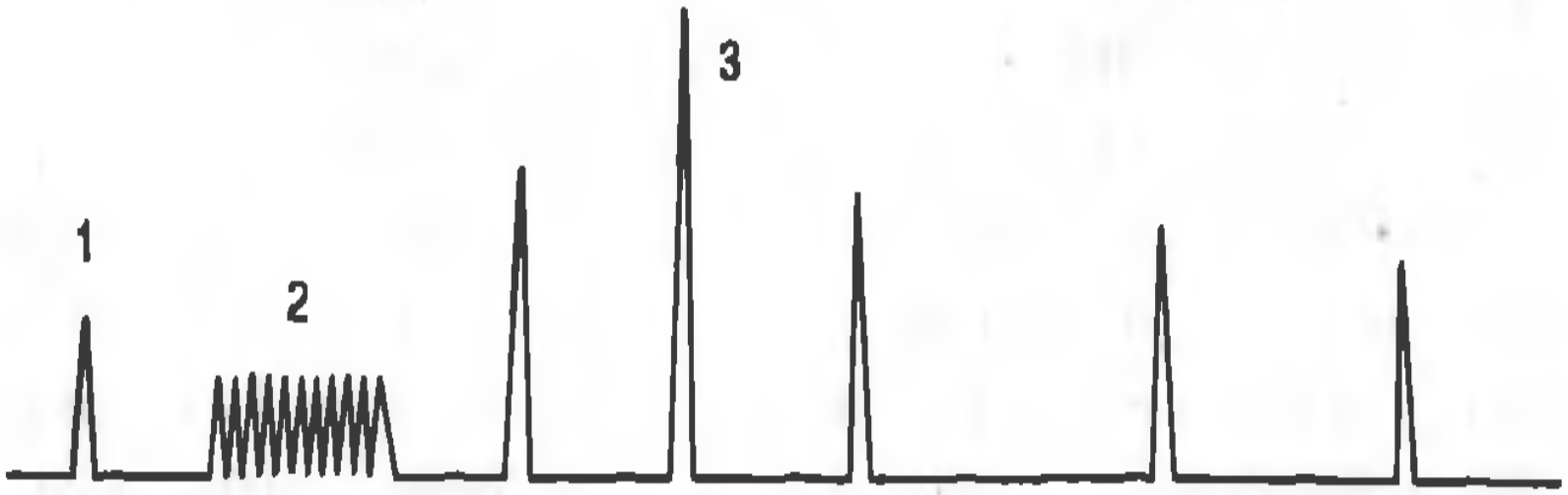


Figure — Posttetanic potentiation:
1 — initial response; 2 — rhythmic stimulation;
3 — increased response of the nerve center

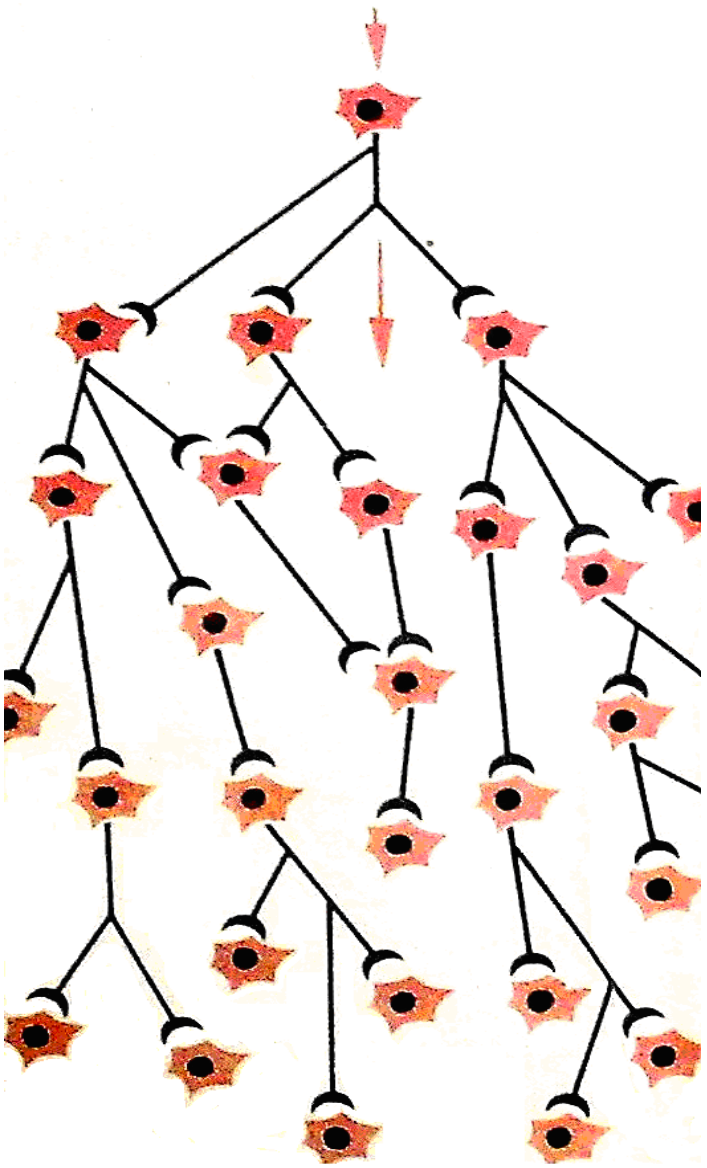
4. The fatigability of the NC is caused by impairment of signal transmission in interneuron synapses or a decrease of the post-synaptic membrane sensitivity to the mediator. Fatigue is also connected with the neuron sensitivity to a lack of oxygen. **The brain consumes 50 ml of oxygen per minute (1/6 from all oxygen consumed by a person at rest).** If the **brain** is not supplied with blood, the cells of the cortex **die within 5–6 minutes; those of the brain stem — within 15–20 minutes**, and the **cells of the spinal cord** are the least sensitive to hypoxia and die within **20–30 minutes**. Hypothermia prolongs the period of tolerable hypoxia by slowing the cerebral metabolic rate for oxygen. The nerve centers are also sensitive to low glucose levels.

5. Neurons and synapses are selectively **sensitive to some chemical substances and poisons**. *Strychnine* blocks the functions of inhibiting synapses, i. e. increases the excitability of the NC. Some substances selectively affect the nerve centers. For example, *apomorphin* affects only the vomiting center, *lobiline* suppresses the respiratory center.

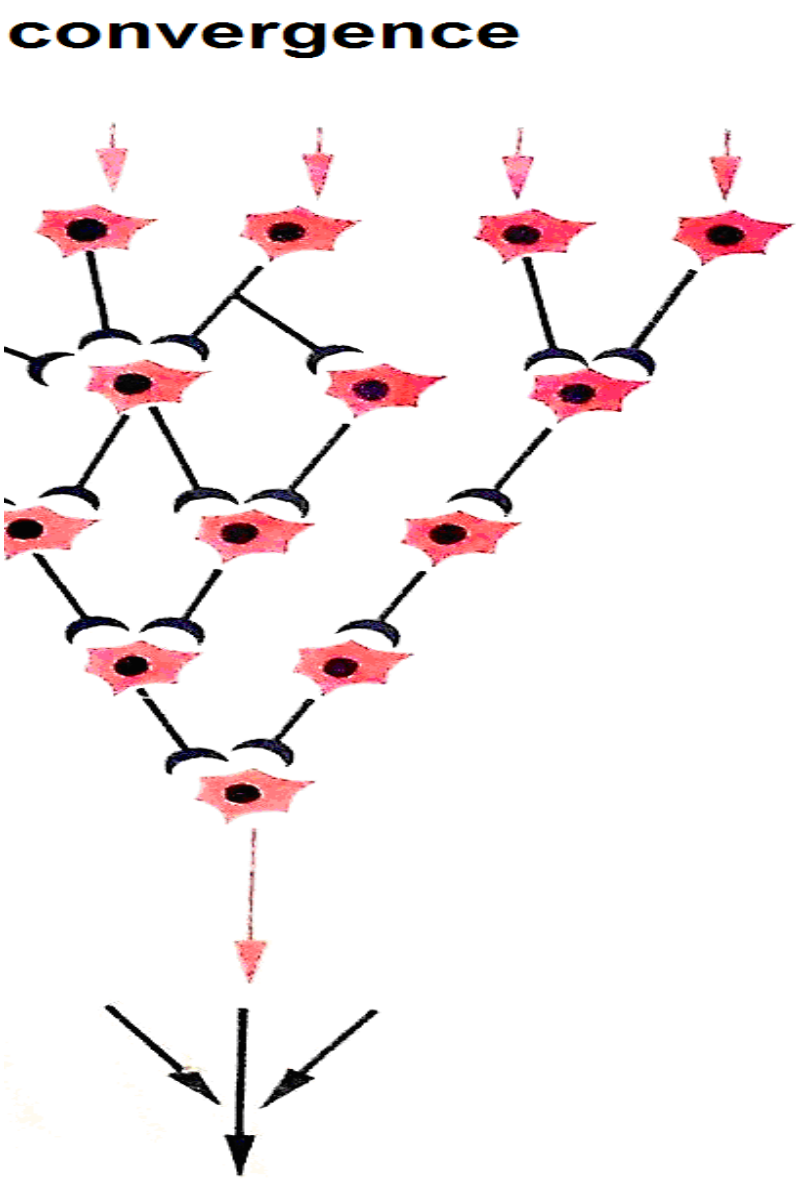
Main principles of excitation transmission in nerve centers

1. **The ability of neurons to establish numerous synaptic links with other neurons is called *divergence*** (Figure), i. e. one cell influences a set of other cells and, therefore, each neuron is capable to redistribute electrical impulses (***irradiation of excitation***).

The divergence



2. The junction of pathways in a neuron is called *convergence* (Figure). Since a number of the pathways join in a motoneuron, Sherrington made up a conclusion that the motor neuron is the final common pathway of the motor system.



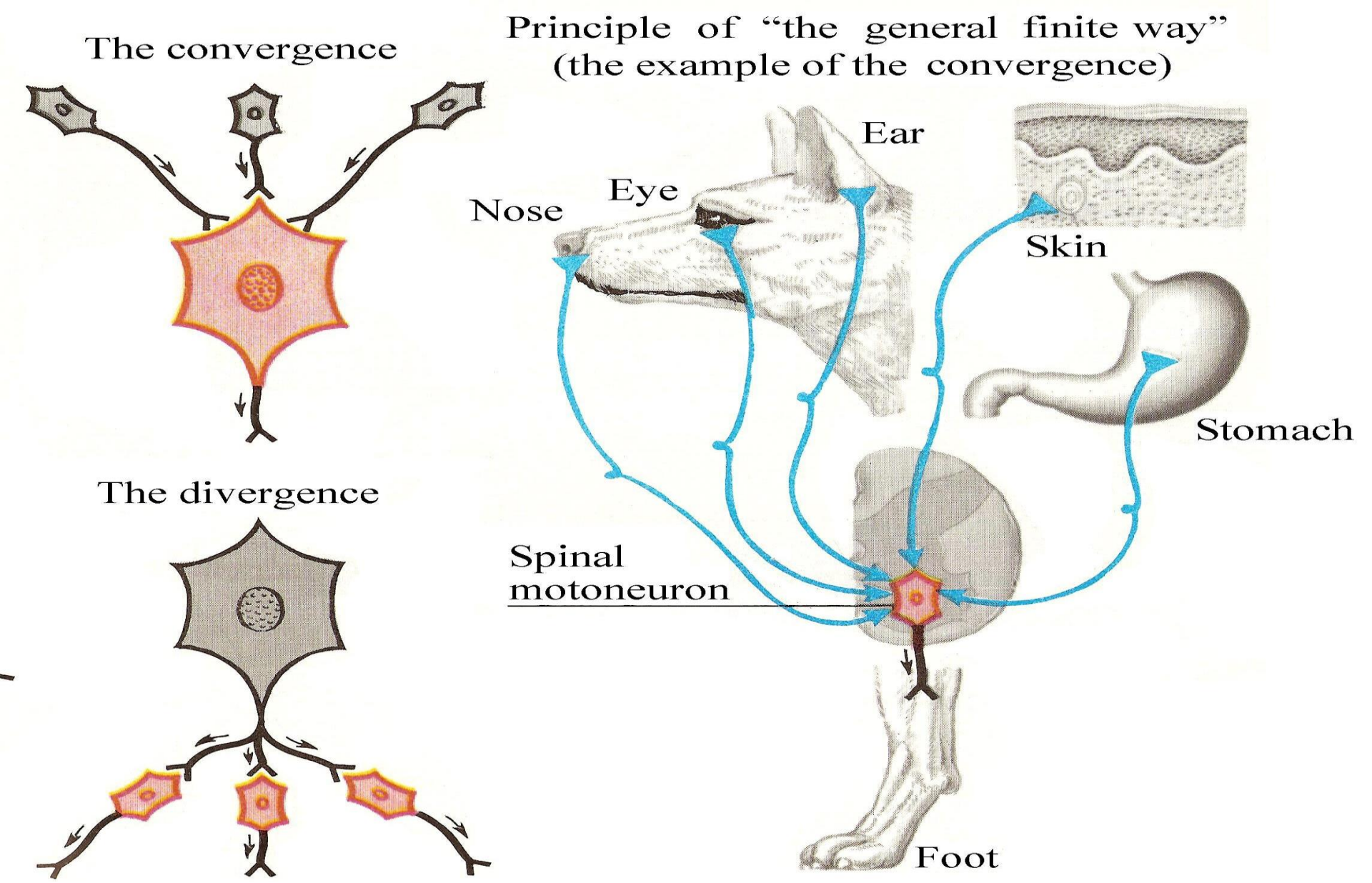


Figure — Types of excitation transmission in the nervous system

3. Through the NC ***excitation is transferred only in one direction*** from the sensory neuron through the interneuron to the efferent one — the law of one-way transmission of signals. It is explained by the mechanism of the functioning of chemical synapses, when mediator is released only from the presynaptic terminal and influences the post synaptic membrane. For example: if to stimulate the posterior (dorsal) roots of the spinal cord, the action potential is registered on the ventral (anterior) roots; in the reverse direction excitation does not extend.

4. In the NC ***signals are transmitted slower than in nerve fibers***. It explains the relative duration of the reflex period. This period includes the following processes:

1) excitation of receptors;

2) conduction of excitation by afferent fibers;

3) conduction of excitation through interneurons;

4) conduction of excitation by efferent fibers;

5) transmission of excitation to the executing organ and its response.

The period during which the intracentral conduction of excitation occurs is called the ***genuine, or central time of the reflex***. For example: the knee reflex is the fastest, as there are no intercalary neurons.

5. The action of a reflex does not end as soon as the extension of excitation is over, but after some time. This is connected with the circulation of excitation in the chains of neurons (Figure). This process is called ***reverberation*** (the basis of short-term memory).

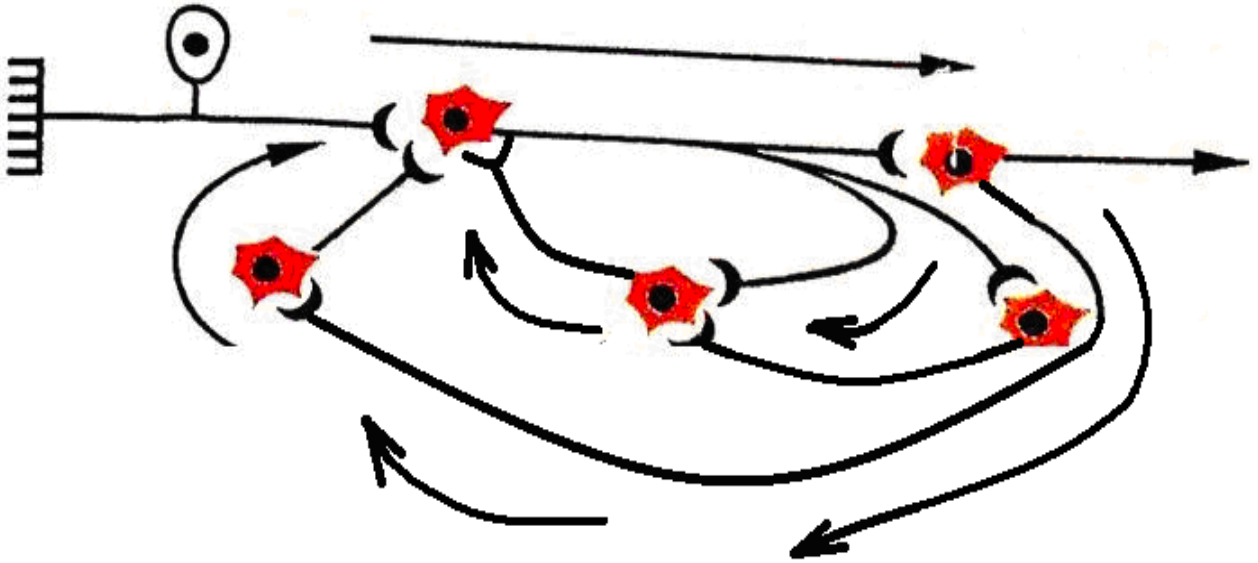


Figure — Reverberation in the nerve center

3. Inhibition in the CNS. Inhibition mechanisms

Inhibition is an important property of the CNS, first studied by **I.M. Sechenov** (Figure). He removed the cerebral hemisphere of a frog at the level of the thalamus. Then he stimulated the posterior leg of the frog, put it into the solution of sulfuric acid and measured the time of the reflex (the defense reflex). After that he put salt crystals on the thalamus and stimulated them with a weak electric current along with putting the posterior leg again into the solution — the time of the reflex was prolonged or absent.

***Conclusion*: <u>the thalamus has nerve centers inhibiting spinal reflexes</u>.**

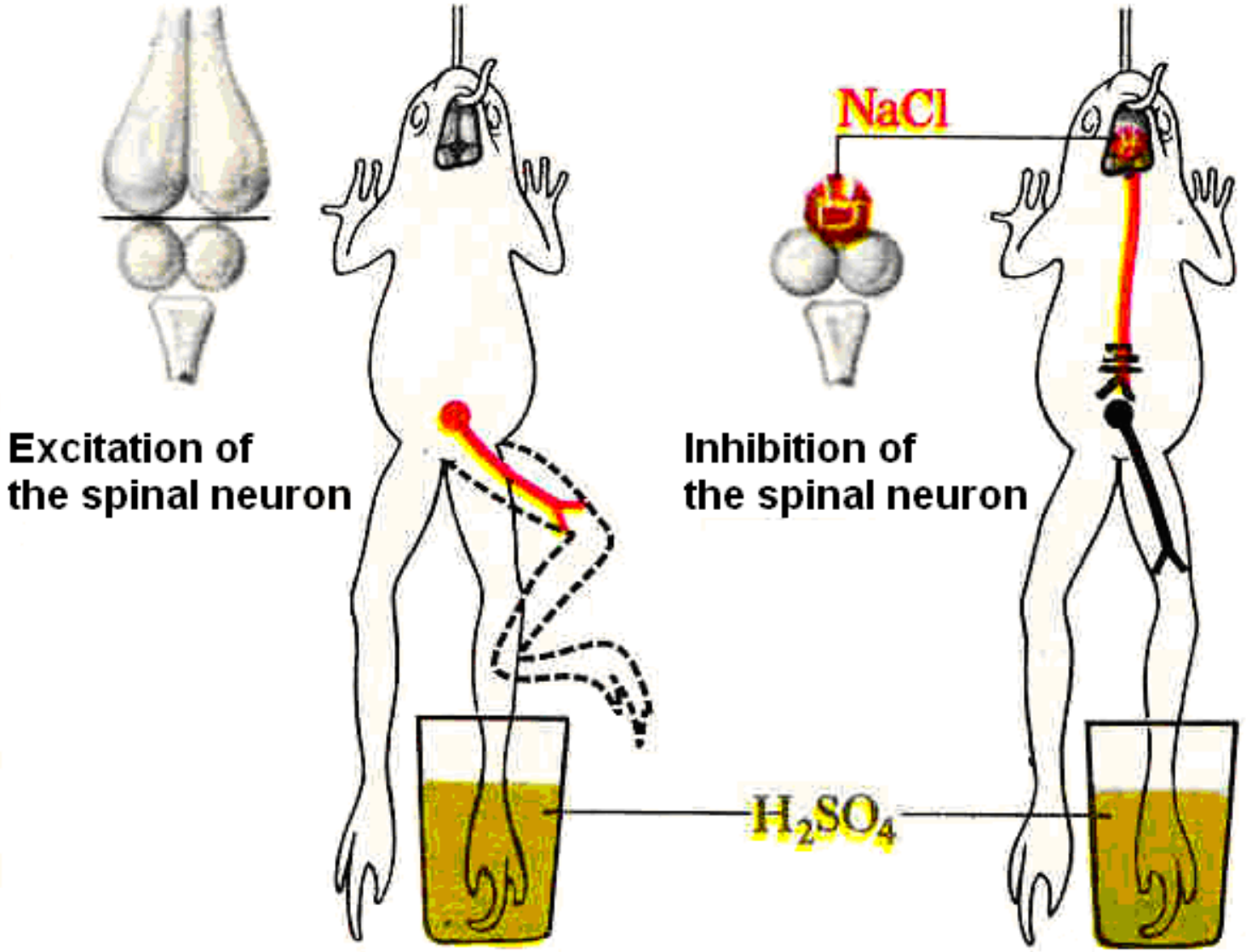


Figure —The inhibition experiment (by I.M. Sechenov)

Later on, inhibition was studied by F. Holtz. He revealed that the defense reflex can be inhibited by strong mechanical stimulation of the other leg as the process of inhibition arises.

Conclusion: inhibition may develop in any part of the CNS when two or several stimulations coincide.

Inhibition is an active process resulting in weakened or depressed excitation.

The role of inhibition in the CNS:

— it decreases the irradiation of excitation and promotes its concentration;

— it protects the CNS from excessive overstrain;

— it switches off the activity of the nerve centers which are unnecessary at this moment.

Kinds of inhibition

1. Antidromic (recurrent): signals from motoneurons together with the activation of muscles through the axon collaterals activate inhibiting cells (**the Renshaw cells**), which form synapses on motoneurons. Inhibition is carried out by the feedback principle (Figure).

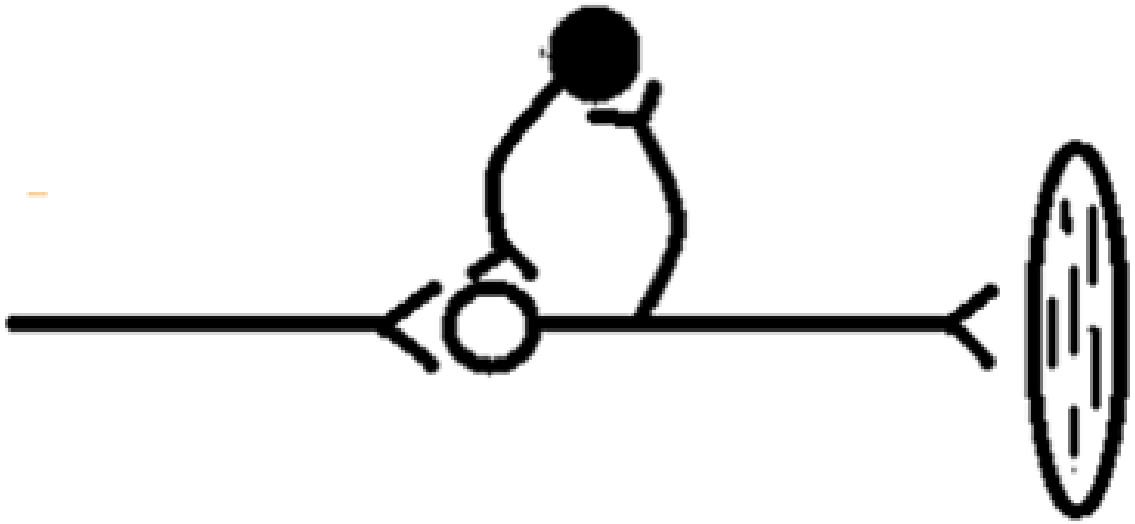


Figure — Antidromic inhibition

2. Reciprocal inhibition (Figure) is based upon the fact that one and the same afferent which stimulates one group of cells through intercalary inhibitory neurons may inhibit other cell groups.

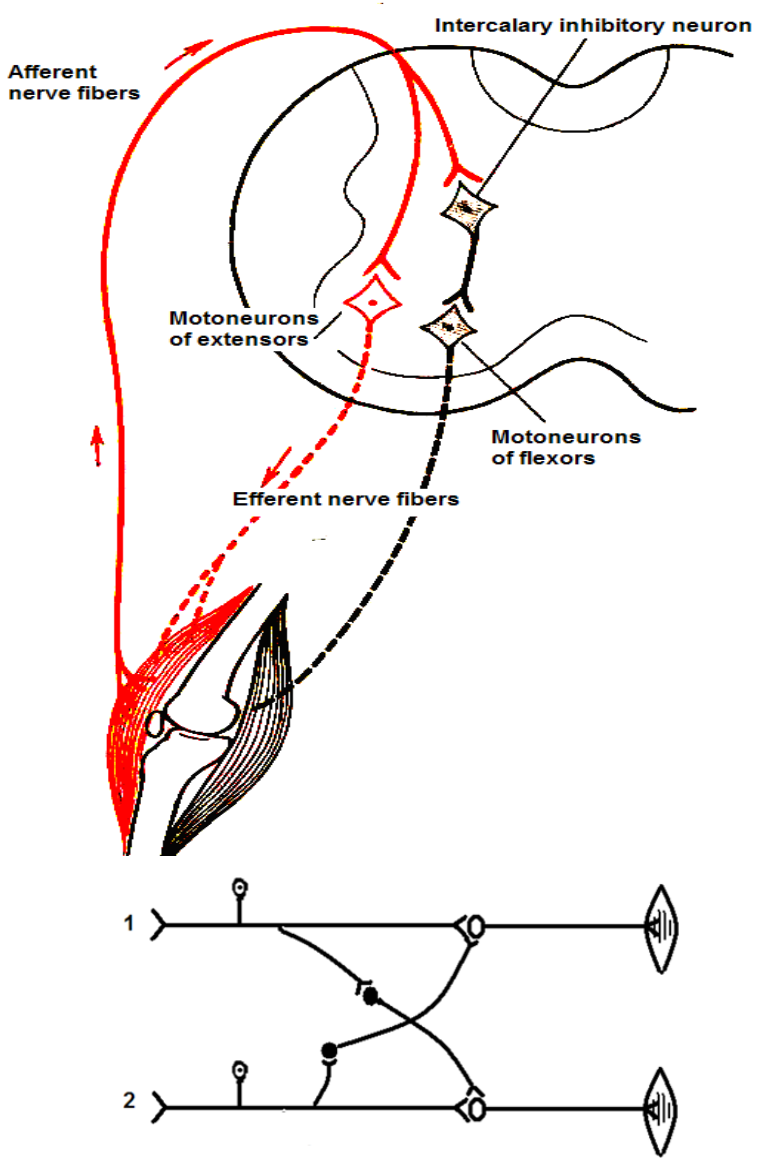


Figure — Reciprocal inhibition

3. Lateral inhibition (Figure) is performed by inhibitory interneurons in parallel nets of neurons. Interneurons can influence not only excitant cells but also closely located cells in which excitation is absent or weak.

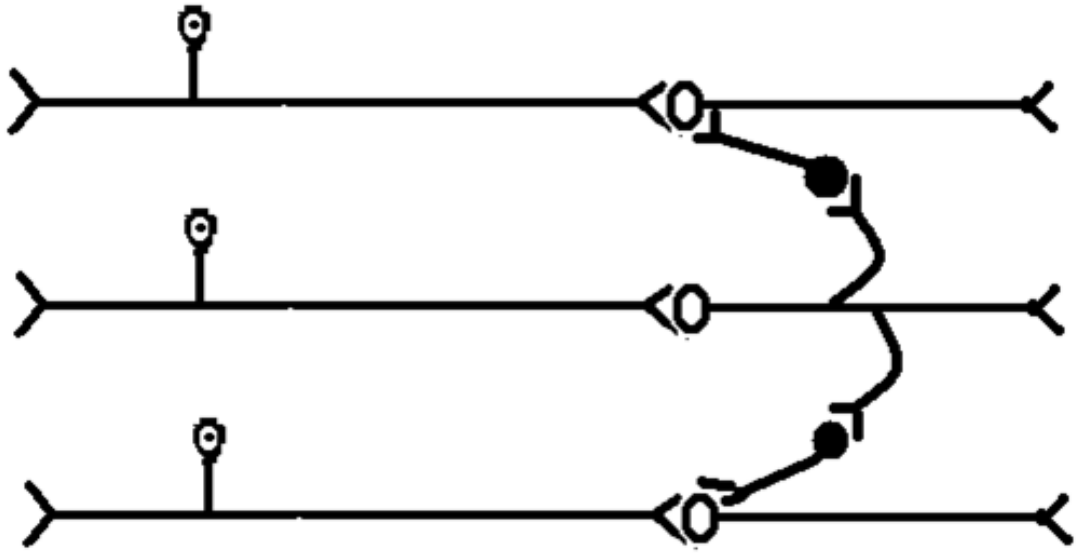


Figure — Lateral inhibition

4. Protective (exorbitant) inhibition is generated by a stimulus exceeding the limit of the working capacity of neurons. It interferes the exhaustion of a neuron and results in strong shock.

5. Cortical inhibition is caused by inhibitory cortical inter-neurons (stellate cells), i.e. excitation does not expand from stellate cells.

6. Pessimal inhibition develops in excitant synapses as a result of strong depolarization of the post-synaptic membrane under the influence of the excessive rhythm of impulses. This inhibition is observed in the spinal cord and reticulum.

7. External and internal types of inhibition are present in the cerebral cortex.

Inhibition mechanisms

In interneuronic synapses two mechanisms of inhibition are possible: post-synaptic and pre-synaptic.

Post-synaptic inhibition develops in response to the action of inhibitory mediators in the synapse (*gamma aminobutyric acid (GABA), glycine, taurine*) (Figure). The permeability of the post-synaptic membrane influenced by these mediators increases for potassium and chlorine ions, potassium is released and chlorine comes inside the cell thus generating ***hyperpolarization*** of the membrane, ***or inhibitory postsynaptic potential (IPP)***, i. e. the *threshold of excitation increases and the inhibiting postsynaptic potential arises*.

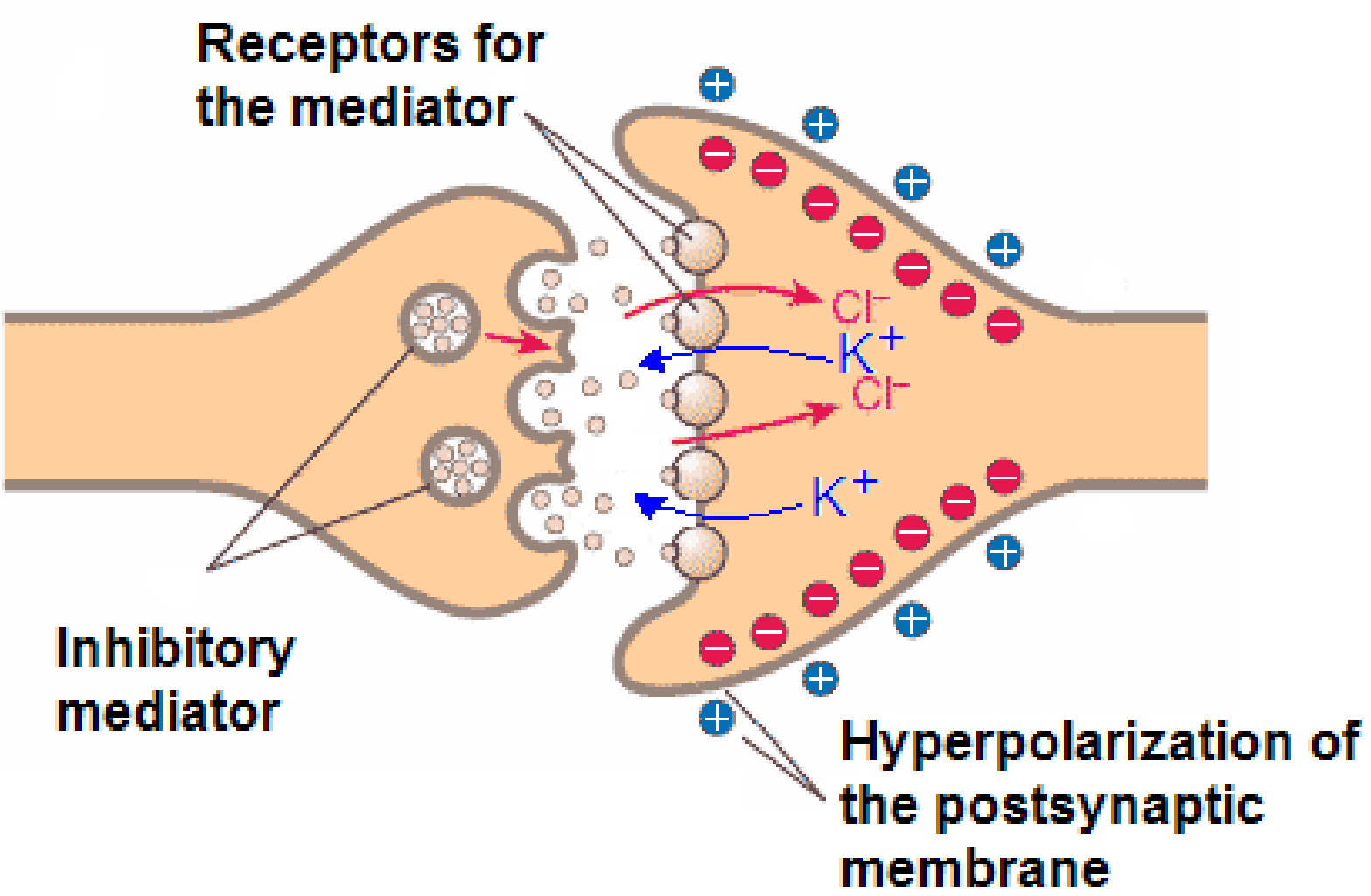


Figure — Mechanism of post-synaptic inhibition

Pre-synaptic inhibition (Figure) arises before the excitatory synaptic contact. Its structural basis is the ***axo-axonal synapse***. The axon terminal of the inhibitory cell forms a synapse on the axon of the excitatory neuron and blocks the transmission of excitation. In the area of the presynaptic contact it causes the membrane ***depolarization***, which decreases the amplitude of the action potential taking place here. The basis: the inhibiting axon releases the inhibiting mediator, which enlarges the membrane permeability of the excitant axon for chlorine ions *coming from the excitant termination,* which *partially depolarizes*. This reduces the amplitude of the action potential and decreases the excitation intensity, because the decreased amount of the released mediator quanta in the excitant synapse is insufficient to induce a response.

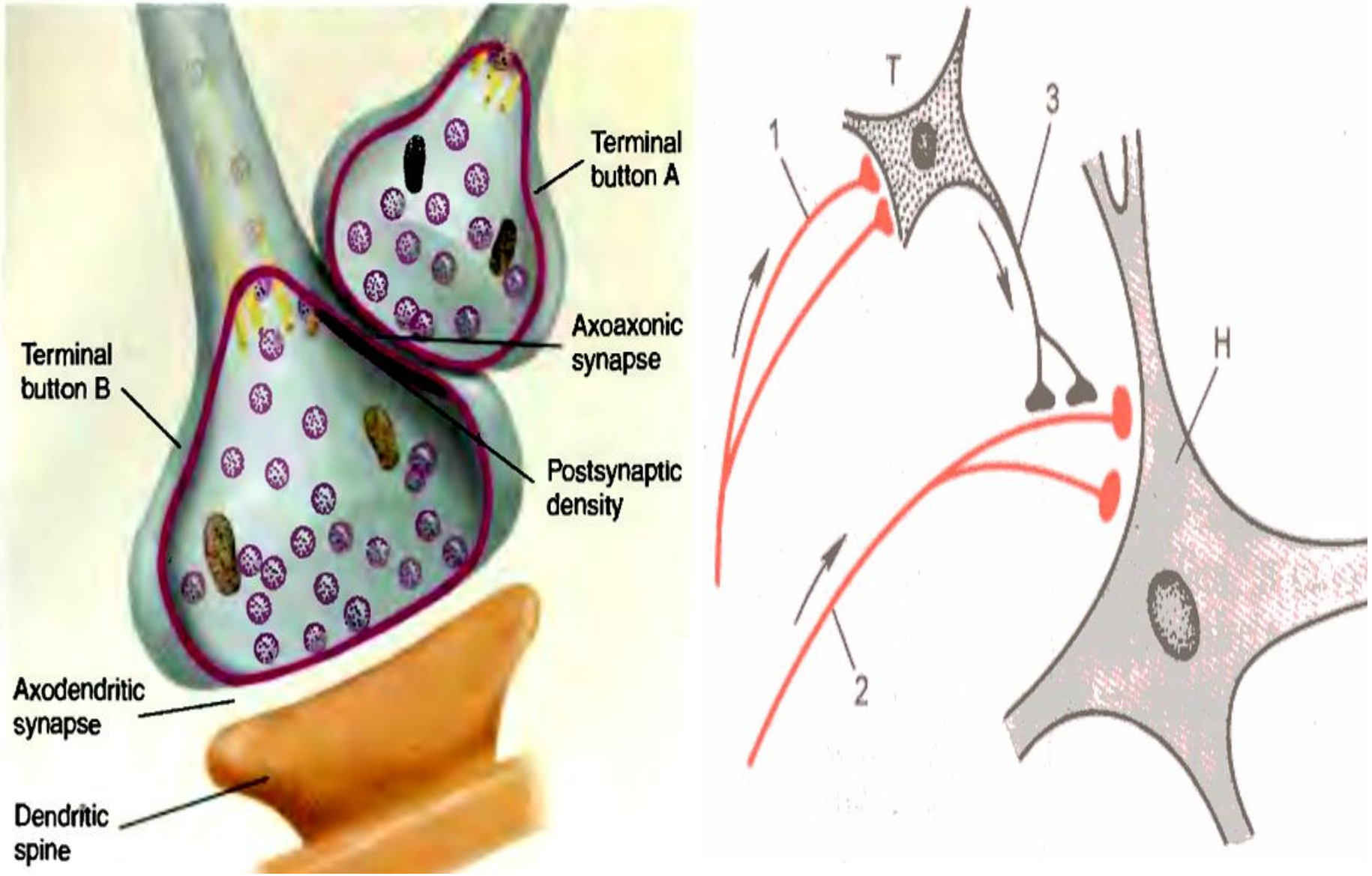


Figure — Mechanism of pre-synaptic inhibition

4. Coordination of reflexes. Dominant.

The mechanism of each reflex depends on the state of the CNS at the given moment of time and on the set of intercentral interactions. **The interaction of neurons, and, therefore, nervous processes, ensuring coordinated activity of the CNS, is called *coordination*.** Its basis is in the interrelations between excitation and inhibition. This question for the first time was studied by ***N. E. Vvedensky***.

The reciprocal principle. In his experiments on animals, N.E. Vvedensky developed the theory of reciprocal innervation of antagonist muscles: the excitation of the motor center of one muscle group is accompanied with ***reciprocal inhibition*** of the center of antagonist muscles. It happens because of the branching of the afferents in the spinal cord. One of them stimulates flexor motoneurons, others form inhibition synapses on extension motoneurons, that is why the excitation of the afferent simultaneously causes the excitation of the flexion center and inhibition of the extension center.

Induction. Induction is dynamic interactions of the nerve processes of excitation and inhibition. *By its effect, induction may have two forms:*

— positive;

— negative.

By its duration, induction may be:

— simultaneous*;*

— successive.

In reflex coordination the inverse change of the state of the nerve center after excitation or inhibition plays an important role. If inhibition in a group of nerve cells induces excitation, it is called ***positive successive induction***, and, conversely, if an initially produced process of excitation induces inhibition, it is known as ***negative successive induction.***

The inter-inhibitory influences of reflexes based on reciprocal inhibition are called ***simultaneous negative induction***.

Strong and long stimulation excite not only the neurons of this center but also those of other centers. This conduction of signals in the CNS is called ***irradiation***.

Hence, inhibition of the nerve centers proceeds due to induction (they are «switched off» from functions), and irradiation involves other nerve centers into this reflex.

Feedback principle.

Any reflex act is controlled due to feedback from the nerve center. The feedback consists in the secondary afferent impulses which come to the CNS from receptors which get excited when the functional activity of the executing organ changes. The afferent impulses arising as a result of the activity of the organs are called *secondary*. They carry out the feedback function and play an important role in the coordination of reflexes providing the interaction between the nerve center and the executing organ.

The feedback can be positive (it increases the reflex reaction which caused the secondary afferent impulses) and negative (it inhibits the reflex which caused the secondary afferent impulses).

Example. Any motor act arises under the influence of impulses from the nervous system to the executing organ. The motor act is accompanied with the excitation of ***proprioreceptors*** from which impulses go to the CNS. If the patient`s proprioceptive system is affected, their movements become jerky, there is no accuracy, i. e., the CNS control over the movements is lost.

The principle of the "final common pathway". It was discovered by C. Sherrington. One reflex (for example, muscle contractions) can be caused by stimulation of different receptors, because the same α-motor neuron of the anterior horns of the spinal cord is a part of many reflex arches (Figure). Sherrington made up a conclusion that the motor neuron is the final common pathway of the motor system.

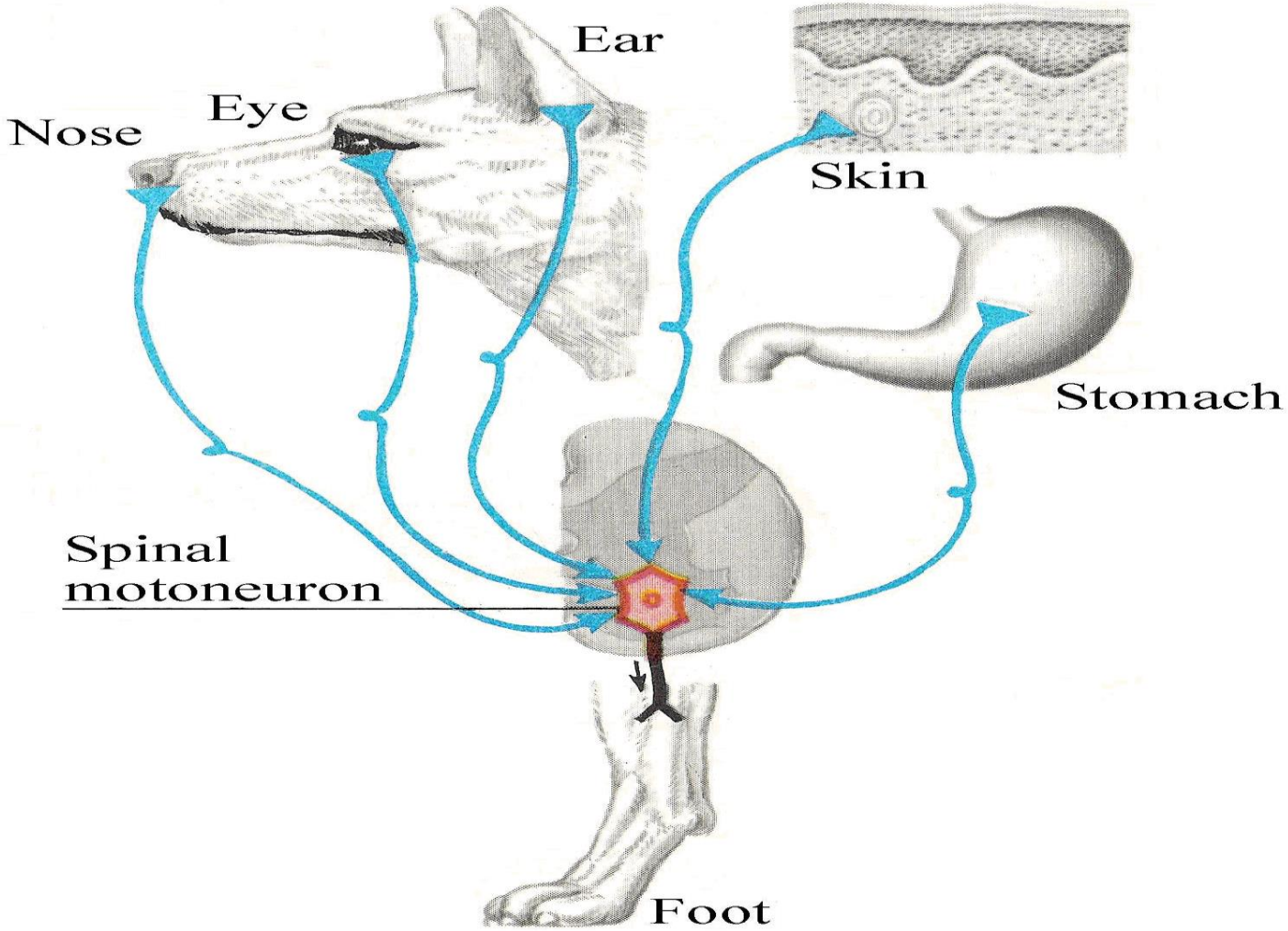


Figure — The principle of the "final common pathway"

Occlusion. If two groups of afferents are stimulated simultaneously, and each of these afferents gives the contractive muscle reflex, it is possible to receive the effect of a smaller force than the sum of the volumes of these reflexes separately. For example: if each afferent excites separately, excitation covers 2 groups of 4 neurons; if two afferents are stimulated simultaneously, excitation covers 6 neurons instead of 8, as two of them, due to convergence, are innervated by both the afferents, and due to the overlap of the synaptic fields the general response is smaller (Figure). Weak stimulation of the afferents leads to summation (i. e. intensified excitation), and strong stimulation to — ***occlusion***, i. e. suppression of excitation (clogging).

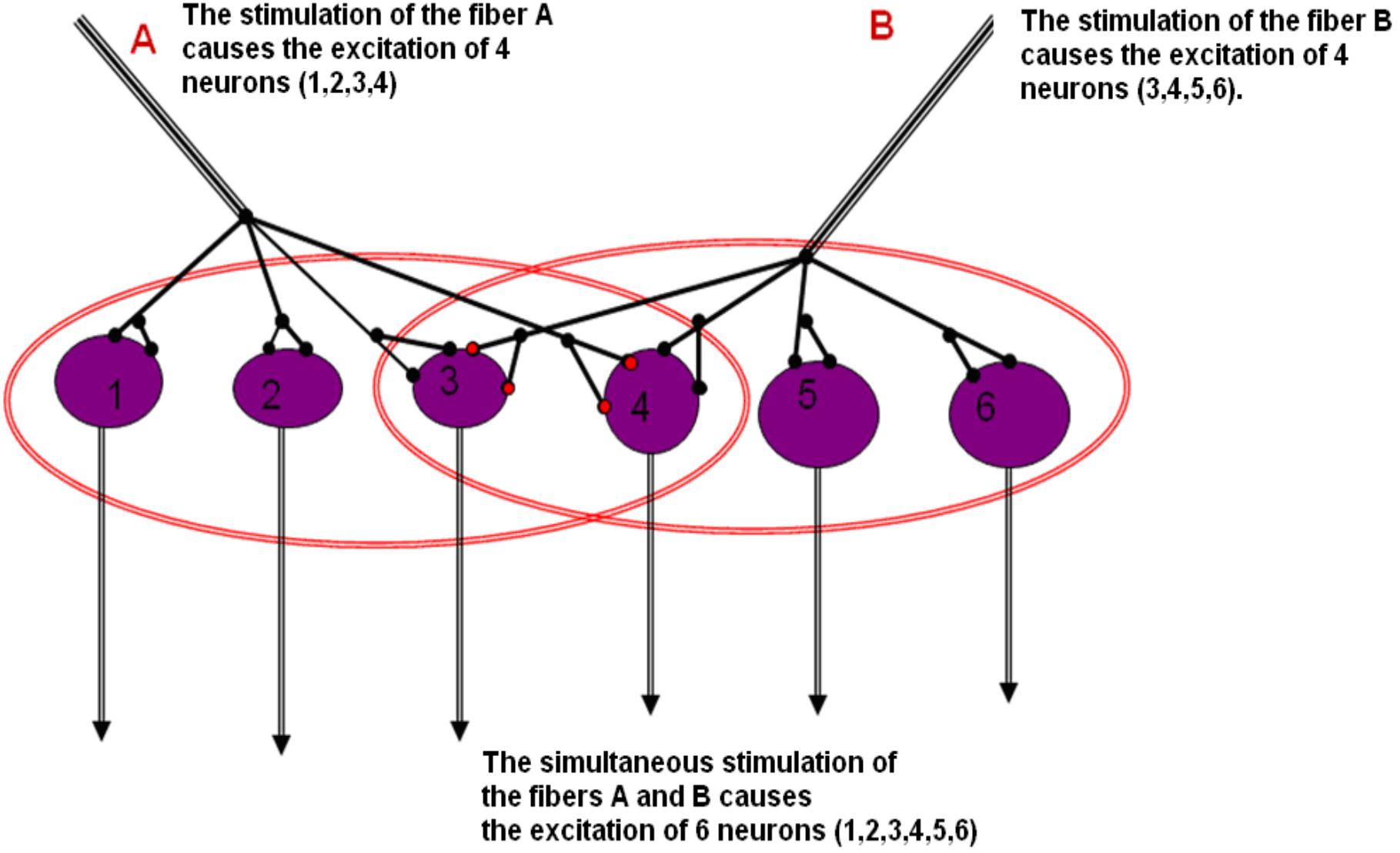


Figure – Occlusion

Dominant

Dominant is the prevailing focus of excitation changing and subordinating the work of all nerve centers. Once the dominant appears, stimulation of any receptors will induce a response typical of this dominant.

The dominant covers large systems of reflexes and is the basis for sexual, alimentary, defense, and other reflexes. But at once only one dominant which is the most essential is realized at the given moment of time and then a new one arises. For example: alimentary and protective reflex. The generation of the dominant always inhibits other centers (a person is thinking and does not hear that somebody is calling them).

The properties of the dominant:

1. Hyperexcitability.

2. Stability of excitation.

3. Ability to sum up excitation.

4. Inertia — ability to keep excitation for a long time once the action of a stimulant is over (hunger dominant).

5. Ability to disinhibit.

6. The ability to inhibit other reflexes in the "final common pathway".