

BASICS OF NEUROBIOLOGY

Zsolt Liposits and Imre Kalló

2017-2018

1. QUO VADIS –NEUROBIOLOGY?
ORGAN SYSTEMS
ORGANIZATION OF THE NERVOUS SYSTEM

Brief summary:

The first lecture provides some hints about the mission of Neurobiology-related courses.

The second lecture illuminates the organization of the human body and the functional units distinguished.

The third lecture explains the development, the structural and functional organization of the nervous system.

One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The modular structure of the body
- 2) The functions required to maintain the body at changing internal and external milieu
- 3) The role played by the nervous system to ensure survival

Test the knowledge you gained:

- 1) *Evaluate the following statements for correctness! (True or False)*

5 points

The modules with the highest complexity in the human body are the organs, which are built from multiple cell types rendered to carry out a single action. False

The basic unit of structure in every living thing are the cells; the human body is composed of both eukaryotes and prokaryotes. False (?)

Multiple organ systems participate in information transmission; these involve e.g. the nervous system, the visceral system, the musculoskeletal system, the lymphatic and immune system. False

The nervous system is connected to organs of special senses collecting information from our external environment. True

There is an arrangement in the nervous system, within a structure possessing a higher hierarchical position can influence the one occupying a lower position, but not *vice versa*. False

- 2) *Identify the part of the nervous system characterized by the following sentences!*

5 points

It hosts monoaminergic and peptidergic cell groups of the arousal system: brain stem

Nuclear complex relaying motor, sensory and limbic information to the cortex: thalamus

Part of the CNS exhibiting a columnar shape with 2 enlargements: spinal cord

Convuluted gyri are formed on the surface of it: cerebral cortex

It controls the pituitary-endocrine axes and autonomic functions: hypothalamus

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2. THE CELL
CELL ORGANELLES I.
CELL ORGANELLES II.

Brief summary:

The first lecture demonstrates cells of the human body, specialised to carry out certain functions. Specialization of the cells means to operate different sets of genes besides those used constitutively in all cell types.

The second and the third lectures provide a brief review of cellular organelles operating in all somatic cell types, including the neurons and glial cells.

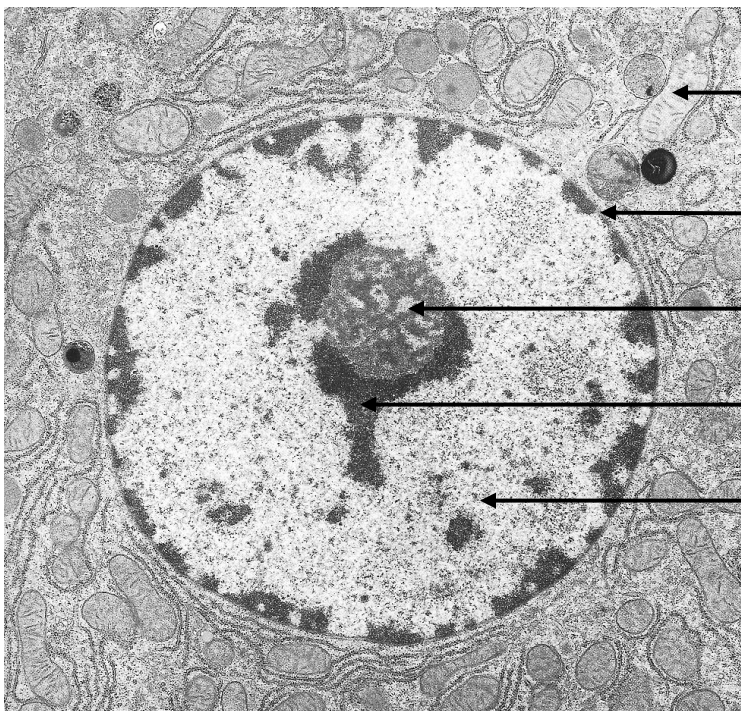
One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The way the cells can specialize to carry out different functions (gain different morphology and chemotype).
- 2) The basic structure and function of cellular organelles.
- 3) The basic process of protein synthesis and modifications.
- 4) The way of energy production to serve cellular events.

Test the knowledge you gained:

- 1) *Electron microscopic image of a somatic cell. Identify the numbered structures!*

5 points



1 mitochondrion

2 nuclear envelope

3 nucleolus

4 heterochromatin

5 euchromatin

2) Identify the cell organelle characterised by the following sentences:

A fiber-like structure with an average of 10 nm diameter, that contributes to the maintenance of the cell's shape: **microfilament**

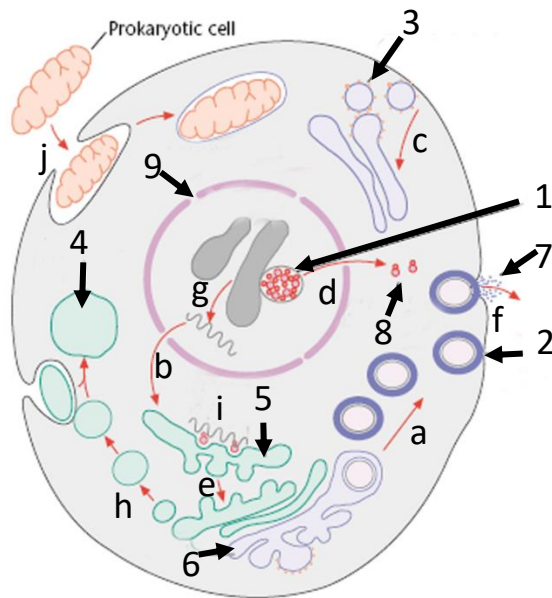
Ion channels belong to this category of membrane proteins: **nuclear pores**

The location of ribosomal RNA synthesis: **nucleoli**

The location of ATP synthesis: **mitochondrion**

The location of degradation of cellular organelles: **lysosome**

3) Identify the organelles labelled with numbers and the cellular events labelled with letters!



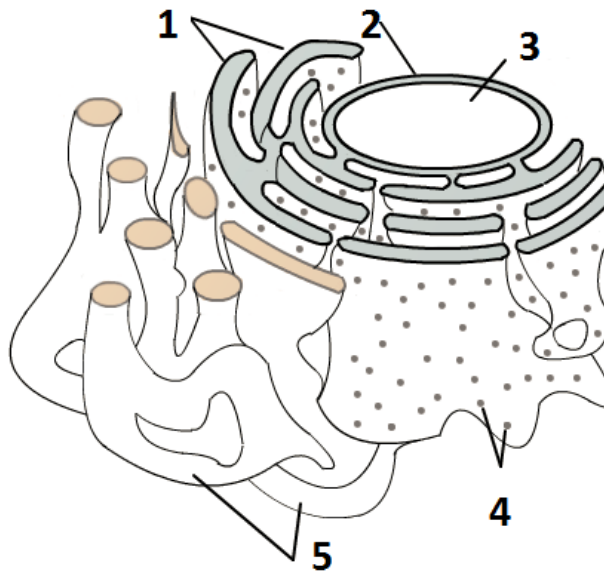
1. nucleolus
2. secretory vesicle
3. endosome
4. endolysosome
5. rough endoplasmic reticulum
6. (trans)Golgi
7. secretum
8. ribosomes
9. nuclear pore

- a. transport of secretory vesicles
- b. mRNA export from nucleus
- c. endocytosis
- d. ribosome export from nucleus
- e. SER -> cis-Golgi vesicle transport
- f. exocytosis
- g. transcription
- h. maturing of lysosomes
- i. translation
- j. phagocytosis

10/

Identify the organelles of the cell numbered in the scheme.

5 points



1 rough endoplasmic reticulum

2 nuclear envelope

3 nuclear matrix

4 ribosomes

5 smooth endoplasmic reticulum

Identify (name) the cell organelle characterised by the following sentences.

5 points

Site of metabolic actions and signal transduction. **cytoplasm**

The rRNA is produced here. **nucleoli**

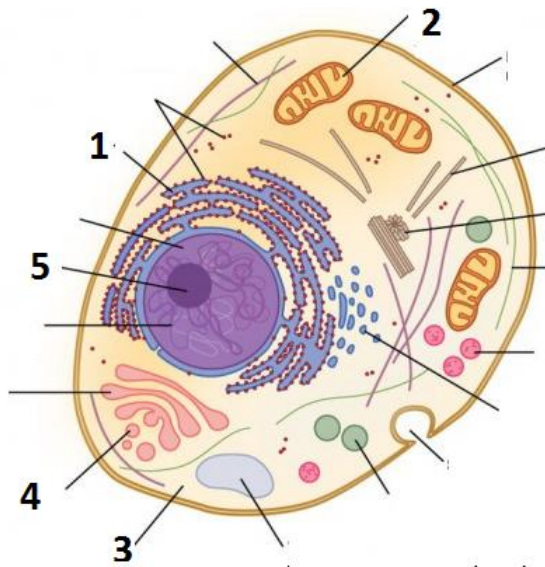
Newly synthesised proteins are trafficked to their inner space. **RER**

It stores and releases calcium in excitable tissues. **SER**

They organize the growth of microtubules. **centriolum**

Identify the organelles of the cell numbered in the scheme.

5 points



1 rough endoplasmic reticulum

2 mitochondrion

3 cytoplasm

4 secretory vesicle/lysosome

5 nucleolus

Identify (name) the cell organelle characterised by the following sentences.

5 points

Macromolecule maturation and tagging, formation of liposomal vesicles are located here. **Golgi complex**

It has glycoproteins and glycolipids embedded. **cell membrane**

Its matrix contains circular DNA, ribosomes and several different types of enzymes. **mitochondrion**

It is composed of alpha and beta tubulin. **microtubules**

Transcription takes place here. **nucleus/nuclear matrix**

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3. NERVOUS TISSUE THE NEURON NERVE FIBERS

Brief summary:

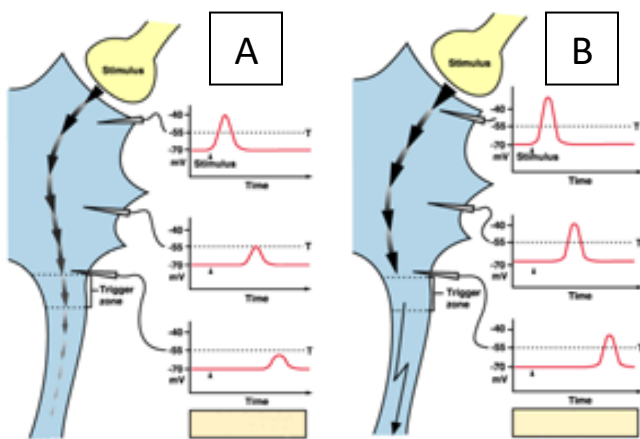
The first lecture characterises the nervous tissue, in which neurons and glial cells exist in structural and functional symbioses. The second lecture demonstrates the unique morphology and the excitability of neurons and some basic networks established by them. The third lecture explains how information is conveyed via nerve fibers between distant locations in the human body.

One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The structural and functional symbioses of neurons and glial cells.
- 2) The morphological and functional diversity of neurons. Mutual definiteness of morphology and function.
- 3) Resting potential and action potential.
- 4) Electrotonic potential, conductance.
- 5) The role of somatodendritic region in information processing.
- 6) The structure of neuropil and events, which take place in the neuropil.

Test the knowledge you gained:

- 1) *These schematic drawings demonstrate electrotonic changes in response to stimuli. There are three electrodes in the cell, each of those measure potential changes in response to the stimulus. Evaluate the following sentences for correctness! (5 points)*



The stimulus evoked electrotonic potential is weakened towards the axon initial segment in both **A** and **B** cases.

True

In the case of **B**, the electrotonic potential is higher than the threshold potential next to the axon initial segment.

True

In the case of **A**, the electrotonic potential can induce action potentials, if it is summed with another electronic potential deriving from another synaptic stimulus.

True

Action potential is generated if the electrotonic potential reaches the axon initial segment.

False

In the case of **A**, the cell is hyperpolarized, in the case of **B**, the cell is depolarized.

False

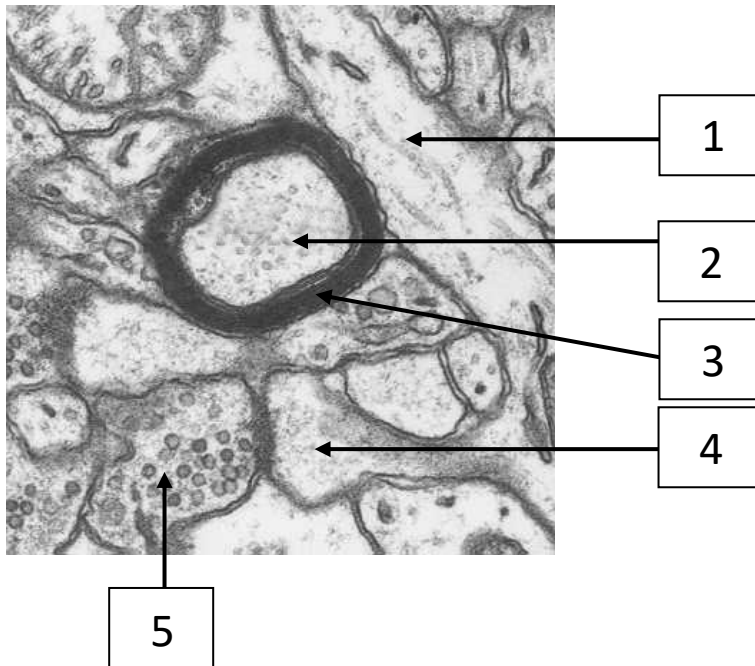
- 2) *Nerve fibers. Supplement the text with the missing words.*

(8 points)

The filament-like structure composed of the **axons** and the **glial cells** is called a nerve fiber. The **axon** is part of the neuron; the larger its diameter, the **slower** is its conductance speed. The **myelin sheath** is produced by glial cells. The glial cells with this function in the peripheral nervous system are called **Schwann cells** whereas the name of the cells with similar function in the

central nervous system is **oligodendrocytes**. The glial cells in the peripheral nervous system are capable to embed several neuronal processes (named above). The latter type of nerve fibers is called **non-myelinated axon**.

- 3) Evaluate the following sentences for correctness! If you think that the statement is true, give the name of the labeled structure. If you think, that the statement is false, then provide a brief explanation why! (10 points)



1. This is an axon, because it is thin and establishes branches.

False

Name/Why? **It is a dendrite, because it has a spine (4).**

2. This is a 25 nm-thick tube, which has transport functions.

False

Name/Why? **It is an axon, because it has a myelin sheath.**

3. Membrane of glial cells, which envelopes structure 2 in multiple layers.

True

Name/Why? **myelin sheath**

4. This is a glial cell, the nucleus of which is not in the plane of the section.

False

Name/Why? **It is a dendritic spine, because it is a part of a synapse.**

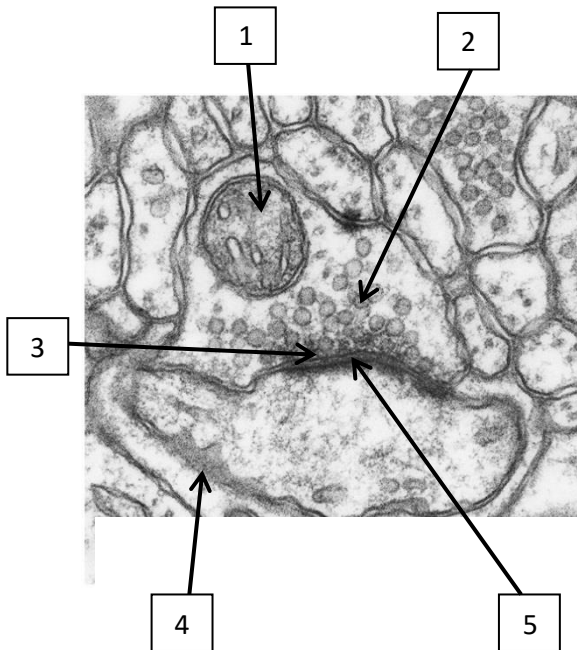
5. In response to action potential, some of the vesicles inside open up and release transmitters into the synaptic cleft.

False

Name/Why? **The vesicles do not open-up inside the axon bouton, they release their contents while fusing with the cell membrane.**

4) Identify the numbered structures!

5 points

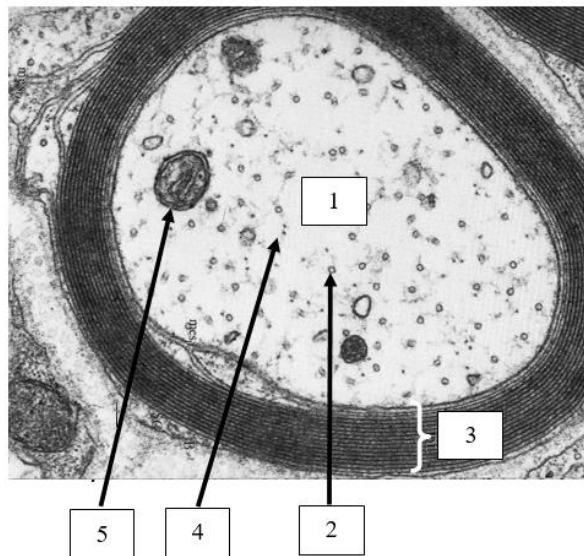


1. mitochondrion
2. synaptic vesicle/granulum
3. presynaptic cell membrane
4. postsynaptic cell/ dendrite
5. postsynaptic membrane/ synaptic cleft

10/

Identify the labelled structures.

5 points



- 1 axon
- 2 microtubule
- 3 myelin sheath
- 4 neurofilament
- 5 mitochondrion

Decide whether the following statements are true (T) or false (F). Give an explanation why.

5 points

Axon hillock is the preterminal conical part of the axon, where the synaptic vesicles accumulate for release.

False, it is the axon terminal (bouton).

Each oligodendrocyte contributes to the formation of the myelin sheath of a single axon.

False, it can cover up to 50 axons with its processes.

The myelin covering of an axon is not totally continuous.

True, there are nodes of Ranvier between myelin sheaths.

Sensory fibers carrying crude touch, pain and temperature sensations are usually naked.

False, they are non-myelinated axons.

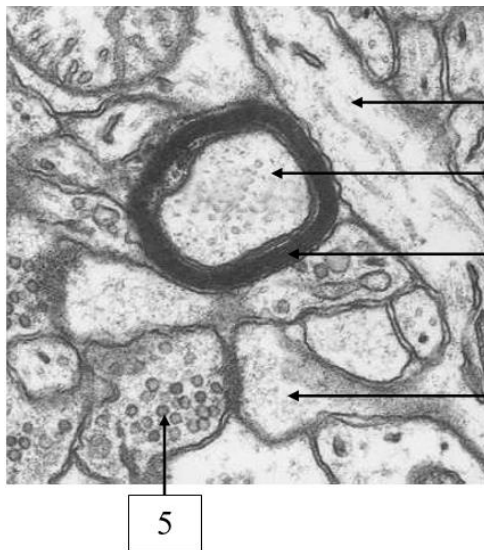
Inflow of potassium ions causes repolarization at the end of AP generation.

False, outflow of potassium (K⁺) ions causes repolarization.

10/

Identify the labelled structures.

5 points



1 dendrite

2 axon

3 myelin sheath

4 dendritic spine

5 synaptic vesicle

Decide whether the following statements are true (T) or false (F). Give an explanation why.

5 points

Neuropil is a region of the neural tissue where perykarion is the dominant structures.

False, neuropil is a region without cell bodies (perikaryons) in the neural tissue.

In case of myelinated axons one Schwann cell can accommodate only a single axon.

True, one Schwann cell wraps around only one axon.

Myelin sheet accelerates the propagation of action potential on the axon.

True, myelin axons propagates action potentials in a saltatory manner from one Ranvier node to the other.

Pseudo-unipolar neurons don't have axons, only dendritic processes.

False, its dendrite and its axon arise from a common stem of the neuron, this is why it is called pseudo-unipolar.

Depolarization in action potential generation is caused by the outflow of sodium ions.

False, inflow of sodium ions (Na^+) causes depolarization. (-70mv + many Na^+ causes a more positive voltage inside, which means depolarization).

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4. NEUROGLIA NERVE ENDINGS SYNAPTIC COMMUNICATION

Brief summary:

The first lecture explains the phenotype and the functions of the different glial cells by emphasizing their essential role in maintaining a healthy nervous tissue and neuronal operation. The second lecture demonstrates the structural elements and molecular mechanisms of neurons, which serve to pick up (from receptors) and transmit (to other neurons and effectors) information. The third lecture summarises the structural and molecular bases of interneuronal communications, which ensure high specificity, controllability, feed-back and plasticity.

One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The way, how different glial cells contribute to the maintenance of neuronal functions.
- 2) The way, how various physical and chemical changes in our close environment are detected and transformed to sensory information.
- 3) The structural elements and the mechanisms, which are involved in the transformation of neuronal activity to muscle contraction or secretion.
- 4) The structure and the operation of chemical synapses.
- 5) The structure and the operation of electric synapses.

Test the knowledge you gained:

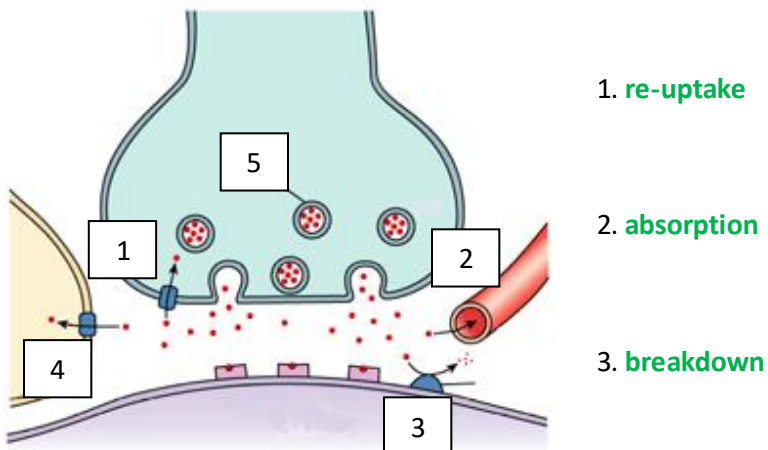
1) *List the different types of glial cells and characterize them by their major function!* (10 points)

- | | | |
|----|------------------------|--|
| a. | astrocyte | form BBB, generate calcium waves, form glial laminae, isolate synapses |
| b. | microglia | resident immune cell in the CNS |
| c. | oligodendroglia | formation of myelin in CNS |
| d. | Schwann cell | formation of myelin in PNS, and m |
| e. | ependyma | form defending surface of the CNS |

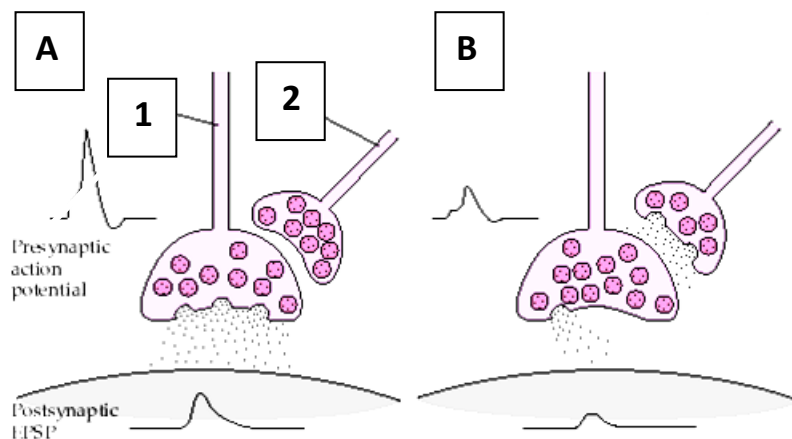
2) *Supplement the text below with the missing words!* (12 points)

The level of exchange of various molecules (nutrients, metabolites, small molecules etc) between the blood and brain is determined by the **BloodBrainBarrier**. Damage of this protective system, e.g. by **infection, inflammation**, results in a(n) **exflow** of the fluid in the extracellular space first around the vessels, which in turn leads disturbance in neuronal functions. This protective system is composed of three cellular and one non-cellular component. The cellular components are the **capillary endothelium** cells, the **basement membrane** cells and **astrocytes**. The non-cellular element is the **tight junction**. The inner layer of the vessels is formed by the **endothelium** cells, which are connected to each other by **tight junctions**; this connection type cannot be observed in the peripheral vessels. The vessels are covered by the processes of **astrocytes**. These cells have two major types: the **fibrous** and the **protoplasmic**. The first type is primarily located in the white matter, whereas the second type of the cells occupies the gray matter.

- 3) This figure shows schematically how neurotransmitters are eliminated from the synaptic cleft. Identify the different physiological processes! (10 points)



- 4) Answer the questions below related to the connection and the measured potential changes, shown in the figures! (10 points)



What kind of process number 1 according to its function? **excitatory presynaptic process**

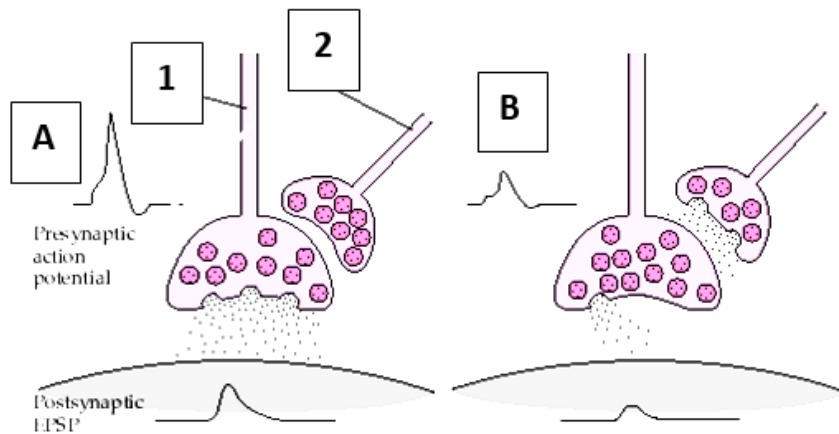
What kind of process number 2 according to its function? **inhibitory presynaptic process**

Which neurotransmitter could be released from process number 1? **serotonin, acetylcholine**

What change can be observed in the charge distribution within the process number 1 in the case of B compared to the case A? **The release of synaptic vesicles on the right side is inhibited by the inhibitory presynaptic process.**

What type of ion channels could be found in the process number one? **Ca⁺⁺, K⁺**

Answer the questions below related to the connection and the measured potential changes, shown in the figures!
5 points



What kind of process is number 1 according to its function? **excitatory**

What kind of process is number 2 according to its function? **inhibitory**

Which neurotransmitter could be released from process number 1? **acetylcholine**

What change can be observed in the charge distribution within the process number 1 in the case of B compared to the case A? **The release of synaptic vesicles on the right side is inhibited by the inhibitory presynaptic process.**

What is the shape of the vesicles generally carried by process number 2? **flattened**

Identify (name) the neuroglial cell type characterised by the following sentences.
5 points

They form the blood brain barrier. **astrocyte**

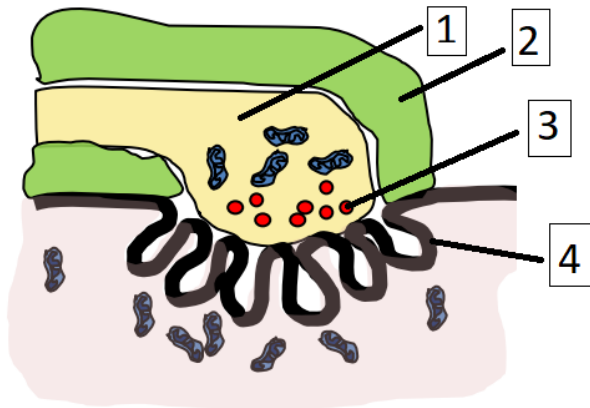
They develop from mesodermal tissue in the red bone marrow. **microglia**

They are situated at the border of the cerebrospinal fluid and the extracellular space liquid compartments. **ependyma**

They act as the resident immune cells in the CNS. **microglia**

They regulate the extracellular potassium ion concentration. **astrocyte**

Name the effector type shown on the scheme, and identify the numbered structures.
5 points



Name of the effector: **motor end-plate**

1: **axon terminal / axon bouton**

2: **Schwann cell**

3: **synaptic vesicle**

4: **folded sarcolemma**

Compare chemical and electrical synapses according to the given aspects.

Quantify your answer where possible.

5 points

	Chemical synapse	Electrical synapse
Distance between pre-, and postsynaptic cell membranes	30-50 nm	3.5 nm
Ultrastructural components	synaptic vesicle	gap junction
Synaptic delay	min: 0.3 ms, avg 1-5 ms	none
Direction of transmission	unidirectional	bidirectional
Cytoplasmic continuity between pre- and postsynaptic cells	no	yes

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5. NEUROTRANSMITTERS I. NEUROTRANSMITTERS II RELEASE OF NEUROTRANSMITTERS

Brief summary:

The first lecture explains and compares the synthesis, intracellular transport, release, effect and fate of amine and peptide neurotransmitters. A general picture is given, which is followed by a detailed description of major amine transmitters and during the second lecture, members of peptide transmitter families. The last lecture will present the molecular mechanisms of transmitter synthesis and release, related pre- and postsynaptic events.

One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The common and differing features of amine and peptide transmitter synthesis and release.
- 2) The spontaneous and action potential-generated transmitter release.
- 3) Involvement of glial cells in transmitter synthesis and elimination from the extracellular space.
- 4) The two basic signal transduction mechanisms of amine transmitters i.e. ionotropic and metabotropic
- 5) Dependence of the transmitter effect on the physiological status of the postsynaptic cells.
- 6) The brain area specific distribution of neurons using specific amine or peptide transmitters.
- 7) Co-existence of amine and/or peptide transmitters in the vast majority of neurons.
- 8) Pathological events may be generated by certain transmitter(s).

Test the knowledge you gained:

- 1) *List five major differences in the synthesis, transport and reuptake processes of amine and peptide transmitters/modulators!* (5 points)

1. **Amine transmitters are synthesised by their synthesising enzymes from cell body, while peptide transmitters are converted from precursors by converting enzymes, which are synthesised in cell body.**
2. **Amine NT's synthesising enzymes and storage vesicles are transported through the axon, while only the storage vesicles (filled with precursors and converting enzymes) are transported in case of peptide NTs.**
3. **Storage vesicles of amine transmitters are much smaller (40-50 nm) than granules (80-200 nm).**
4. **Amine NTs are often recycled by re-uptake processes, while peptide NTs can not be re-uptaken.**
5. **Amine NTs are synthesized in the axon terminal and in the perikaryon, while peptide NTs can not be synthesised in the axon terminal, only in the cell body.**

- 2) *Fill in the form with the missing component of receptor-ligand relationships:* (5 points)

Muscarinic receptor

NMDA receptor

α -/ β -adrenergic receptors

GABA-A / GABA-B

acetylcholine

glutamate

Adrenaline (Epinephrine)

GABA

(?no receptor needed, it diffuses into cell?)

Nitrogen monoxide

3) Name two examples for peptide transmitters produced by hypothalamic cells!

(1 point)

vasopressin (ADH/AVP)

oxytocin

4) Supplement the text below with the missing words!

(11 points)

Neuropeptides are synthesized in the **cell body** of the neurons in the form of **precursor proteins**. They are transported in the axons towards the **axon terminal**, while smaller peptides are cleaved off the **precursor** molecule. They are transported and stored in **granules**. In contrast, most of the amine transmitters are synthesized in the **axon terminal** of the neurons and stored in **classical transmitter vesicles**. The membrane of the storage organelles is synthesized in the **cell body** of the neurons; the neurotransmitter transporters are also built in the membrane here. A subset of amine transmitters undergoes a process called **re-uptake**, through which it enters the **presynaptic axon terminal** via plasma membrane transporters. In addition to neurons, **astrocytes** also participate in the elimination of transmitters from the synaptic cleft.

5) Complete the text below!

10 points

The main inhibitory neurotransmitter in the CNS is **GABA**, which is stored in **flattened synaptic** vesicles within the axon terminals. It is formed by decarboxylation of **L-glutamate** by the enzyme called **glutamate-decarboxylase (GAD)**. Its ionotropic receptors are the **GABA-A** receptors that act as **chloride** ion channels. Its metabotropic receptor is coupled to **G-proteins**. The transmitter gets into the synaptic vesicles by the aid of **vesicular GABA transporter**. The neurotransmitter occurs in **neuraxial** cells of the cerebellum. The synapses established by these inhibitory axons belong to the **axo-axonous** category.

Complete the table with the missing information/definition!

5 points

Glutamate	
Derivative of	alpha-ketoglutarate / glutamine
Synthesized by	aminotransferase / glutaminase
Inactivated by	neuronal uptake by plasma membrane transporters
Its ionotropic receptors	AMPA, Kainate, NMDA
Packed into synaptic vesicles by	vesicular glutamate transporter

Complete the text below.

5 points

The synthesis of **peptide** neurotransmitters starts at the RER in the cell body of the neuron, where first its **precursor** molecule is produced. During the **anterograde axonal** transport of the maturing proteins to the axon terminal, further processing of them may occur. In the axon terminal they are stored in **granules**, whose diameter is about **80-200 nm**.

Complete the table with the missing information/definition! 5 points

GABA	
Derivative of	L-glutamate
Synthesized by	glutamate-decarboxylase
Inactivated by	GABA aminotransferase
Its receptors	GABA-A (ionotropic), GABA-B (metabotropic)
Packed into synaptic vesicles by	vesicular GABA transporter

Complete the text below.

5 points

Amine neurotransmitters are synthesised in the (mostly) axon terminal of the neuron. They are packed into synaptic vesicles of the size 40-50 nm. Inflow of Ca⁺⁺ ion to the terminal frees the vesicles from actin filaments of the cytoskeleton. After this, the vesicles get inserted into the presynaptic web (grid) (in active zone) and establish contact with the presynaptic membrane. This process is called docking.

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6. IONOTROPIC RECEPTORS METABOTROPIC RECEPTORS NEURODEGENERATION

Brief summary:

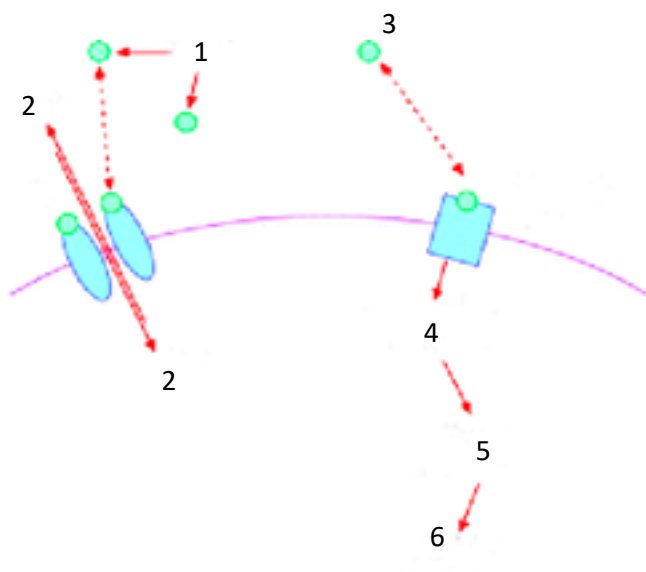
The first lecture lists the different subclasses of ion channels and presents detailed description of the ligand gated channels, the ionotropic receptors. The second lecture describes the other major class of receptors, the metabotropic receptors, which transmit the intercellular signal via different G-proteins. Information about the two waves of intracellular signaling pathways (the systems of second and third messengers) are also given. The third lecture analyses the consequences of cellular distress in the central and peripheral nervous systems, which ultimately leads to cell death. Tissue damage and tendency for regeneration in the PNS and CNS are also explained giving clues, why this field is a major target of current research.

One has gained sufficient knowledge, if understand and can explain the followings:

- 1) The difference between ion channels and ion pumps.
- 2) Regulation of ion channels.
- 3) Majority of amine transmitters targets both ionotropic and metabotropic receptors.
- 4) Peptide transmitters target metabotropic receptors.
- 5) The signalling waves of first, second and third messengers.
- 6) The complex role of calcium played in signalling.
- 7) Regulation of protein functions by phosphorylation and dephosphorylation.
- 8) The difference between necrosis and apoptosis.
- 9) Tissue damage and tendency for regeneration in the PNS and CNS.

Test the knowledge you gained:

- 1) *Ionotropic and metabotropic receptors. Answer the following questions. If the answer is no, exemplify the numbered element with another ion/molecule/protein/event!* (6 points)



Can the element number 1 be serotonin? **yes**

Can the element number 2 be potassium ion? **yes**

Can the element number 3 be GABA? **yes**
Can the element number 4 be cAMP? **yes** (the figure skips G-protein and adenylylcyclase activation)
Can the element number 5 be sodium channel? **no, but it can be protein phosphorylation**
Can the element number 6 be dephosphorilation of proteins? **no, but it can be ion channel activation**

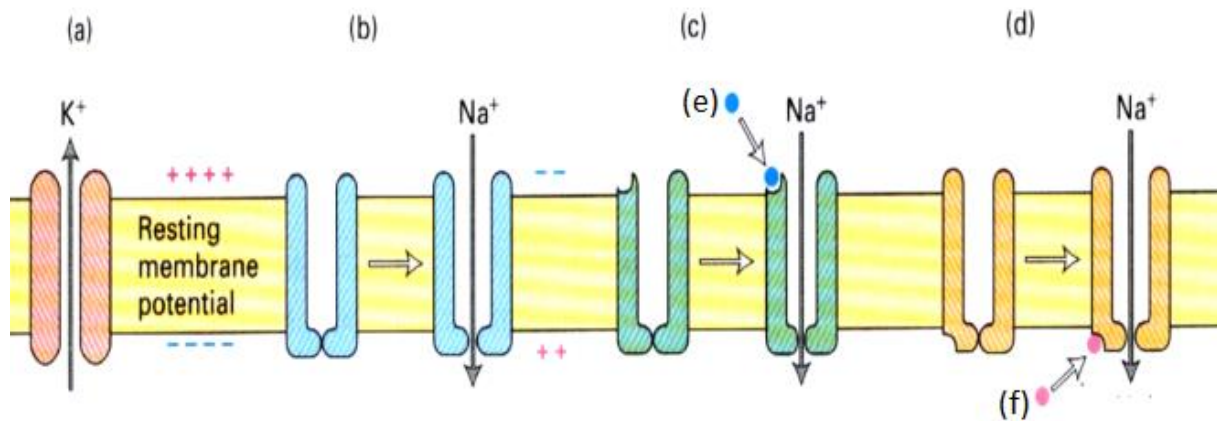
2) *List some second messengers together with target molecules!*

(8 points)

2 nd messenger	target molecule
a. cAMP	protein kinase A (PKA)
b. Ca²⁺	protein kinase C (PKC)
c. diacylglycerol	protein kinase C (PKC)
d. inositol-triphosphate (IP3)	Ca²⁺ channels on SER

Identify the different ways of ion channel activation!

5 points



(a) **resting K⁺ channel**

(b) **voltage-gated ion channel**

(c) **ligand-gated ion channel**

(d) **signal-gated ion channel**

Write an example for (e), which can trigger Na⁺ flow into the cell:

glutamate, acetylcholine, serotonin

Fill in the form with the missing component of receptor-ligand relationships!

5 points

Receptor

Ligand

nicotinic receptor

acetylcholine

GABA-A/GABA-B

GABA

NMDA

glutamate

5HT₁ receptor

serotonin

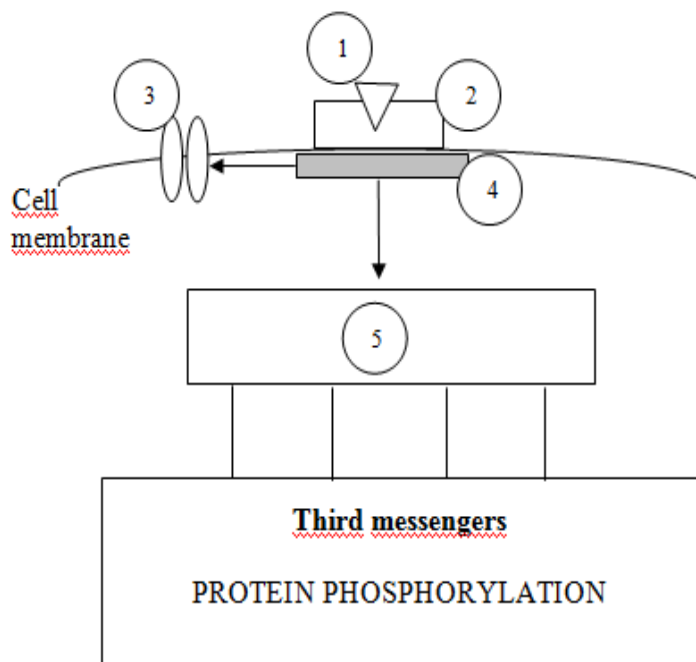
adrenergic receptor

noradrenalin

10/

Steps of signal transduction. Numbers next to a symbol mark a **particular class** of the cascade. Pair each of the listed members of different signalling pathways with the correct number(s)!

9 point



Adrenergic receptors: **2**

Epinephrine or norepinephrine: **1**

Ca²⁺: **5**

GABA_B receptors: **2**

G protein: **4**

Second messengers: **5**

AMPA receptors: **3**

cAMP: **5**

muscarinic acetylcholine receptors: **2**

List two possible causes of neural tissue damage.

1 point

genetic mutations
traumatic brain injury
tumor
infection
oxidative stress
chemical damage
ischemia
hypoxia
aging

Corrected by:

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7. DEVELOPMENT OF THE NERVOUS SYSTEM SPINAL CORD INTERNAL STRUCTURE OF SPINAL CORD

Brief summary:

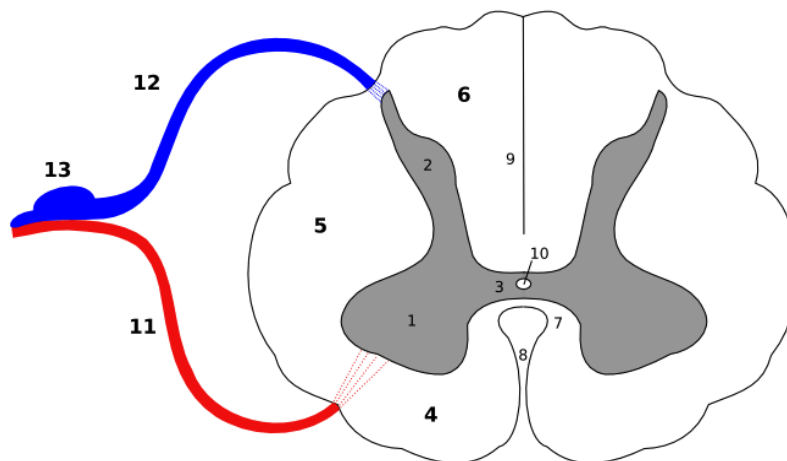
The first lecture describes the major steps of nervous system development from the formation of neural plate till the cyto-differentiation of the cerebral cortex. The second lecture provides an overview about the structural organization of the spinal cord, and explains the term of spinal cord segments, which receives sensory input from and send motor commands to well defined portions (segments, the existence of which is not obvious in humans) of the human body. The third lecture demonstrates the location of spinal cord neurons, which send information to peripheral targets, form local connections or establish ascending pathways to send information to supraspinal centers. Descending pathways are also described, which bring information from supraspinal centers.

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The development of the central nervous system from a tube-like structure, the wall of which host initially stem cells. After multiplication, cells differentiate into neurons and glial cells and establish function-related connections with the capacity of plastic changes.
- 2) The basic structure of spinal cord is organised to support body segments. The term of reflex arch, and the difference between somatic and autonomic reflex arches.
- 3) The arrangement of nerve fibers within the spinal cord carrying motor and/or sensory informations from and to supraspinal centers.

Test the knowledge you gained:

- 1) *Identify the selected numbered structures by using the schematic drawing of the spinal cord! Then, associate the statements with the corresponding numbers of the figure. Finally depict the locations of the Substantia gelatinosa Rolandi and the Tractus fundamentalis in the schematic drawing.* (10 points)



1. **Ventral horn / cornu anterior**

8. **fissura mediana anterior**

9. **sulcus medianus posterior**

13. **dorsal root ganglion**

In this structure fibers connect the right and the left halves of the spinal cord: **3**

Both ascending and descending fibers can be found in this structure: **4**

The cell body of the sensory neurons is located here: **2**

Cerebrospinal fluid can be found in this(ese) space(s): **8**

2) Give a short definition for the following terms!

(10 points)

Reflex arch: **<out of view>**

Axon initial segment: **Part of the neuron, where the axon hillock with dense sodium channels can generate action potential.**

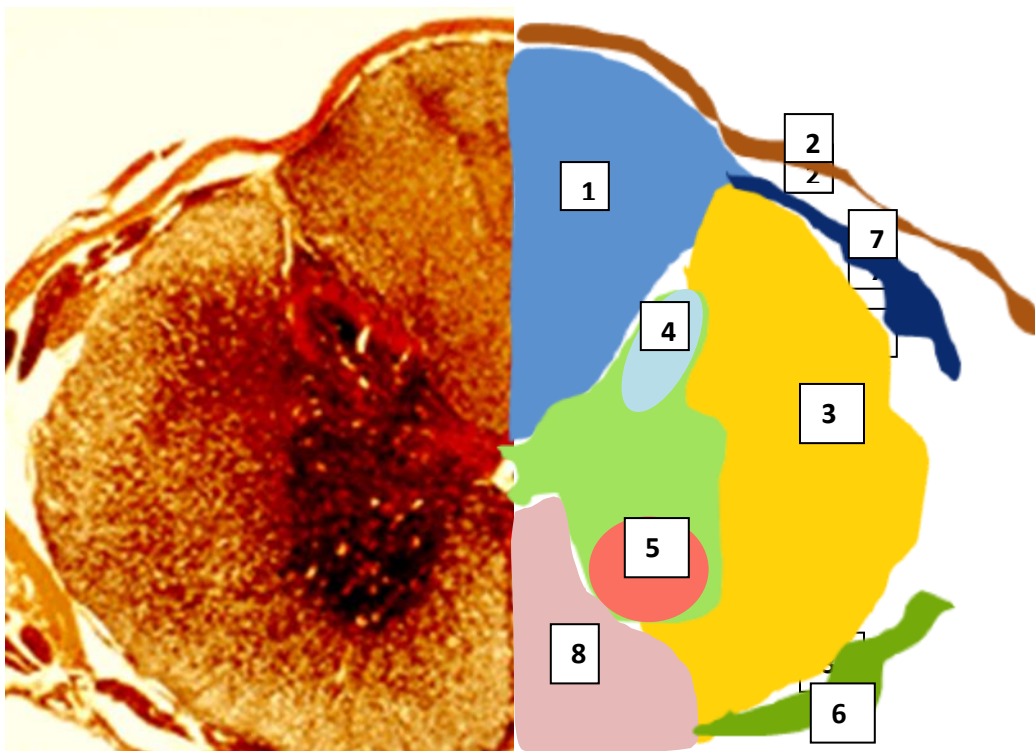
Ranvier nodes: **Naked parts of axon process between myelin sheaths, they cause propagation in a saltatory manner.**

Resting membrane potential: **Approx. -90mV in neurons, comes from inside and outside ion concentrations . When it is depolarized, action potentials can be generated.**

Second messenger: **Second step of signal transduction, usually activated by G-proteins. For example: cAMP, Ca++**

3) Associate the statements below with the corresponding numbers of the figure.

(13 points)



Nerve fibers, which derive from the spinal ganglion

Connective tissue, which encapsules the subarachnoid space

Nerve fibers, most of which terminate in the cuneate and gracile nuclei

This structure contains somatomotor axons

The crossed pyramidal tract runs in this compartment

Nerve fibers, which project to the cerebellum, are found here

It contains gamma-type motor fibers

It contains the rubrospinal tract

7

2

<out of view>

6

<out of view>

1

6

<out of view>

Perikarya of the somatomotor neurons are located here
It contains fibers from the lateral vestibular fibers
It participates in filtering pain
This structure may convey autonomic, preganglionic fibers
It conveys nerve fibers projecting to the thalamic VPL nucleus

5

<out of view>

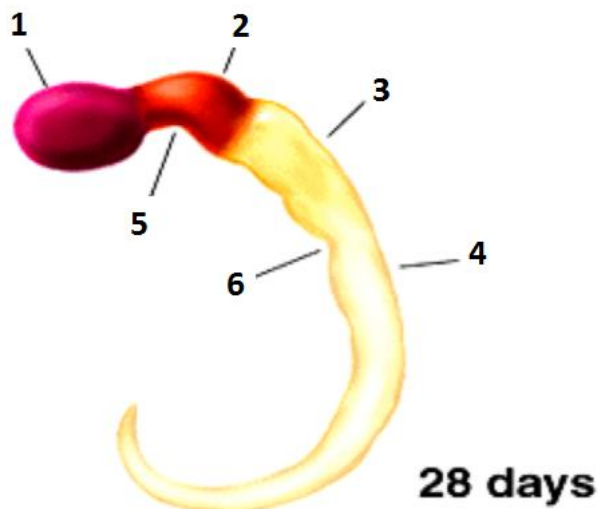
<out of view>

3

<out of view>

10/

Identify the numbered structures, and render the number of the structures to the statements. 8 points



- 1) prosencephalon
- 2) mesencephalon
- 3) rhombencephalon
- 4) spinal cord
- 5) (mesen)cephalic flexure
- 6) cervical flexure

The frontal lobe develops from its derivative secondary vesicle: 1

From its derivative secondary vesicle, the medulla oblongata develops: 3

Answer the questions! 2 points

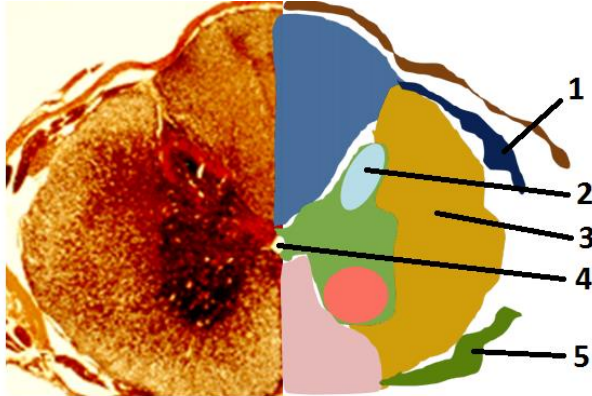
Which microscopic method employing fluorescent dyes has the following advantages: no fading, no phototoxicity, increased focal depth?

Two-Photon Microscopy

What is the basic principle of immunohistochemical labeling?

Detecting molecules with antigenic properties.

Name the numbered parts of the spinal cord, and render the number of the structures to the statements (multiple answers are possible). 8 points



- 1: dorsal root
- 2: posterior/dorsal horn
- 3: lateral funiculus
- 4: central canal
- 5: ventral root

The fibres of this structure carry motor commands:

3, 5

Conveys sensory information:

1, 3

Derives from the alar plate:

2

Answer the questions!

2 points

What is the aim of next generation sequencing compared to older methods?

Reducing time required for sequencing with several new approaches.

Describe briefly the Brainbow method!

3 or more fluorescent proteins (XFPs) are combined in this method (combinatorial expression). As a result, it is easier to distinguish adjacent neurons and visualize other cellular interaction due to many colors.

BASICS OF NEUROBIOLOGY

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2017-2018

8. TRACTS OF SPINAL CORD STRETCH REFLEX FLEXOR AND AUTONOMIC REFLEXES

Brief summary:

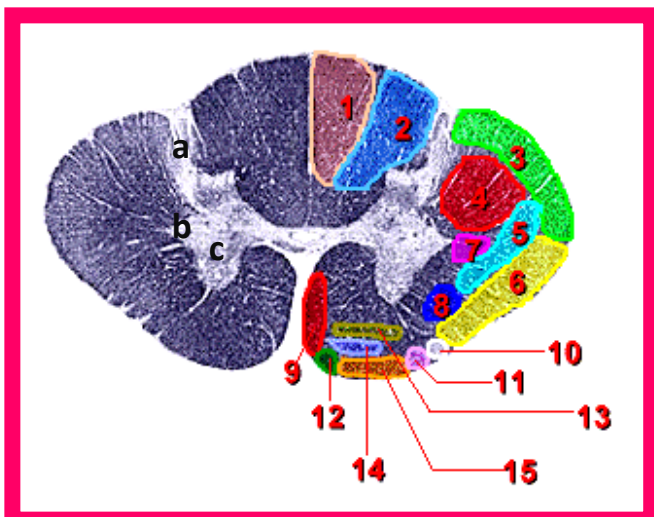
The first lecture explains the organization of the white matter of spinal cord and demonstrates the major ascending and descending pathways with the location of contributing neurons and the functions provided. The second and the third lectures introduce the term reflex arc, which is a multicellular pathway capable to trigger actions in response to internal or external stimuli. Five basic elements are described morphologically as well as functionally; the receptors (the sensor of the internal and external stimuli), the afferents (carrying the information to the center), the center (mono- or polysynaptic connections, which allow processing and distributing the incoming signal), the efferents (carrying the information from the center) and the effectors (the executive units – usually muscles or glands).

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) At some extent, the human body preserved the segmental organization of phylogenetically more ancient creatures. The segments became more or less reorganised, but kept their controlling neuronal pathways with sensory and motor innervation.
- 2) The spinal cord collects sensory information from the body and the limbs. The information is conveyed to higher brain centers via ascending pathways.
- 3) There are pathways selective for the different sensory modalities. Some sensory modalities are carried by parallel pathways to different brain centers.
- 4) The spinal cord sends motor commands to the body and the limbs. The information is conveyed from higher brain centers via descending pathways.
- 5) There are pathways, which carry motor information from different higher brain centers.
- 6) Reflex arcs have five basic elements.
- 7) The generation of specific responses to stretch, pain or visceral sensations.
- 8) The consequences of spinal cord injury.

Test the knowledge you gained:

- 1) *List the major parts of the white matter and the grey matter (the area/volume occupied by the numbered pathways or cell groups marked by letters):* (10 points)



Major parts of the white matter:

1, 2: **dorsal funiculus/funiculus posterior**

3,4,5,6,7,8: **lateral funiculus / funiculus lateralis**

9,10,11,12,13,14,15: **ventral funiculus / funiculus anterior**

Major parts of the grey matter:

a) **dorsal horn / cornu posterius** b) **lateral horn / cornu laterale** c) **ventral horn / cornu anterius**

List the major parts of the spinal cord and the segments, which build up these parts!

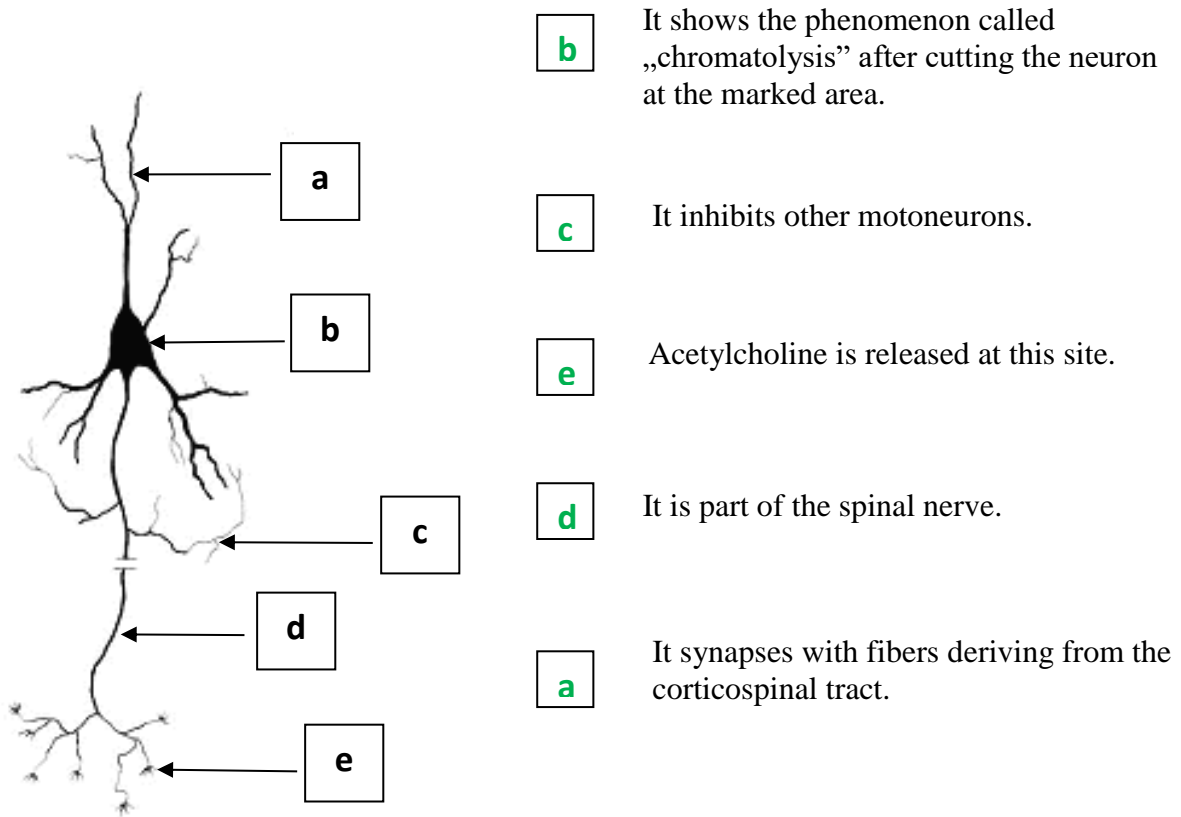
dorsal horn: **substantia gelatinosa, nucleus proprius, nucleus dorsalis**

lateral horn: **nucleus intermedio-lateralis**

ventral horn: **nucleus motorius**

This is a spinal cord motoneuron. Write the letter of specific parts of this motoneuron into the corresponding squares!

(5 points)



2) *Identify the parts of the spinal cord (white or grey matter), where the following structures are located:*

4 points

a. Cell bodies of motoneurons of the autonomic nervous system: **grey matter**

b. Fasciculus gracilis: **white matter**

c. Crossed pyramidal tract: **white matter**

d. Substantia gelatinosa Rolandi: **grey matter**

BASICS OF NEUROBIOLOGY

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9. BRAIN STEM STRUCTURE OF CEREBELLUM NETWORKING OF CEREBELLUM

Brief summary:

The first lecture gives a detailed description of the brain stem including the surface structures, the major constituents, its cavity, the cranial nerves originating from and the supplying vessels. The second and the third lectures describe the location and major parts of the cerebellum; parcellation is explained on the bases of phylogenetic development and functional connections with the spinal cord and other brain regions. The cerebellar cell types, their afferent and efferent connections are also explained.

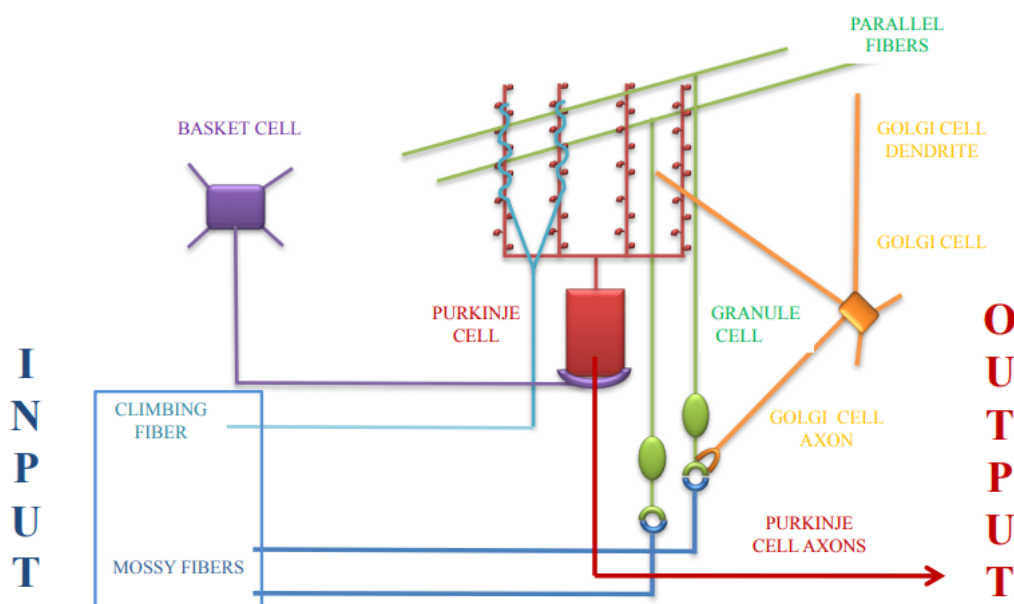
One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The brain stem has three parts, which develop from the midbrain and the hindbrain (rhombencephalon).
- 2) The brain stem hosts 10 out of 12 cranial nerves, which ensure all functions for the neck and the face, as spinal neurons do for the body and the limbs.
- 3) The brain stem level is the site, where CSF moves in and out of the 4th ventricle and the subarachnoidal space.
- 4) The cerebellum establish connection with all three parts of the brain stem, through which it can gain essential somatosensory, vestibular and higher cortical informations to carry out its motor control.
- 5) The different cell types, and the functional interconnections in the cerebellar cortex.

Test the knowledge you gained:

- 1) *Make a schematic drawing of the neuronal circuits of the cerebellum. Depict the following structures and their specific connections.* 10 points

1. Purkinje cell. 2. Granule cell. 3. Golgi cell. 4. Basket cell. 5. Dentate nucleus 6. Climbing fiber. 7. Mossy fiber. 8. Glomerulus. 9. Parallel fiber. 10. Termination site of the Purkinje axon.



2) List the number of cranial nerves characterised by the following sentences!

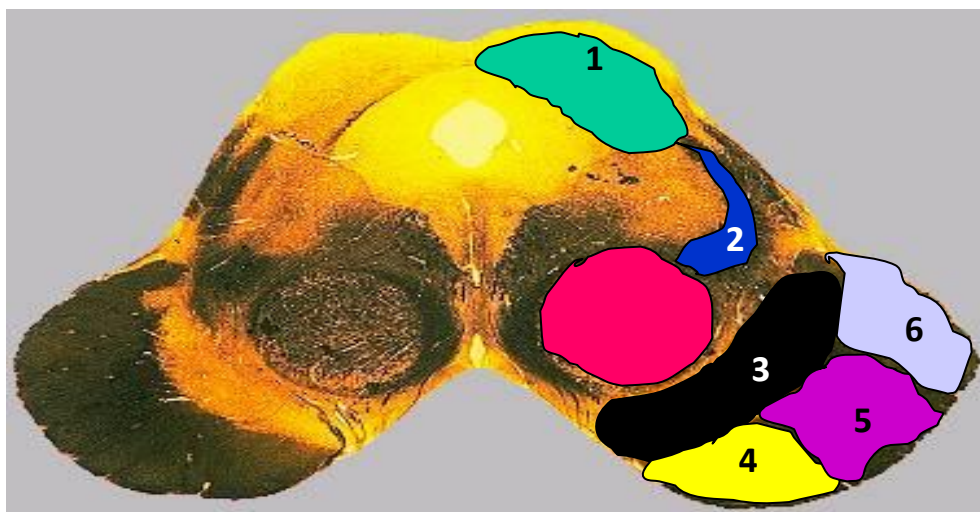
5 points

- a. It has purely sensory functions: _____
- b. It has purely motor functions: _____
- c. It has autonomic motor functions: _____
- d. It participates in the eye(ball) movements: _____
- e. They share the same somatomotor nucleus in the brain stem: _____

3) This figure shows the coronal section of the midbrain at the level of the superior colliculus. Associate the statements with the corresponding brain stem structure!

5 points

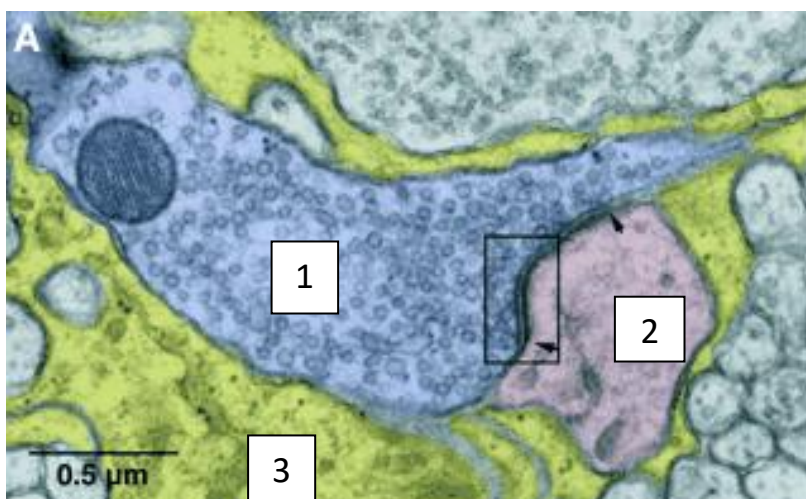
- a. It conveys the fibers of the pyramidal tract: _____
- b. It is a relay station of the visual pathway: _____
- c. It is a somatosensory pathway: _____
- d. It terminates in the pons: _____
- e. It's dopamine content is high: _____



4) This electron micrograph shows a climbing fiber (No 1).

Answer the following questions:

8 pont



Where is located the somatodendritic part of the neuron, which is giving rise to this process? **inferior olive**

Which neuron's process is No.2. ?

Purkinje cell

What kind of processes (No. 3.) do surround No. 1. and 2.?

parallel fibers

List three more functions of No.3. cells: ???

What kind of transmitter is stored in the synaptic vesicles of No1. process? **glutamate**

What other cells contribute to the innervation of No2. process? **basket cells, stellate cells**

5) Identify the neurons characterised by the following statements!

4 points

The neurons from this nucleus can activate individual Purkinje cells selectively and very efficiently, even in an inhibited zone of the cerebellar cortex.

The name of the nucleus: **inferior olivary nucleus (climbing fiber)**

These neurons are capable to establish inhibited areas on both side of the activated Purkinje cells.

The name of the neurons: **basket cells ???**

These neurons collect information from the spinal cord, brainstem as well as the neocortex and can activate several Purkinje cells, but only with concurrent, additional inputs.

The name of the neurons: **mossy fibers ???**

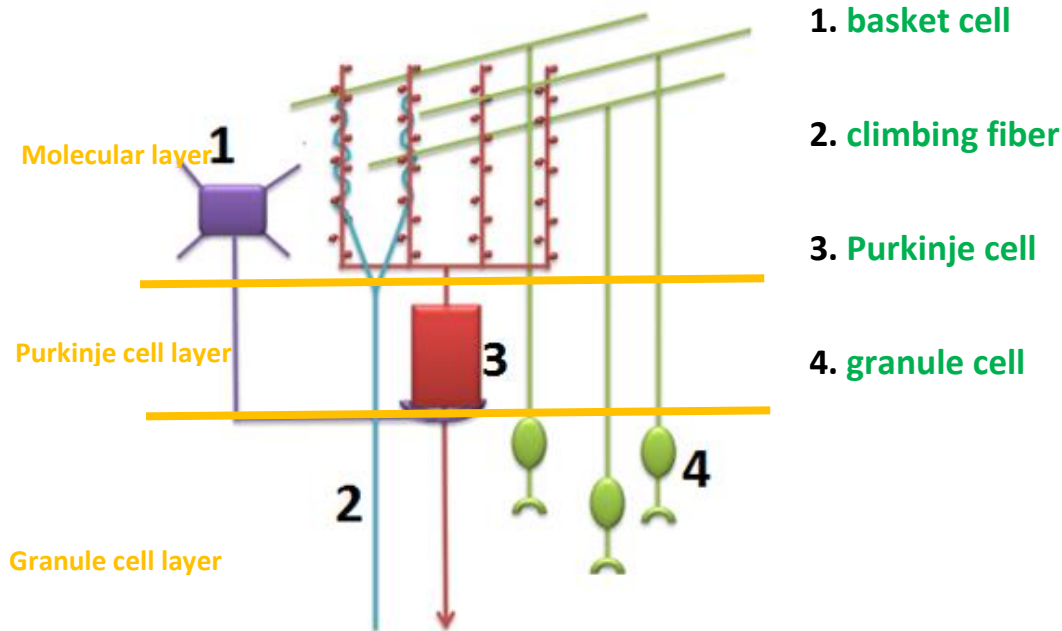
These neurons establish a long pathway, which carries information from the periphery direct to the brainstem.

The name of the neurons: **???**

Name the numbered cell types or afferents of the cerebellar network!

Separate the cortical layers by drawing lines and name the different layers next to the scheme!

7 points



Answer the questions!

3 points

List the ascending spinal cord tracts that convey conscious sensory information.

fasc. gracilis, fasc. cuneatus, spinothalamic tract

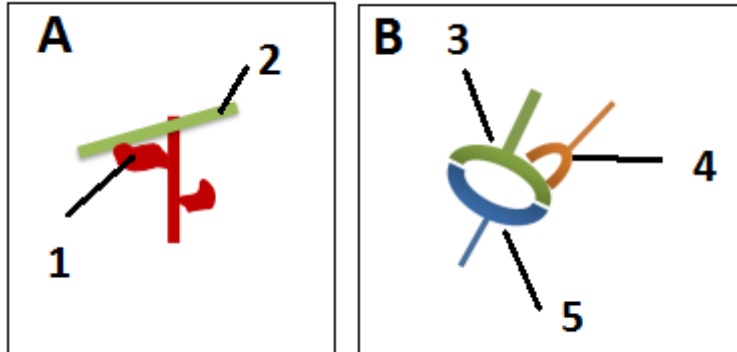
What is the function of the rubrospinal tract?

conveying motoric information from red nucleus to lower motoneurons
(descending motor pathway)

What is the efferent path of the nociceptive reflex?

axons of alpha motoneurons (ipsilateral flexor and contralateral extensor innervations)

Synaptic specializations in the cerebellar cortex. Identify the type of synapses (A, B) and the components (contributing neuronal processes). 7 points



A: cross-over synapse

1: Purkinje cell's dendritic spine

2: parallel fiber of granule cell

B: cerebellar glomerulus

3: granule cell's dendrite

4: Golgi cell's axon

5: mossy fiber (axon)

Answer the questions!

3 points

At which part of the central nervous system does the tractus corticospinalis cruciatus and the tractus corticospinalis directus decussates?

cruciatus: medulla oblongata

directus: innervated spinal segment

Name the spinal cord tracts that carry information from the vestibular system.

vestibulospinal tract

What is the afferent path of the autonomic reflex?

processes of pseudo-unipolar cells of spinal ganglia

BASICS OF NEUROBIOLOGY

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10. ORGANIZATION OF THE BRAIN STEM NETWORKING OF BRAIN STEM CRANIAL NERVES

Brief summary:

The first lecture demonstrates the brain stem's major constituents i.e. the neuronal clusters, the ascending and descending pathways, decussations and the origin of cranial nerves at different rostro-caudal levels. The neuronal clusters either appear as nuclei or interconnected cells forming a reticulum i.e. reticular formation.

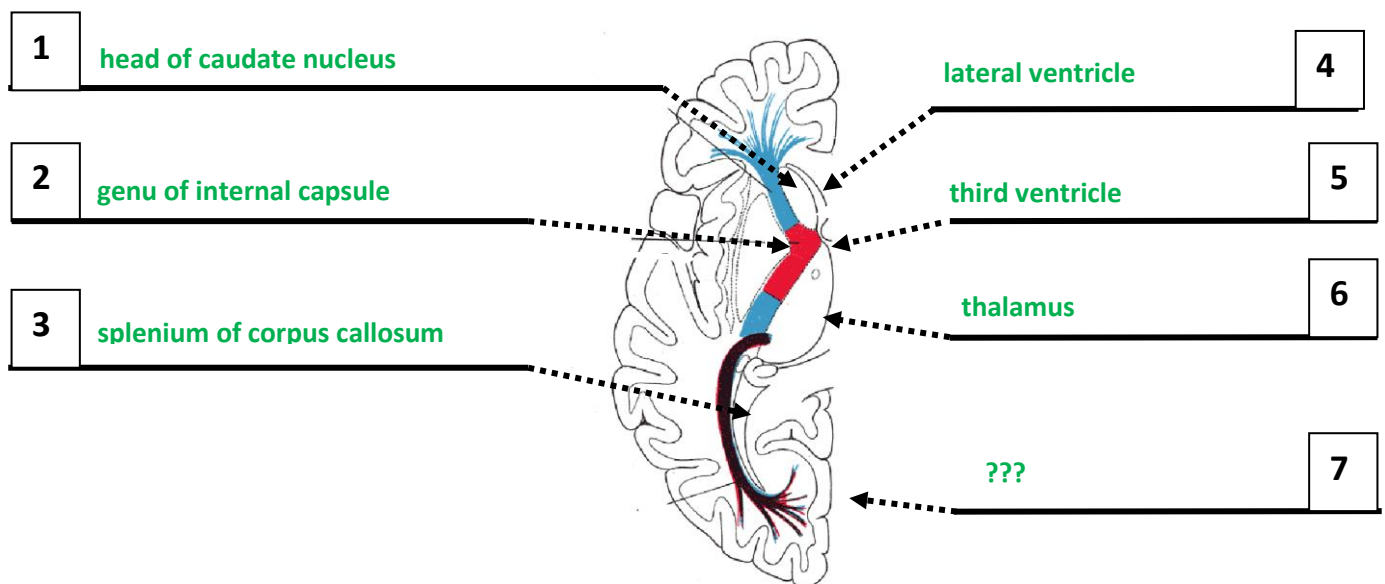
The second lecture demonstrates the ascending and descending pathways, which either terminate in the brain stem or path through it at a relayed manner or without being relayed. The third lecture explains the functional constituents and the location of the different cranial nerves.

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The brain stem has inherent regulatory functions i.e. it controls somatic (e.g. coordinated eye movements) and vital autonomic functions (e.g. respiration, circulation, feeding, state of consciousness, arousal)
- 2) The brain stem transmits motor and sensory pathways.
- 3) There are motor cranial nerves carrying out either single (somatic) or multiple motor (somato and autonomic) functions.
- 4) There are sensory cranial nerves carrying out either single, or multiple sensory (somatic and autonomic) functions.

Test the knowledge you gained:

- 1) *Scheme of a horizontal slice of the left hemisphere! Identify the numbered structures (write the name of the structure next to the number) and answer the related questions!* 10 points



Structural component of the corpus striatum:

striatum + globus pallidus

It contains descending pathways from the cerebral cortex:

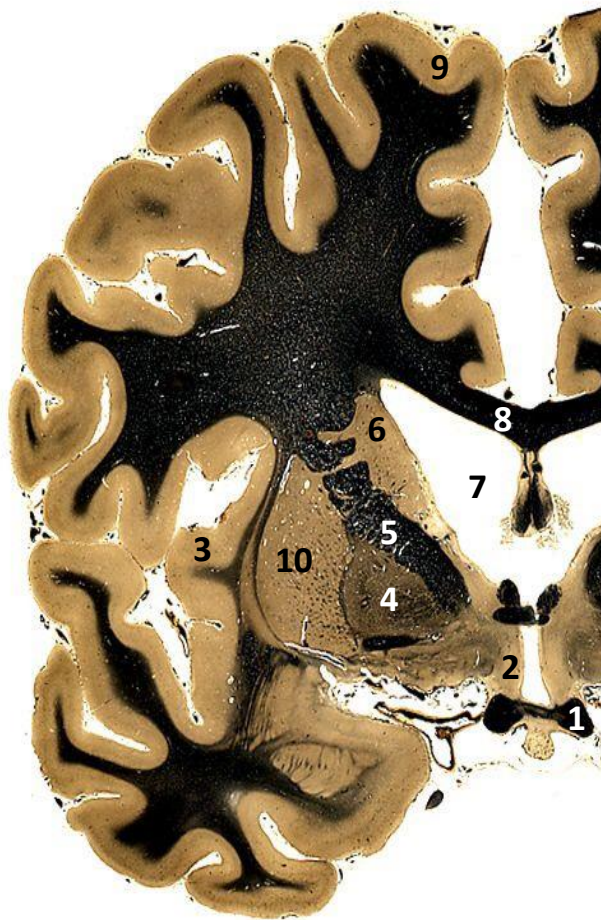
internal capsule

It provides a stimulatory input of the cerebral cortex:

???

2) Identify the names of the numbered structures!

10 points



1. mammillary body

2. diencephalon

3. insular cortex

4. globus pallidus

5. internal capsule

6. nucleus caudatus

7. lateral ventricle

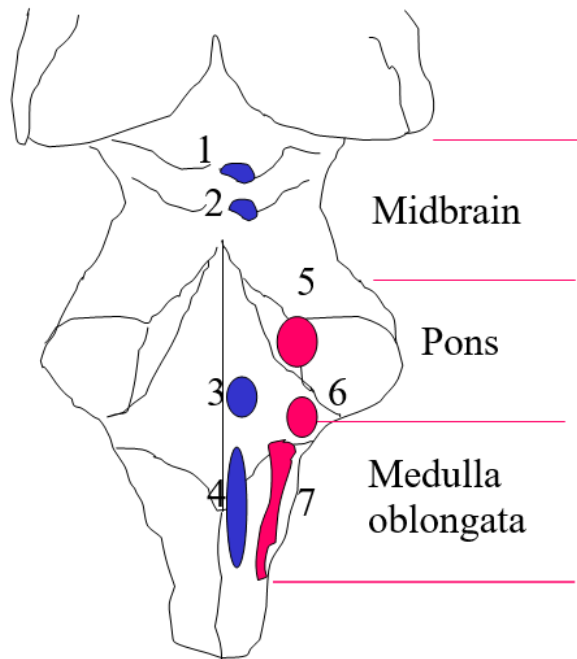
8. corpus callosum

9. parietal cortex

10. putamen

10/

The brainstem scheme shows the location of motor nuclei of cranial nerves.
Render the number of the nuclei to their name! 7 points



nucleus trochlearis IV	2
nucleus hypoglossus XII	4
nucleus facialis VII	6
nucleus abducens VI	3
nucleus oculomotorius III	1
nucleus ambiguus IX, X, XI	7
nucleus trigeminus V	5

Identify the cranial nerves characterised by the following statements! 3 points

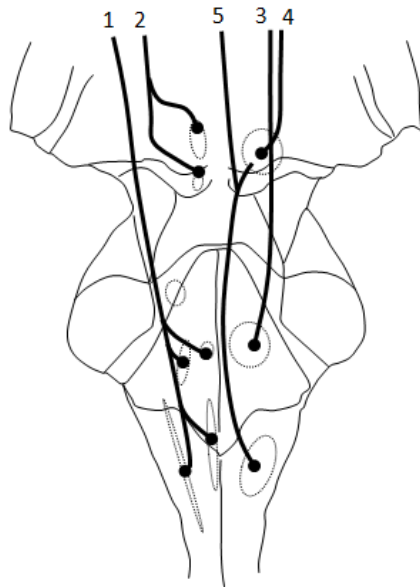
This(se) neuron(s) innervate(s) the masticatory muscles: V

It has purely sensory function: I, II, VII

It participates in the eye(ball) movements: III, IV, VI

Corrected by:

The brainstem scheme shows the descending pathways terminating in the brain stem. Render the number of the pathways to their name and answer the question!
6 points



tractus corticopontinus	3
tractus corticobulbaris	1
tractus corticomesencephalicus	2
tractus tegmentalis centralis	5
tractus corticorubralis	4

What pathway is tract number 3 relayed to in its target nuclei in the brain stem?

Identify the cranial nerves characterised by the following statements! 4 points

It has autonomic motor functions: III

It is a prosencephalic derivative: I, II

It is responsible for the movement of the tongue: XII

This(se) neuron(s) convey(s) signals to the brain about balance: VIII

BASICS OF NEUROBIOLOGY

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11. DIENCEPHALON DIVISIONS OF THE TELENCEPHALON CYTOARCHITECTURE OF CEREBRAL CORTEX

Brief summary:

The first and the second lectures describe the two major derivatives of the prosencephalon; the diencephalon which is the rostral enlargement of the neural tube positioned in front of the mesencephalon and the telencephalon which shows up as two lateral enlargements of the diencephalon. The macroscopy, subdivisions and cavity of both diencephalon and telencephalon are demonstrated; and subdivision-specific functions are explained. The third lecture demonstrates the structural organization of cerebral cortex including regional differences, and the morphology, connectivity and function of the various cell types. The cortical column as the putative functional unit is also explained.

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The thalamus is a complex nucleus; each of its nuclei are in reciprocal connection with the corresponding areas of the cerebral cortex.
- 2) There is a functional distinction among the thalamic nuclei; there are nuclei with primary motor, sensory or limbic functions, each transmit excitatory signal to target areas.
- 3) The thalamic inhibitory neurons are segregated into the reticular nucleus.
- 4) The hypothalamus, besides being regulatory center of several autonomic functions (i.e. thermoregulation, metabolism), it controls the peripheral endocrine organs via the hypothalamo-hypophyseal axis.
- 5) The telencephalic grey matter forms an internal core, the basal ganglia, and an outer folded mantle, the cerebral cortex. The telencephalic white matter is composed of nerve fibers connecting either contralateral cortical areas (commisural pathways), ipsilateral cortical areas (associative pathways) or cortical areas to subcortical regions (projecting pathways).
- 6) The structural components of the basal ganglia and the internal capsule.
- 7) The morphology, connectivity and function of the various cortical cell types and the putative model of the cortical column.
- 8) Topography of functionally different cortical areas.

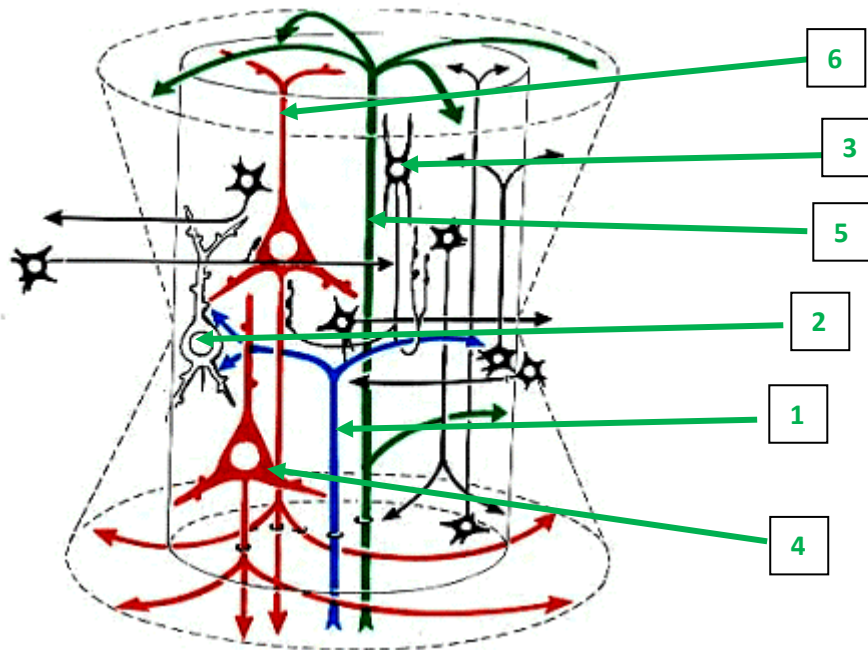
Test the knowledge you gained:

1) Features of the basal ganglia!

5 points

The corpus striatum is composed by the **striatum** and **globus pallidus**. Its major dopaminergic input derives from the **substantia nigra (and ventral tegmental area)**. The main efferents of the system take their origin from the **pallidum** and project to the **thalamus VA/VL**.

Label the listed elements in the scheme of a cortical module with numbers and arrows!
6 points



- 1) Specific afferents from subcortical centers.
- 2) Excitatory interneurons.
- 3) GABAergic interneuron establishing axo-axonic synapses.
- 4) Neurons establishing large projection pathways.
- 5) Terminal fibers of commissural and associative pathways.
- 6) Apical dendrites establishing „cross-over” synapses.

List 4 of the 5 major subdivisions of the diencephalon and one of their characteristic function (very briefly).
4 points

thalamus – consciousness

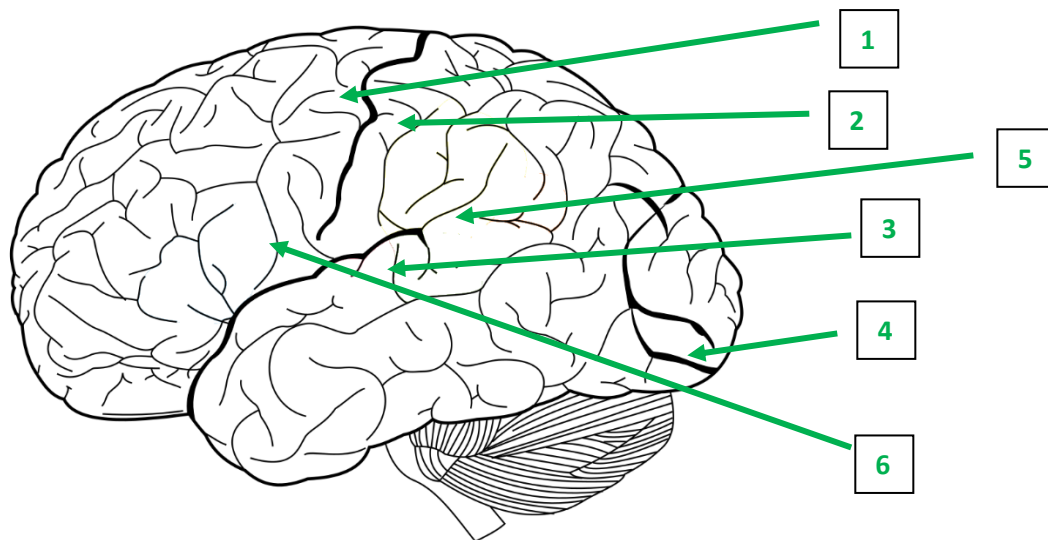
hypothalamus – neuroendocrine

subthalamus – DBS

metathalamus – visual and auditory

epithalamus – melatonin

Mark the brain region on the scheme associated with the following functions. 6 points



- 1) Primary motor centre.
- 2) Primary somatosensory centre.
- 3) Hearing centre.
- 4) Visual centre.
- 5) Sensory speech field.
- 6) Motor speech field.

List the main parts of the limbic system and describe briefly its function. 4 points

olfactory bulbs, **hippocampus**, hypothalamus, **amygdala**, anterior thalamic nuclei, **fornix**, columns of fornix, mammillary body, septum pellucidum, habenular commissure, **cingulate gyrus**, parahippocampal gyrus, entorhinal cortex, and limbic midbrain areas -> **emotion, behavior, motivation, long-term memory, and olfaction**

Corrected by:

BASICS OF NEUROBIOLOGY

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12. SENSORY SYSTEMS MOTOR SYSTEMS HIPPOCAMPAL FORMATION

Brief summary:

The first lecture gives a comparative description of the two major pathways (i.e. the medial lemniscus and the spinothalamic systems) which mediate different modalities of the sensory information towards the brain. The second lecture demonstrates the brain centers and pathways involved in different aspects of motor control. The third lecture provides basic information about the hippocampal formation. This ancient part of the cortex creates memory traces from information packages collected from, processed and redirected to neocortical areas of the brain.

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The sensory modalities, which stimulate the medial lemniscus system.
- 2) The sensory modalities, which stimulate the spinothalamic tract.
- 3) The receptors, first, second and third order neurons and their terminal fields within both systems.
- 4) The multi-center aspect of motor control.
- 5) The upper and lower motor neurons.
- 6) The trisynaptic neuronal network of the hippocampus.

Test the knowledge you gained:

1) *Complete the text below!*

10 points

The hippocampal formation is formed by the **hippocampus** and the **dentate gyrus**. The hippocampus is divided into four **CA** sectors, whose principal neuron type is the **pyramidal** cell. The perforant path carries information from the territory of the **entorhinal cortex**, its fibers synapse with **granule** cells of the **dentate gyrus**. Pyramidal neurons of the CA3 sector receive **mossy** fibers from the dentate gyrus. The Schaffer collaterals communicate with apical dendrites of **pyramidal** neurons in the **CA1** sector.

2) *Complete the text below!*

10 points

The upper cortical motoneuron control of somato-motor nuclei of the medulla is supplied by the **corticobulbar tract**, while motoneurons of the spinal cord receive this regulatory influence via the **corticospinal** tract. Fibers descending from the primary motor cortex of the latter tract enter first the **internal capsule**, then the **cerebral peduncle** part of the midbrain. In the medulla, the majority of the descending fibers **crosses over**, orienting the projection toward the **lower-motoneurons** of the spinal cord. The descending motor fibers originate from the **fifth (V)** layer of the cerebral cortex and use the neurotransmitter **glutamate** for communication. The archicerebellum provides motor control via

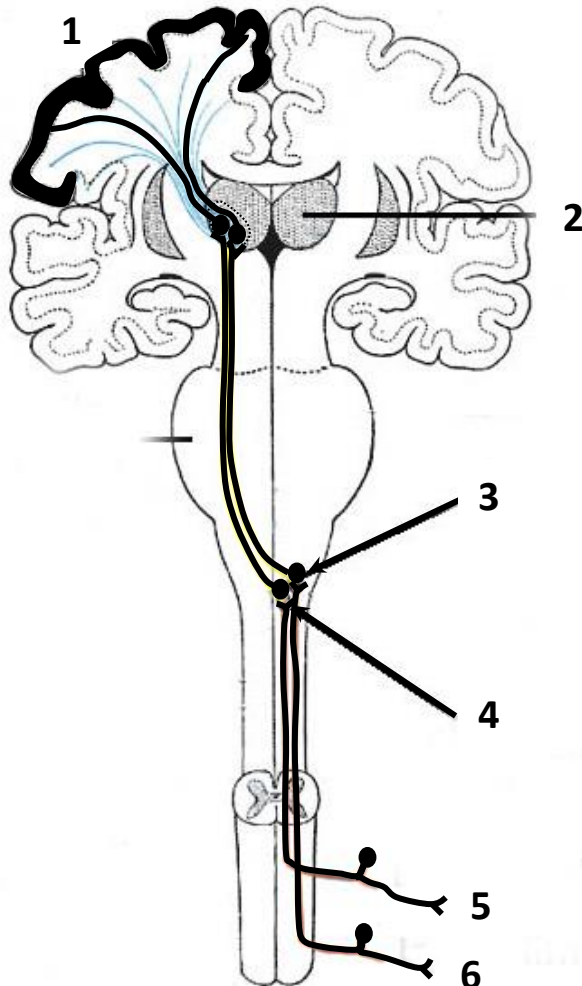
the **vestibulospinal** pathway. The lower motoneuron system utilizes **acetylcholine** as neurotransmitter in the control of skeletal muscle function.

3) *Complete the text below!*

10 points

The main conscious sensory system of the spinal cord is composed by the **spinothalamic** and **medial lemniscus** pathways. The first order neurons of these systems are **pseudo-unipolar** in shape and reside in the **spinal ganglia**. The proper nucleus (*nucleus proprius*) of the spinal cord is associated with the **spinothalamic** tract. Harmful, tissue damaging stimuli are sensed by **nociceptors**. The spinal reflex mechanism protecting the body from severe tissue damage is called **nociceptive** reflex. In terms of function, it is a **flexor**, crossed **extensor** reflex. The information carried by the medial lemniscus system is relayed by **the ventral postero-lateral** nucleus of the thalamus.

Identify the neuronal pathway and the brain areas participating in the information processing. 8 points



The name of the pathway: **medial lemniscus system**

The function of the pathway: **discriminative touch, vibration, proprioception**

1. **primary somatosensory cortex (postcentral gyrus)**

2. **thalamus**

3. **nucleus cuneatus**

4. **nucleus gracilis**

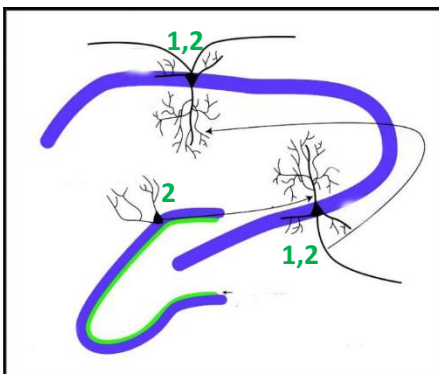
Information source of number 5:

lower part of body (T6-Coccyx segments) (fasciculus gracilis)

Information source of number 6:

upper part of body (C1-T6 segments) (fasciculus cuneatus)

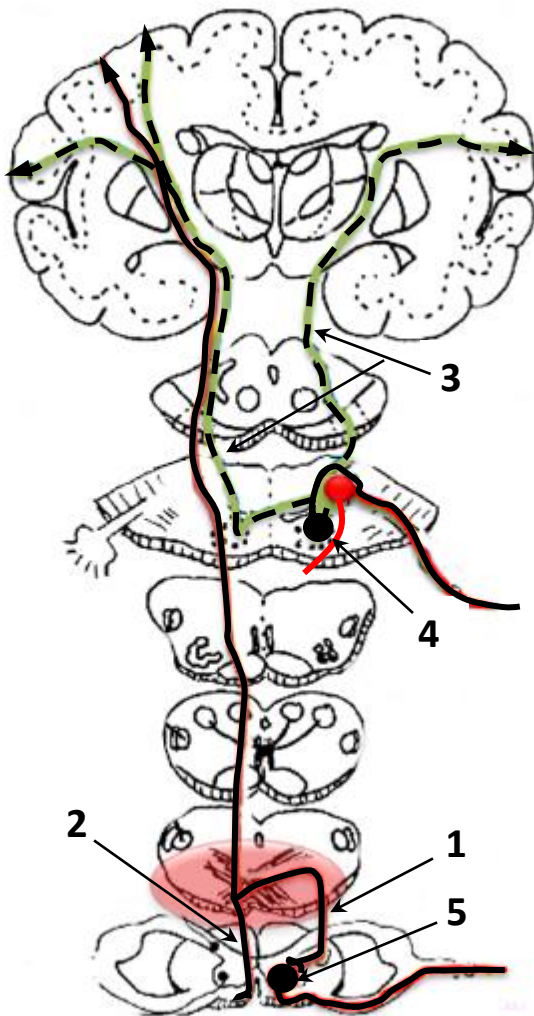
Identify the members of neuronal network and answer the following questions. 2 points



Name and label with number(s) the cell type, which directly communicate with cells in the mammillary bodies:
pyramidal cell of CA1 and CA3 (1)

Name and label with number(s) the cell type, which directly communicate with cells of the entorhinal cortices:
granule cell (hilar mossy cell) in dentate gyrus, pyramidal cell of CA1 and CA3 (2)

Identify the neuronal pathways and the CNS regions participating in the information transmission. 8 points



The name of pathway 1: **lateral corticospinal tract**

The function of the pathway: **voluntary motor control of muscles of limbs (contralateral)**

The name of pathway 2: **anterior corticospinal tract**

The function of the pathway: **voluntary motor control of muscles of trunk (ipsilateral)**

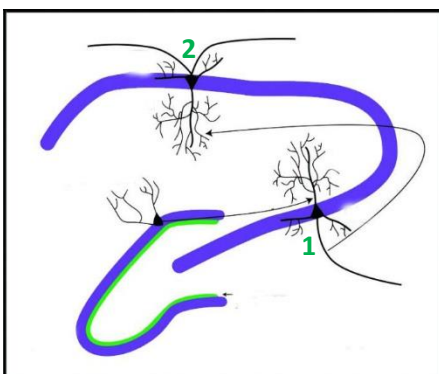
The name of pathway 3: **corticobulbar tract**

The function of the pathway: **voluntary motor control of muscles of head (via cranial nerves)**

4. **lower motoneuron of brainstem**

5. **alpha motoneuron (lower motoneurons of spinal cord)**

Identify the members of neuronal network and answer the following questions. 2 points



Name and label with number(s) the cell type, which directly receive input from hilar mossy cells:

pyramidal cell of CA3 (1)

Name and label with number(s) the cell type, which directly receive information from pyramidal cells of CA3 region:

pyramidal cell of CA1 (2)

BASICS OF NEUROBIOLOGY

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13. OLFACTORY SYSTEM VISUAL SYSTEM COCHLEAR AND VESTIBULAR SYSTEMS

Brief summary:

The last three lectures demonstrate the main sensory organs and the basic information processing taking place at their level. The olfactory system recognizes the chemical environment; the visual system detects certain spectrum of electromagnetic waves and the cochlear and vestibular system turns mechanical waves into cellular activity and nerve impulses.

One has gained sufficient knowledge, if understands and can explain the followings:

- 1) The structure of the receptor organ, which translate and enhance the olfactory, visual, auditory and vestibular signals to cellular activity.
- 2) Signalling mechanism(s) in the receptor cells.
- 3) Basic information processing at the level of receptor organs.

Test the knowledge you gained:

- 1) *Sensory organs. Evaluate the following statements for correctness: 8 points*
If is not correct, give a short explanation why!

Signal amplifiers can be found in most of the sensory organs. **True ???**

All sensory pathways are relayed in the thalamus. **True**

Thermo-sensation is bound to subcortical areas, such as the striatum. **???**

Decussations characterize all sensory pathways. **False**

There is no decussation in the olfactory system.

Most of the environmental information is collected by the visual system. **False**
Also olfactory and auditory systems are important in collecting information about environment.

The auditory information is transmitted via a fast, monosynaptic pathway. **False**
The information is transmitted through spiral ganglion, cochlear nucleus, superior olivary complex, lateral lemnisci and medial geniculate body, terminating in the primary auditory complex.

Injury of the optic tract on one side results in blindness in the visual field of both eyes on the side of the injury **False**

It results in blindness in the visual field of both eyes on the opposite side of the injury.

High frequency tones are detected at the base of the snail, whereas low frequency tones are detected at the top of the snail. **True**

- 2) *Features of the pupillary reflex! 10 points*

Intense illumination of one eye results in the **constrict** of the pupil on **both** side/s/. The receptors are the **ganglion cells** located in the retina. These receptors do not contribute to sight directly. Photo transduction for the visual pathway instead is carried out by **rods** and **cones** which are wired to **bipolar** cells that converge to the main efferent cell type of the retina, the **ganglion** cells. The optic afferents convey the information to the **pretectal** nucleus which innervates bilaterally the **Edinger-Westphal** nuclei. The preganglionic fibers reach the neurons of the **ciliary** ganglia that, in turn, innervate the constrictor muscles of the pupils.