In the animals of highly developed organization consisting of complex organs and organ systems, develops a special system, which connects these organs and organ systems, correlates their functions and finally completes the individual life, that is the **nervous system**. The nervous system consists exclusively of the nervous tissue and a few connective tissue accompanying the blood vessels.

- The nervous tissue consists of the nerve cells, neurons, nerve fibers and their supporting cells, neuroglia cells. They compose the central nervous system, the brain and the spinal cord, and the peripheral nervous system, which comprises all nerve cells and nerve fibers being outside of the central nervous system.

- The central nervous system, brain and spinal cord, develops very early embryonic period from the ectoderm as the neural tube and the peripheral nervous system from the neural crest cells, that originates from the place where the neural tube separates from the ectoderm.
The central nervous system (CNS) consists of the brain and the spinal cord and is composed of the nerve cells, neurons, and a host of supporting cells, neuroglia. As the other components there are only blood vessels and a few concomitant connective tissue.
The most conspicuous function of nerve cells is the excitation by stimuli from outside and the communication of this excitation to the other cells. The nerve cells, neurons, consists of cell body, perikarion, and two kinds of protoplasmic processes: dendrites and neurite or axon.

Cell body: The form and largeness of the nerve cells vary extremely; from round to polygonal in shape and several μm to several ten μm in diameter. At the center of cell body there is a round nucleus with a conspicuous nucleolus; around the nucleus the cytoplasm is filled with coarse granules staining deeply with basic dyes. As these granules were first reported by Fr. Nissl in 1884, they are named Nissl bodies or Nissl substance. These are highly developed rER. Besides these, well developed Golgi complex surrounds the nucleus. When silver impregnation is performed, fine fibrils appear around the nucleus very densely, and run in all directions in cell body and through there from dendrites into dendrites and from cell body into the neurite; these are called neurofibrils.

Dendrites: These are protoplasmic processes, radiating from the cell body in all directions and tapering in some long distance. In the beginning portion they contain Nissl substance. They contain neurofibrils and are regarded as the enlargements of the cell body. In the specimens impregnated by Golgi method dendrites appear deep black and have a lot of small processes, spines.

Neurite: This is a very long single protoplasmic process transporting and communicating the excitation to the distant cells. The neurite contains no Nissl
bodies nor spines; with silver impregnation, it stains deep black and shows a smooth contour. At the starting region, the neurite contains no Nissl bodies; this region is called the axon hillock.
• In the center left a large polygonal nerve cell is shown. A large round nucleus with a conspicuous nucleolus locates in the center of the cell body. Around the nucleus the cell body is filled with coarse granules stained deeply with basic dye. At the periphery of the cell body seven dendrites (short arrows) and one neurite (long arrow) are recognized. At the beginning portion of the axon no basophilic granules are seen. This portion is called axon hillock. At right one smaller more darkly stained neuron is seen. They both are embedded in a dense meshwork of the nerve fibers, dendrites and neurites of other nerve cells. This is called the neuropil, in which capillaries and nuclei of supporting cells are scattered. Double arrows indicate the blood capillaries.
This is an anterior horn cell of human spinal cord, stained by Nissl stain. Fixed with a high concentration alcohol and stained with basic aniline dye, for example, toluidinblue, deeply stained coarse granules appear in the cytoplasm of nerve cells. They are Nissl bodies. In this stain nucleolus is deeply stained but not the nucleus. The dendrites contain the Nissl bodies whereas the neurite does not. In the unstained neuropil nuclei of the supporting cells are scattered. An arrow indicates the axon.
• This is also an anterior horn cell. In this figure three long dendrites (long arrows) containing the Nissl bodies and three short dendrites (short arrows) are recognized. The cytoplasm is densely packed with the Nissl bodies. The nucleolus is conspicuous but nucleus itself is not stained.
• Bodian’s silver impregnation visualizes the neurofibrils. This is an anterior horn cell impregnated by this method. The anterior horn cell is multipolar having several dendrites and one neurite (arrow). The cytoplasm is filled with neurofibrils, that run densely around the nucleus and from dendrites into dendrites through the perikaryon. The neuropil consisting of the dendrites and neurites of other neurons is a very dense meshwork.
• This figure shows three anterior horn cells, of a little lower magnification, to demonstrate the wide spread of the dendrites. In this figure a neurite is perceived upper right (red arrow).
This is a giant pyramidal cell in the cerebral cortex, Area 4, of about 60 $\mu$m in length and about 40 $\mu$m in width. It has a big and long apical dendrite (long arrow), arriving at the surface of the cortex, and several basal dendrites (short arrows), radiating from the basal portions of the cell body. The perikaryon is filled with the coarse Nissl bodies; the nucleolus is conspicuous but the nucleus itself is not stained. The neurite, axon, does not appear by this staining. Around this neuron there are smaller neurons and nuclei of supporting cells, neuroglia cells, scattered. The neuropil is not stained. Compare this figure with 05-07.
In 1883 C. Golgi invented an impregnation method to plate the surface of nerve cells with osmium or silver resulting in visualization of the entire form of neurons. Although the results of this method are capricious and not always well, but if this impregnation is succeeded, some neurons appear in full view, cell body, dendrites with innumerable spines and axon until its terminal endings. About the inner structure of the cell body this method gives no information.

This figure shows two giant pyramidal cells. Their cell bodies, apical and basal dendrites with innumerable spines, and a smooth axon (arrow) are clearly seen. The axon of the right cell is out of focus.
• This is a portion of the cerebellar cortex, stained by Nissl method. The cerebellar cortex consists of three layers from the surface to the deep: ① molecular layer, ② layer of Purkinje cells, or ganglionic layer and ③ granular layer.
  ① Molecular layer is wide light zone consisting of small neurons scattered loosely.
  ② Layer of Purkinje cells or ganglionic layer consists of one row of big fusiform or pear-form cells, called Purkinje cells. Around the Purkinje cells there are numerous small cells with scant cytoplasm.
  ③ Granular layer consists of unnumbered small cells of about 5μm in diameter and they are very densely packed. Usual staining methods can demonstrate only the nuclei and not their cytoplasm.
• Compare this figure with 05-09.
The Bodian’s silver impregnation method visualizes the neurofibrils; so cell bodies, dendrites and axons appear in full view. The Purkinje cells send one or two apical dendrites toward the surface, that ramify repeatedly and fine terminal branches occupy the entire molecular layer. Very specifically these terminal branches are exactly oriented in the sagittal plane. Such arborization can not be imagine from the 05-08.

In the lower one third of the molecular layer there are numerous horizontal fibers, some of which ramify and form the fiber baskets surrounding the cell bodies of the Purkinje cells. But by this method no spines projecting from the dendrites are demonstrated. About the cells of the granular layer, the granule cells, this method gives us few information.
This is a portion of human cerebellar cortex stained by Prof. K. Suzuki by himself using his own impregnation method.

The complex features surrounding the Purkinje cell body and fine arborization of the dendrites are demonstrated more in detail.
• One Purkinje cell is demonstrated in full view. The cell body with a short axon, two principal apical dendrites and huge dendritic arborization with spines are distinct. Beside this Purkinje cell four more Purkinje cell bodies are perceived, but not stained. No granule cells are demonstrated.
• A Purkinje cell is well demonstrated in full view. The pear-formed cell body locates bottom center, sending one main apical dendrite upward which gives the lateral branches one after another and then final arborization with spines. Such huge arborization is not able to imagine from the figures of H-E stain or Nissl stain.

• The black shadow overlapping on the main apical dendrite is a blood vessel.
• Higher magnification of the lower right portion of 05-12.
• In the lower region of this figure runs one secondary dendrite right upward sending several tertiary dendrites downward as well as upward in turn that give birth the final arborization with unnumbered tiny spines. These spines are the accepting apparatuses of stimuli from the other neurons.
• This specimen is of an aged person, in which the arborization of Purkinje cells is fully developed. Compare this with 05-11, which belongs to a puppy.
• In this specimen only one Purkinje cell is insufficiently demonstrated; but the basket cells and small cortical cells in the molecular layer are numerous demonstrated. And more, some of the granule cells in the granular layer are well visualized; the granule cells have three or four short dendrites which terminate in the vicinity of the cell body. Their axons start from one dendrite, go upward into the molecular layer, then bifurcate in the frontal direction running forward as well as backward through the terminal spines of the Purkinje cells.
This is a scheme showing the three dimensional structure of the cerebellar cortex, based on the findings of the specimens from 05-06 to 05-14.

To clarify the structure of the central nervous system we should study using various staining methods and also sections at least of frontal and sagittal planes.

Abbreviations: cin: molecular layer; gan: Purkinje cell layer; grn: granule layer; Cz: small critical cell; Gr: granule cell; Gz: Golgi cell; Kf: climbing fiber; Kz: basket cell; Mf: mossy fiber; Pz: Purkinje cell; ax: axon of Purkinje cell; den: arborization of dendrites of Purkinje cell.
• These are nerve cells in the Nucl. caeruleus of the human medulla. They contain in the cytoplasm, beside the Nissl substance, melanin granules, functional significance of that is not still clarified. Because of these melanin granules the Nucl.caeruleus shows macroscopically bluish gray hue.
In the central nervous system (CNS), nerve cells and nerve fibers are supported by the special cell groups, collectively called neuroglia. Usual connective tissue, fibroblasts and reticular and/or collagen fibers, is only found surrounding the blood vessels. In the histological specimens stained by the routine staining methods using dyes only the small round or elongated elliptic nuclei are observed, but the cytoplasm surrounding them does not appear. To demonstrate the cytoplasm of the neuroglia numerous silver impregnation methods have been devised. Using these methods three kinds of neuroglia cells are detected: ① astrocytes, ② oligodendroglia and ③ microglia.

① Astrocytes, the star-shaped glia cells, are divided in two groups:
  a) Fibrous astrocytes are mainly found in the white matter. They have numerous long thin processes radiating in all directions, among which one or two are relatively thick and attach to the blood vessels.
  b) Protoplasmic astrocytes are mainly found in the gray matter. They have a stellate form with multiple highly branched processes, some of which attach to the blood vessels.

② Oligodendrocytes are found in the white matter and are now believed to give the myelin sheath to the nerve fibers in the CNS. The oligodendrocytes also give the sheath to the unmyelinated nerve fibers.

③ Microglia is composed of small cells scattered throughout the CNS. They have a dense oval, elongated nucleus, scant cytoplasm and short tortuous processes. The cell body and processes have minute spines. In the
inflammatory changes of the CNS the microglia cells proliferate greatly, enlarge, and become phagocytic, clearing up cellular debris and ingesting damaged myelin. The microglia cells are now considered as phagocytic cells of mesenchymal origin.
• This is a fibrous astrocyte in the subcortical white matter. Numerous fibrous processes radiate from the cell body in all directions but cell body itself is not perceived. The thick black rods are blood vessels. The horizontal parallel lines indicate the nerve fibers.
This figure shows the fibrous astrocytes in the subcortical white matter surrounding a blood vessel (arrow). Using this method the fibrous astrocytes appear with numerous long thin processes radiating in all directions from the cell body. Some of them send one or two thick processes to attach to the blood vessel (arrow).
• Higher magnification of 05-18. The thick processes connecting the astrocyte cell body and blood vessel (arrow) are very conspicuous. By this method the contour of the cell body appears somewhat clear. The thin processes are long and smooth and without numerous branchings.
The protoplasmic astrocytes found in the same specimen of 05-17, but in the cortical gray matter. They have multiple highly branched processes but not as long as fibrous astrocytes. They also attach to the blood vessels (thick black rods) with short thick processes. Among and around these structures numerous nerve cells are faintly perceived.
The oligodendrocytes are one of the most difficult objects of visualization. In H-E preparations only their nuclei appear as densely stained small round nuclei among the nerve fibers. In the special silver impregnation specimens they appear as blackened small round cells with several short processes. Electron microscopy clarified that they provide the myelin sheath to the plural nerve fibers.

In this figure of the cross section of the spinal cord, numerous blackened small round cells are oligodendrocytes projecting only a few short processes among the myelinated nerve fibers.
The microglia cells are also difficult to demonstrate their entire picture. As they increase in number in the pathological condition, they have been investigated eagerly by neuropathologists and various silver impregnation methods were proposed.

This is a microglia cell demonstrated by Yano’s silver impregnation. It has a dense elongated nucleus, scant cytoplasm and tortuous processes.
• These are microglia cells demonstrated in the cerebral cortex of a dementia paralytica patient. They increase in number and show the activated form.
• The peripheral nervous system consists of the nerve cells, nerve fibers and special supporting cells, called Schwann cells, existing outside of the brain and spinal cord. They all originate from the neural crest cells. In the peripheral nervous system there are also myelinated and unmyelinated nerve fibers. The Schwann cells give both myelin sheath and sheath of Schwann.
05-0021
Nerve Cell
This is a spinal ganglion cell, a large round cell containing a big spherical nucleus with a conspicuous nucleolus. The cytoplasm is filled with dark violet stained fine and coarse granules and an axon starts from its left extremity, where axon hillock is conspicuous (arrow). The cell body is tightly enclosed by mantle cells. As the axon divides into two branches, shortly after the departure, and the one runs to the periphery arriving at the sensory terminal organs, the other comes into the spinal cord as the dorsal root fibers arriving at the terminal nuclei in the spinal cord or brain stem. This type of nerve cells are called “pseudo-unipolar nerve cells”.

Except for the axon, they have no protoplasmic processes.
• In the ganglia of the eighth cranial nerve, vestibulo-acoustic nerve, the neurons are bipolar, having two axons, one peripheral axon starting one pole of the neuron as the centrifugal axon and arriving at the end-organs in the internal ear; the other, as the centripetal axon, constitutes the vestibulo-acoustic nerve entering into the medulla oblongata and arriving at the vestibulo-acoustic nuclei.

• In this figure the neurons of the ganglion spirale are shown. At lower middle a thick spindle-shaped neuron with two axons, from the upper and lower pole, is indicated with long arrows (① and ②). In the eighth cranial nerve ganglia, the cell body of neuron is wrapped by the Schwann cell (short arrows).
• This is a nerve cell in the sympathetic ganglion. It resembles roughly with the nerve cell of the spinal ganglion. But this kind of nerve cells have the several protoplasmic processes (short arrows) beside the axon (long arrow). A large round nucleus with a very conspicuous nucleolus locates in the middle of the cytoplasm filled with dark stained granular substance.
• This is a sympathetic ganglion cell containing brownish colored granules that react with the di-chromate ion. This nature is common with that of the adrenal medulla cells.
• This is a nerve cell found in the cardiac ganglion. A large round nucleus with a distinct nucleolus locates eccentrically and the abundant cytoplasm is filled with basophilic fine and coarse granules. At lower left of the cell body starts the axon with axon hillock. The surface of the cell body is wrapped tightly with the mantle cells (arrows).
These are nerve cells of the Meissner’s plexus. Throughout the alimentary tract, from esophagus until rectum, in the tela submucosa small groups of nerve cells and nerve fibers are scattered. They are called Meissner’s plexus, and control the condition of the mucous membrane and especially the secretion of the glands.

This is a Meissner’s plexus found in the human jejunum, consisting of three nerve cells and scant nerve fibers.
• The Auerbach’s plexus locates between the inner circular and outer longitudinal muscle layers throughout the alimentary tract, and consists of several number of nerve cells and nerve fibers. This plexus controls the movement of alimentary tract.

• This is a relatively large Auerbach’s plexus found in the Monkey ileum, consisting of several large and small nerve cells.
The special supporting cells in the peripheral nervous system are called Schwann cells.

A nerve fiber consists of an axon enveloped in a sheath of Schwann cells from near its origin to near its termination. This type is the unmyelinated fiber and axons lie simply in deep grooves in the surface of the Schwann cells. Often multiple axons are enveloped by the one same Schwann cell.

Another type of nerve fibers, the myelinated nerve fibers, have a myelin sheath between the Schwann cells and axon, which is derived from the Schwann cells. Because of the high refractivity the bundles of myelinated fibers appear brilliant white in the fresh condition.
• This is an unmyelinated nerve fiber isolated from a bovine spleen nerve. In the center of this figure there is a nucleus of Schwann cell attaching to the faintly stained axon. The cytoplasm of the Schwann cell is beyond the resolving power of the light microscope.
There are four unmyelinated nerve fibers, three of them have the nucleus of Schwann cells and the resting one (arrow) lacks the nucleus in this field.
• This is a portion of longitudinal section of the sympathetic trunk and unmyelinated fiber bundles with rows of nuclei of the Schwann cells are seen. On the top a concomitant blood vessel is distinct (arrow).
• Higher magnification of 05-33. The horizontal parallel arrangement of the nuclei of the Schwann cells is conspicuous but axons are not perceived. The fine tortuous red lines between the nuclei are the connective tissue wrapping each of the sheath of Schwann, endoneurium.
• This is a transverse section of the spleen nerve. The axons are not stained, the red lines separating the each axon are connective tissue wrapping the surface of the sheath of Schwann, the endoneurium. In these connective tissue several elongated or spindle shaped and faintly stained nuclei are seen. They are the nuclei of fibroblasts (arrows). The small round and deeply stained nuclei belong to the cells of Schwann.
This is a myelinated nerve fiber, fixed with OsO₄ and isolated in the saline. In the center a node of Ranvier is seen, where the myelin sheath is interrupted. The myelin sheath is blackened with OsO₄ and there are oblique lines from opposite sides of the fiber, the incisure of Schmidt-Lantermann (arrows), here and there. The nucleus of Schwann cell is not seen in this figure. Compare this figure with 05-39.
• A fresh sciatic nerve is soaked in a thin AgNO₃ solution, then, after brief washing with water, reduced with thin formalin, it appears a black cross at the place of the node of Ranvier. This is called “silver cross of Ranvier”. Because of the narrowness of the node of Ranvier, the AgNO₃ solution penetrated into the node remains even after washing and by reduction becomes blackened and appears the “silver cross of Ranvier”.

• The same procedure as 05-37. When the soaking time in AgNO₃ solution is enough long, AgNO₃ penetrates deep into the gap between the axon and myelin sheath, resulting in blackening of the axon. At the center is the “silver cross of Ranvier”.

05-38. Myelinated nerve fiber 3, silver cross of Ranvier. Frog, silver impregnation, x 160.
These are the myelinated nerve fibers departing from the trigeminal ganglion. In the middle a myelinated nerve fiber runs horizontally, and at the center of it is a node of Ranvier (long arrow). On this fiber several widened incisures of Schmidt-Lantermann are distinct. The myelin is extracted entirely by the procedures of preparation making, and leaves behind an artifactitious meshwork of residual protein, called “neurokeratin meshwork”. At lower right a thin unmyelinated nerve fiber with the nucleus of Schwann cell is perceived (double arrows).

Each nerve fiber, myelinated and unmyelinated, is wrapped by scant connective tissue, endoneurium, but in this figure it is difficult to perceive distinctly.
• This is a part of transverse section of a spinal nerve, consisting of numerous thick and thin nerve fibers. As the myelin is entirely extracted, each fiber shows a concentric figure, the deep stained axon in the middle, surrounding empty ring, rest of myelin, and circular contour, cytoplasm of the Schwann cell and wrapping endoneurium. In a few cases nucleus of the Schwann cell are seen attaching to the contour of nerve fibers (arrows). The neurokeratin meshwork appears very variously (see 05-41).
• This is a higher magnification of a part of transverse section of a myelinated nerve. The axons, both thick and thin, are blackened by silver and the other tissue components are stained with Kernechtrot deep red. The thick axons are enclosed usually with thick myelin sheaths and here neurokeratin meshworks appear as a radiating pattern. A long arrow indicates a nucleus of the Schwann cell, attaching to a medium-sized myelinated nerve fiber. Interspace among the nerve fibers is filled with fine connective tissue, called endoneurium. At bottom of the figure is a layer of relatively coarse connective tissue, perineurium and a small blood vessel locates in the middle (short arrow).
• This is a part of a transverse section of a frog sciatic nerve, fixed with OsO₄. The myelin is blackened with OsO₄. There are numerous myelinated nerve fibers here, thick and thin, encircled with blackened myelin. The thick fibers have usually the thick myelin sheath.
05-43. Myelinated nerve 1. Human ischiadicus nerve, H-E stain, x 64.

- This is a part of human sciatic nerve. At upper center there is a primary nerve fiber bundle enclosed by perineurium (long arrow). Each nerve fiber wrapped by scanty connective tissue (endoneurium). They are tied up by this connective tissue and form a primary nerve fiber bundle. The primary nerve fiber bundle is enveloped with perineurium, whose cavity is filled with lymph. At lower middle there is a small nerve fiber bundle; that is also enveloped by perineurium. Outside of the primary bundle is filled with coarse connective tissue.
• This is higher magnification of 05-43. Numerous myelinated nerve fibers, transversely and obliquely sectioned, are enveloped by the perineurium at the left extremity of this figure (long arrow). Each nerve fiber is wrapped by scant connective tissue, endoneurium, but we can scarcely perceive it as the contour of the fiber. Between the fiber bundle and perineurium there is a narrow cavity, filled with lymph.
• Short arrows indicate the lymphatic cavity.
• This is a whole view of transverse section of human sciatic nerve. Numerous primary nerve fiber bundles enveloped by the perineurium are tied by the coarse connective tissue and form the secondary bundles; and as a whole they are all enclosed by coarse connective tissue, epineurium (arrows), and thus the macroscopic nerve is formed.

05-45. N. ischiadicus, transverse section, general view. Human, H-E stain, x 3.5.