Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 05, August, 2025
Website: usajournals.org

MORPHO-FUNCTIONAL CLASSIFICATION OF NEURONS: HISTOLOGICAL APPROACHES

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Abstract
Neurons are the fundamental functional units of both the central and peripheral nervous systems. They are classified based on their morphological structure and physiological functions. This article discusses the histological organization of neurons, their morphological and functional classification, and their role in neural activity. In addition, clinical relevance and recent advances in the study of neuronal differentiation and pathology are also reviewed.

Keywords: Neuron, unipolar, bipolar, multipolar, sensory, efferent, interneuron.

Introduction

The central and peripheral nervous systems represent the primary regulatory and coordinating centers of the human body. At the core of essential functions such as movement, sensation, reflexes, homeostasis, and cognition lies the activity of neurons. Neurons are highly specialized cells capable of generating, transmitting, and receiving electrical and chemical signals. The morphological structure,

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ISSN (E): 3067-803X
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function, and interconnections of each neuron determine its role within the organism.

Histologically, neurons are characterized by a distinct nucleus, cytoplasm, axon, and dendrites, and they vary in shape and size. This morphological diversity is directly linked to their functional specialization. Based on their structural characteristics, neurons are classified into unipolar, bipolar, pseudounipolar, and multipolar types. Additionally, depending on their functional roles, neurons are grouped as afferent (sensory), efferent (motor), and associative (interneurons) [1,2].

Diseases resulting from the disruption or degeneration of neuronal structures—such as Alzheimer's and Parkinson's diseases—are among the most pressing clinical challenges today [3]. Therefore, a comprehensive understanding of the histological and functional classification of neurons is essential not only for theoretical purposes but also for practical medicine.

Neurons. Neurons are the principal specialized cells of nervous tissue, playing a crucial role in transmitting information throughout the body via electrical and chemical signals. They are central to reflex responses, movement coordination, cognitive processes, and homeostatic regulation. Each neuron consists of the following major components:

Soma (Cell Body / Perikaryon). The soma serves as the metabolic center of the neuron. It is typically large, spherical or pyramidal in shape. The nucleus is centrally located, prominent, with open chromatin and a well-defined nucleolus—indicating high transcriptional activity [10].

Within the cytoplasm of the soma are Nissl bodies (also called tigroid substance), corresponding to granular endoplasmic reticulum, which reflect the cell's synthetic activity [1]. These structures are found in the soma and dendrites but are absent in the axon. The Golgi apparatus is involved in the modification of neurotransmitters and other proteins.

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Dendrites. Dendrites are short, branched projections that receive signals from other neurons or sensory cells. Their surfaces often contain synaptic spines—microscopic sites of synaptic contact. The dendritic arbor is especially well-developed in pyramidal neurons. Histologically, dendrites contain Nissl bodies, making them similar in appearance to the soma. However, their degree of branching, number, and presence of spines reflect the functional plasticity of the neuron [2].

Axon (Neurite). The axon is a single, often long and unbranched projection responsible for transmitting impulses to other cells. It originates from the axon hillock, which is structurally distinct from the soma due to the absence of Nissl substance—a key diagnostic marker. This is the site of action potential initiation. If the axon is myelinated (by oligodendrocytes in the CNS or Schwann cells in the PNS), conduction is facilitated through the nodes of Ranvier, significantly increasing impulse velocity [3].

Axon terminals (Telodendria). At the end of the axon, numerous fine branches known as telodendria form. Each telodendron ends in a synaptic bouton, which contains synaptic vesicles filled with neurotransmitters. These vesicles transmit impulses to the postsynaptic cell via efferent or associative connections [9].

Neurofibrillar structures. Within the cytoplasm of neurons are three major cytoskeletal components:
Microtubules (tubulin): Serve as tracks for axonal transport.
Neurofilaments (intermediate filaments): Help maintain the neuron's shape.
Actin filaments: Play a role in synaptic plasticity and the movement of spines.
These structures are visualized using electron microscopy and are known to undergo changes in degenerative diseases such as Alzheimer’s [4].
In aging neurons, the following inclusions may appear:
Lipofuscin: Age-related pigment accumulation.
Neuromelanin: Found in dopaminergic neurons.

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Inclusion bodies (e.g., Lewy bodies): Seen in Parkinson's disease. These features have diagnostic significance in clinical neurology.
Clinical note: Disruption in the structure or function of any neuronal component can impair signal transmission, leading to slowed conduction, desynchronization, and degeneration—hallmarks of neurodegenerative diseases such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), and Alzheimer's disease [5].

Morphological classification of neurons. Neurons are morphologically classified based on the number and arrangement of their processes (axons and dendrites). This classification directly influences how neurons receive and transmit nerve impulses. The main morphological types include the following:

Unipolar neurons. Unipolar neurons possess a single process that serves both axonal and dendritic functions. These neurons are more commonly found in lower organisms.
Histological features: A single process emerges from the soma; usually smooth and unbranched.
Clinical significance: Unipolar neurons are rare in the human body and are primarily observed during developmental stages [1].

Bipolar neurons. Bipolar neurons have two distinct processes: one axon and one dendrite. They typically serve sensory (afferent) functions and are found in specialized sensory systems.
Common locations: Retina (photoreceptors of the eye), olfactory epithelium (nasal cavity), spiral ganglion of the cochlea.
Histological features: Elongated, slender cell body with two processes arising from opposite poles [2].

Pseudounipolar neurons. Although these neurons appear to have a single process morphologically, it bifurcates into two branches—peripheral and central—thereby supporting bidirectional information flow.
Location: Spinal (dorsal root) ganglia and cranial nerve ganglia (V, VII, IX, X).

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Clinical relevance: They transmit sensory (afferent) impulses from the periphery to the central nervous system. Damage to these neurons may result in pain or sensory deficits [3].

Multipolar neurons. This is the most common type of neuron, characterized by one axon and multiple dendrites. They perform motor, associative, and integrative functions.
Location: Cerebral cortex (pyramidal cells), anterior horn of the spinal cord (motor neurons), Purkinje cells of the cerebellum.
Histological features: Large cell body, extensively branched dendritic tree, and often a myelinated axon [4].
Clinical note: Damage to multipolar neurons can result in motor dysfunction, loss of reflexes, or paralysis. Such impairments are observed in diseases like amyotrophic lateral sclerosis (ALS) and poliomyelitis [5].

Table 1. Morphological Classification of Neurons (Summary)

Neuron Type	Processes	Location	Function	Clinical Relevance
Unipolar	One process (axon = dendrite)	Mainly in invertebrates; rarely in human development	Primitive signal conduction	Rare in humans; seen during embryogenesis [1]
Bipolar	One axon, one dendrite	Retina, olfactory epithelium, cochlear (spiral) ganglion	Sensory transmission	Damage may cause sensory deficits (e.g., vision, smell, hearing) [2]
Pseudounipolar	One process bifurcating into two	Dorsal root ganglia, cranial nerve ganglia (V, VII, IX, X)	Afferent (sensory) transmission	Lesions may lead to impaired pain or tactile sensation [3]
Multipolar	One axon, multiple dendrites	Cerebral cortex, spinal cord (anterior horn), cerebellum	Motor, integrative, associative	Degeneration causes paralysis, reflex loss (e.g., ALS, polio) [4,5]

Functional classification of neurons. Neurons are classified not only by their structure but also based on the roles they perform within the body. This functional classification is primarily determined by the direction of information flow and the

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nature of the neuron's connections with other cells. Functionally, neurons are divided into three major groups:

Sensory (afferent) neurons. These neurons receive stimuli from the external or internal environment and transmit the signals to the central nervous system (CNS). They gather information through sensory receptors located in the skin, internal organs, and sensory organs such as the eyes, ears, and nose.
Common morphology: Often pseudounipolar or bipolar in structure [1].
Function: Conduct incoming (afferent) impulses toward the CNS.

Motor (efferent) neurons. Motor neurons transmit information from the CNS to effector organs such as muscles or glands, thereby generating a response (e.g., movement, secretion).
Location: Anterior horn of the spinal cord, pyramidal layer of the cerebral cortex.
Morphology: Typically multipolar [2].
Function: Conduct outgoing (efferent) impulses from the CNS to the periphery.

Associative (interneurons). Interneurons form the connecting network between sensory and motor neurons. They analyze, integrate, and process information, playing a critical role in reflexes and decision-making mechanisms.
Location: Primarily in the gray matter of the brain and spinal cord.
Characteristics: Highly diverse in both structure and function; morphologically complex [3].
Function: Facilitate communication within the CNS and modulate neural circuits.

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Table 2. Functional Classification of Neurons (Summary)

Neuron Type	Function	Direction of Signal	Typical Morphology	Main Locations	Clinical Relevance
Sensory (Afferent)	Transmit sensory input from receptors to CNS	Periphery → Central Nervous System (CNS)	Pseudounipolar / Bipolar	Skin, sensory organs (eyes, ears, nose), visceral receptors	Damage causes loss of sensation or neuropathy [1]
Motor (Efferent)	Transmit motor output from CNS to muscles or glands	Central Nervous System (CNS) → Periphery	Multipolar	Anterior horn of spinal cord, motor cortex	Damage results in motor deficits, weakness, or paralysis [2]
Interneurons (Associative)	Analyze, integrate, and relay signals between sensory and motor neurons	Within CNS	Highly variable / Multipolar	Gray matter of brain and spinal cord	Dysfunction can impair reflexes, coordination, or cognition [3]

Clinical importance of neuronal types in neurological disorders

Damage to sensory neurons leads to the loss of pain and tactile sensation, while injury to motor neurons results in paralysis. Interneuron dysfunction contributes to disturbances in complex reflexes and cognitive processes [4,5]. The morphological and functional diversity of neurons determines their selective vulnerability to different diseases. A reduction in neuron numbers, degeneration of their processes, disruption of synaptic connections, or imbalance in neurotransmitter levels can all contribute to the development of various neurological and neurodegenerative disorders.

Sensory (afferent) neurons transmit information from peripheral receptors to the brain and spinal cord. Their impairment can result in conditions such as:

Diabetic polyneuropathy: Degeneration of the distal axons of long sensory neurons leads to sensory loss, itching, and pain [1].

Herpes zoster (shingles): The virus targets pseudounipolar neurons in the spinal ganglia, causing sharp pain and vesicular skin eruptions [2].

Motor (efferent) neurons control voluntary movement. Their degeneration results in muscle weakness and paralysis:

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Amyotrophic lateral sclerosis (ALS): Progressive degeneration of motor neurons in the spinal cord and motor cortex leads to gradual loss of movement and respiratory failure [3].
Poliomyelitis: A viral infection that destroys motor neurons in the anterior horn of the spinal cord, resulting in asymmetric paralysis [4].
Interneurons are essential for processing, integrating, and coordinating information within the brain. Dysfunction in these neurons is associated with several neuropsychiatric and neurodegenerative conditions:
Alzheimer's disease: Accumulation of β-amyloid plaques and neurofibrillary tangles around pyramidal (multipolar) cells and interneurons results in progressive memory loss, impaired speech, and cognitive decline [5].
Schizophrenia and autism spectrum disorders: An imbalance of interneurons in the prefrontal cortex and limbic system has been identified, contributing to disruptions in social behavior and emotional processing [6].

Clinical Summary. The morphology, location, and function of different neuron types are key to understanding the pathogenesis of neurological disorders. Each type of neuron has specific vulnerabilities, and these structural-functional characteristics form the basis for modern approaches to diagnosis and treatment in neurology [7].

Modern research and neuronal differentiation. For many years, neurons were considered post-mitotic cells—incapable of division. However, recent studies, particularly in the fields of regenerative medicine and cell therapy, have significantly expanded our understanding of neuron derivation from stem cells, their differentiation pathways, and the potential for neurogenesis.
Neurogenesis, the process by which new neurons are formed, is most active during the embryonic period. Yet, modern investigations have confirmed the occurrence of neurogenesis in adults as well. This phenomenon has been primarily identified in the following regions:
Hippocampus (dentate gyrus)
Olfactory bulb

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Adult neurogenesis has been linked to cognitive performance, memory, and mood regulation. However, its activity can be suppressed by factors such as stress, inflammation, or exposure to toxins [1].

Stem cells and neuronal differentiation. Induced pluripotent stem cells (iPSCs) can be differentiated into neuronal lineages under laboratory conditions. This technique holds significant promise for replacing damaged neurons in diseases such as Parkinson's and Alzheimer's [2].
Differences between iPSCs and mature neurons—such as genetic profiles and expression of molecular markers like Nestin and βIII-tubulin—can be identified through advanced histochemical and molecular biology techniques [8].

Neuronal plasticity. Although neurons do not proliferate, they possess the remarkable ability to reorganize their synaptic connections, dendritic structures, and functional activity—a property known as neuroplasticity. This capacity underlies learning, memory formation, and functional recovery after injury. For example, in post-stroke rehabilitation, surviving neurons may form new synapses to compensate for lost function [3].

Optogenetics and neural circuit manipulation. Optogenetics is a cutting-edge technique that enables the activation or inhibition of genetically modified neurons using light. This method allows researchers to investigate the specific roles of individual neurons and their networks in real time. It is revolutionizing experimental approaches in psychiatry and epileptology [4].

Gene therapy against neuronal degeneration. Gene therapy aims to deliver genes encoding deficient or therapeutic proteins directly into neurons. For instance:
SMN1 gene therapy is used in spinal muscular atrophy
GDNF gene therapy shows promise in protecting neurons in Parkinson's disease [5]

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Contemporary neuroscience reveals that neurons are far more than passive signal transmitters—they are dynamic, adaptable, and highly specialized information-processing units. Research into their differentiation and regeneration is opening new frontiers in neurological rehabilitation, transplantation, and gene therapy.

Conclusion

Neurons are the fundamental and most critical functional units of the nervous system, responsible for receiving, transmitting, and processing information. Their morphological classification into unipolar, bipolar, pseudounipolar, and multipolar types, as well as their functional division into sensory, motor, and interneurons, provides a deeper understanding of their specific roles in the body. Each neuronal type has a unique structure and localization that enables it to fulfill specialized tasks.

Moreover, their selective vulnerability to certain diseases, susceptibility to degeneration, and associated clinical consequences are of great importance in modern neurology. Neuronal histology plays a central role not only in structural analysis but also in understanding their physiological behavior and clinical manifestations.

Recent scientific advances—such as **neurogenesis, stem cell therapy, optogenetics**, and **gene therapy**—have opened new possibilities for the regeneration and detailed study of neurons. These developments not only reinforce fundamental histological knowledge but also pave the way for novel approaches in medical treatment and rehabilitation.

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ISSN (E): 3067-803X
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Website: usajournals.org

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