Nervous System Basics:

Neuron parts and classifications

Excerpts and study notes from **Organization of the Nervous System** by Jay B. Angevine Jr. U. of Arizona
p. 313 Volume3 **Encyclopedia of the Human Brain**
Images from Google images

INTRODUCTION

"The human nervous system is a hierarchy, culminating in the brain, of 100 billion or more neurons of 10,000 types, 1-10 trillion neuroglial cells, 100 trillion chemical synapses, 160,000 kn of neuronal processes, thousands of neuronal clusters and fibers tracts, hundreds of functional regions, dozens of functional subsystems, 7 central regions, and 3 main divisions. All of these parts form a coherent, bodily pervasive, diversified, complex *epithelium* with interdependent connectivity of neurons, mostly neither sensory nor motor but anatomically and functionally intermediate. The key organizing principles of the system are *centralization* and *integration*. The nervous system performs two roles: *regulation* and *initiation*. In the first, it *counteracts*: responsively and homeostatically, gathering stimuli from outside and inside the body (including the brain), assessing their short-term and long-range significance, generating activity from faster breathing to stock trading, even to functional plasticity in learning or after brain damage. In the other, it *acts*: endogenously, not so homeostatically, replacing one state of neural activity with another, generating activity from doing nothing at all to creative thinking and extraordinary achievement, even talking steps toward understanding how itself, the nervous system, works. Although the divisions and regions of the nervous system are identical in all normally developed humans, their genetic specification and personal history are unique, as are the permutations and combinations of their unified function. Each human nervous system is unprecedented. The work of each (expressed or hidden) is unpredictable, ever-different, surprising, startling, at times horrifying, but not infrequently magnificent." *- Jay B. Angevine*

Complexity and Individuality of Neurons (p. 343)

"Neurons typically emit many highly branched, intermingling processes. This complexity, along with their sheer size, is a problem in studying them and a reason why the neuron doctrine was controversial. Many studies, experiments and years of bitter debate took place before the idea that nerve cells were separate was generally accepted. Even then, some doubted it. Only with the demonstration by electron microscopists in the mid- 1950s of the minute cleft between neurons at the synapse was the physical individuality of neurons established."

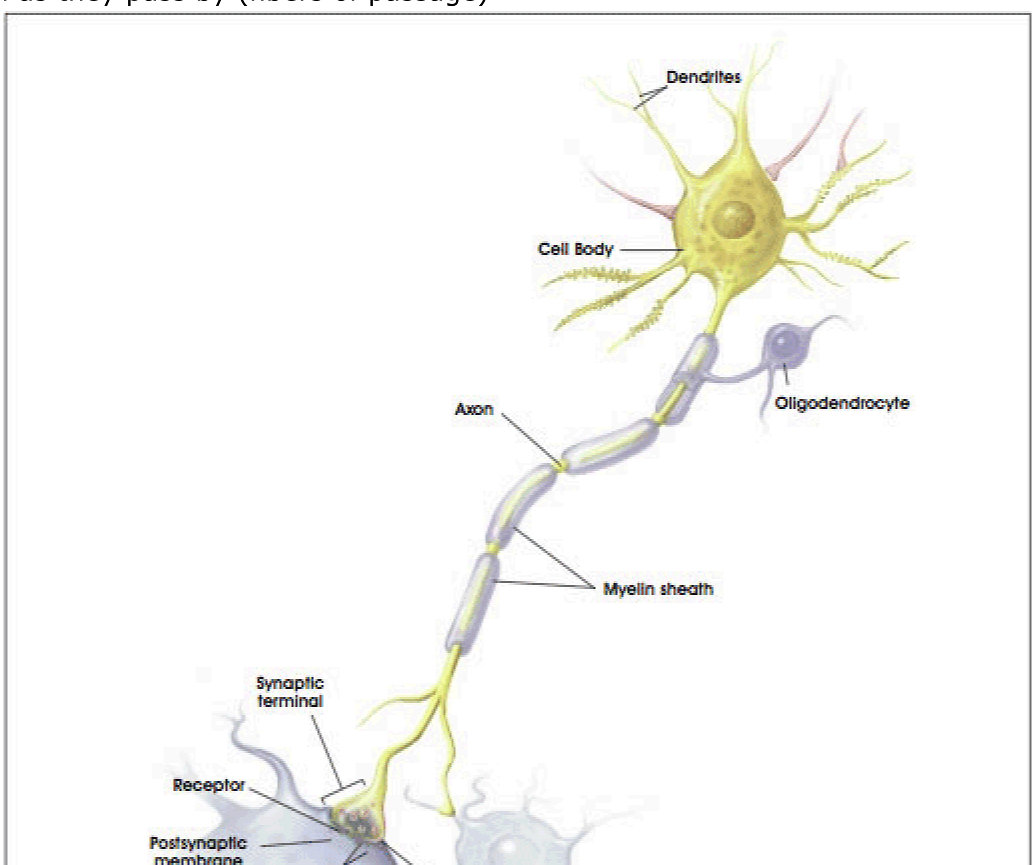
Parts and functional dependencies of neurons

1. The cell body

- during development the soma is the first part of the cell to arise
- throughout the life of the cell it is the irreplaceable trophic part that maintains the structural integrity and health of the neuron with its far-reaching processes

2. Dendrites

- these are relatively short processes that taper slightly, extend from the soma and branch obliquely like the limbs of a tree
- they contain the organelles seen in the soma in varying proportions
- in a few neurons they arise at the end of an axon: a dorsal root ganglion cell has dendritic tufts or a specialized nerve ending (free or encapsulated axonal tip) in such an axon in the dermis, wall of a viscus, or other peripheral area
- dendrites are the main receptive processes of a neuron although other parts may also receive inputs
- their branching pattern signifies the relationship of their neuron to others, and its integration
- they offer points of contact (synapses) for axon terminals and for axons grazing them as they pass by (fibers of passage)
- they are the



prime integrative components of neurons; they...

- receive
- combine
- summate

......and otherwise regulate neuronal input

- dendrites originate from the soma as one or more primary branches
- these continue to ramify into finer and finer twigs
- total dendritic surface area and volume may exceed those of soma by many times
- incoming axons end on the dendritic shaft or on *spines*, minute thorns which give dendrites a studded appearance
- role of spines not well understood:

- they do not serve as way to increase the surface area further and usually there are few synaptic areas on them
- spine synapses are the major sites of excitation - each spine usually has one input but may have several
- they have electrical properties that may be modified by slight changes in the form of the spine neck
- spine necks show changes in learning and in aging
- they seem to be specialized ports of entry for currents into the dendritic shaft
- they may be bounded by astrocytic processes

- astrocytes play vital roles in communication, serve as "sponges":

- they take up excess potassium ions that might interfere with local neuronal activity
- localize glutamate release for optimal elicitation of excitation in target cells
- prevent glutamate-induced toxicity that would be life-threatening to neurons

3. Axons and axonal collaterals

- out of the soma of most neurons emerges a relatively long, single cable-like process called the axon or axis cylinder
- it arises from a small conical elevation (axon hillock) or from the stem of a major dendrite
- it may be straight (a clearly directed flight to a distant location) or it may meander (as if lost in the neuronal shrubbery near its origin)
- these provide the long-distance trunk lines and myriad local circuits over which neuronal signaling and communication take place
- the conductile axon conveys impulses to other neurons, a muscle, or a gland
- in primary sensory axons in axonal endings innervating the skin, impulses arise in axonal endings: naked, with minute expanded tips, or encapsulated as shown
- the action potentials travel to the CNS via a cranial or sensory nerve

- the axons vary in length from 2-3 μm to 1 meter, and in width from 0.1 to 20 μm and do not taper
- the axon may have axon collaterals which stick out at right angles rather than branch at acute angles
- collaterals distribute neuronal output to several or many places depending on circuit design and how many collaterals there are
- axonal collateralization expresses neuronal relationship as much as does dendritic

branching
- dendrites signify integrative power of a neuron, whereas axons and their collaterals signify its distributive power, and the routes and addresses of impulse dissemination

- there can be two axons (bipolar) or none (amacrine); the latter intercommunicate through their dendrites
- the axon is thinner and a lot longer than any dendrite, but most CNS neurons have a greater total length of dendrites than axons

- axon no matter what its shape is the functional axis of the neuron, the hub along which nerve impulses travel, the all-or-none action potentials or spikes
- these encode output in spike trains or bursts superimposed on a discharge frequency characteristic of the neuron under given conditions
- in motor neurons and other large nerve cells, these spike potentials originate in the axon hillock and axon initial segment, the "spike trigger zone"

4. Axon terminals
- Axon terminals are the effector parts of neurons, whereas dendrites are the receptive, the cell body is the trophic, and axons are the conductile parts
- axon terminations are described by their shapes: button-like, claw-shaped, bulbous etc.
- similar beaded structures may lie along the course of an axon
- all are sites where frequency-coded messages are transmitted chemically to some part of a target neuron or muscle fiber across a synapse or neuromuscular junction and where trophic effects may be bidirectional

5. Flexibility of the parts of neurons
- the parts of neurons are adaptable, and there are lots of exceptions to the definitions as outlined above
- awareness of the exceptions enhances understanding of neural function and neurologic disease
- certain regions of the axon may serve receptive function - there can be axoaxonic input at the axon hillock or on its presynaptic end bulbs
- dendrites may conduct impulses swiftly in an all-or-none manner like axons (as in the towering hippocampal pyramidal cells)
- they can act as effectors (like axon terminals) and transmit activity fractionately, as in dendrodenritic synapses
- this means, the parts of a neuron can be thought of as a functional mosaic

- neuronal design is strikingly flexible
- almost any part can perform any communication function if circumstances or circuit design makes it advantageous
- the only inflexibility is the cell body which is always trophic

- only serial progressions of neurons through axodendritic and axosomatic synapses and similar sequences through axonal collateral channels used to be considered
- some other arrangements which illustrate cell-cell interplay, gap junction unpredictability, and neuronal versatility are:

- parallel coupling - axoaxonic and somatosomatic synapses
- reciprocal coupling - dendrodendritic synapses

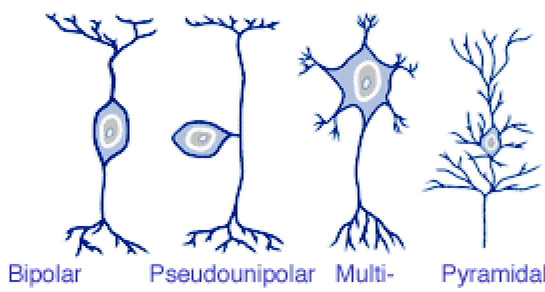
- parallel-serial coupling - axodendritic synapses
- atypical coupling - somatoaxonic synapses

6. Polarity of Neurons

- Three kinds: uni-, bi- and multipolar:

1. **unipolar** neurons:
    - are found mostly in invertebrates
    - in vertebrates can be noted at developmental stages only
    - in invertebrates they represent the dominant population and comprise the largest number of nerve cells on earth

2. **bipolar** neurons:
    - are simple modifications, have fusiform cell bodies of the columnar epithelial cells from which they evolved
    - in humans they form the primary sensory neurons in the olfactory epithelium, retina and vestibulocochlear ganglia
    - terminal ramifications in the periphery (e.g. organ of Corti) respond fractionately to stimuli and may be considered distant dendrites
    - the long process leading to the soma is by all criteria axonal, even has a myelin sheath for faster transmission
    - with the interposition of an axonal cable between the receptive organ and the cell body, spikes triggered peripherally pass swiftly to the soma and flow to the other process and onto the CNS, wherein their central ramifications distribute impulses to secondary sensory neurons

    - **pseudounipolar** neurons:
        - these are modified bipolar neurons
        - during development opposing processes shift round the soma and become united proximally
        - this united process extends out a bit from the soma then branches into a T-shape
        - one branch goes to the periphery and the other to the CNS as in bipolar neurons
        - nerve impulses in these neurons pass quickly from one branch to the other and send a backfire up the single process and into the soma

3. **multipolar** neurons
    - have many variably branched processes into all directions
    - most common type is the vertebrate neuron comprising virtually all neurons of the human CNS
    - their diversified input (10^4 to $3x10^5$ apiece) gives them tremendous integrative capacity

- their variety is extraordinary, but their vast number (100 billion or maybe as high as a trillion) are of two main kinds:
  - about 2 million motor neurons sending axons to muscles and glands
  - the rest mostly interneurons
- the dendrites on these vary from few to profuse, from straight to smooth to curving and spiny, from "meagre shrubbery to magnificent arboreal extravaganzas"
- the axon is either short or long, unbranched or rectilinearly collateralized, ruler-straight and departing the locale or else sinuous and wandering through local neuropil
- the soma can be ovoid, spherical, pyriform, fusiform, fat skinny big small, minuscule (4μm, half the size of a red blood cell) or huge (150 μm in giants - Betz cells can be seen with the naked eye)

- pseudounipolar and bipolar neurons make up all the sensory neurons in the PNS
- both have limited integrative domains in distant dendritic tufts and no input on their somata
- somata are limited to trophic duties, housekeeping
- their central terminals however receive presynaptic endings which provide efferent modulation of their transmission to secondary sensory neurons
- **this arrangement is important in suppressing the receipt of nociceptive stimuli**
- it is an enkephalinergic component of a complex brain stem analgesia system

7. Specialization of neurons

- the variety of cell types in the human nervous system is far more complex than in other tissues
- cells elsewhere (e.g. erythrocytes, hepatocytes) are highly redundant, but neurons are highly individualized
- invertebrate nervous systems (e.g., certain arthropods) have indispensable, decision-making command neurons, but vertebrates simply keep a whole lot of neurons to iron out individual peculiarities
- human nervous system has many neuronal subpopulations
- a neuron shows its individuality by form, function (speed of response, endurance, fatigability), position in a circuit, chemical coding of impulses and sheer size
- neuronal specialization gives our nervous system speed, flexibility, fidelity and staggering integrative power.

8. Schemes of classifying neurons

- many classifications exist each with advantages and limitations
- neurons are grouped as to:

- size
- shape
- polarity
- dendritic pattern
- axonal length
- long-distance or local circuit

- presence and nature of neurosecretory service
- identifiability as a circuit component from one nervous system to another

- perhaps the most useful scheme is its position in the fundamental circuit plan, a functional classification into sensory, motor or intermediate neuron:

a) Sensory neurons:

- *primary sensory neurons* (first-order) are the initial neurons in sensory data processing
- derived from neural crest cells near the embryonic neural tube their cell bodies remain outside the CNS
    - rod cells of the olfactory membrane
    - bipolar ganglion cells of the vestibulocochlear nerve (cranial nerve VIII)
    - pseudounipolar cells of spinal nerves
    - cranial nerves V, VII, IX, and X
- they are sentinels posted outside the CNS, reporting news (good and bad) from the periphery
- there are only about 20 million of them

- *secondary sensory neurons* (second-order) are the next echelon in sensory data processing
- these cells are in the CNS - the first-order cells terminate on them
- clusters of them lie in the dorsal horn of the spinal gray and brain stem nuclei (e.g. cochlear nuclei)
- whereas their afferent domain is weighted by sensory input they are **interneurons**, between the first and last neurons in the plan of the nervous system
- they receive input from sources beside primary sensory neurons, even from the cerebral cortex
- they are multipolar, not bipolar or pseudounipolar, thus meet the criteria for being interneurons

b) Motor neurons:

- these are multipolar in design
- soma are located entirely within CNS
- sensory neurons are the first cells in neural processing and motor neurons are the last
- they send impulses to effector organs; muscles and glands
- there are only about 2 million, like sensory neurons, but their role is profound
- they derive from the mantle layer of the neural tube
- they include the large ɑ and small γ motor neurons in the spinal cord and brainstem that innervate extrafusal and intrafusal skeletal muscle fibers, those that work and those that report stretch, respectively
- they include the visceral motor fibers of the ANS, the dual arrangement of a preganglionic motor neuron in the CNS and a postganglionic one in an autonomic ganglion

c) Interneurons

- were once called internuncial or "go-between" neurons
- their somata is in the CNS - neuroanatomy is mostly to do with the study of this class of neuron and its connections; they comprise almost all of our neurons
- their number is extremely large: 10^{11} is the figure currently cited
- some of the neurons are so minute and in such large populations in the hippocampus and cerebellum the real number may be closer to 10^{12} (a trillion)

- "These countless separate, yet richly interconnected cells are more than responsive to stimuli, though they serve homeostasis with computer speed and reliability and in ways nineteenth century opponents of the neuron doctrine could hardly have comprehended. Interneurons are the source of endogenous neural activity, the cells that initiate new programs of behavior and if need be, abandon old ones."
- 'interneurons' is a useful term for invertebrates but loses a lot of meaning because of their staggering numbers, especially in human vertebrates where they comprise 99.9997% of the total number
- it is now used for neurons confined to particular regions of vertebrate nervous systems

- a newer classification recognizes two major kinds: **projection** and **local circuit**
- projection neurons are interneurons in the original sense and also include sensory and motor neurons
- local circuit neurons have axons restricted in their sphere of influence to other neurons nearby
- size and shape, length of axon or type of contact have no bearing on their classification - only service in long-distance or local communication

d) Projection neurons (example)
- most large neurons are of this class
- they fit the classic mold of a neuron:
  - multipolar
  - ample cell body
  - many dendrites
  - long axon
  - the amino acid, glutamate, as the primary transmitter (usually eliciting excitation of target cell)
- familiar examples are the pyramidal cells in the cerebral cortex and Purkinje cells in the cerebellum
- also, motor neurons in the brain stem and spinal cord
- they perform long-range signaling in the CNS (the corticospinal tract) or from CNS to muscles (e.g., the sciatic nerve)
- other cells arise from these cells:
  - central projection fibers (region to region)
  - association fibers (area to area within a region)
  - commissural fibers (association fibers that cross midline)
- projection fibers originate earlier than local circuit fibers during neural development

e) Local circuit neurons
- usually have a short axon or none (e.g., amacrine cells)
- are involved in local activity within a group of cells, not transactions with distant groups
- far more numerous than cells
- arise later and for a longer time in neural development
- the dentate gyrus in the hippocampal formation and cerebellar cortex have huge numbers of these
- also are numerous in the cerebral cortex but are only 20-25% of the grand total in this region noted for its long-distance direct output
- some of these large subpopulations take a long time to grow; millions of LCNs

arise after birth and even in adulthood in some mammals including humans

- with the growing appreciation that regions of the CNS are specialized for different functions, LCN roles in circuits peculiar to these regions are now high-priority issues
- general structure and connections of these have been known for years, but their functions were elusive because they were hard to study
- some LCNs elicit inhibitory effects with GABA (γ- aminobutyric acid) whereas others elicit excitatory effects with glutamate
- many LCNs are recognized in the cerebral cortex, and certain ones in the cerebellum are well known; e.g. the GABAergic basket cell in the cerebellar cortex exerts *surround inhibition* on rows of Purkinje cells, providing *enhanced contrast* between them and the excited Purkinje cells in nearby rows

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