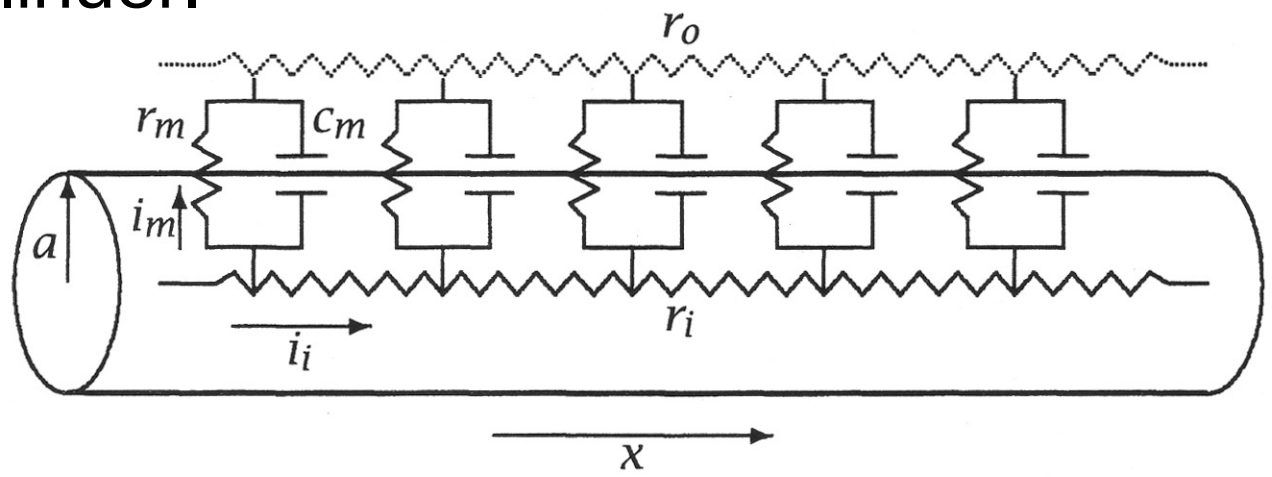
EE 791 Lecture 2

Jan 19, 2015

Action Potential Conduction And Neural Organization

Core-conductor model:

In the *core-conductor model* we approximate an axon or a segment of a dendrite as a uniform cylinder.



(from Johnston and Wu)

Figure 4.6 Diagram for current flow in a uniform cylinder such as an axon or segment of dendrite.

Each small (cylindrical) segment of membrane is electrically linked (axially) to the next segment by the intra- and extra-cellular electrolytes.

Core-conductor model (cont.):

If a single fiber described by the core-conductor model lies in a restricted extracellular space, then longitudinal current flow can occur in the extracellular electrolyte and longitudinal variations in the extracellular potential can result.

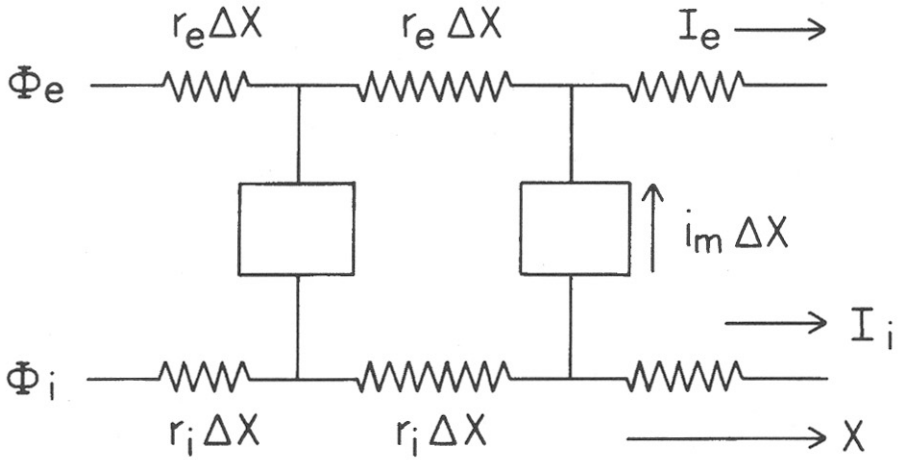


Figure 6.1. The linear core-conductor model for a single fiber lying in a restricted extracellular space. Longitudinal extracellular and intracellular currents are I_e and I_i, while extracellular and intracellular potentials per unit length are designated Φ_e and Φ_i, respectively.

Local circuit currents:

Propagation of action potentials can be understood qualitatively by considering the patterns of local currents that are produced by an action potential (site A in the figure below).

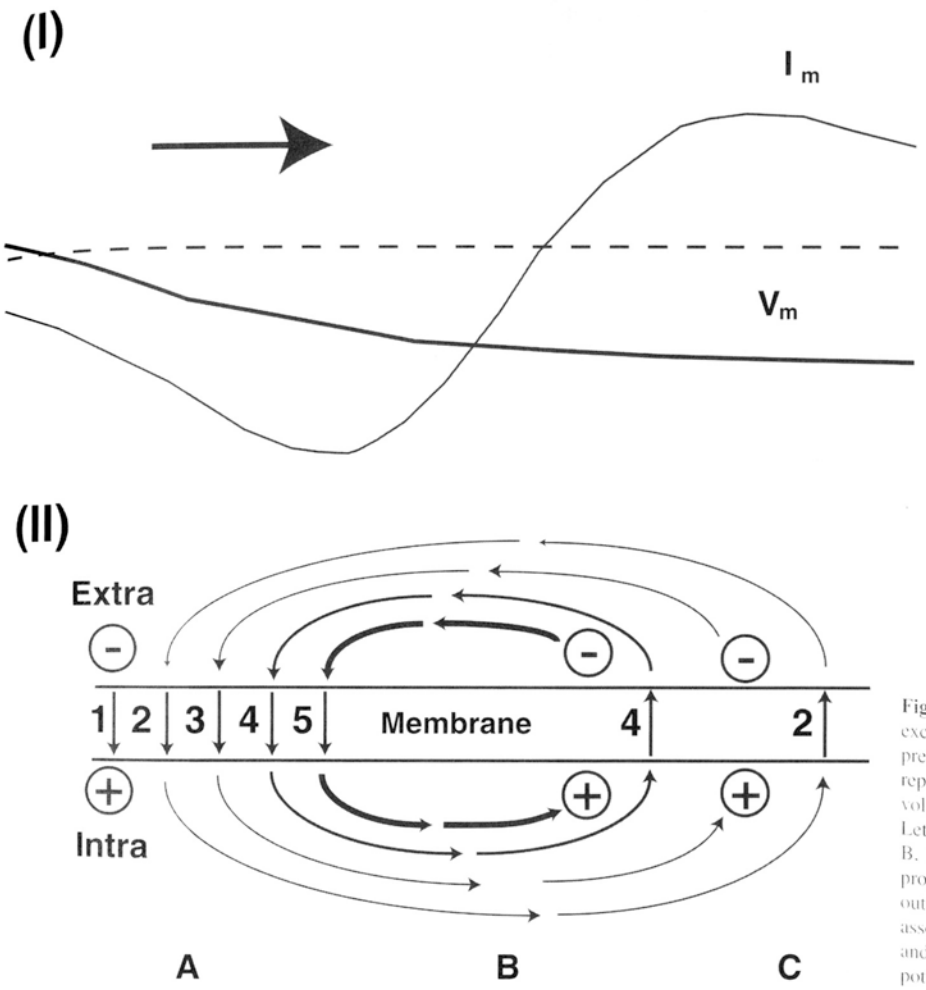
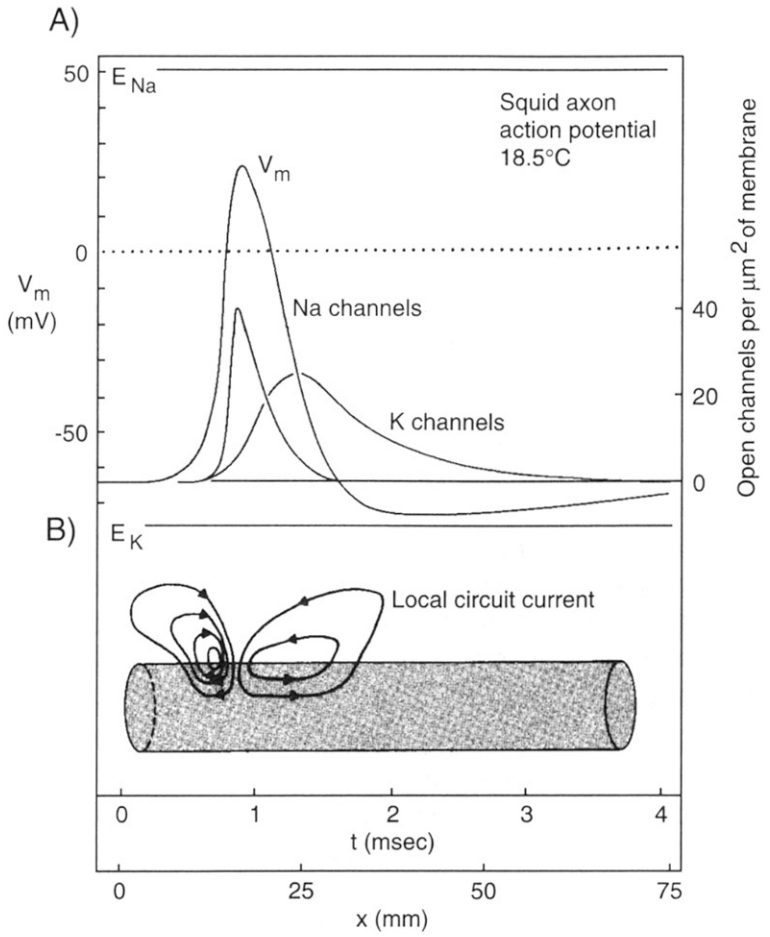


Figure 6.8. Local Circuit Pattern. Panel I (top): The arrow indicates the direction of excitation. Sketches from Figure 6.7 of a segment of the V_m and I_m curves also are present. Panel II (bottom) is a sketch of possible current pathways. The two horizontal lines represent the fiber's membrane, with the extracellular volume above and the intracellular volume below. Five possible current flow pathways are depicted (and discussed in the text). Letters A, B, and C along the axis at bottom identify three major regions as A, sodium influx; B, transition; C, potassium outflux. Along the fiber at the moment depicted, currents of propagation are inward at A, due to the inward movement of sodium ions. At B there is an outward movement of potassium ions. At C there is in effect an outward capacitative current associated with axial current down the longitudinal pathways. Horizontal locations A, B, and C drawn in panel II show currents that correspond approximately to the transmembrane potentials and currents at the same horizontal position.

Local circuit currents (cont.):



(from Koch)

Fig. 6.13 Local Circuit Current in the Squid Axon Illustration of the events occurring in the squid axon during the propagation of an action potential. Since the spike behaves like a wave traveling at constant velocity, these two panels can be thought of either as showing the voltages and currents in time at one location or as providing a snapshot of the state of the axon at one particular instant (see the space/time axes at the bottom). **(A)** Distribution of the voltage (left scale) or the number of open channels (right scale) as inferred from the Hodgkin–Huxley model at 18.5° C. **(B)** *Local circuit currents* that spread from an excited patch of the axon to neighboring regions bringing them above threshold, thereby propagating the action potential. The diameter of the axon (0.476 mm) is not drawn to scale. Reprinted by permission from Hille (1992).

Propagation in myelinated nerve fibers:

In vertebrates, Schwann cells produce myelin which wraps around an axon to produce an insulating sheath. The regularly-space breaks in the myelin are called *nodes of Ranvier*, and the axon segments between nodes are referred to as *internodes*.

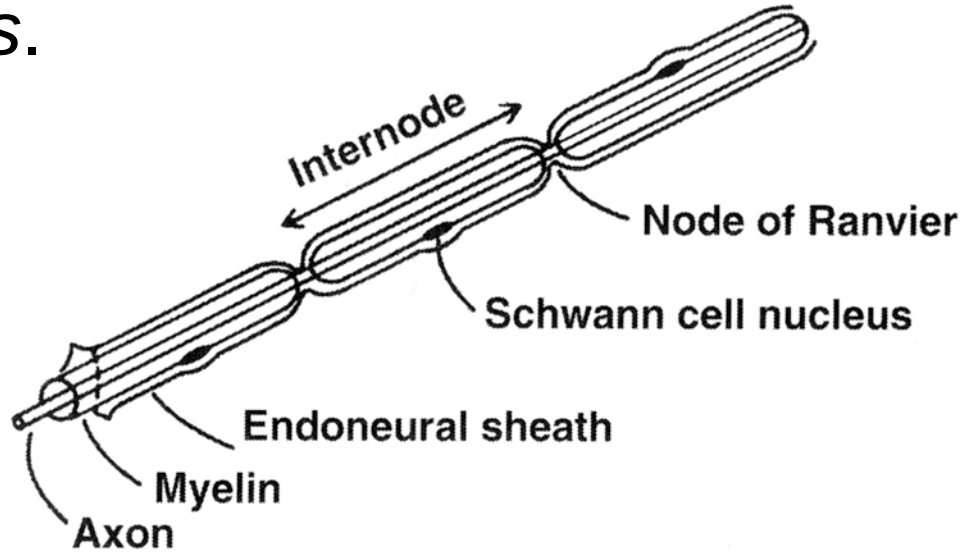


Figure 6.11. Diagram Showing the Structure of a Myelinated Nerve Fiber. Reprinted with permission from Aidley DJ. 1978. *The physiology of excitable cells*. Cambridge: Cambridge UP.

Propagation in myelinated nerve fibers (cont.):

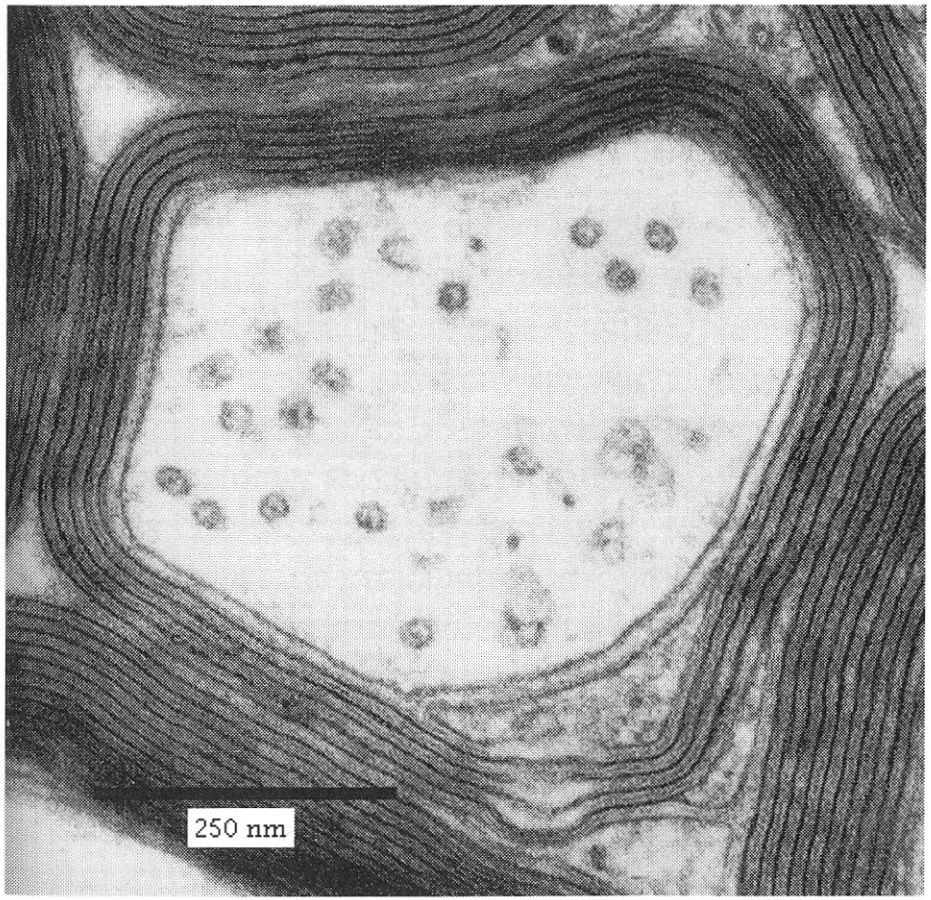


Fig. 6.14 MYELINATED AXONS Electron micrograph of a cross section through a portion of the optic fiber in an adult rat. The complete transverse section through a single myelinated axon is shown in close neighborhood to other axons. About four wrappings of myelin insulation are visible. The circular structures inside the axonal cytoplasm are transverse sections through microtubules. Reprinted by permission from Peters, Palay, and Webster (1976).

(from Koch)

Propagation in myelinated nerve fibers (cont.):

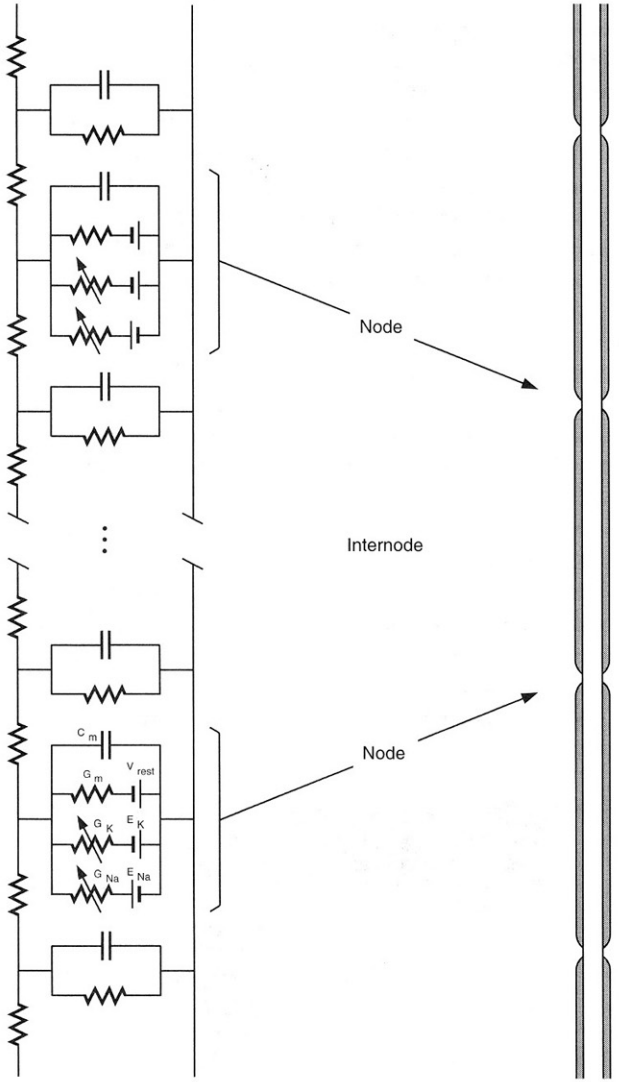


Fig. 6.15 Electrical Circuit for a Myelinated Axon Geometrical and electrical layout of the myelinated axon from the frog sciatic nerve (Frankenhaeuser and Huxley, 1964; Rogart and Ritchie, 1977). The diameter of the axon and its myelin sheath is 15 μm, the diameter of the axon itself 10.5 μm, the difference being made up by 250 wrappings of myelin. The myelin is interrupted every 1.38 mm by a *node of Ranvier* that is 2.5 μm wide. The total distributed capacitance for the internode (2.2 pF) is only slightly larger than the capacitance of the much smaller node (1.6 pF). The same is also true of the distributed resistance. At each node, the spike is reamplified by a fast sodium current and is repolarized by a potassium current. Little or no potassium current is found at the nodes of Ranvier in mammalian myelinated axons. There, repolarization is accomplished by rapid sodium inactivation in conjunction with a large effective "leak" current.

(from Koch)

Propagation in myelinated nerve fibers (cont.):

The specific leakage resistances and specific capacitances of the myelin sheath and cell membrane shown below are consistent with the myelin sheath being equivalent to around 100 layers of cell membrane.

Table 6.2. Electrical Properties of Myelin Sheath and Cell

	Specific leakage resistance (Ω cm^2)	Specific capacitance (F/cm^2)
Myelin sheath	10^5	10^{-8}
Cell membrane	10^3	10^{-6}

Propagation in myelinated nerve fibers Note:-

- Nodes of Ranvier are around 1 μm in length.
- Internodal distances are on the order of 1 to 2 mm. (A rough empirical rule is that the internodal length equals 100d, where d is the fiber diameter.)

Although internodes are much longer than nodes, the much smaller specific capacitance of the former means that an internode and a node have approximately the same capacitance.

Propagation in myelinated nerve fibers (cont.):

The purpose of the myelin is clearly to:

1. reduce the capacitance of long stretches of membrane, the *internodes*, such that they are more easily charged up as an AP propagates through, and
2. increase the membrane leakage resistance so that there is less leakage across the membrane of the intracellular longitudinal current.

Consequently, the “local circuit currents” extend over much longer lengths of the fiber.

Propagation in myelinated nerve fibers (cont.):

Because the local circuit currents extend from one node to the next node (or several nodes ahead in some cases):

1. action potentials propagate faster, and
2. a “failsafe” mechanism may be provided – if one node is blocked, the action potential may be regenerated at the next node along the axon.

Propagation in myelinated nerve fibers (cont.):

Propagation along a myelinated axon has historically been referred to as *saltatory propagation*, as if APs effectively jump or skip from node to node.

This is based on the observations that:

1. the extracellular potential outside an internode does not change much as the AP propagates by, and
2. the voltage-gated sodium channels are concentrated at the nodes of Ranvier.

Velocity of Propagation

- .25 m/sec in small unmyelinated fibres to >100 m/sec in large myelinated fibres
- Varies as diameter of fibre in myelinated
- Varies as square root of diameter of fibre in unmyelinated

Central Nervous System

- More than 100 billion neurons
- From hundreds to 100K inputs to neuron dendrites and cell body.
- Separated into (i) sensory system – signals received from sensory receptors, causing immediate response or stored in memory and (ii) motor system – contraction of skeletal muscle, smooth muscle in internal organs, or secretion by exocrine and endocrine glands.

Somatic Sensory Axis

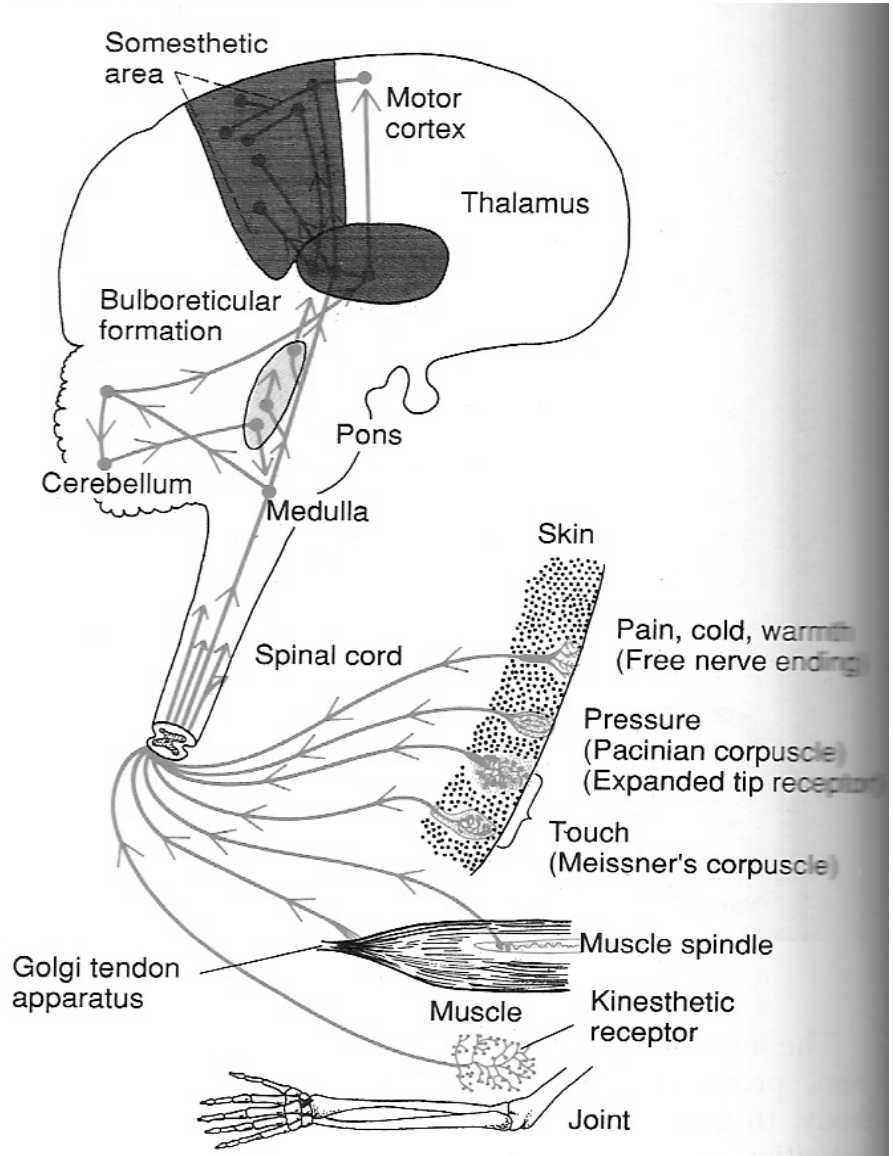


Figure 45–2. Somatic sensory axis of the nervous system.

Motor Axis

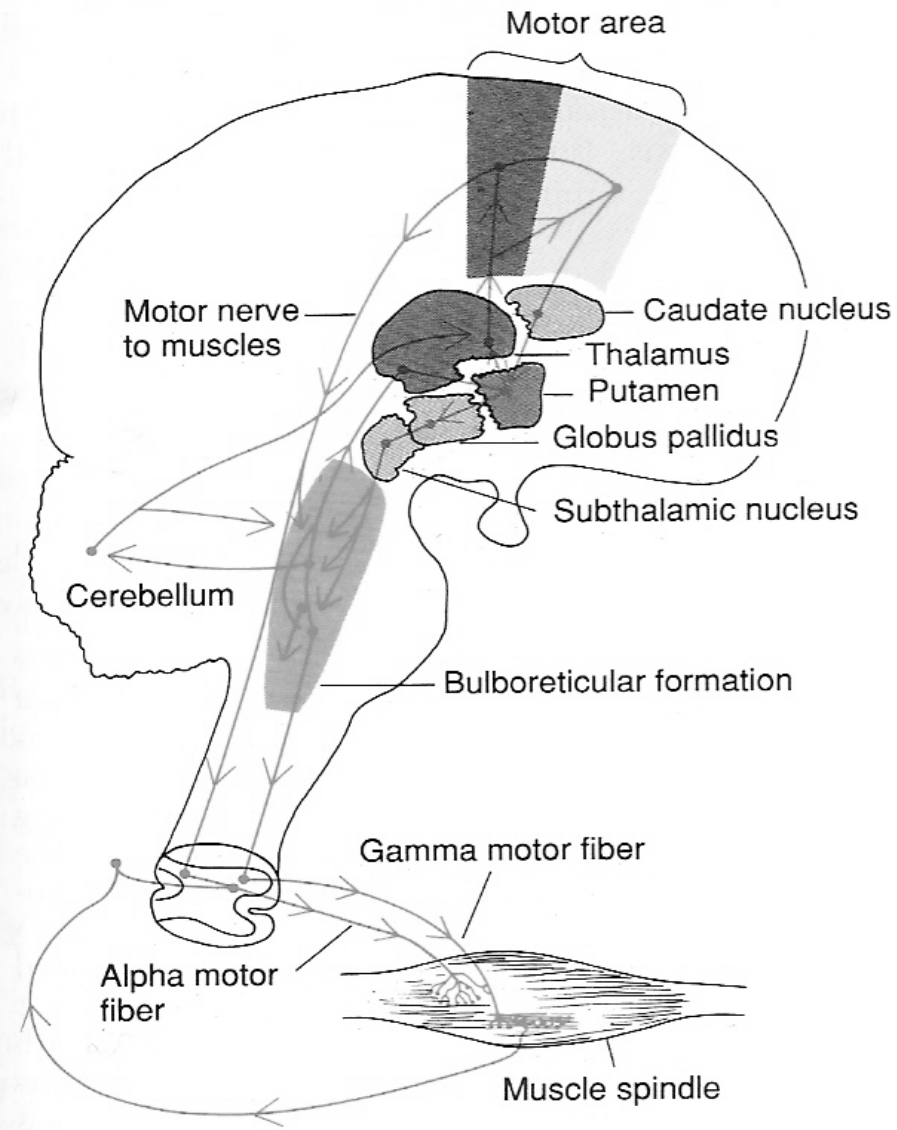


Figure 45–3. Motor axis of the nervous system.

Integrative Function of Nervous System

- Nervous system processes incoming information
- Produces appropriate motor response
- More than 99% of incoming information ignored, e.g. visual, tactile, auditory
- Integration and control effected through synapses – neuron-neuron connections
- Memory initiated through synapses

Major Levels of CNS

- Spinal cord – conduction of signals to and from brain and control centres for reflex and movement (e.g. walking)
- Lower brain level for subconscious activities – medulla, pons, mescephalon, hypothalamus, thalamus, cerebullum and basal ganglia
- Cortical level – memory, thought processes, planned movements, interacts with lower levels

Synapses

- Connections between cells with excitable membranes
- Chemical – cover almost all connections in CNS - Action potential causes release of neurotransmitter in axon endings, transmitted across the synaptic cleft to receptor proteins in next cell, excites or inhibits or modulates this cell.
- Electrical – direct electrical connections between two cells (gap junctions – smooth muscle and cardiac muscle)

Synapses (cont'd)

- Ensures one way communication
- Many different neurotransmitters, especially in central nervous system
- Excitatory – open Na^+ channels or inhibit CL^- or K^+ channels and depolarize cell
- Inhibitory – open CL^- channels and K^+ to hyperpolarize cell.
- Rapidly acting small molecules for signal transmission
- Slowly acting large neuropeptide modules for long term cell function modulation

Structure of the neuromuscular junction (cont.):

The nerve terminal contacts the muscle fiber at an *end plate*.

The pre- and post-synaptic membranes form a specialized "gutter".

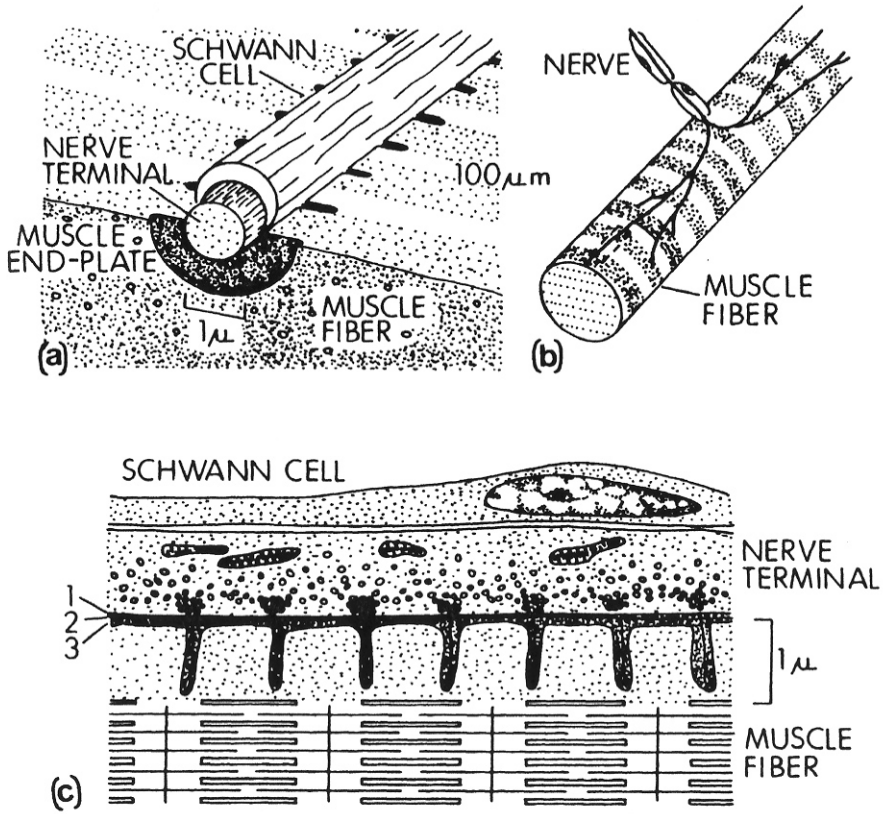


Figure 10.2. Neuromuscular junction of frog. (a) One portion of the junction. (b) General position of endings of motor axon on muscle fiber, showing portion (a) as a small rectangle. (c) Schematic drawing from electron micrographs of a longitudinal section through the muscle fiber. 1, terminal axon membrane; 2, "basement membrane" partitioning the gap between nerve and muscle fiber; 3, folded post-synaptic membrane of muscle fiber. (From B. Katz, *Nerve, Muscle, and Synapse*, McGraw-Hill, New York, 1966. Copyright 1966, McGraw-Hill with permission of the McGraw-Hill companies.)

Structure of the neuromuscular junction (cont.):

The pre- and post-synaptic membrane formations are similar to nerve-to-nerve chemical synapses, except for the synaptic gutter.

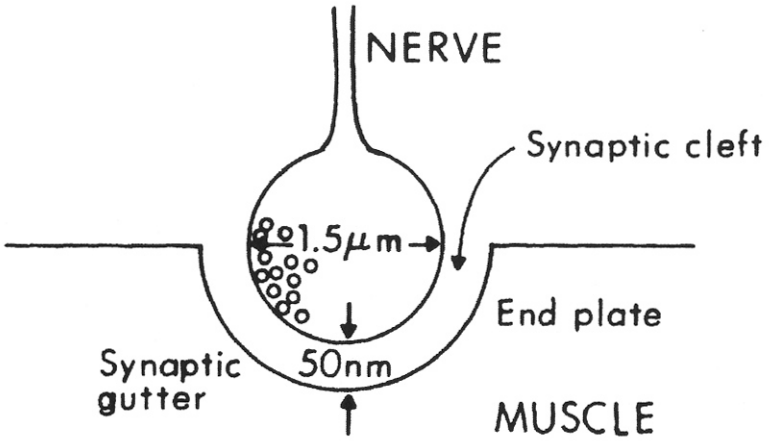


Figure 10.3. Details of the neuromuscular junction at a single nerve terminal.

Structure of the neuromuscular junction (cont.):

Muscle fiber end-plate potentials (EPPs) are similar to EPSPs in neurons—note that they are always excitatory.

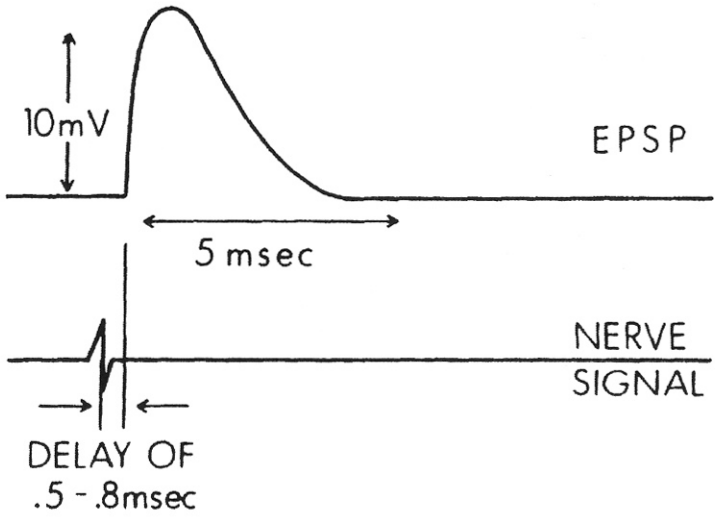


Figure 10.4. The end-plate potential arising from the neural action potential. The EPP is from an intracellular recording while the action potential is recorded separately with extracellular electrodes. The latter is included for timing; its relative amplitude is uncalibrated. [From L. G. Brock *et al.*, The recording of potentials from motoneurons with an intracellular electrode, *J. Physiol.* **117**:431–460 (1952).]

Rapidly Acting Neurotransmitters

Table 45–1 SMALL-MOLECULE, RAPIDLY ACTING TRANSMITTERS

Class I:
Acetylcholine
Class II: *The Amines*
Norepinephrine
Epinephrine
Dopamine
Serotonin
Histamine
Class III: *Amino Acids*
γ-Aminobutyric acid (GABA)
Glycine
Glutamate
Aspartate
Class IV:
Nitric oxide (NO)

Slowly Acting Neurotransmitters

45–2 NEUROPEPTIDE, SLOWLY ACTING TRANSMITTERS

Hypothalamic-releasing hormones
Thyrotropin-releasing hormone
Luteinizing hormone–releasing hormone
Somatostatin (growth hormone inhibitory factor)
Pituitary peptides
ACTH
β-Endorphin
α-Melanocyte-stimulating hormone
Prolactin
Luteinizing hormone
Thyrotropin
Growth hormone
Vasopressin
Oxytocin
Peptides that act on gut and brain
Leucine enkephalin
Methionine enkephalin
Substance P
Gastrin
Cholecystokinin
Vasoactive intestinal polypeptide (VIP)
Neurotensin
Insulin
Glucagon
From other tissues
Angiotensin II
Bradykinin
Carnosine
Sleep peptides
Calcitonin

Neuronal Cell Body properties

- Resting membrane potential -65 mV (vs -90 mV for large peripheral axons) to allow both excitation and inhibition
- Cell dendrites and body (soma) have few sodium channels so individual excitatory post synaptic potentials (EPSP) do not result in action potentials
- Cell body potential is uniform because of geometry and electrolytic conductance
- Action potential generated in initial segment of axon (axon hillock) because it has 7 times number of sodium gates as cell body

Summation of Inputs

- EPSPs and IPSPs from typically ACh rise in 1-2 ms and return to baseline within 15 ms due to diffusion of ions
- Other neurotransmitters can excite or inhibit for 100s of ms, sec, min or hours
- A single input only raises or lowers post synaptic membrane by .5 to 1 mV
- Many simultaneous inputs are spatially summated
- If a presynaptic neuron fires at a high enough rate the single synapse response can be temporally summated giving that synapse much greater possibility of exciting the cell to produce an AP

Multiple Input Effect on Cell

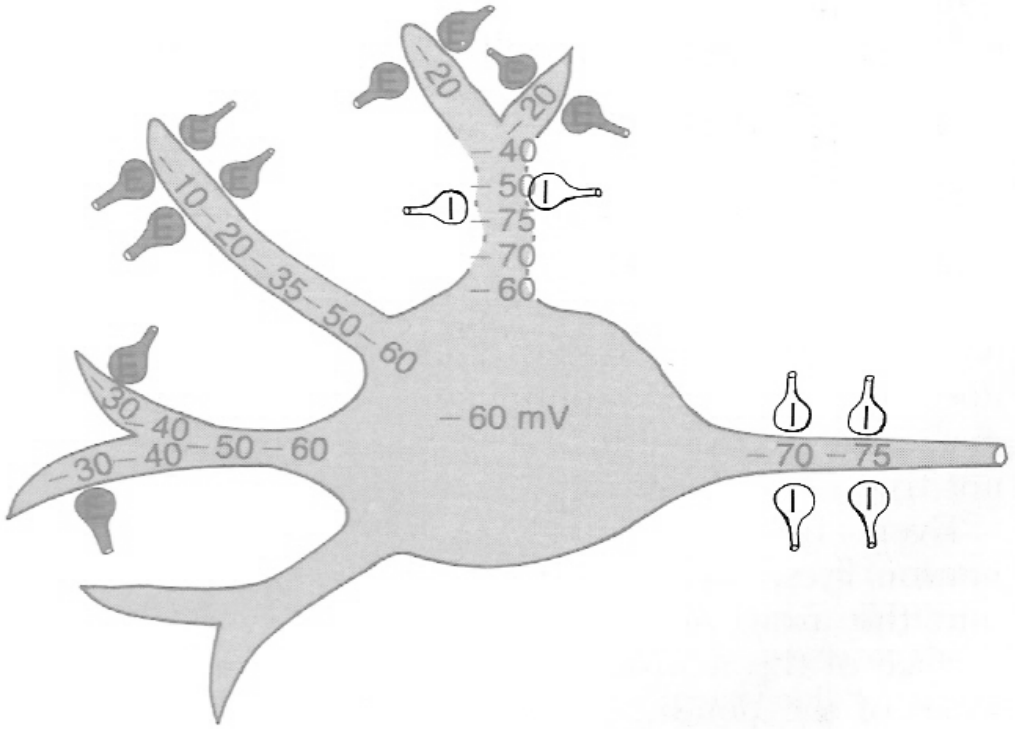


Figure 45–11. Stimulation of a neuron by presynaptic terminals located on dendrites, showing, especially, decremental conduction of excitatory electrotonic potentials in the two dendrites to the left and inhibition of dendritic excitation in the dendrite that is uppermost. A powerful effect of inhibitory synapses at the initial segment of the axon is also shown.

Neuronal Firing Rates

- When AP generated it travels down axon and also back through soma resulting in depolarization thus inhibiting successive firing
- Neurons have different inherent firing rates or thresholds
- Neurons have different rates of firing increase with excitation

Sensory Inputs

- Sensory receptors are highly differentiated
- Generally consist of an axon with a special peripheral end or transducer responsive to a certain type of input
- Transducer can generate a maximum of 100 mv
- Sensory signals travel to specific brain areas which interpret a signal as specific to the transducer – e.g. a pain sensor signal interpreted as pain even if signal results from mechanical deformation, electrical stimulation or heat
- Cell body in ganglion outside e.g. spinal cord

Sensory Receptors

Table 46–1 CLASSIFICATION OF SENSORY RECEPTORS

- Mechanoreceptors
  - Skin tactile sensibilities (epidermis and dermis)
    - Free nerve endings
    - Expanded tip endings
      - Merkel's discs
      - Plus several other variants
    - Spray endings
      - Ruffini's endings
    - Encapsulated endings
      - Meissner's corpuscles
      - Krause's corpuscles
    - Hair end-organs
  - Deep tissue sensibilities
    - Free nerve endings
    - Expanded tip endings
    - Spray endings
      - Ruffini's endings
    - Encapsulated endings
      - Pacinian corpuscles
      - Plus a few other variants
    - Muscle endings
      - Muscle spindles
      - Golgi tendon receptors
  - Hearing
    - Sound receptors of cochlea
  - Equilibrium
    - Vestibular receptors
  - Arterial pressure
    - Baroreceptors of carotid sinuses and aorta
- Thermoreceptors
  - Cold
    - Cold receptors
  - Warmth
    - Warm receptors
- Nociceptors
  - Pain
    - Free nerve endings
- Electromagnetic Receptors
  - Vision
    - Rods
    - Cones
- Chemoreceptors
  - Taste
    - Receptors of taste buds
  - Smell
    - Receptors of olfactory epithelium
  - Arterial oxygen
    - Receptors of aortic and carotid bodies
  - Osmolality
    - Probably neurons in or near supraoptic nuclei
  - Blood CO_2
    - Receptors in or on surface of medulla and in aortic and carotid bodies
  - Blood glucose, amino acids, fatty acids
    - Receptors in hypothalamus

Somatic Sensory Nerve Endings

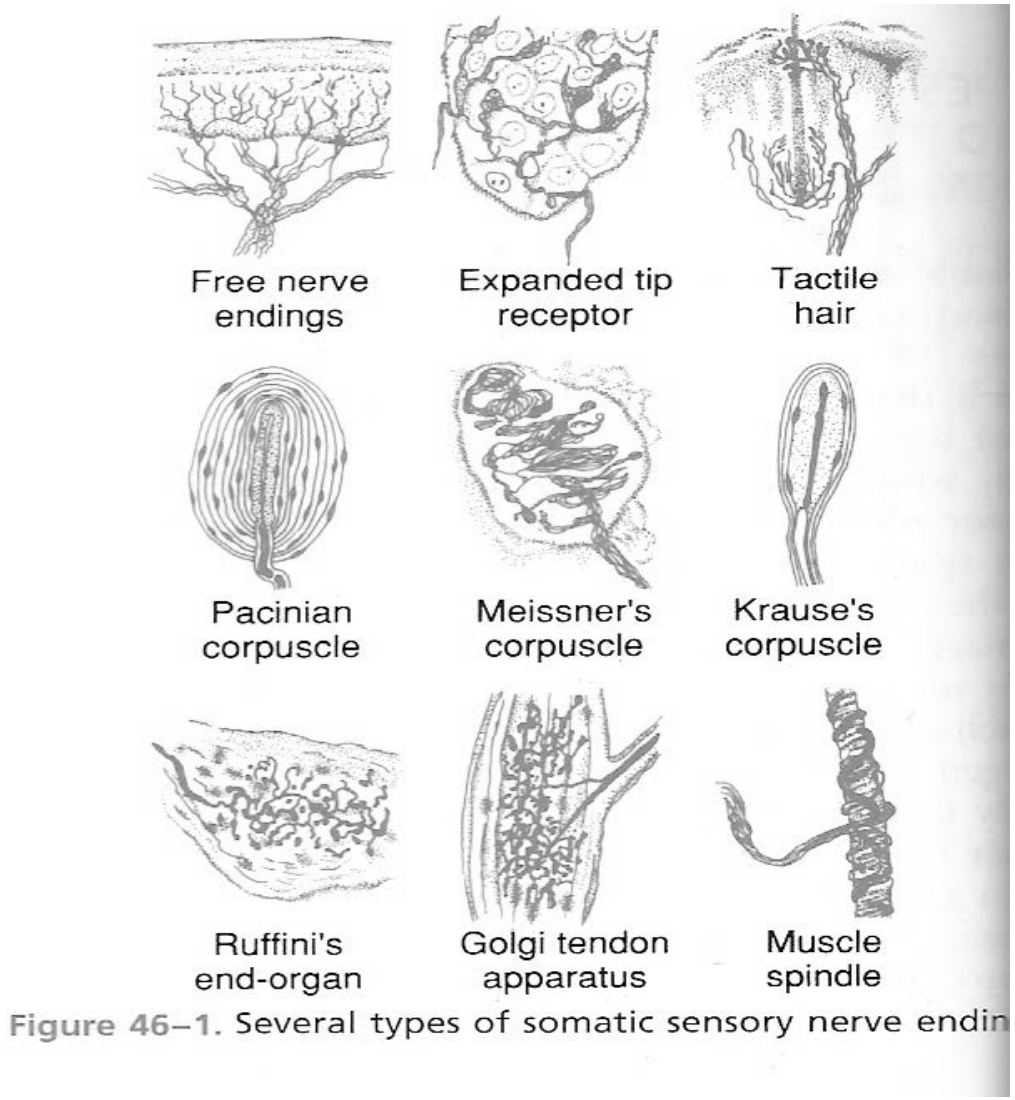


Figure 46–1. Several types of somatic sensory nerve endin

Pacinian Corpuscle

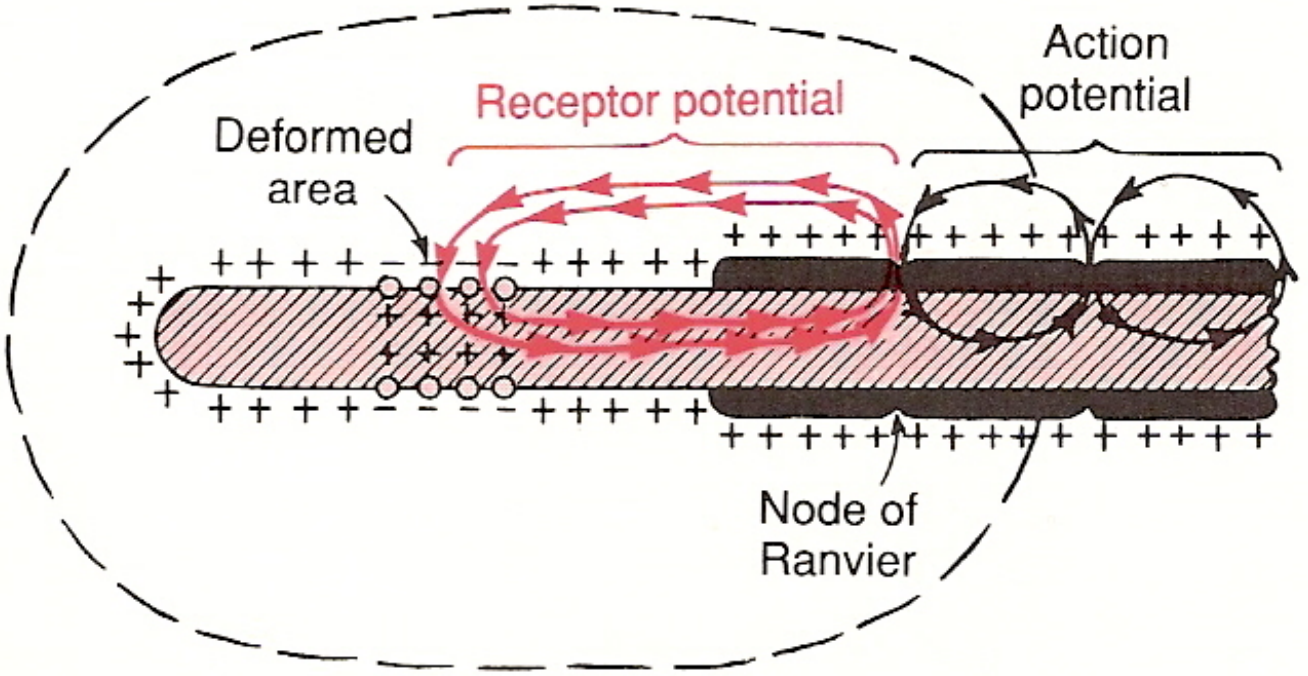


Figure 46–3. Excitation of a sensory nerve fiber by a receptor potential produced in a pacinian corpuscle. (Modified from Loëwenstein: *Ann. N. Y. Acad. Sci., 94:*510, 1961.)

Receptor Potential of Pacinian Corpuscle

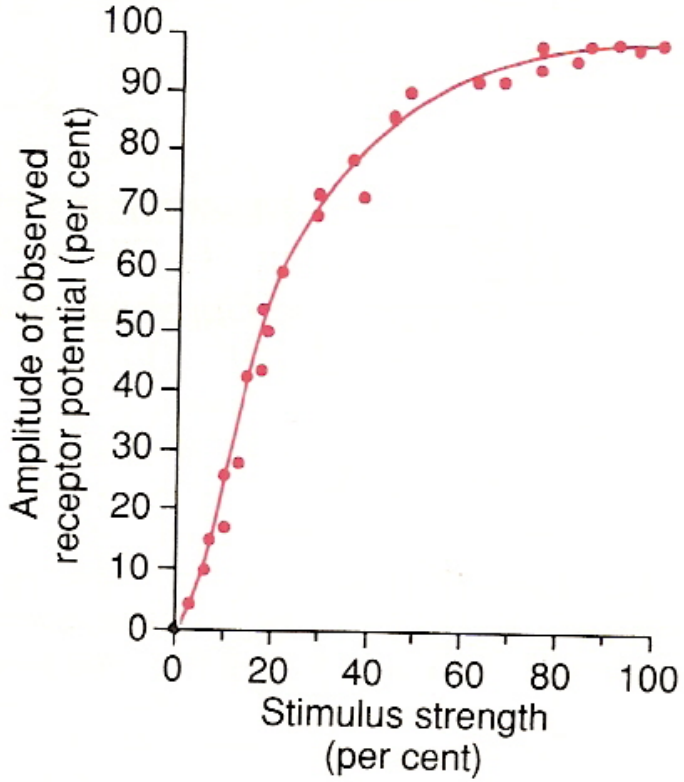


Figure 46–4. Relation of amplitude of receptor potential to strength of a mechanical stimulus applied to a pacinian corpuscle. (From Loëwenstein: *Ann. N. Y. Acad. Sci., 94:*510, 1961.)

Receptor Potential and Firing Rates

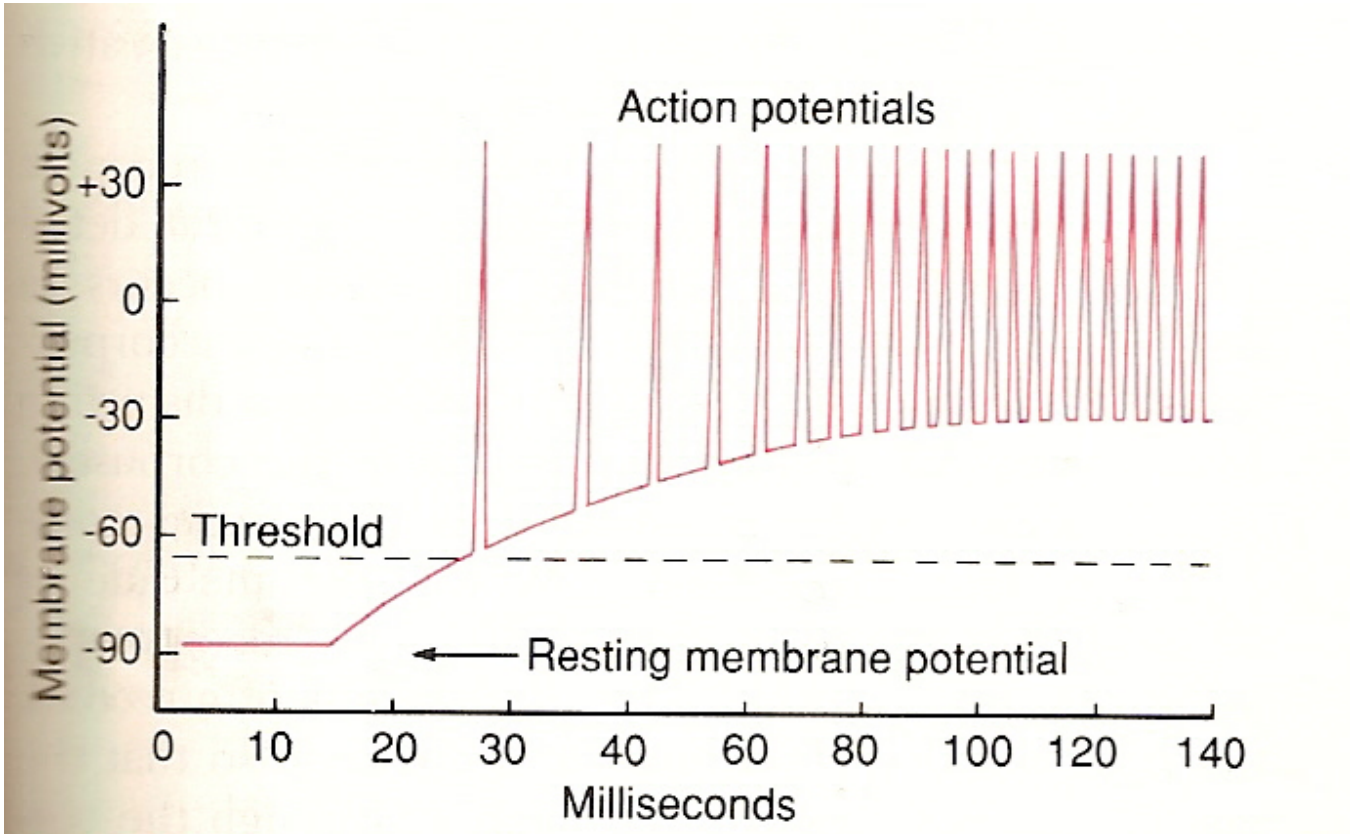


Figure 46–2. Typical relation between receptor potential and action potentials when the receptor potential rises above the threshold level.

Receptor Adaptation

- Decay of response when sensory stimulus is continuous
- For Pacinian corpuscle fluid redistributes in receptor to make pressures equal
- Slowly adapting receptors provide continuous input to brain (tonic – e.g. muscle spindles)

Receptor Adaptation

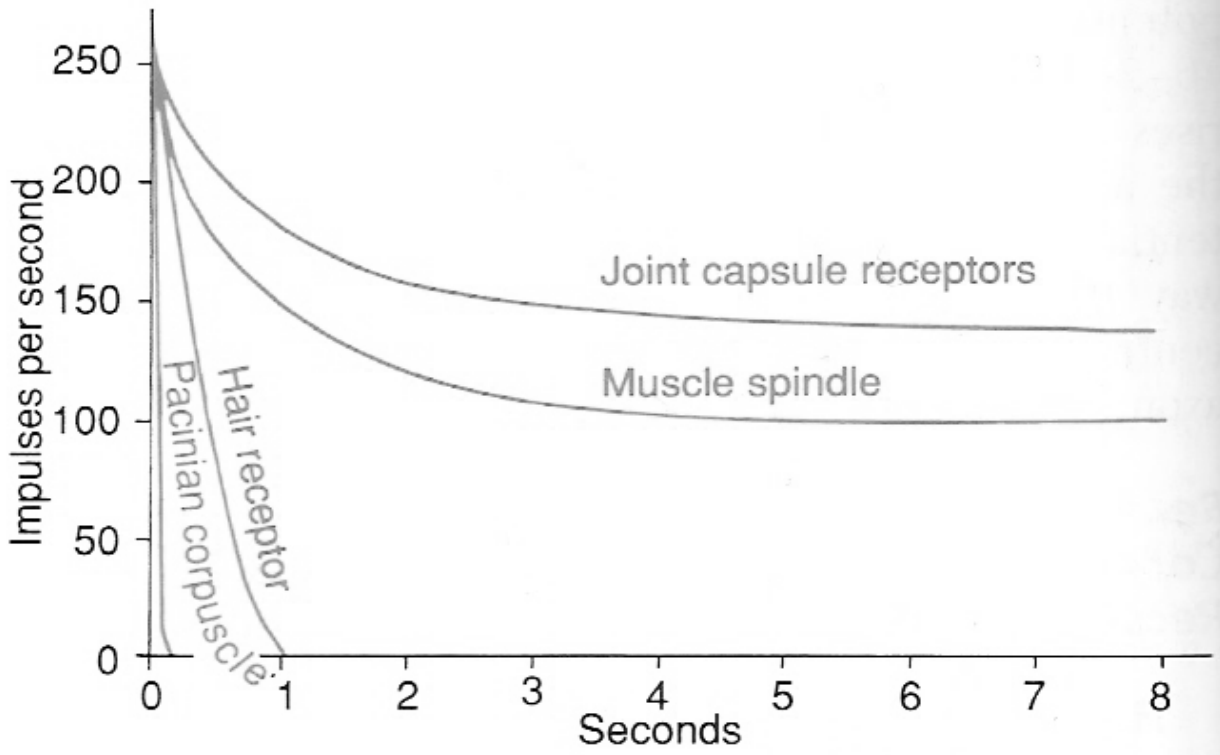


Figure 46–5. Adaptation of different types of receptors, showing rapid adaptation of some receptors and slow adaptation of others.

Physiological Classification of Nerve Fibres

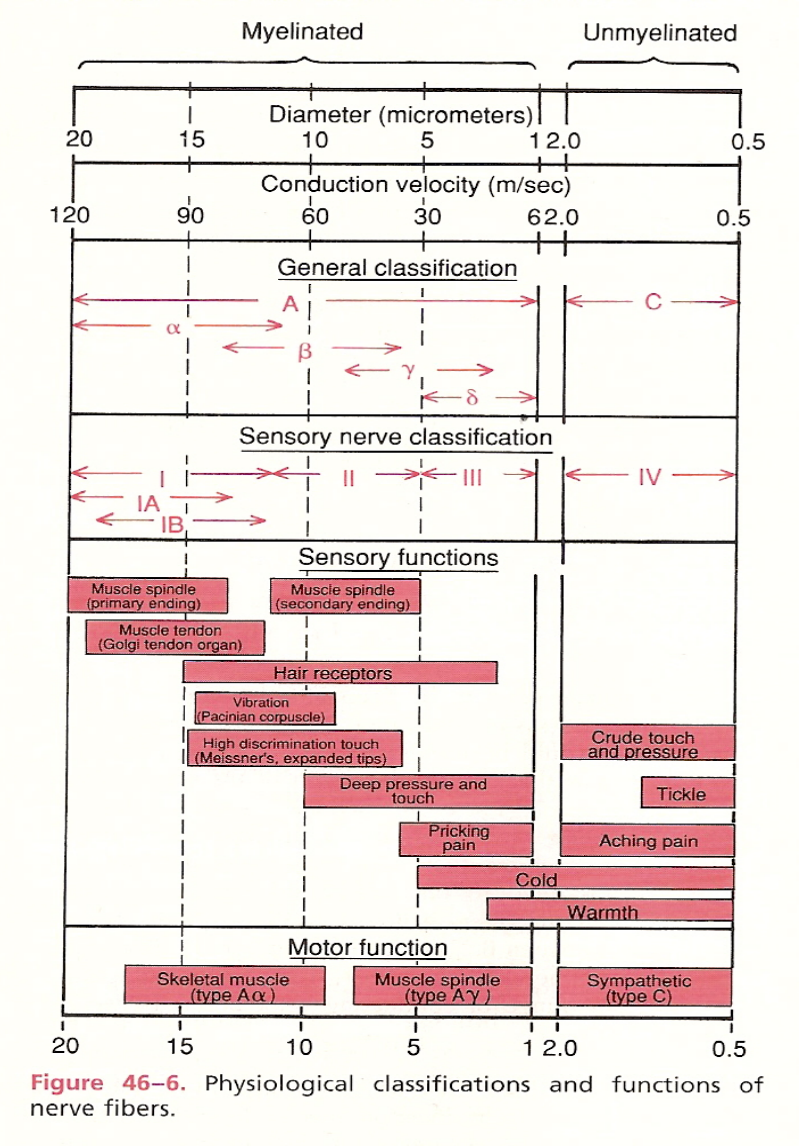


Figure 46–6. Physiological classifications and functions of nerve fibers.

The Neuronal Pool

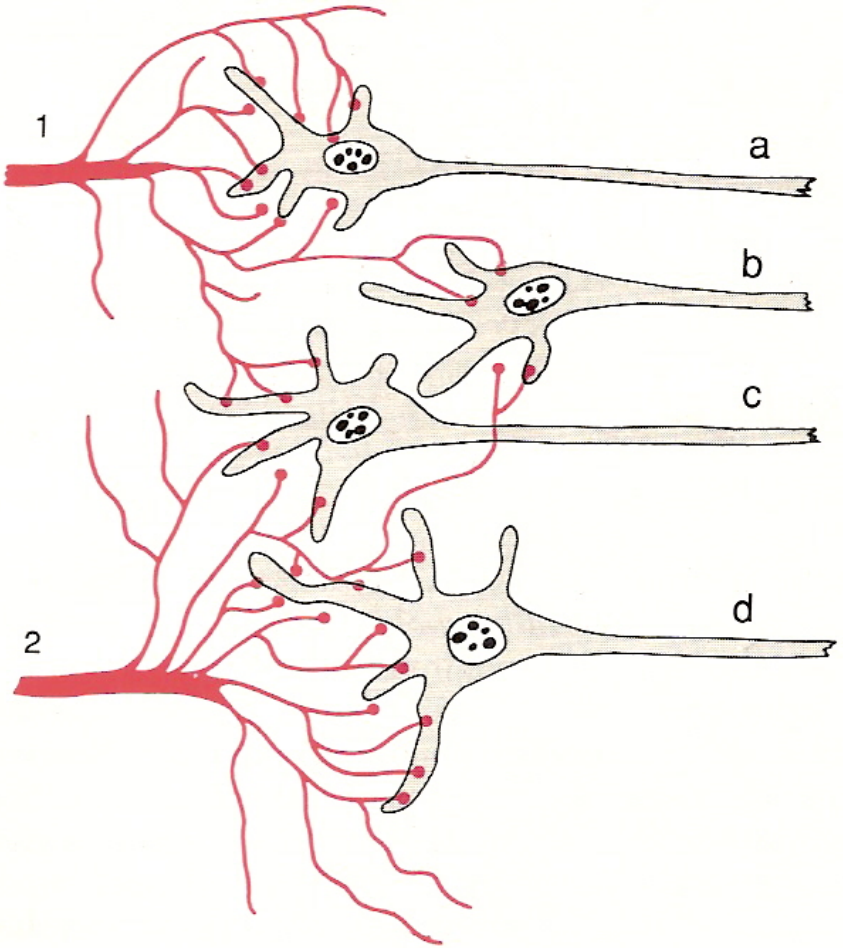


Figure 46–9. Basic organization of a neuronal pool.