Peripheral Neurology

SIU SOM Neurology Neuroscience Course

2018

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SIU SOM

No Disclosures

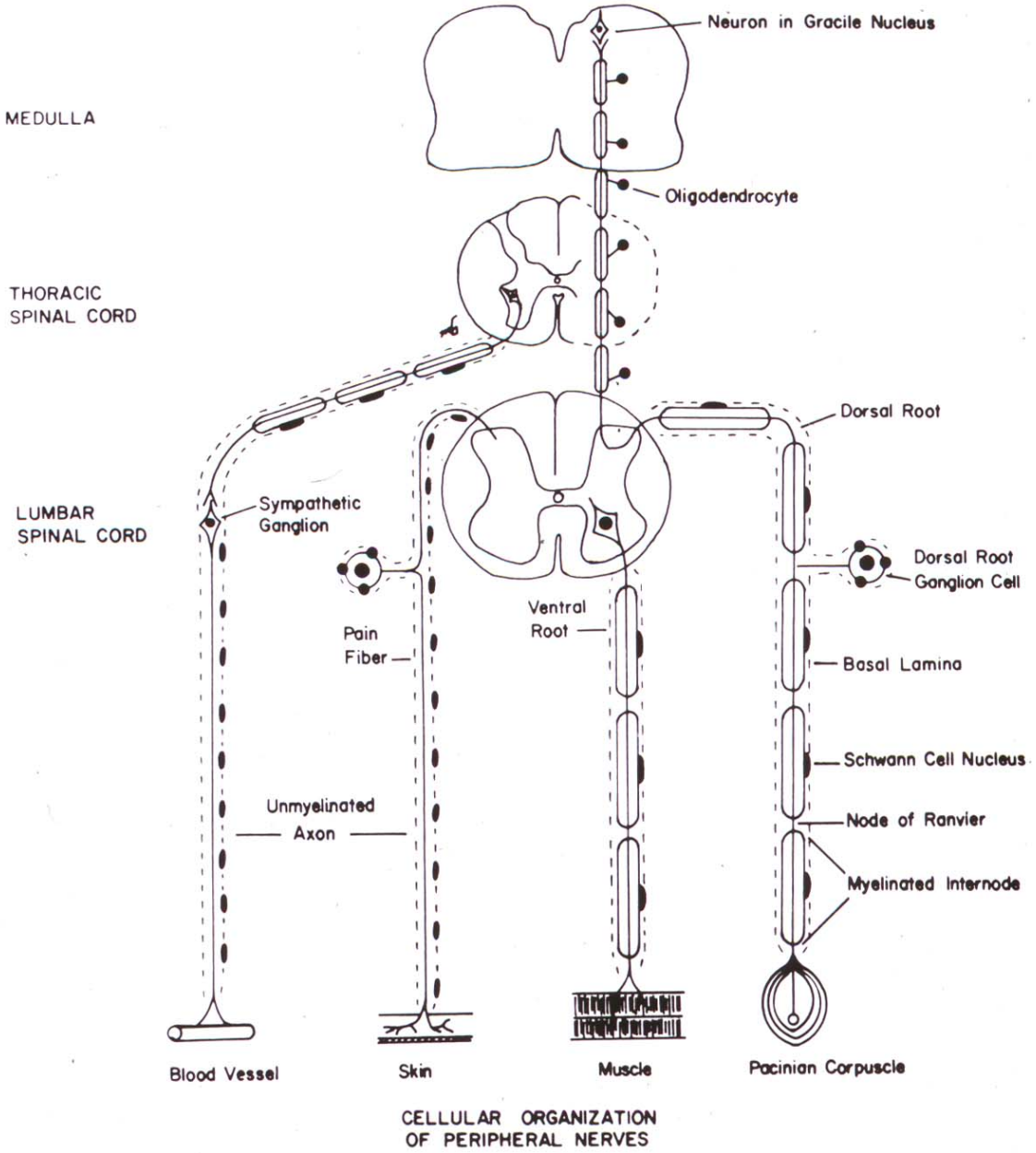


FIGURE 1. A diagram of the principal components of the peripheral nervous system.

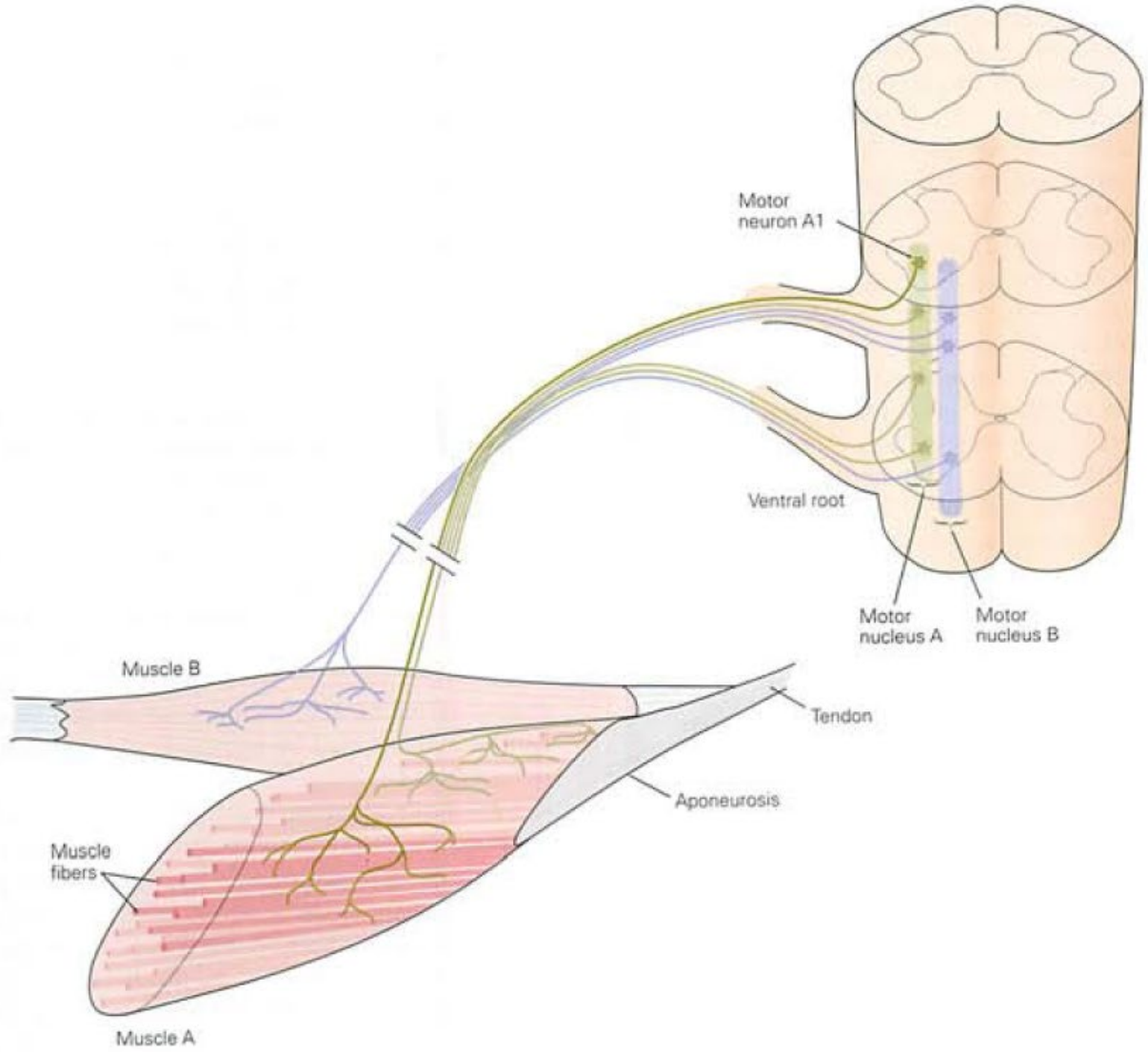
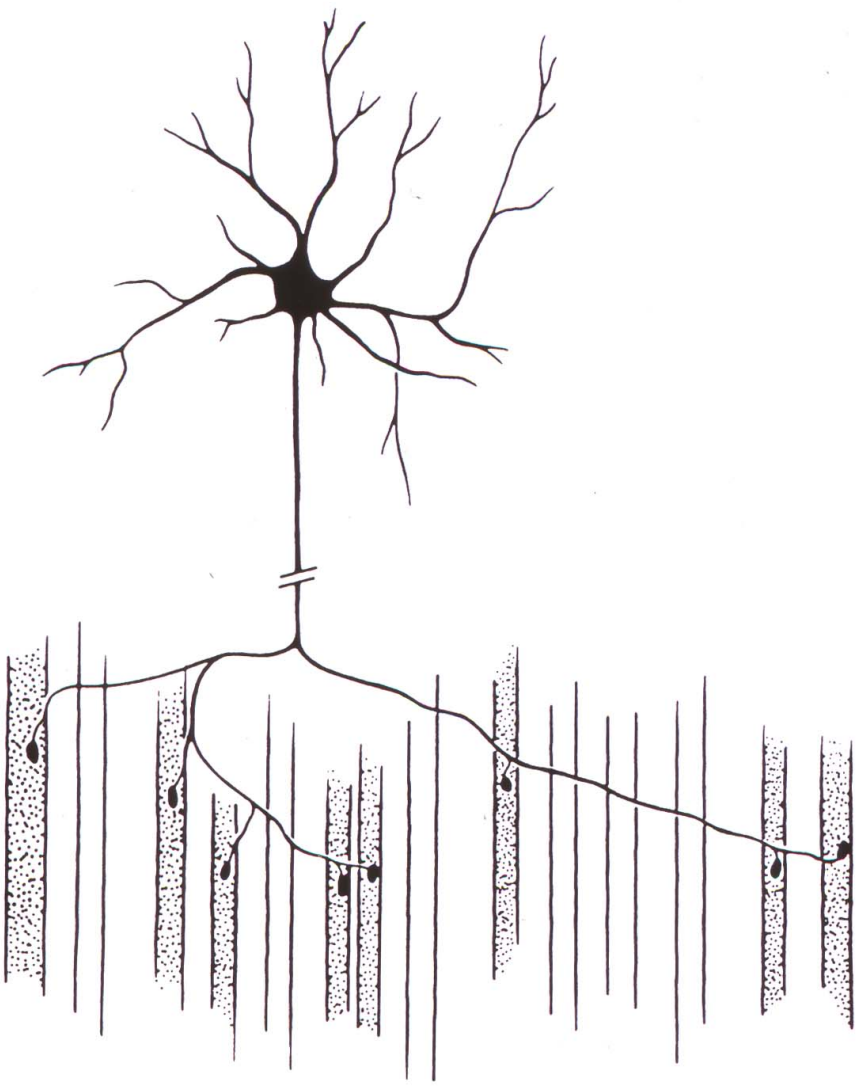


Figure 34–1 A typical muscle consists of many thousands of muscle fibers working in parallel and organized into a smaller number of motor units. A motor unit consists of a motor neuron and the muscle fibers that it innervates, illustrated here by motor neuron A1. The motor neurons innervating one muscle are usually clustered into an elongated motor nucleus that may extend over one to four segments within the ventral spinal cord. The axons from a motor nucleus exit the spinal cord in several ventral roots and peripheral nerves but are collected into one nerve bundle near the target muscle. In the figure, motor nucleus A includes all those motor neurons innervating muscle A; muscle B is innervated by motor neurons lying in motor nucleus B. The extensively branched dendrites of one motor neuron tend to intermingle with those of motor neurons from other nuclei.



Differential signs of the peripheral nervous system

	Strength	DTRs	Sensory	Cranial nerves
Anterior horn cell (ALS)	↓ diffusely	↓ diffusely (↑ diffusely)	normal	motor affected
Root/plexus	↓ regional	↓ regional	↓ regional	normal
Nerve fiber	↓ distally	↓ distally	↓ distally	affected if severe
Neuromus-cular junction	↓ diffusely	↓ diffusely	normal	motor affected
Muscle	↓ proximal	↓ proximal	normal	normal

Table 34–1 Innervation Numbers in Human Skeletal Muscles

Muscle	Alpha motor axons	Muscle fibers	Innervation number
Biceps brachii	774	580,000	750
Brachioradialis	333	>129,200	>410
Cricothyroid	112	18,550	155
Gastrocnemius (medial)	579	1,042,000	1,800
Interossei dorsales (1)	119	40,500	340
Lumbricales (1)	96	10,269	107
Masseter	1,452	929,000	640
Opponens pollicis	133	79,000	595
Platysma	1,096	27,100	25
Posterior cricoarytenoid	140	16,200	116
Rectus lateralis	4,150	22,000	5
Temporalis	1,331	1,247,000	936
Tensor tympani	146	1,100	8
Tibialis anterior	445	272,850	613
Transverse arytenoid	139	34,470	247

(Adapted, with permission, from Enoka 2008.)

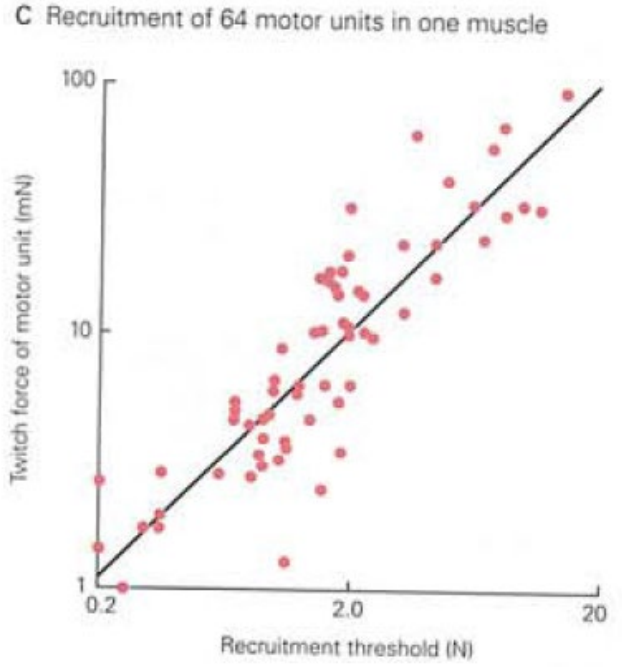
The response to a single action potential is known as a *twitch contraction*. The time it takes the twitch to reach its peak force, the *contraction time*, is one measure of the contraction speed of the muscle fibers that comprise a motor unit. Slow-twitch motor units have long contraction times; fast-twitch units have shorter contraction times. A rapid series of action potentials elicits superimposed twitches known as a *tetanic contraction* or *tetanus*.

Two types of Muscle fibers

to identify type I and type II muscle fibers. Slow contracting motor units contain type I muscle fibers, and fast contracting units include type II fibers. The type II fibers can be further classified into the least fatigable (type IIa) and most fatigable (type IIb, IIx, or IId). Another commonly used scheme distinguishes muscle fibers on the basis of genetically defined isoforms of the myosin heavy chain. Those in slow contracting motor units express myosin heavy chain-I, those in fast contracting and least fatigable units express myosin heavy chain-IIa, and fibers in fast contracting and most fatigable units express myosin heavy chain-IIb or -IIx. There is a high degree of correspondence between the two classification schemes for muscle fibers.

Changes in the contractile properties of motor units involve adaptations in the structural specializations and biochemical properties of muscle fibers. The

The order in which motor units are recruited is highly correlated with several indices of motor unit size, including the size of the motor neuron cell bodies, the diameter and conduction velocity of the axons, and the amount of force that the muscle fibers can exert. Because the recruitment threshold of a motor unit depends on the membrane resistance of the motor neuron, which is inversely related to its surface area, a given synaptic current will produce larger changes in the membrane potential of small-diameter motor neurons. Consequently, increases in the net excitatory



neuron size: The smallest motor neuron is recruited first and the largest motor neuron last (Figure 34–5). This effect is known as the size principle of motor neuron recruitment, a principle enunciated by Elwood Henneman in 1957.

First, the sequence of motor-neuron recruitment is determined by spinal mechanisms and not by higher regions of the nervous system. This means that the brain cannot selectively activate specific motor units. Second, motor units are activated in order of increasing fatigability, so the least fatigable motor units available produce the initial force required for a specific task.

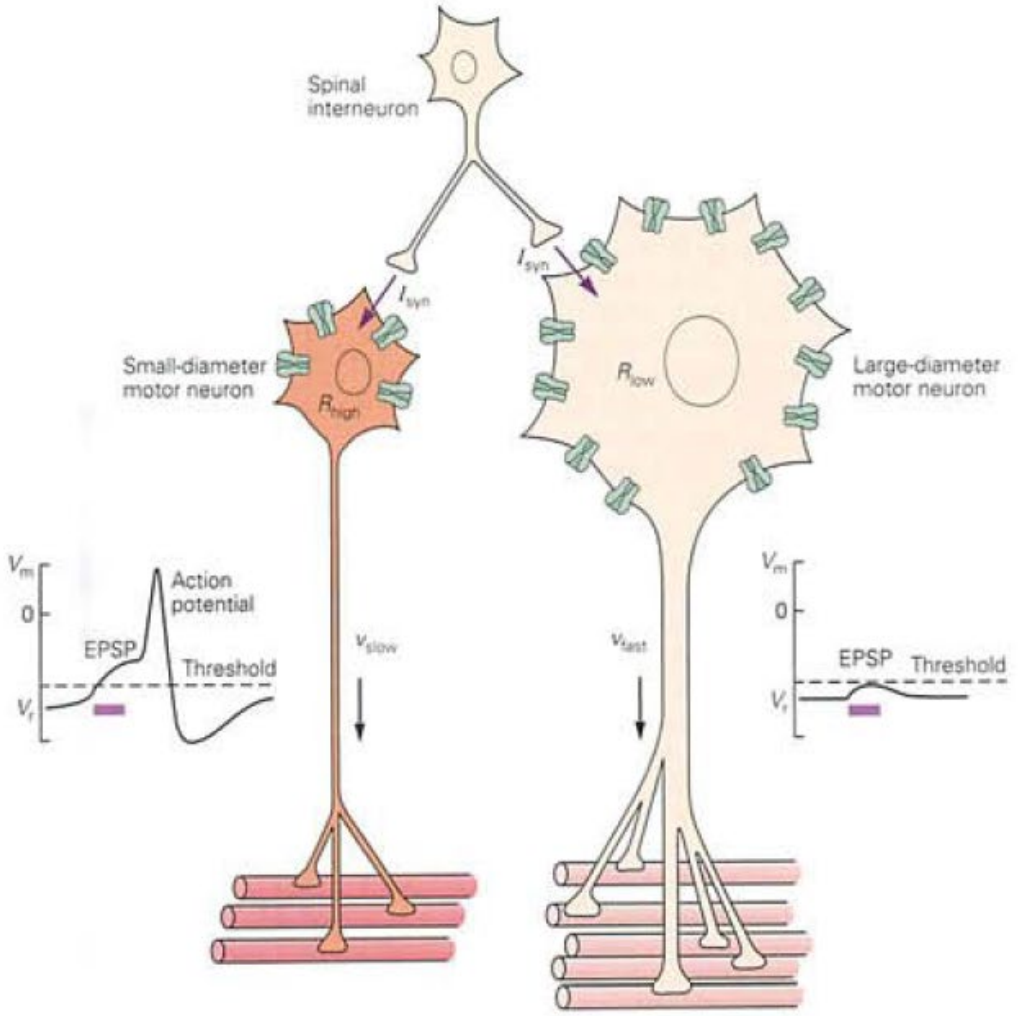


Figure 34–5 The response of a motor neuron to synaptic input depends on its size. Two motor neurons of different sizes have the same resting membrane potential (V_r) and receive the same excitatory synaptic current (I_{syn}) from a spinal interneuron. Because the small motor neuron has a smaller surface area, it has fewer parallel ion channels and therefore a higher resistance (R_{high}). According to Ohm's law ($V = IR$), I_{syn} in the small neuron produces a large excitatory postsynaptic potential (EPSP) that reaches threshold, resulting in the discharge of an action potential. The small motor neuron has a small-diameter axon that conducts the action potential at a low velocity (v_{slow}) to fewer muscle fibers. In contrast, the large motor neuron has a larger surface area, which results in a lower transmembrane resistance (R_{low}) and a smaller EPSP that does not reach threshold in response to I_{syn}.

TABLE 28.1 Size-Related Properties of Motor Neurons

Properties that Increase with Size	Properties that Decrease with Size
Diameter of soma and axon	Resistance to fatigue
Conduction velocity	Ia EPSP amplitude
Complexity of axonal collaterals	Input resistance
Membrane area, dendritic extent	Membrane resistance
Rheobase	Time constant
Muscle fiber diameter	Duration of after-hyperpolarization
Maximum force output	Twitch contraction time
	Twitch relaxation time

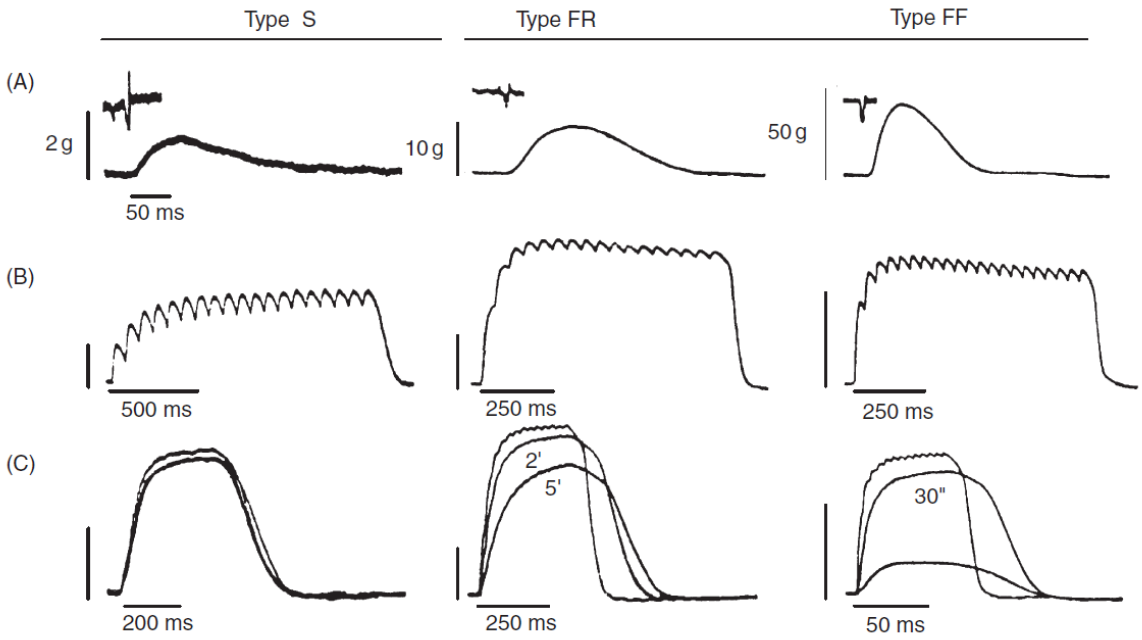
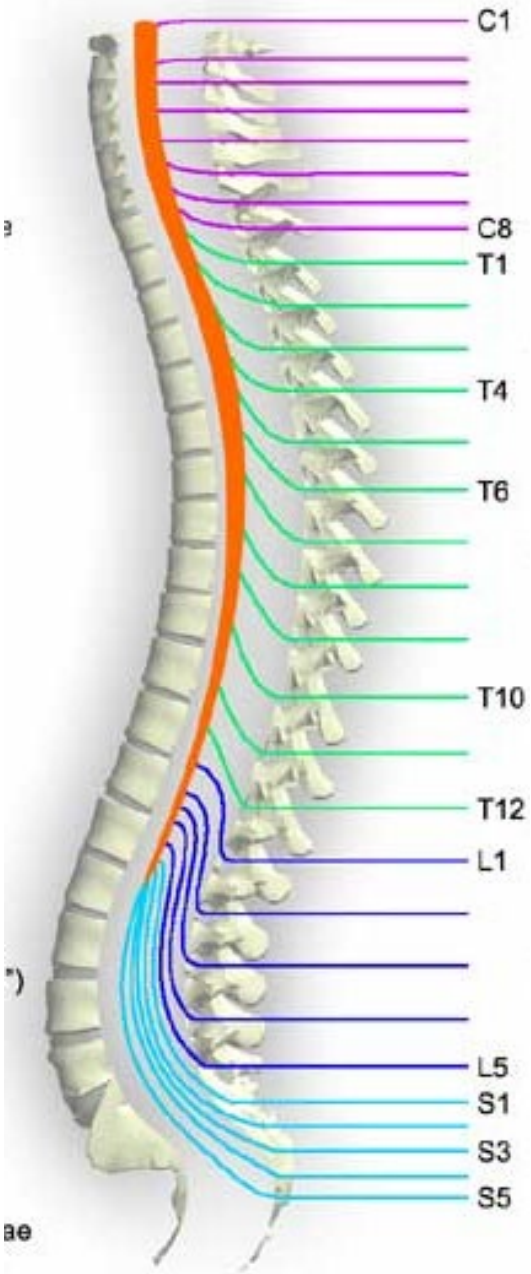
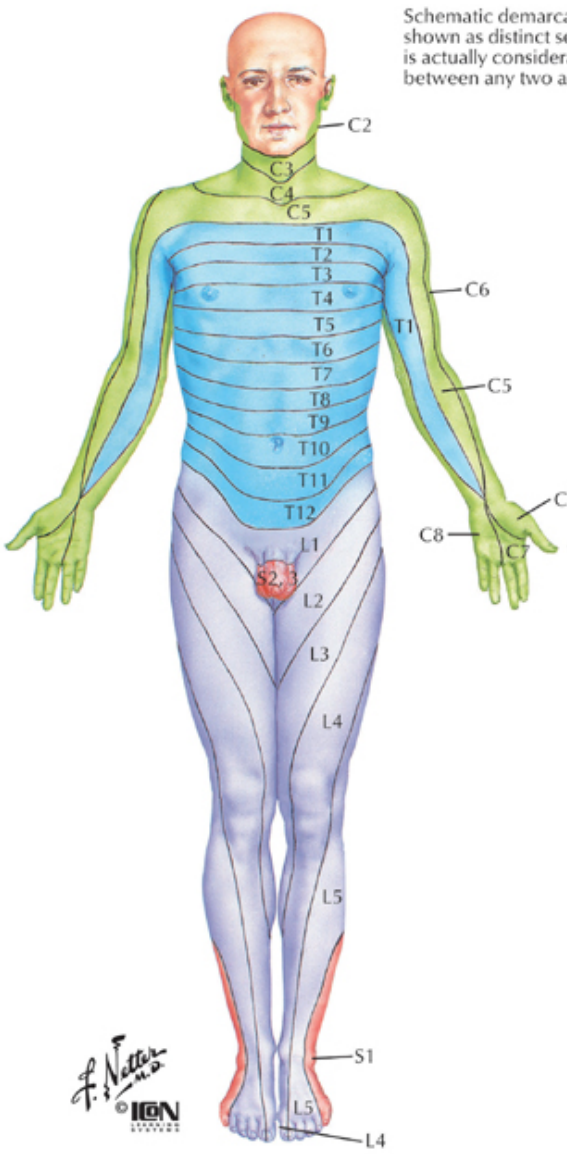
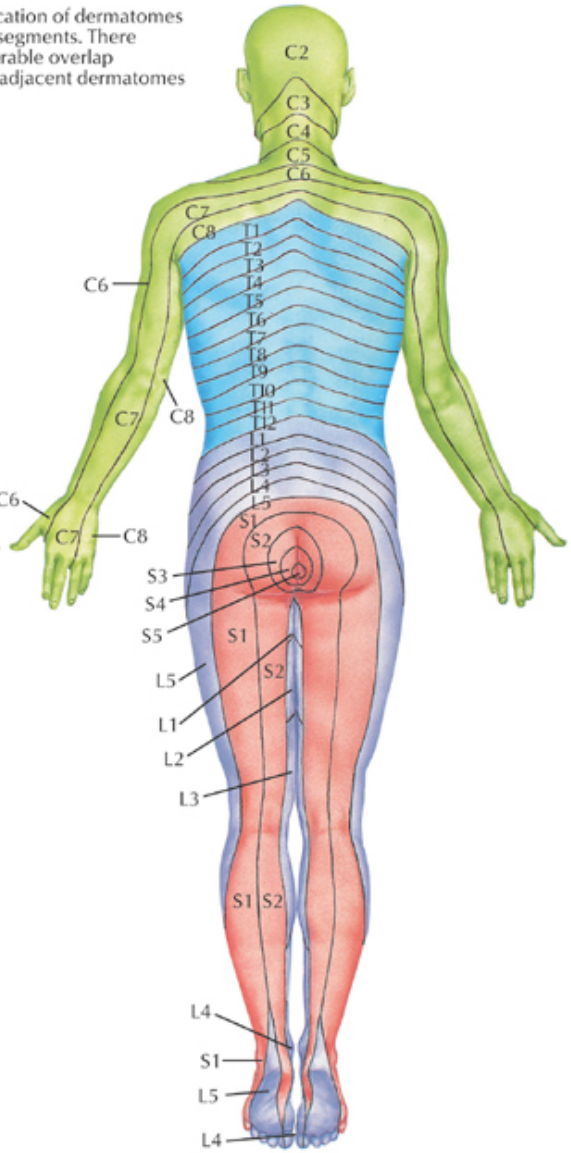


FIGURE 28.4 The three motor unit types (S, FR, and FF) can be defined experimentally by measuring their contractile properties and fatigability. Panels A–C show recordings of muscle force, with insets in A showing recordings of motor neuron action potentials. Note different time and amplitude calibration scales for each of the motor units. (A) Single twitches produced by one action potential of the motor neuron. (B) Maximal force produced by repetitive stimulation of the motor neuron to produce an unfused tetanus. In addition to differences in maximal force, the "sag" property, a dropping off of tension during maintained stimulation, is seen in FR and FF units. (C) Fatigability is demonstrated by a drop in the tension produced by a single twitch after short periods of activation, as noted. Note that S units show little fatigue, whereas FF units fatigue within 30 s. *Reproduced with permission from Burke, Levine, Tsairis, and Zajac (1973).*



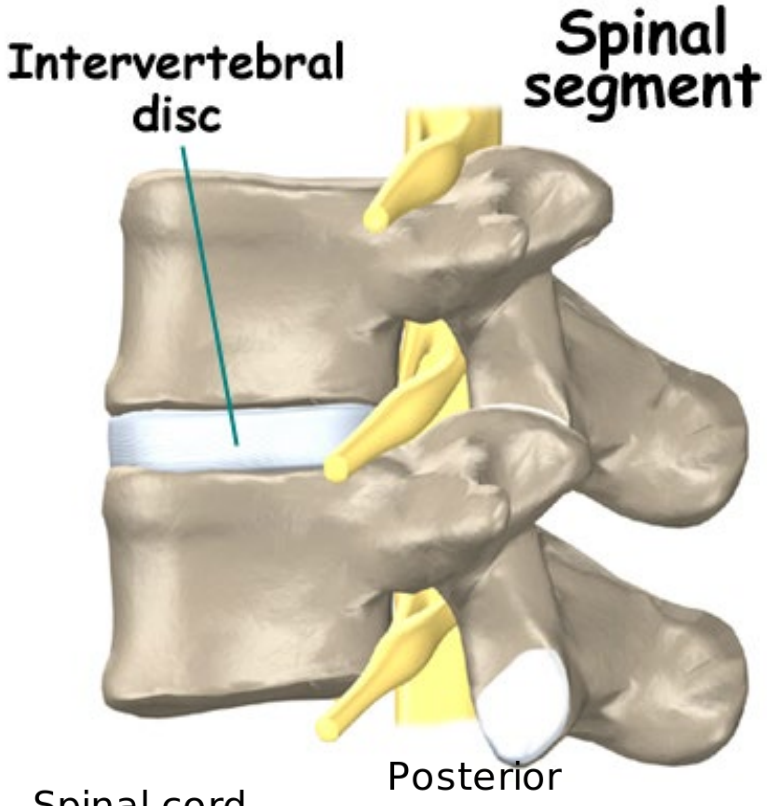


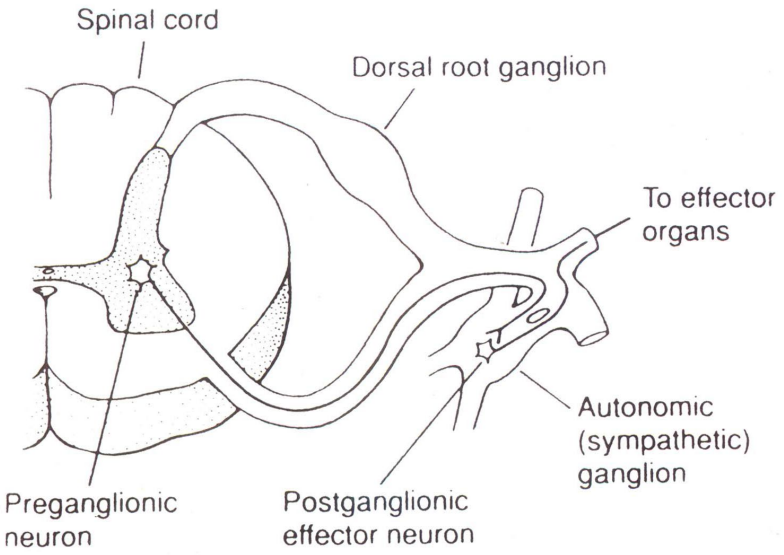
Schematic demarcation of dermatomes shown as distinct segments. There is actually considerable overlap between any two adjacent dermatomes

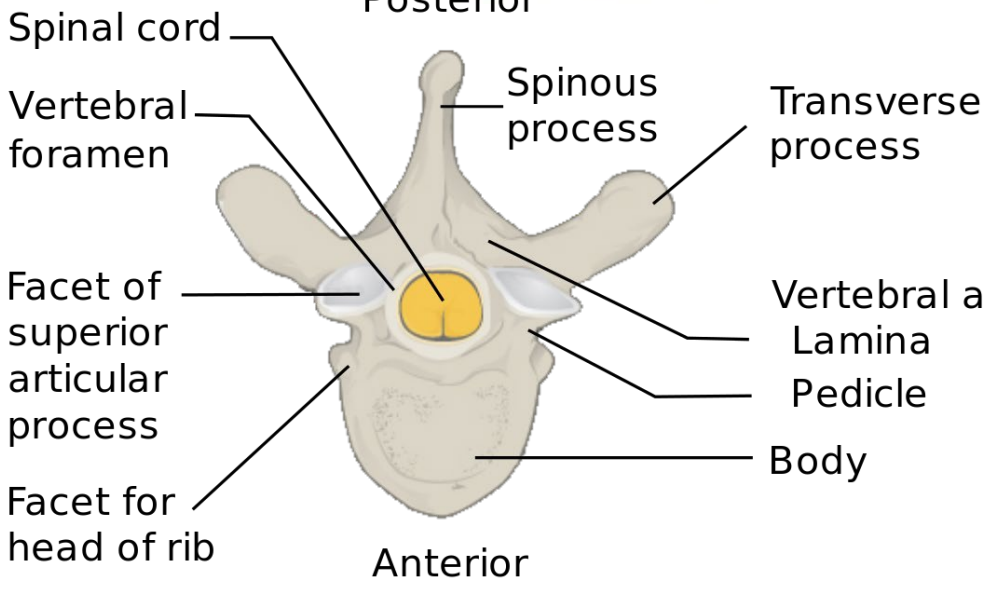


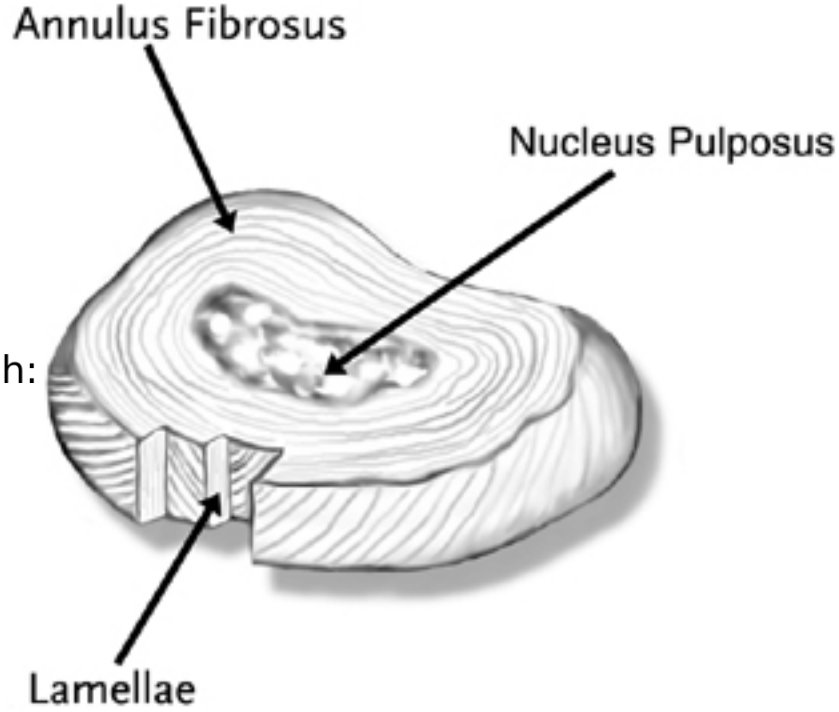
Levels of principal dermatomes

C5	Clavicles
C5, 6, 7	Lateral parts of upper limbs
C8, T1	Medial sides of upper limbs
C6	Thumb
C6, 7, 8	Hand
C8	Ring and little fingers
T4	Level of nipples
T10	Level of umbilicus
T12	Inguinal or groin regions
L1, 2, 3, 4	Anterior and inner surfaces of lower limbs
L4, 5, S1	Foot
L4	Medial side of great toe
S1, 2, L5	Posterior and outer surfaces of lower limbs
S1	Lateral margin of foot and little toe
S2, 3, 4	Perineum

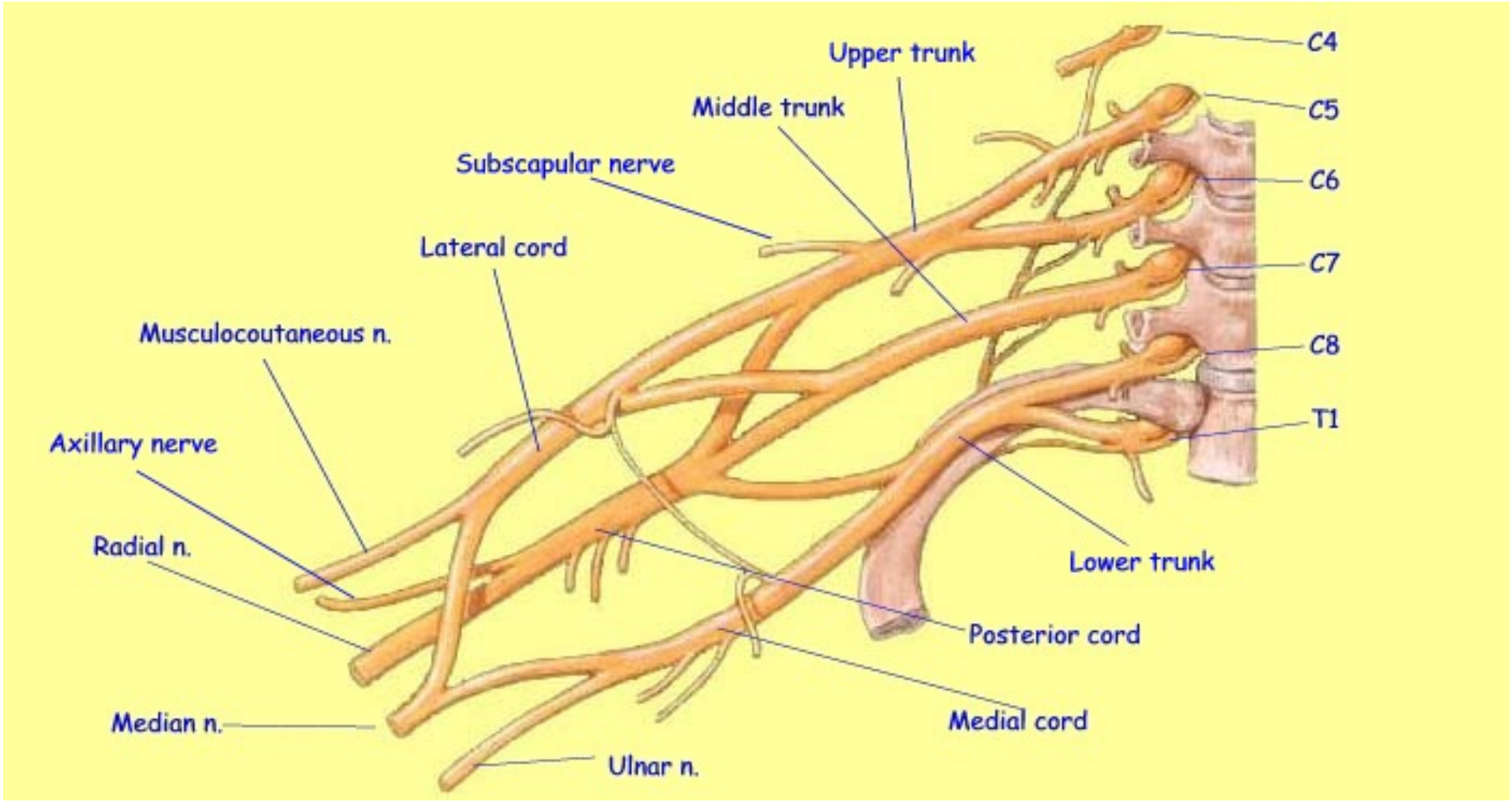

Intervertebral disc
Spinal segment
Posterior

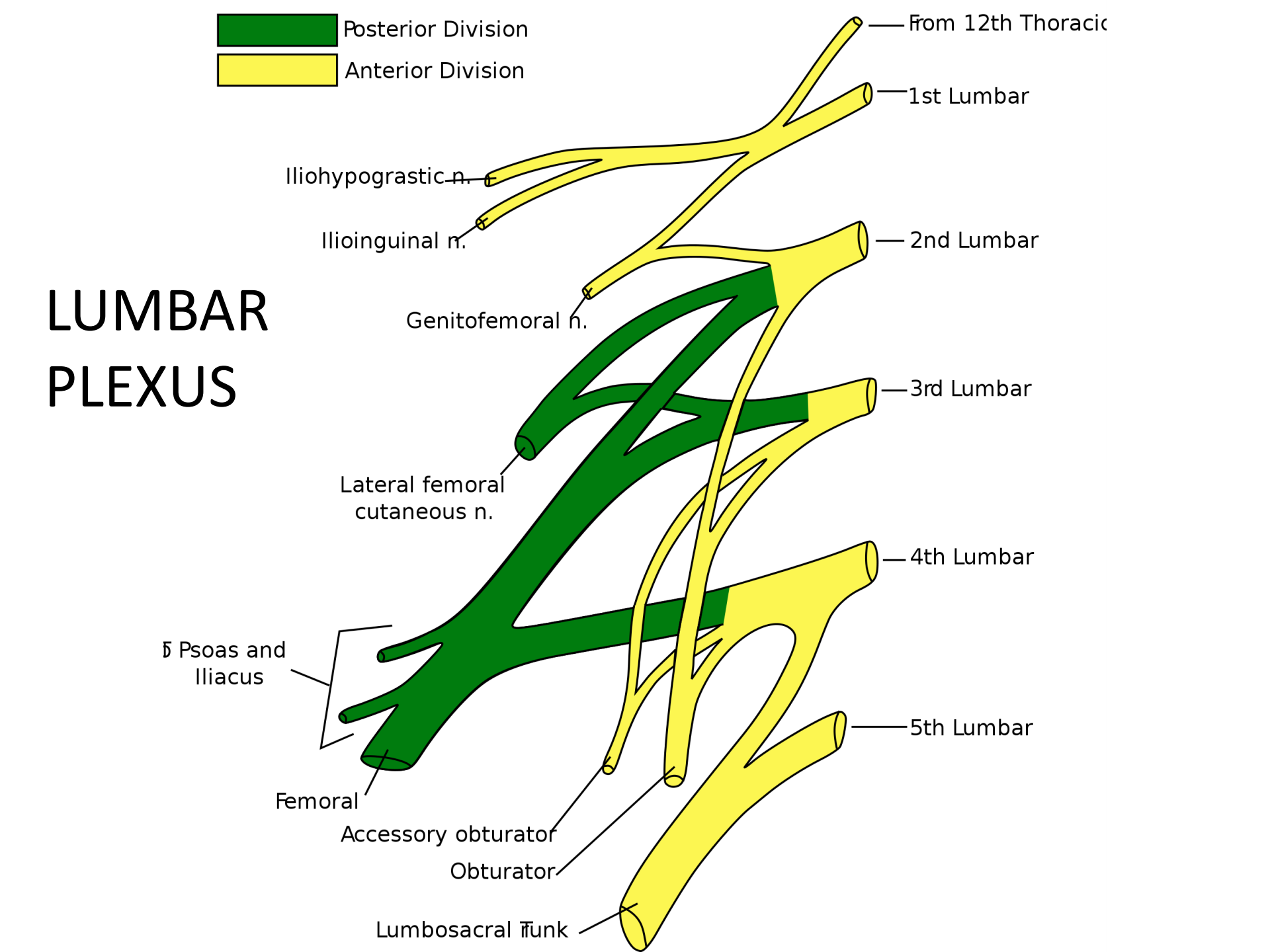

Spinal cord
Dorsal root ganglion
To effector organs
Autonomic (sympathetic) ganglion
Preganglionic neuron
Postganglionic effector neuron


Spinal cord
Vertebral foramen
Spinous process
Transverse process
Facet of superior articular process
Vertebral arch:
Lamina
Pedicle
Body
Facet for head of rib
Anterior

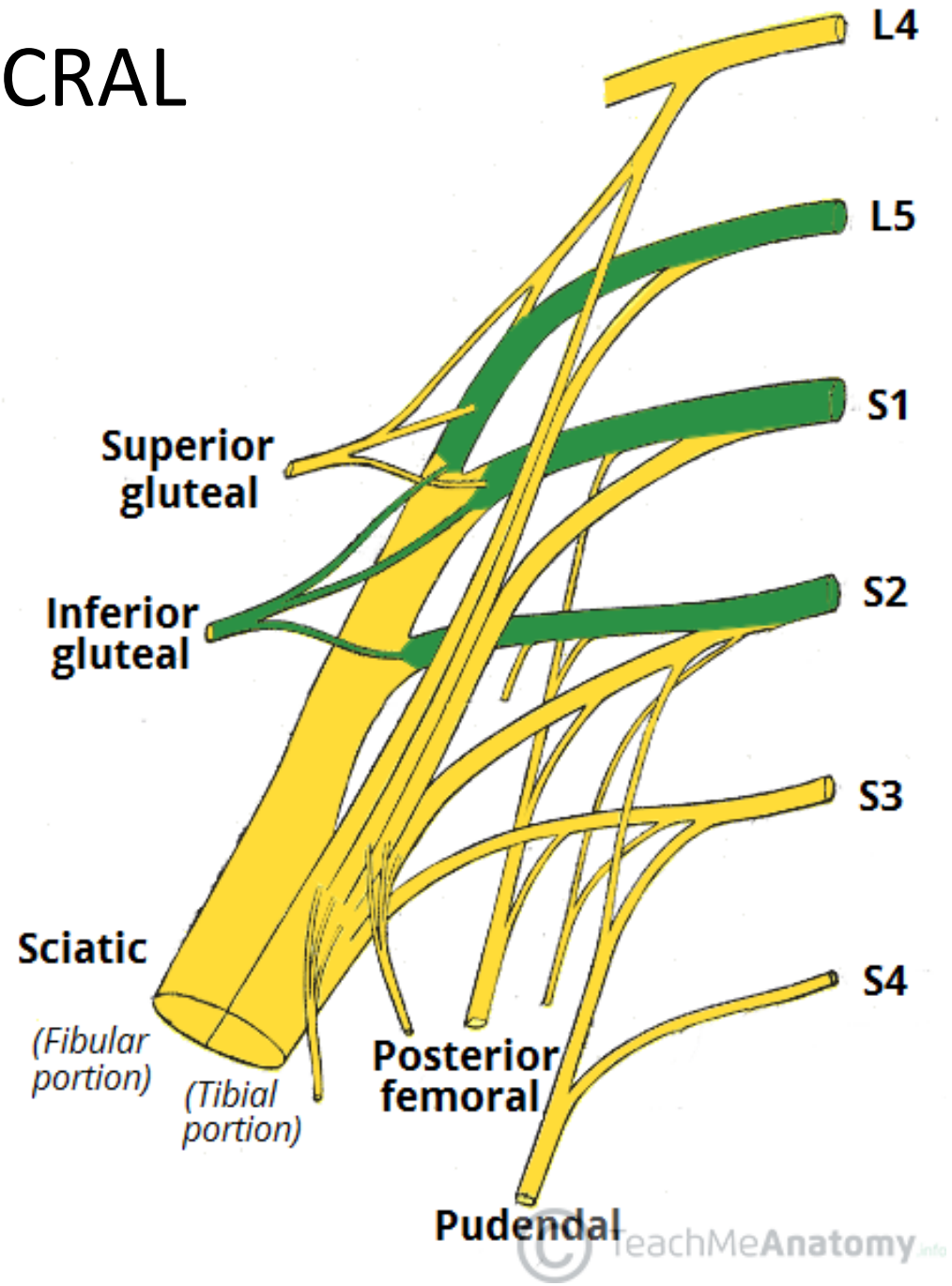

Annulus Fibrosus
Nucleus Pulposus
Lamellae

BRACHIAL PLEXUS

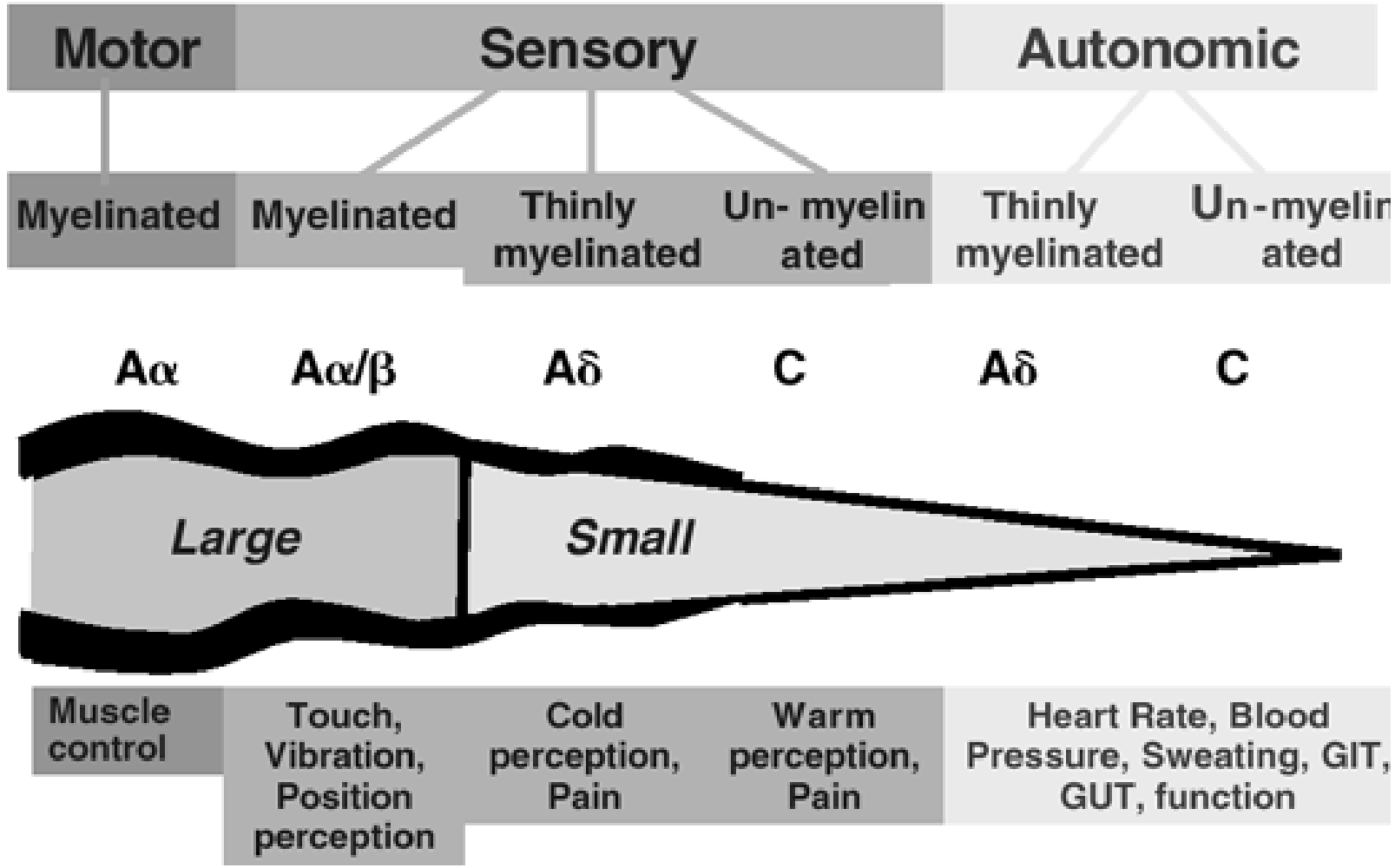



Posterior Division
Anterior Division
LUMBAR PLEXUS
From 12th Thoracic
1st Lumbar
Iliohypograstic n.
Ilioinguinal n.
2nd Lumbar
Genitofemoral n.
3rd Lumbar
Lateral femoral cutaneous n.
4th Lumbar
Psoas and Iliacus
5th Lumbar
Femoral
Accessory obturator
Obturator
Lumbosacral Trunk

LUMBOSACRAL PLEXUS



A Simplified View of The PNS



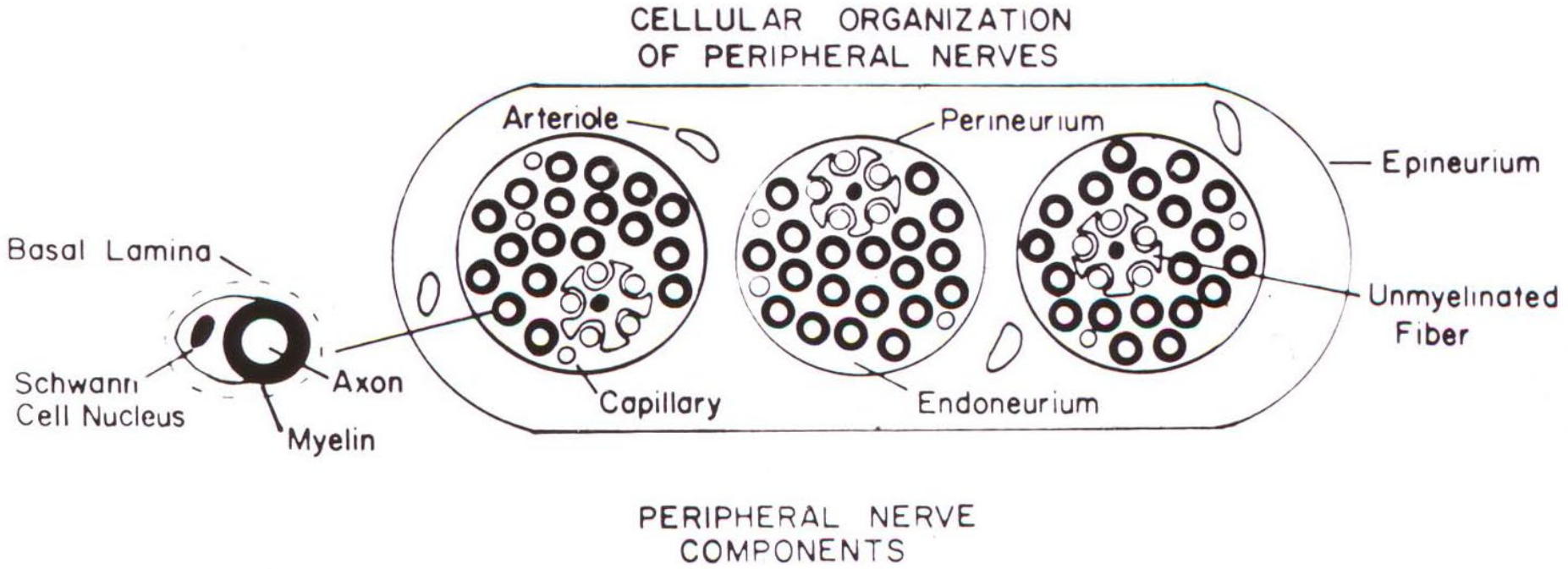
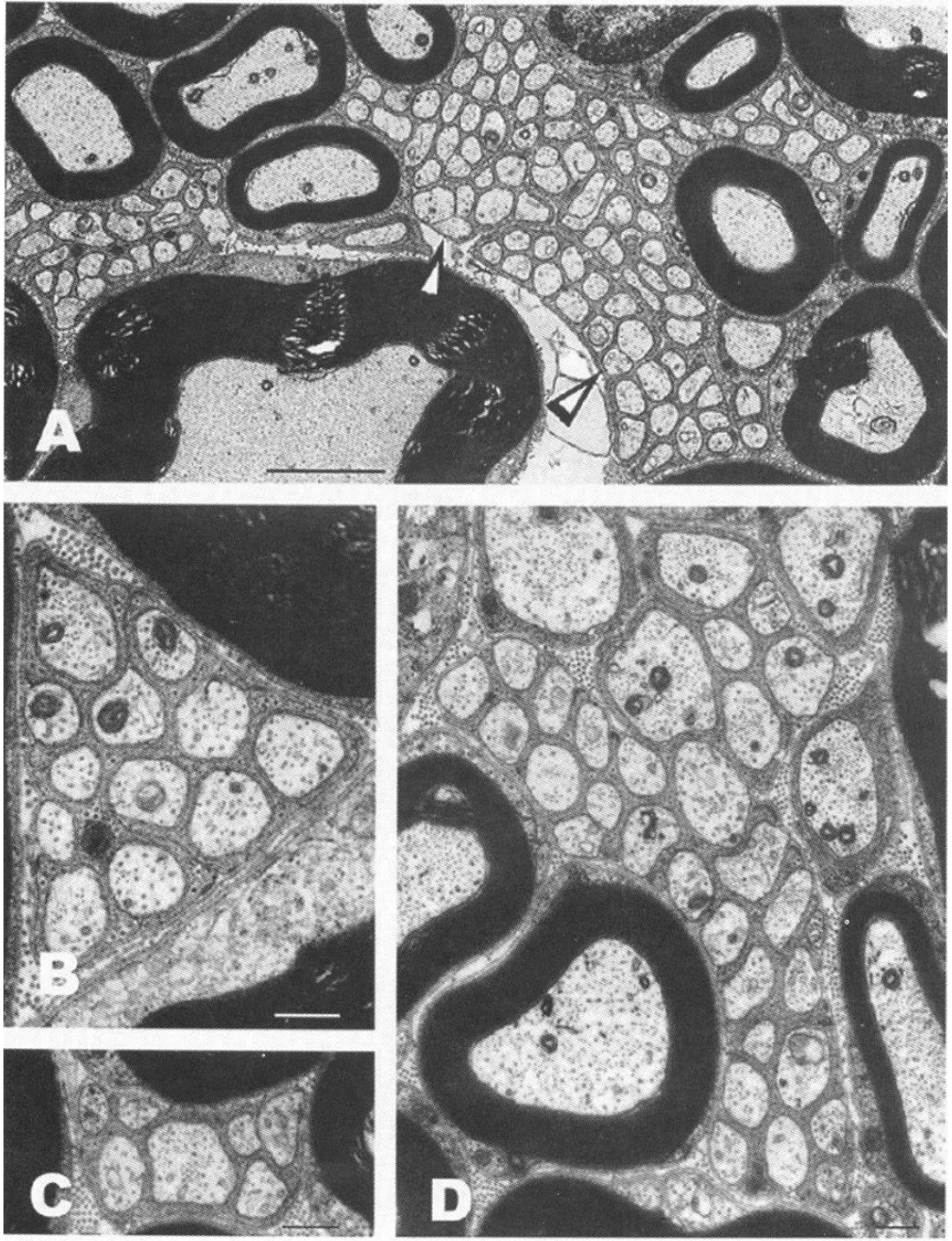


FIGURE 2. A diagram of a peripheral nerve in cross section. The nerve contains three fascicles. The figure on the left represents a high magnification of a myelinated axon in cross-section.

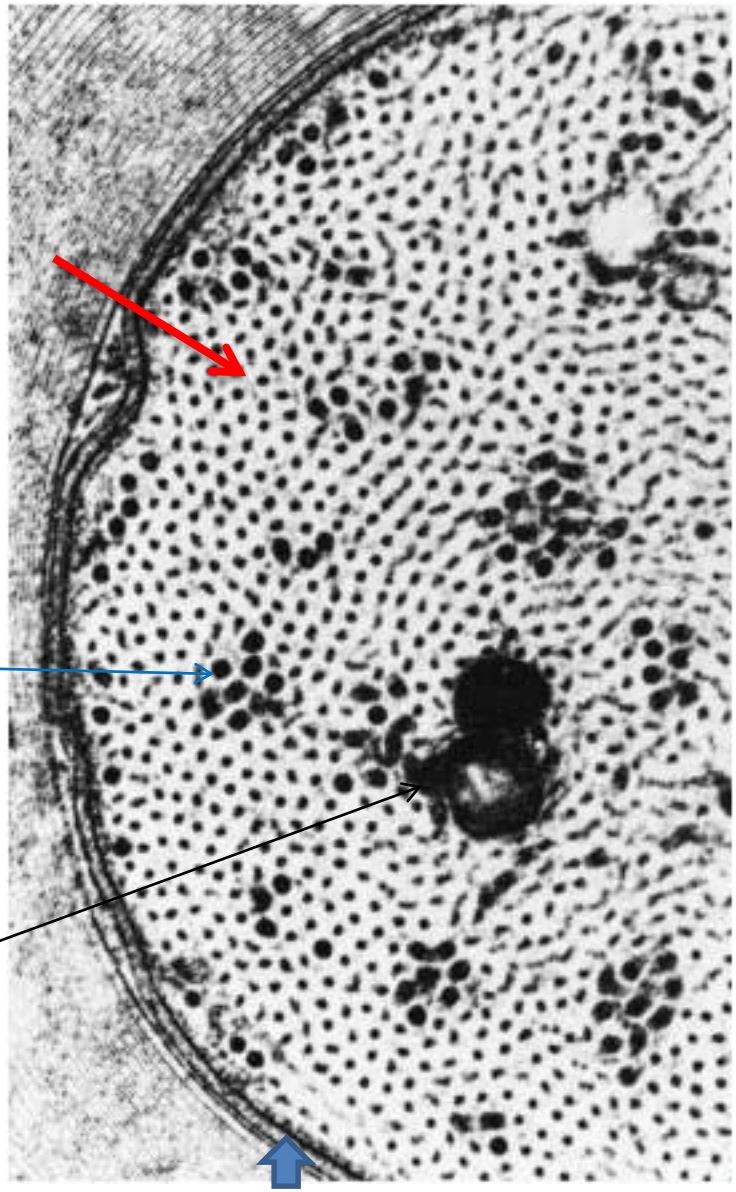
Arrowheads point to Remak Bundles



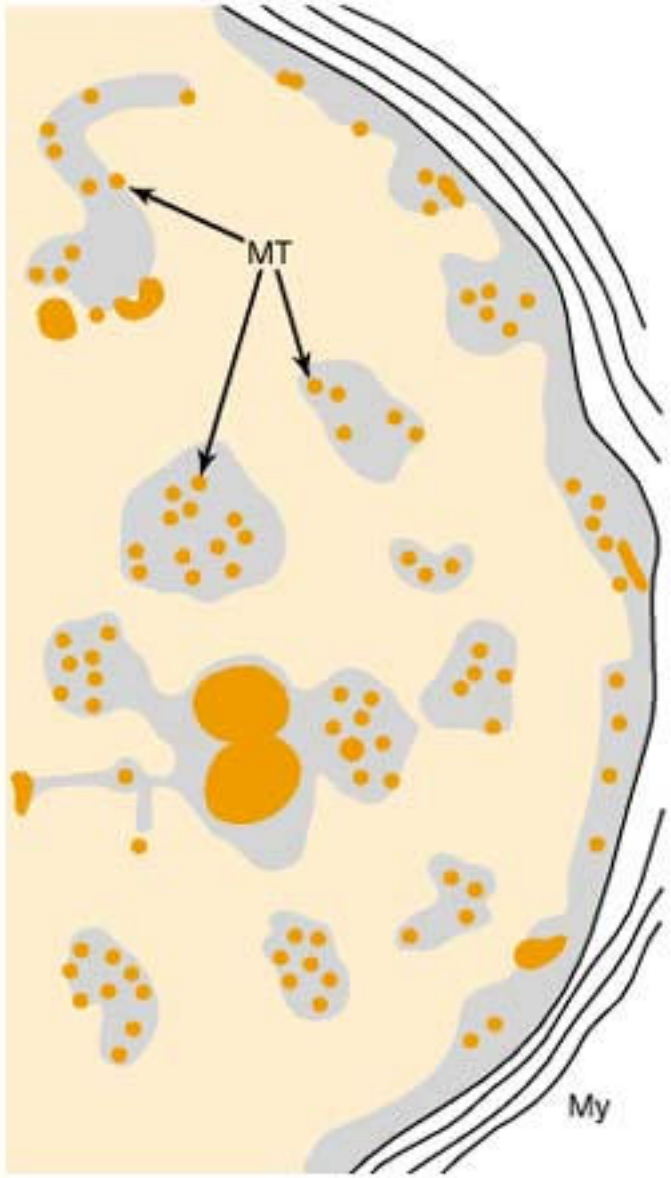
Neurofilaments

Microtubules

Organelles in fast axoplasmic transport



Microfilaments



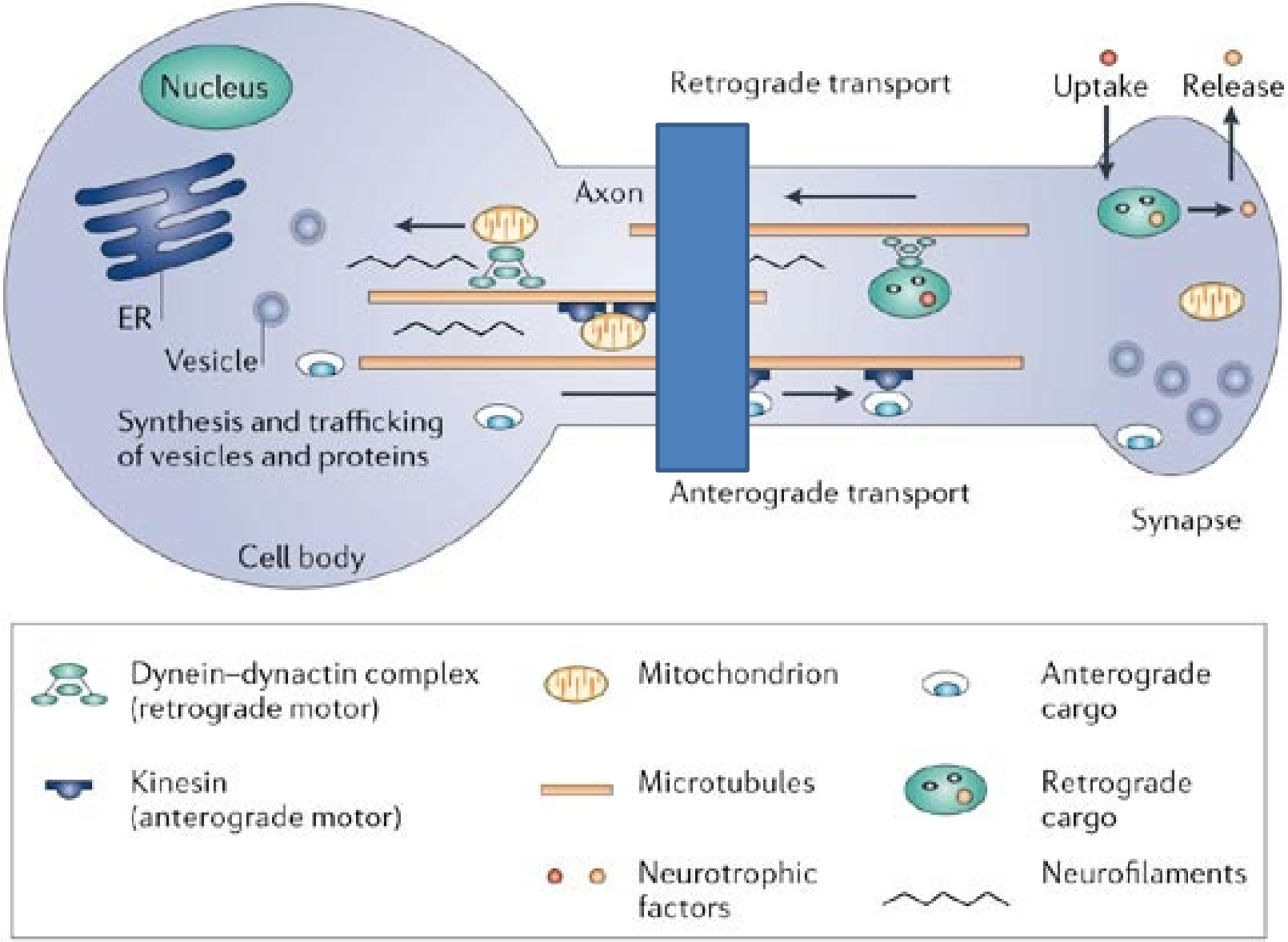


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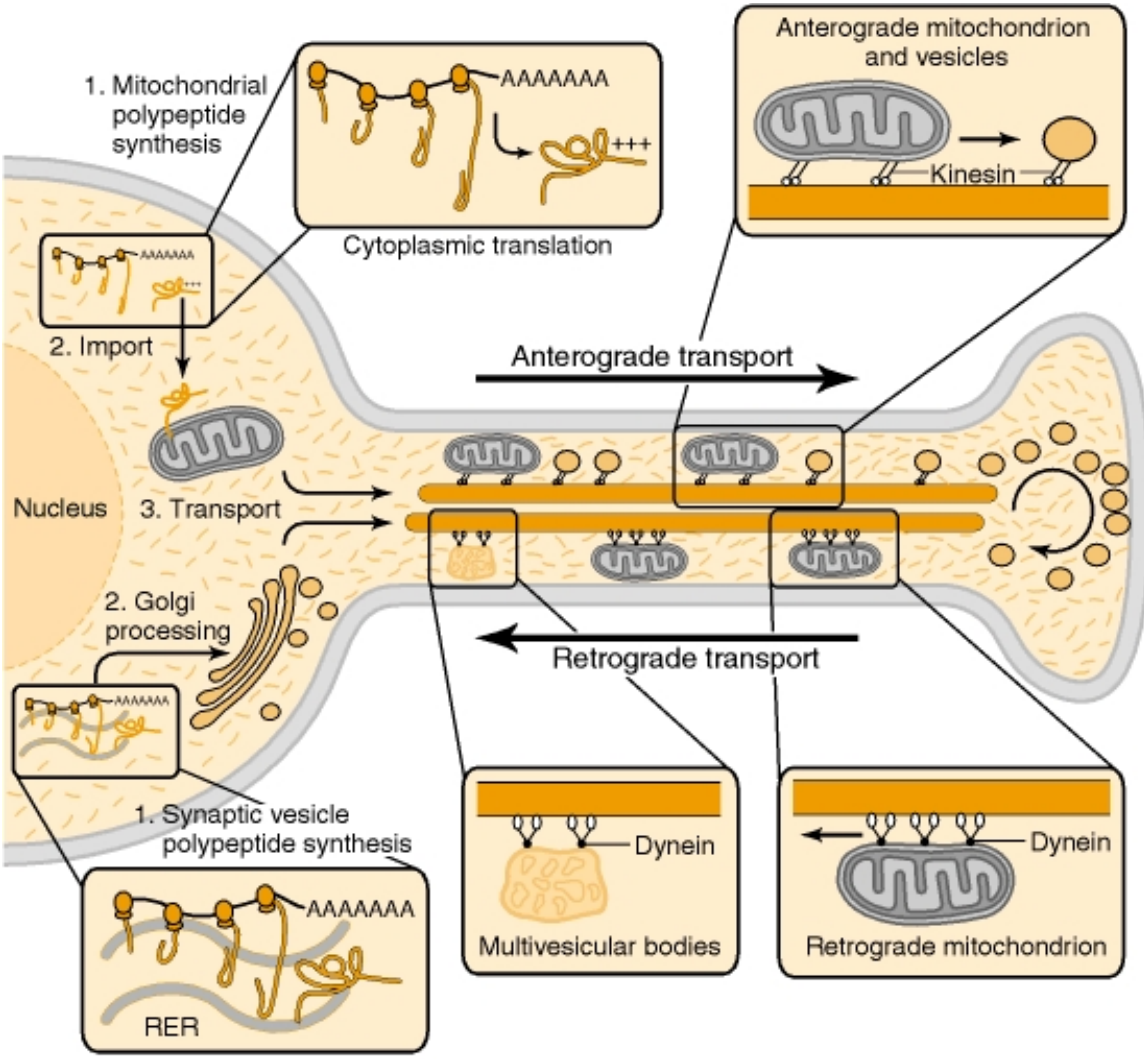
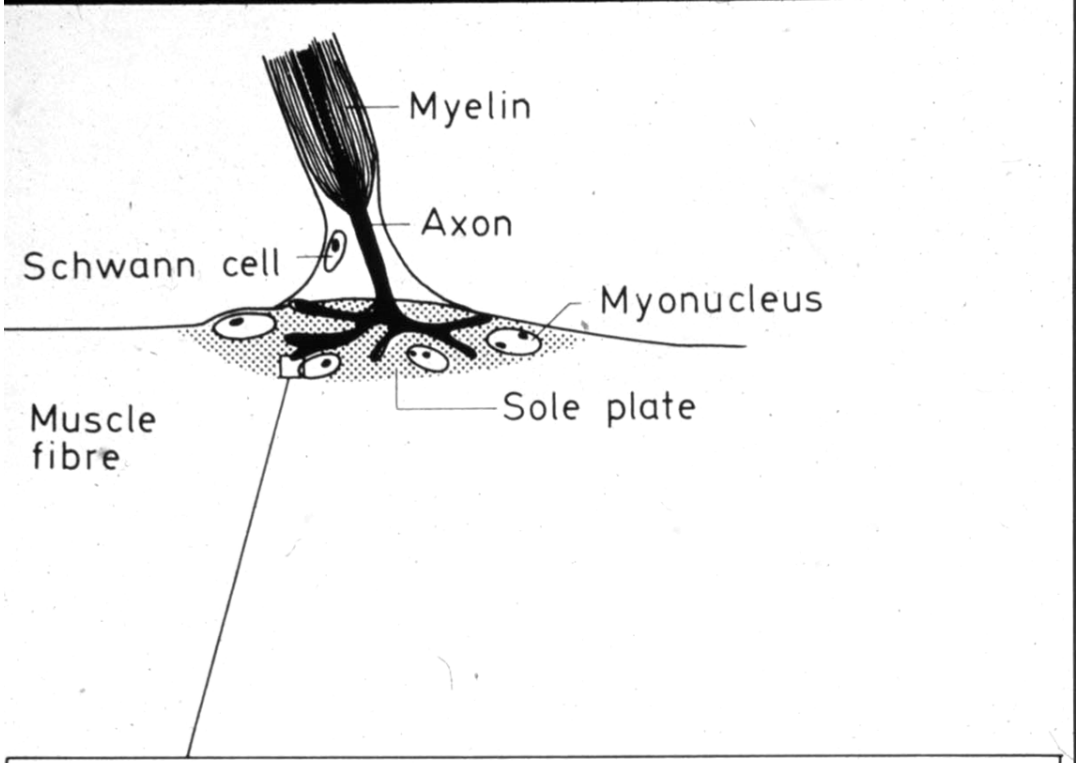
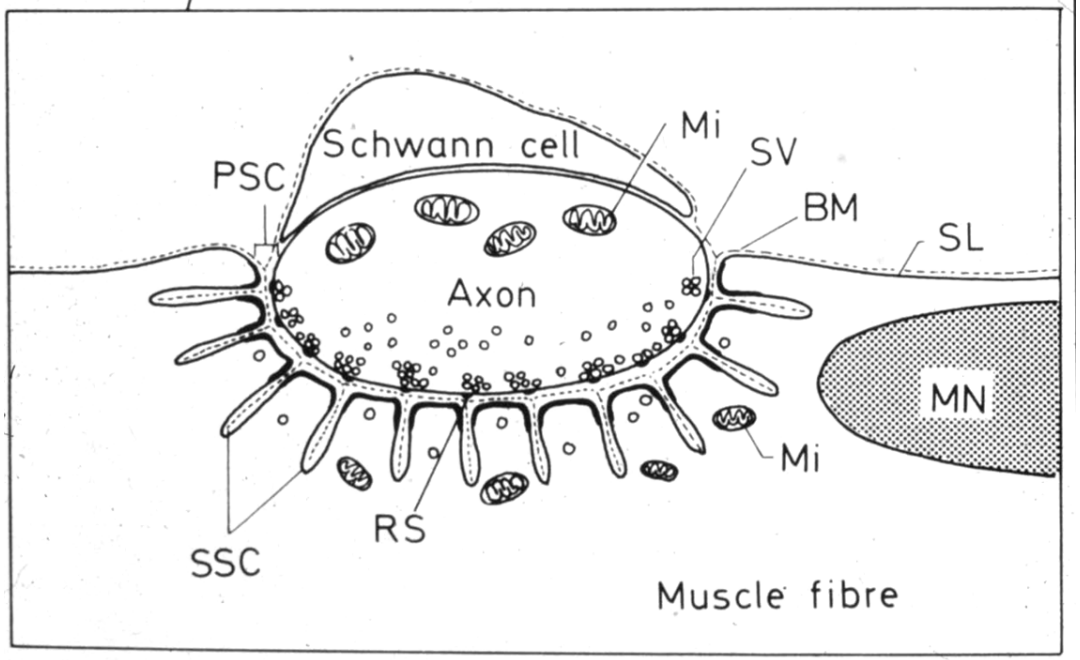
Table 1 | **The moving structures of axonal transport***

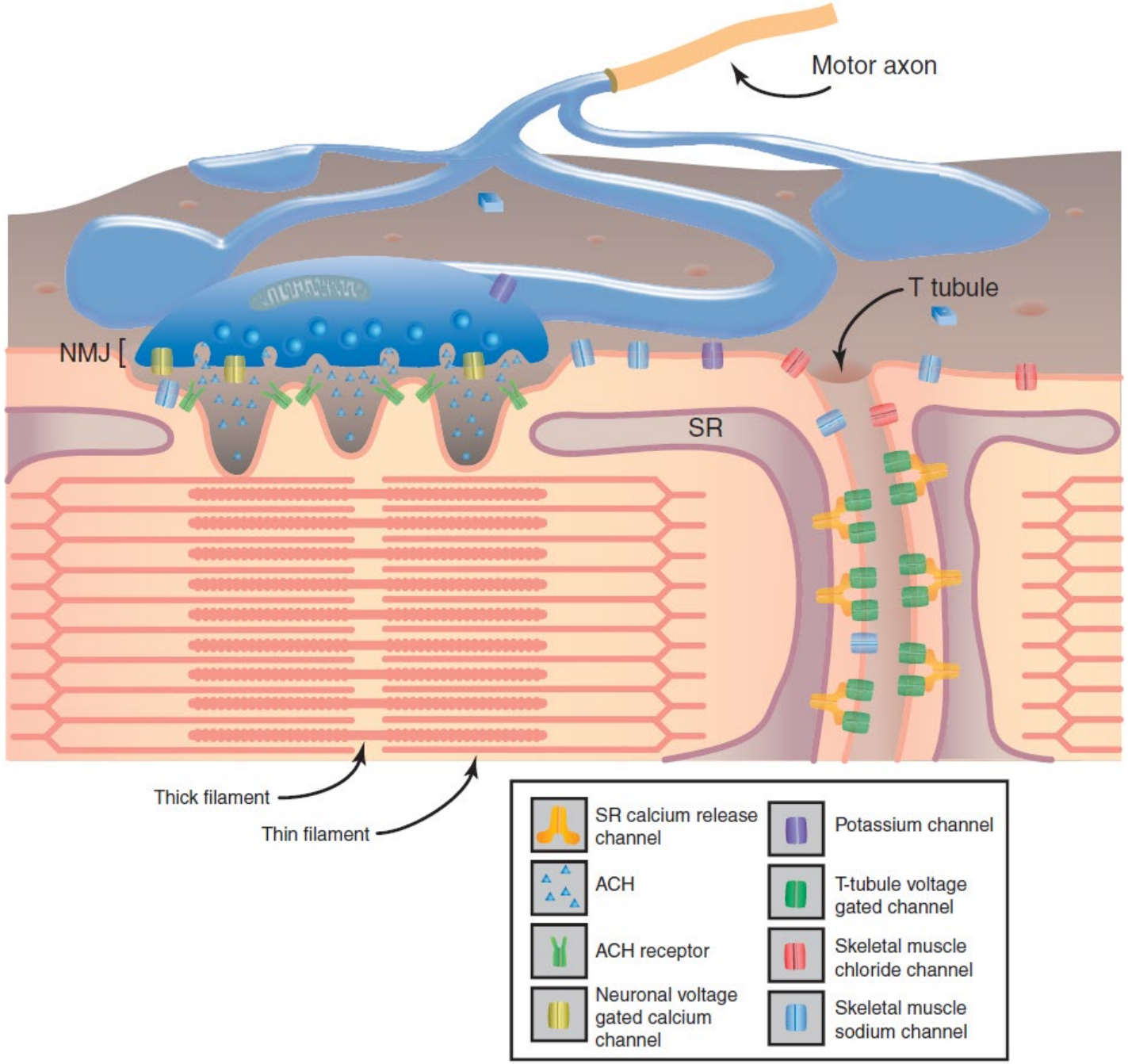
Rate class	Average rate	Moving structures	Composition (selected examples)
Fast components			
Fast anterograde	200–400 mm day^{-1} (≈2–5 μm s^{-1})	Golgi-derived vesicles and tubules (secretory pathway)	Synaptic vesicle proteins, kinesin, enzymes of neurotransmitter metabolism
Bi-directional	50–100 mm day^{-1} (≈0.5–1 μms^{-1})	Mitochondria	Cytochromes, enzymes of oxidative phosphorylation
Fast retrograde	200–400 mm day^{-1} (≈2–5 μm s^{-1})	Endosomes, lysosomes (endocytic pathway)	Internalized membrane receptors, neurotrophins, active lysosomal hydrolases
Slow components			
Slow component 'a'	0.3–3 mm day^{-1}	Neurofilaments, microtubules‡	Neurofilament proteins, tubulin, spectrin, tau proteins
Slow component 'b'	2–8 mm day^{-1} (≈0.02–0.09 μm s^{-1})	Microfilaments, supramolecular complexes of the cytosolic matrix	Actin, clathrin, dynein, dynactin, glycolytic enzymes

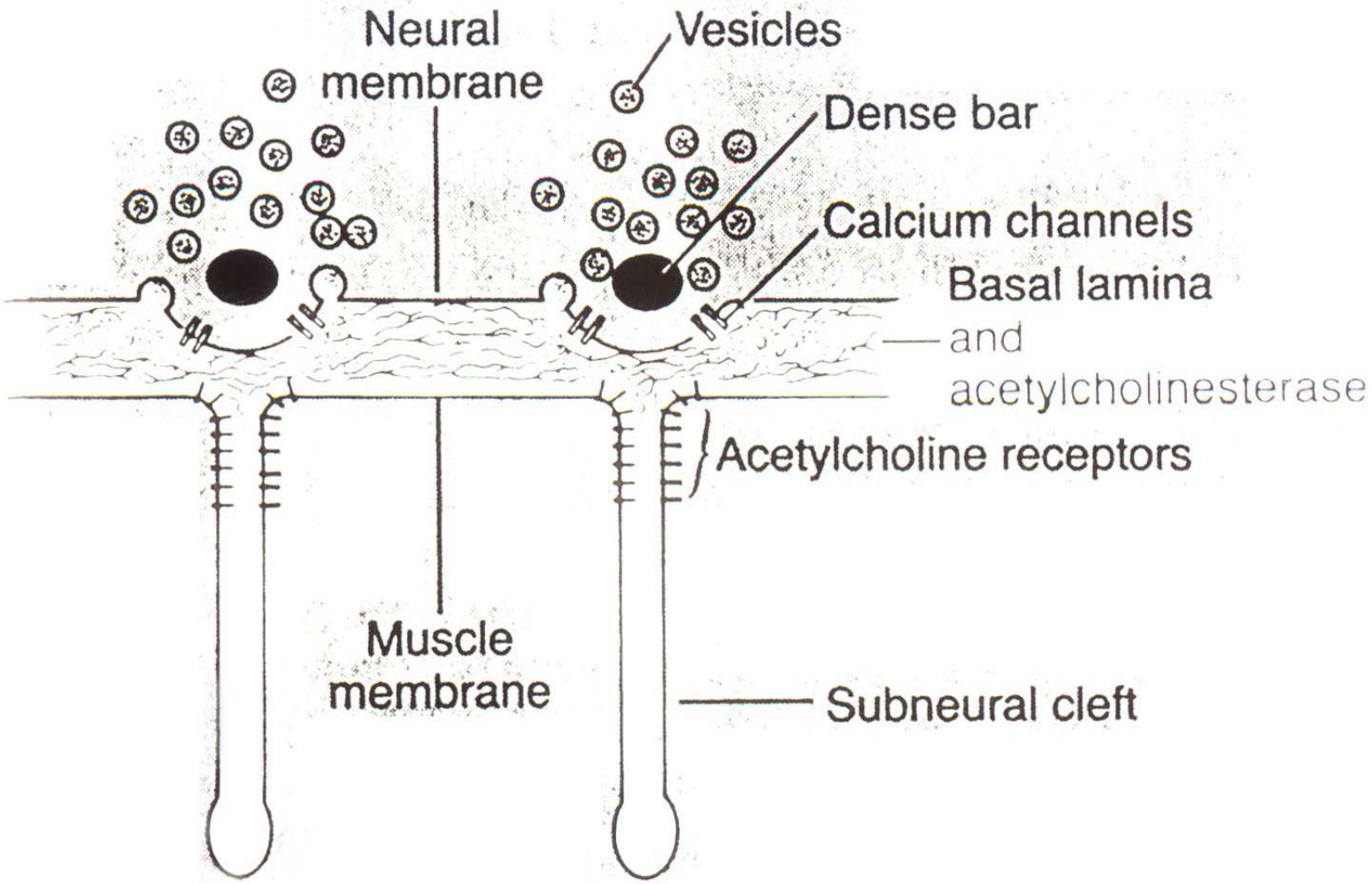
*Data compiled from REFS 1,41,44. ‡ In some neurons, microtubule proteins are transported in slow component 'b' as well as slow component 'a'.

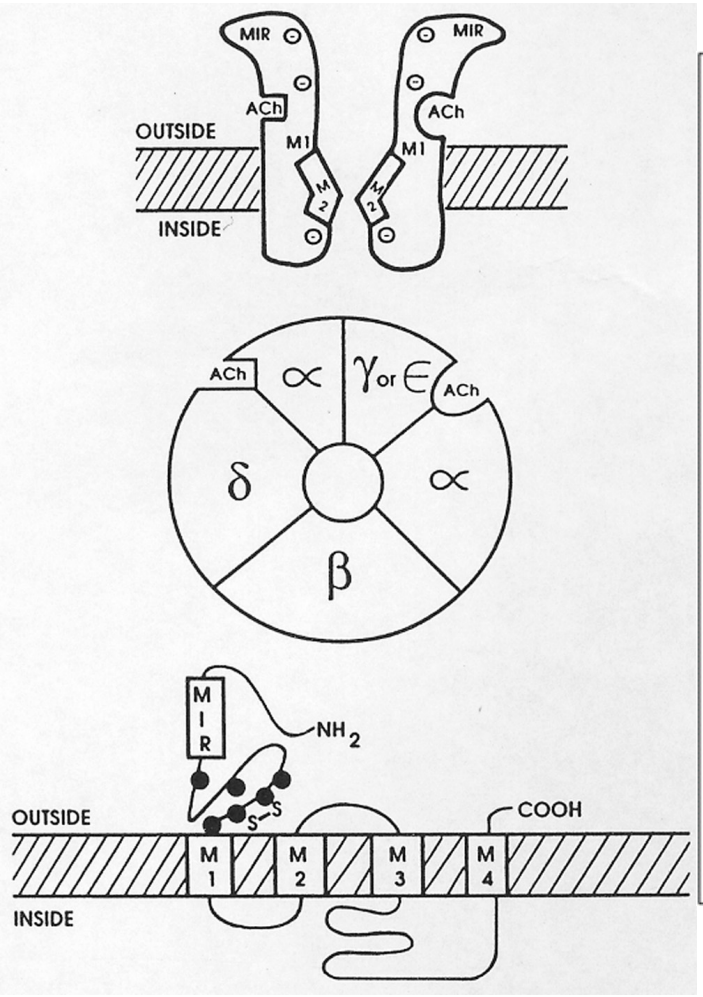


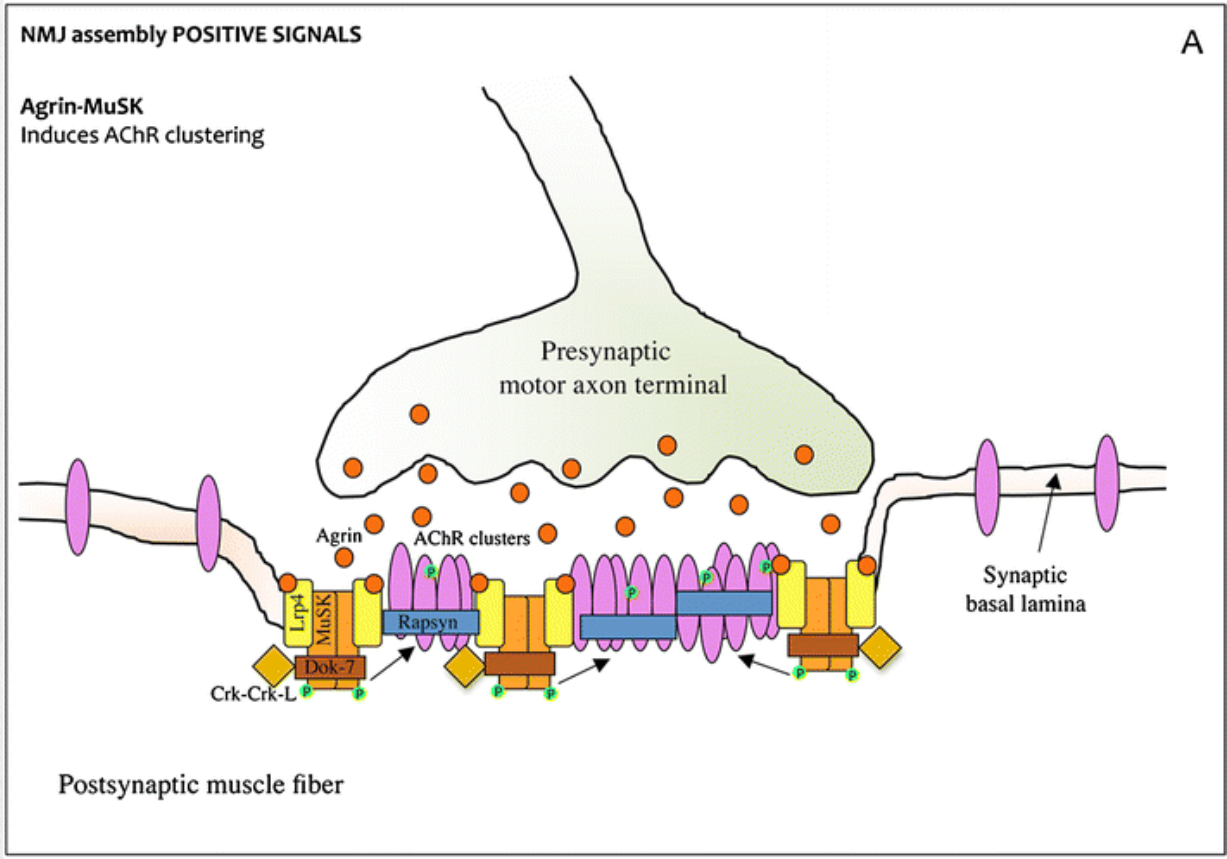

Myelin
Axon
Schwann cell
Myonucleus
Sole plate
Muscle
fibre


Schwann cell
PSC
Mi
SV
BM
SL
Axon
MN
Mi
RS
SSC
Muscle fibre


Motor axon
T tubule
NMJ [
SR
Thick filament
Thin filament
SR calcium release channel
ACH
ACH receptor
Neuronal voltage gated calcium channel
Potassium channel
T-tubule voltage gated channel
Skeletal muscle chloride channel
Skeletal muscle sodium channel

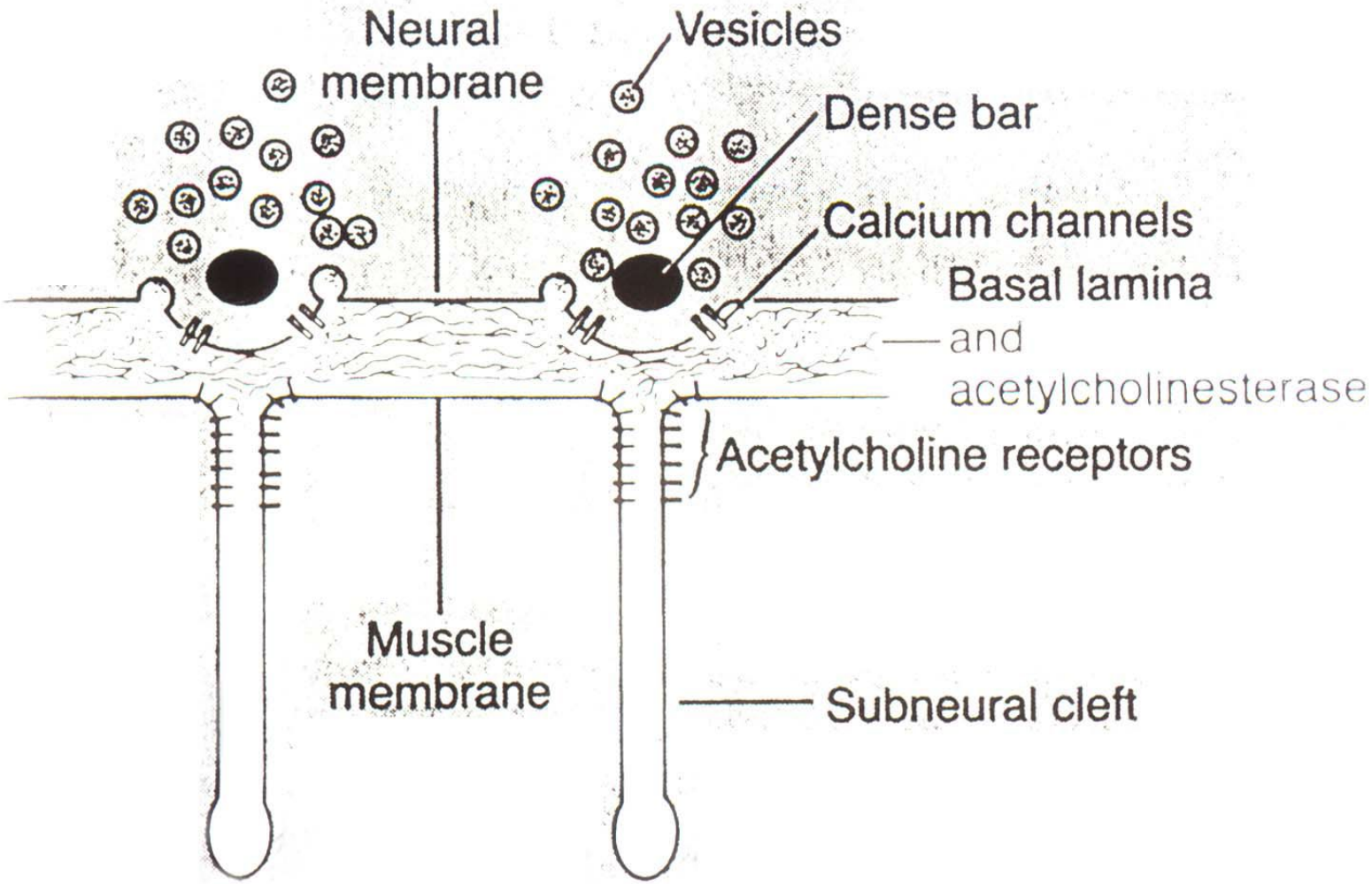

Neural membrane
Vesicles
Dense bar
Calcium channels
Basal lamina
and
acetylcholinesterase
Acetylcholine receptors
Muscle membrane
Subneural cleft

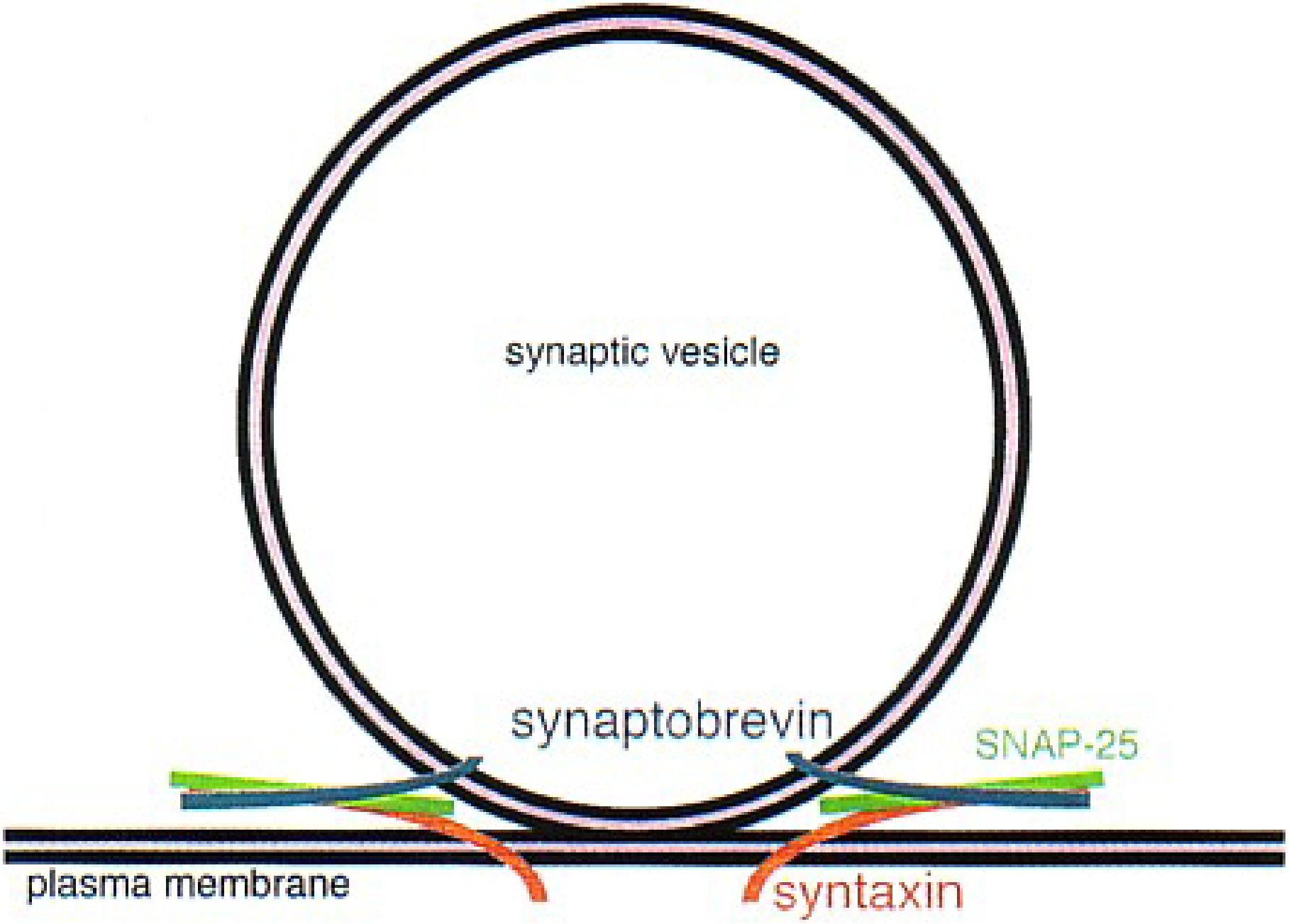




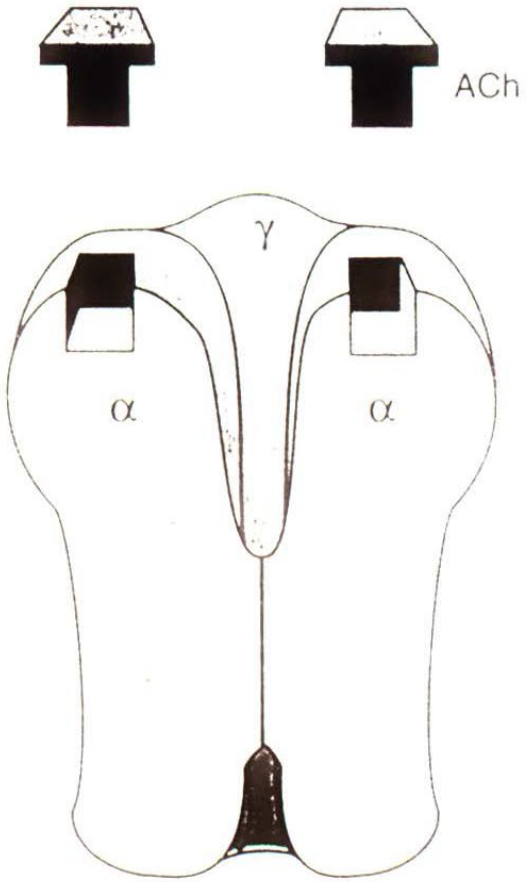
Engel A, ed. Myasthenia Gravis and Myasthenic Disorders, 1999

Ferraro, et al JCSM 2011

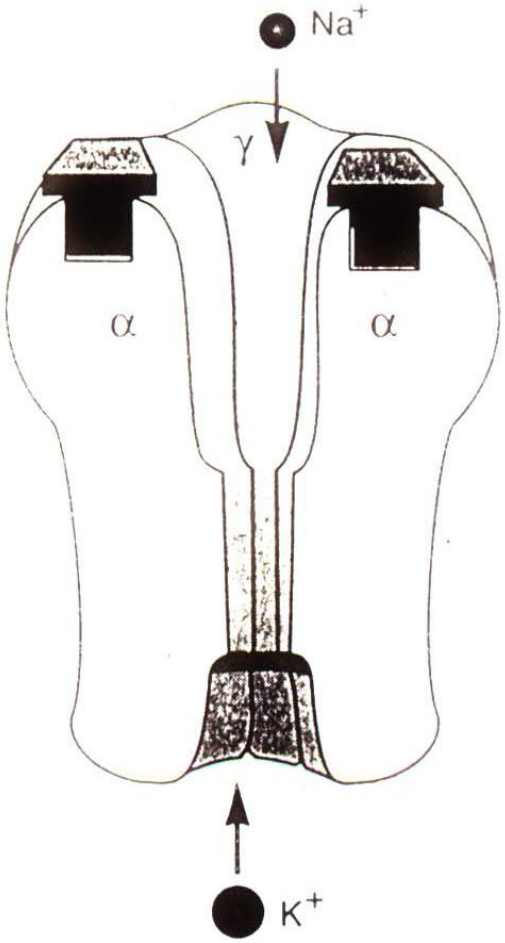

Neural membrane
Vesicles
Dense bar
Calcium channels
Basal lamina
and
acetylcholinesterase
Acetylcholine receptors
Muscle membrane
Subneural cleft

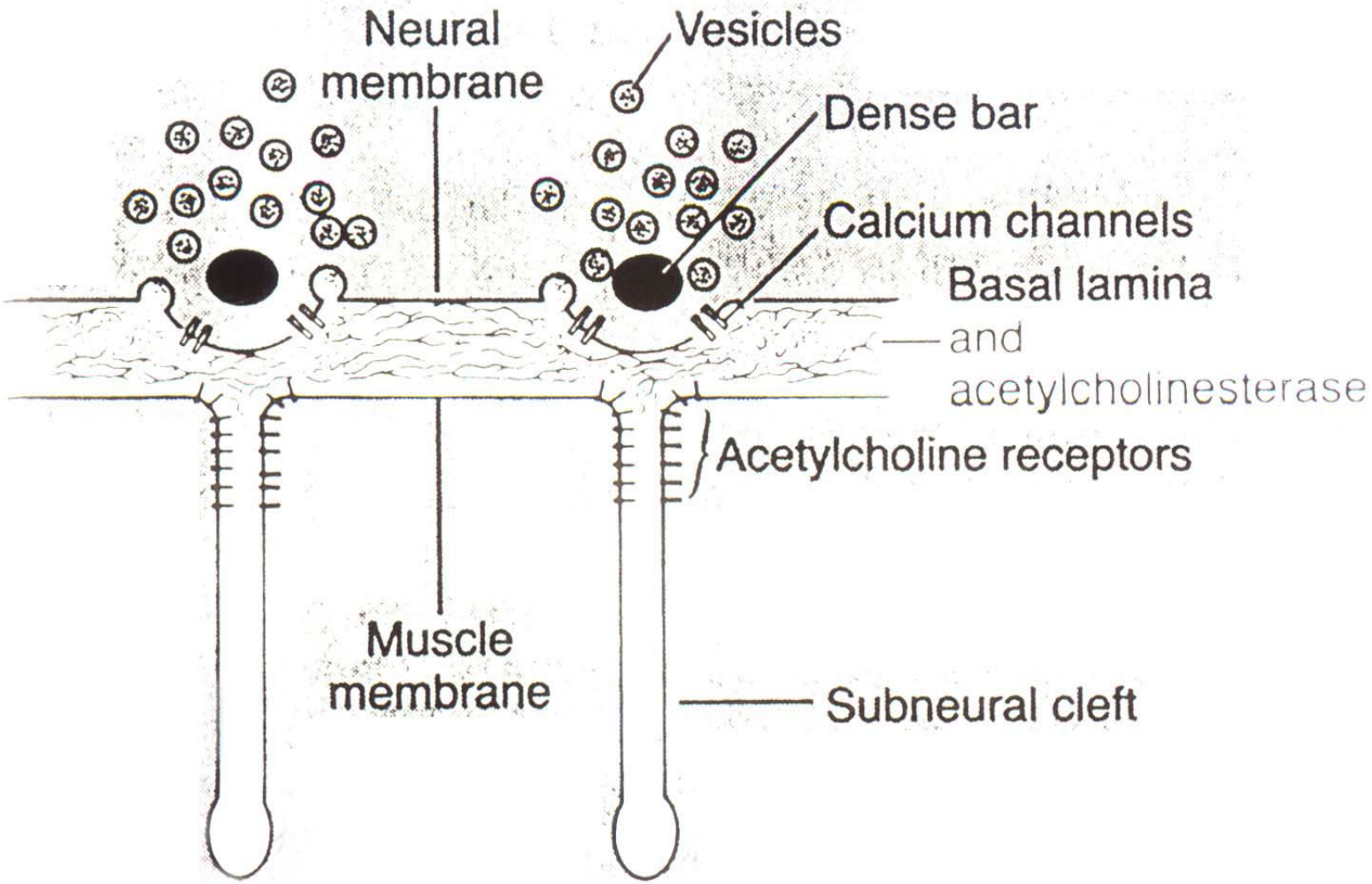

synaptic vesicle
synaptobrevin
SNAP-25
plasma membrane
syntaxin

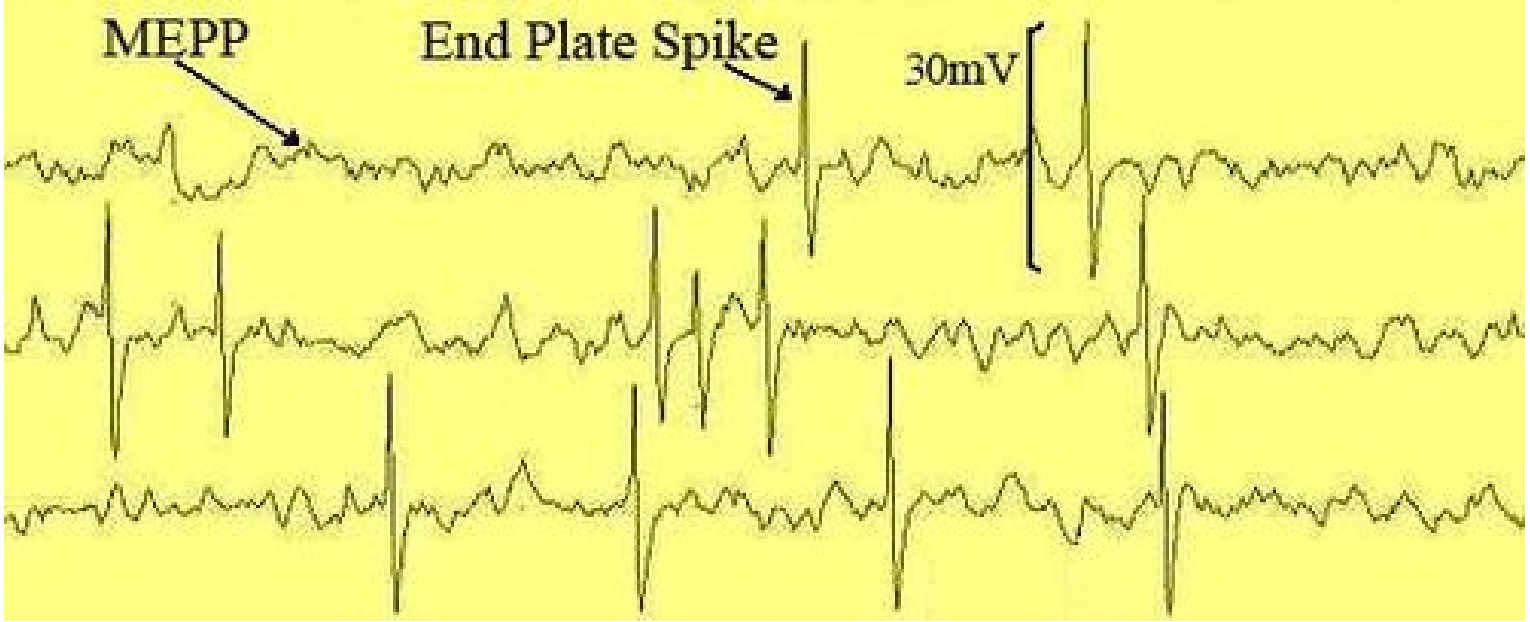
B_1 No ACh bound:
Channel closed



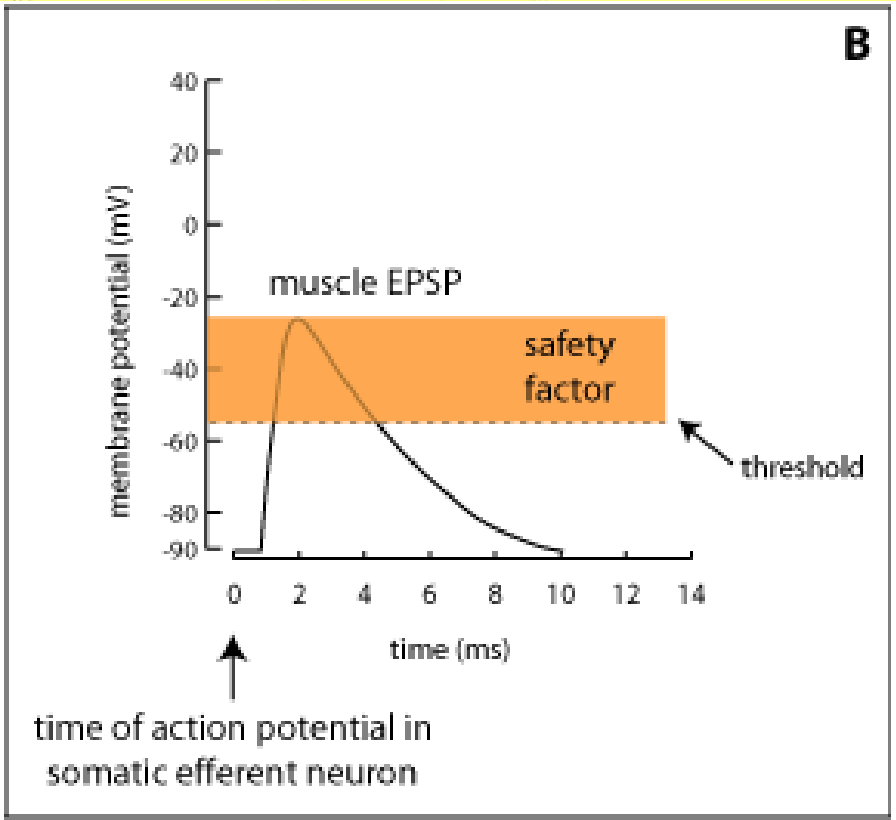
B_2 2 ACh molecules bound:
Channel open



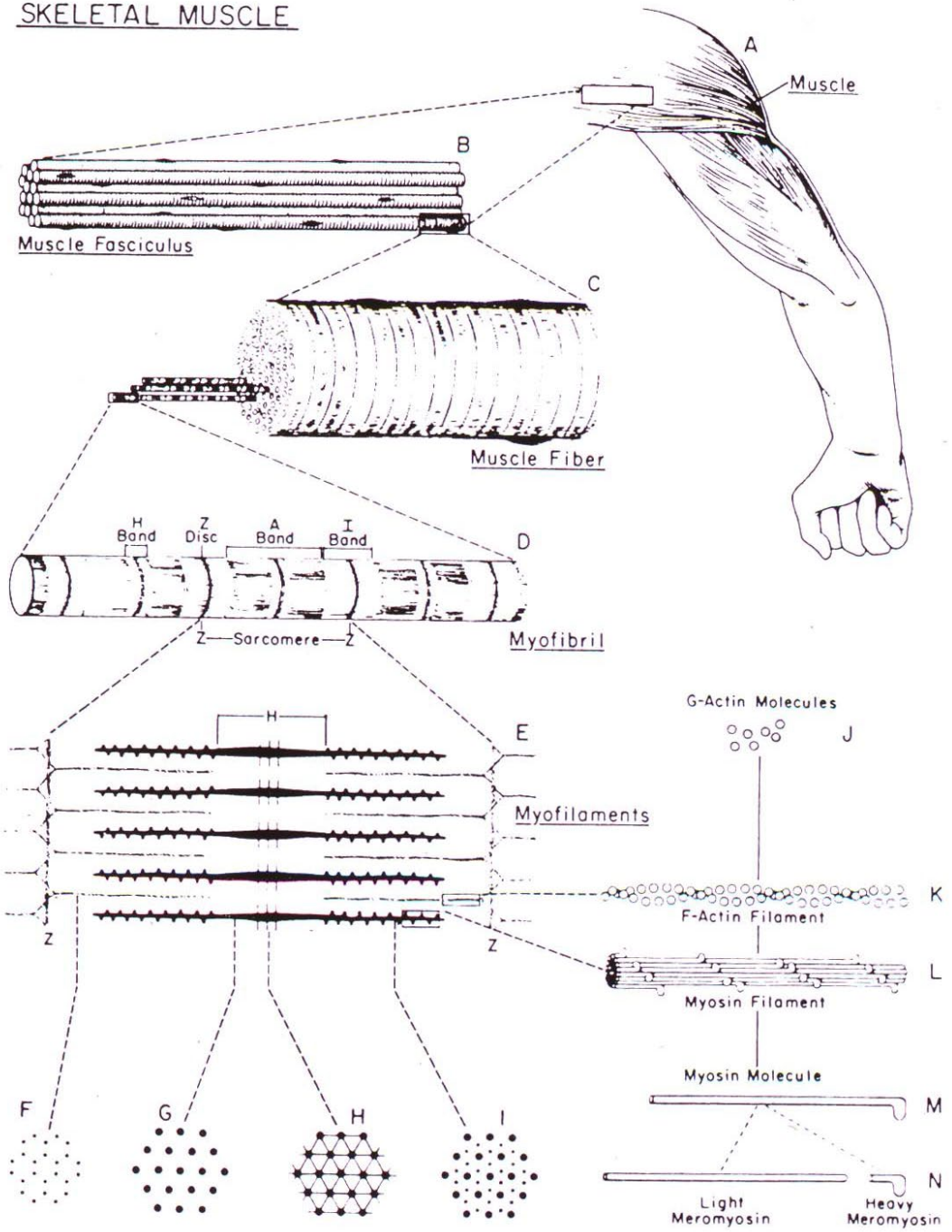

Neural membrane
Vesicles
Dense bar
Calcium channels
Basal lamina
and
acetylcholinesterase
Acetylcholine receptors
Muscle membrane
Subneural cleft



Neuromuscular Junction Safety Factor



SKELETAL MUSCLE



Because one sarcomere can shorten by a certain length with a given maximal velocity, both the range of motion and the maximal shortening velocity of a muscle fiber are proportional to the number of sarcomeres in series. The force that a myofibril can exert is equal to the average sarcomere force and is not influenced by the number of sarcomeres in series. The force capacity of a fiber, however, depends on the number of sarcomeres in parallel and hence on the diameter or cross-sectional area of the fiber.

At the level of the muscle, the functional attributes of the fibers are modified by the orientation of the fascicles to the line of pull of the muscle and the length of the fiber relative to the muscle length. In most muscles the fascicles are not parallel to the line of pull but fan out in feather-like (pennate) arrangements (Figure 34–11).

more fibers can fit into a given volume as the pennation angle increases, muscles with large pennation angles typically have more myofibrils in parallel and hence large cross-sectional areas. Given the linear relation between cross-sectional area and maximal force (~0.25 $N \cdot mm^{-2}$), these muscles are capable of a greater maximal force. However, the fibers in pennate muscles are generally short and have a lesser maximal shortening velocity than those in nonpennate muscles.

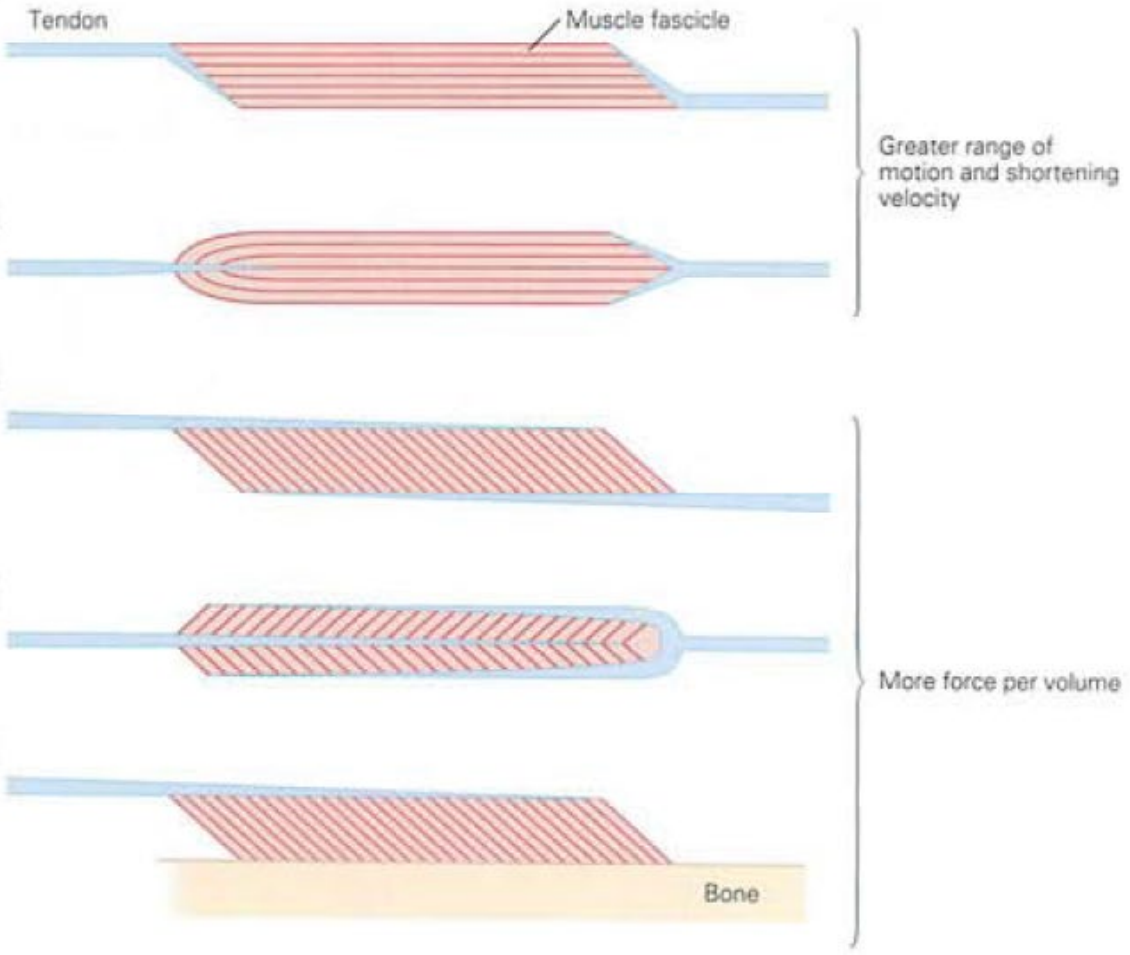
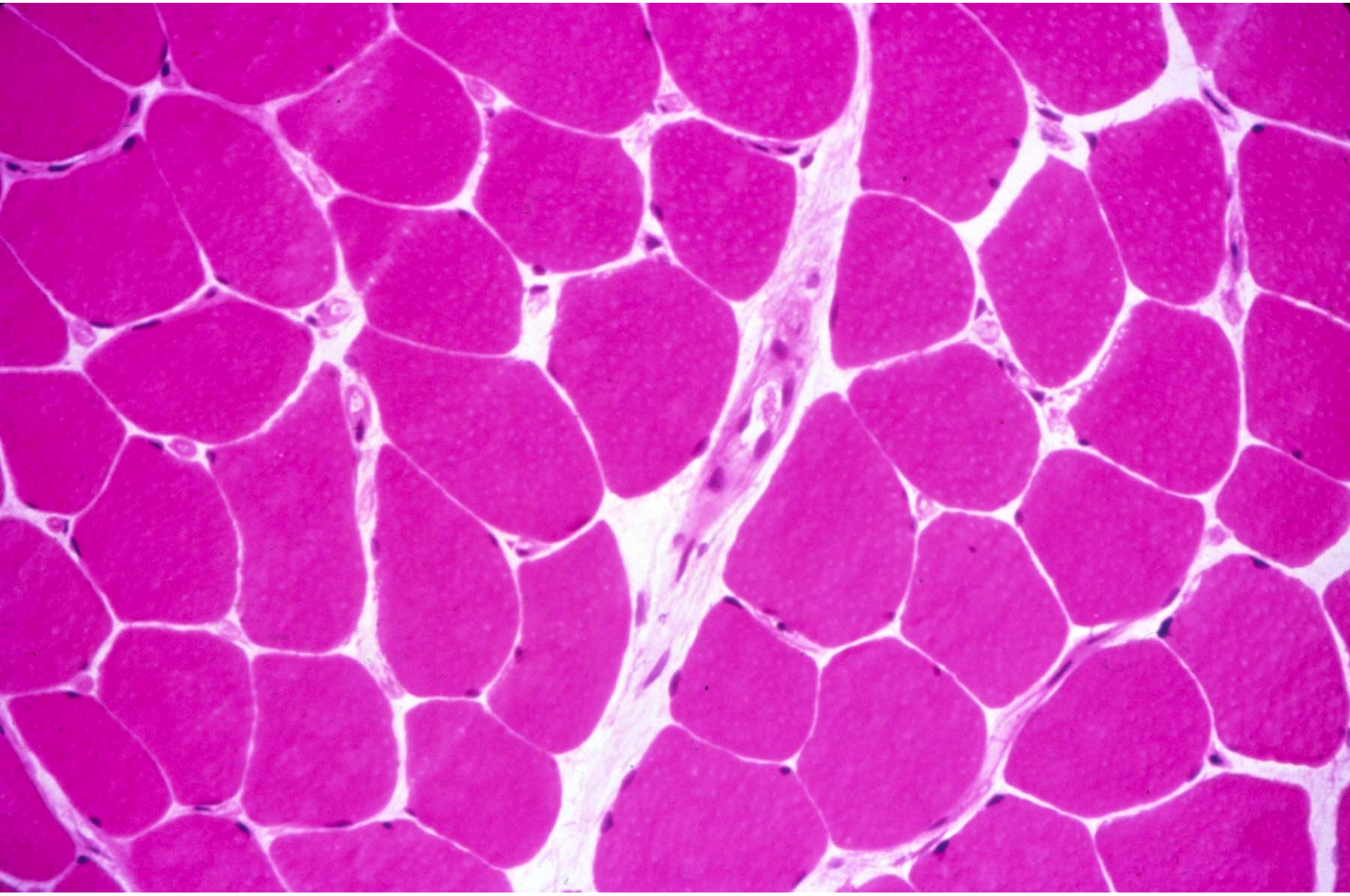
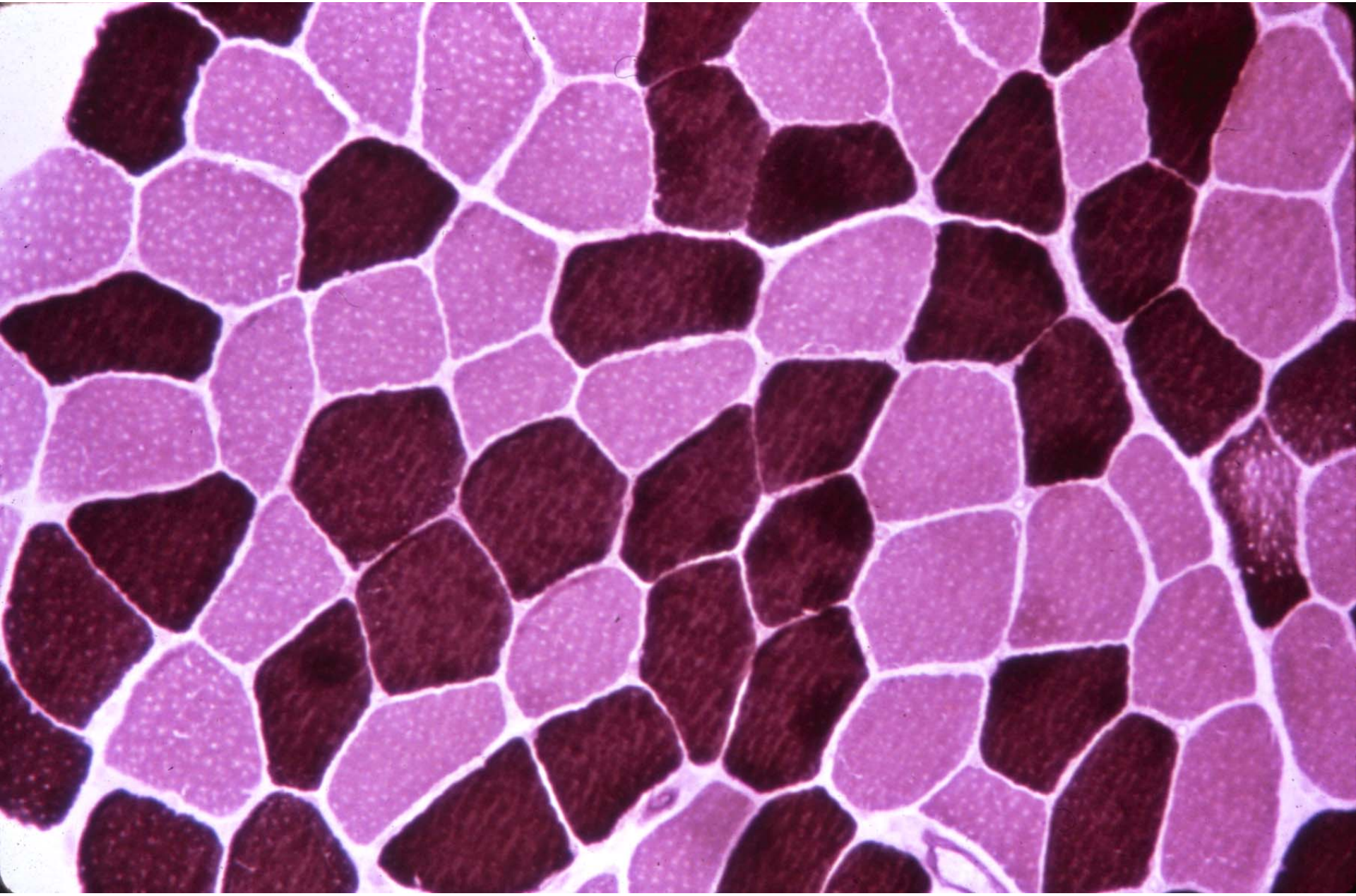
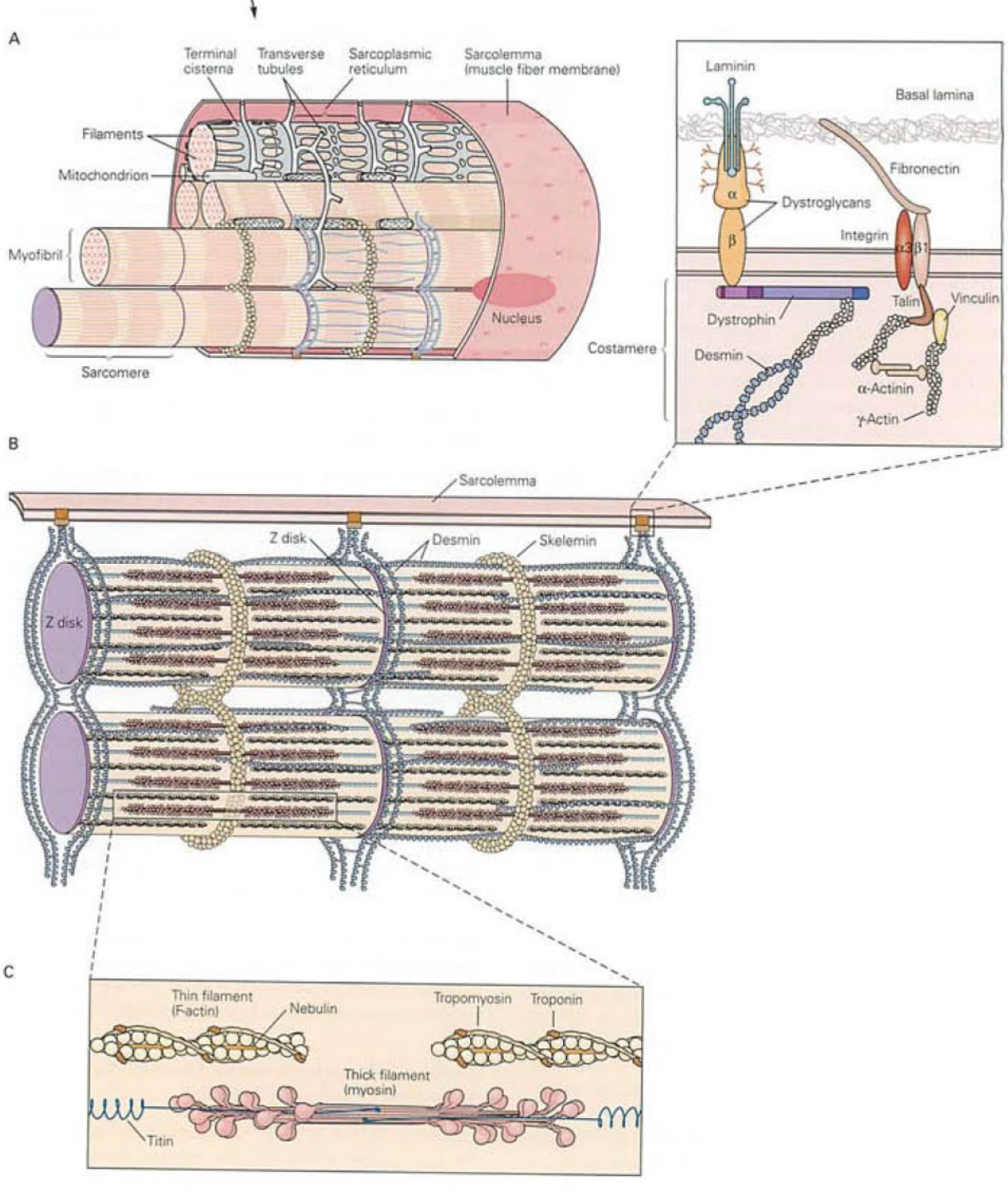
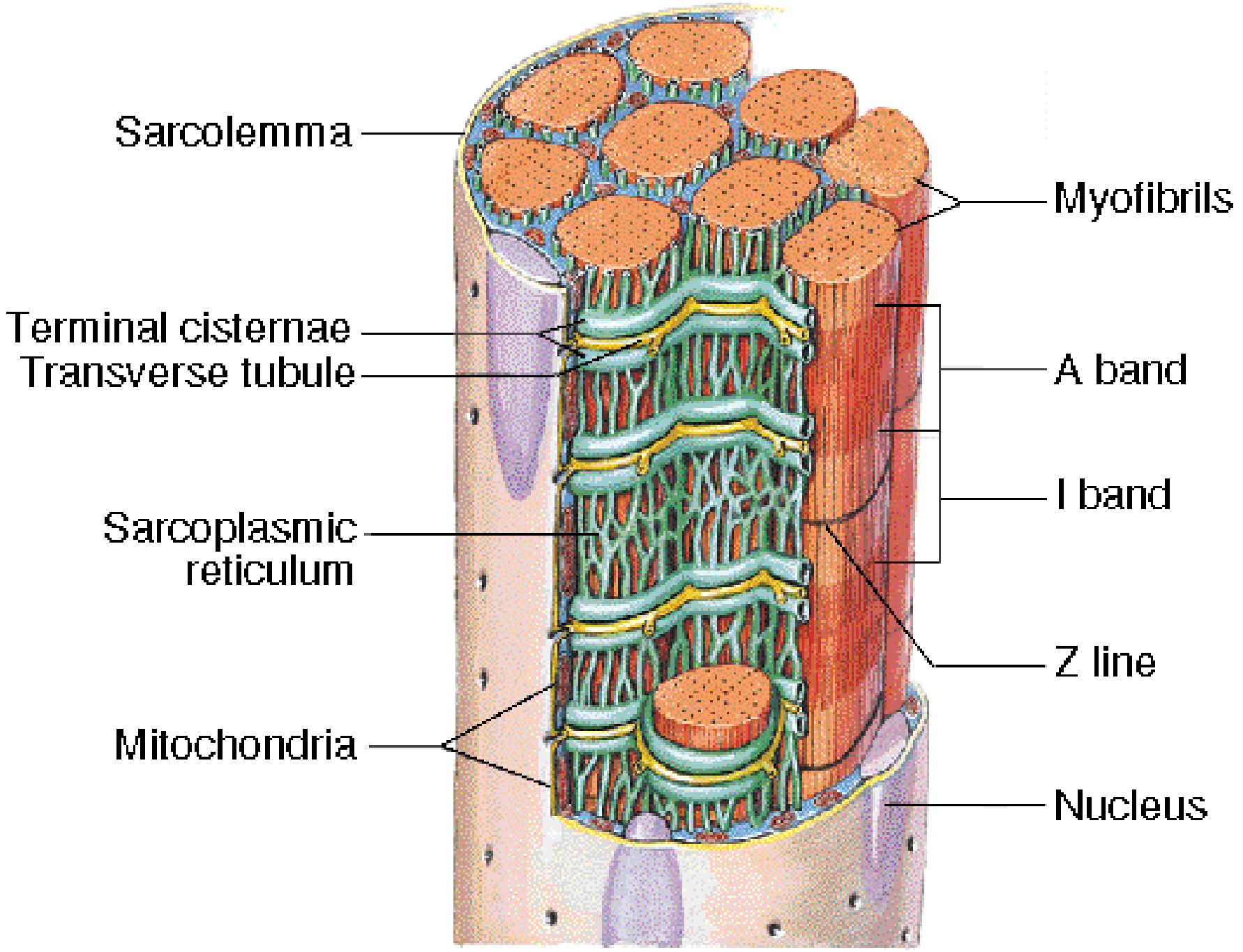


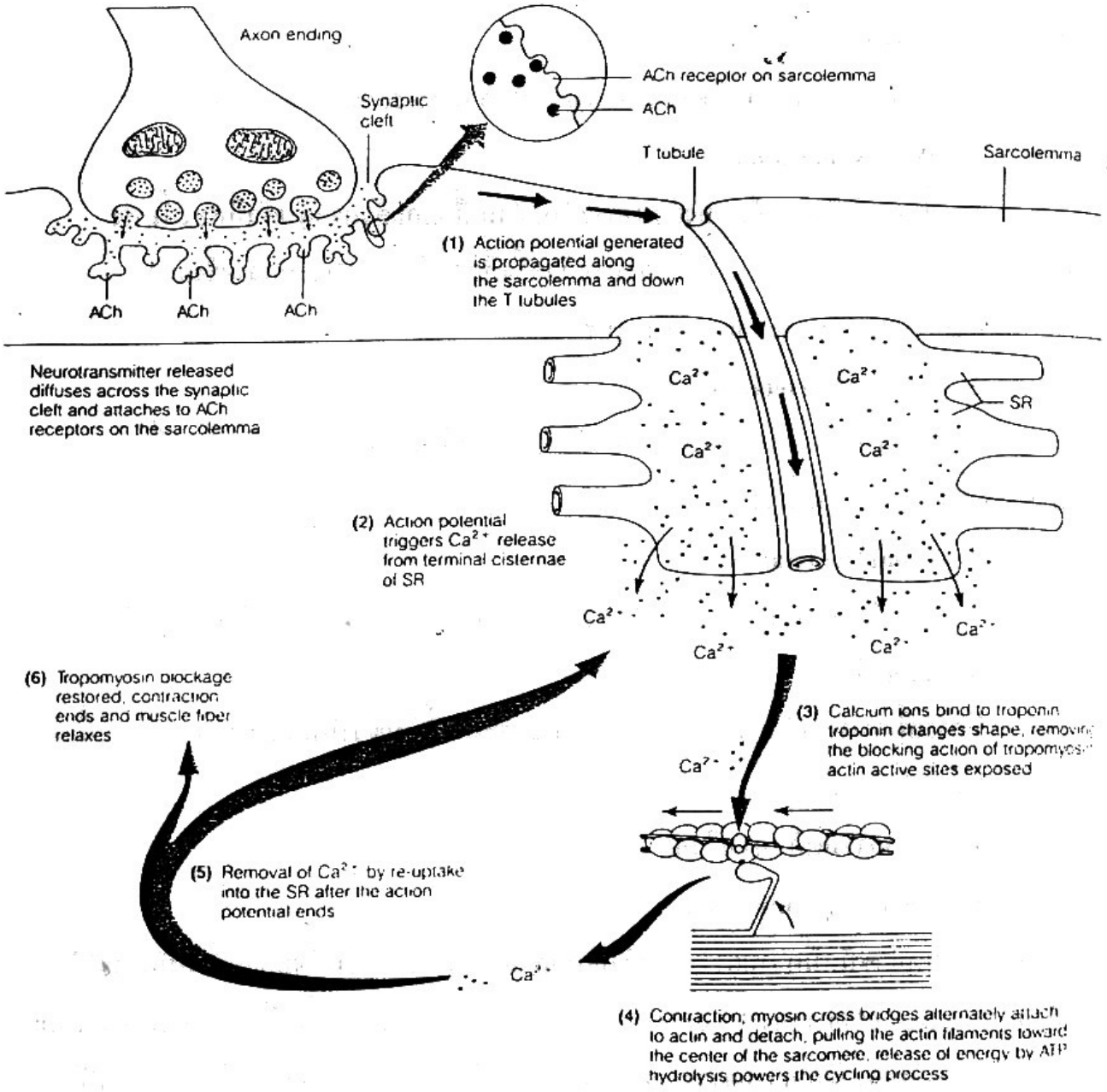
Figure 34–11 Five common arrangements of tendon and muscle. (Reproduced, with permission, from Alexander and Ker 1990.)

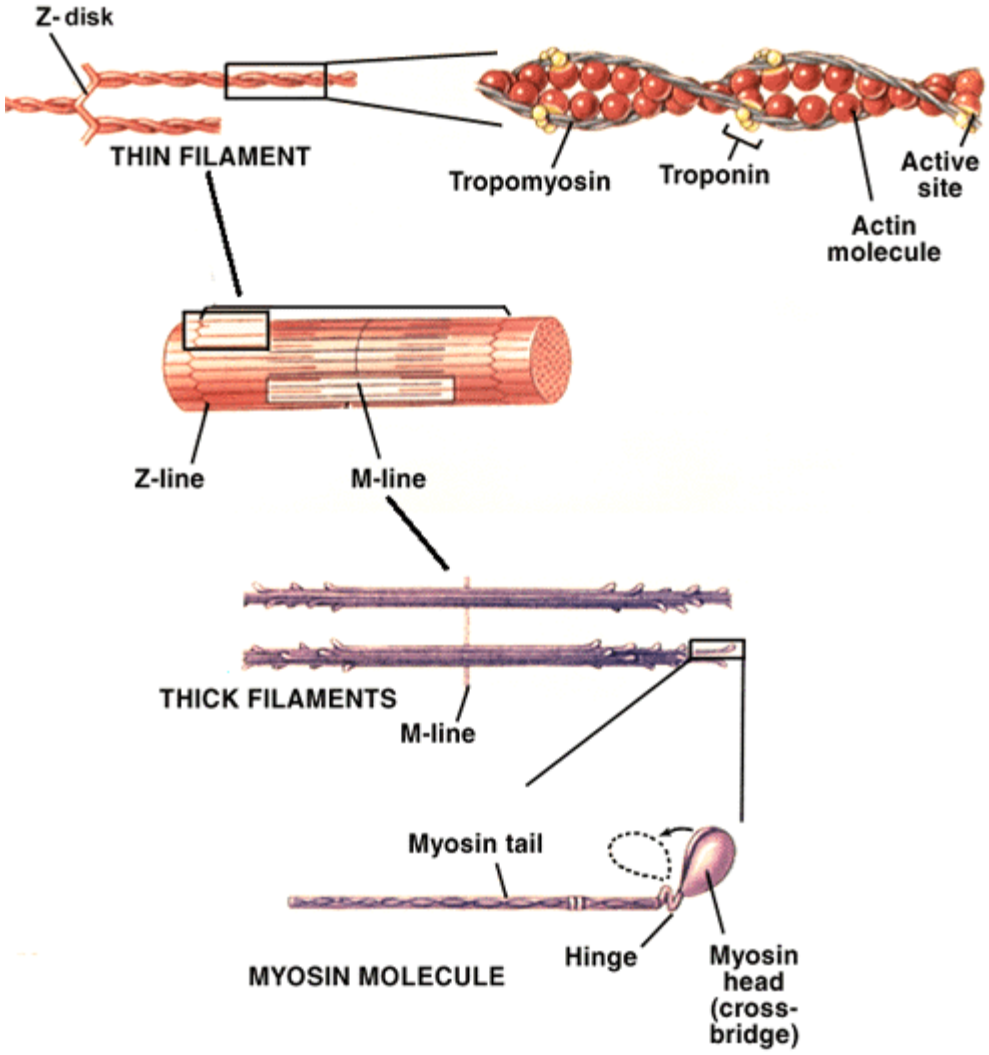


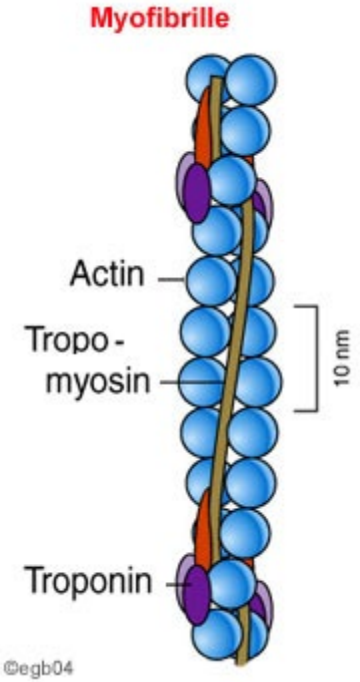



A
Terminal cisterna
Transverse tubules
Sarcoplasmic reticulum
Sarcolemma (muscle fiber membrane)
Filaments
Mitochondrion
Myofibril
Nucleus
Sarcomere
Laminin
Basal lamina
Fibronectin
α
Dystroglycans
β
Integrin
α3β1
Talin
Vinculin
Dystrophin
Costamere
Desmin
α-Actinin
γ-Actin
B
Sarcolemma
Z disk
Desmin
Skelemin
Z disk
C
Thin filament (F-actin)
Nebulin
Tropomyosin
Troponin
Thick filament (myosin)
Titin

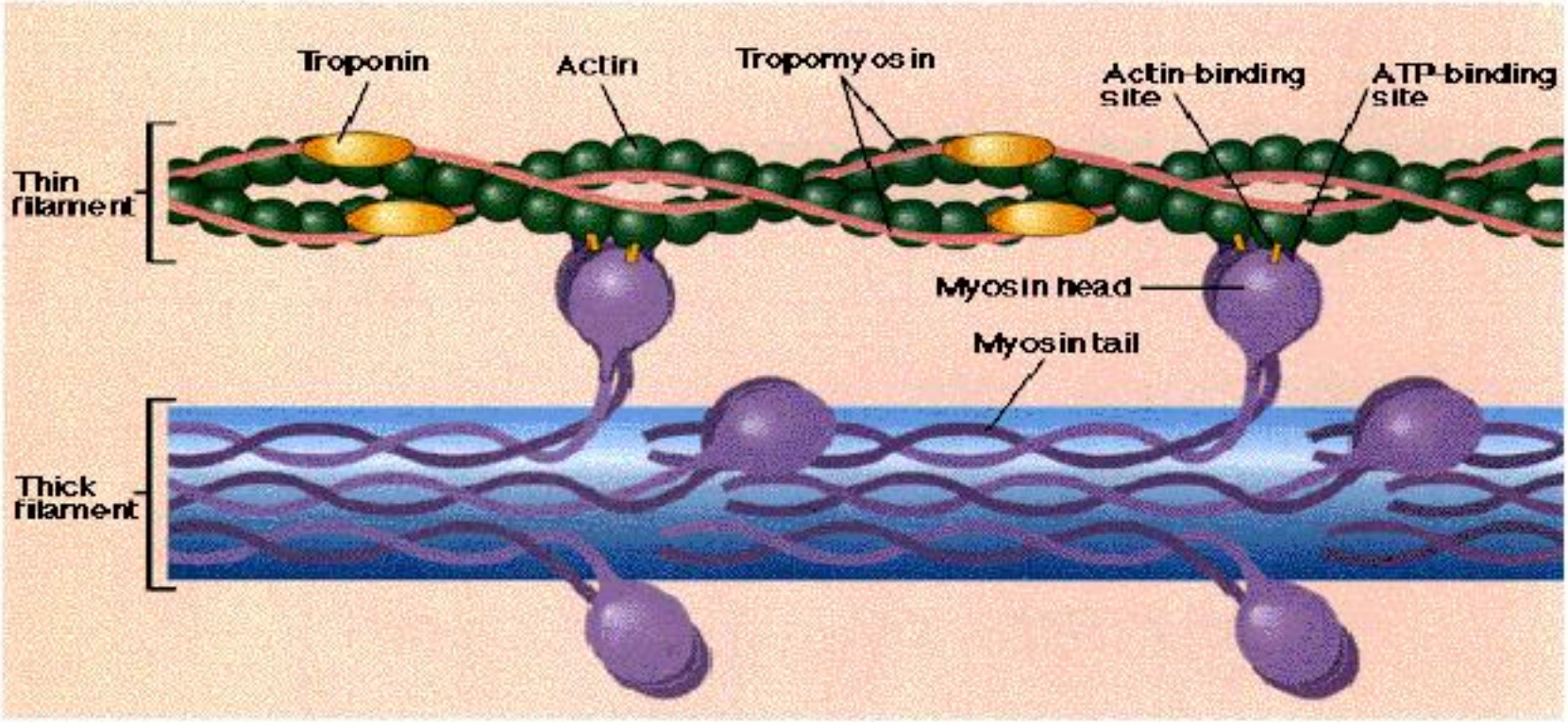

Sarcolemma
Myofibrils
Terminal cisternae
Transverse tubule
A band
I band
Sarcoplasmic reticulum
Z line
Mitochondria
Nucleus

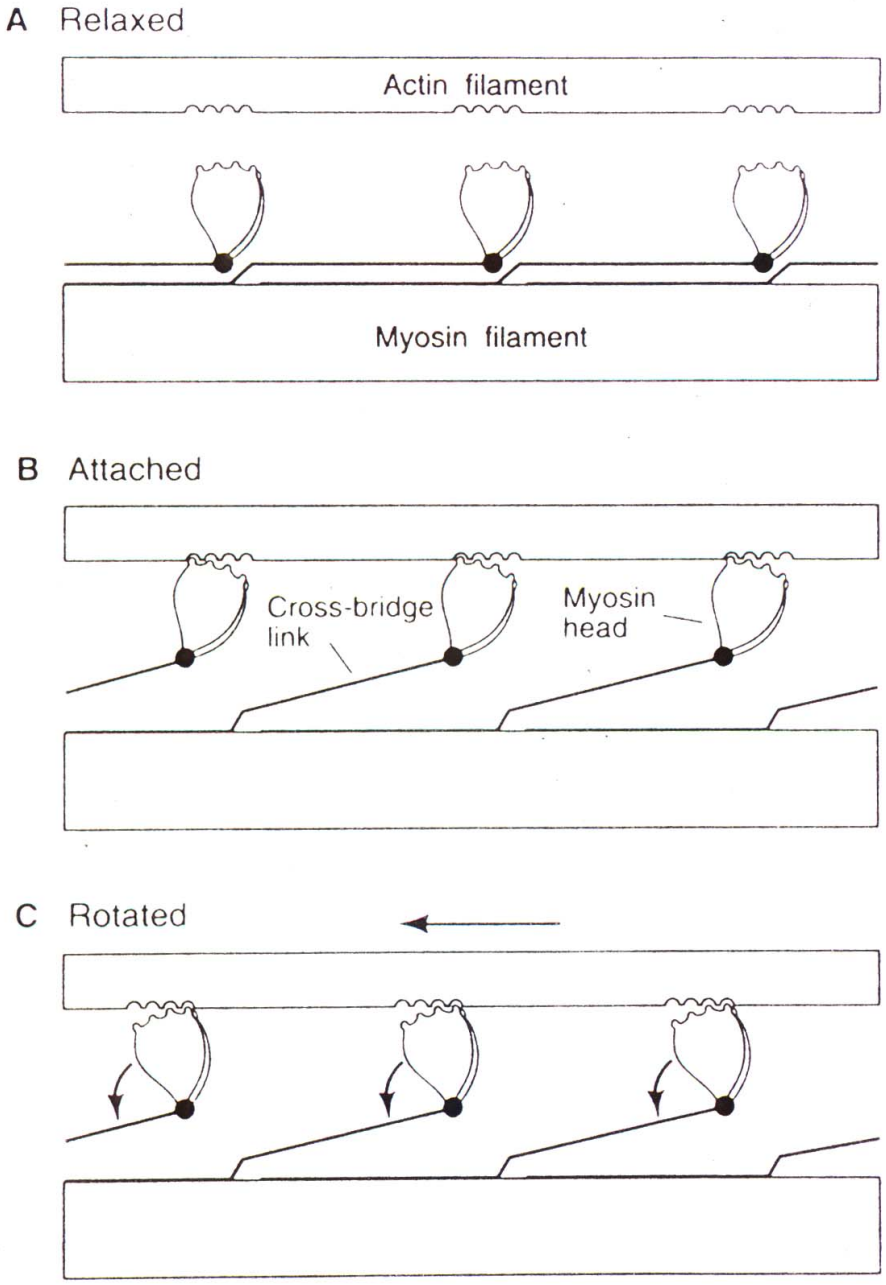

Axon ending
Synaptic cleft
ACh receptor on sarcolemma
ACh
T tubule
Sarcolemma
(1) Action potential generated is propagated along the sarcolemma and down the T tubules
ACh
ACh
ACh
Neurotransmitter released diffuses across the synaptic cleft and attaches to ACh receptors on the sarcolemma
Ca2+
SR
(2) Action potential triggers Ca2+ release from terminal cisternae of SR
(3) Calcium ions bind to troponin troponin changes shape, removing the blocking action of tropomyosin actin active sites exposed
(4) Contraction; myosin cross bridges alternately attach to actin and detach, pulling the actin filaments toward the center of the sarcomere, release of energy by ATP hydrolysis powers the cycling process
(5) Removal of Ca2+ by re-uptake into the SR after the action potential ends
(6) Tropomyosin blockage restored, contraction ends and muscle fiber relaxes

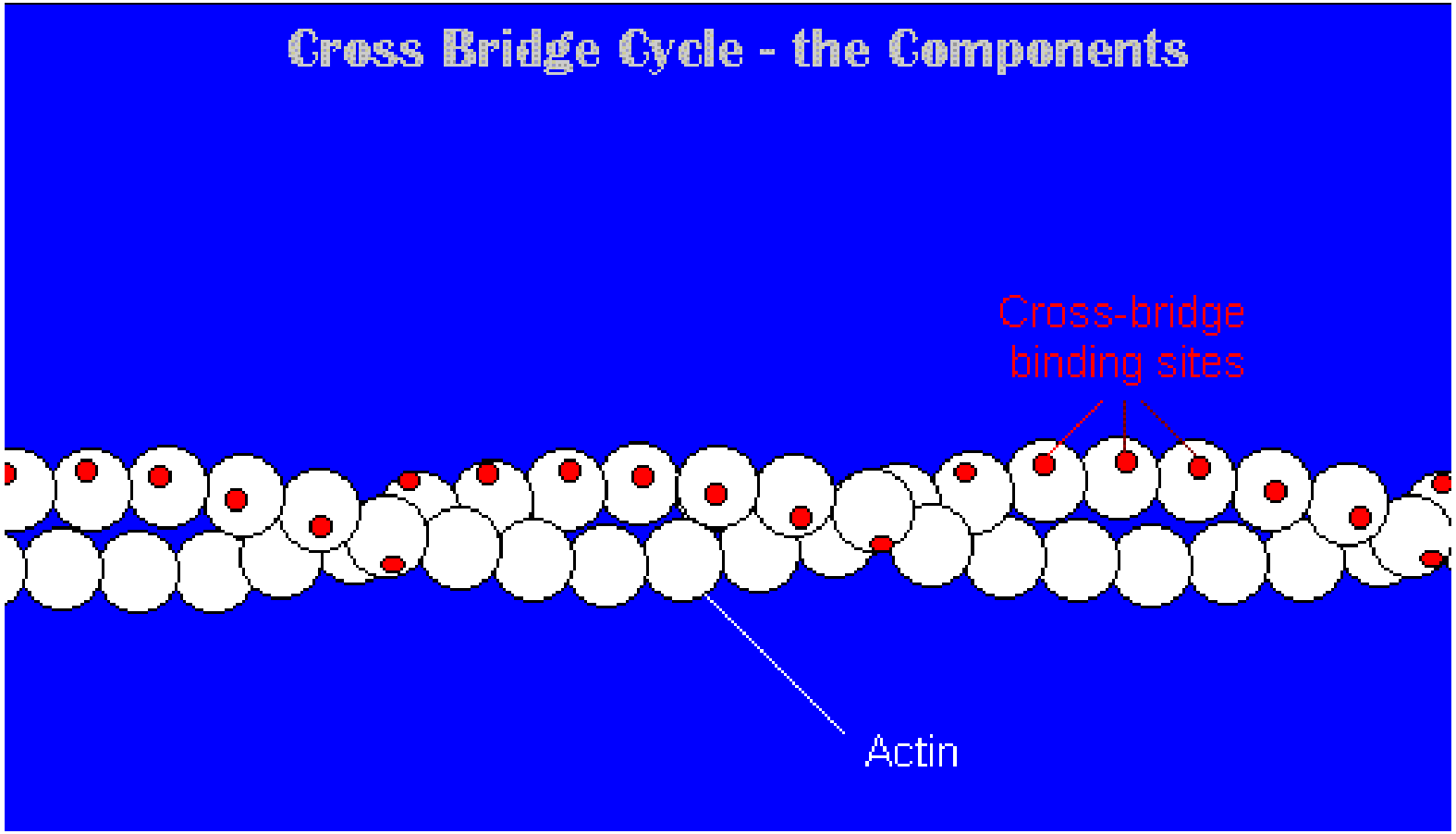

Z-disk
THIN FILAMENT
Tropomyosin
Troponin
Active site
Actin molecule
Z-line
M-line
THICK FILAMENTS
M-line
Myosin tail
Hinge
Myosin head (cross-bridge)
MYOSIN MOLECULE

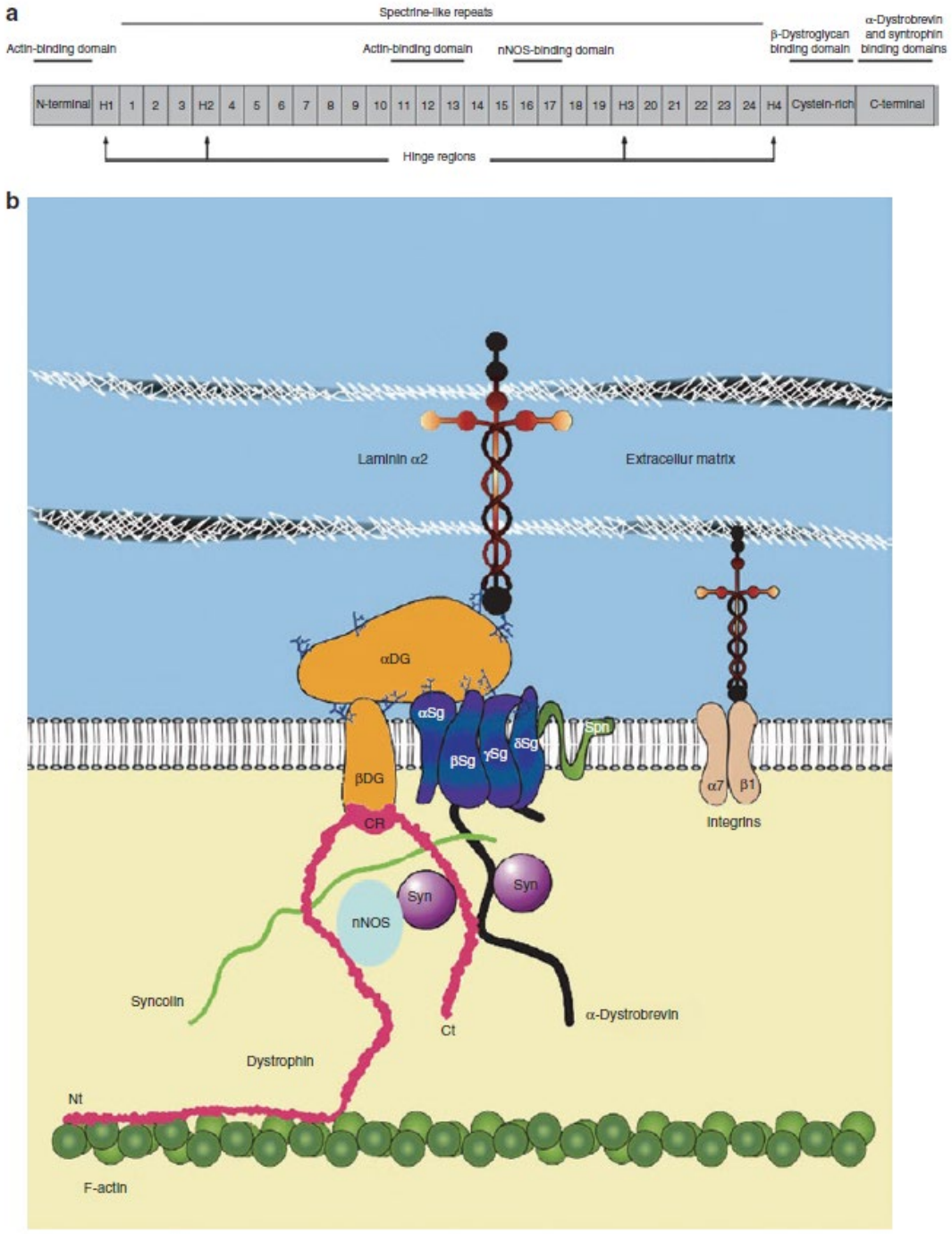

Myofibrille
Actin
Tropo-myosin
Troponin
10 nm
©egb04

Myosin & the Thick Filament




A Relaxed
Actin filament
Myosin filament
B Attached
Cross-bridge link
Myosin head
C Rotated

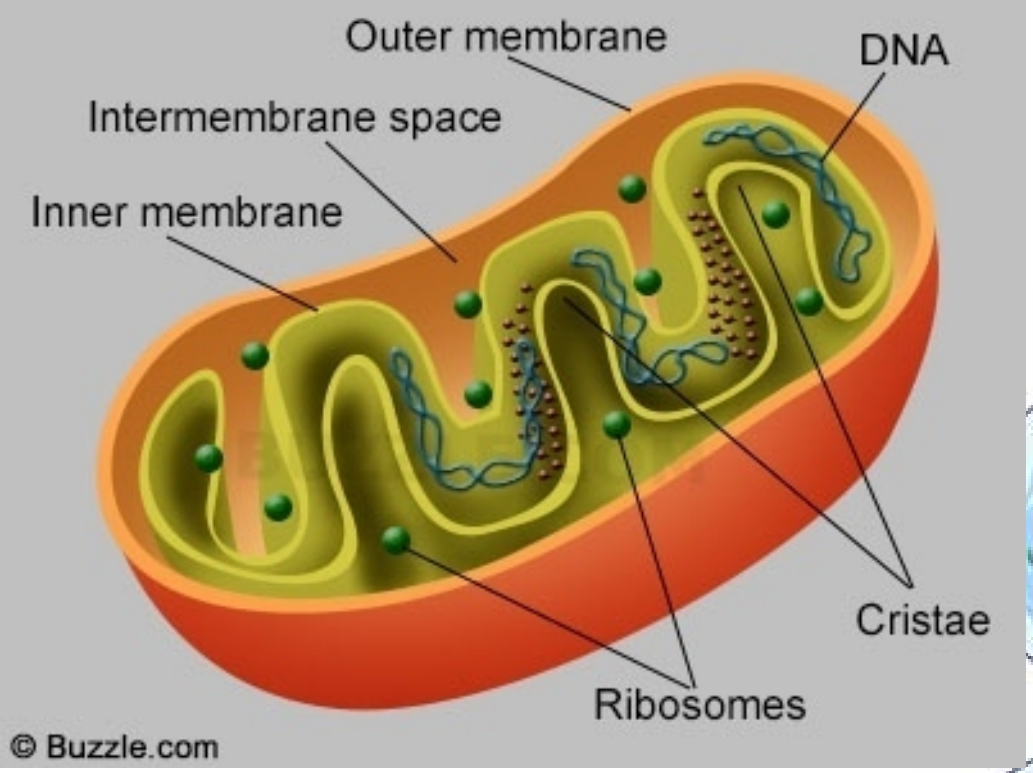

Cross Bridge Cycle - the Components
Cross-bridge
binding sites
Actin

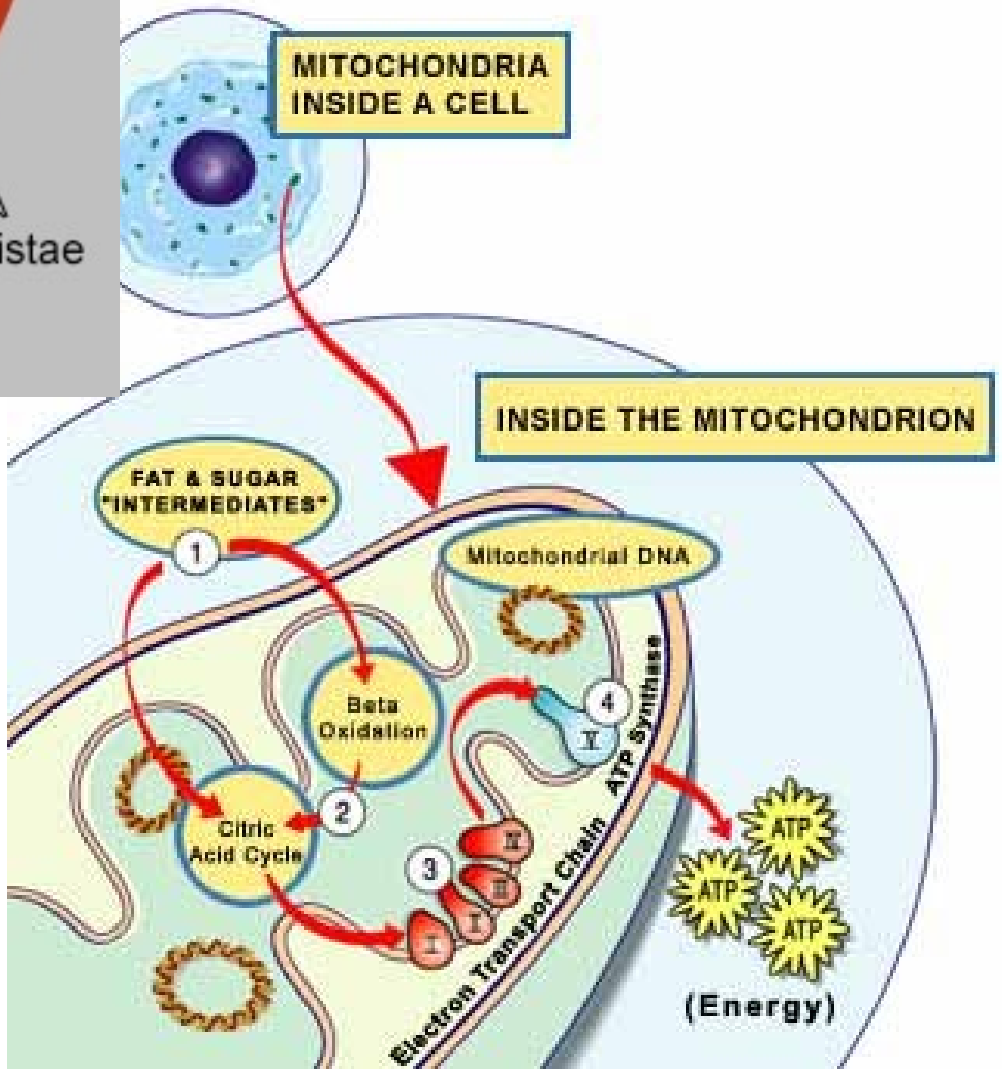


Dystrophin is very large molecule at 479 kD and has 4 domains

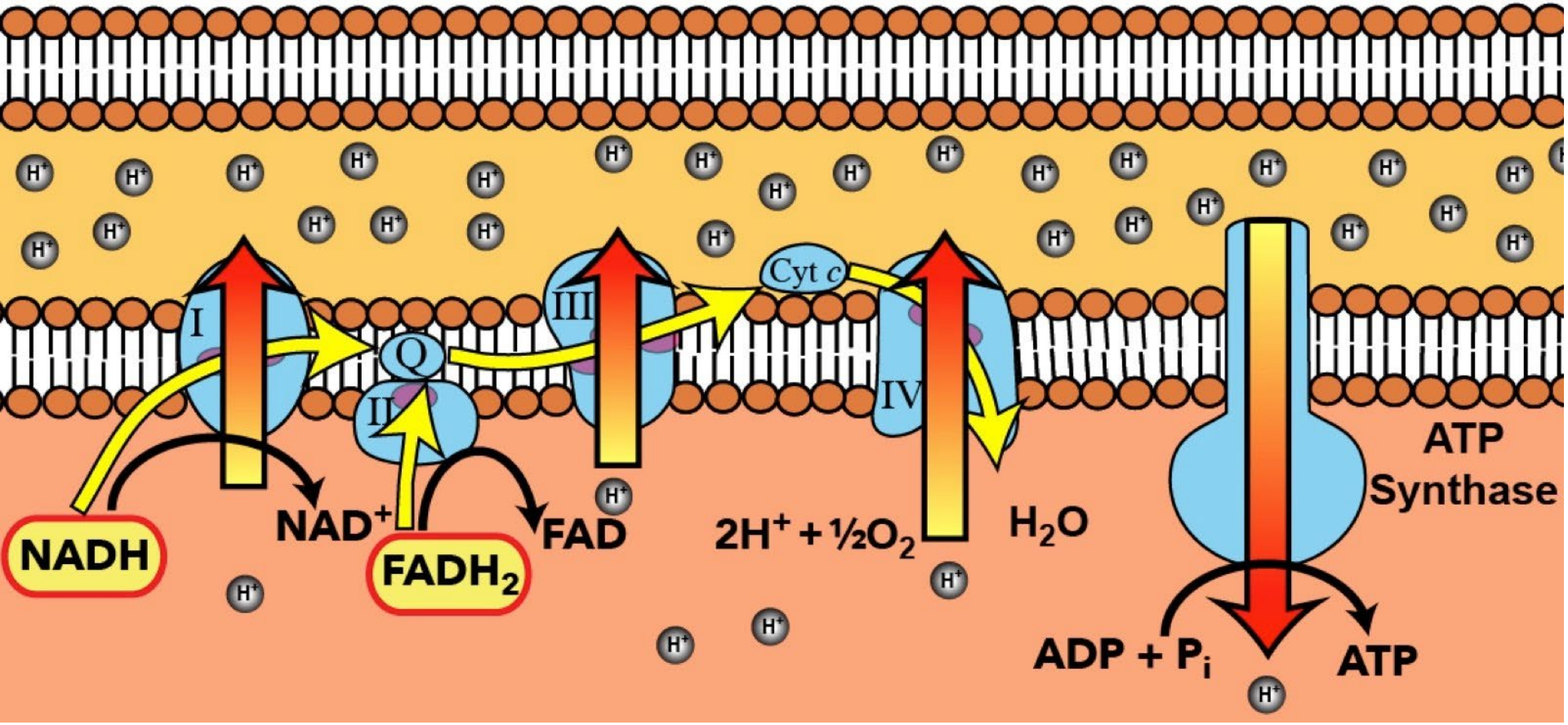
- N terminus
- Central Rod with 4 hinge zones
- Cysteine rich region
- C terminus

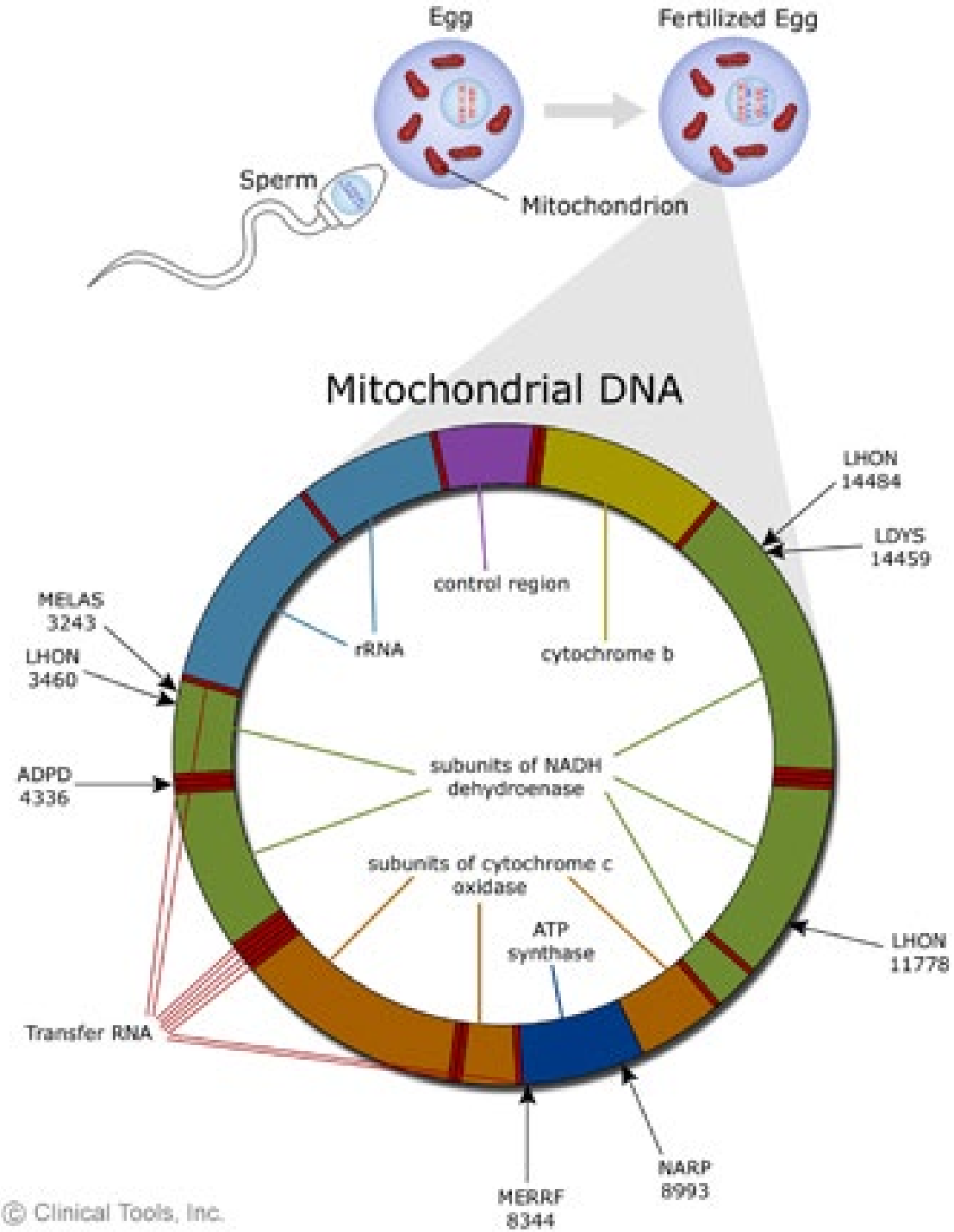
Mol Ther 5:830;2011


Outer membrane
DNA
Intermembrane space
Inner membrane
Cristae
Ribosomes
© Buzzle.com


MITOCHONDRIA INSIDE A CELL
INSIDE THE MITOCHONDRION
FAT & SUGAR "INTERMEDIATES"
1
Mitochondrial DNA
Beta Oxidation
2
Citric Acid Cycle
3
4
ATP Synthase
Electron Transport Chain
ATP
ATP
ATP
(Energy)

Electron Transport Chain




Egg
Fertilized Egg
Sperm
Mitochondrion
Mitochondrial DNA
LHON
14484
LDYS
14459
control region
MELAS
3243
rRNA
cytochrome b
LHON
3460
ADPD
4336
subunits of NADH
dehydroenase
subunits of cytochrome c
oxidase
ATP
synthase
LHON
11778
Transfer RNA
MERRF
8344
NARP
8993
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Maternal Inheritance