ANSC (FSTC) 607
Physiology and Biochemistry of Muscle as a Food
MOTOR INNERVATION AND MUSCLE CONTRACTION

I. Motor innervation of muscle

A. Motor neuron

1. Branched (can innervate many myofibers) → terminal axons.
2. Absolute terminal innervation ratio: one myofiber innervated by one terminal axon.

B. The motor unit

1. Each motor neuron innervates several muscle fibers within a muscle.
2. Size of motor unit varies with muscle and fineness of movement.
   a. There are 100 to 200 myofibers per motor neuron in larger muscles.
      -- *rat soleus, 200 fibers/neuron; rat gastrocnemius, 1,000 fibers/neuron*
   b. There are fewer in muscles such as ocular muscles.

C. The neuromuscular junction

1. Terminal axon
   a. Vesicles (contain acetylcholine)
   b. Presynaptic membrane
   c. Synaptic cleft

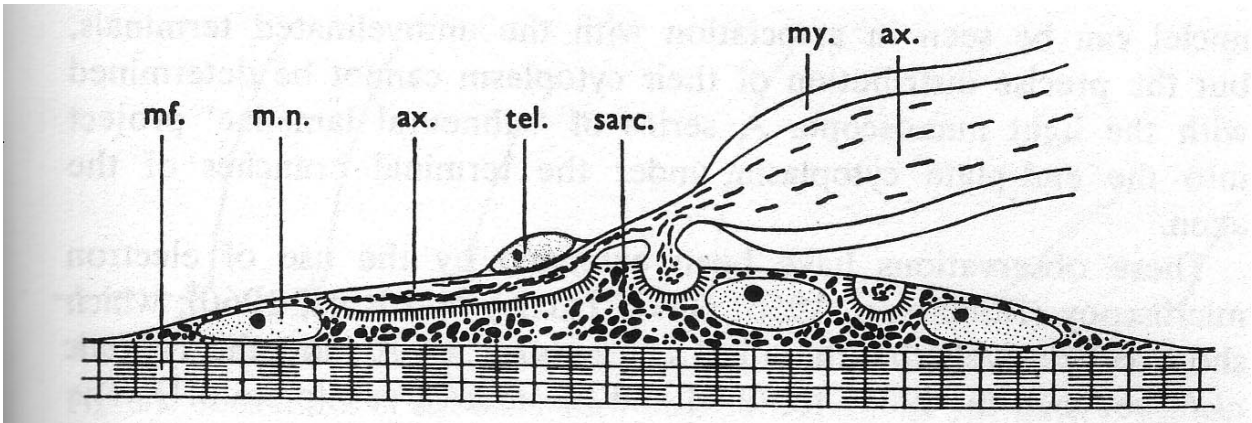
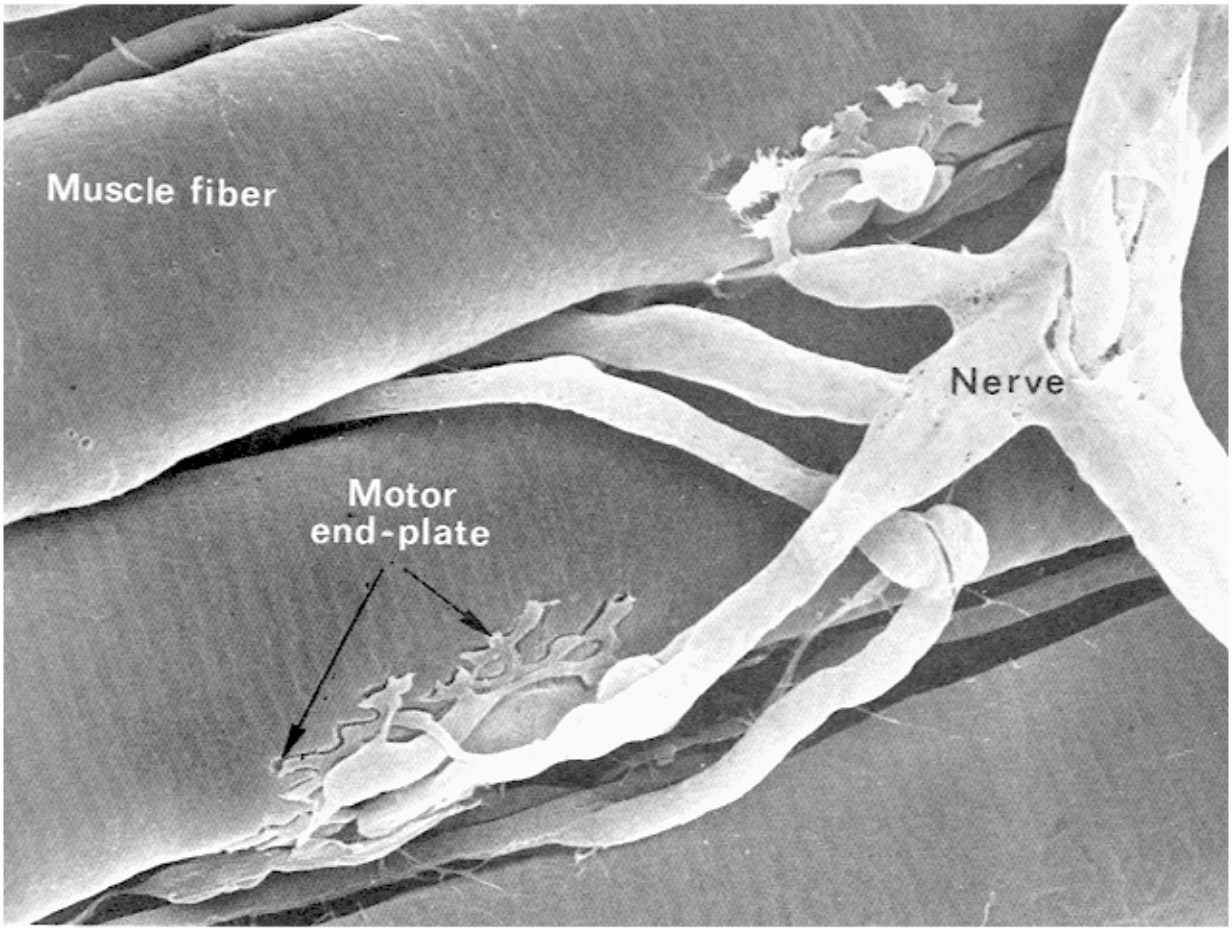
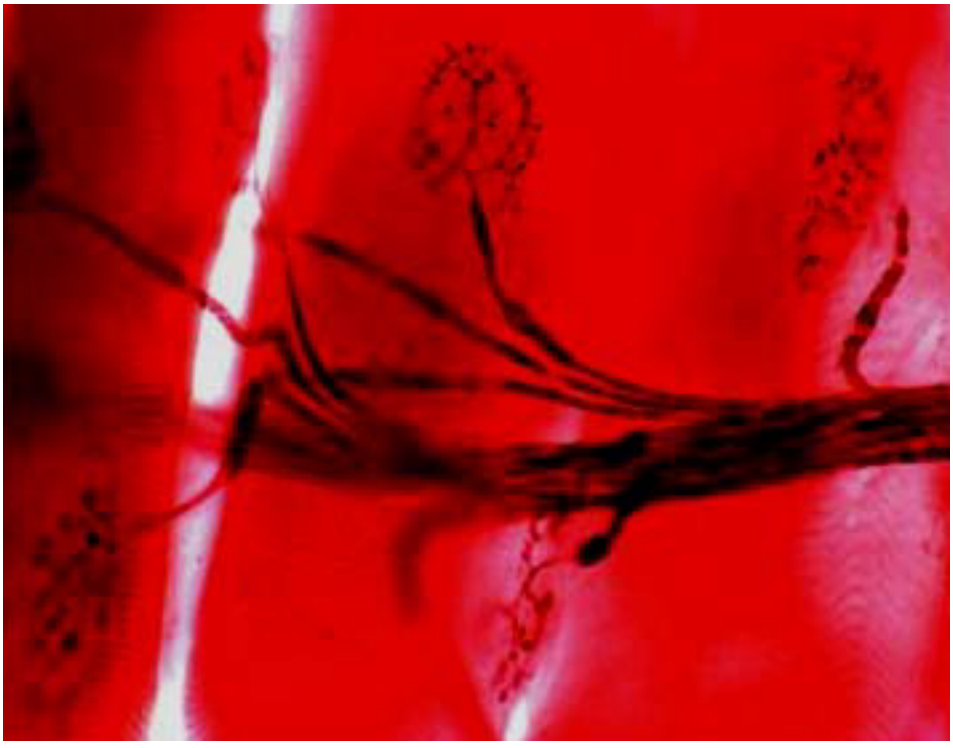
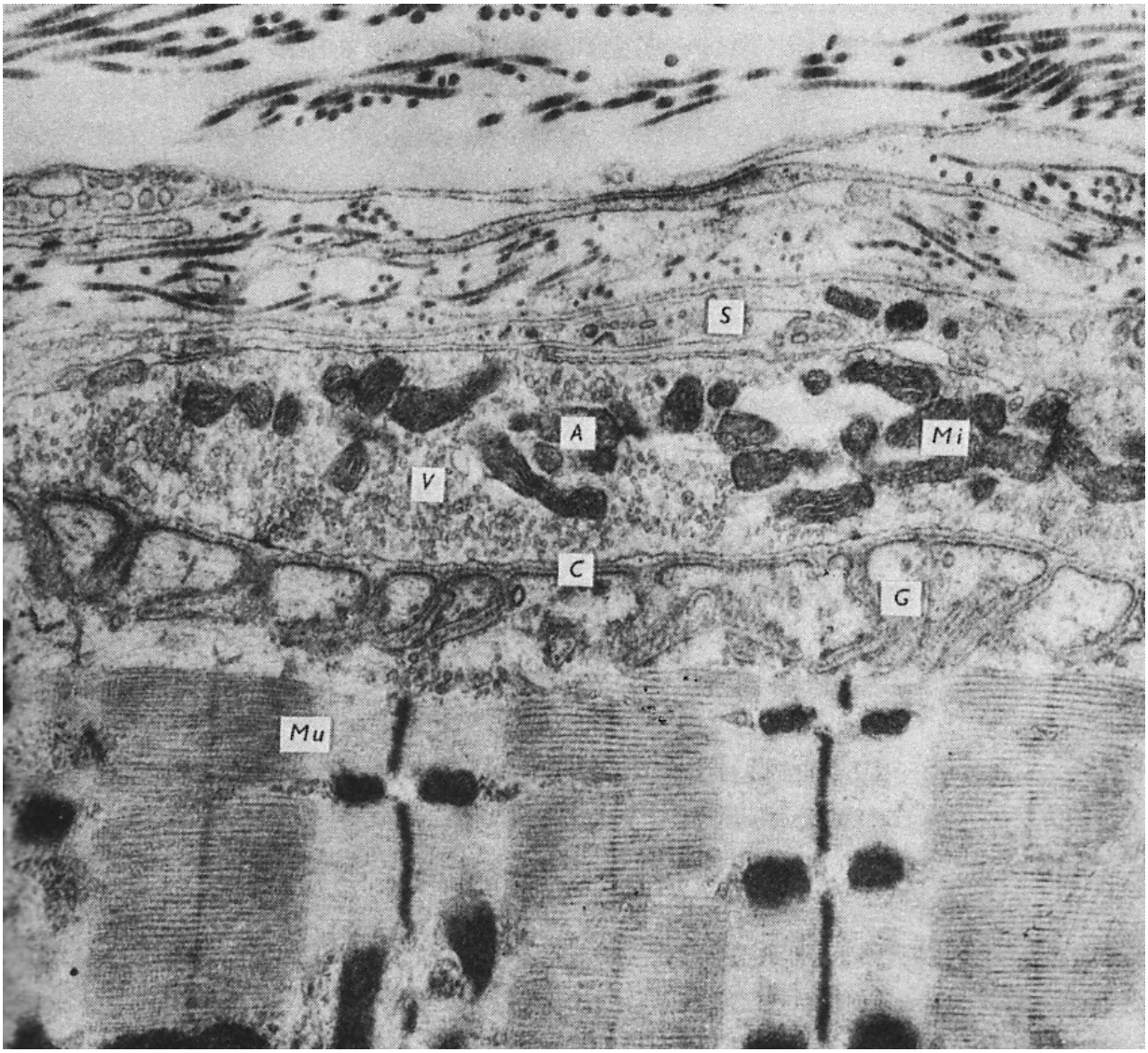


Fig. 6.2. The fine structure of a vertebrate motor end-plate and nerve ending, seen in longitudinal section, as determined by light microscopy. *mf*, myofibril; *m.n.*, muscle nucleus; *ax*, axon; *tel*, Schwann cell (teloglia) nucleus; *sarc*, sarcoplasm; *my*, myelin sheath. (From Couteaux, 1960.)

2. Myofiber
   a. Postsynaptic membrane – *sarcolemma*
   b. Synaptic clefts – *increase surface area*


Muscle fiber
Nerve
Motor
end-plate





D. Transmission of impulse across the synaptic cleft – *synaptic delay of the action potential*

1. Acetylcholine
    a. End-plate potentials
    b. Quantal nature of transmitter release – each vesicle contains 10^3 to 10^4 molecules of acetylcholine
2. Acetylcholinesterase
    a. In synaptic cleft degrades acetylcholine
    b. Stops transmission signal, contraction

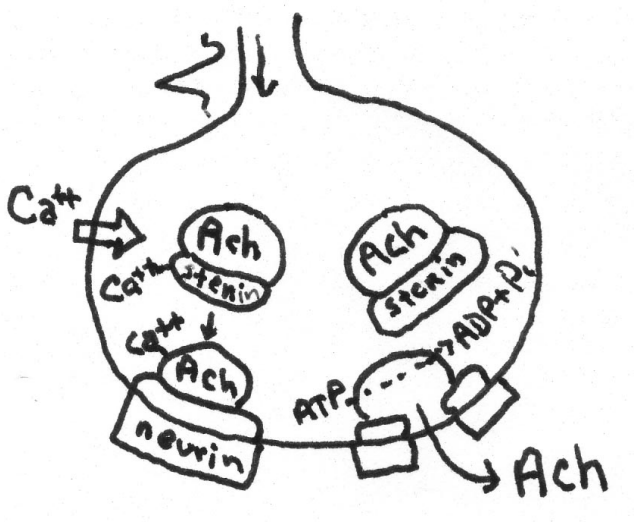
II. Neurotransmitter release

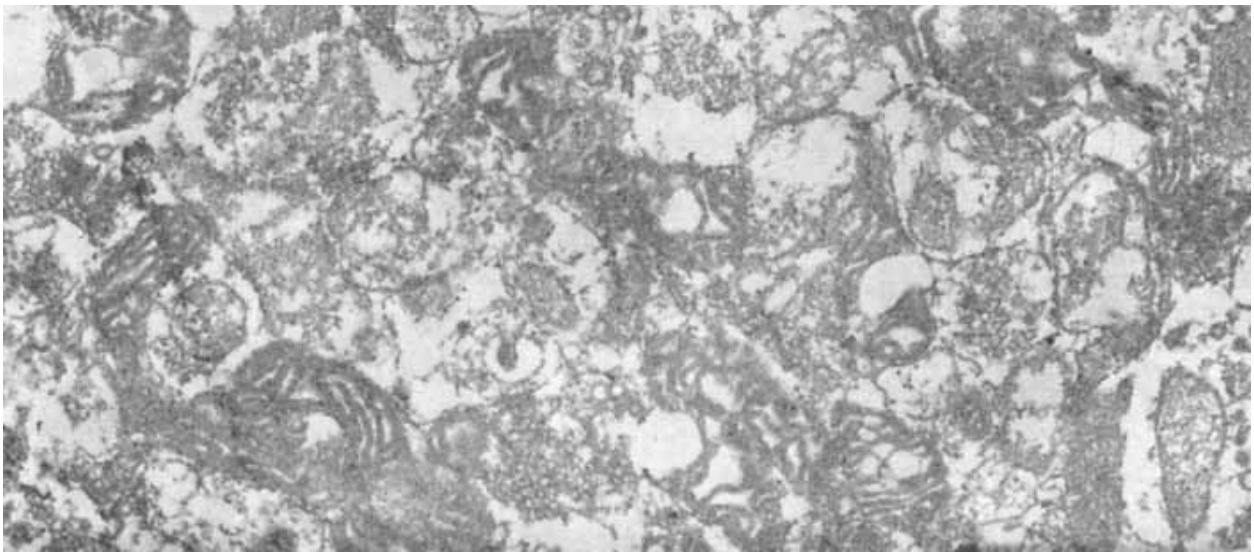
A. Neurotransmitter released from the presynaptic vesicles

B. Stenin (myosin-like) is associated with vesicles and neurin (actin-like) is associated with the presynaptic membrane.

C. Calcium influx causes stenin to fuse with neurin.

D. This activates neurostenin ATPase; vesicles expel 1,000 to 10,000 molecules of acetycholine into cleft.





Electron micrograph of synaptosomal-enriched fraction from bovine brain. Neurin and stenin were enriched from this fraction. Puszkin et al. (1972) J. Neurochemistry 19:1319-1333

IV. Depolarization of the sarcolemma

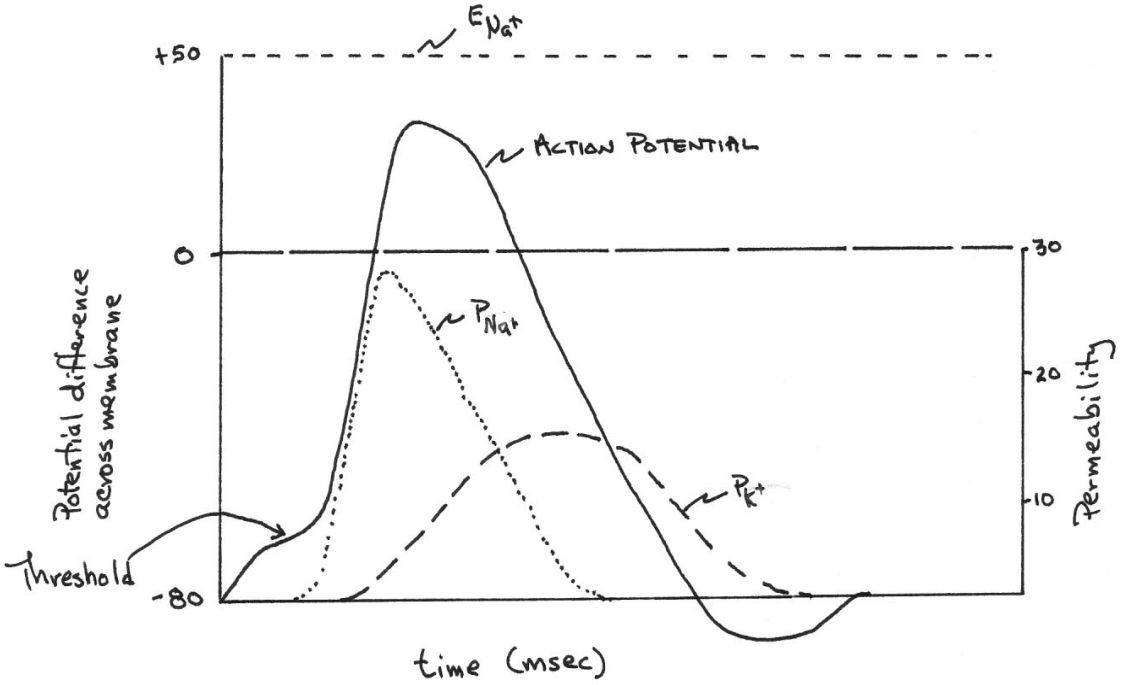
A. Depolarization of postsynaptic membrane

1. Causes local depolarizaton (miniature end-plate potentials).
2. Miniature end-plate potentials are caused by the quantal release of acetylcholine.

B. Depolarization of sarcolemma

1. Depolarization = summation of miniature end-plate potentials leads to action potential.
2. Action potential spreads across sarcolemma.

3. Action potential reaches interior via the t-tubules.



VI. Generation of the resting membrane potential

A. Resting state (steady state)

requirements

1. Equimolarity
2. Electrical neutrality
3. Zero electrochemical gradient

B. Basis for the resting membrane potential

1. Ions responsible are primarily Na^+ and K^+.
2. Factors influencing magnitude of the action potential are primarily the concentrations of Na^+ and K^+.

Fig. 2–3.—Schematic representation of the distribution of major ions on either side of the membrane of a frog muscle cell. The column to the right of the ions indicates the concentration of each, in millimoles per liter. Pn^- is intracellular protein; the number in parentheses is the number of millequivalents of protein; i.e., the equivalent concentration of univalent ion. Note that intracellular fluid is rich in potassium (K^+) and that the extracellular medium is high in sodium (Na^+) and chloride (Cl^-).

Na^+ 117.5	Na^+ 10
K^+ 2.5	K^+ 140
Cl^- 120	Cl^- 2.5
	Pn^- 97.5 (147.5)

C. Calculation of the resting membrane potential

1. Nernst equation: $E = (-RT)/zF)ln[K_i]/K_o]$

Where E = potential difference across the membrane (usually in mV)
R = gas constant
T = absolute temperature

F = Faraday's constant (# charges per mole ion)
z = valence of ion

2. Modified Nernst equation

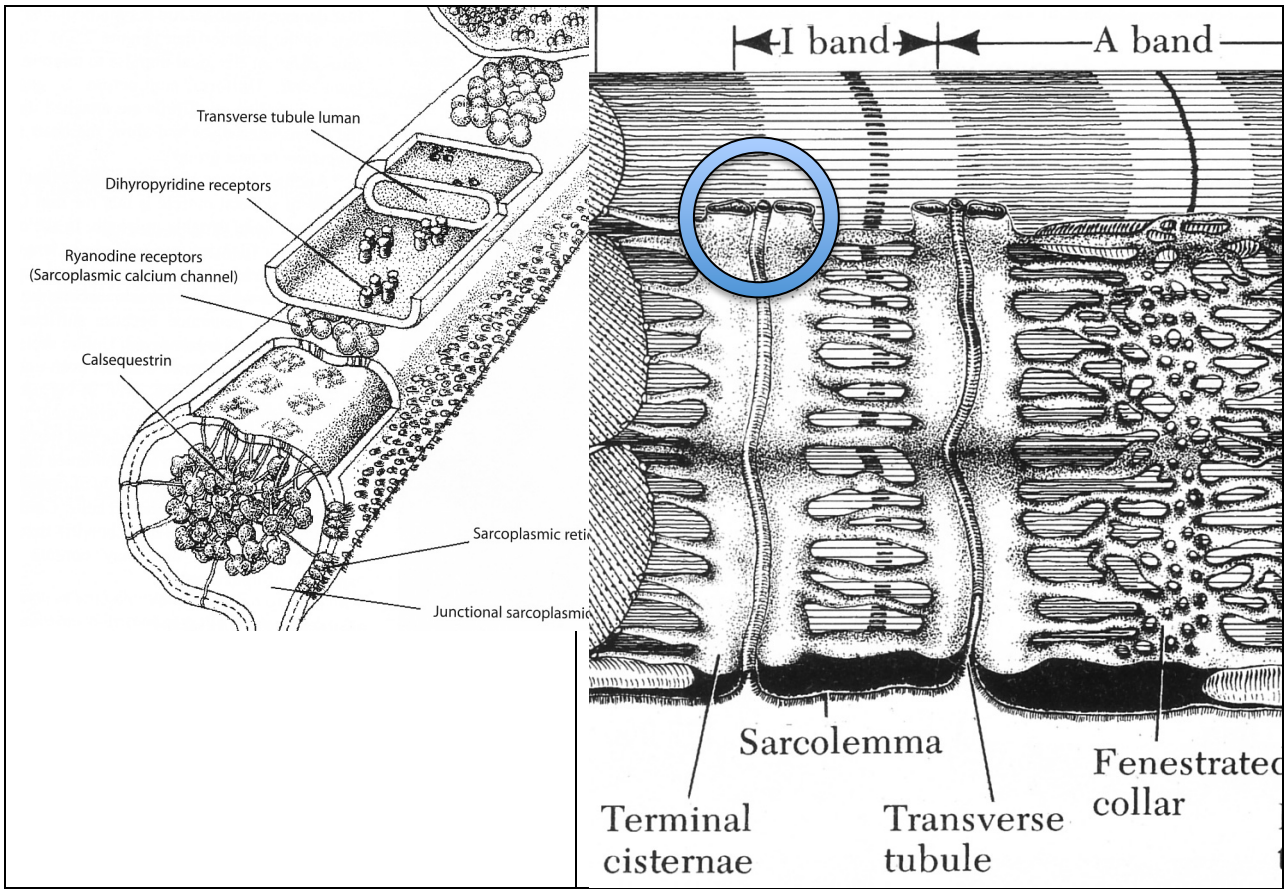
R and F = constants
T (20°C) = 293 absolute
z for K^+ = 1

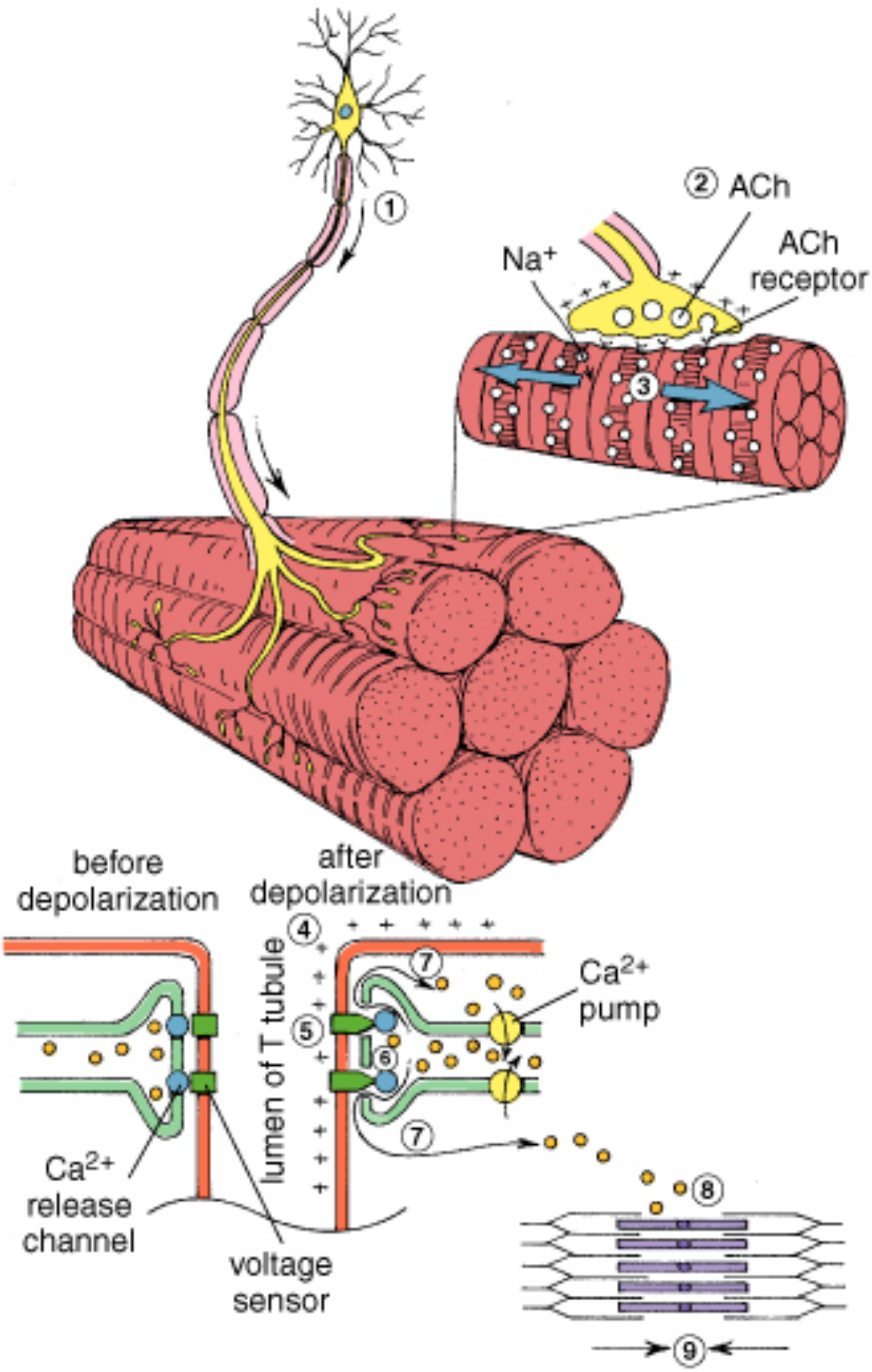
Convert *ln* to $\log_{10}$, so that: E (in mV) = -58 $\log_{10}[K_i]/[K_o]$

VI. The triad

A. Junction of the terminal cisternae of the sarcoplasmic reticulum and the transverse tubule (t-tubule)

B. Site of transmission of the action potential to the sarcoplasmic reticulum, via the t-tubule.




①
② ACh
ACh receptor
Na+
③
before depolarization
after depolarization
④
lumen of T tubule
⑤
⑥
⑦
Ca2+ pump
⑦
⑧
Ca2+ release channel
voltage sensor
⑨

VII. Initiation of contraction

A. Action potential causes release of Ca^{++} from the sarcoplasmic reticulum.

1. Release of Ca^{++} occurs in area of triad (at A band-to-I band interface in mammals).
2. The dihydropyridine receptor (embedded in the T-tubule) is altered by the incoming action potential.
2. This causes the ryanodine receptor (underlying the T-tubule) to open, allowing calcium release from the sarcoplasmic reticulum.
3. Ca^{++} follows its electrochemical gradient into the sarcoplasm.
4. The sarcoplasmic concentration of Ca^{++} increases from 10 nM to 10 μM (1,000-fold increase).

B. Ca^{++} binds to troponin C, which initiates contraction.

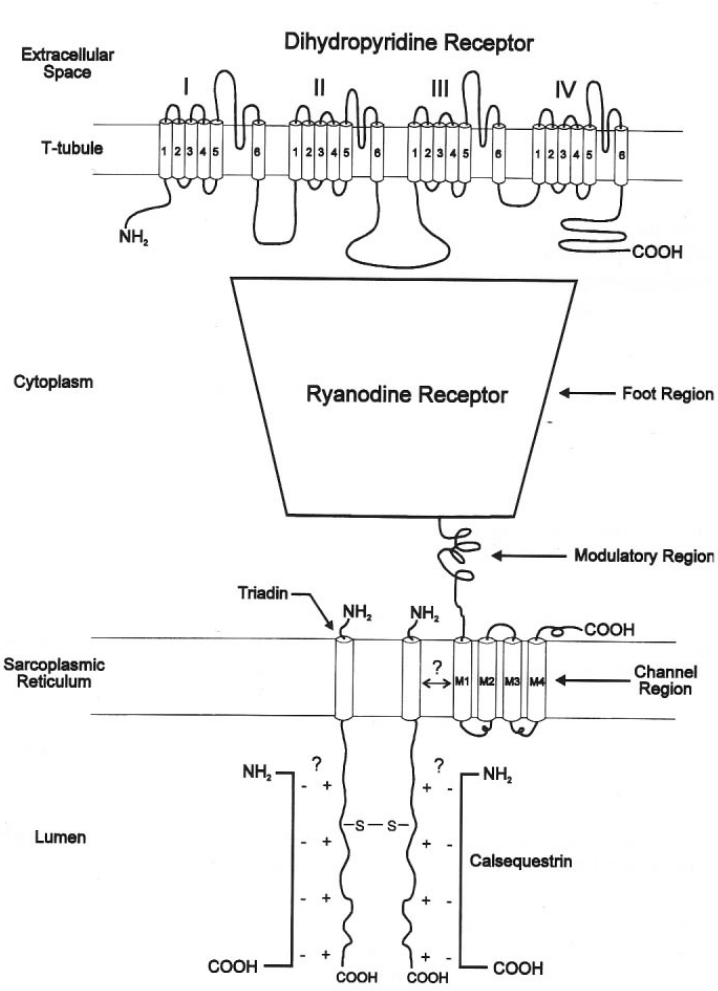


FIG. 1. **Model of the triad junction.** For simplicity, only the α_1 subunit of the dihydropyridine receptor and only one subunit of the ryanodine receptor homotetramer are shown. The ryanodine receptor is modeled after that of Takeshima *et al*. (17) although alternative models suggest as many as 12 transmembrane domains (18) and predict other regulatory domains within the foot region (19). *Question marks* indicate the speculative nature of the interaction between 94-kDa glycoprotein (triadin) and the ryanodine receptor as well as between triadin and calsequestrin.

VIII. Return to resting state

A. Acetylcholine levels are reduced.

1. Acetylcholine is repackaged into vesicles.
2. Acetylcholine also can be degraded to acetate and choline by acetylcholinesterase.

B. Sarcoplasmic Ca^{++} resequestered in sarcoplasmic reticulum by:

1. Ca^{++}-Mg^{++}-ATPase (active pumping)
2. Calsequestrin
   a. Binds 43 Ca^{++}/mol of protein.
   b. Helps to concentrate Ca^{++}.
3. High-affinity Ca^{++}-binding protein also helps to sequester Ca^{++}.