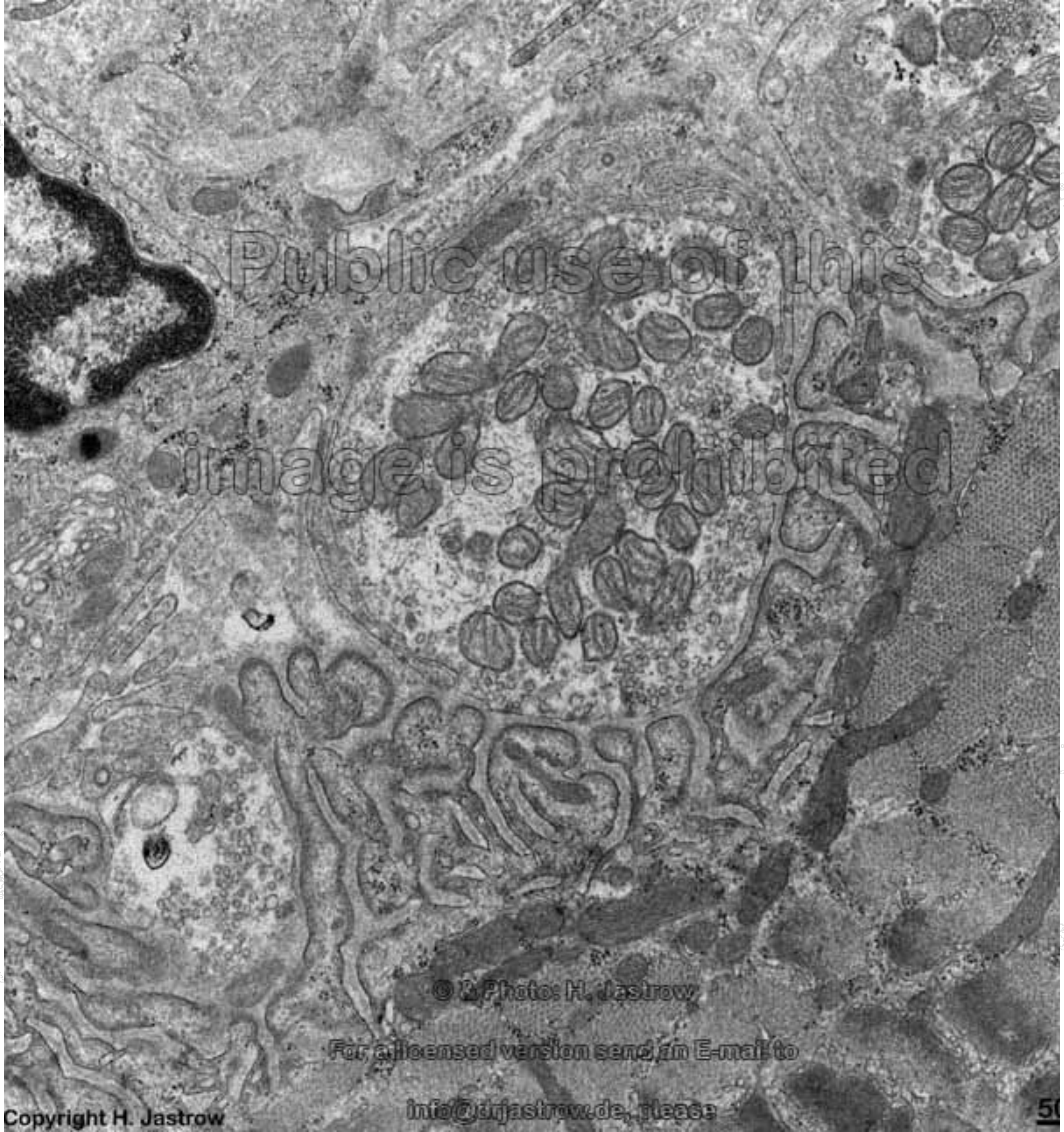
NEUROMUSCULAR TRANSMISSION IN SKELETAL MUSCLE

Simon Frei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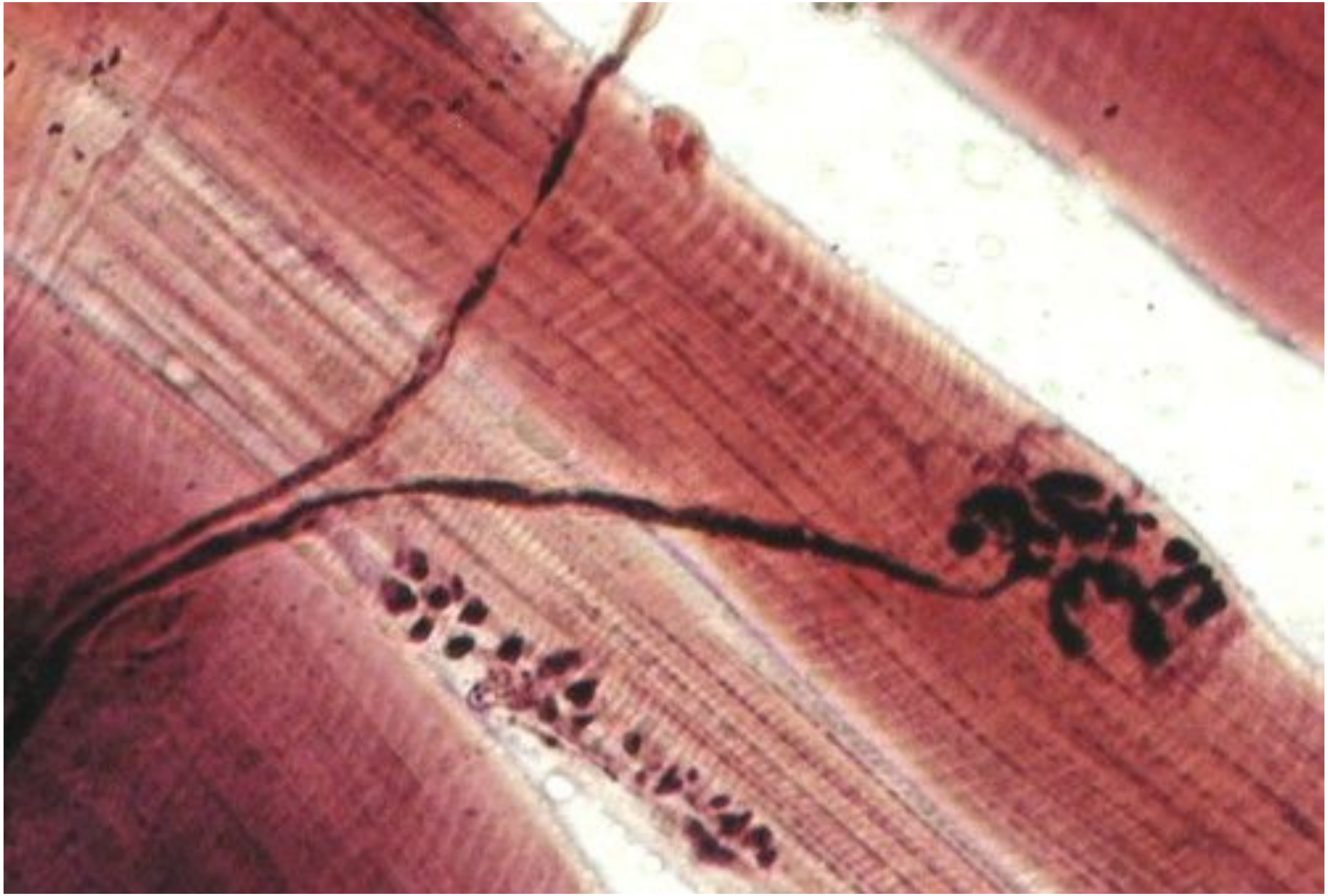
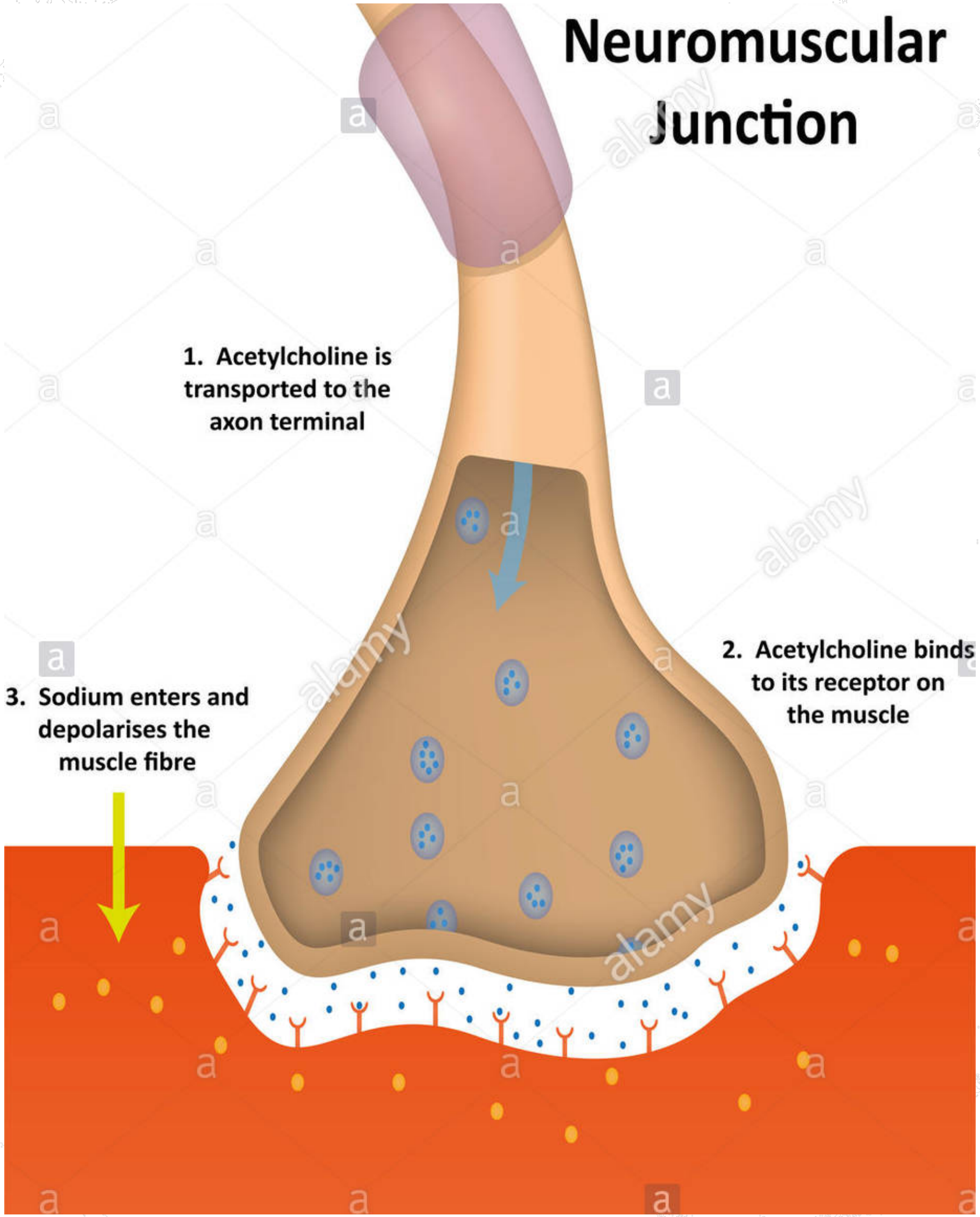
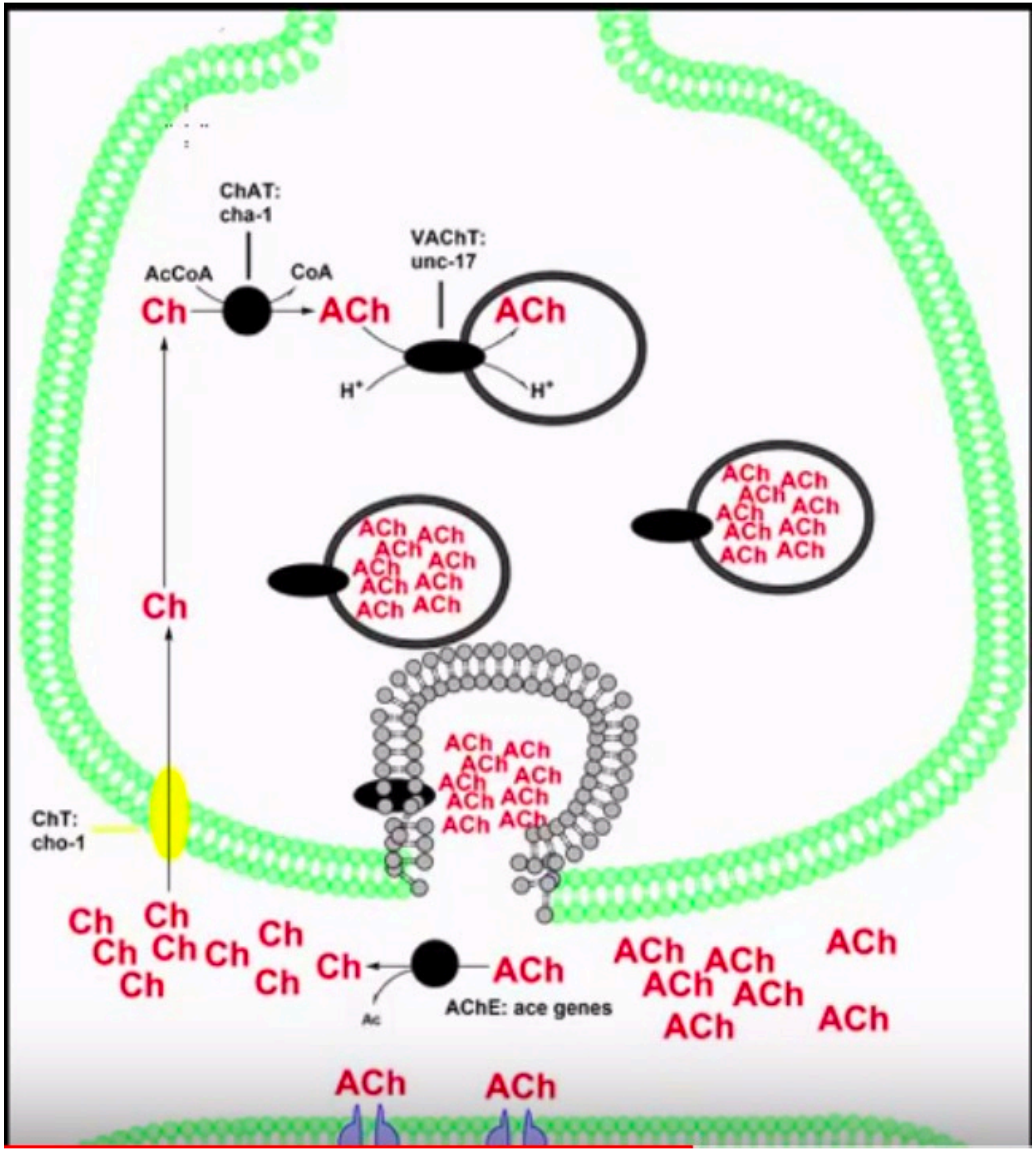


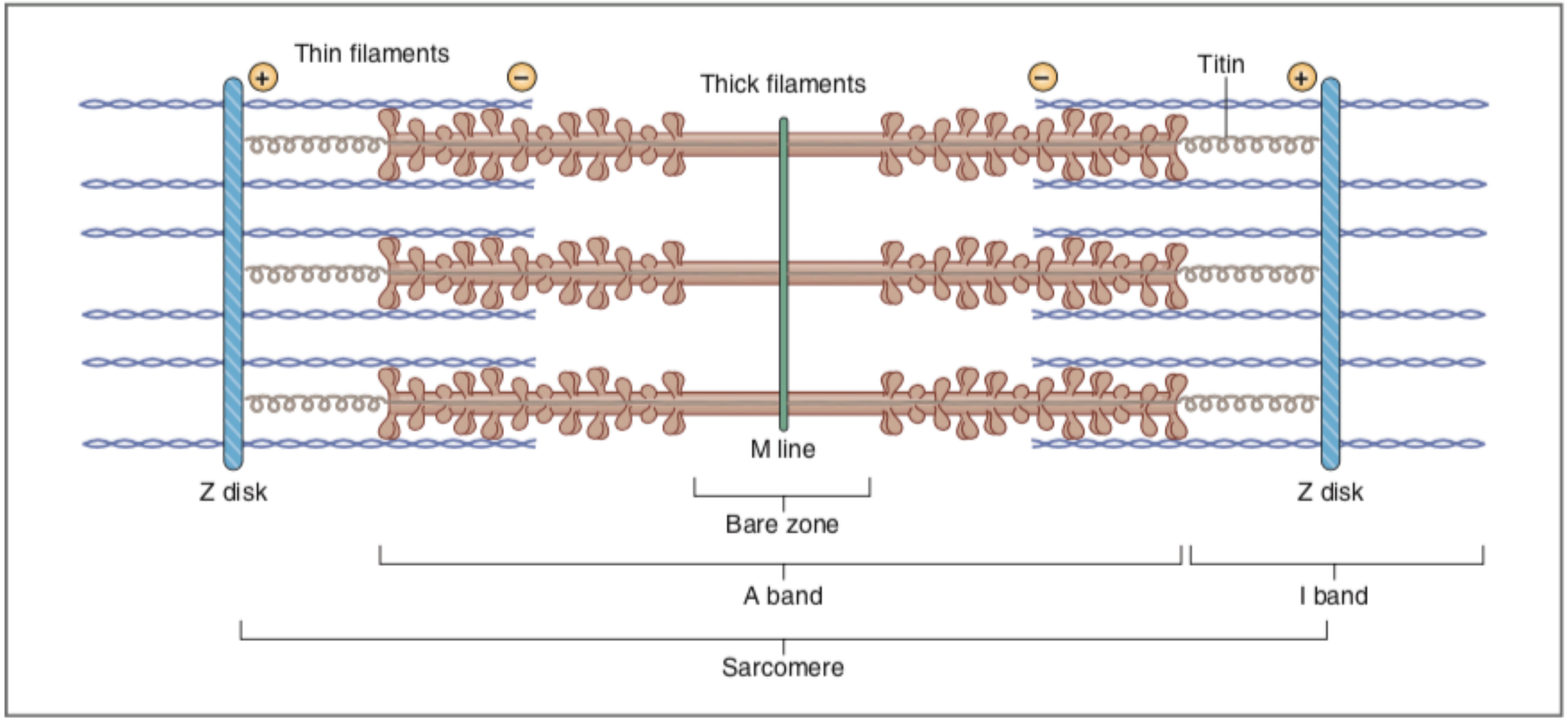

Neuromuscular Junction
1. Acetylcholine is transported to the axon terminal
2. Acetylcholine binds to its receptor on the muscle
3. Sodium enters and depolarises the muscle fibre


ChAT:
cha-1
AcCoA
CoA
Ch
ACh
VAChT:
unc-17
ACh
H+
H+
ACh ACh ACh ACh ACh ACh ACh ACh
ACh ACh ACh ACh ACh ACh ACh ACh
Ch
ChT:
cho-1
ACh ACh ACh ACh ACh ACh ACh ACh
Ch Ch Ch Ch Ch Ch Ch Ch Ch
ACh
Ac
AChE: ace genes
ACh ACh ACh ACh ACh ACh ACh
ACh ACh

EXCITATION-CONTRACTION COUPLING IN SKELETAL MUSCLE

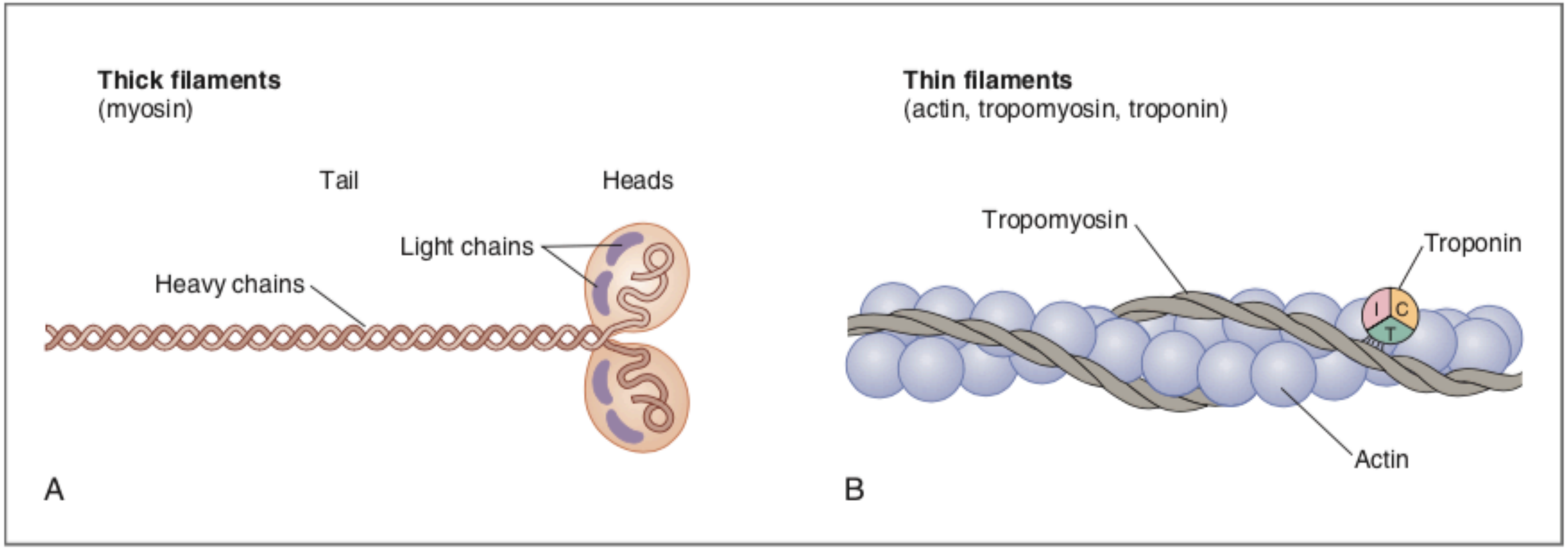
Konrad Riesenhuber

Sarcomere



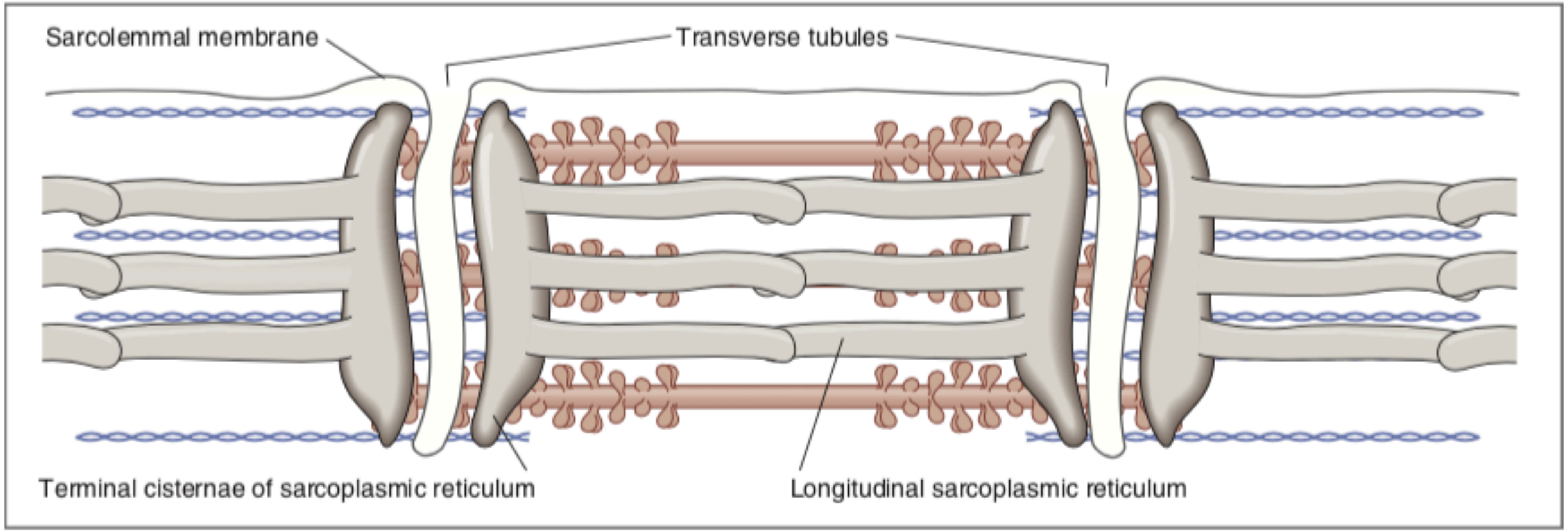
Linda S. Costanzo Physiology, Sixth edition, 2018; p. 35, fig. 1.22

Thick And Thin Filaments



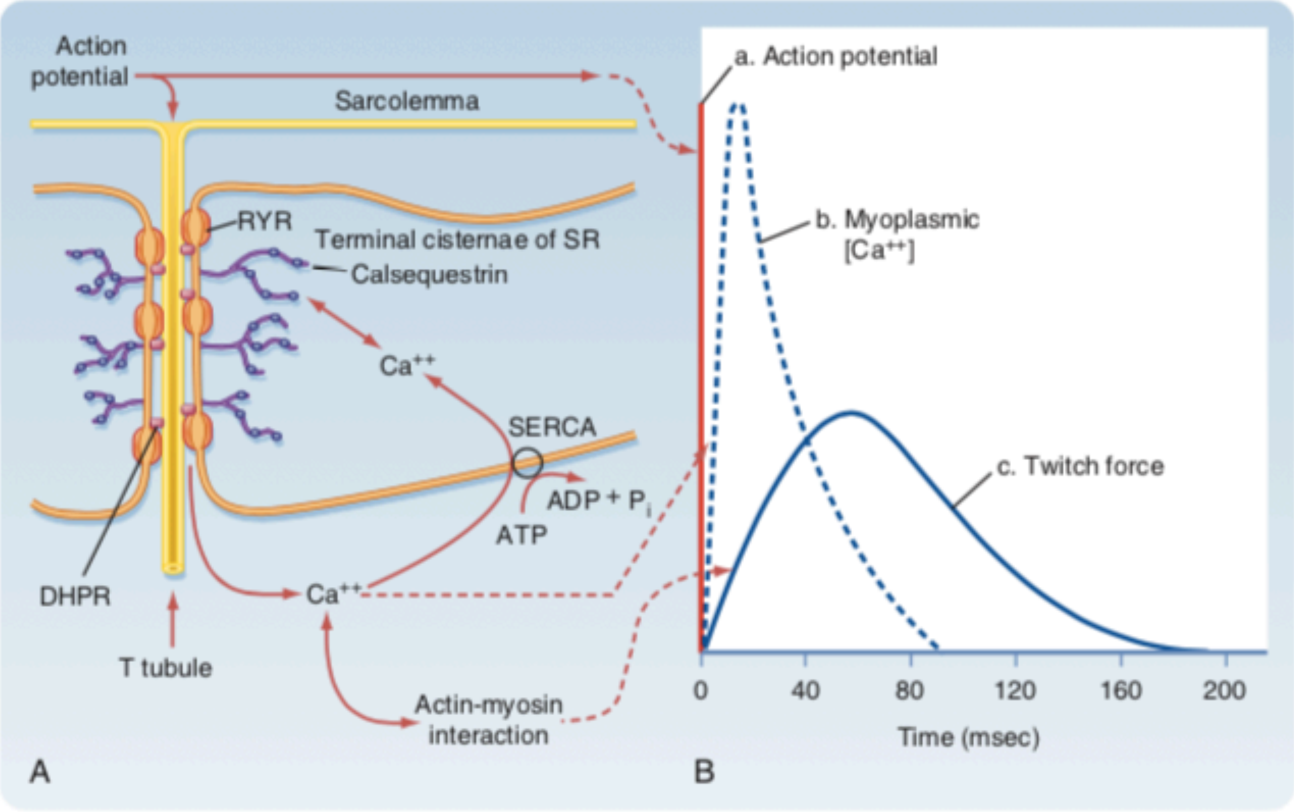
Linda S. Costanzo Physiology, Sixth edition, 2018; p.34 fig. 1.21

Transverse Tubules, Terminal Cisternae



Linda S. Costanzo Physiology, Sixth edition, 2018; p. 36 fig. 1.23

Excitation-Contraction Coupling



Berne & Levy Physiology, Seventh edition, 2018; p. 250 fig. 12.8

EXCITATION – CONTRACTION IN SKELETAL MUSCLE

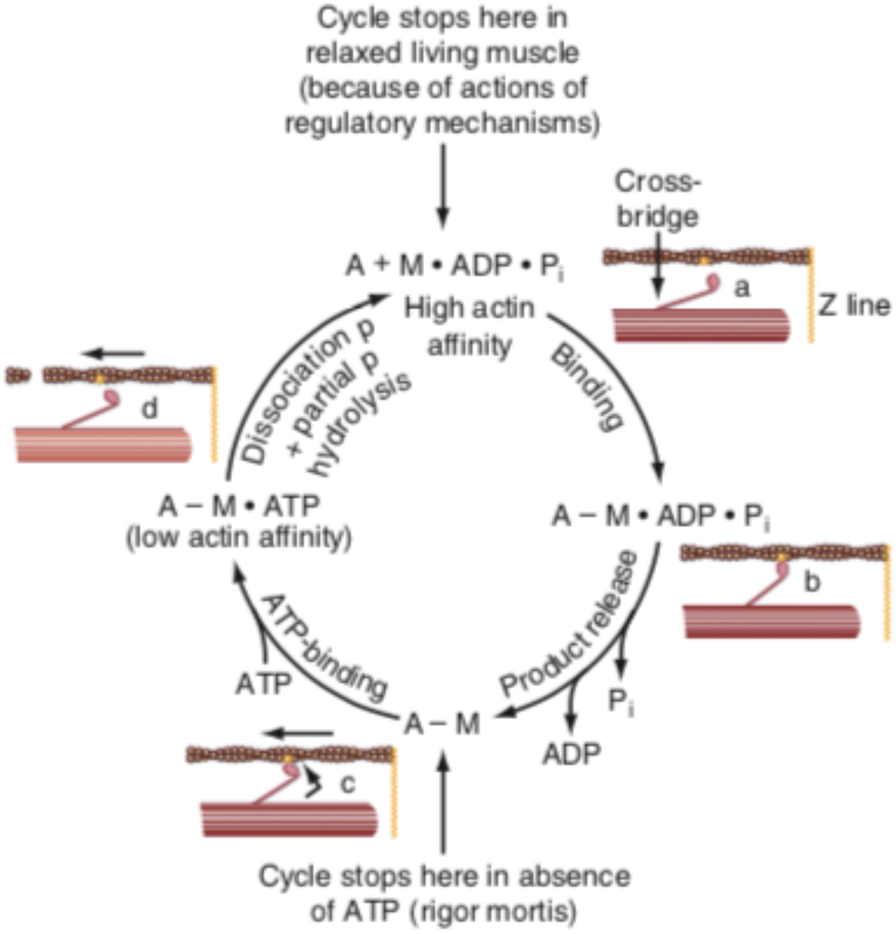
1. Action potential in muscle membrane
   ↓
2a. Depolarization of T tubules
   ↓
2b. Opens SR Ca^{2+} release channels (ryanodine receptors)
   ↓
3. ↑ Intracellular Ca^{2+} concentration
   ↓
4. Ca^{2+} binds troponin C
   ↓
5. Tropomyosin moves and allows interaction of actin and myosin
   ↓
6. Cross-bridge cycling and force-generation
   ↓
7. Ca^{2+} reaccumulated by SR ⟶ relaxation

Linda S. Costanzo Physiology, Sixth edition, 2018; p. 37, fig. 1.25

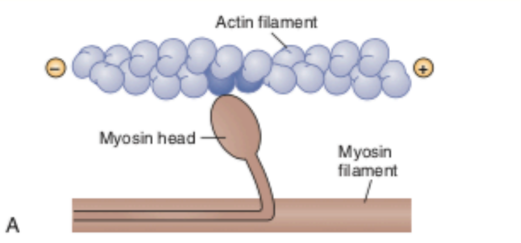
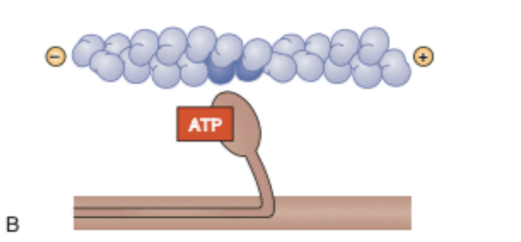
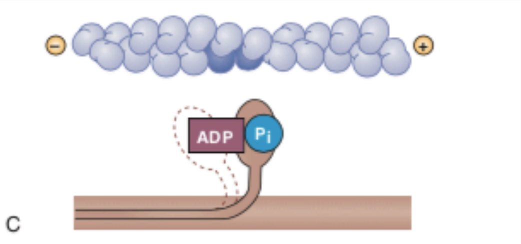
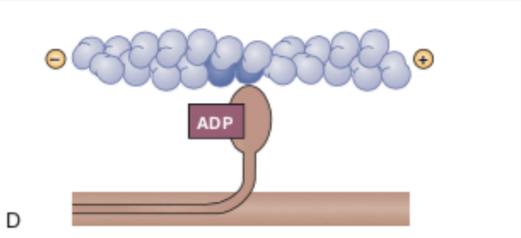
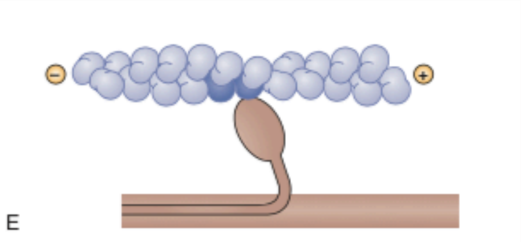
Excitation-Contraction Coupling

- Action potential is propagated along sarcolemma
- depolarization of T-tubule
- conformational change in DHPR of T-tubule —> opening of nearby RYR on sarcoplasmic reticulum (Ca^{2+} -release channels)
- Ca^{2+} is released from SR into myoplasm —> increase in intracellular [Ca^{2+}] (from 0,01-0,1μmol/l to 1-10μmol/l)
- Ca^{2+} binds to Troponin-C —> conformational change in troponin complex —> Troponin-I changes position —> Troponin-T passes change onto Tropomyosin —> moves „out of way“ to expose myosin binding site
- cross-bridge cycle
- Ca^{2+} is reaccumulated in SR with help of SERCA —> relaxation

Cross-Bridge Cycle



Berne & Levy Physiology, Seventh edition 2018; p. 254, fig. 12.13

Position of Actin and Myosin During Cross-Bridge Cycling	Events	ATP/ADP
	Rigor	No nucleotides bound
	ATP binds to cleft on myosin head Conformational change in myosin Decreased affinity of myosin for actin Myosin released	ATP bound
	Cleft closes around ATP Conformational change Myosin head displaced toward ⊕ end of actin ATP hydrolysis	ATP → ADP + P$_i$ ADP + P$_i$ bound
	Myosin head binds new site on actin Power stroke = force	ADP bound
	ADP released Rigor	No nucleotides bound

Linda S. Costanzo Physiology, Sixth edition 2018; p.38, fig. 1.26

SUMMATION

THE CONVERSION FROM AN “ALL OR NOTHING” SIGNAL TO A GRADED MUSCLE CONTRACTION

Lukas Lexmann

Frequency Of Motor Neuron Stimulation

- **Latent** period

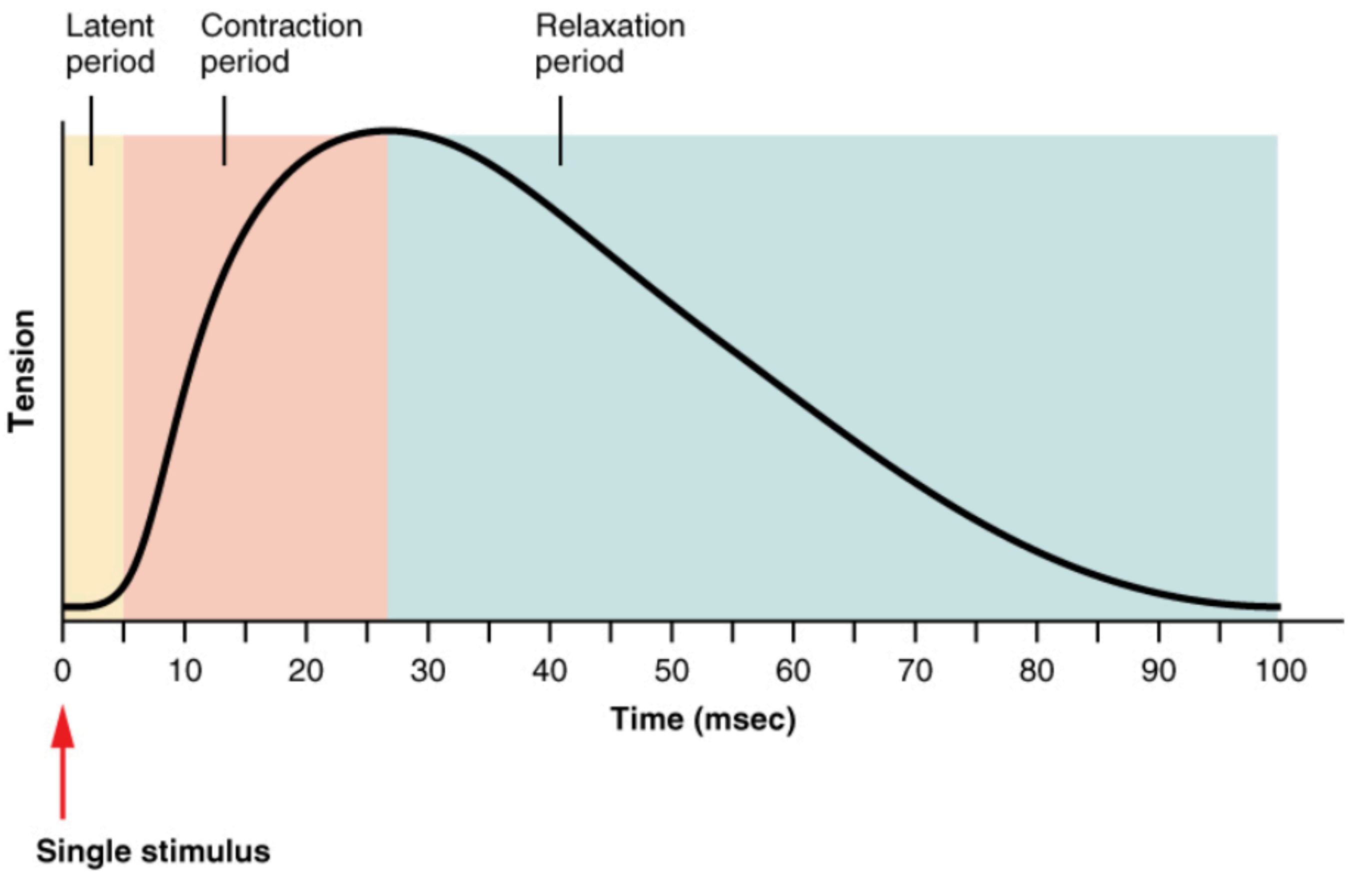
- action potential propagated along Sarcolemma

- **Contraction** period

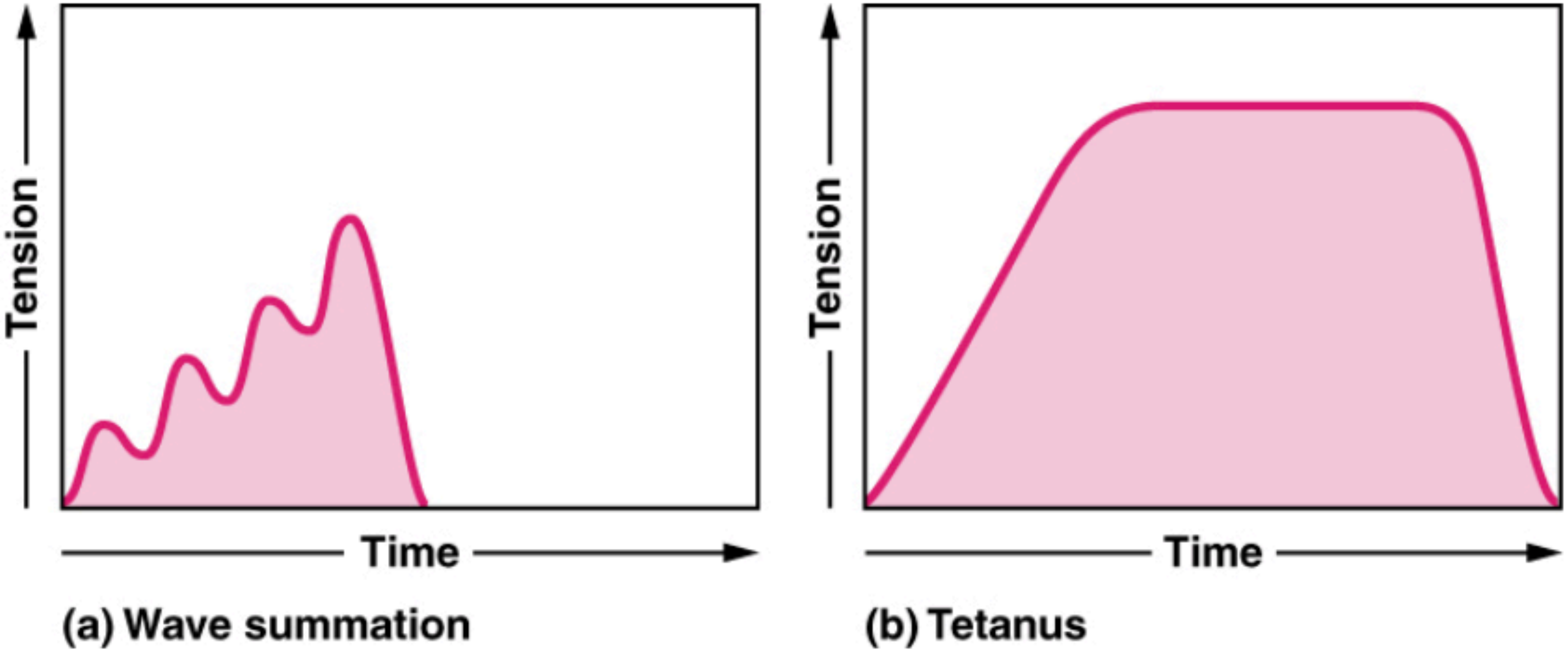
Cross-bridges form

- **Relaxation** period

Ca++ are pumped out Of sarcoplasm



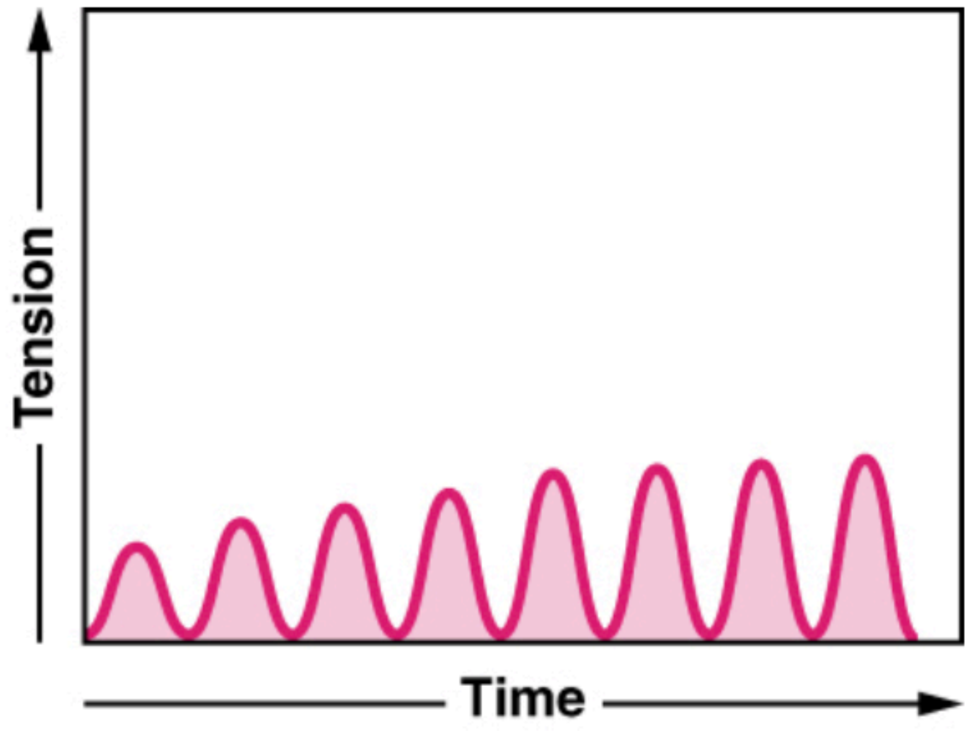
Principle of **Summation**
The **rate** of the motor neuron potential determines the **tension** produced in the **skeletal muscle**



Wave summation/Temporal summation

Treppe - Principle Of Skeletal Muscle

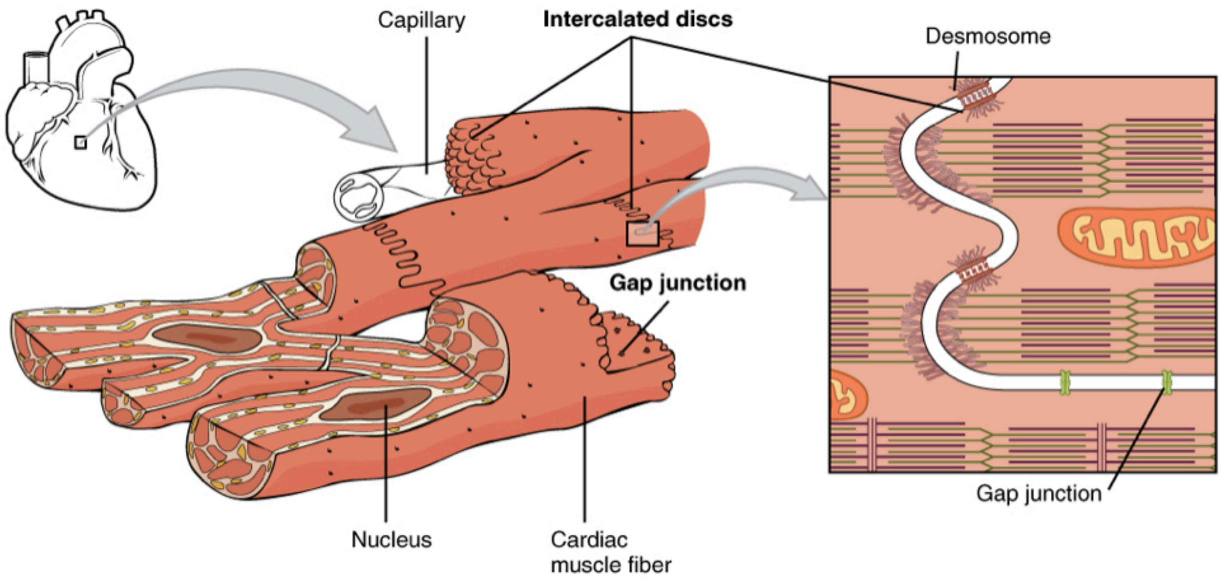
- Treppe = „stairs“
- In a resting state: the generated force that a muscle is able to perform is lower than the force of later contractions
- Why does it result?



Treppe

Cardiac Muscle In Comparison To Skeletal Muscle

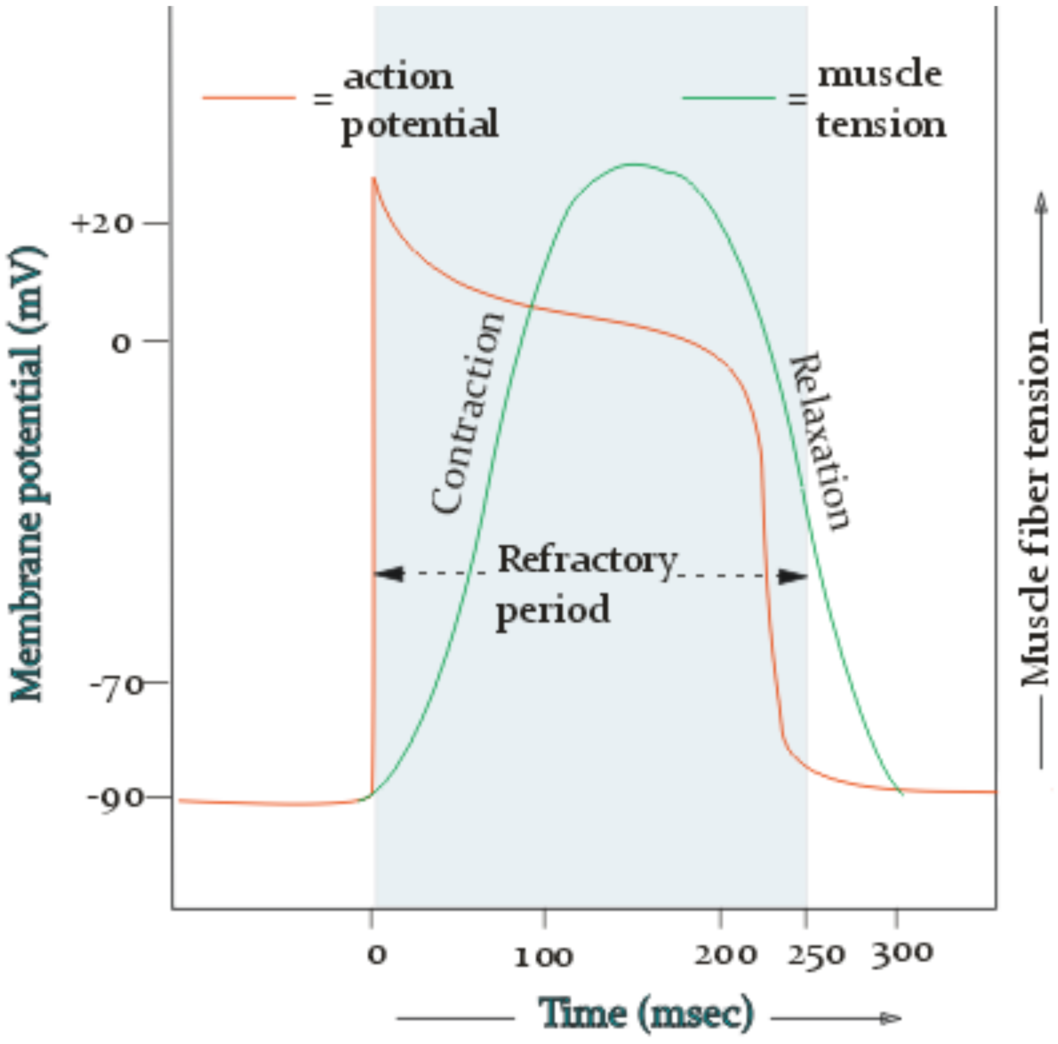
	Cardiac muscle	Skeletal muscle
Nuclei	1 (max.2)	Multi-nucleated
Innervation	Auto-rhytmic	Alpha-neurones
AP	300ms	1ms
Features	Intercalated discs Gap junctions	



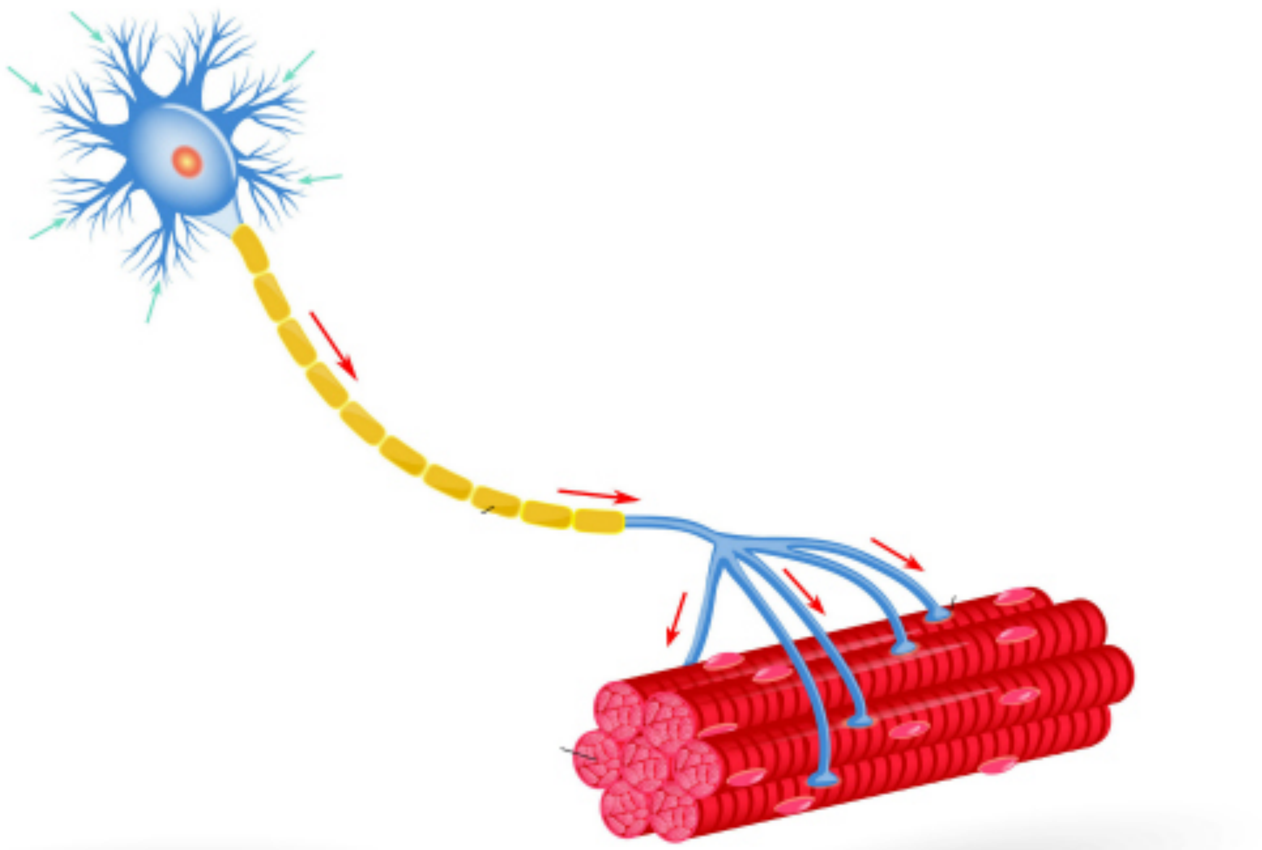
The Cardiac Action Potential

- Phase 4: RMP -85mV
- Phase 0: Depolarization (Na influx)
- Phase 1: voltage-gated K channels open (slight Repolarization), Na-channels inactivated,
- Phase 2: Plateu (Ca influx, K efflux)
- Phase 3: Voltage-gated Calcium Channels close, only K channels open

—> Is tetanus (summation of contractions) possible in myocytes?



The relationship between an action potential and the refractory period to the duration of the contractile response in cardiac muscle



COMPARING MUSCLE TO NERVE I

Tonio Naka

- Transmission in both directions
- Longer action potential duration – 1~5 milliseconds
- And slower velocity – 3~5m/s

SIGNAL TRANSMISSION IN SMOOTH MUSCLE

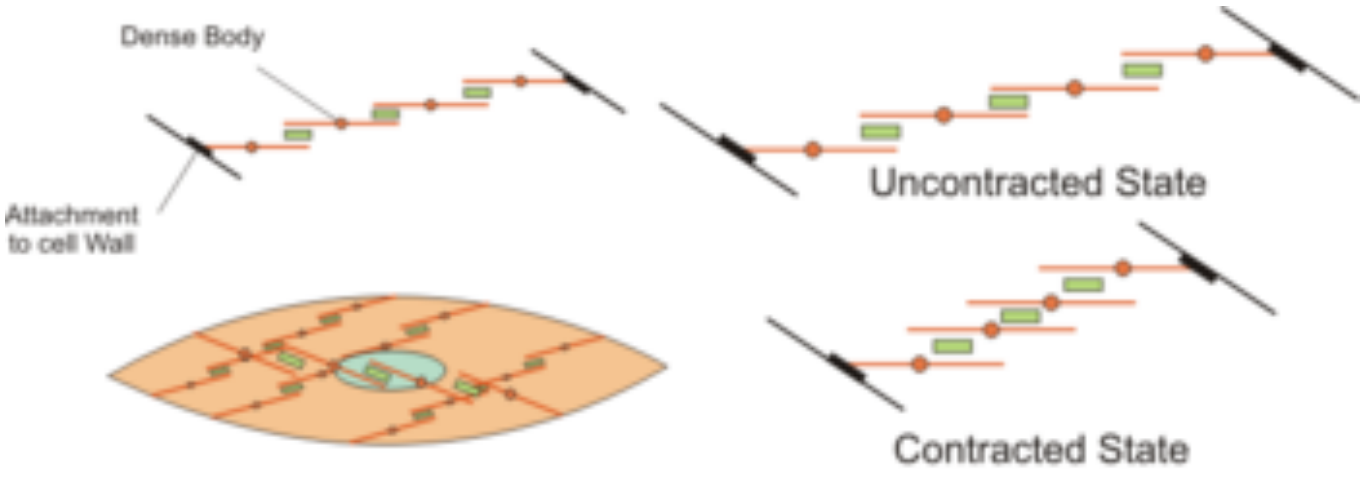
COMPARING MUSCLE TO NERVE II

Smooth Muscle Contraction Mechanism + Alpha

- Calmodulin instead of troponin
- Scares Sarcoplasmic reticulum

-> influence from external environment

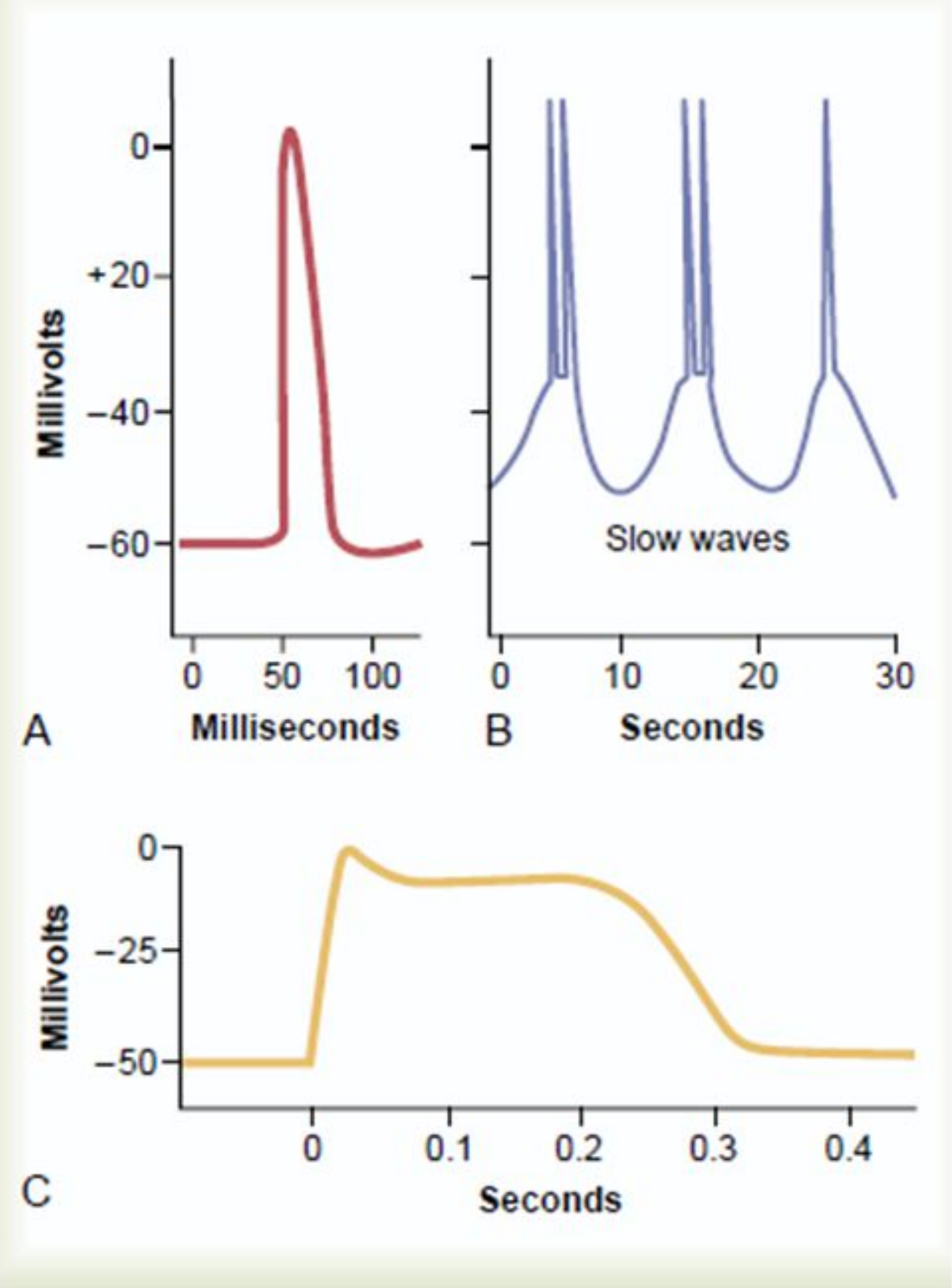
- Prolonged more powerful contraction with less ATP degredation



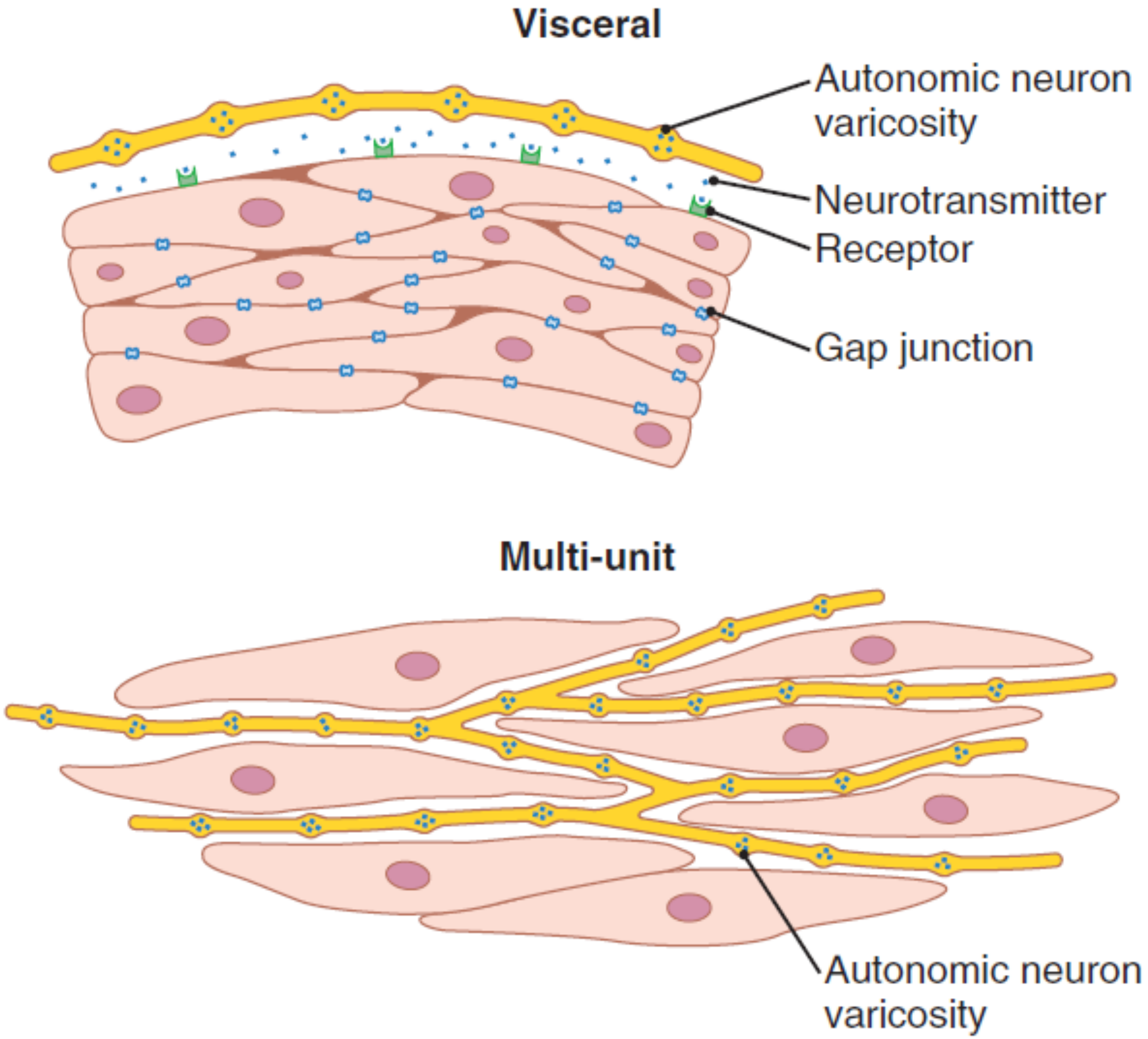
Actin-myosin filaments

Action Potential In Smooth Muscle

- Only seen in unitary smooth muscle
- Longer duration ~50 msec
- Can have plateau
- Can be elicited by different sources



Neuromuscular Junction Of Smooth Muscle

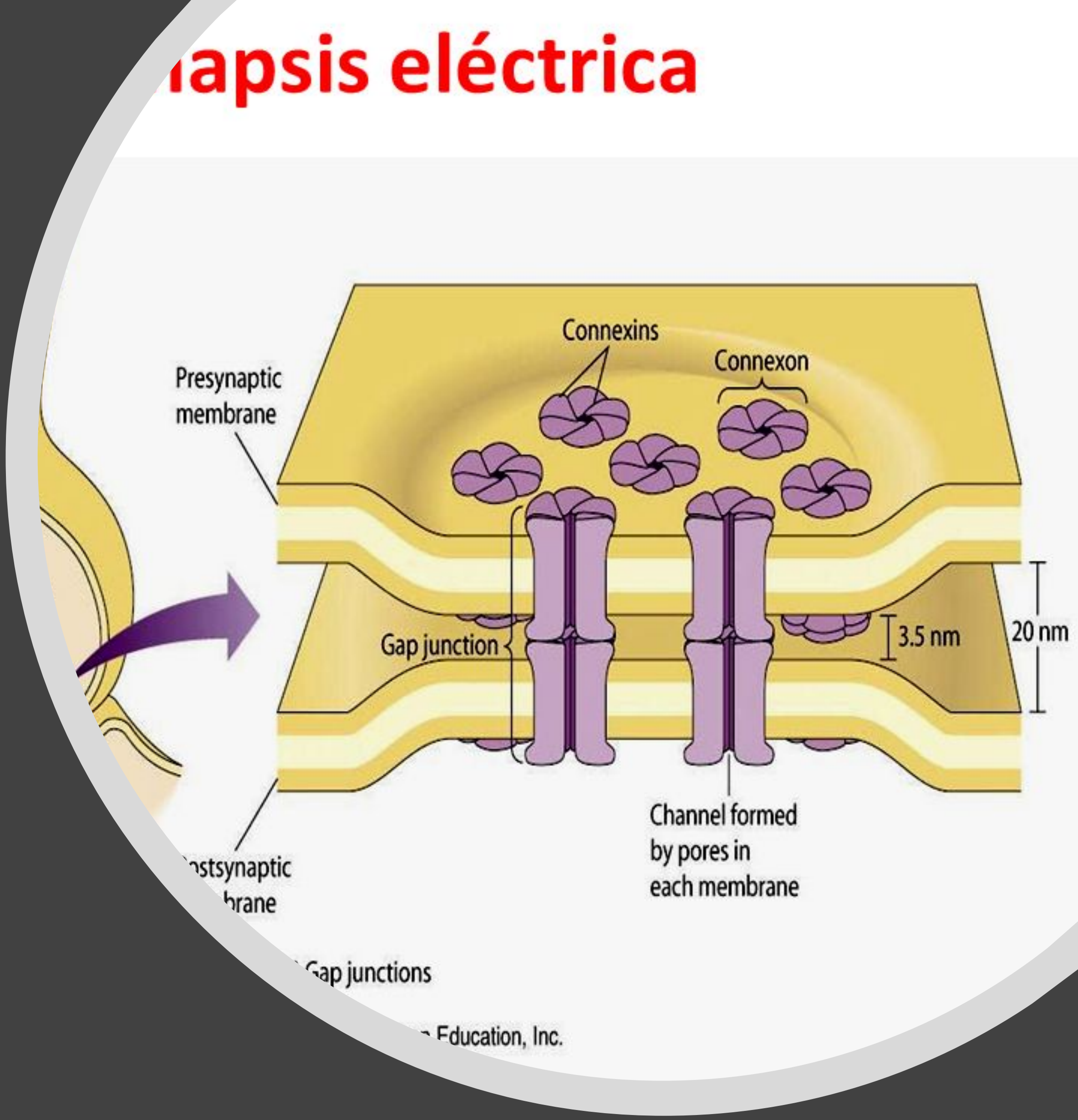


Back Two Slides For Slow Wave Potential

COMPARING MUSCLE TO NERVE III

SIGNAL TRANSMISSION IN THE HEART

- Specialized junctions (gap junction)
- Low resistance pathways connecting cardiomyocytes
- Depolarization can spread quickly
- Example of electric synapse

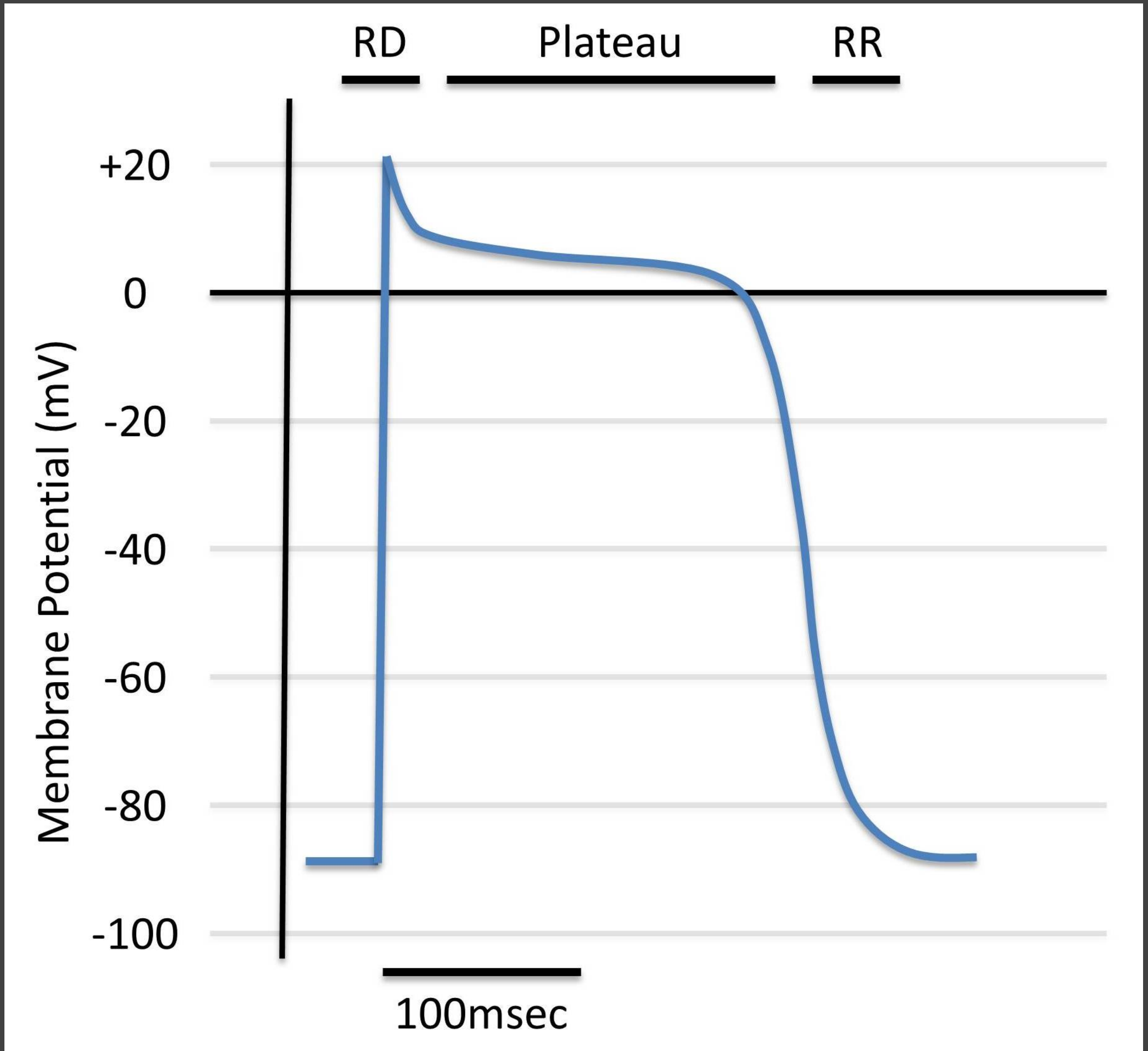


Distinct Action Potential

- A prolonged plateau phase

-> prevention of tetanus

- Fast & L type channels



SKELETAL MUSCLE TONE REGULATION, GAMMA SYSTEM

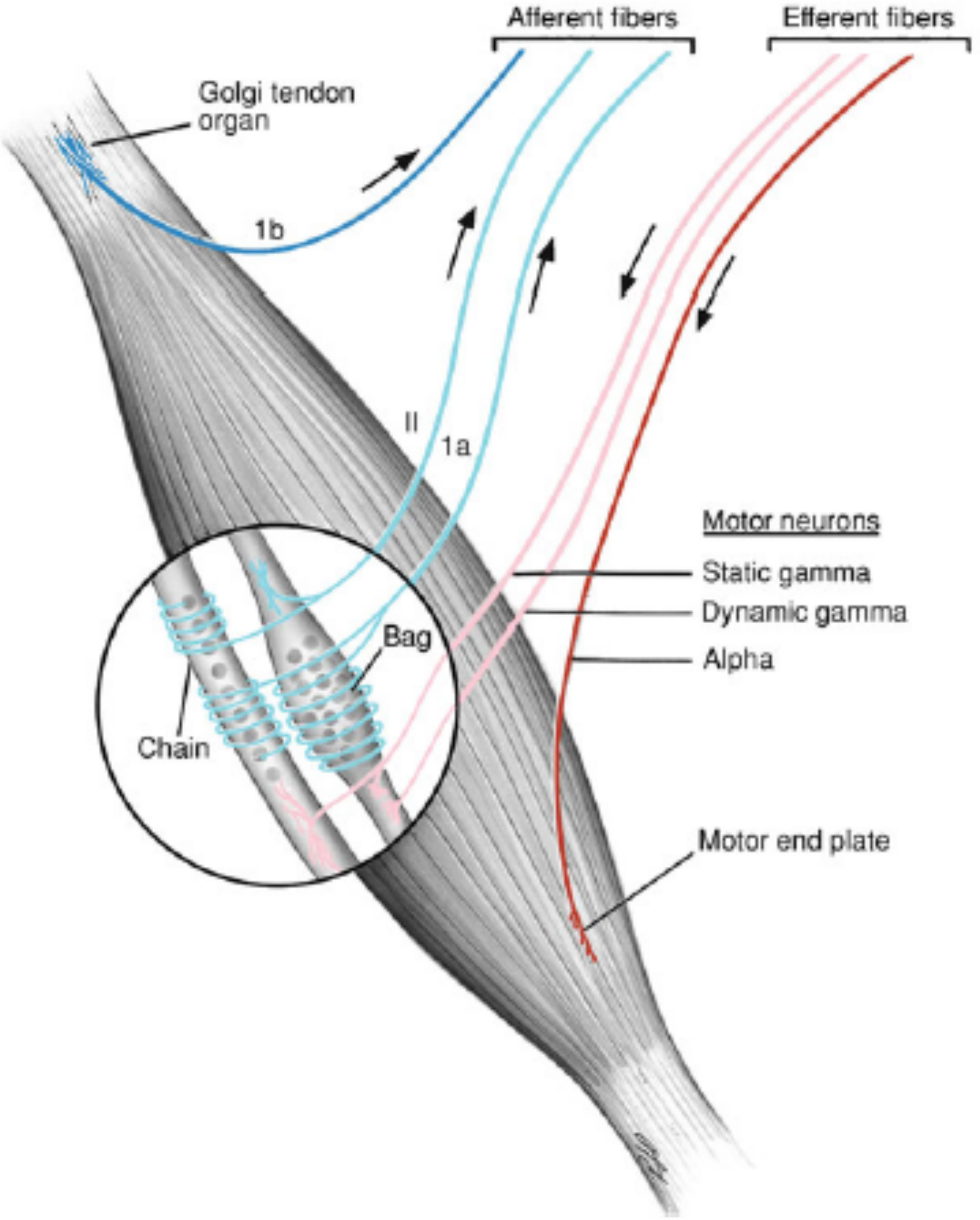
Camilla Rossi

Polar ends

Central portion

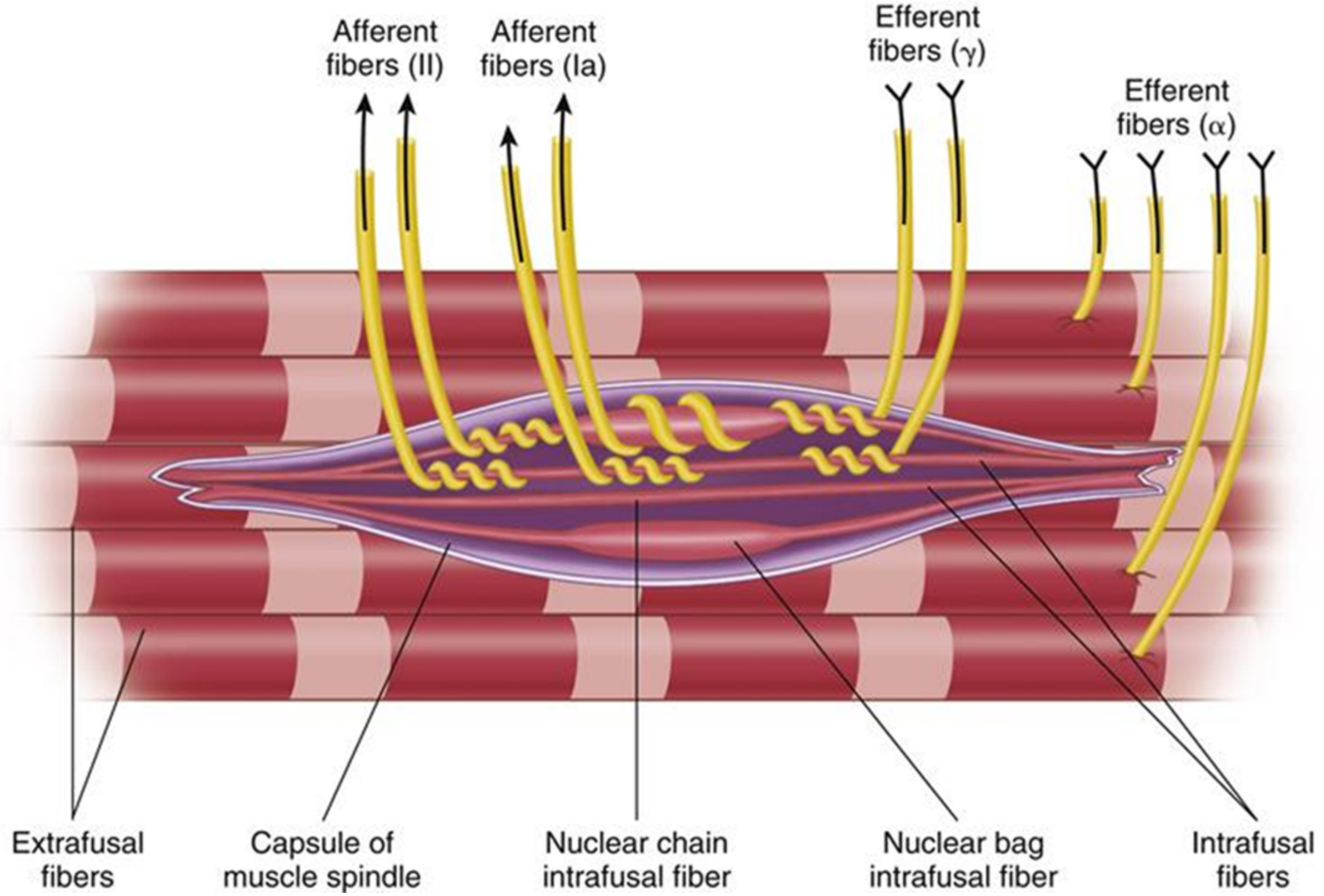
Nuclear bag fibers

Nuclear chain fibers



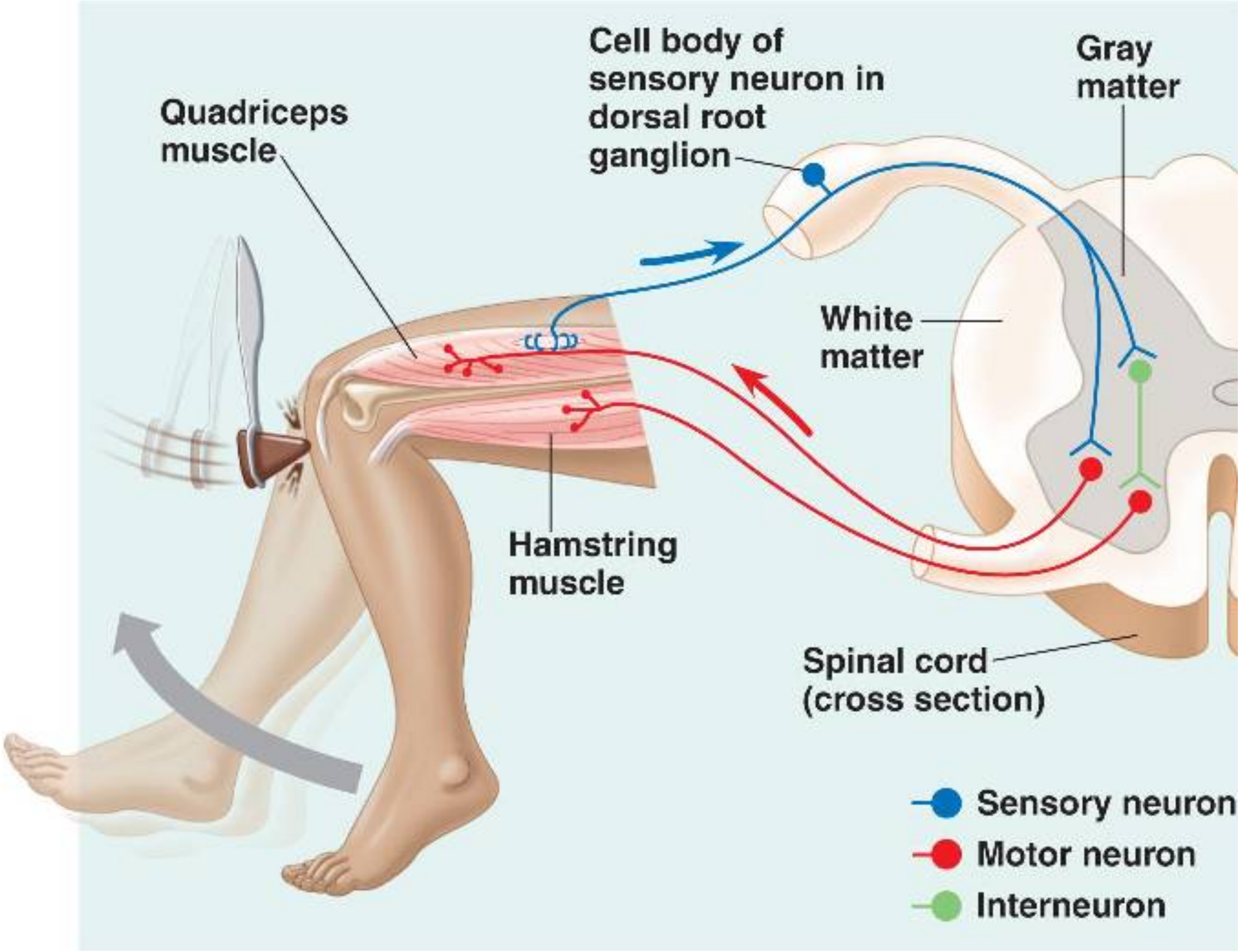
Stretch Reflex

Reflexive contraction following stretching



Knee Jerk

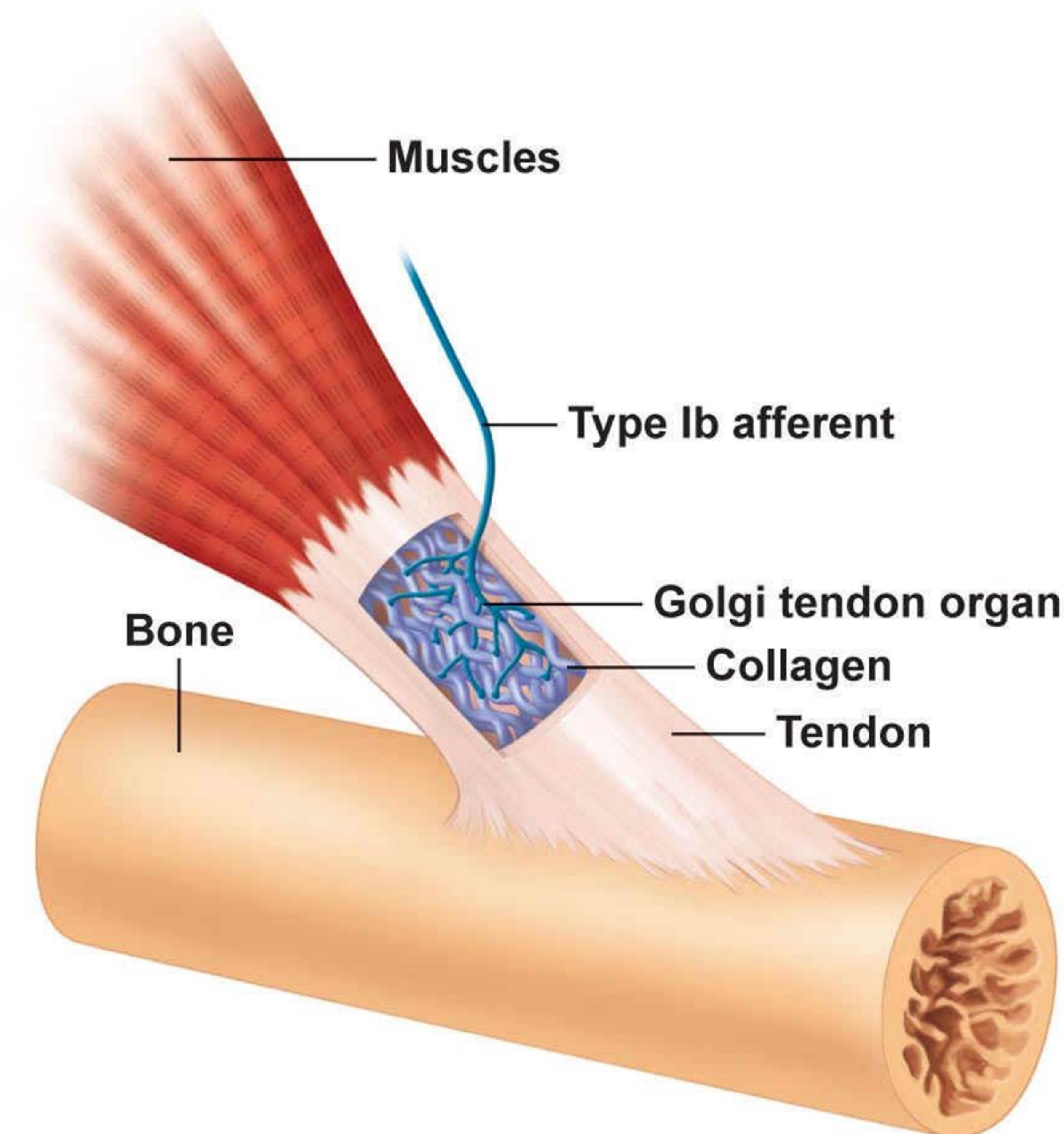
- Hyperreflexia
- Hyporeflexia



Golgi Tendon Organ

Tension and change in tension

Autogenic inhibition/ inverse myotatic reflex

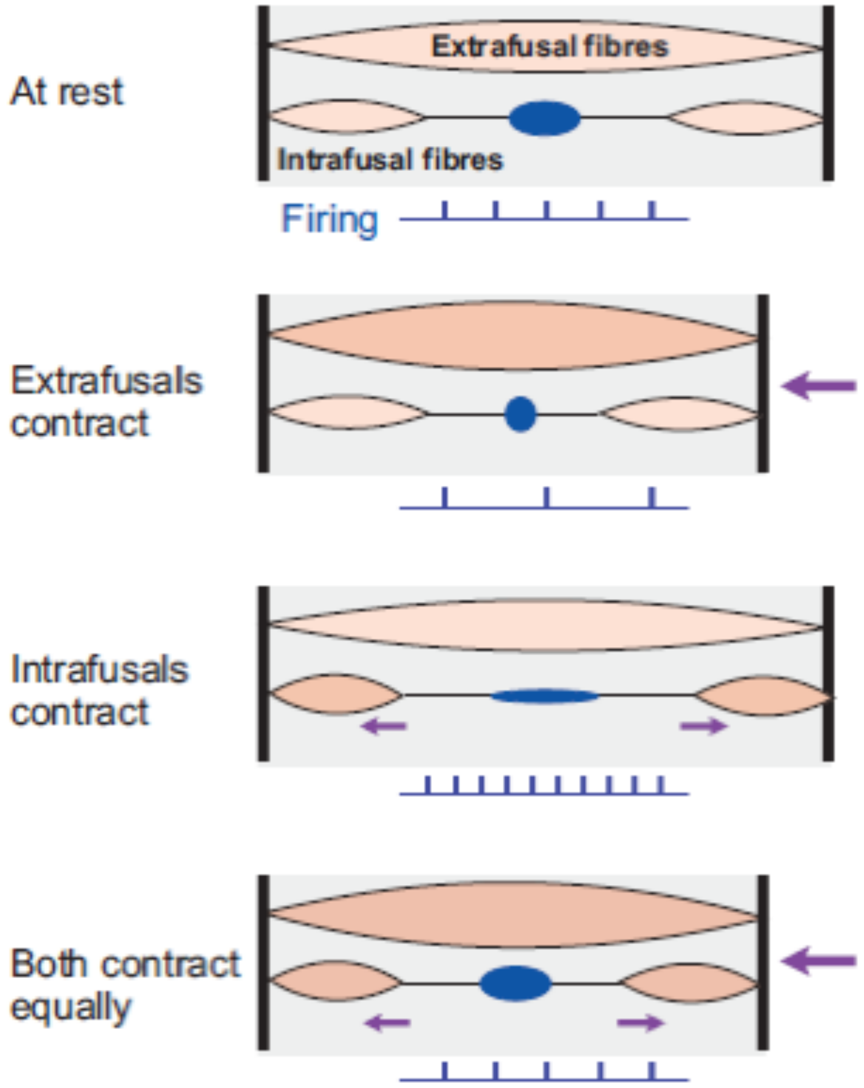


Gamma Neurons

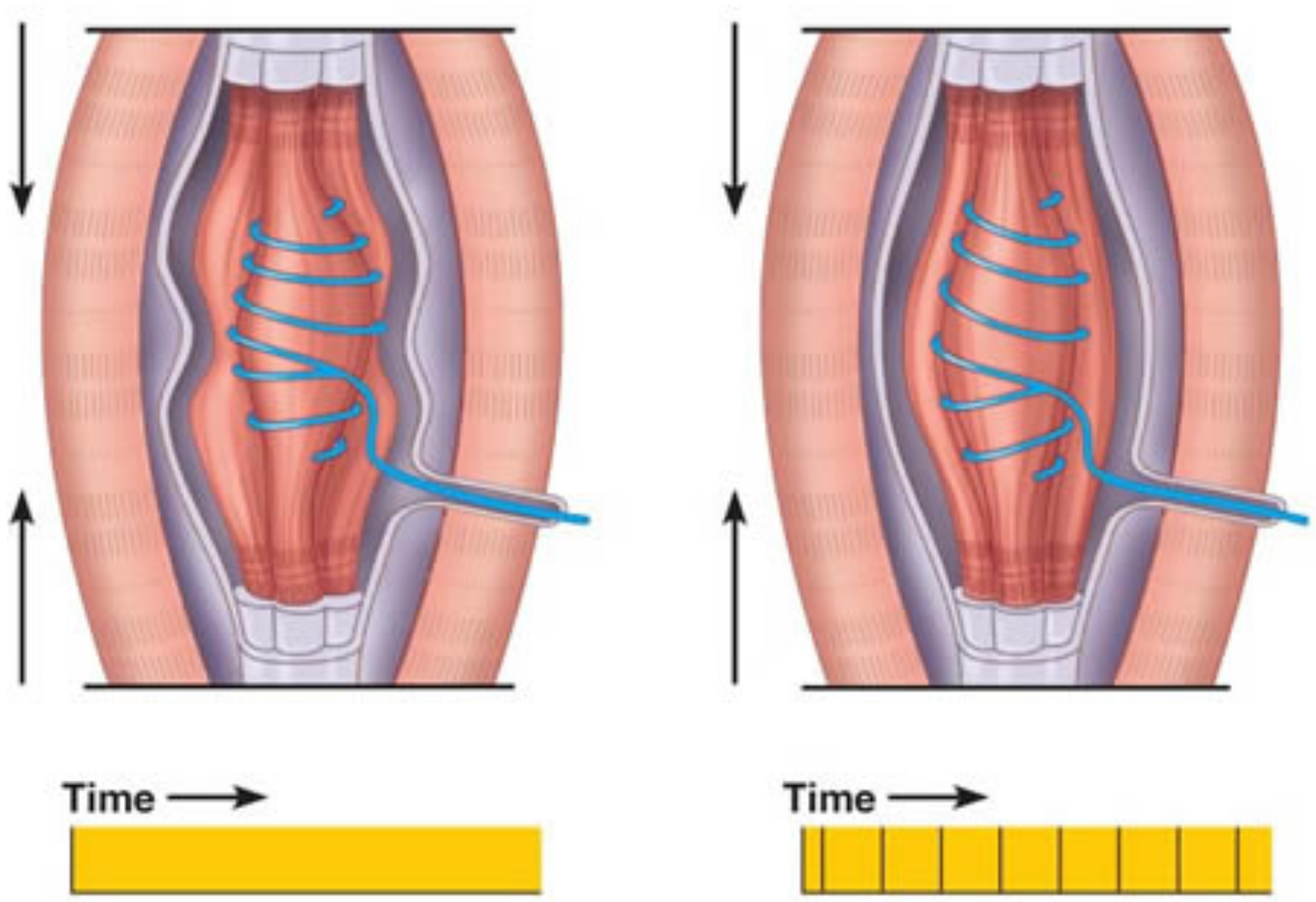
Spindle remains taut

sensitive over a wide range

of muscle lengths



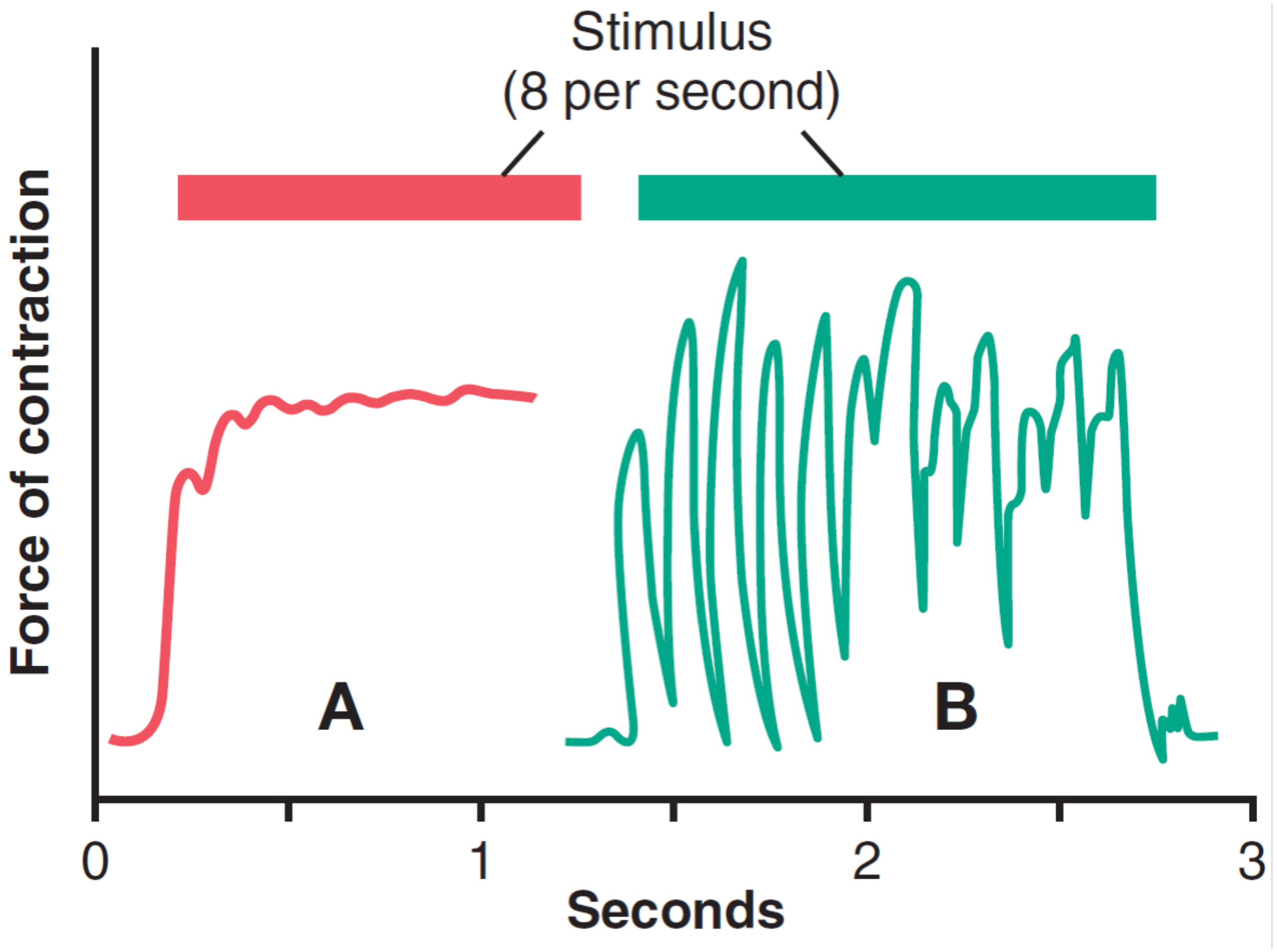
Alpha-Gamma Coactivation



Damping Function

The myotatic reflex acts in the coarse adjustment of muscle tension.

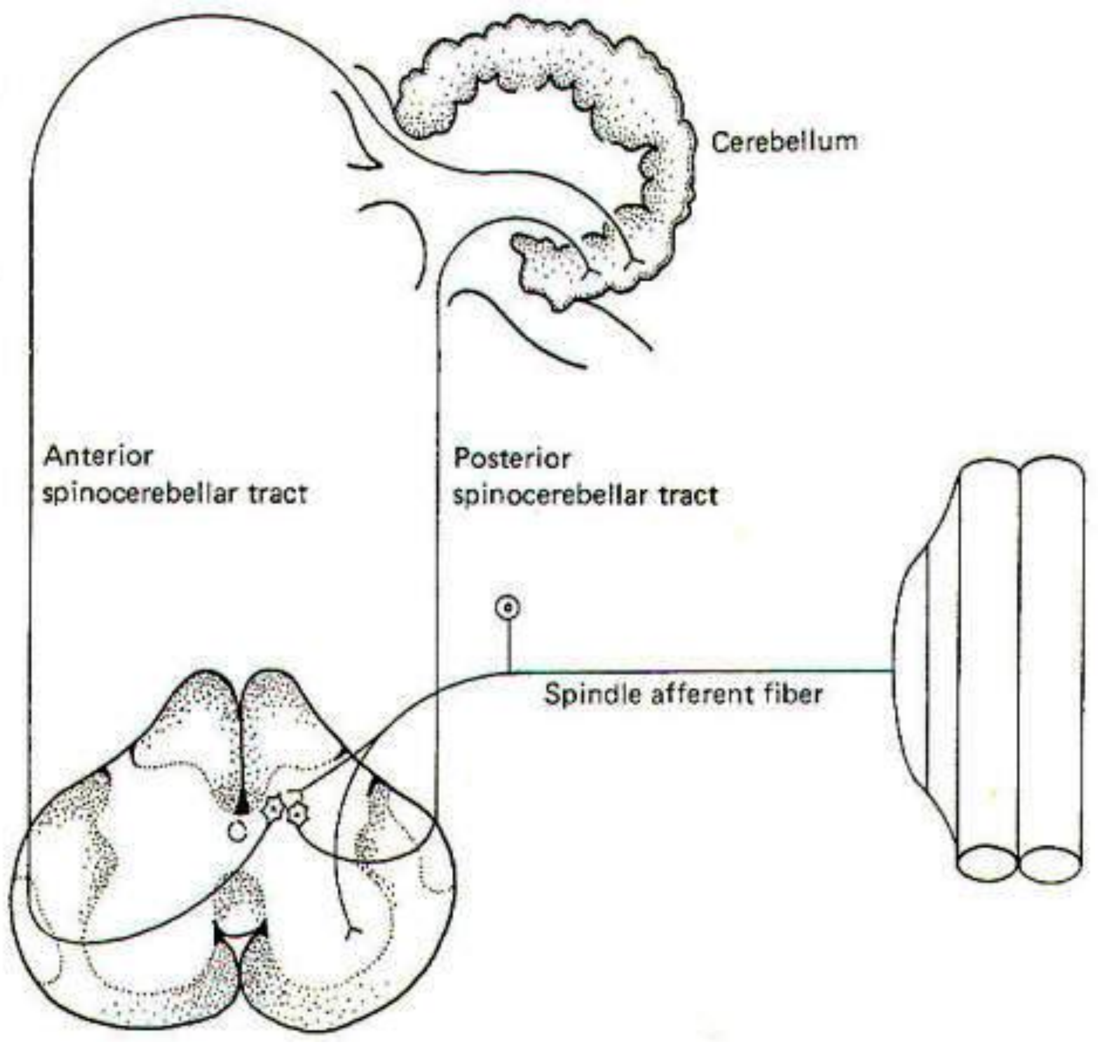
The fine adjustment in muscle activity is dependent on the integrity of the gamma loop.



Supraspinal Influences

Cerebellum mainly influences muscle tone through its connection with reticular and vestibular nuclei.

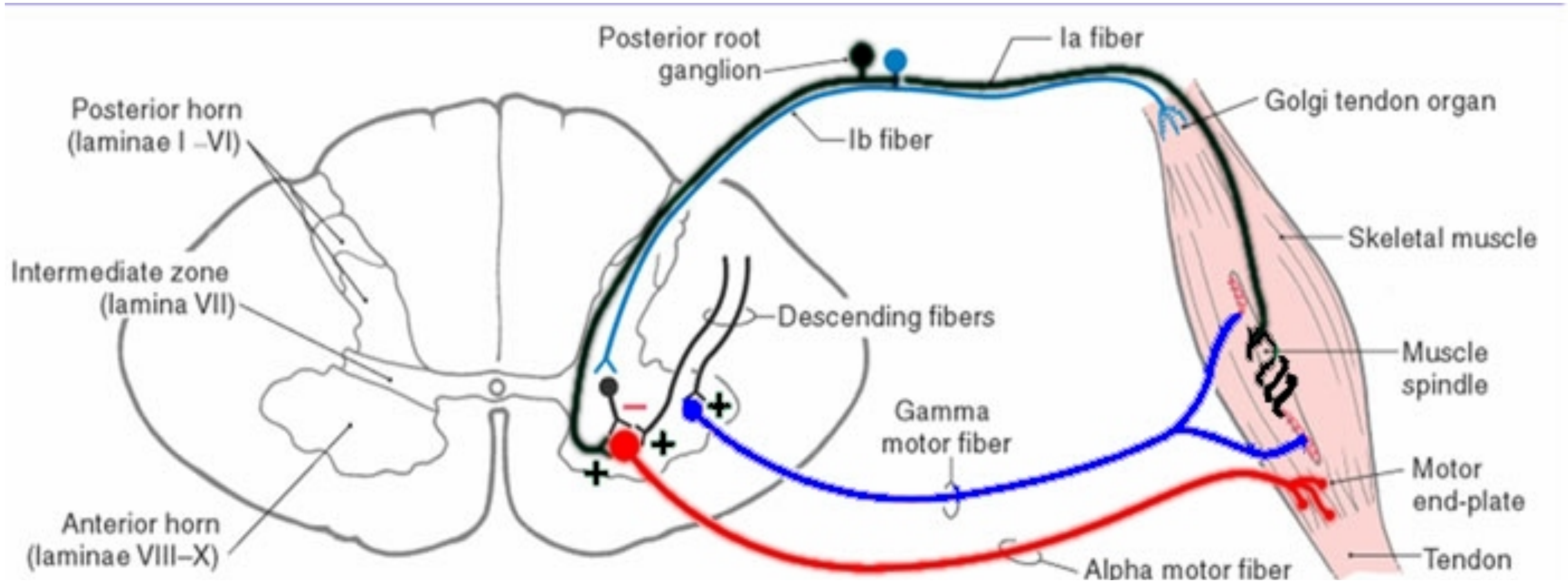
Muscles have a pre-set length determined by gamma motor neurons, indirectly controlled by the cerebellum.



Gamma Loop Spindle As A Comparator

Signalling difference between the desired length of the muscle and its actual length.

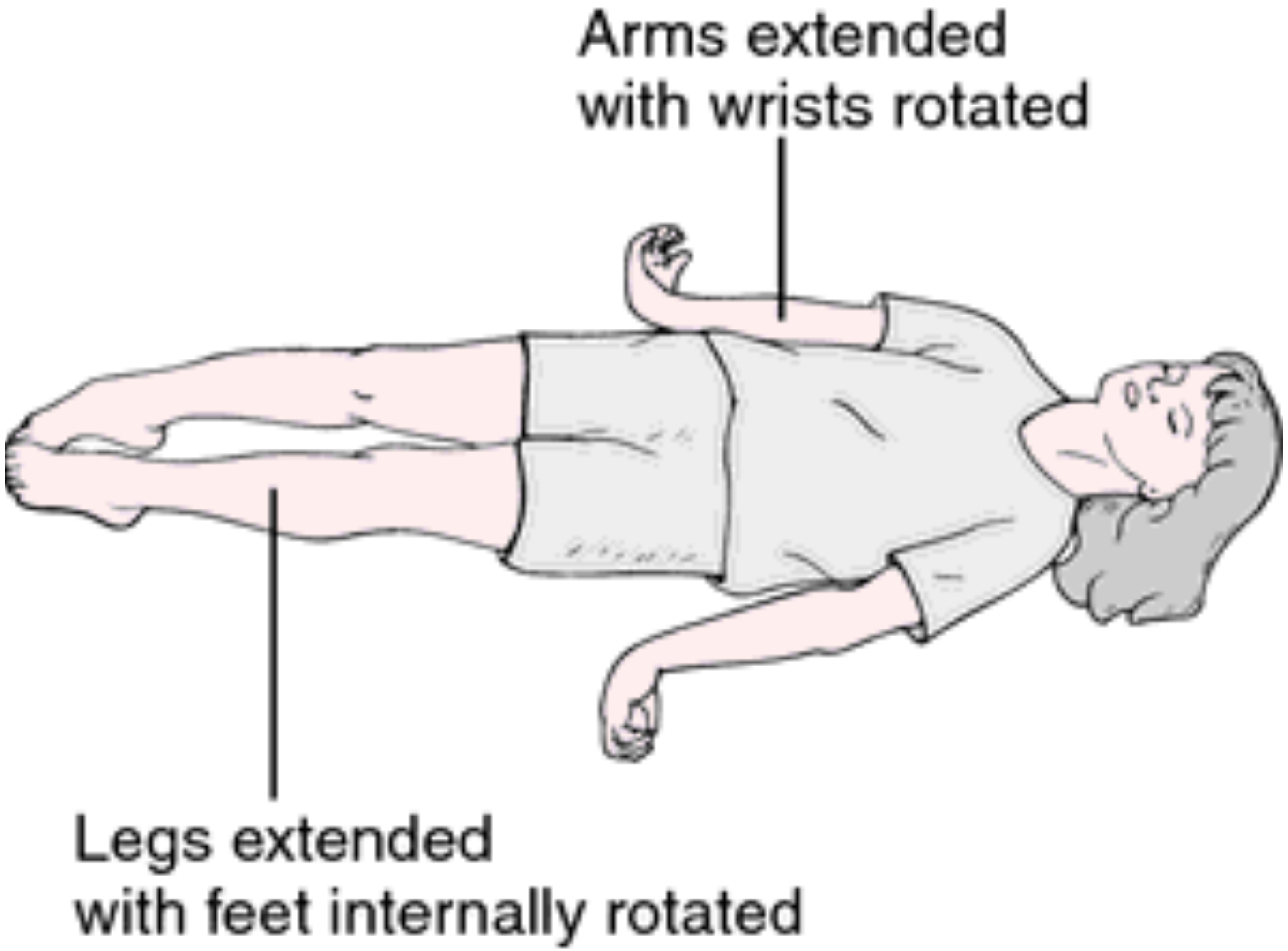
If shorter than the actual length, the spindle afferents stimulate the motor neurons to generate a force that makes the muscle contract.



Decerebrate Posture

Compression of the brainstem at a low level.

Increased discharge from gamma motor neurons, which facilitates the stretch reflex.



Cerebellar Disease

Cerebellum fine tuning motor activities

- Ataxia
- Hypotonia
- Dysdiadochokinesia
- Dysmetria
- Intention Tremor