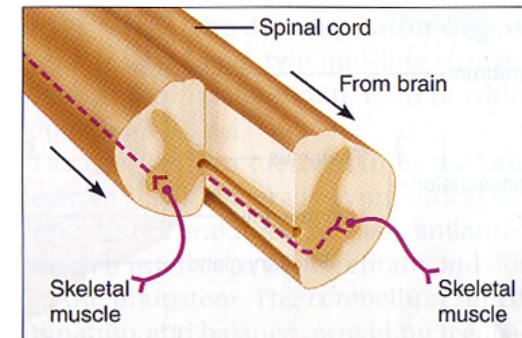
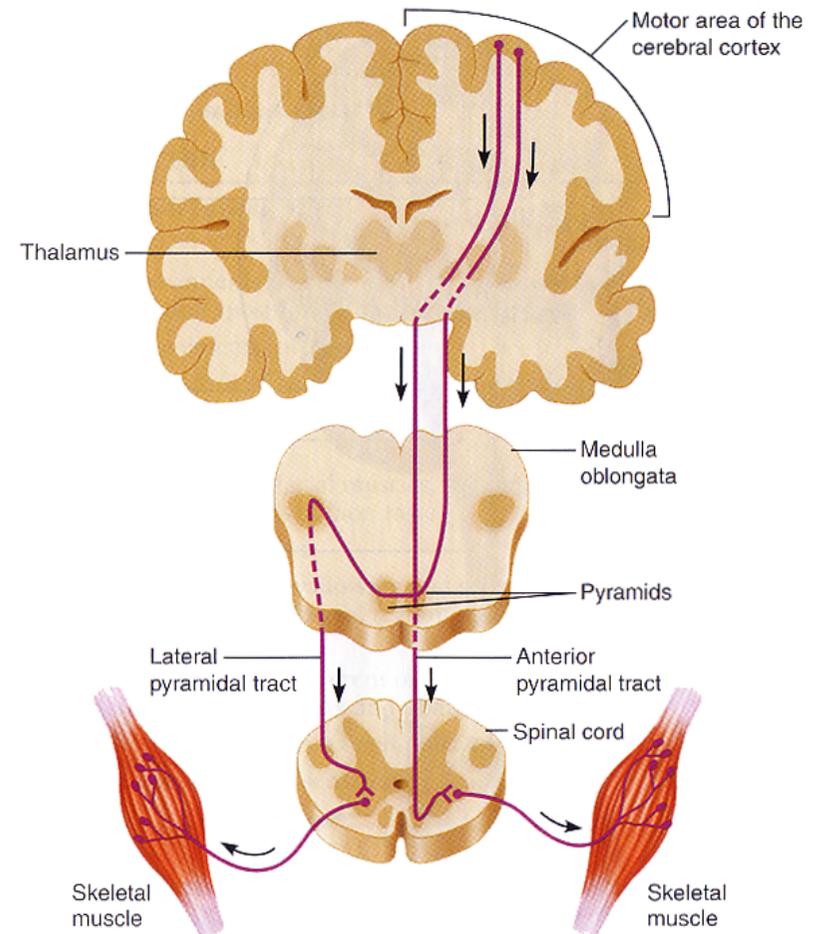


# Le vie nervose efferenti (o discendenti) motorie

## Omeostasi

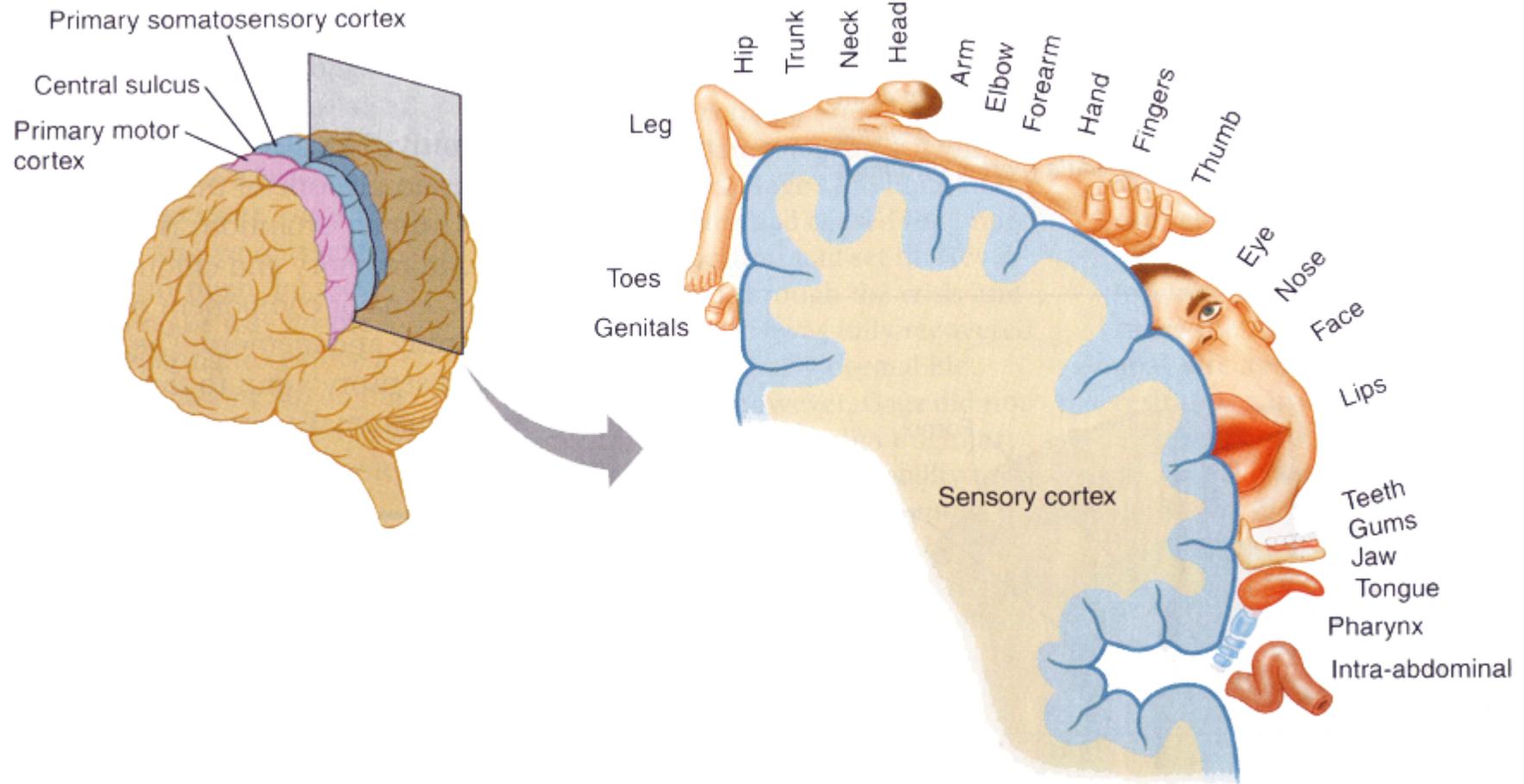
“Mantenimento di condizioni stabili  
mediante  
meccanismi fisiologici coordinati”

- 1) Comunicazione tra cellule
- 2) Interazione con l'esterno
- 3) Reazione agli stimoli ←
- 4) Autoritmicità (cuore, respiro)



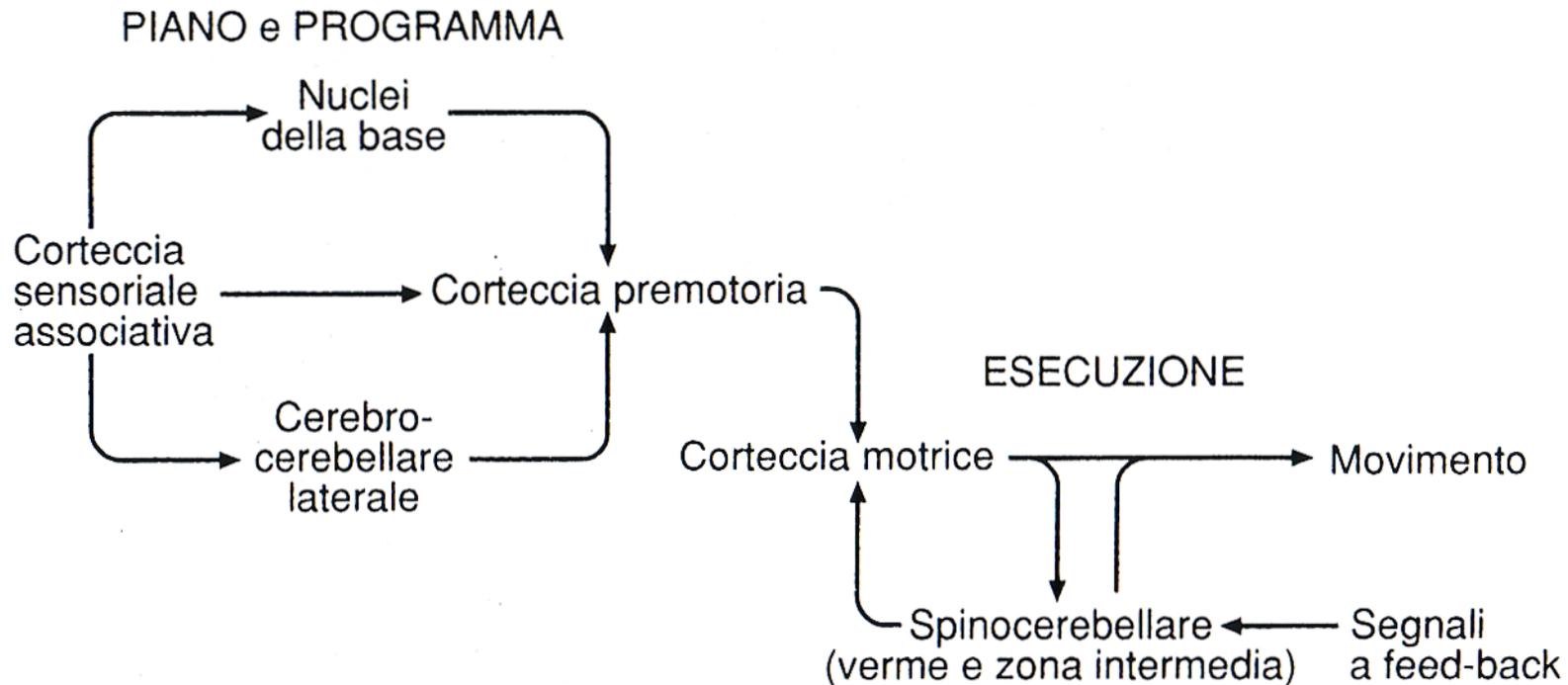
(b) Descending tracts

# La corteccia motoria primaria



# Il controllo dell'ideazione e dell'esecuzione del piano motorio

---



**Figura 12-15** Rappresentazione ipotetica del flusso di informazione che governa l'inizio e l'esecuzione del movimento volontario. Per semplicità di circuito è stata omessa la stazione talamica di relais per i nuclei della base, per il cervelletto e per le stazioni somestesiche. (Da E.R. Kandel e J.H. Schwartz, op. cit.)

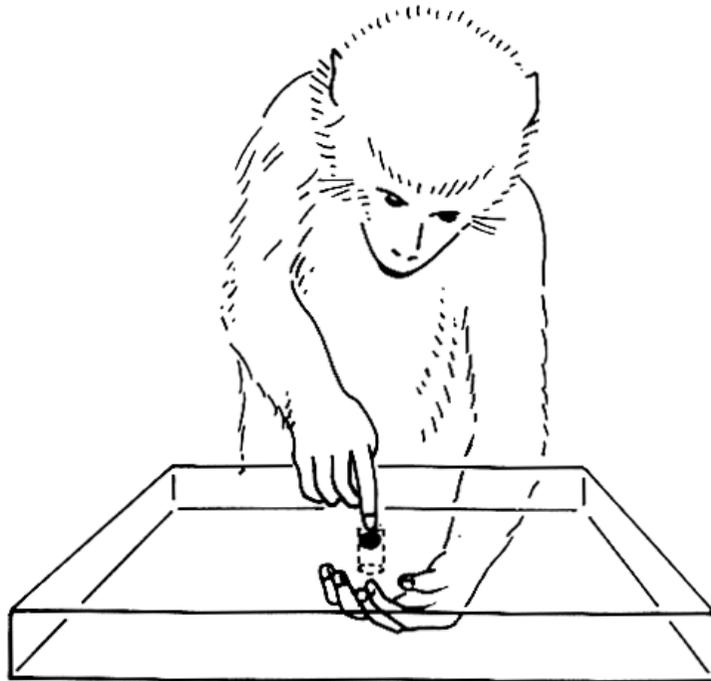
# Il ruolo della corteccia premotoria nell'ideazione del piano motorio

**FIGURA 40-15**

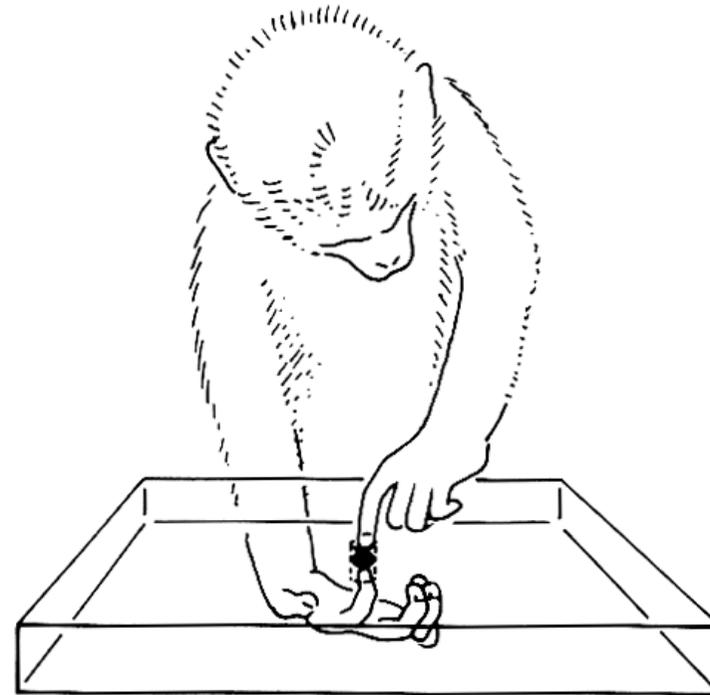
A seguito della lesione unilaterale dell'area motrice supplementare si hanno deficit della coordinazione bimanuale. Una scimmia normale spinge il cibo attraverso il foro con una mano e lo afferra con l'altra. L'animale lesionato utilizza gli indici di entrambe le mani per spingere il cibo dall'alto e dal basso.

(Modificata, da Brinkman, 1984).

Animale normale



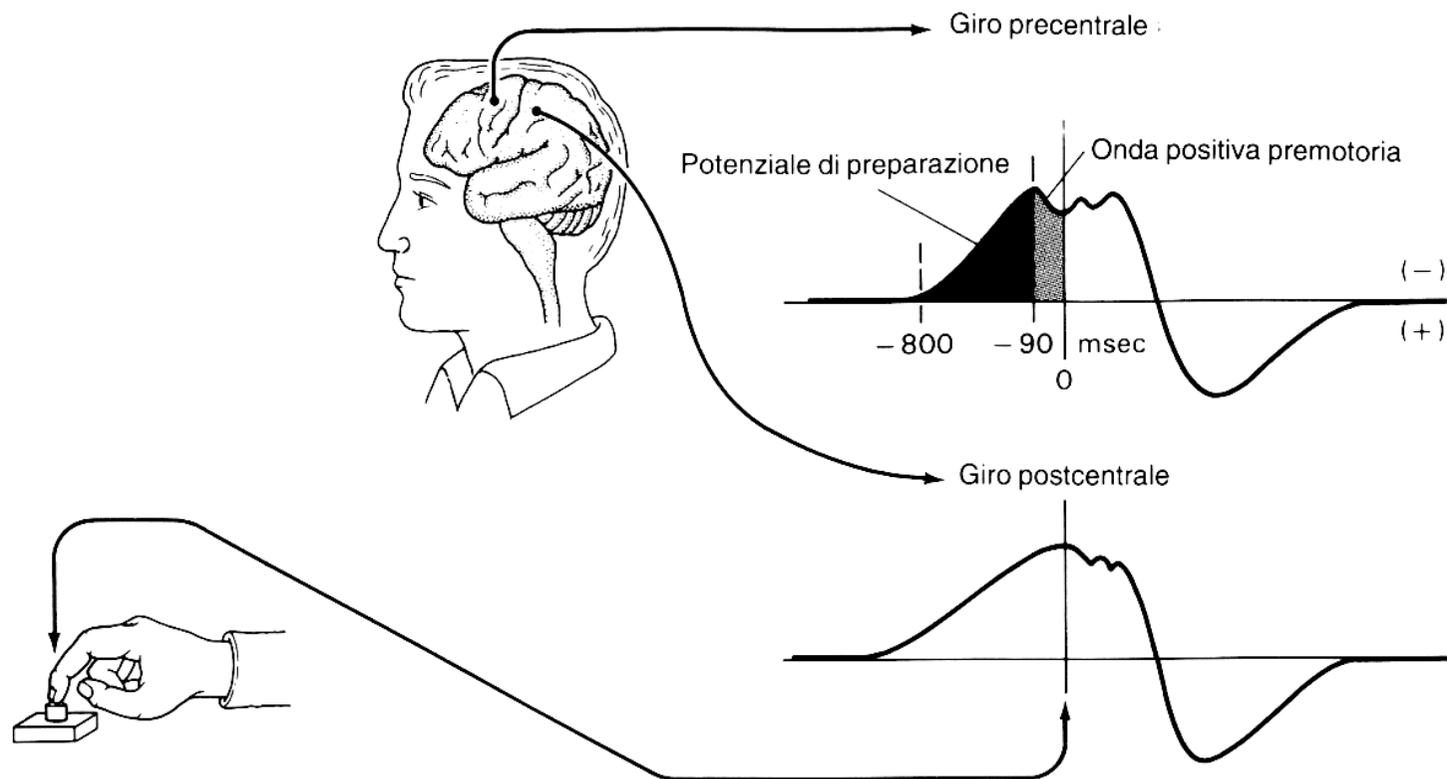
5 mesi dopo la lesione dell'area motrice supplementare di destra



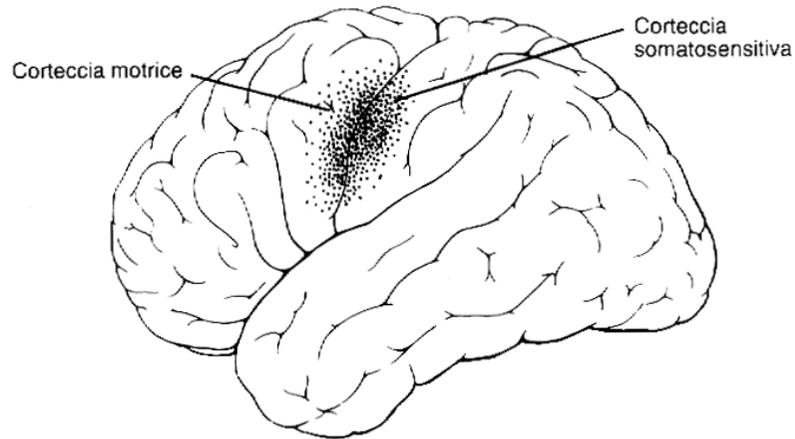
# L'attivazione dell'area premotoria precede l'attivazione dell'area motoria primaria

**FIGURA 40-12**

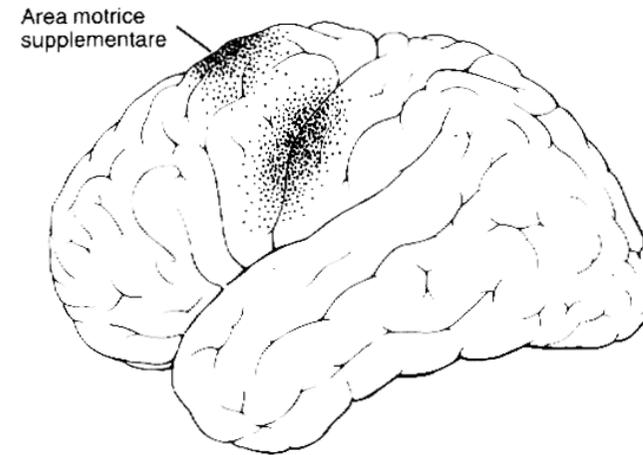
I neuroni dell'area premotoria laterale cominciano a scaricare circa 800 ms prima dell'inizio del movimento volontario del dito. I tracciati sono stati ottenuti eseguendo nell'Uomo registrazioni mediante elettrodi posti sullo scalpo in corrispondenza della corteccia frontale. (Modificata, da Deecke et al., 1969).



**A** Semplice flessione delle dita (esecuzione)



**B** Sequenza di movimenti delle dita (esecuzione)



**FIGURA 40-14**

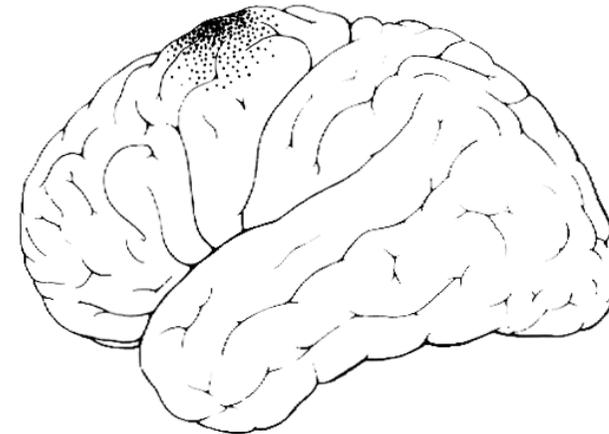
Gli aumenti localizzati del flusso ematico cerebrale durante l'esecuzione di particolari comportamenti indicano quali aree della corteccia cerebrale sono implicate in quei comportamenti. (Modificata, da Roland et al., 1980).

**A.** Quando un dito viene tenuto premuto contro una molla, si osserva un aumento del flusso ematico a livello delle aree della mano delle cortecce motrice primaria e somatosensitiva primaria. L'aumento a livello dell'area motrice è in rapporto con l'esecuzione della risposta motoria, mentre quello a livello dell'area sensitiva è la conseguenza dell'attivazione dei recettori periferici.

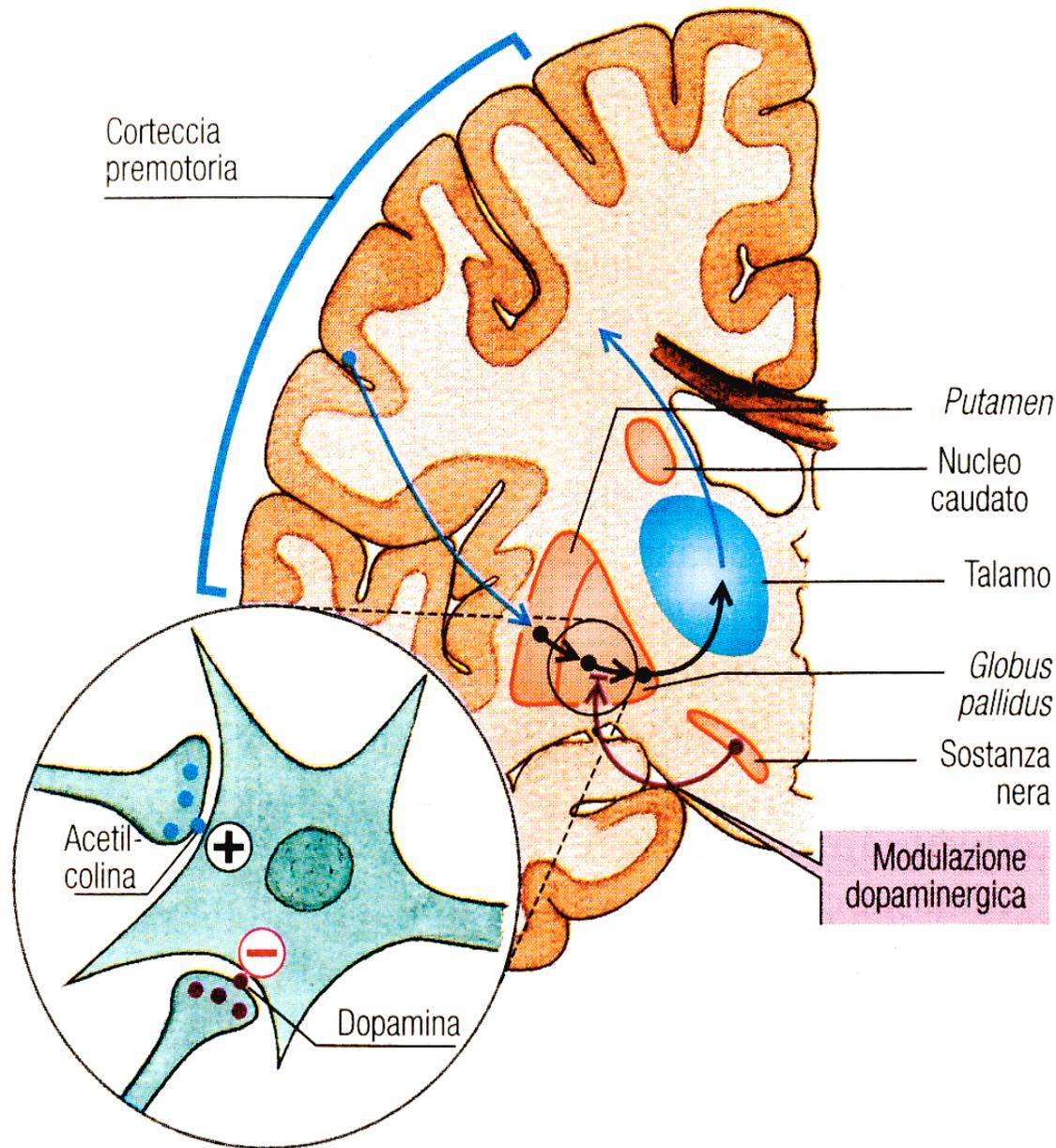
**B.** Durante l'esecuzione di una complessa sequenza di movimenti delle dita l'aumento del flusso ematico interessa anche l'area motrice supplementare.

**C.** Durante la ripetizione mentale della stessa sequenza di movimenti il flusso ematico aumenta solo a livello dell'area motrice supplementare. Per determinare il flusso ematico si procedeva ad iniettare per via endovenosa una soluzione salina contenente xeno radioattivo e a misurare la radioattività a livello di parti diverse della corteccia cerebrale mediante una serie di rivelatori posti sullo scalpo. Poiché il flusso ematico locale aumenta con l'aumento dell'attività nervosa, la misurazione della radioattività fornisce un indice attendibile dell'attività nervosa in corrispondenza della superficie cerebrale.

**C** Sequenza di movimenti delle dita (ripetizione mentale)



# I nuclei della base



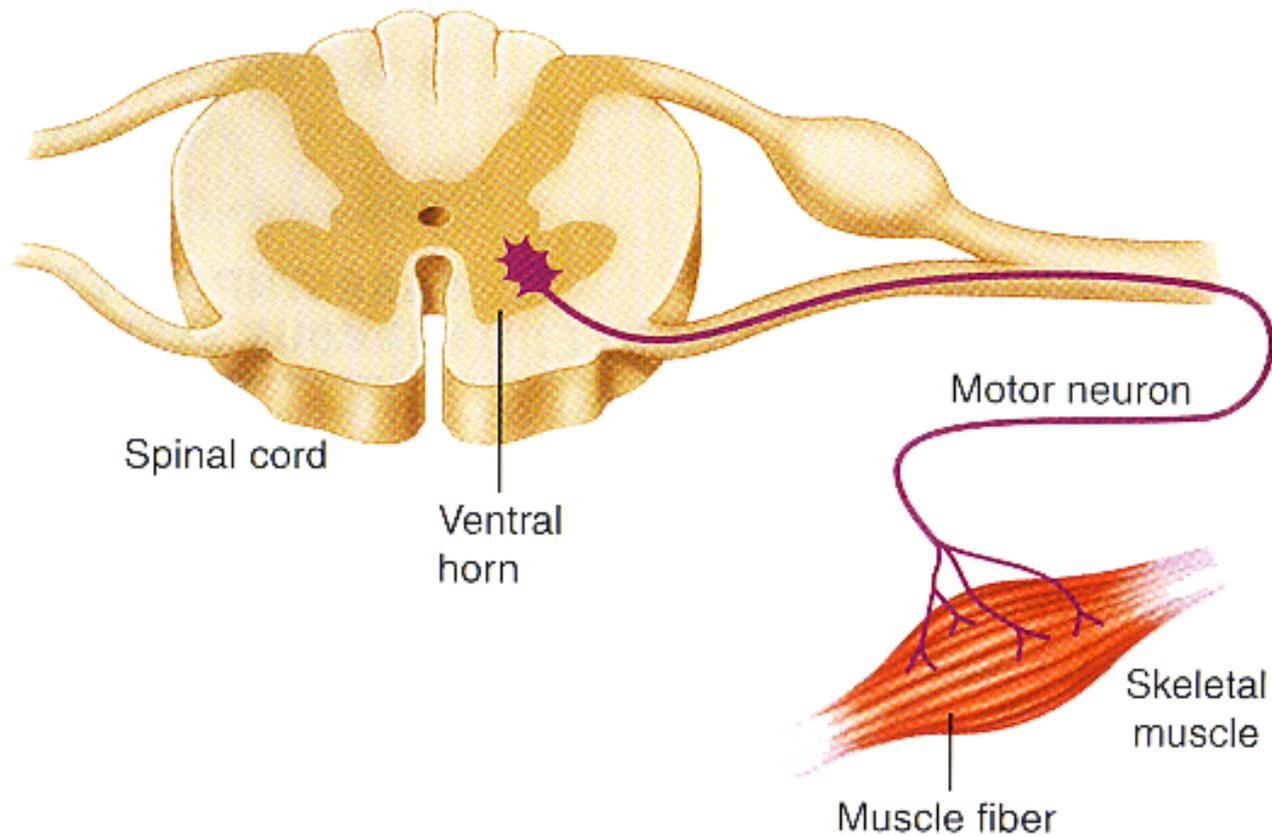
## Il morbo di Parkinson

**Figura 27.22** Schema di alcuni circuiti del "sistema extrapiramidale" a livello dei nuclei basali dello striato. Il *putamen* e il nucleo caudato ricevono informazioni dal complesso della corteccia telencefalica. Dal *globus pallidus* parte una via che, tramite il talamo, raggiunge la corteccia premotoria. Questi circuiti sono modulati da assoni provenienti dalla sostanza nera mesencefalica, i quali rilasciano la dopamina come neurotrasmettitore (inserto).

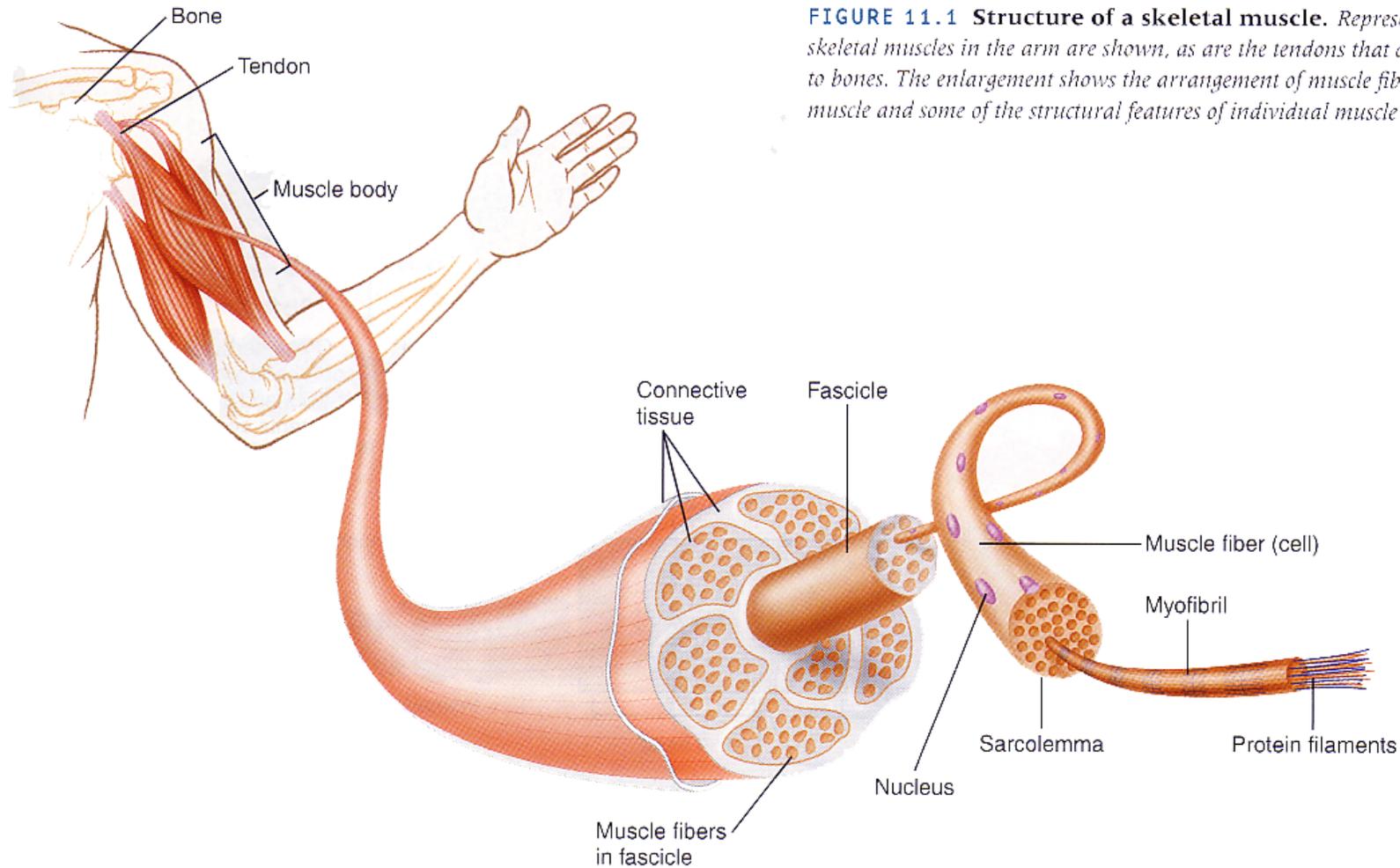
## La localizzazione dell' $\alpha$ -motoneurone

**FIGURE 10.13** Anatomy of somatic nervous system pathways.

*The somatic nervous system consists of motor neurons, which originate in the ventral horns of the spinal cord and terminate on skeletal muscle fibers throughout the body.*

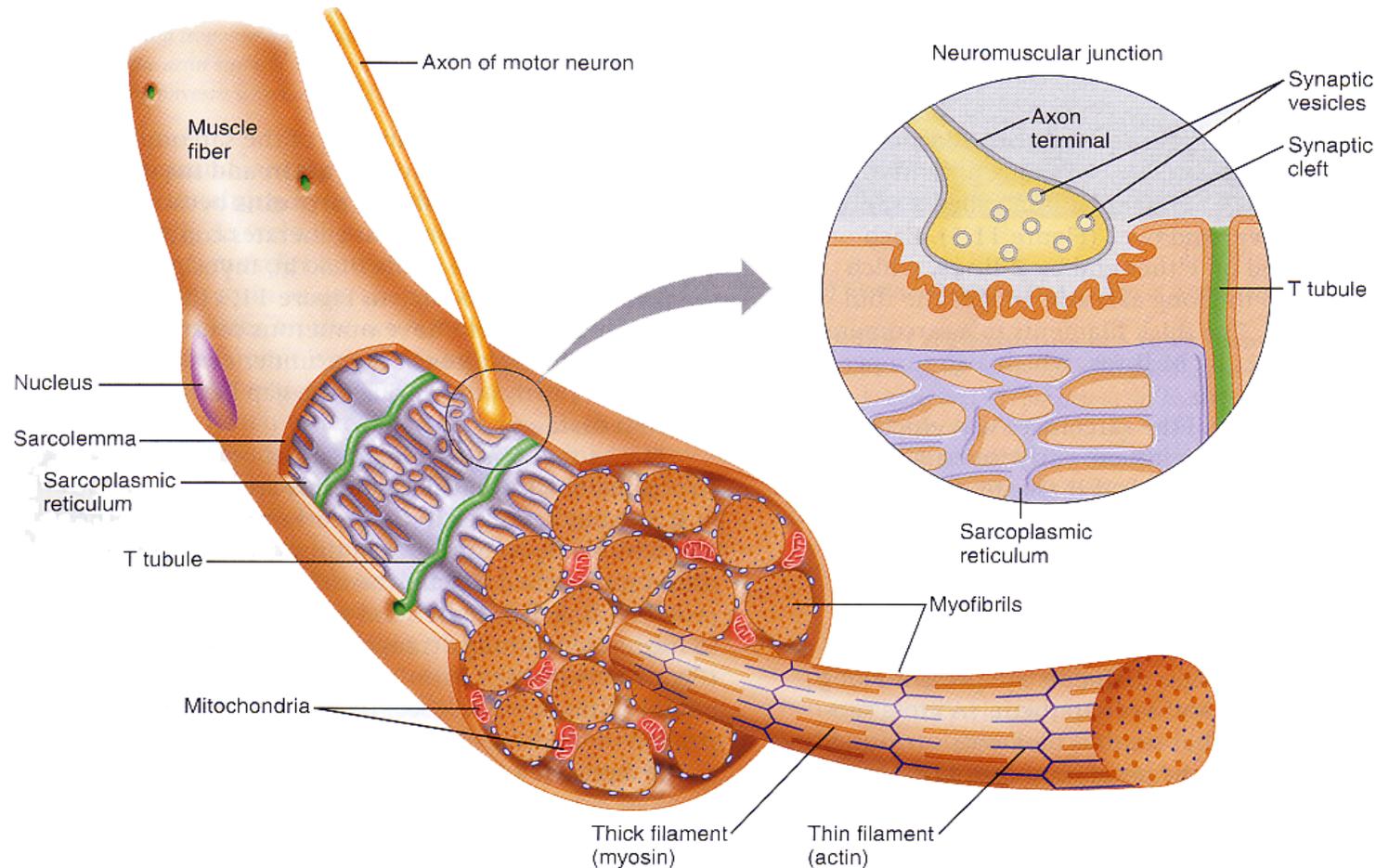


# L'organizzazione anatomo-funzionale del tessuto muscolare scheletrico

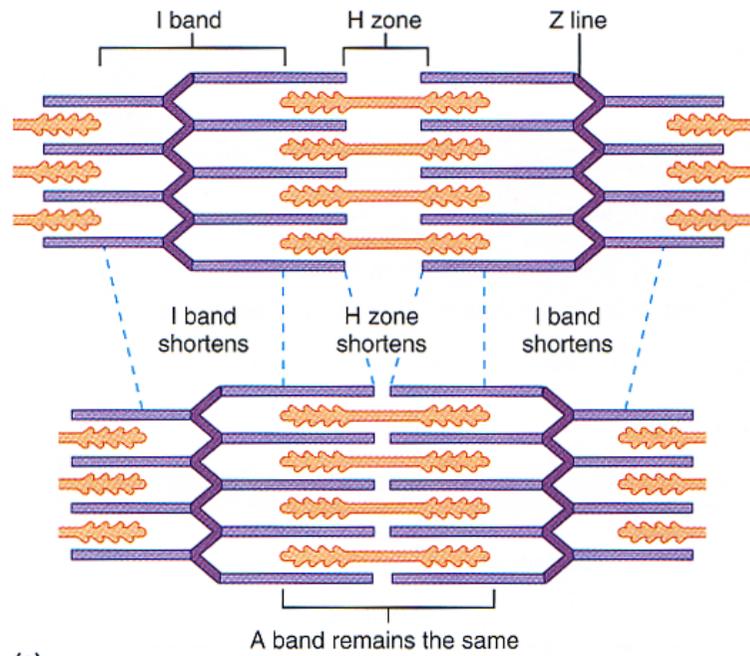


**FIGURE 11.1 Structure of a skeletal muscle.** Representative skeletal muscles in the arm are shown, as are the tendons that connect them to bones. The enlargement shows the arrangement of muscle fibers within a muscle and some of the structural features of individual muscle fibers.

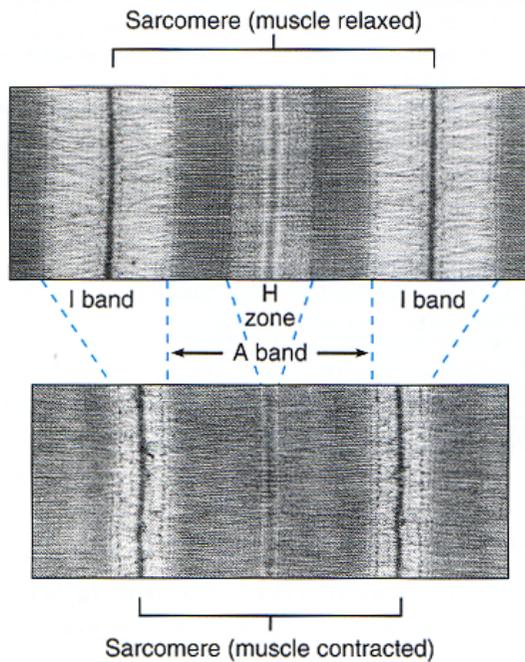
# Il sarcomero è l'unità funzionale della fibra muscolare scheletrica



**FIGURE 11.2 Structure of a skeletal muscle fiber.** Major internal components of a muscle fiber are shown. A single myofibril in the muscle fiber has been extended and slightly enlarged to reveal the arrangement of thick and thin filaments within it. The enlarged view shows a magnified image of a neuromuscular junction.



(a)



(b)

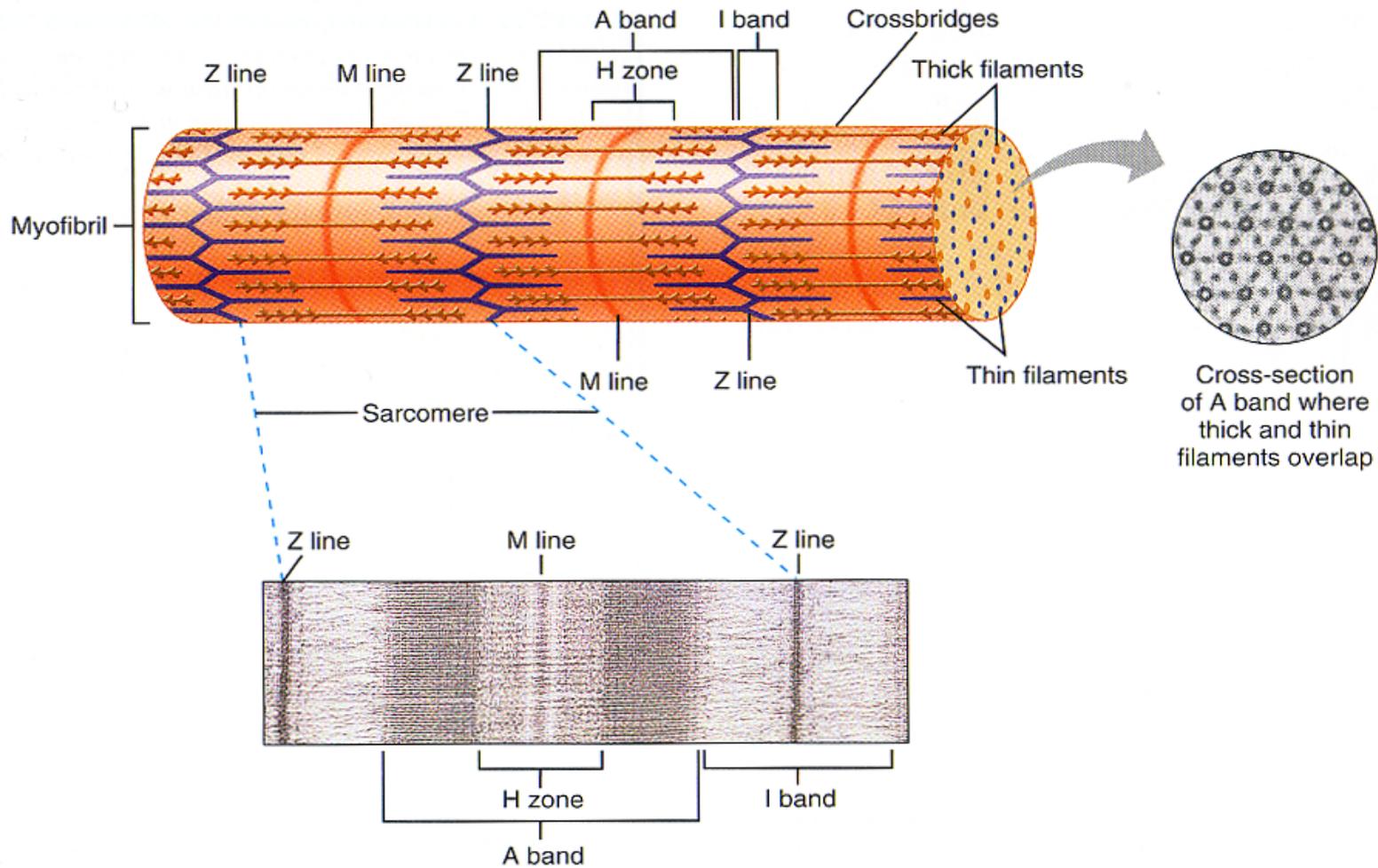
## I filamenti contrattili del sarcomero:

- l' actina (filamenti sottili)
  - la miosina (filamenti spessi)
- (proteine accessorie)

**FIGURE 11.6** How changes in striation pattern are explained by the sliding-filament model of muscle contraction. A schematic drawing (a) and photomicrographs (b) showing the relative positions of the thick and thin filaments in sarcomeres in relaxed muscle (top) and contracted muscle (bottom).

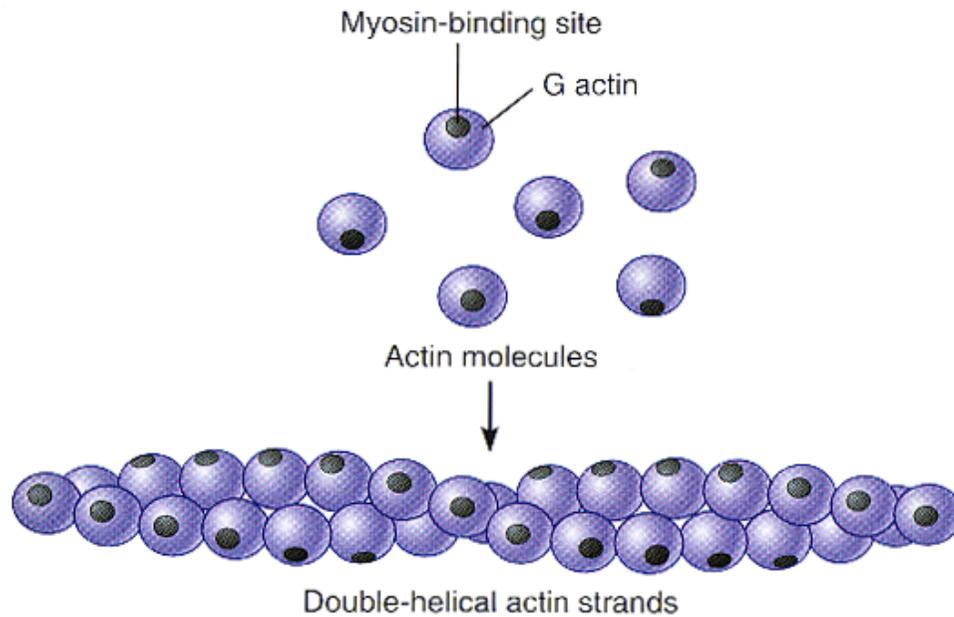
# L'arrangiamento geometrico dei filamenti contrattili

**FIGURE 11.3 Sarcomere structure.** A drawing of a myofibril, showing the regular arrangement of protein filaments within sarcomeres. The lower photomicrograph shows the banding pattern typical of striated muscle; the photomicrograph at right shows a cross section through the A band of a myofibril, in which the three-dimensional arrangement of thick and thin filaments can be clearly seen.



## La struttura dell'actina:

- l'actina G (monomero)
- l'actina F (polimero)



**FIGURE 11.4 Structure of a thin filament.** (a) *The backbone of a thin filament consists of two strands of polymerized actin molecules wound together to form a double helix. Myosin-binding sites on individual actin molecules (G-actin) are represented by dark dots.*

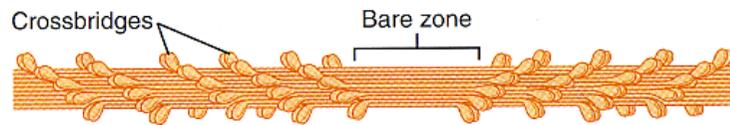
## La struttura della miosina:



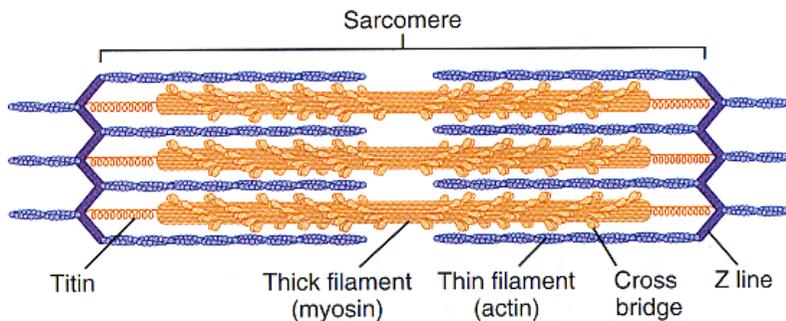
(a) Myosin molecule



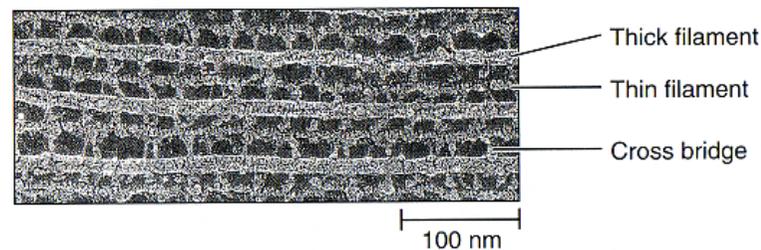
(b) Two myosin molecules bound at their tail ends



(c) Portion of thick filament



(d) Sarcomere

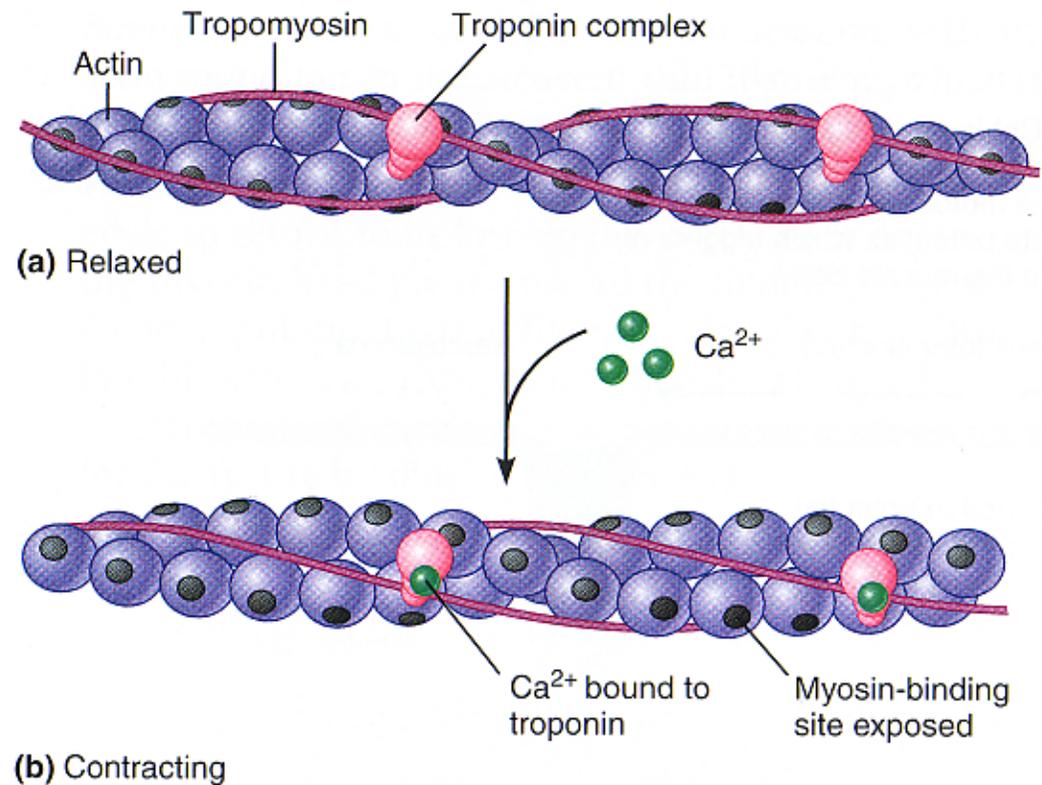


(e) Electron micrograph of portion of sarcomere

- la regione testa (“head”)
- la regione coda (“tail”)

**FIGURE 11.5 Structure of a thick filament.** (a) A myosin molecule, a dimer composed of two subunits wound together. Note the actin-binding and ATPase sites in the head region. (b) Two myosin molecules joined tail to tail. (c) A portion of a thick filament showing myosin heads (crossbridges) protruding at either end but not in the middle region (the bare zone). (d) A detailed view of a sarcomere showing the relative positions of thick and thin filaments and the protein titin, which anchors the thick filaments in place. (e) A photomicrograph of a sarcomere showing thick and thin filaments and crossbridges.

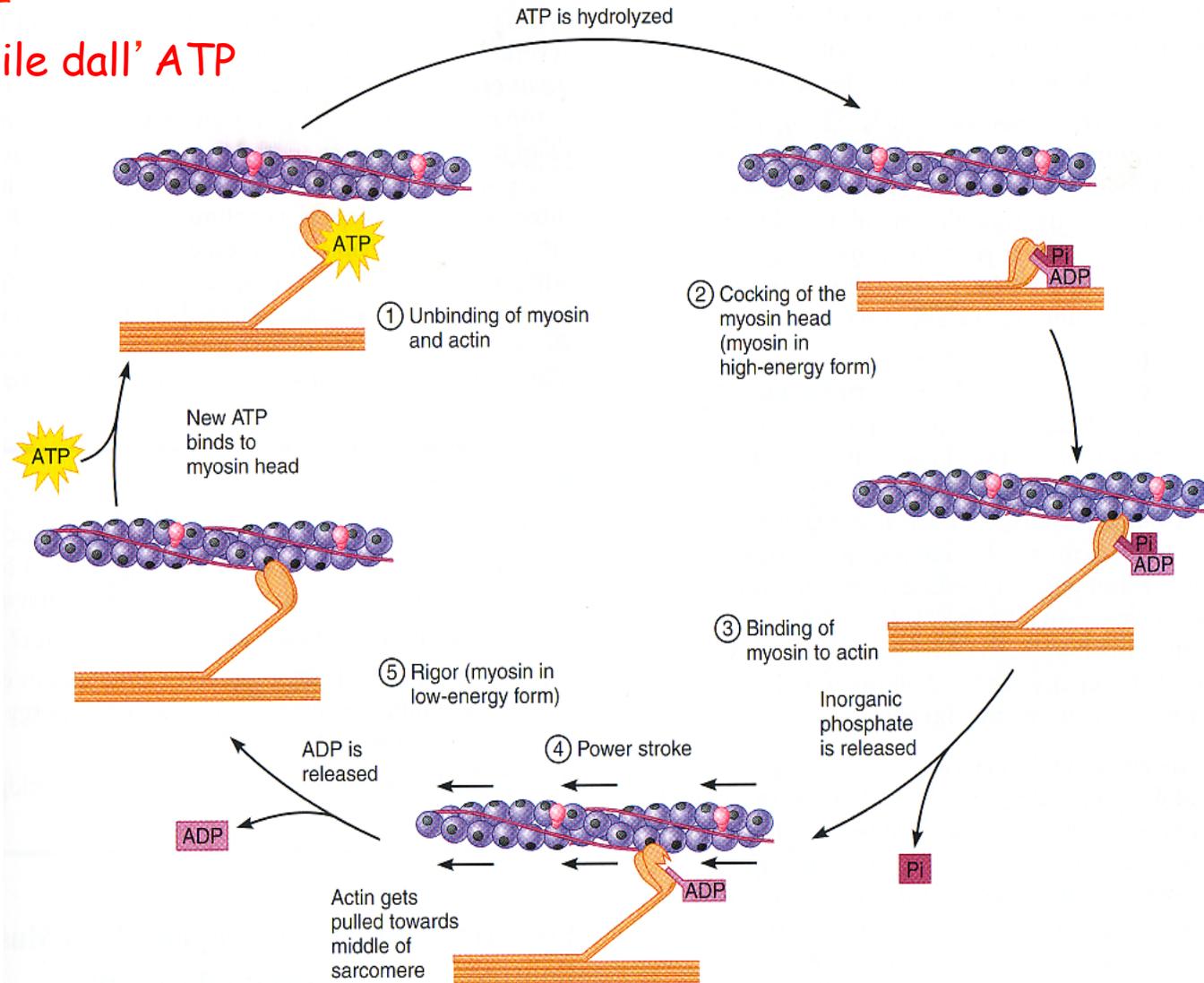
# Il complesso troponina-tropomiosina



**FIGURE 11.9** Actions of troponin and tropomyosin in excitation-contraction coupling. **(a)** In relaxed muscle, tropomyosin covers up actin's myosin-binding sites, which prevents the crossbridge cycle from occurring. **(b)** Following their release from the sarcoplasmic reticulum, calcium ions bind to troponin, causing a conformational change in the troponin complex that shifts tropomyosin's position on the actin filament and exposes the myosin-binding sites.

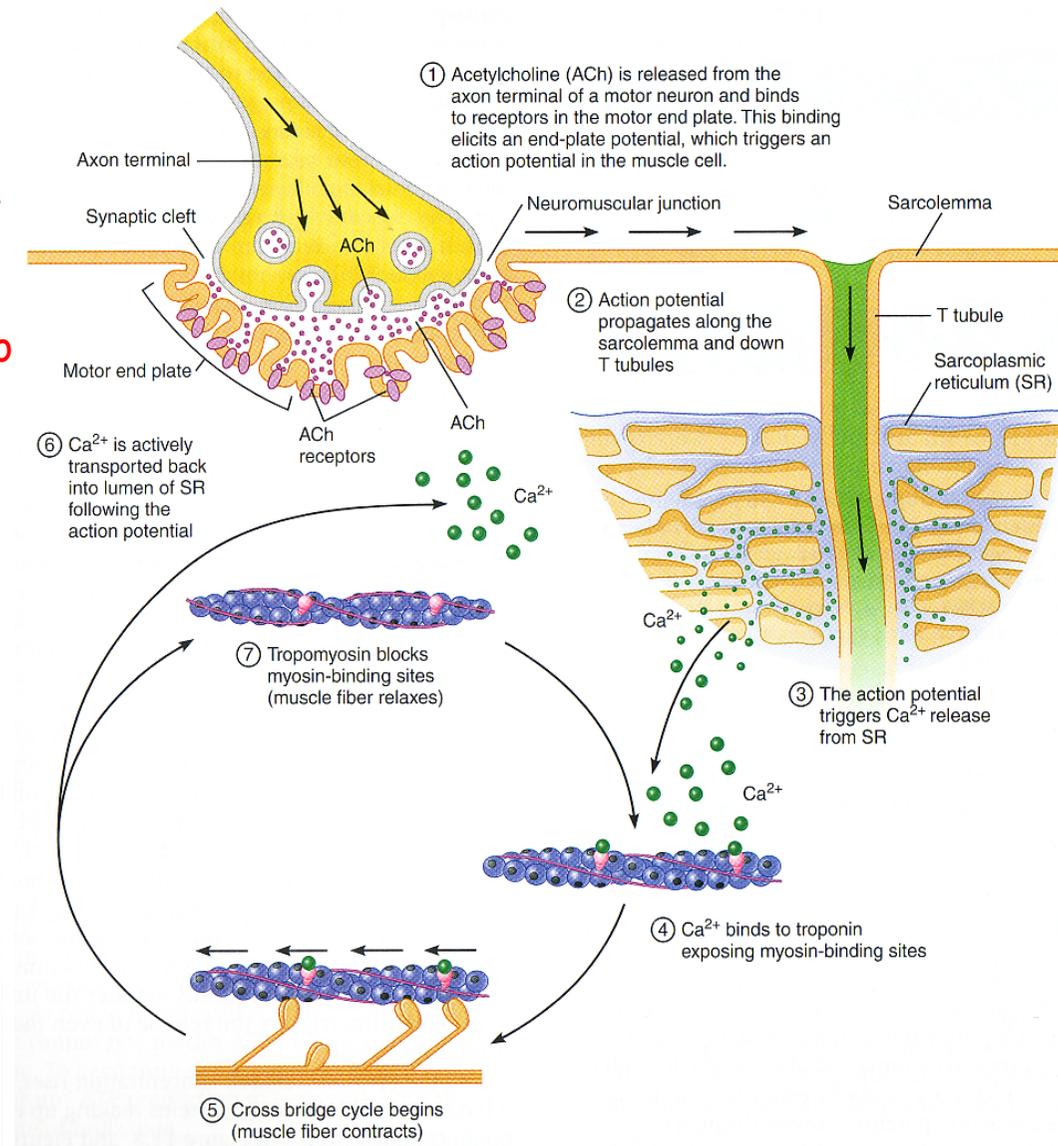
# La formazione del ponte acto-miosinico

- necessita di  $\text{Ca}^{2+}$
- è reso reversibile dall' ATP



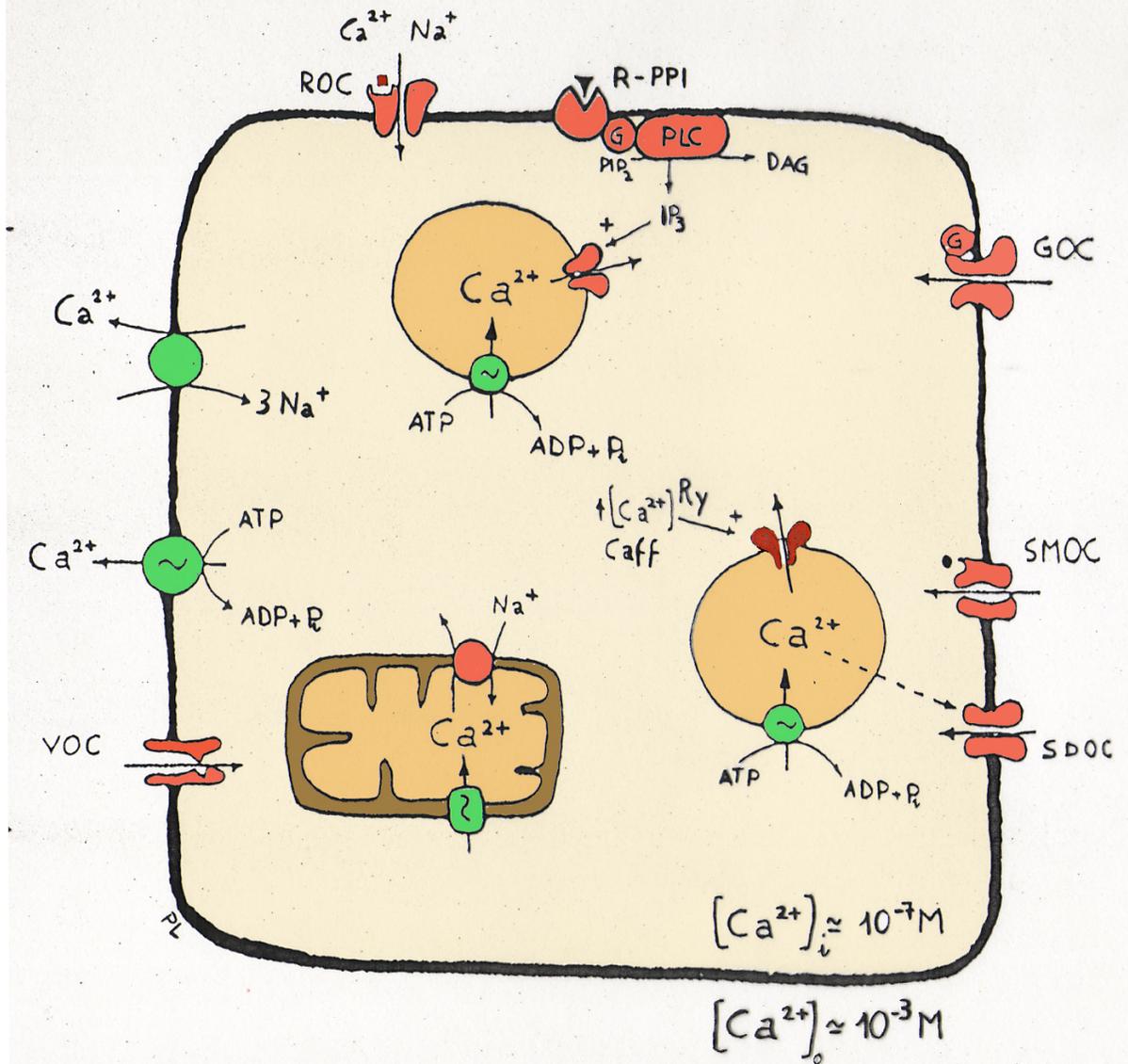
# Il meccanismo di accoppiamento eccitazione-contrazione

- 1) Rilascio di acetilcolina
- 2) Potenziale d'azione muscolare
- 3) Liberazione di  $\text{Ca}^{2+}$  dal reticolo
- 4) Interazione  $\text{Ca}^{2+}$ -troponina
- 5) Interazione actina-miosina
- 6) Contrazione



# I meccanismi coinvolti nell'omeostasi della $[Ca^{2+}]_i$

Fig 1. Overall picture of the control of  $Ca^{2+}$  homeostasis in nerve cells. A large number of mechanisms operate coordinately to keep  $[Ca^{2+}]_i$  about four orders of magnitude lower than the concentration of free  $Ca^{2+}$  in the extracellular space,  $[Ca^{2+}]_o$ . At the plasma membrane  $Ca^{2+}$  influx can occur through a variety of channel types, some of which voltage gated (VOC, lower right side), others ligand- or receptor-gated such as the nicotinic cholinergic and the NMDA glutamate receptors (ROC, upper side). In addition, activation of receptors coupled to the hydrolysis of polyphosphoinositides (R-PPI, upper side) causes the stimulation of  $Ca^{2+}$  influx apparently mediated by various types of channels: activated by G proteins (GOC), by second messengers (SMOC) and by the discharge of intracellular stores (SDOC), all depicted on the right side. Efflux across the plasmalemma is sustained by both the  $Ca^{2+}$  pump and the  $Ca^{2+}/Na^+$  exchanger (left side). Within the cell only three membrane-bounded structures are depicted. Mitochondria accumulate  $Ca^{2+}$  at the expenses of their membrane potential, while the organelles sensitive to  $IP_3$  (upper cytoplasm) and ryanodine (Ry, lower right cytoplasm), here shown separate from each other, are endowed with  $Ca^{2+}$  pumps. In some cell types (eg PC12 cells)  $Ca^{2+}$  stores exist sensitive to both  $IP_3$  and Ry, suggesting colocalization of the two receptors in their limiting membrane. The intracellular release channels are depicted white for the  $IP_3$  receptor, black for the Ry receptor. For the latter is indicated the sensitivity to both changes in  $[Ca^{2+}]_i$  (calcium-induced- $Ca^{2+}$ -release) and caffeine (Caff), a drug that lowers the  $Ca^{2+}$  threshold of the latter process).



# La contrazione della cellula muscolare scheletrica non richiede $\text{Ca}^{2+}$ extracellulare

*Biochim. Biophys. Acta*, 267 (1972) 605–608

Twitches in the presence of ethylene glycol bis( $\beta$ -aminoethyl ether)- $N,N'$ -tetraacetic acid

C.M. ARMSTRONG, F.M. BEZANILLA and P. HOROWICZ

## SUMMARY

Single muscle fibers continue to twitch for up to 20 min when immersed in ethylene glycol bis( $\beta$ -aminoethyl ether)- $N,N'$ -tetraacetic acid (EGTA) solutions containing less than  $10^{-8}$  M free calcium. Failure of the twitch results from reversible depolarization, which occurs after 15–20 min in EGTA. The results make it clear that external calcium or calcium in the transverse tubules play no essential part in action potential propagation or excitation–contraction coupling.

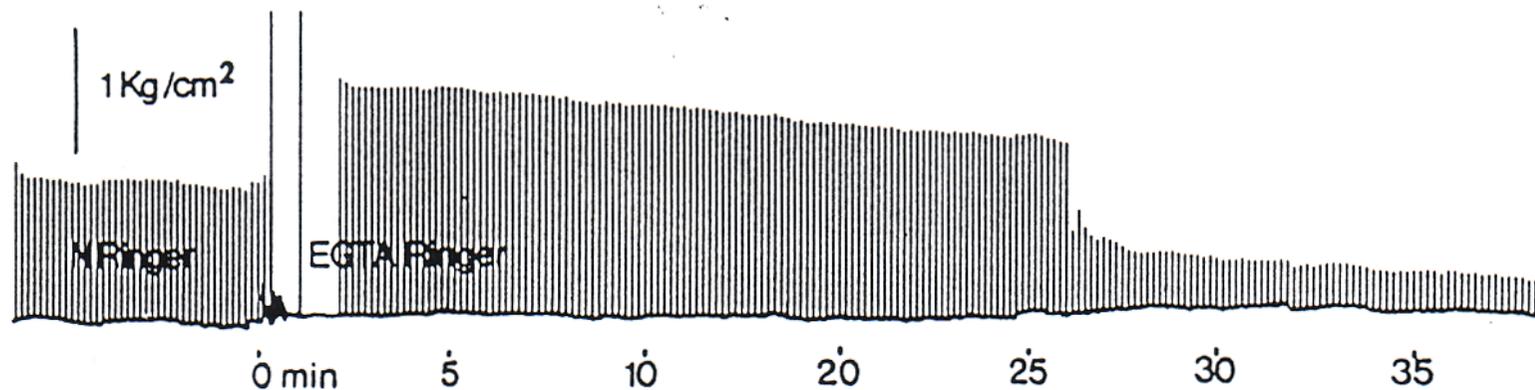
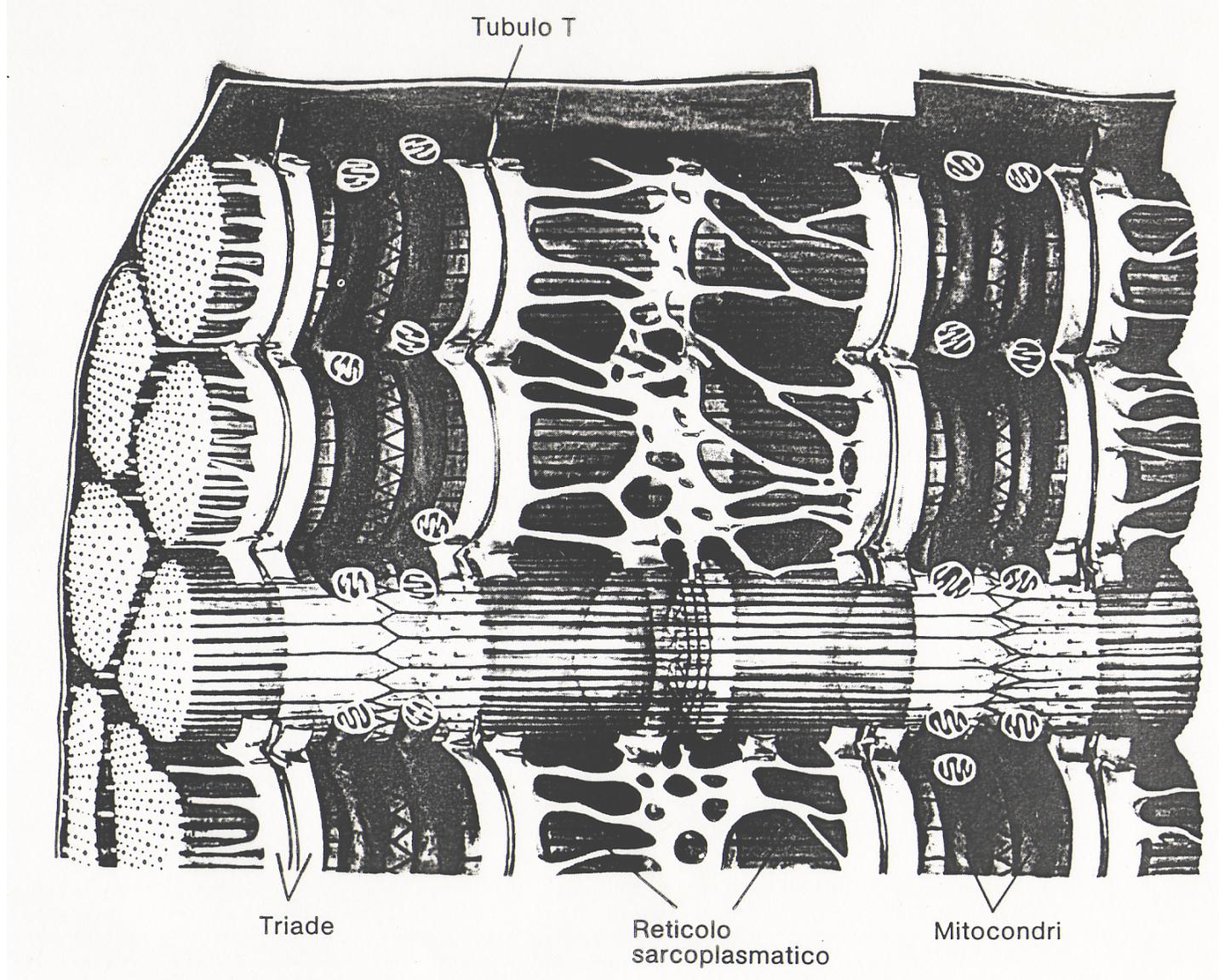


Fig. 1. Twitches in a single fiber on changing from normal Ringer's fluid to one containing 1 mM EGTA and no added calcium. Stimulation frequency, 0.1 Hz.

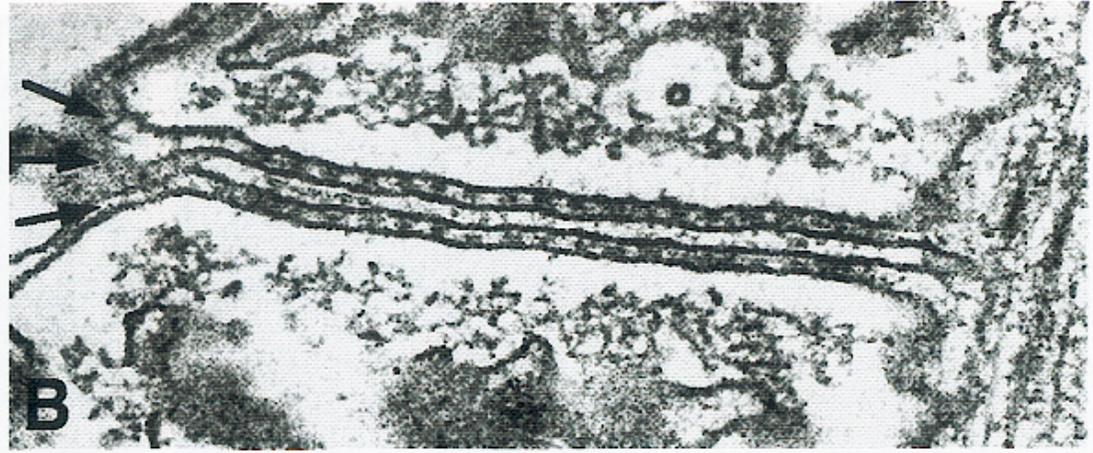
## Il deposito intracellulare di $\text{Ca}^{2+}$ : il reticolo sarcoplasmatico



## La triade osservata al microscopio elettronico

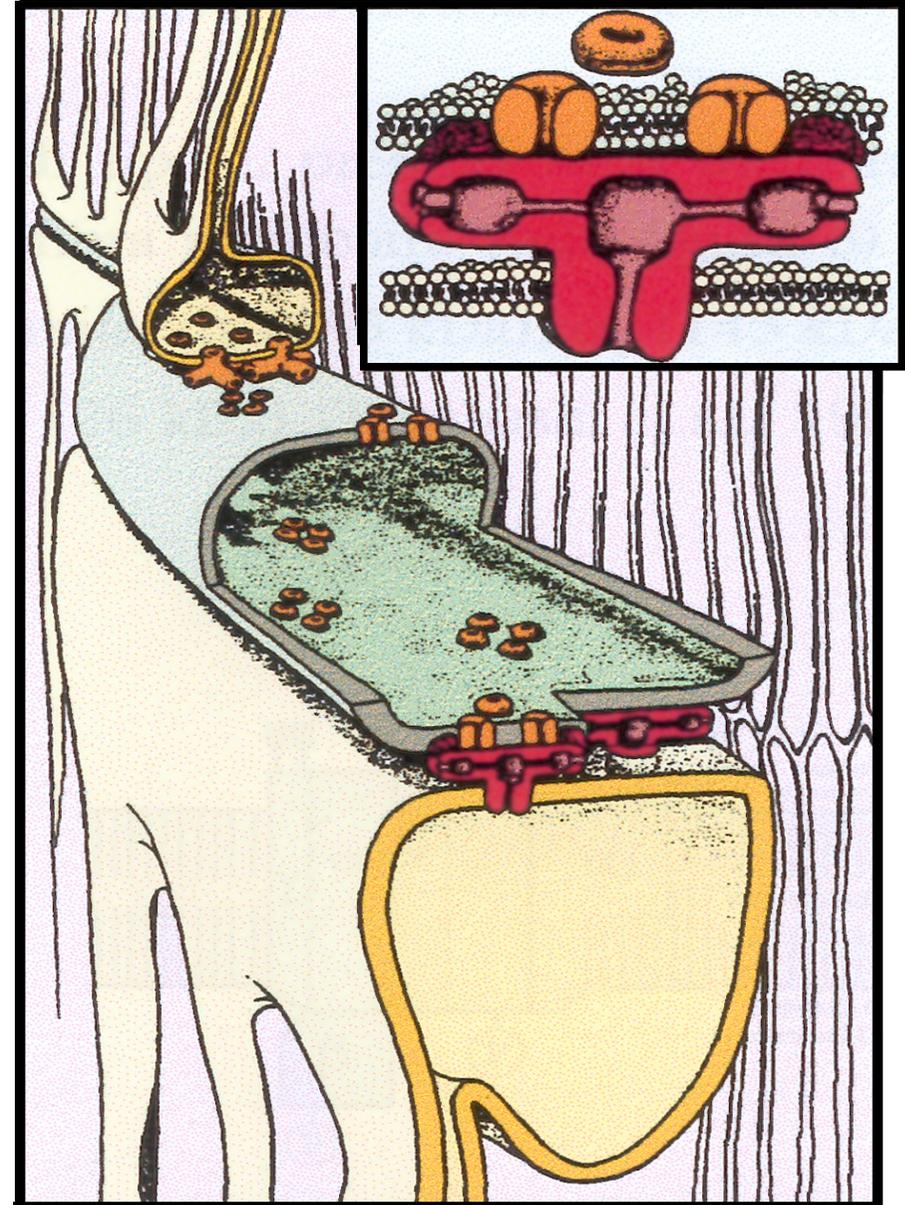
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*- foot and feet*



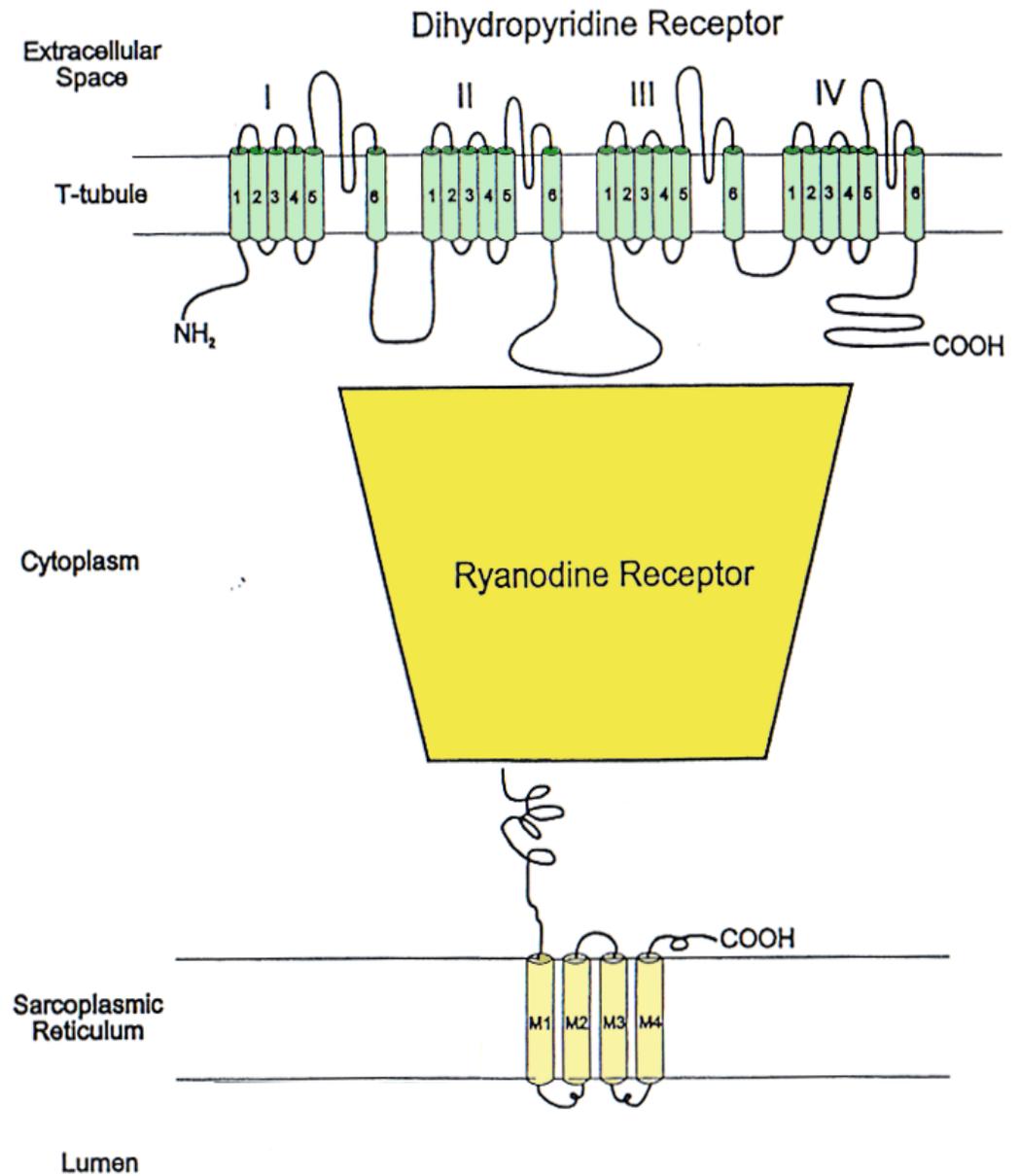
## La triade ed i canali ionici:

- canali voltaggio-dipendenti per il  $\text{Ca}^{2+}$  (DHPR)
- canali per il  $\text{Ca}^{2+}$  rianodina-sensibili o canali caffeina-sensibili (RyR)

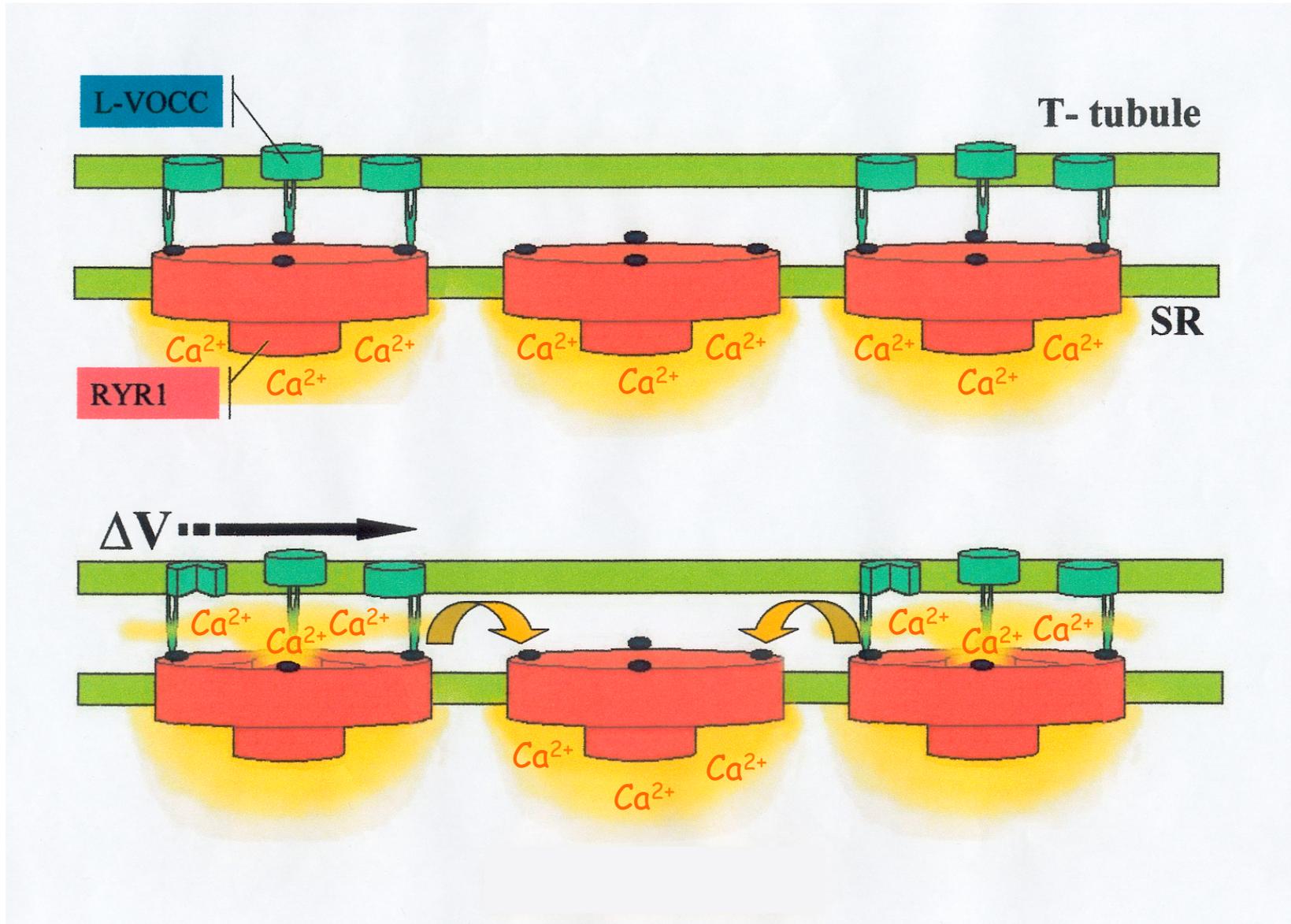


(modificata da Ríos and Pizarro, 1991)

# L' interazione DHPR-RyR ("foot" o piede)

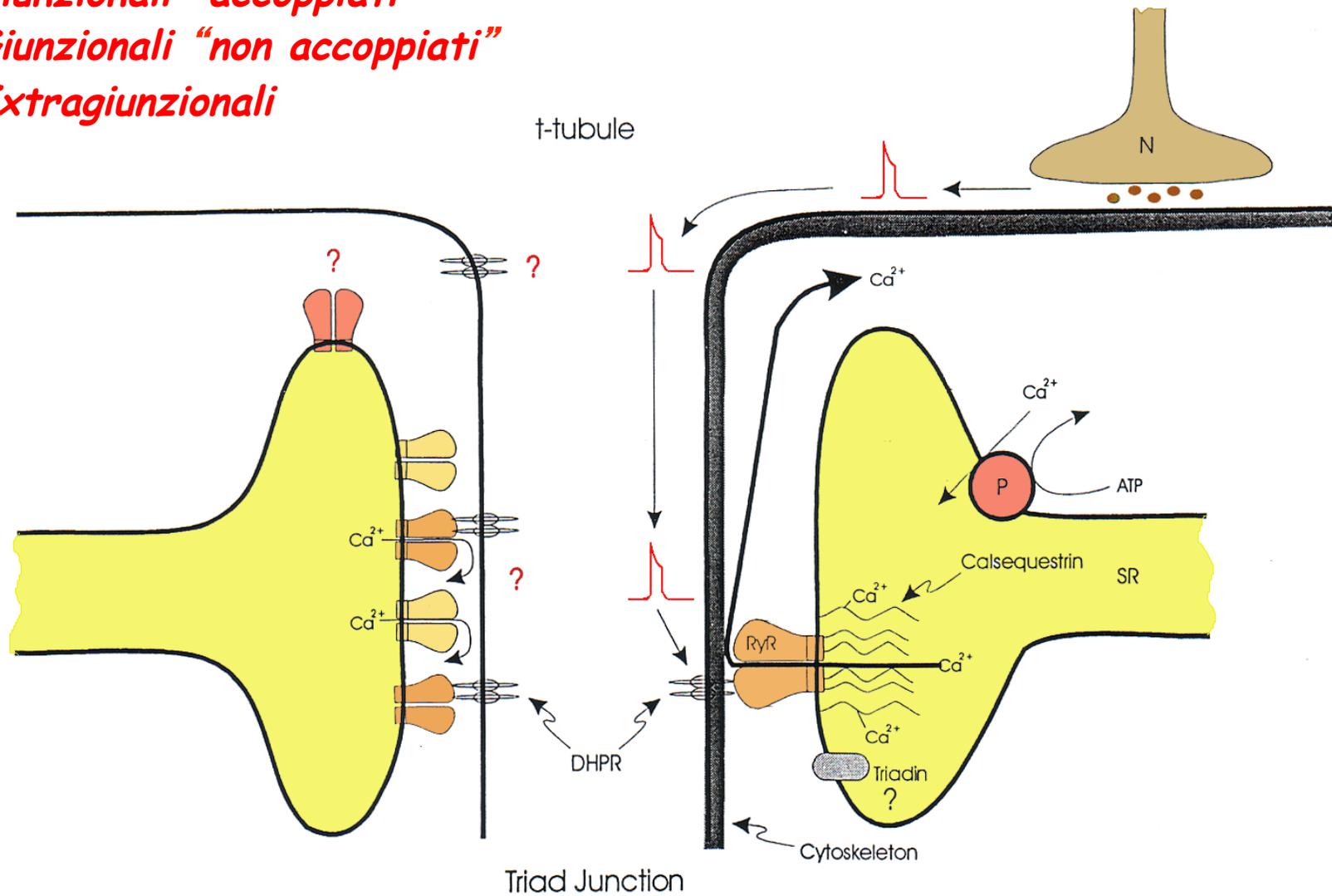


# La trasformazione del segnale elettrico in calcio



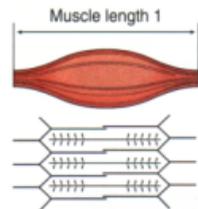
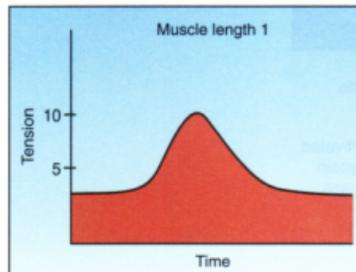
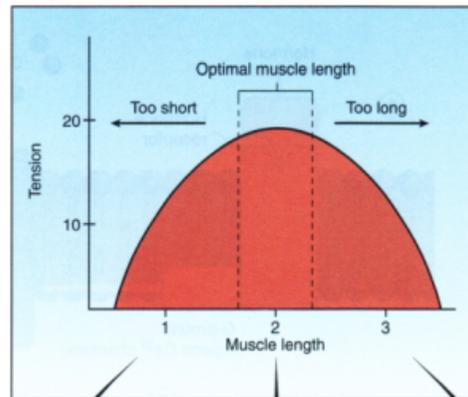
# I diversi tipi di RyR

- Giunzionali "accoppiati"
- Giunzionali "non accoppiati"
- Extragiunzionali

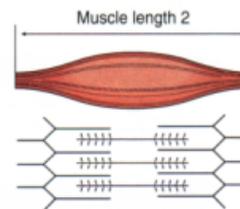
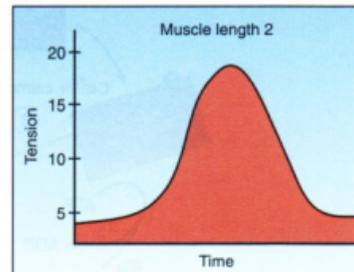


# La modulazione della forza sviluppata dal muscolo: il ruolo della lunghezza del sarcomero

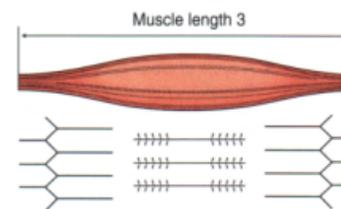
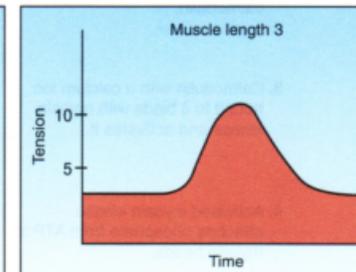
There is an optimal muscle length at which the muscle produces a maximal tension in response to a maximal stimulus.



At muscle length 1, the muscle is not stretched, and the tension produced when the muscle contracts is small because the actin and myosin myofilaments are already overlapping nearly as much as they can and the sarcomere cannot shorten much more.



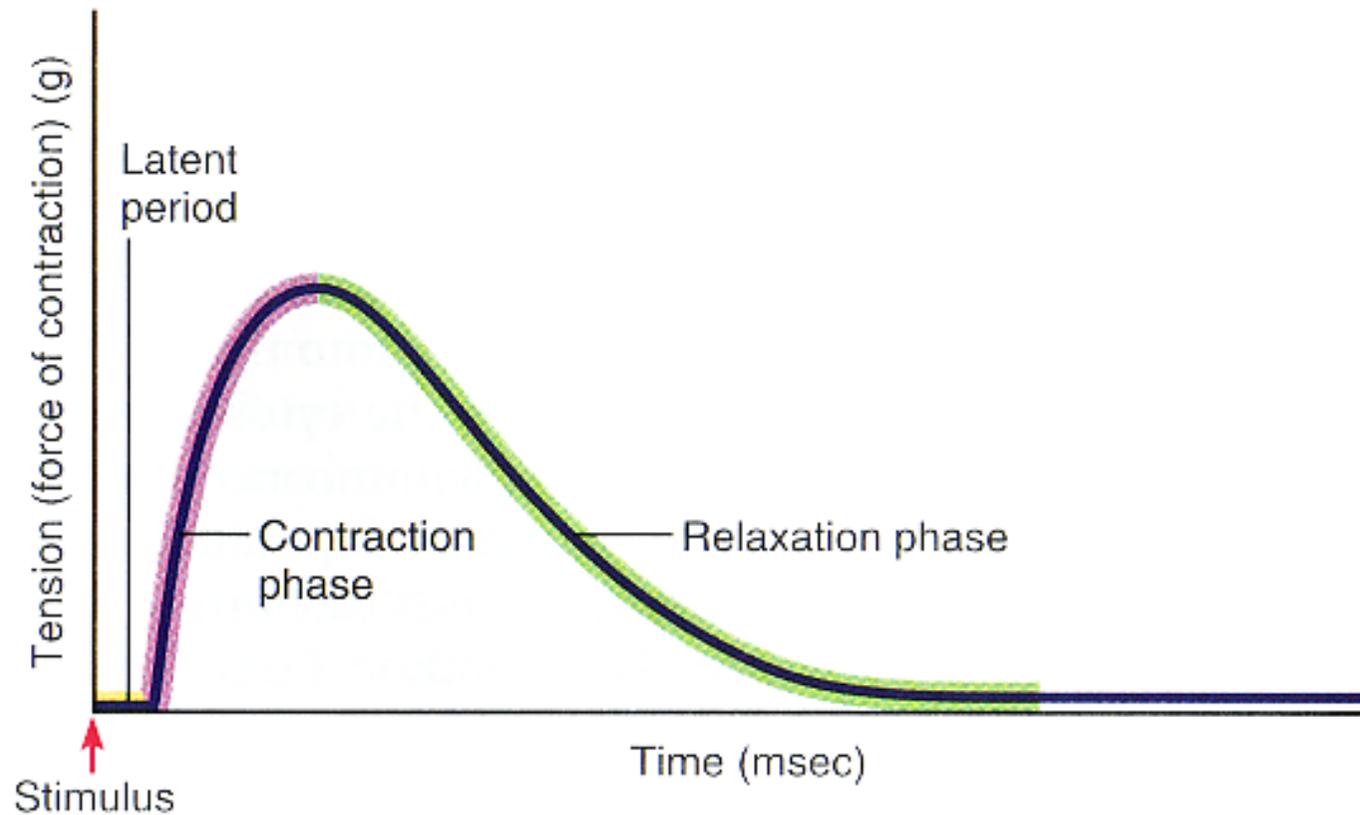
At muscle length 2, the muscle is optimally stretched, and the tension produced when the muscle contracts is maximal because the number of cross bridges that can form is maximal.



At muscle length 3, the muscle is stretched severely, and the tension produced is small because the actin and myosin myofilaments only slightly overlap and the number of cross bridges that can form is small.

## La diversa durata del segnale elettrico (potenziale d'azione) e dell'evento meccanico (contrazione)

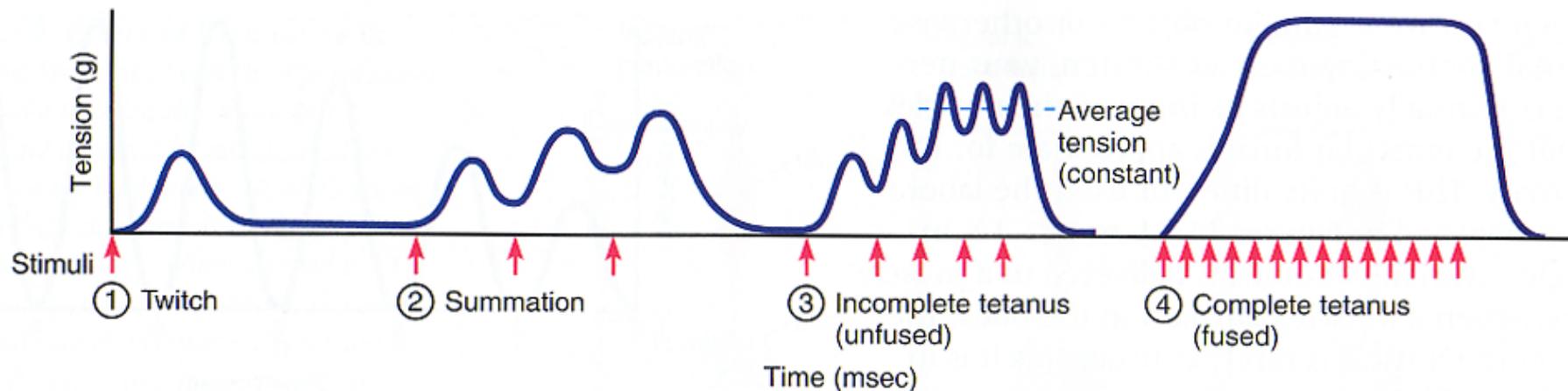
**FIGURE 11.10 Phases of a twitch.** *The tension that is actively generated by a muscle in response to a single stimulus is plotted as a function of time.*



## La modulazione della forza sviluppata dal muscolo: la sommazione dei transienti di $\text{Ca}^{2+}$

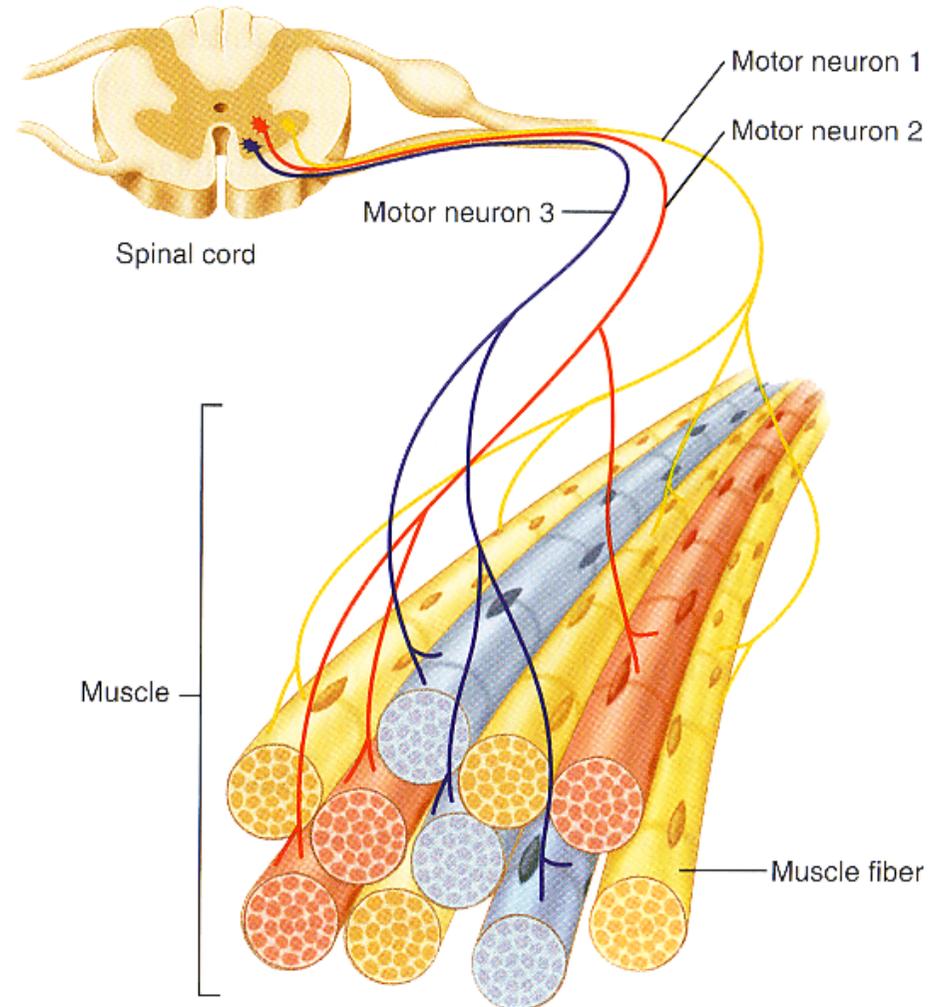
**FIGURE 11.15** Effects of high stimulus frequency: summation and tetanus.

*In response to repetitive stimuli (arrows) delivered close together in time, muscle twitches superimpose in summation. A train of more frequent stimuli causes tension to rise with each twitch until the muscle reaches incomplete tetanus, characterized by a plateau composed of individually distinguishable twitches. Still greater stimulus frequency produces complete tetanus, in which force increases swiftly and smoothly to a plateau in which individual twitches are no longer distinguishable.*



## Ogni muscolo è un insieme di unità motorie

**FIGURE 10.14 Motor units.** A motor unit consists of a motor neuron and all the muscle fibers it innervates. Whereas a single neuron innervates many muscle fibers, a given muscle fiber is innervated by one motor neuron only. Note that the muscle fibers within a given motor unit are scattered throughout the muscle.



# La modulazione della forza sviluppata dal muscolo: il reclutamento delle unità motorie

**FIGURE 11.18** Increases in force generation with recruitment of motor units. (a) A hypothetical motor unit consisting of a motor neuron and a single muscle fiber. (b) Motor units X and Y, which possess five fibers and seven fibers, respectively. (c) Tension developed by the single fiber, by motor unit X, by motor unit Y, and by motor units X and Y together.

