MSS MODULE
PHYSIOLOGY (LECTURE 2)
PHYSIOLOGY OF MUSCLE II

BY

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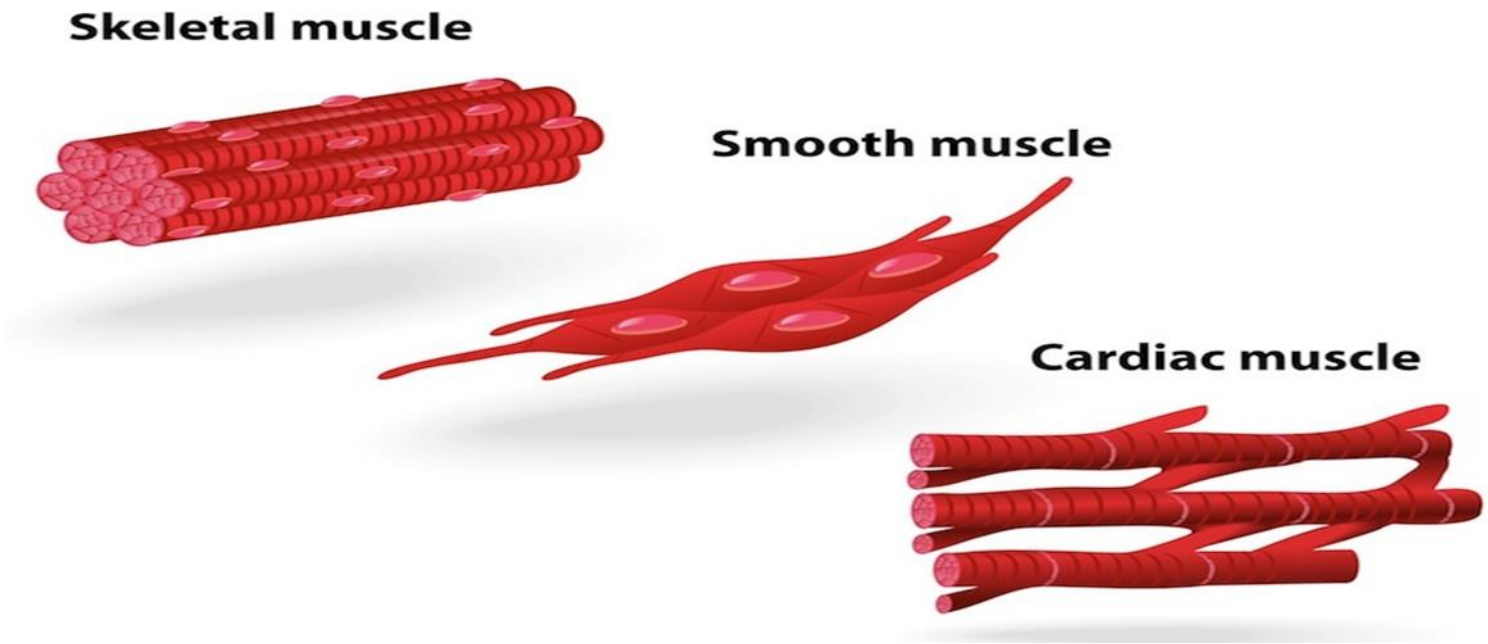
2024-2025



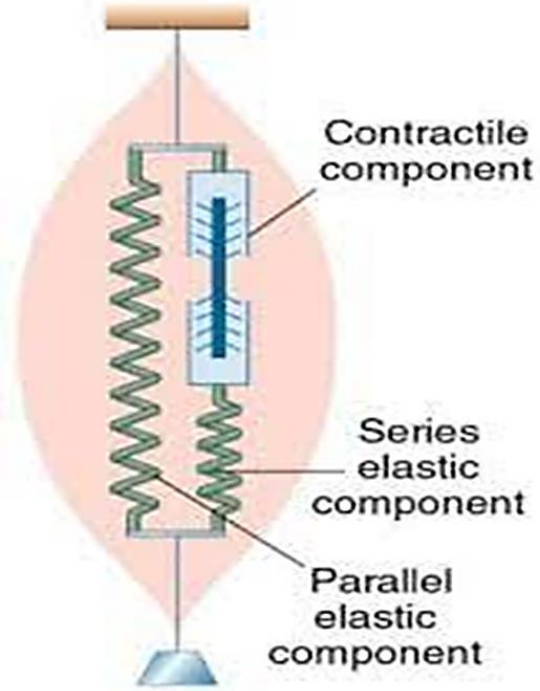
TYPES OF MUSCLE CONTRACTION

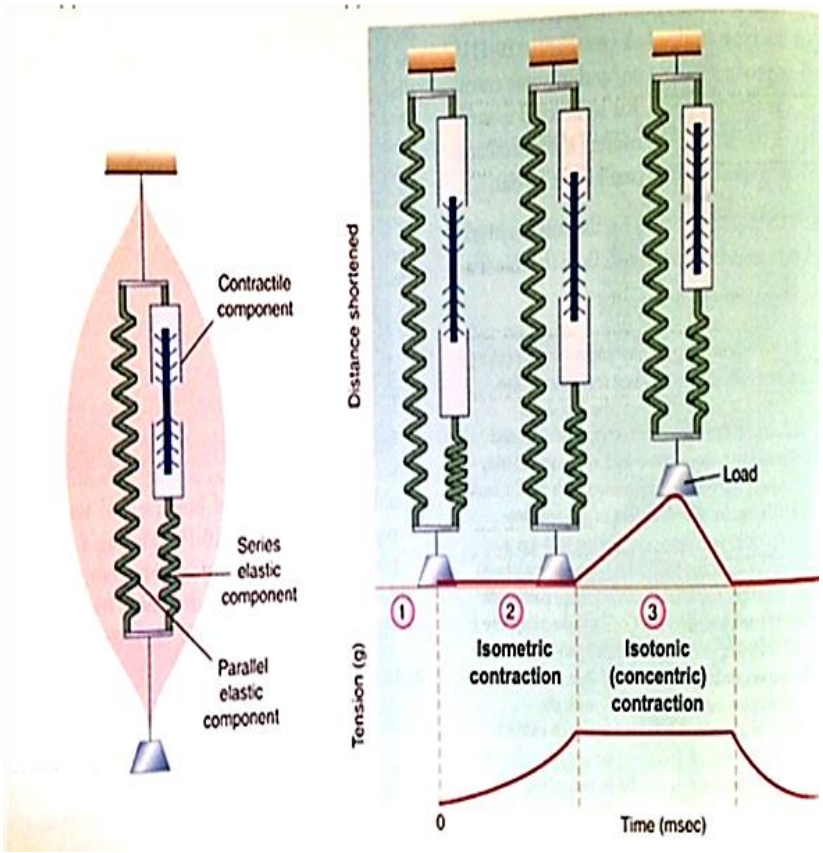
- **There are TWO TYPES of muscle contraction:**

❑ **Isometric contraction.**

❑ **Isotonic contraction.**

- **Normal muscle activity is a combination of isometric and isotonic contractions.**


Contractile component
Series elastic component
Parallel elastic component


Contractile component
Series elastic component
Parallel elastic component
Distance shortened
Load
1
2
3
Isometric contraction
Isotonic (concentric) contraction
Tension (g)
0
Time (msec)

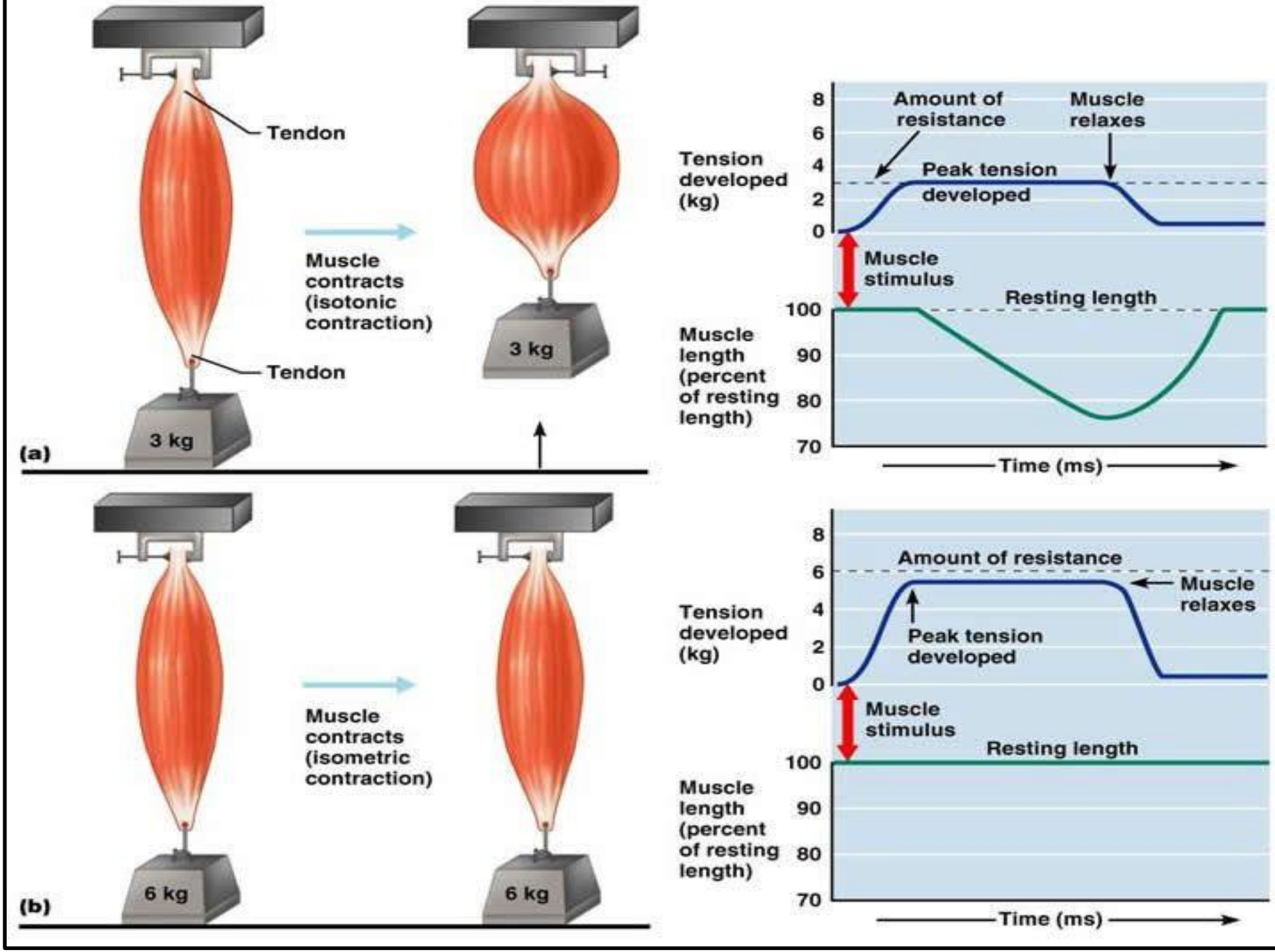
ISOMETRIC CONTRACTION

- Involves the **development of tension without** any **change in length (constant length).**
- The muscle **contract without shortening** but the **tension is much increased.**
- **Mechanism**: The muscle fibers are formed of **contractile** parts (CE) and elastic tissue (SE). When the contractile part (sarcomere) is shortened → **pull** on the elastic tissue which is markedly **stretched (because the load is not moved)→** so that the **total length** of the muscle fiber **doesn't** change (i.e. length is constant **but** tension is increased).

ISOTONIC CONTRACTION

- Involves the **change in length without any change in tension (constant tension).**
- The muscle **shortens** and carries a weight (i.e. **mechanical work is done**) **without** change in tension.
- **Mechanism:**

The CE shortens and SE is not markedly stretched (because load is moved)→ the whole muscle is shortened and tension remains constant.


Tendon
Tendon
3 kg
3 kg
(a)
Muscle contracts (isotonic contraction)
Amount of resistance
Muscle relaxes
Peak tension developed
Tension developed (kg)
8
6
4
2
0
Muscle stimulus
Resting length
100
90
80
70
Muscle length (percent of resting length)
Time (ms)
6 kg
6 kg
(b)
Muscle contracts (isometric contraction)
Amount of resistance
Muscle relaxes
Peak tension developed
Tension developed (kg)
8
6
4
2
0
Muscle stimulus
Resting length
100
90
80
70
Muscle length (percent of resting length)
Time (ms)

Types of Muscle Contraction

Item	Isotonic	Isometric
Length of muscle	Decreases; the muscle shortens	Constant length
Tension	Constant	Much increased
Work	The muscle performs external work	No work is done
Mechanical efficiency	20-25% The rest of energy production is released as heat	Zero Though energy is consumed
Example	Carrying a weight against gravity	Carrying a weight that is too heavy to be carried

Load–Velocity Relation

- **A load** on a contracting muscle is **a reverse force** that opposes the contractile force caused by muscle contraction.
- As the load increases → Velocity of shortening is decreased.
- **At zero load**, the muscle contracts with **a maximal velocity of shortening**.
- **A heavy load that cannot be lifted** doesn't allow shortening of the muscle → **isometric contraction**.

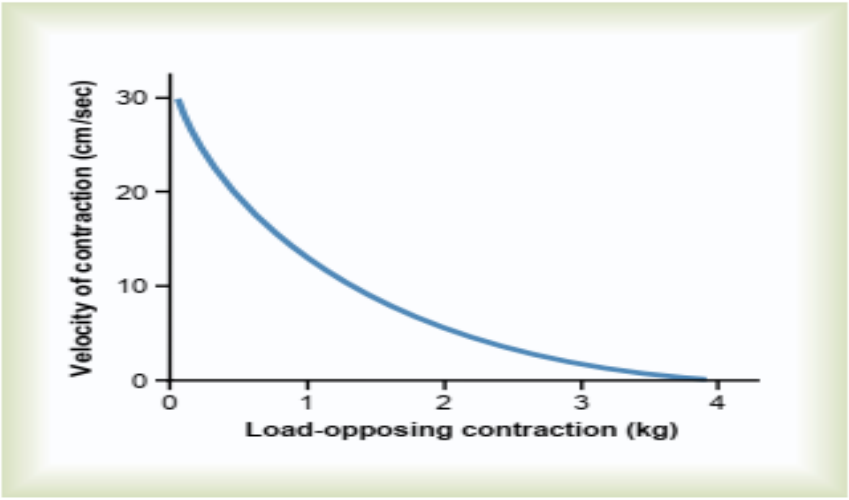
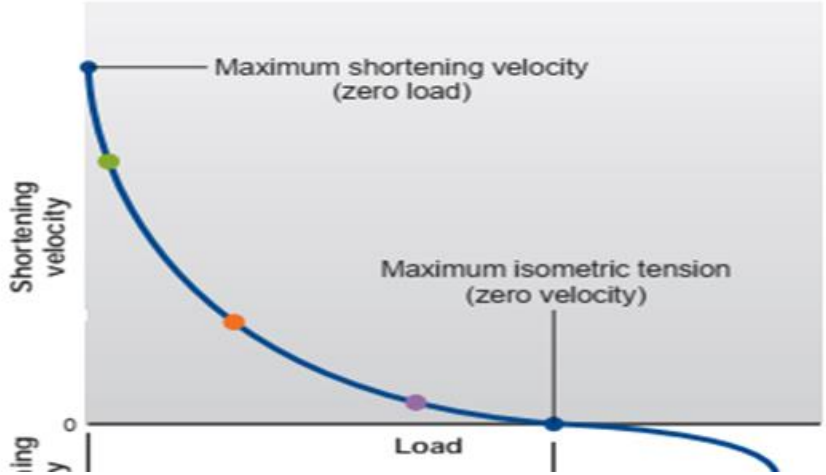

Velocity of contraction (cm/sec)
30
20
10
0
0
1
2
3
4
Load-opposing contraction (kg)

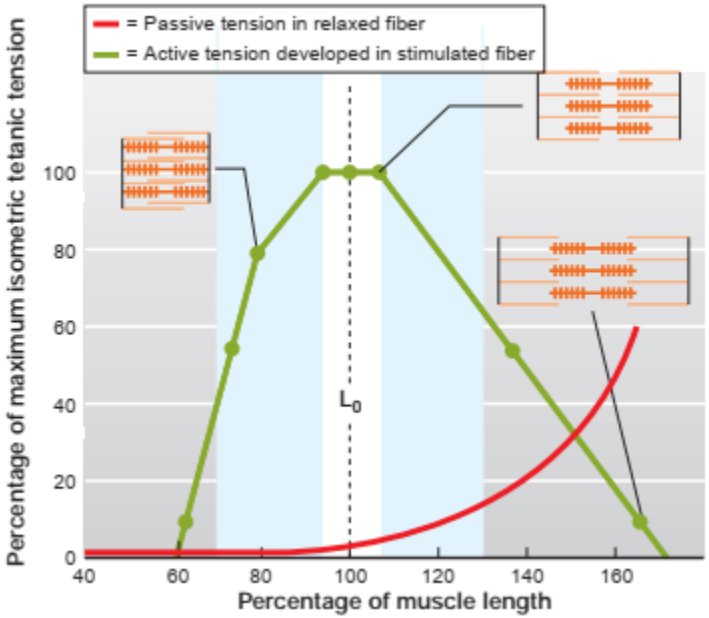
Figure 6–10


Maximum shortening velocity
(zero load)
Shortening
velocity
Maximum isometric tension
(zero velocity)
0
Load

Length–Tension Relation

- The **tension developed** by a contracting muscle **depends** on the **number of points of attachment** between **actin** and **myosin** during the myosin **power stroke.**
- The **maximum amount of tension** developed by the sarcomere is where **every myosin head** is **across from** an **actin molecule** (at the optimal length of the muscle; L_0).
- **At lengths longer than the optimal length (L_O)** → some myosin heads are **NOT** across from actin (filaments apart)→ these heads **cannot** participate in the power stroke → the **tension developed** by the contracting sarcomere is **diminished**.

- **At sarcomere lengths shorter than optimal (L_o)** → the myosin filaments are **already** approaching the point of attachment for the actin filaments, **overlap** occurs between actin molecules → **tension decreases**.
- **Both overstretch** and **understretch** of resting muscle→ **↓ the developed tension**.
- The **resting length** of the muscle (before contraction is initiated) helps to determine the **maximal amount of tension** that can be developed during contraction.
- **For skeletal muscle**→ the **optimal length (L_o)** is the **normal resting length** of the muscle (i.e. inside the body).



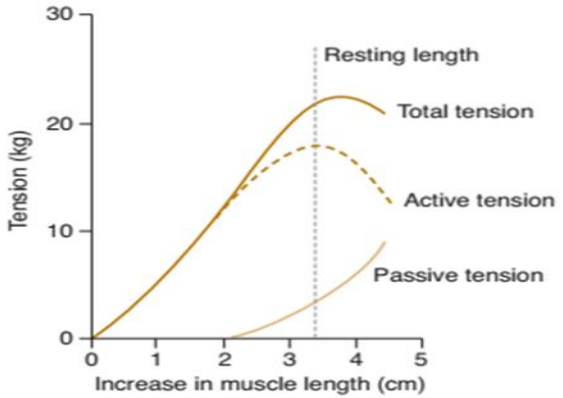


FIGURE 5–11 **Length–tension relationship for the human triceps muscle.** The passive tension curve measures the tension exerted by this skeletal muscle at each length when it is not stimulated. The total tension curve represents the tension developed when the muscle contracts isometrically in response to a maximal stimulus. The active tension is the difference between the two.

TWITCH CONTRACTIONS

- The RMP of skeletal muscle is -90 mV.
- Initiation of muscle contraction begins with action potential (AP) in the muscle fiber that is conducted from the surface to the interior of the muscle fiber along the T-tubule.
- The mechanical response of a muscle fiber to a single action potential is known as a twitch.
- Following the action potential, there is an interval of a few milliseconds known as the latent period before the tension in the muscle fiber begins to increase.
- During this latent period, the processes associated with excitation–contraction coupling (ECC) are occurring.
- The time interval from the beginning of tension development at the end of the latent period to the peak tension is the contraction time.
- The muscle regains its excitability completely just after beginning of the contraction phase and can respond to a second stimulus.

- **Not all skeletal muscle fibers have the same twitch contraction time.**
- **Some fibers have contraction times as short as 10 msec, whereas slower fibers may take 100 msec or longer.**
- **The total duration of a contraction depends in part on the time that cytosolic Ca^{2+} remains elevated so that cross-bridges can continue to cycle. This is closely related to the Ca^{2+} -ATPase activity in the sarcoplasmic reticulum; activity is greater in fast-twitch fibers and less in slow-twitch fibers.**

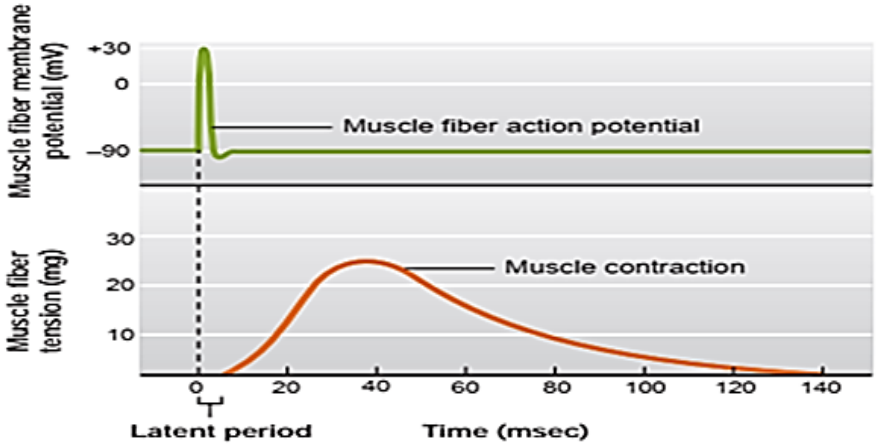


Figure 9.10 Time relationship between a skeletal muscle fiber action potential and the resulting contraction and relaxation of the muscle fiber. The latent period is the delay between the beginning of the action potential and the initial increase in tension.

Frequency–Tension Relation

- A single action potential in a skeletal muscle fiber lasts only 1 to 2 msec but the twitch may last for 100 msec.
- It is possible for a second action potential to be initiated during the period of mechanical activity.
- Following the first stimulus, S1→ isometric twitch lasts 150 msec.
- When the second stimulus, S2, applied to the muscle fiber 200 msec after S1→ the fiber has completely relaxed, → causes a second identical twitch.
- When a stimulus is applied before a fiber has completely relaxed from a twitch, → it induces a contractile response with a peak tension greater than that produced in a single twitch (S3 and S4).
- If the interval between stimuli is reduced further →the resulting peak tension is even greater; mechanical summation (S5 and S6).

- At **low stimulation frequencies→ the muscle fiber partially relaxes** between stimuli → producing an **unfused tetanus**.
- At **higher stimulation frequencies→ tetanus** is produced.
- **Tetanus** (tetanic contraction): **A maintained contraction in response to repetitive stimulation**.
- Different muscle fibers have different contraction times, so the stimulus frequency that will produce a maximal tetanic tension differs from fiber to fiber.

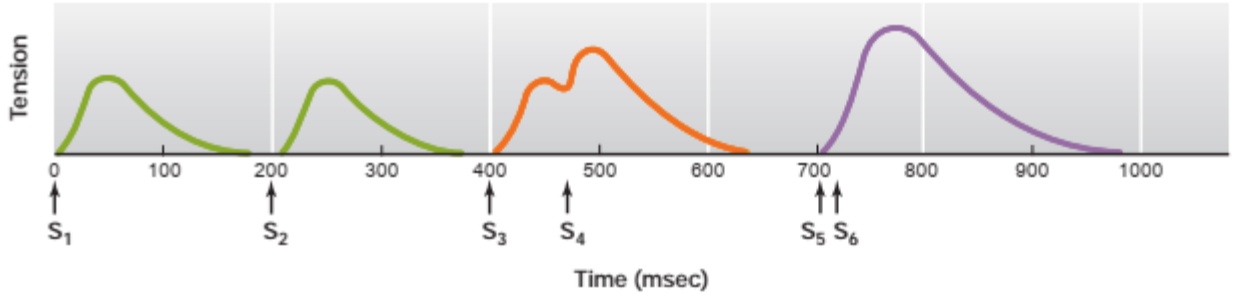


Figure 9.19 Summation of isometric contractions produced by shortening the time between stimuli.

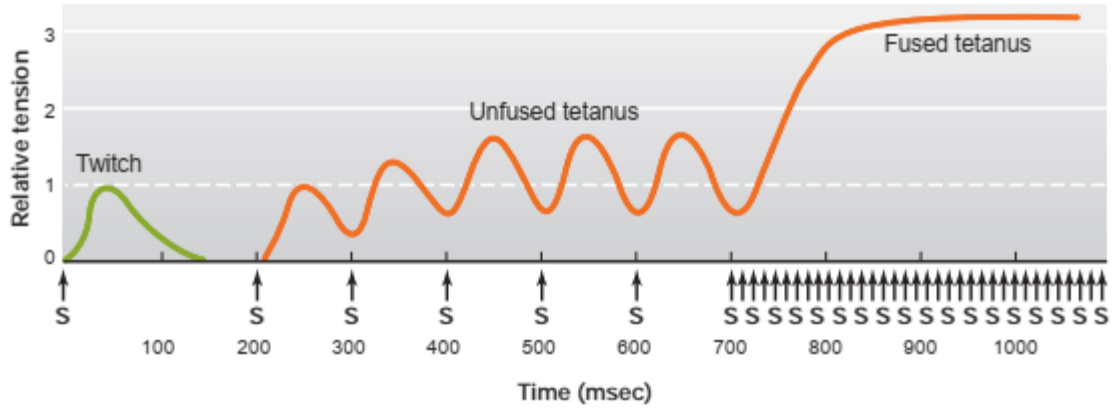


Figure 9.20 Isometric contractions produced by multiple stimuli (S) at 10 stimuli per second (unfused tetanus) and 100 stimuli per second (fused tetanus), as compared with a single twitch.

Types and causes of fatigue

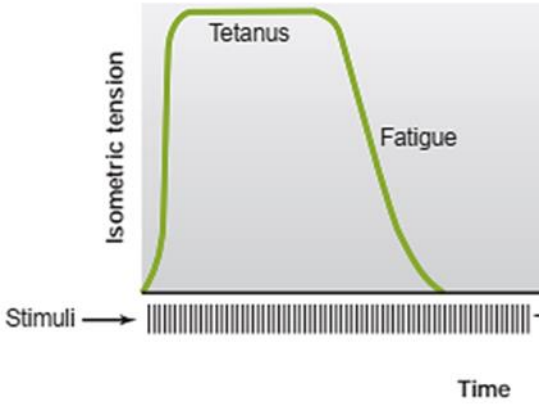
Fatigue: A temporary state of reduced work capacity.

- Muscle fatigue:

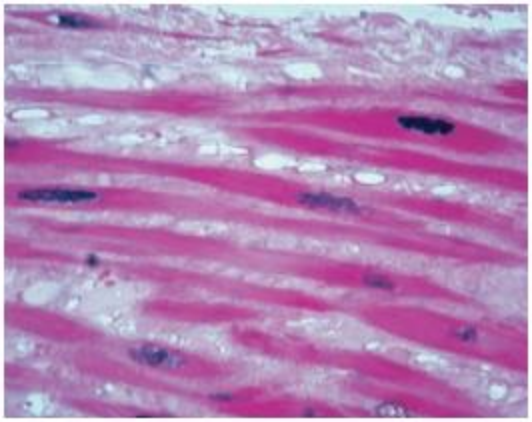
Due to depletion of the energy stores (ATP, CP and glycogen) and accumulation of metabolites (e.g. lactic acid).

- MEP fatigue:

Due to depletion of chemical transmitter (ACh) at the MEP.



SMOOTH MUSCLE



- **Two characteristics are common to all smooth muscles:**
- They lack the cross-striated banding pattern found in skeletal and cardiac fibers (which makes them “smooth”).
- The nerves to them are part of the **autonomic division of the nervous system** rather than the somatic division. Thus, **smooth muscle is not under voluntary control**.
- Just like skeletal muscle fibers, smooth muscle cells have thick myosin-containing filaments and thin actin-containing filaments.
- Although tropomyosin is present in the thin filaments, the regulatory protein **troponin is absent**.

SMOOTH MUSCLE CONTRACTION

- **Smooth muscle contraction is controlled by multiple neurotransmitters and other chemical ligands that affect cytosolic Ca^{2+} concentration**.
- Some of these substances produce **depolarization of the cell membrane, resulting in opening of voltage-gated membrane Ca^{2+} channels and release of Ca^{2+} from intracellular stores**, in a process similar to that in skeletal muscle.
- **Binding of a ligand to a membrane receptor produces an increase in intracellular Ca^{2+} concentration, and thus smooth muscle contraction, without altering membrane potential**.
- **Ligand binding activates membrane phospholipase C→↑ IP3 which releases Ca^{2+} from intracellular stores.**
- **Therefore, depolarization or binding of a ligand to a membrane receptor leads to elevation of intracellular Ca^{2+} → the common signal in smooth muscle contraction.**

Cross-bridge activation

The following sequence of events occurs after an increase in cytosolic Ca^{2+} in a smooth muscle fiber:

(1) **Ca^{2+} binds to calmodulin**, a Ca^{2+}-binding protein that is present in the cytosol of most cells and whose structure is related to that of troponin.

(2) **The Ca^{2+}–calmodulin complex** binds to another cytosolic protein, **myosin light-chain kinase**, thereby activating the enzyme.

(3) **Active myosin light-chain kinase** then uses ATP to phosphorylate myosin light chains in the globular head of myosin.

(4) **Phosphorylation of myosin** drives the cross-bridge away from the thick filament backbone, allowing it to bind to actin.

(5) Cross-bridges go through repeated cycles of force generation as long as myosin light chains are phosphorylated.

✓ A key difference here is that Ca^{2+}-mediated changes in the thick filaments turn on cross-bridge activity in smooth muscle, whereas in striated muscle, Ca^{2+} mediates changes in the thin filaments.

- ✓ **The smooth muscle form of myosin has a very low rate of ATPase activity less than that of skeletal muscle myosin**.
- ✓ Because **the rate of ATP hydrolysis determines the rate of cross-bridge cycling and shortening velocity, smooth muscle shortening is much slower than that of skeletal muscle**.
- ✓ Due to this **slow rate of energy usage, smooth muscle does not undergo fatigue during prolonged periods of activity**.

SMOOTH MUSCLE RELAXATION

- To relax a contracted smooth muscle, **myosin must be dephosphorylated** because dephosphorylated myosin is unable to bind to actin.
- This dephosphorylation is mediated by the enzyme **myosin light-chain phosphatase**, which is continuously active in smooth muscle during periods of rest and contraction.
- When **cytosolic Ca^{2+} concentration increases, the rate of myosin phosphorylation by the activated kinase exceeds the rate of dephosphorylation by the phosphatase** and the **amount of phosphorylated myosin in the cell increases, producing an increase in tension**.
- When the **cytosolic Ca^{2+} concentration decreases, the rate of phosphorylation decreases below that of dephosphorylation and the amount of phosphorylated myosin decreases, producing relaxation**.

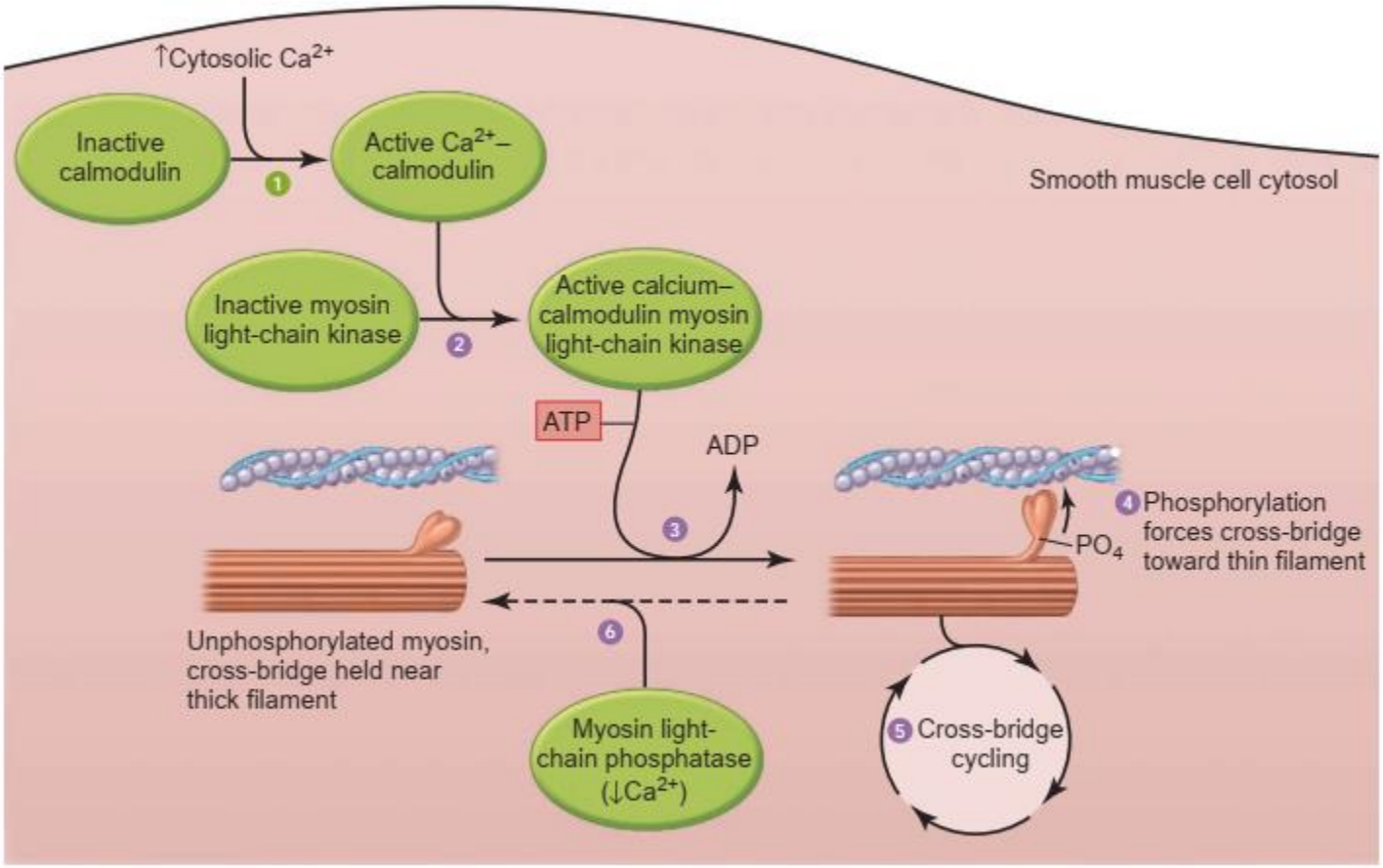


Figure 9.34 Activation of smooth muscle contraction by Ca^{21}. See text for description of the numbered steps.

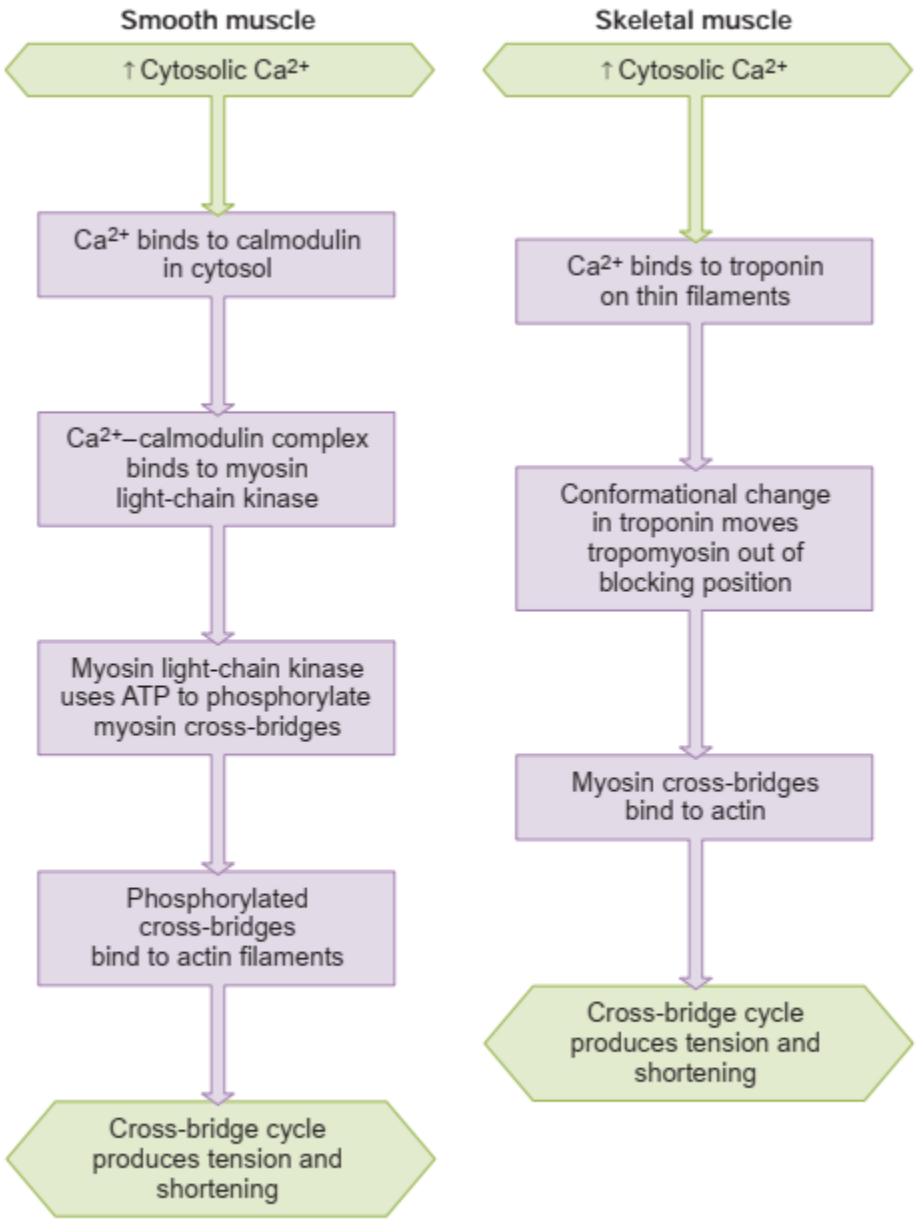


Figure 9.35 Pathways leading from increased cytosolic Ca^{21} to cross-bridge cycling in smooth and skeletal muscle fibers.


Thank you