Muscle biophysics.

The striated muscle. Smooth muscle and smooth-muscle-based organs.

Notice of a lecture

Presented by Professor D.R. Wilkie to the Institution of Electrical Enginers in London

Available now. LINEAR MOTOR. Rugged and dependable: design optimized by world-wide field testing over an extended period. All models offer the economy of "fuel cell" type energy conversion and will run on a wide range of commonly available fuels. Low stand-by power, but can be switched within msecs to as much as 1 kW/kg (peak, dry). Modular construction, and wide range of available subunits, permit tailor-made solutions to otherwise intractable mechanical problems:

Choice of two control systems:

(1) Externally triggered mode. Versatile, general-purpose units. Digitally controlled by picojoule pulses. Despite low input energy level, very high signal-to-noise ratio. Energy amplification 10^6 approx. Mechanical characteristics: (1 cm modules) max. speed optional between 0.1 and 100 mm/sec. Stress generated: 2 to 5 x 10^5 N/m^2.

(2) Autonomous mode with integral oscillators. Especially suitable for pumping applications. Modules available with frequency and mechanical impedance appropriate for:

(a) Solids and slurries (0.01-1.0 Hz)

(b) Liquids (0.5-5 Hz): lifetime 2.6 x 10^9 operations (typical) 3.6 x 10^9 (maximum) independent of frequency

(c) Gasses (50-1,000 Hz)

Many options: e.g., built-in servo (length and velocity) where fine control is required. Direct piping of oxygen. Thermal generation, etc.

Good to eat.

Muscle

Tissue and/or cell specialized for the generation of force and movement.

It can only pull, not push (...).

Hungarians in muscle research

Albert Szent-Györgyi
(Actomyosin superprecipitation)

Straub F. Brunó
(Actin)

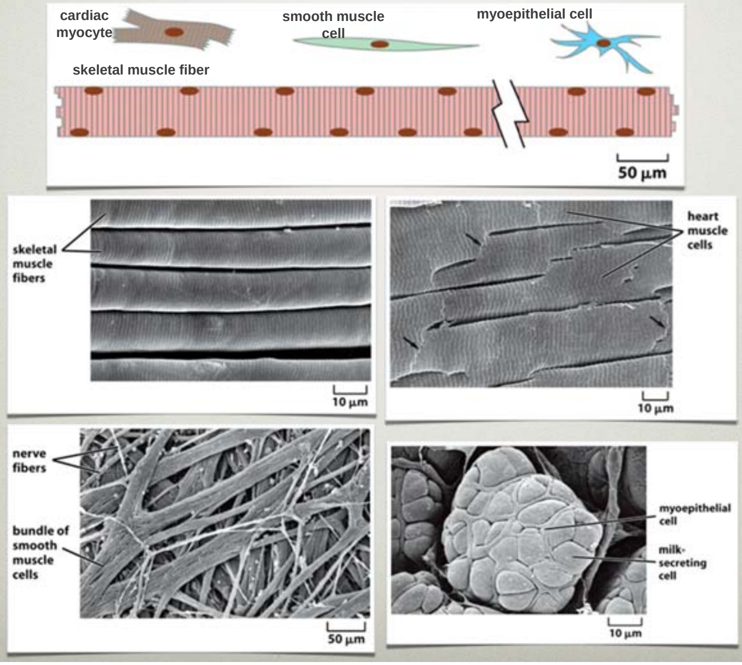
András Szent-Györgyi
(Smooth muscle myosin)

János Gergely
(Calcium regulatory system)

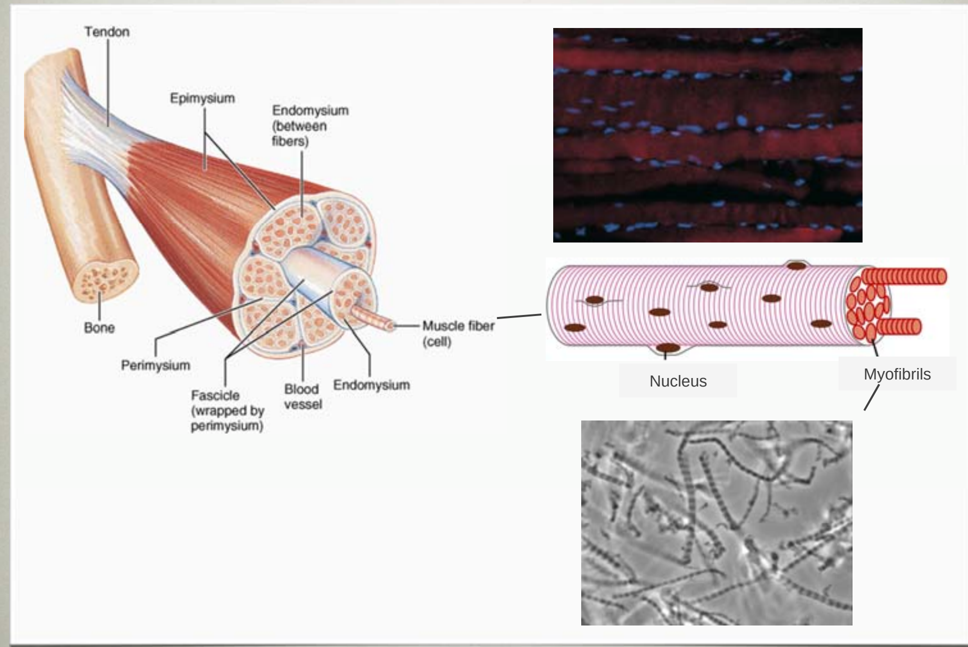
Katalin and Mihály Bárány
(Myosin isoforms and contraction speed)

Ferenc Guba
(Fibrillin)

Types of muscle

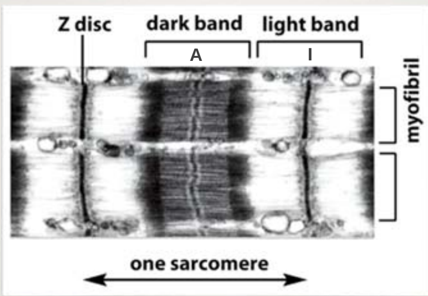


Skeletal muscle



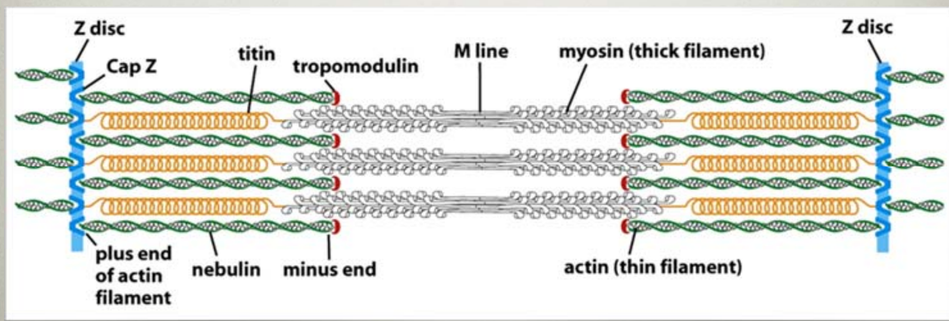
The sarcomere

sarcos: meat (Gr)
mera: unit
the smallest structural and functional unit of striated muscle.

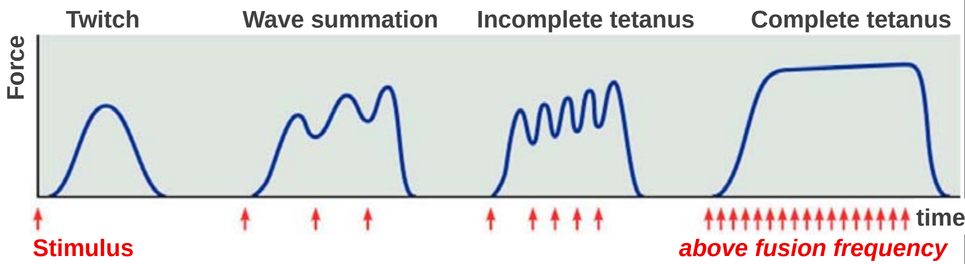


A-band: Isotropic-band
Thick filaments (myosin II.)

I-band: Anisotropic-band
Thin filaments (actin, tropomyosin, troponin)



Basic phenomena of muscle function I.



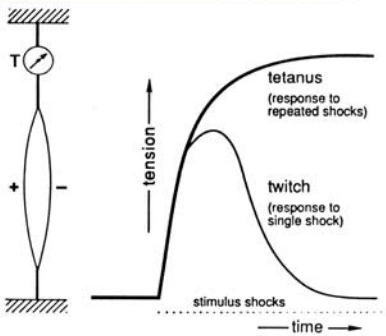
A single stimulus results in a single contractile response – a muscle **twitch** (contracts and relaxes).

More frequent stimuli increases contractile force – **wave summation** - muscle is already partially contracted when next stimulus arrives and contractions are summed.

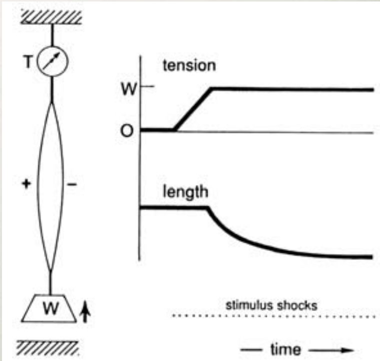
A sustained contraction that lacks even partial relaxation is known as **tetanus.**

Basic phenomena of muscle function II.

1. Isometric contraction
The muscle does not or cannot shorten, but the tension on the muscle increases.



2. Isotonic contraction
Tension remains unchanged while the muscle's length changes.



Auxotonic contraction (simultaneous shortening and force generation)

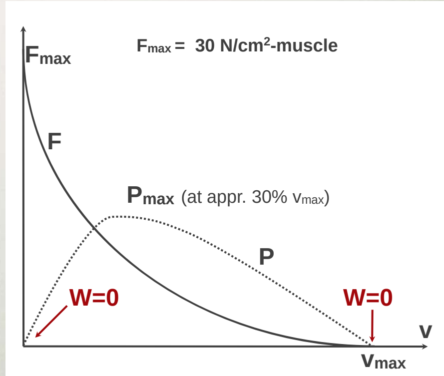
Basic phenomena of muscle function III.

1. Work, Power

$$W=Fs$$

$$P=Fs/t=Fv$$

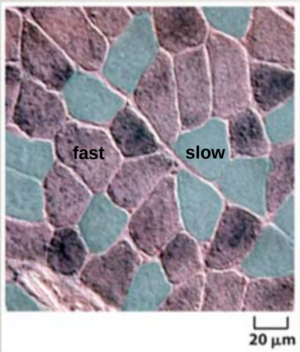
2. Force-velocity diagram



Energetics of muscle I.

Source of energy:

$Mg.ATP^{2-} + H_2O \rightleftharpoons Mg.ADP^{1-} + Pi^{2-} + H^+$



Type I fibers

- rich in mitochondria
- ATP generation by respiratory mechanisms
- slow fatigue
- rich in myoglobin: "red muscle"
- innervated by thin, slow nerves
- slow fiber
- dominates in postural muscles

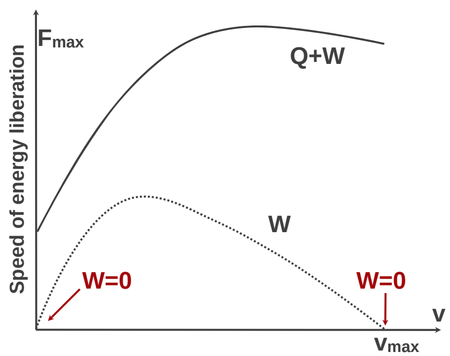
Type II fibers

- few mitochondria
- rich in glycogen
- ATP generation by glycolysis
- rapid fatigue due to lactate
- devoid of myoglobin: "white muscle"
- innervated by large, fast neurons
- fast fiber
- present in fast muscles

Energetics of muscle II.

Fenn effect

The increased liberation of heat in a stimulated muscle when it is allowed to do mechanical work.
Liberation of heat increases with increasing speed of contraction.



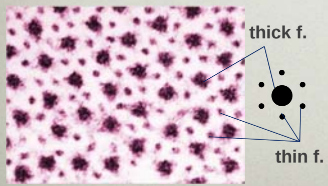
Mechanisms of muscle shortening

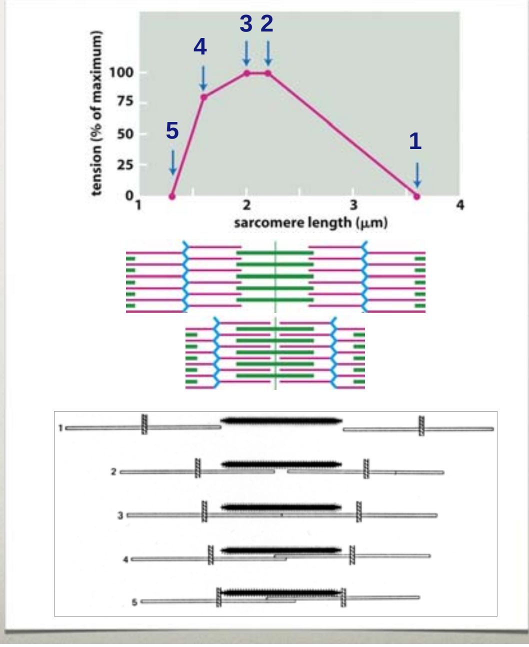
Phenomenological mechanism:

Sliding filament theory

Andrew F. Huxley, Jean Hanson, Hugh E. Huxley

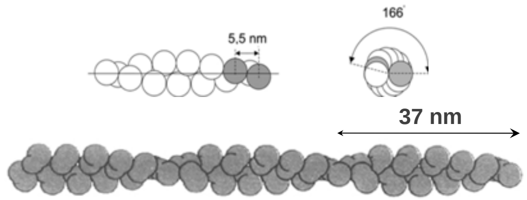
Sarcomere cross section

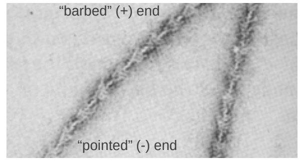




Molecular mechanisms of muscle contraction: Cyclic, ATP-dependent actin-myosin interaction

The actin filament





~7 nm thick, length *in vitro* exceeds 10 μm, *in vivo* 1-2 μm

Right-handed double helix.

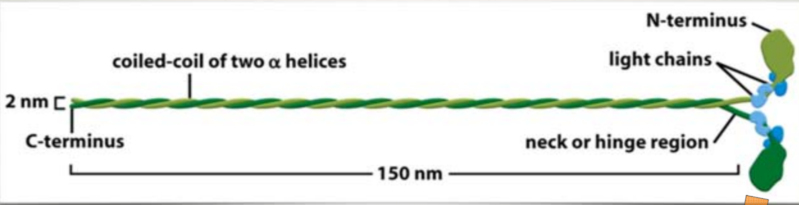
Semiflexible polymer chain (persistence length: ~10 μm)

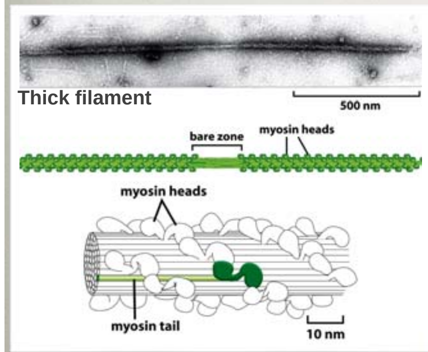
Structural polarity ("barbed", "pointed" ends)

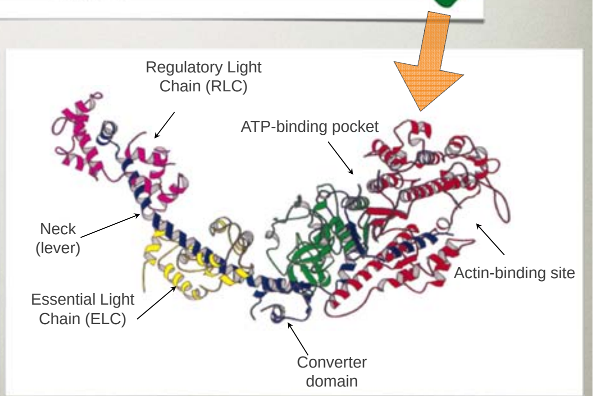
Tensile strength of actin: appr. 120 pN (N.B.: under isometric conditions up to 150 pN force may reach a filament.

Number of actin filaments in muscle: 2 x 10^{11}/cm^2-muscle cross section.

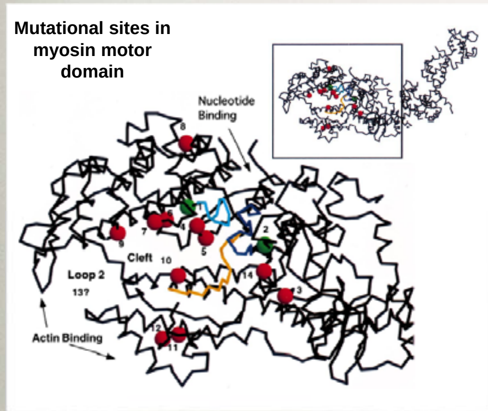
Myosin II





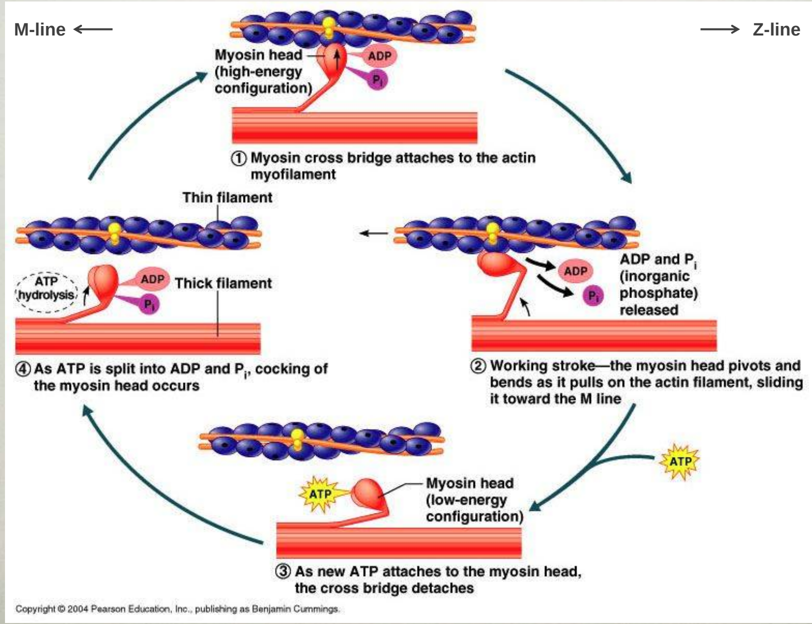


Myosin mutation - pathology

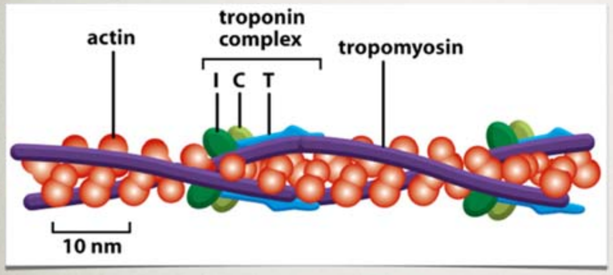


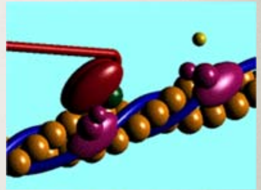
Arg403Gln mutation: hypertrophic cardiomyopathy

The myosin "cross-bridge" cycle



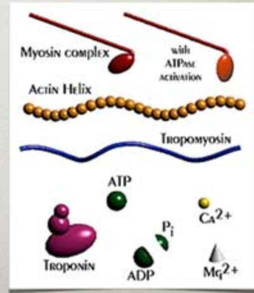
Contraction regulation in striated muscle



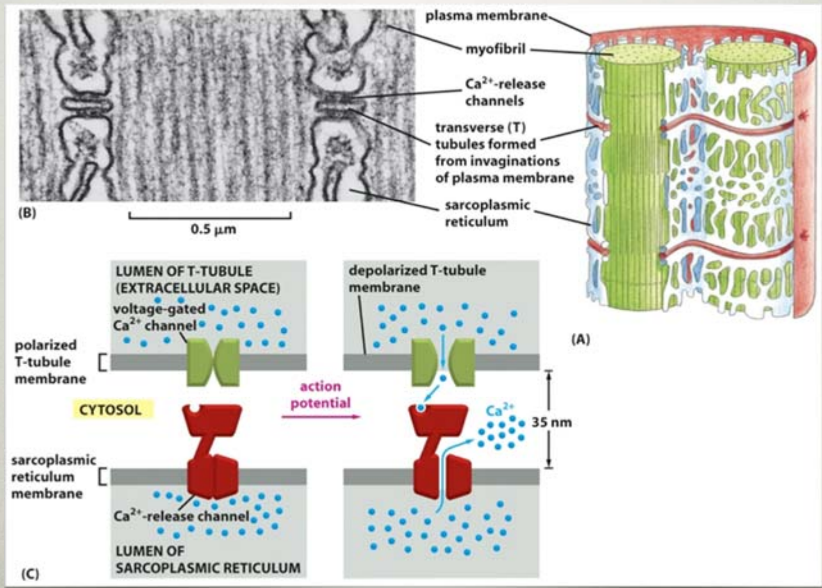


Tropomyosin: blocks myosin-binding site on actin

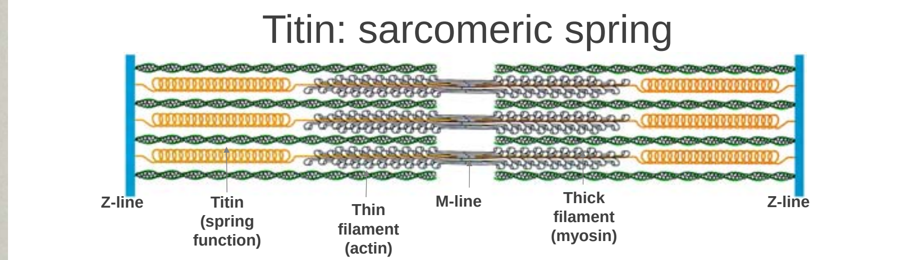
Troponin complex: 3 subunits, (C, T, I)
Troponin C binds free Ca^{2+}, which causes the conformational change of tropomyosin, thus myosin-binding sites expose.

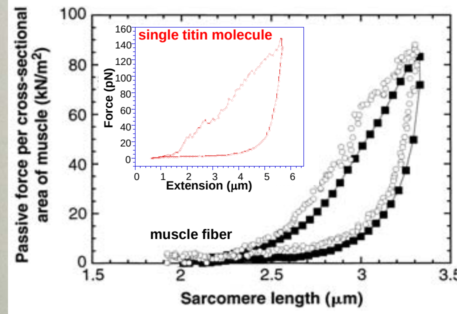


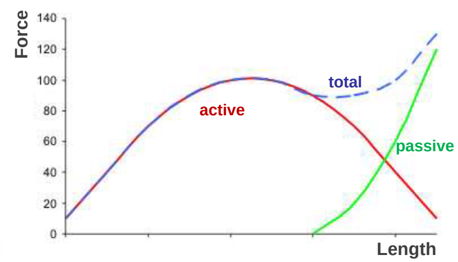
Excitation-contraction coupling



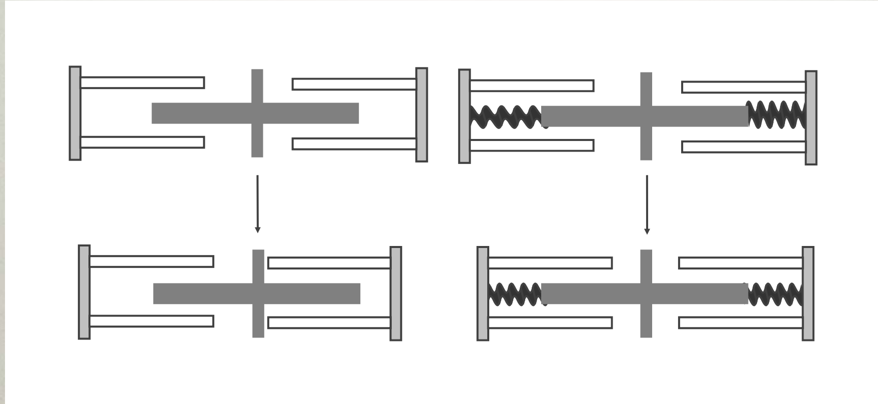
Elasticity of striated muscle



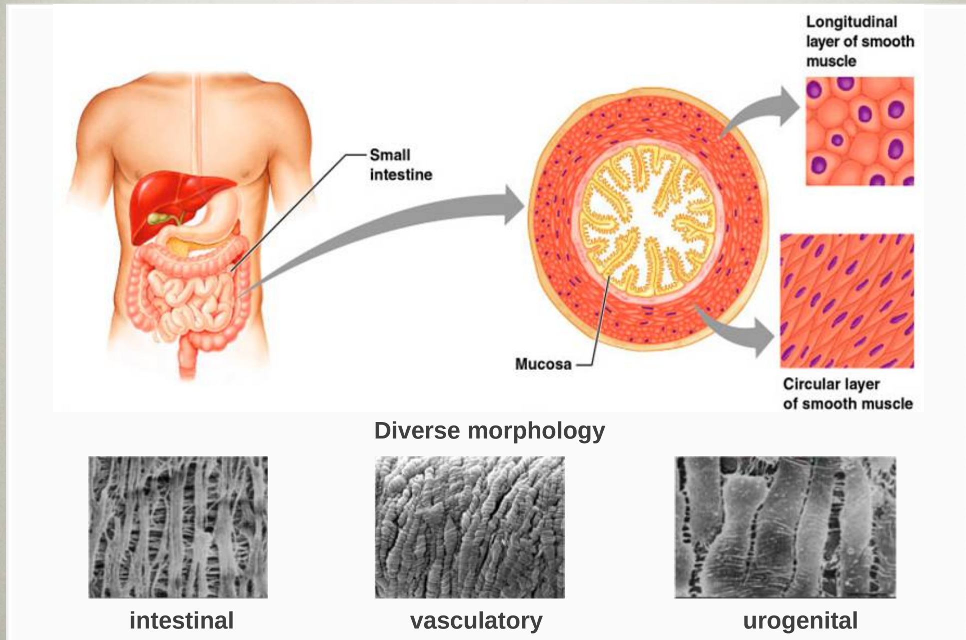




Role of titin in sarcomere: Limitation of A-band asymmetry



Smooth muscle

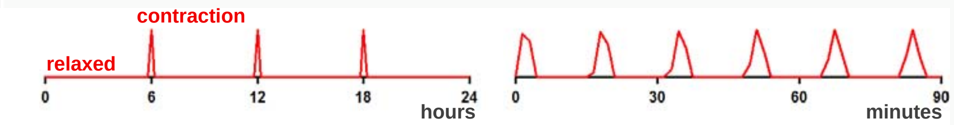


Smooth muscle classification

Phasic: Relaxes most of the time, contracts only periodically.

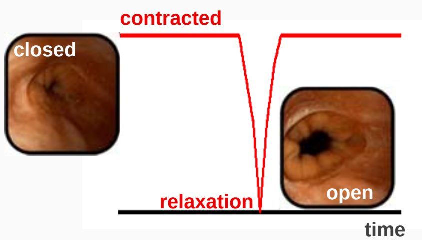
urinary bladder (few times a day)

GI tract (few times an hour)



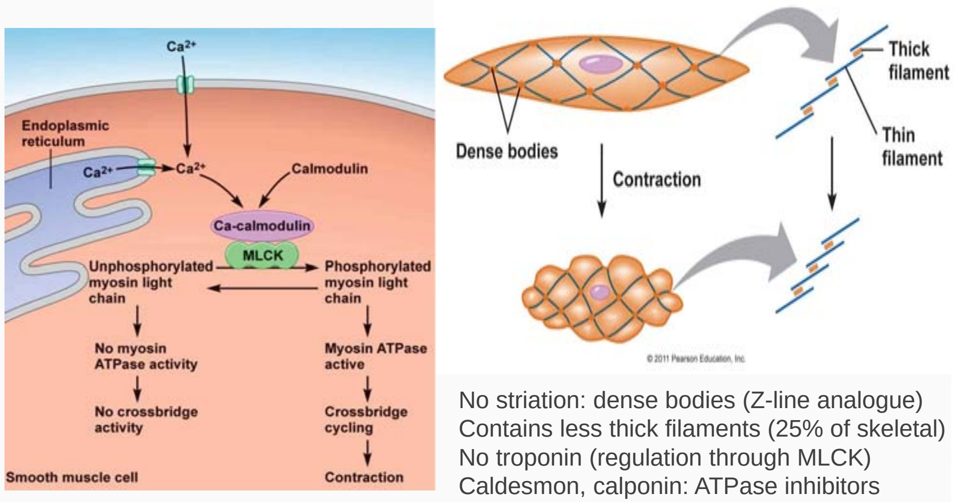
Tonic: Contracted most of the time, relaxing only briefly.

lower oesophageal sphincter



vascular smooth muscle
maintain and tune vascular tension

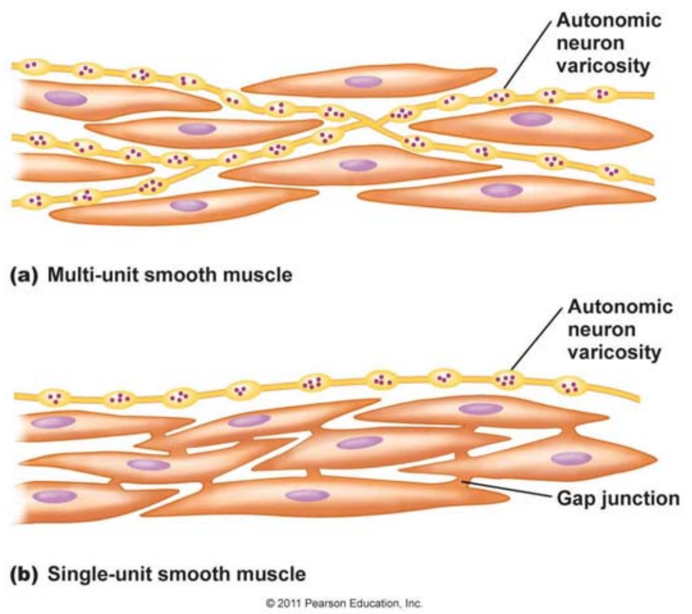
Smooth muscle contraction



No striation: dense bodies (Z-line analogue)
Contains less thick filaments (25% of skeletal)
No troponin (regulation through MLCK)
Caldesmon, calponin: ATPase inhibitors

Desmin: main intermediate filament of smooth muscle
Smooth muscle myosin: lower actin affinity, regulated by phosphorylation

Smooth muscle contraction



Independent mechanical activity of cells

Airways, vasculature

Synchronized contraction, by gap junctions.

GI tract: peristaltic motion (Basal Electrical Rhythm – BER)

Urogenital tract

Smooth muscle energetics

Source of energy:

$$Mg.ATP^{2-} + H_2O \rightleftharpoons Mg.ADP^{1-} + Pi^{2-} + H^{+}$$

Skeletal muscle	**Smooth muscle**
1 ATP per crossbridge cycle by myosin ATPase	1 ATP per crossbridge cycle by myosin ATPase
	~ 1 ATP per crossbridge cycle by MLCK

Smooth muscle consumes more ATP than skeletal?

ATPase activity and crossbridge formation rate is significantly slower, thus fewer crossbridge cycles occour in a time period.

Smooth muscle can sustain long or even extreme-long contractions at lower ATP consumption rate.