Muscle Contraction

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Introduction

Muscle – *contractile tissue*; Muscle are of 2 varieties: striated (striped) or nonstriated (smooth) muscle and make up to 50% of adult body mass.

Muscle tissue can be divided into 3 types of muscle:

i. skeletal muscle – attached to skeleton , functions as a unit,
morphologically striped muscle,
voluntary muscle under conscious control.
skeletal muscle fibre types:
- slow type muscle fibres
- twitch-type muscle fibres
  - fast fatigable fibres
  - slow fatigue-resistant fibres
  - fast fatigue-resistant fibres.

ii. cardiac muscle – myocardium, generate contraction of
atrial and ventricle muscle,
morphologically striped muscle.

iii. smooth muscle - involved in involuntary process (blood vessels, gut)
divided into unitary (visceral) and multi-unit smooth muscle (iris, ciliary muscle, piloerector muscles), morphologically nonstriped muscle.

Muscle properties[1-2]

Characteristics	Skeletal *m.*	Cardiac *m.*	Smooth *m.*
Anatomy:			
Cell shape/size	Long cylindrical cells, up to 30 cm long, 100 µm wide	Irregular, branched, rod-shaped cells, up to 100 µm long, 20 µm wide	Spindle shaped cells up to 400 µm long, 10 µm wide
Nuclei	Multinucleated	Mostly single	Single
Actin & myosin filaments	Yes	Yes	Yes
Sarcomeres present (striated)	Yes	Yes	No
Myogenic activity	No	Yes	Yes

- **sarcomere** is the basic unit of muscle contraction and is enclosed by adjacent Z-lines. Each sarcomere consists of one A band and two I band halves. Myosin forms the A band (thick filaments) and actin filaments (thin) form the I band. The actin filaments are anchored at the Z lines, with M lines formed by the connecting thick myosin filaments together. [3]
- **smooth muscle** – lack of cross striations, actin and myosin filaments arranged randomly.

A reductionist approach to skeletal, cardiac and smooth muscle morphology will be discussed during the presentation.

Characteristics	Skeletal *m.*	Cardiac *m.*	Smooth *m.*
Signaling:			
Initiation of contraction	Extrinsic (somatic, neural)	Intrinsic (muscle origin), but influenced by extrinsic autonomic (sympathetic & parasympathetic)	Intrinsic via nerve plexus, extrinsic via autonomic (sympathetic & parasympathetic), hormones or stretch
Depolarization/ *stimulation of contraction	Nerve action potential to each muscle cell, then to muscle endplate	Spread by specialized muscle cells in the conducting system, then spreads cell to cell	*Often spontaneous, sensitive to circulating chemical agents
Gap junctions (electronic coupling)	No, connective tissue separate adjacent cells	Yes (functional syncytium)	Yes – few in multi-unit, many in unitary
Hormonal influence on contraction	Small	Large	Large
Effect of nerve stimulation	Excitatory	Excitatory or inhibitory	Excitatory or inhibitory
Extent of innervation	Each cell innervated	Variable	Almost every cell in multi-unit, sparse in unitary
Spontaneous electrical activity	No	Yes	No in Multi-unit, Yes in unitary
Resting membrane potential	Stable RMP	Stable RMP in ventricular muscle. Not stable RMP in SA and AV node due to automaticity/rhythmicity	No RMP as potential tends to wander
Control	Voluntary control	Involuntary (and automatic contractions due to pacemaker cells)	Involuntary control only

- **gap junction** – also called a electrical synapse and provide connections between the cytoplasm of adjacent cells.

  It consists of a functional unit called connexion.

  This electrical conduction is much more rapid than the chemical synapses at the NMJ as it allows for:
  a) rapid depolarisation from cell to cell
  b) passage of ions and small molecules between cells.

- **motor unit** – consists of a single anterior horn α-motor neurone, its axon and all the muscle fibres it innervates, it is considered the functional unit of contraction.[3]

- **cardiac muscle has several special intrinsic properties –** automaticity, rhythmicity, conductivity, contractility and excitability. The nerves innervating the heart can only speed up or slow down the rhythm (chronotropy) and can modify the force of contraction (inotropy).

- **smooth muscle** – more sensitive to circulating chemical mediators.

Characteristics	Skeletal *m.*	Cardiac *m.*	Smooth *m.*
Muscle contraction physiology:			
Major source of Ca^{2+}	Sarcoplasmic reticulum	ECF and sarcoplasmic reticulum	ECF (sarcoplasmic reticulum poorly developed)
Ca^{2+} binds to	Troponin C	Troponin C	Calmodulin
Function of this binding by Ca^{2+}	Removes the inhibition of troponin I and exposes myosin binding sites	Removes the inhibition of troponin I and exposes myosin binding sites	Ca^{2+}-calmodulin activates myosin light chain kinase
Mechanism of excitation-contraction coupling	Via action potentials and t-system	Via action potentials and t-system ('calcium-triggered calcium release')	Via action potentials, calcium channels and/ or 2nd messengers
Activation of myosin ATPase	Phosphorylation not required	Phosphorylation not required	Requires phosphorylation which is catalyzed by active myosin light chain kinase
Duration of muscle contraction	Brief – 7,5 – 100 msec. depending on fibre type	300 msec. in the ventricle at normal heart rate	Last for long periods (tonic contraction)
Type of contraction	Phasic	Rhythmic	Tonic with some phasic
Basic muscle tone	Neural activity	None	Intrinsic and extrinsic factors
Speed of contraction	Fast	Slow	Very slow
Muscle spindles	Present and important in regulation of contraction	Not present	-

- Excitation-contraction coupling collectively refers to the sequential series of steps from the action potential to the subsequent muscle contraction.

Molecular machinery

Muscle contraction requires interaction between Ca^{2+}, troponin, tropomyosin, actin and myosin.

Myosin is a large complex protein, consisting of a long tail and 2 globular heads which each bind actin and ATP.

Two F-actin chains twisted together make up the thin filaments. Actin potentiates the ATPase activity of myosin.

Tropomyosin prevents interaction of myosin with actin and is modulated by troponin.
Troponin is a globular protein present on the thin filament (1:7 actin molecules), with 3 sub-units Troponin-T (binds tropomyosin), troponin-I (inhibits actomyosin ATPase) and troponin-C (binds Ca^{2+}).

Ca^{2+} alters the troponin-tropomyosin complex configuration, so that myosin can interact with actin. Ca^{2+} binds to troponin C on the thin actin filaments. This interacts with troponin I and tropomyosin and this complex moves away to expose the sites on actin where myosin heads bind. Actin and myosin form a cross-link.

Both muscle contraction and relaxation are energy processes requiring ATP.

Muscle contraction persists until the cytoplasmic Ca^{2+} concentrations fall, Ca^{2+} is released from troponin C and actin is unable to interact with the myosin heads. This occurs due to rapid pumping of Ca^{2+} back into the SR via Ca^{2+}-Mg^{2+} ATPase pump, and Ca^{2+} diffuses to the terminal cisternae (t-tubules), ready for release with the next contraction.

Mechanism responsible for skeletal muscle contraction

This can be explained by the sliding filament theory. Muscle contraction occurs because of the sliding of the thin filaments and thick filaments along each other. This sliding is produced by myosin head cross-bridges pulling the actin fibers toward the centre of the sarcomere. The sliding is powered by the hydrolysis of ATP by the ATPase activity of the myosin heads.

The sliding filament theory is confirmed by the observation that developed tension during isometric contraction depends on initial muscle length.

Skeletal muscles are arranged near their optimal length.

Cardiac action potential and contraction

In the absence of extracellular Ca^{2+}, cardiac muscle doesn't contract (Ca^{2+} triggered Ca^{2+} release). Cardiac muscle cannot exhibit tetanic contraction due to a prolonged refractory period.

Smooth muscle contraction considerations

There is twice as much actin and tropomyosin in smooth muscle compared to striated muscle, but no troponin.

- **calmodulin** – an intracellular Ca^{2+} binding protein, with 4 Ca^{2+} binding sites. Calcuim binding to calmodulin can activate 5 different calmodulin-dependant kinaseses – myosin light chain kinase, phosphorylase kinase, Ca^{2+}-calmodulin kinase I,II, and III.
  Smooth muscle contraction is initiated by this activation of myosin light chain kinase, resulting in phosphorylation of myosin and causes the cross-bridge mechanism to operate.
- **latch bridge mechanism** – a sustained smooth muscle contraction, where the myosin heads remain attached to actin despite becoming dephosphorylated and the fall in cytoplasmic Ca^{2+} concentrations.

Smooth muscle tends to contract in response to increased tension.

- **plasticity** – refers to the variable tension that develops in visceral smooth muscle at a given length.

Nitric oxide – plays an important role in vascular smooth muscle; (i) local control of vascular tone and (ii) contributes to vascular wall thrombo-resistance. In the latter it inhibits platelet aggregation and adhesion to the vascular wall.
It is produced from L-arginine in the vascular endothelium by nitric oxide synthase, and diffuses to the vascular smooth muscle. It stimulates guanylate cyclase forming cGMP, causing relaxation of vascular smooth muscle.

Topics for interactive discussion during the 2nd part of the presentation and/or further consideration:

i) What is a muscle spindle?
ii) Describe the stretch reflex?
iii) Physiology of neuromuscular transmission, action potentials and developed tension in skeletal and smooth muscle.
iv) Drugs affecting excitation-contraction coupling in cardiac and skeletal muscle.

References

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