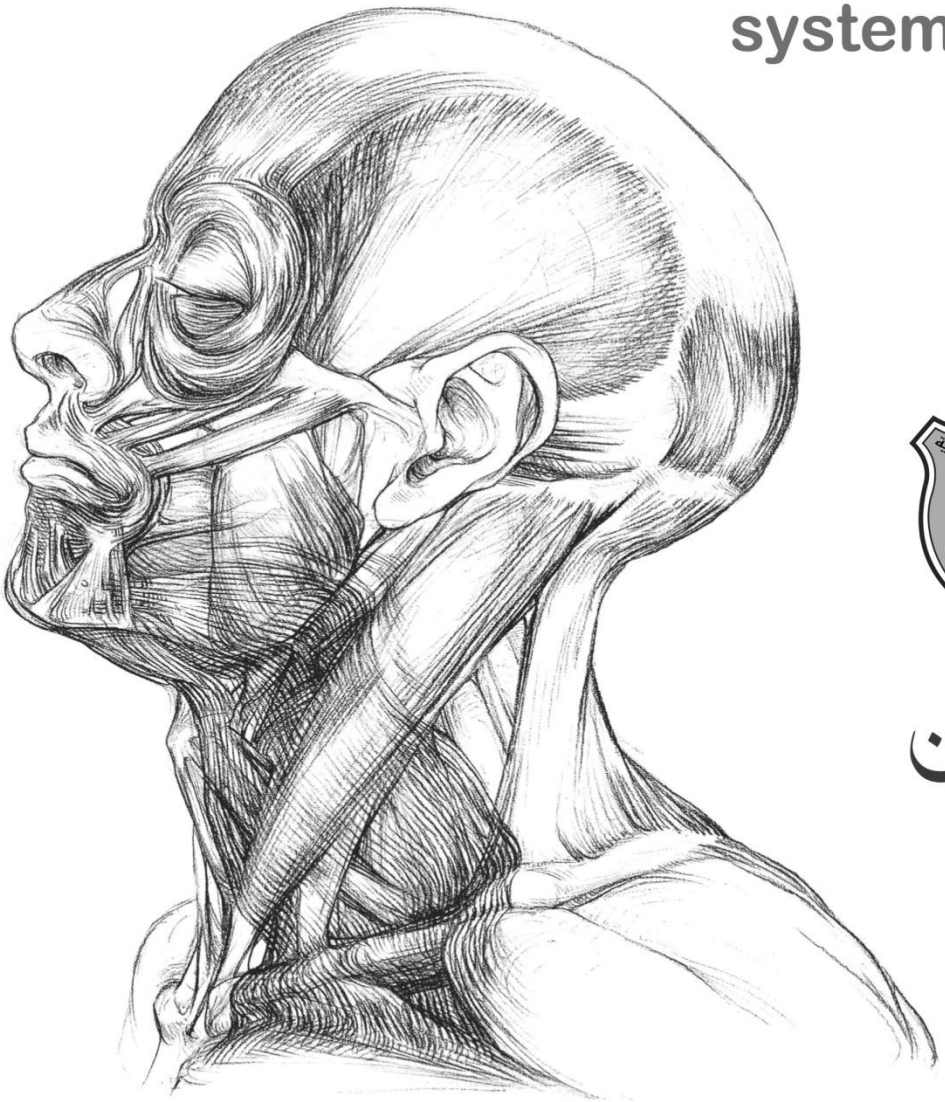
The skin & Muscloskeletal system



PHYSIOLOGY

SLIDES ☐
SHEET ■
LECTURE # 2

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Introduction

Previously, we discussed the physiology of excitable membranes and action potential. In this sheet, we are going to discuss skeletal muscle's structure and contraction.

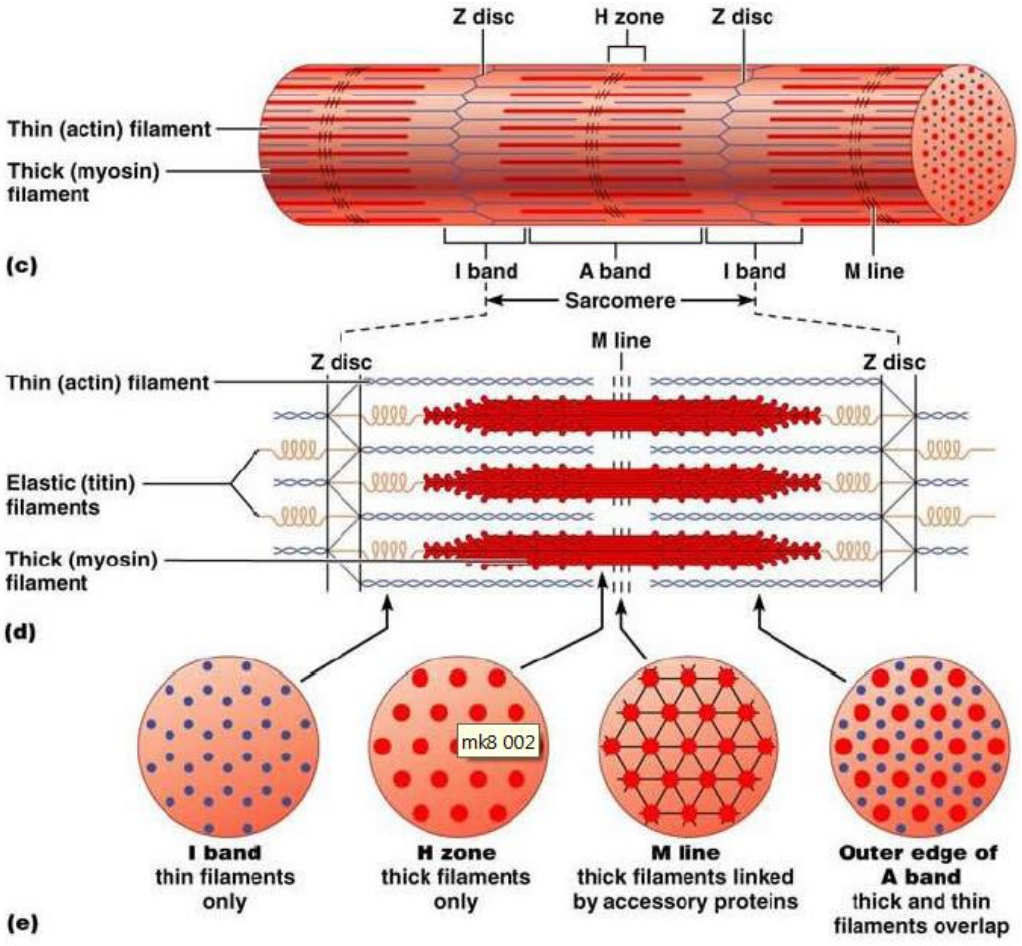
Muscles and neurons are excitable cells. Muscles can be classified in many ways (**microscopic appearance**, *innervation*). Skeletal muscles are **striated** *voluntary* muscles. Note that we are not going to discuss the detailed anatomical aspects of this topic.

Structure of skeletal muscle

Skeletal muscles are composed of muscle fibers (muscle cells; myofibers), which *contain* myofibrils, which are striated ultra-structural cylinders. Skeletal muscles are striated; dark and light areas can be noticed in an alternative way when viewing muscle fibers or myofibrils under the microscope. Such striation is due to the organization of the contractile proteins, which are either thick (dark) or thin (light).

The sarcomere: the functional unit

The organization of the contractile proteins constructs fundamental structures. Such structures are illustrated as follows.

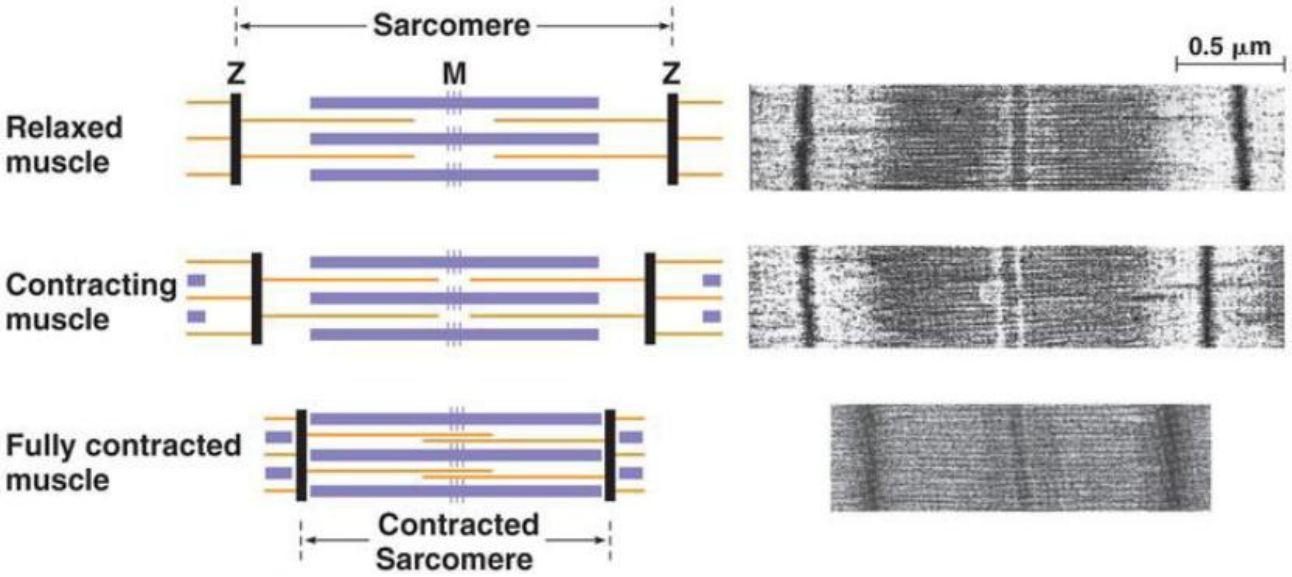


1- **I-band**: (the lighter region) this region contains only thin filaments with **no** overlapping (notice the first cross section of figure **(e)**). In the middle of the I-band presents the *Z-disc* when viewed in 3D (or line when viewed in 2D.
2- **Z-disc**: holds the thin filaments.
3- **A-band**: this region extends between the thick filaments margins. There are regions of overlapping between thick and thin filaments in this region (notice the last cross section of figure **(e)**). Notice in this cross section that each thick filament is surrounded by 6 thin filaments, and each thin filament is surrounded by 3 thick filaments. So, we can conclude that the ratio of thick filaments to thin filaments equals 1:2.
4- **H-zone**: In the middle of the A-band we can notice a region with **no** overlapping (only thick filaments), which is this zone.
5- **M-line**: this line is in the middle of the H-zone, and functions in holding thick filaments.

The sarcomere is the functional unit of the myofibrils. It extends from a Z-disc to the following Z-disc. Its midline is the M-line.

Other structures of the myofiber will be discussed later. Those include the *sarcolemma* (= plasma membrane of the muscle cell), the *sarcoplasm* (= cytoplasm of the muscle cell) and the *sarcoplasmic reticulum* (ER of the muscle cell).

Muscle's Contraction and the Sarcomere components



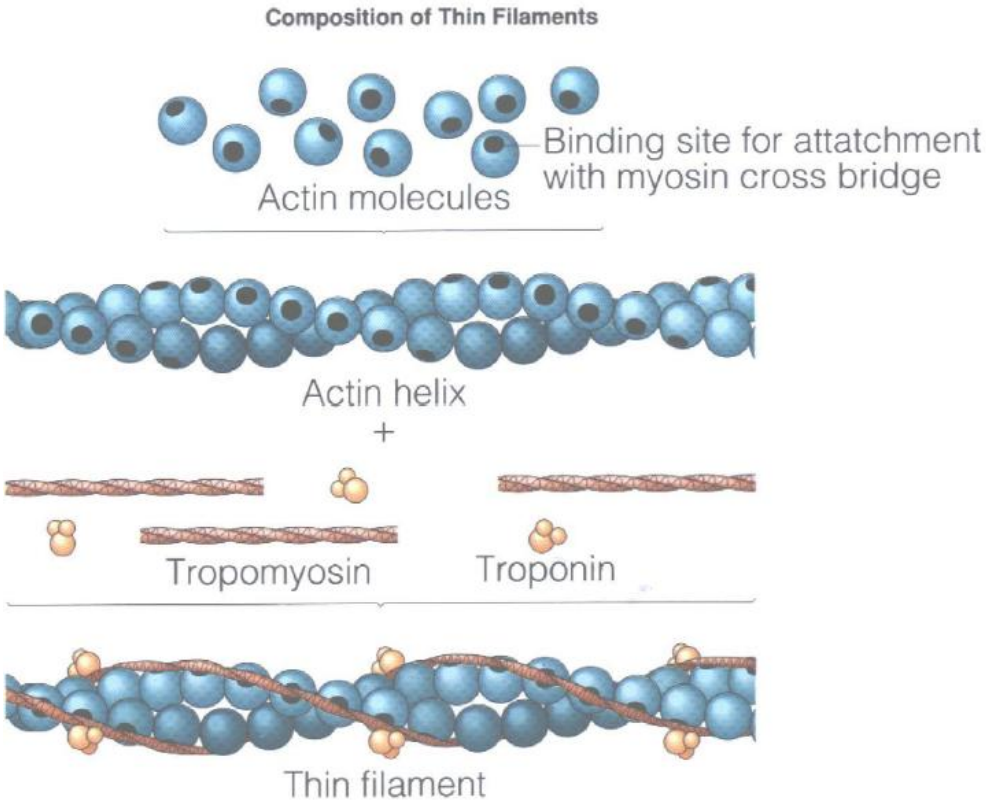
As the muscle contracts, thick-thin filaments overlapping area increases; so we can expect the following changes:

1- Length of the sarcomere decreases.
2- Length of the I-band decreases.
3- Length of the H-zone decreases.
4- Length of the A-band does ***not*** change (= length of thick filaments).
5- Z-discs approximate to each other and towards the M-line. (Notice the figure.)

Thick-Thin Filaments Interaction Process

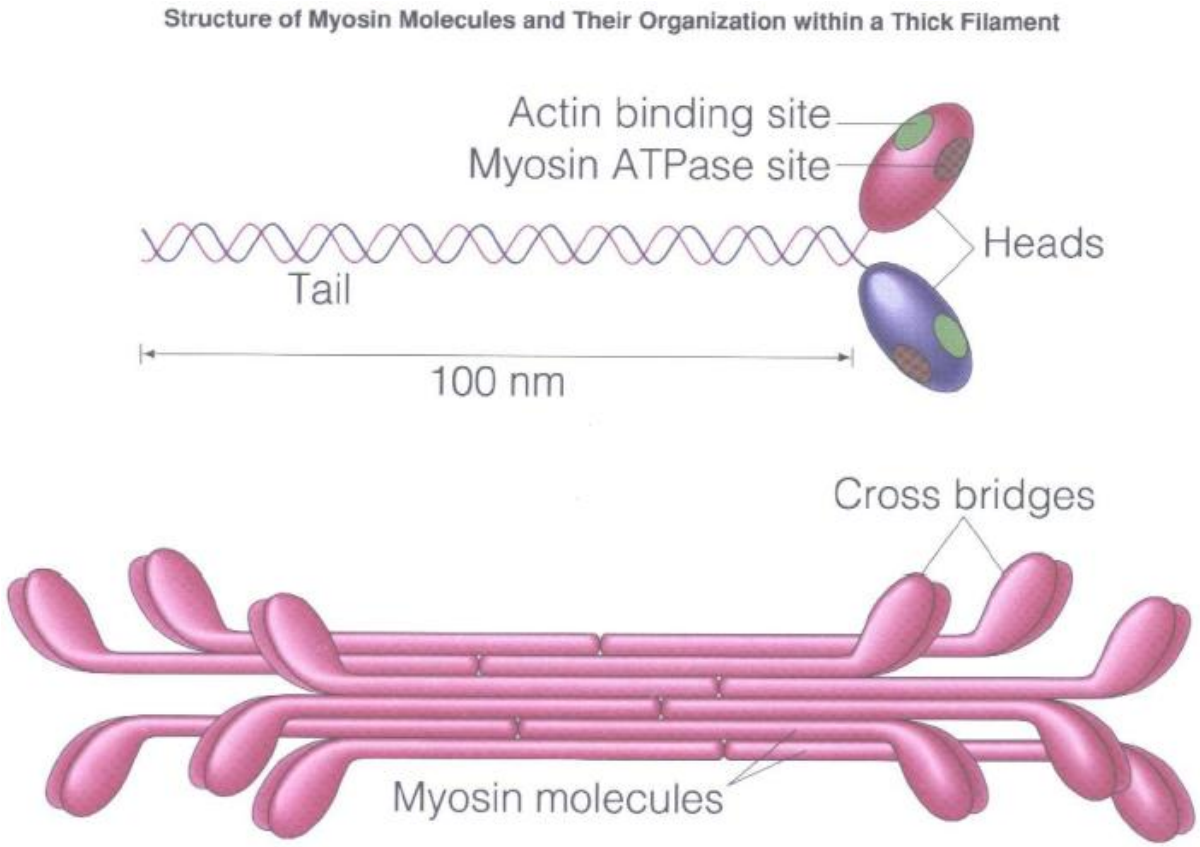
Structure of contractile filaments

1- Thin filaments: contain more than one type of proteins:
a- **Actin**: Actin molecules polymerize to form a helix structure; which forms the backbone of the thin filament. Notice from the figure below that Actin molecules have a binding site for interaction with the thick filaments.
b- Regulating proteins: have a regulatory function on the interaction process;
***Troponin**: has 3 subunits; **C** subunit for Ca^{++} binding, **T** subunit for *tropoMyosin* binding and **I** subunit, which is the intermediate subunit which binds the two other subunits.
***TropoMyosin**.



Notice that in the normal relaxed settings, TropoMyosin covers the binding sites on the Actin, which prevents the interaction process.

2- Thick filaments: contain so many units of one type of proteins; *Myosin*. Myosin has 2 globular heads, and a helical tail (α-helix) which participates in the formation of the backbone of the thick filament. The heads protrude to the outside in all directions, and this is what forms the *cross bridges*. These heads have 2 sites of interaction; **Actin binding site**, and **Myosin ATPase site**; which splits ATP to phosphorylate the heads.



Interaction process

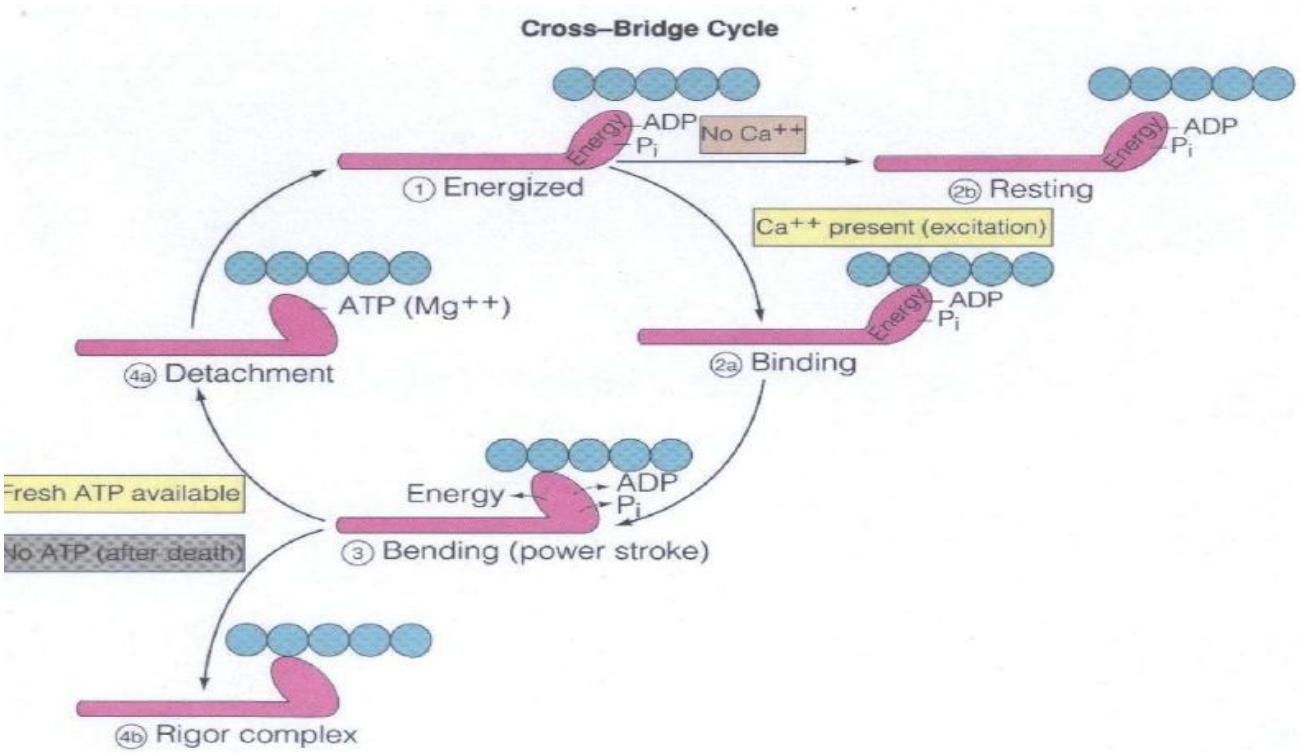
To accomplish the interaction process, Ca^{++} ions are needed. When Ca^{++} ions are available, the following steps take place:

1- Ca^{++} ions bind to troponin C subunit; conformational changes occur to the regulating proteins.

2- These conformational changes result with changing the place of Tropomypsin and uncovering Actin binding sites to myosin. This exposure of the interaction sites leads to the binding of Myosin heads to them; because both sites have high affinity to bind each other, so exposing the sites is enough to result with the binding. Note that **4 Ca^{++} ions** are needed to bind to each Troponin molecule to get the needed conformational changes.

3- **Cross-bridge cycle**: after *(a) binding*, Myosin heads automatically (b) bend as a result of a conformational change, and this is called *bending* or *power stroke*. This results with the shortening of the sarcomere. After this, thick and thin filaments must (c) *detach*, and that is done by decreasing the affinity between them. To perform that, the bound ADP and phosphate are exchanged with ATP, which results with decreasing the affinity and detaching the filaments from each other. Then, the ATPase part of Myosin consumes the added ATP to phosphorylate the head (the resulting ADP stays bound), returning back to its original high-affinity position (the energized position). In this position (it is also the position of the resting state), the heads are ready for the interaction. After that:

- If Ca^{++} levels are still elevated, the cycle will loop again and again (step 3).
- If Ca^{++} levels are decreased, everything will stay at this position. The system will be ready for subsequent interaction (then, it undergoes all the steps - from step 1).



Rigor Mortis: if ATP was not available for step 3 c (Detachment), then everything stays as it is; the sites are stuck (no detachment) and the heads are bent, so the muscle will stay contracted, and no relaxation will take place. This happens after few hours (4 to 5 hours) of death (*rigor* from contraction; *mortis* from death).

Mg^{++} ions and muscle contraction: ATPase of Myosin requires Mg^{++} ions to function. Hypomagnesaemia can result with spasm, but that is not because of ATPase functionality, but rather because of its effect on CNS (elevates neurons excitability). Hypocalcaemia also results with spasm.

Energy usage and sources

ATP is used by the ATPase in the cross-bridge cycle. ATP is also needed to normalize the sodium and potassium levels after the action potential, in addition to the need of ATP to pump back Ca^{++} ions to its stores in the sarcoplasmic reticulum. So, huge amounts of ATP are needed to help muscles function well.

Normal ATP levels in the muscle cell are enough for few seconds of contraction only, so the muscle needs to replenish its ATP pool fast to perform its function, and that is done by the phosphorylation of ADP with the presence of creatine phosphate. An enzyme (creatine kinase) catalyzes the reaction of phosphate group transfer from creatine phosphate to ADP to re-produce ATP. Creatine phosphate stores last for a few minutes.

The other two sources of energy are anaerobic glycolysis and oxidative phosphorylation. In contrast to oxidative phosphorylation, anaerobic glycolysis produces small amount of energy at a frequent rate. Anaerobic glycolysis is the continuous source of energy in the 'fast' muscle fibers; whereas oxidative phosphorylation is the continuous source in the 'slow' fibers, see the table.

Difference	Fast fibers	Slow fibers
Properties	Faster energy production, but with less amounts	Slower energy production, but with higher amounts
Energy source	Anaerobic glycolysis	Oxidative phosphorylation
Presence of mitochondria	Less	More
Vascularization	Less	More; oxygen-dependent
Presence of myoglobin*	No	Yes
Color	White	Red
* Myoglobin is a globular protein, similar to Hemoglobin; it binds and stores oxygen; it gives slow fibers a reddish color.		

These fibers also differ in the size of cells. Notice that fast fibers require less vascularization; because anaerobic glycolysis does not need oxygen, and glucose is made available by the presence of muscular glycogen. But their high production of lactate renders them more prone to fatigue.

Some sports depend more on one type of these fibers than the other; for example, marathons depend on the presence of more slow fibers, whilst fast races for short distances require more fast fibers.

Here we finish our topic for the second lecture. Note that you have got to refer to the doctor's slide while studying. If you find any mistakes or edits, please refer it to the sheet's writer and corrector. Thank you, and good luck.

"Because they accept what is transient, they become firmly rooted in the silent unchanging awareness that is at the core of their being; the space in which all that is transient comes and goes"