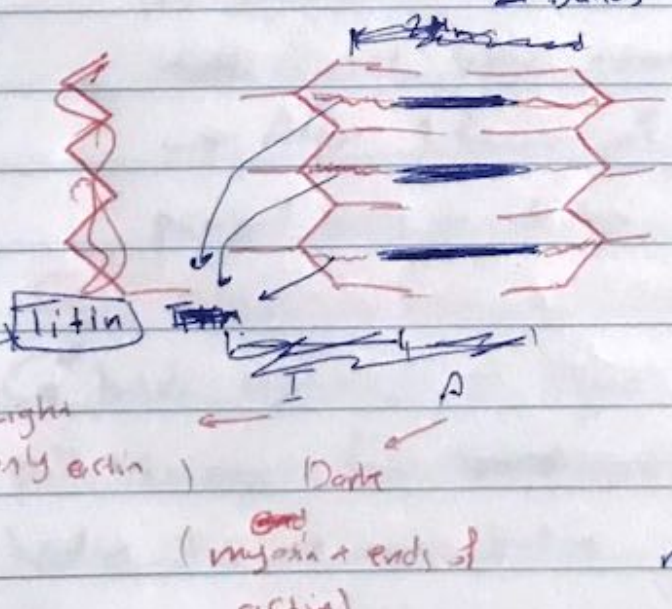
Physiology

- 40% of body weight → skeletal muscles
  10% → Cardiac & smooth.

skeletal
- Muscle fibers (cells) 10-80 micron in diameter (ماشية عطول العضلة الخلية الوحيدة) takes the length of the muscle, except 2% of the muscle fibers.
- Sarcolemma consist of → true plasma membrane
  → thin polysaccharide with collagen fibrils
- Each muscle fiber (cell) ends in tendon (tendon fiber) that collect with other tendon fibers to form muscle tendon. تجمع الخيوط بالوتر
- Muscle fiber → hundreds to thousands of myofibrils
  1500 myosin, 3000 actin
  thick filaments thin filaments

Sarcomere in myofibril: distance bet. 2 successive Z bands (lines),



- Z lines is continuous along the muscle fiber → the whole fiber (not only fibrils) has dark and light areas.
- At contracted state sarcomere may reach 2 μm → at this length actin completely overlap myosin.

- the largest protein molecule in the body (3 million) MW
- Springy → holds actin & myosin

20, 21, 22

- Each muscle fiber is innervated by one nerve in the middle part
- One end of titin protein is elastic, attached to Z line.
  - Other end tethers it to myosin
  - Act as a template for initial formation & portions of contractile filaments of the sacromere.

يعني بيساعد على تكوين actin & myosin in their place

- Sarcoplasm: Intercellular fluid between myofibrils, containing: Na^+, Mg^{+2}, PO_4, multiple proteins & enzymes, and tremendous amounts of mitochondria → ATP supply.

Action potential in muscle fiber

Action potential from nerve to muscle fibers → At end of nerve fiber it secrets Acetylcholine → Ach act on local area of the muscle fiber to open Ach-gated channels → opening of these channels leads to large quantities of Na^+ entry → local depolarization by Na^+ → opening of voltage-gated channels → Action potential in muscle fiber. → AP travel along the muscle fiber membrane (T-tubules) → depolarizations of the membrane, and the centre → Sarcoplasmic reticulum release large amounts of Ca^{+2} → contraction

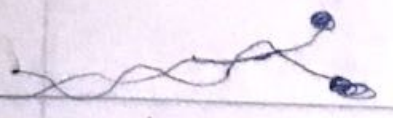
→ After 1 fraction of second (0.1s) Calcium ions are pumped back to reticulum.

Ca^{++} from sarcoplasmic reticulum

- Ca^{++} binds troponin C → Troponin T pull tropomyosin from myosin-binding sites → myosin bind to Actin → Contraction.
- Ca^{++}

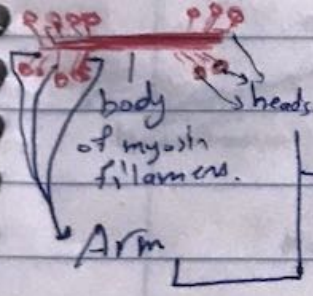
Tropomyosin at myosin-binding sites of Actin

- Troponins → I attaches tropomyosin to actin
  - C to which Ca^{+2} binds
  - T binds tropomyosin



Myosin

- Myosin 480,000 in MW 2 heavy chains, 6 light chains (200,000 × ½ + 200,000 × 6)
- * 2 heavy chains wrap each other → helix "tail" → only at head
- * One of each end of these 2 heavy chains will form globular head.
- * Two light chains to each head. → helps in control the function of the head during contraction.
- * One myosin filament (thick filament) is formed of ≥ 200 myosin molecule
- * Tails of myosin molecules → (body) of myosin (thick) filament.



→ Arm + head → Cross-bridge

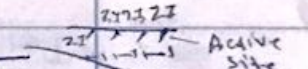
- * Each cross-bridge has 2 Hinges "flexible point" The first at body-arm junction, the other at arm-body.
- * Hinges allow head of myosin to be away or close to myosin filament body
- * Myosin filament length = 1,6 microns, Body apart from heads by 0,2 micron "arms"
- * Each cross-bridge pair is axially displaced by 120° from the previous one.
- * Myosin head has ATPase activity

Actin

* Backbone of actin (thin) filament is double-strand F-actin protein molecule → (two lighter-colored strands forming helix)

2 F-actin → actin filament

* Each strand of F-actin is formed of: Polymerized G-actin molecules
* Each strand is 42,000 in MW.
* Attached to ADP → active sites of actin that bind to cross-bridges of myosin
* Active sites of F-actin strands of the double helix are staggered, giving one active site on the overall actin filament about every 2.7 nanometers.



* Between F-actin strands, Tropomyosin molecules lie.
* ~~At end of each tropomyosin molecule Tropo~~
* Actin filament is 1 micron in length.

Myosin 1.6 microns

* Tropomyosin covers active sites of actin
* Attached intermittently along the sides of tropomyosin proteins, called troponin
* Troponin C binds 4 Ca^{++} ions. → conformational change of troponin complex → moves tropomyosin deeper in groove bet. the 2 actin strands (F-actin)

(Walk-along) (Ratchet) theory

Power stroke

1

2

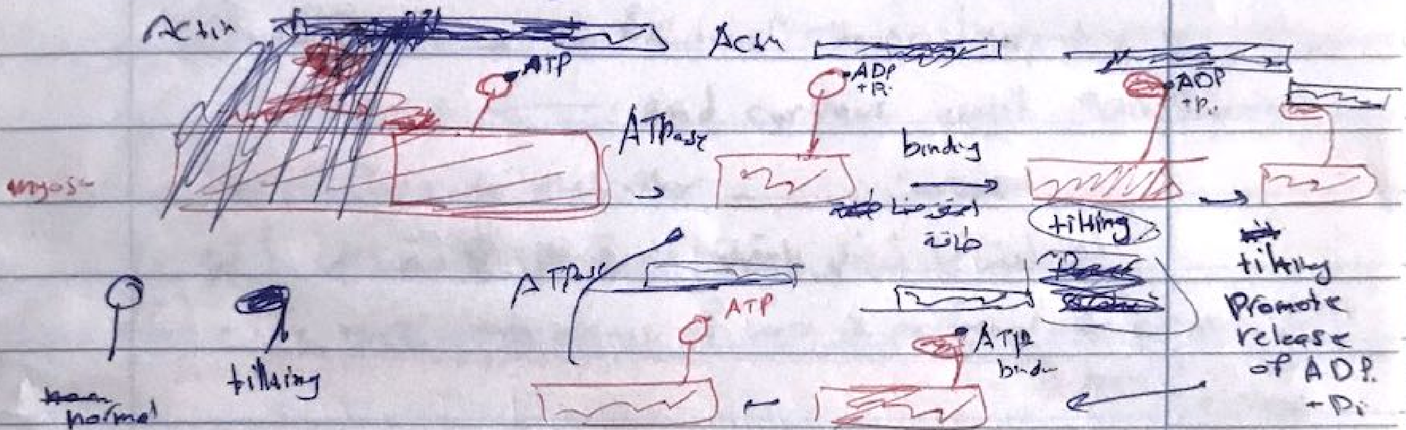
Myosin cross-bridges binding to Active sites on actin

* A Cross-bridge binding to actin → profound changes in intermolecular forces between the head & arm → Head tilt toward arm and drag the actin filament along with it. This is called Power stroke

* Immedialy after tilting ~~head~~ head breaks away from the active site, then return to it's extended direction and repeats the cycle وبظل يسحب بالأكتين للداخل

Pulling the ends of actin ~~fil~~ filaments toward the centre of myosin filaments

* The greater the number of cross bridges in contact with actin → the greater the contraction.



(1) ATP bound to head of myosin before ~~binding~~ binding to actin → ATPase leaves the head with ADP + Pi → Conformational change of the head (يقرب عن الأكتين) Perpendicular toward actin

(2) Tropon-tropomyosin complex binds with Ca^{++} → Actin is ~~f~~ free to bind to myosin

(3) Myosin ~~h~~ cross-bridge binds actin → tilting the head toward the arm of cross-bridge هذه الخطوة 2 تحتاج طاقة

ATP ~~...~~ ويحصل عليها من الطاقة المخزنة الناتجة عن

(4) Conformational change of the head at Step 1 (becoming Perpendicular facing actin)

~~(4) Once the head tilts → release of ADP+Pi from myosin head~~

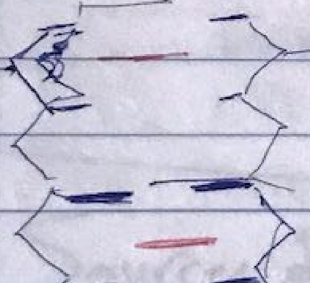
(4) Tilting the head of myosin will activates power stroke → pulling actin toward centre.

(5) After tilting has occured → head release ADP + Pi, and a new molecule of ATP binds to head → detachment of the head from actin.

(6) ATPase → conformational change (perpendicular) → tilting and continue until actin filaments are close to each other

أو لعند ما تبطل العضلة قادرة عن الإنقباض أكثر.

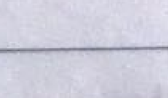
Fenns effect • The more amount of work is performed, the greater ATP needed to be cleaved



• No actin - myosin overlap → tension is Zero

• كل ما صغر طول ال sarcomer وقرب ال actin وصار overlap مع الميوسين بزيد ال tension لعند ما يوصل طول ال sarcomere 2.2 μ → maximum tension

• From 2.2 → 2.0 micr the tension is constant "maximum".



At sarcomere length = 2 the actin filaments starts to overlap each over ويقل عدد ال cross-brige المرتبطة من الميوسين مع الأكتين

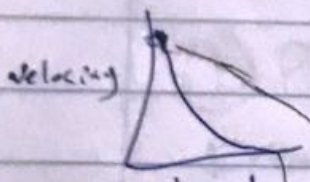
• بعدين كل ما قصر ع

يظل يتداخل ال actin في بعض وال myosin لبيأ ينضغط ← بقل ال tension لعند ما يوصل صفر

Increase in whole muscle length & tension

At normal muscle length, sarcomeres length considered 2 micron "maximum tension"

→ Any tension that occurs during contraction "Active tension" decreases as the muscle is stretched beyond normal 2.2



→ Velocity maximum at load = zero

→ Velocity 0 at load = maximum ability of the muscle

Work = L X D (distance)

"The energy transfered from muscle to external load to lift an object or to overcome resistance to movement.

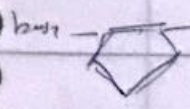
Sources of energy:

① Muscles depend on ATP; most of energy from ATP is used in walk-along mechanism.

- Small amounts of energy needed to: 1) Pumping Ca from sarcoplasm to sarcoplasmic reticulum

2) Pumping Na & K through muscle fiber membrane to maintain appropriate ionic environment for propagation of action potential

- The concentration of ATP is 4 milli molar → maintain full contraction for 1-2 sec at most.
- only 1-2 sec at most.
- ATP $\xrightarrow{ATPase}$ ADP + H_3PO_4 + 12 k cal
- ADP → ATP "rephosphorylation"



Rephosphorylation
- creatine phosphate
- glycolysis
- oxidative phosphorylation

(1) Phosphocreatine : carries a high energy phosphate bond

Creatine ~P ~~higher~~ Similar to the bonds of ATP (~P), that has slightly higher free energy than that each ATP bond.

- Thus cleavage of phosphocreatine → energy.
- It's present in very little levels (five times as great as ATP) → 20 millimolar
- ATP + Phosphocreatine combined → maximal muscle contraction for 5-8 sec.

Anaerobic

(2) Glycolysis: Rapid enzymatic breakdown of glycogen to pyruvate & lactic acid → energy → ADP to ATP ~~+ Reformation~~

This resultant ATP → directly to energize muscle contraction
or → Reformation of Phosphocreatine.

- Two-fold mechanism of glycolysis

(1) Occurs in absence of O_2, muscle contraction sustained for many seconds up to minutes, even in the absence of O_2

Cont

المصدر الثالث لـ ATP في العضلات — Oxidative phosphorylation — أسرع بحوالي مرتين ونص

② Rate of ATP formation is 2.5 times as rapid as ATP formation in response to cellular foodstuffs reacting with oxygen.
- Loses its capability to sustain maximum contraction after 1 minute, due to accumulation of glycolysis end products as lactic acid.

③ Oxidative phosphorylation.
- Combining food stuffs & glycolysis end products with O_2.
- More than 95% of all energy used in sustained, long term contraction comes from this source.
- Acting for sustained contraction for so many hours, and major source is fat.

لأوقات طويلة الدهون هي مصدر الطاقة للعضلات الأكبر

for a period 2-4 hours → half of energy comes from carbohydrates. بعديه بصير الدهون هو المصدر الرئيسي وبطلع ATP بالـ oxidative phosphorylation

Efficiency of muscle contraction

Percentage of energy that can be converted to work instead of heat. (The percentage of input energy that can be converted into work)

* Under best conditions efficiency ≤ 25%, due to:

1) 50% of energy during ATP formation from foodstuffs are lost. 100-50 = 50%

2) Only 40-45% of the residual 50% can be converted to work

40% of the 50% → ≤ 25%

Velocity of contraction الانقباض [crossed out] سرعة المقصودة السرعة مثلا

- Maximum efficiency can be realized when the muscle contracts at a moderate velocity.

⟹ If the muscle contracts slowly or without movement "isometric" → small amounts of maintenance heat are released during contraction → little or no work is performed

الحرارة بتلزمنا عشان ال enzymatic reactions and to overcome viscosity

Distance = 0

W = L × D

⟹ If the muscle contracts rapidly → to much energy used to overcome viscous friction within the muscle itself → reduces efficiency.

→ Maximum efficiency at velocity ≈ 30% of maximum

Isometric & Isotonic Contractions

	Isometric	Isotonic
length of muscle	Constant	shortens
Tension	increases within limits → then decreases	Constant

"بتزيد ال tension مع زيادة ال load لحد ما يعني ال sarcomere ال C.C متكونه لحدها بصير تقل.

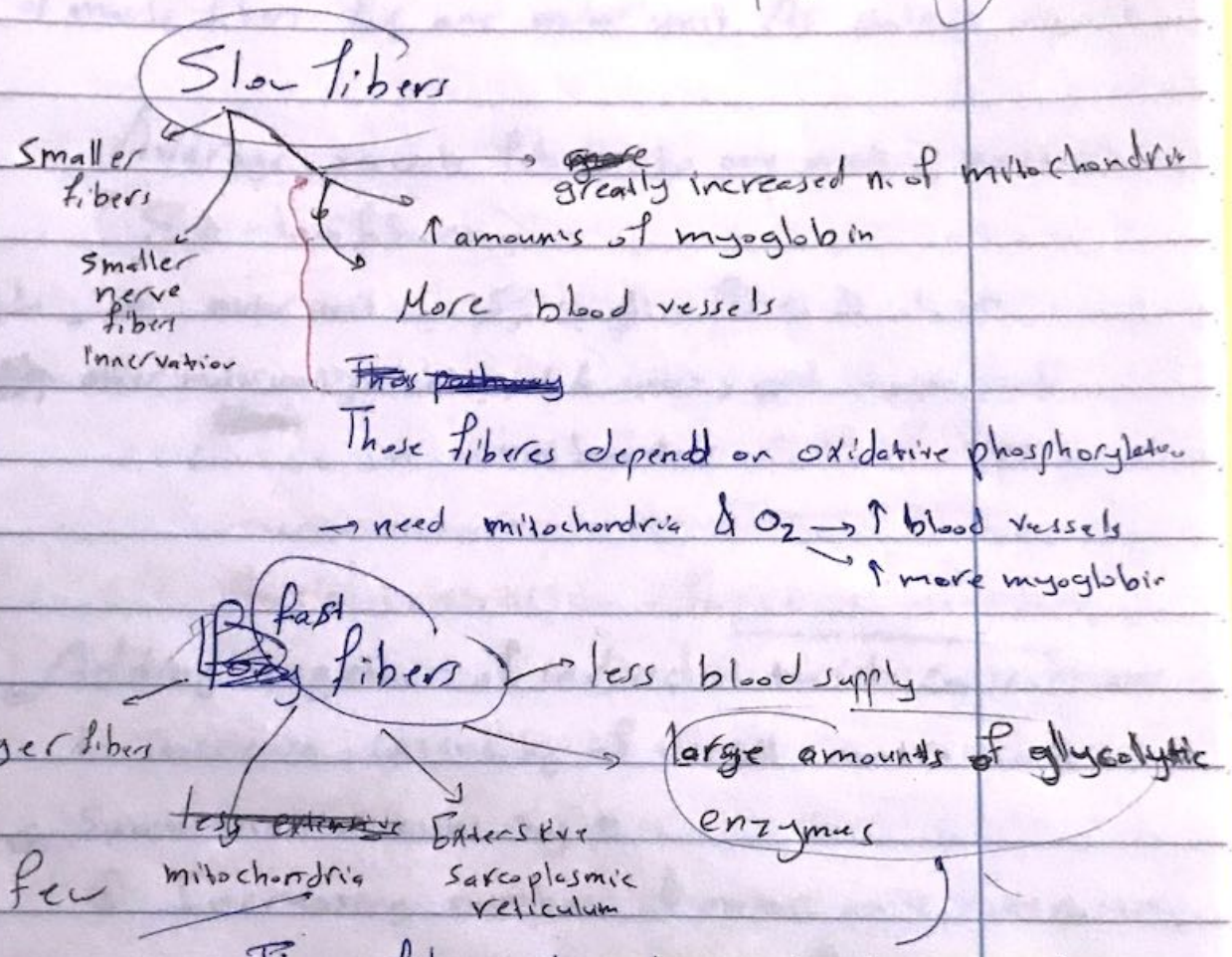
[crossed out] myosin

Isometric system records strictly changes in force of muscle contraction itself.

↳ • Isometric ~~contraction~~ system is used when comparing the functional characteristics of different ~~[crossed out]~~ muscle types.

Type 2 | Type 1
white | Red
long | short
Fast | slow fibers

- Each muscle is composed of fast & slow fibers.



Motor unit: mutiple muscle fibers innervated by single nerve fiber,

∈ Number of fibers in one unite depends one the type of muscle.

∈ Small muscle fibers that require exact control have one motorneuron for fewer fibers

e.g. In laryngeal muscles 2 or 3 fibers for one motorneuron "motor unit"

hundreds

- Large fibers, that need less control have hundreds of muscle fibers for one motor unit. As soleus muscle.

Avarage muscle fibers to one motor unit is (80-100 fibers.)

صدول الـ fibers اللي بشتركوا ب motor unit مش شرط

يكونوا معزولين لحالهم وملقيين لا بيختلطوا مع other motor units (overlap)

in microbundels 3-15 fiber.

Muscle contraction - Force summation

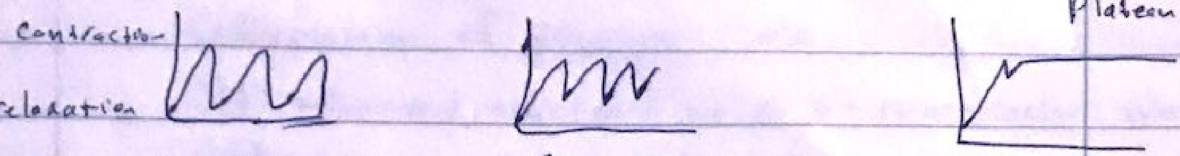
- Adding together of individual twich contractions to increase intensity of overall contraction.
- Summation occurs by:
  1. Increasing number of motor units contracting simultaneously, called multiple fiber summation.
  2. Increasing frequency of contraction, called frequency summation, can lead to tetanization "تضل العضلة contracted ← بتصير plateau).

1) Multiple fiber summation:

- Weak signal → contract weak or smaller motor units.
- Larger motor units need stronger signal, with larger motor units have as much as 50 times the contractile ability of smallest units. Size principle
  - It allows gradation of muscle force.

← الـ small motor units بتنشطوا أسرع ب signal ضعيفة من تنشيط الـ Large units

2) Frequency summation



Twitch	Clonus	Tetany
Complete contractions and relaxations	incomplete relaxations	No relaxation

- Maximum strength of contraction, any addition of increase in contraction will have no effect. Because Ca^{++} ions are maintained in enough the muscle sarcoplasm, even bet. action potentials.
- Maximum strength of contraction of muscle operating at a normal muscle lengh (bet. 3-4 kg/cm²) ال avarage of maximum contraction.

العضلة لما تبدأ شغل بعدما كانت مرتاحة رح تعطي أولها نص قدرتها في الانقباض مع الوقت باقي الـ fibers بتشترك (10-50 fibers) بيصيرلها twitch

→ ↑ muscle strength of contraction → وصولاً للـ plateau "tetany"

- This is called Staircase effect or treppe phenomenon.
- It's belived to be caused by ↑ Ca^{++} in sarcoplasm, beacause of → ↑ Ca release from sarcoplasmic reticulum, and failure of sarcoplasm to recapture Ca^{++}.
- Some degree of tautness remains in muscle even at rest → muscle tone, results from low rate of nerve impulses coming from the spinal cord.

Prolonged muscle contraction → fatigue

Fatigue may caused by:

1) Depletion of glycogen stores

2) Diminished transmission at neuromascular junction.

- Also interruption of blood flow through a contracting muscle leads to almost complete fatigue within 1-2 minutes ~ loss of nutrients, especially O_2.

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① Only few strong contractions each day are required to cause significant hypertrophy within 6-10 weeks

② During muscle hypertrophy, the rate of contractile protins synthesis increases too much. → leading to greater number of actin & myosin in myofibrils as much as 50%.

Along with increasing size of myofibrils the enzyme system that provides energy also increases → especially enzymes for glycolysis.

③ When muscle remain unused for weeks → atrophy, due to degredation of contractile proteins

Protein degredation pathway in muscle undergoing atrophy is called ATP-dependent ubiquitin-proteasome Pathway.

Rigor mortis

- Detachment of myosin cross-bridges from actin needs energy.
- After death → no energy → no detachment → muscles contract and become rigid.
- ~~After~~ This rigidity lasts 1-4 hours.
- After 15-25 hours Rigor mortis disappears due to autolysis of proteins by proteolytic enzymes from lysosomes.
- All these events occur more rapidly at higher temperatures.