Molecular mechanisms of biological motion

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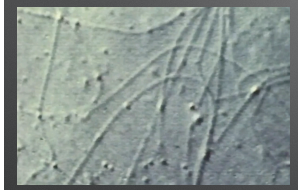
1

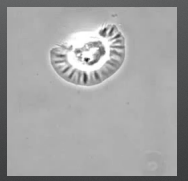
Various levels of biological motion

Molecular motion



Axoplasm

Cellular motion



crawling keratinocyte

Body motion

2

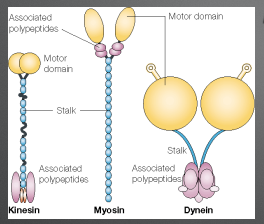
Motor proteins

Mechanoenzymes capable of converting chemical energy into mechanical work.

1. Specifically attach to a cytoskeletal filament or other biopolymer (DNA).
2. They generate force when moving along the filament.
3. They utilize energy from nucleotide cleavage for force generation.

3

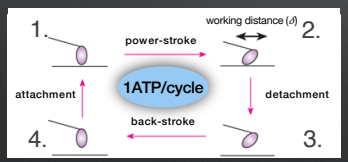
Common characteristics of motor proteins



I. Structural homology

The globular head at the N-terminus is the ***motor domain*** (ATPase) and provides a specific binding-site for the respective cytoskeletal filament.

The C-terminus binds to the surface that is being moved

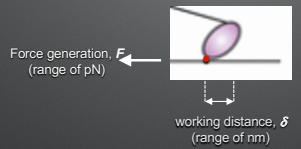


II. Cyclic operation

1. Attachment
2. Power-stroke (pull)
3. Detachment (dissociation)
4. Back-stroke (relaxation)

4

Force generation of motor proteins



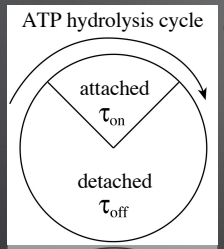
Work done by a single motor protein, ***W***

$$W = F \cdot \delta$$

range of 10^{-20} J *(zeptojoule* = 10^{-21}J*)*

5

Duty cycle of motor proteins



Duty ratio (r):

$$r = \frac{\tau_{on}}{\tau_{on} + \tau_{off}} = \frac{\tau_{on}}{\tau_{total}}$$

Processive motor protein: r~1
F.e. kinesin, DNA-, RNA-polymerase.
They remain attached in most of the cycle time. They function individually.

Non-processive motor protein: r~0
F.e. conventional myosin (skeletal muscle myosin II.) They remain detached in most of the cycle time. They function in ensembles.

$$v_{stroke} = \frac{\delta}{\tau_{on}} \qquad \tau_{on} = \frac{\delta}{v_{stroke}} \qquad \tau_{total} = \frac{1}{k_{ATPase}} \qquad r = \frac{\delta k_{ATPase}}{v_{stroke}}$$

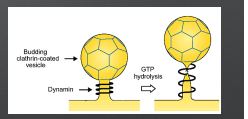
δ = working distance
v_{stroke} = stroke velocity
k_{ATPase} = ATPase rate

6

Types of motor proteins

1. Actin based
- ***Myosins:*** They move towards the plus end along the actin filament.
(lamellipodium formation, muscle contraction)

2. Microtubule based
- ***Dyneins:*** Ciliary (flagellar) and cytoplasmic dyneins. They move towards the minus end along the microtubule. (*axonal retrograde transport)*
- ***Kinesins:*** They move towards the plus end along the microtubule.
(*axonal anterograde transport)*
- ***Dynamins:*** Microtubule activated GTPase function. *(pinchase)*



3. DNA based mechanoenzymes
- They exert force and move along the DNS double helix.
(*DNA- and RNA-polymerases, viral capsid portal motor)*

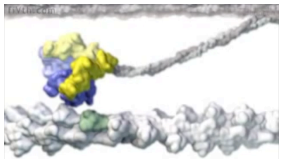
4. Rotary motors
- They are transmembrane mechanoenzymes that utilize the proton gradient across the membrane.
F1Fo-ATP synthase, bacterial flagellar motor

5. Mechanoenzyme complexes
- *Ribosome*

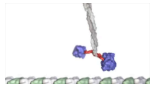
7

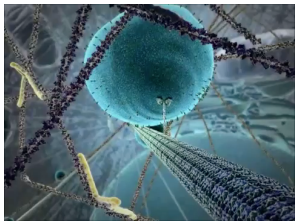
Citoskeleton based motors

Non-processive motor
Skeletal myosin II.
Moves along the actin filament



Processive motor
Kinesin
Moves along the microtubule

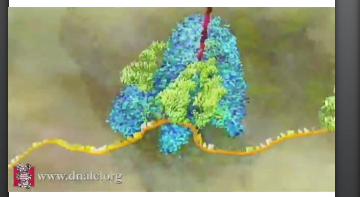




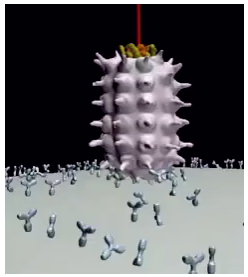
8

Nucleic acid based motors

Ribosome
mechanoenzyme complex



Virus portal motor
DNS „packaging"

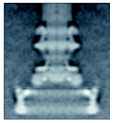


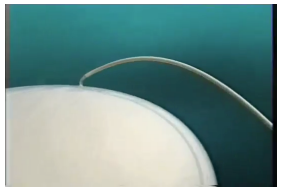
9

Rotating motors

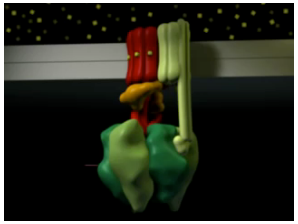
driving force: proton gradient

Flagellar motor
bacterial movement



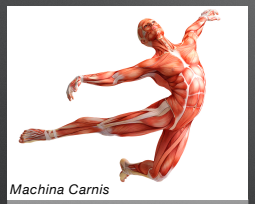


F_1F_o ATP synthase



10

Muscle biophysics

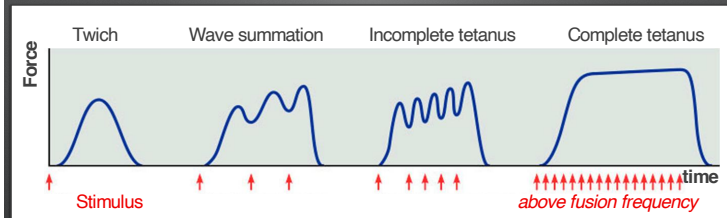


Cell and tissue specialized for movement.

It can only pull, not push!

11

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.

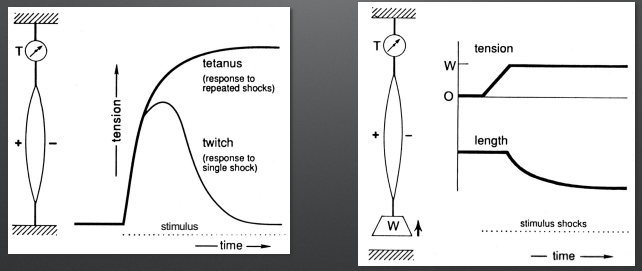
A sustained contraction that lacks even partial relaxation is known as **tetanus**.

12

Basic phenomena of muscle function II.

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

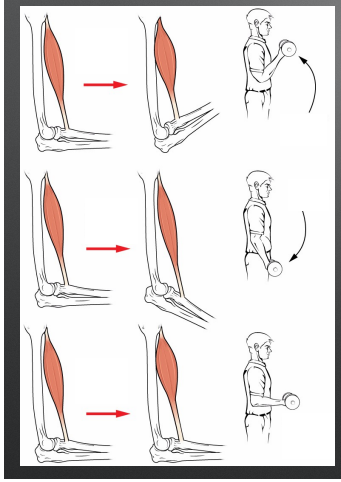
2. Isotonic contraction
Tension remains unchanged while the muscle's length changes.



Auxotonic contraction (simultaneous shortening and force generation)

13

Basic phenomena of muscle function III.



1.Concentric muscle action
The muscle shortens during force generation

2. Excentric muscle action
The muscle elongates during force generation

3. Isometric muscle action
The muscle length remains constant during force generation

14

Basic phenomena of muscle function IV.

1. Work and Power

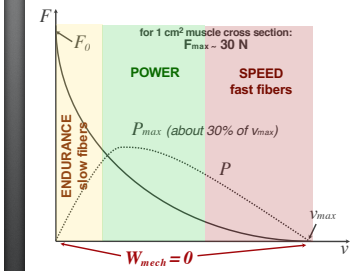
$$W = F \cdot s$$

$$P = \frac{W}{t} = \frac{F \cdot s}{t} = F \cdot v$$

If the shortening velocity is zero, the force is maximal: maximal isometric force (F_0)

If v = maximum, than $F = 0$

2. Force - velocity diagram



Hill equation:

$$(F + a)(v + b) = (F_0 + a)b$$

F: force, v: shortening velocity
a and b: constants,
F0: maximal isometric force

$$v_{max} = \frac{bF_0}{a}$$

15

Energetics of muscle contraction

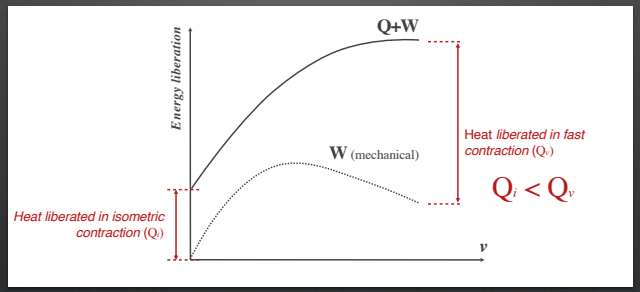
ATP hydrolysis, heat liberation

Source of energy:

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

Fenn effect: The liberation of heat increases when the muscle is doing work during shortening. The amount of heat liberated increases with increasing speed of contraction.

The majority of chemical energy used by the muscle is dissipated as heat

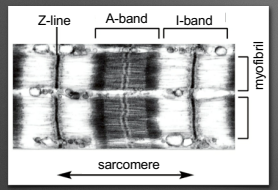


16

The mechanism of muscle shortening

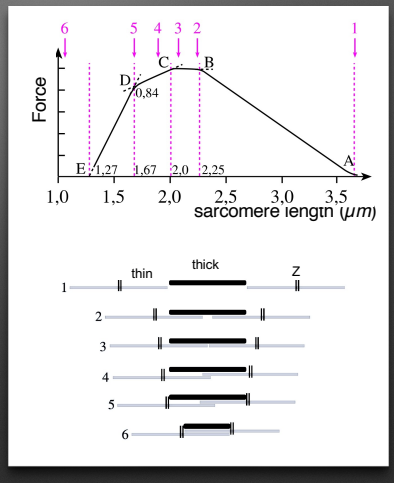
Phenomenological mechanism: sliding filament model

Sarcomere



Relaxed

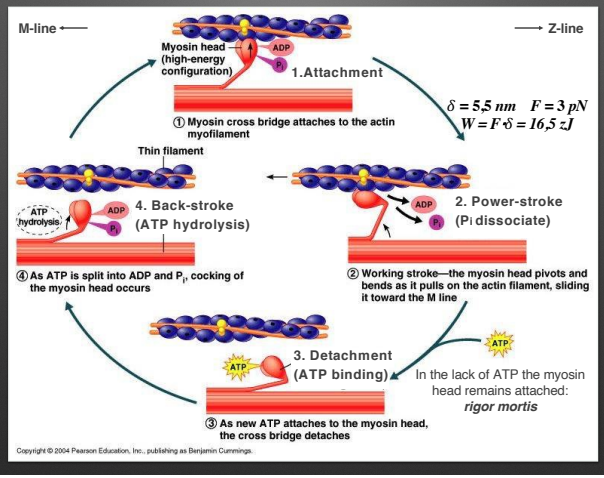
Contracted



17

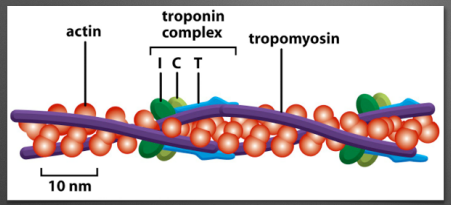
The myosin „cross-bridge“ cycle

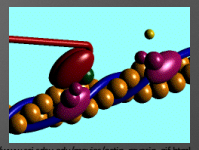
Molecular bases of muscle contraction



18

Regulation of muscle contraction

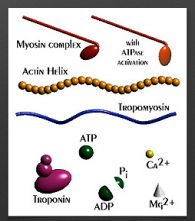




http://www.sci.sdsu.edu/movies/actin_myosin_gif.html

Tropomyozin: *Blocks the myosin binding sites on actin filament.*

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



19