

Molecular mechanisms of biological motion

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Various levels of biological motion

Molecular motion

Bacterial Flagellar Motor

Cellular motion

「ERATO 株式会社プロトニックス/マシンプロジェクト終了報告ビデオ」より

Bacterial flagella



ceratocyte crawling on surface

Body motion



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Motor proteins

Mechanoenzymes capable of converting chemical energy into mechanical work.

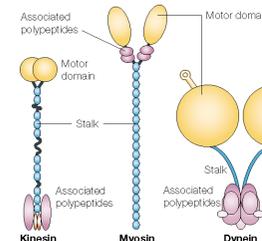
1. Specifically attach to a cytoskeletal filament or other biopolymer (DNA).
2. They generate force when moving along the filament.
3. They utilize energy from ATP for force generation.

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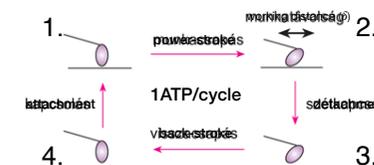
Common characteristics of motor proteins

I. Structural homology

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



The C-terminus contains functional binding sites.



II. Cyclic operation

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

Work done by a single motor protein can be calculated from: $W = F \cdot \delta$

pulling force (F): in the range of pN

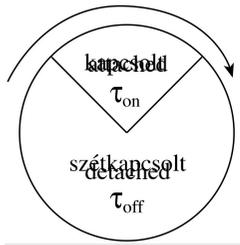
working distance (δ): in the range of nm

W : in the range of μJ ($zeptojoule = 10^{-21} J$)

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Duty cycle of motor proteins

ATP hydrolysis cycle



Duty ratio (r):

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

Processive motor protein: $r \sim 1$

F.e. kinesin, DNA-, RNA-polymerase.

They remain attached in most of the cycle time. They function individually.

Non-processive motor protein: $r \sim 0$

F.e. conventional myosin (skeletal muscle myosin II.) They remain detached in most of the cycle time. They function in ensembles.



$$v_{stroke} = \frac{\delta}{\tau_{on}}$$

$$\tau_{on} = \frac{\delta}{v_{stroke}}$$

$$r = \frac{\delta k_{ATPase}}{v_{stroke}}$$

$$\tau_{total} = \frac{1}{k_{ATPase}}$$

δ = working distance

v_{stroke} = stroke velocity

k_{ATPase} = ATPase rate

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Types of motor proteins

1. Actin based

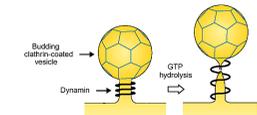
Myosins: They move towards the plus end along the actin filament. (lamellipodium formation, muscle contraction)

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

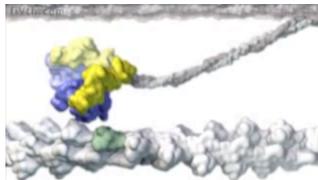
Ribosome

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Cytoskeleton based motors

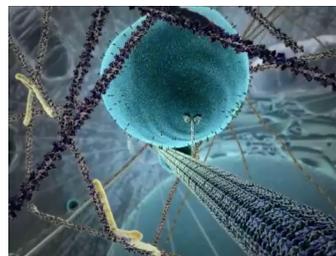
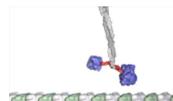
Non-processive motor

Skeletal muscle myosin II.
Moves along the actin filament



Processive motor

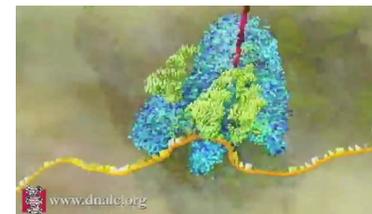
Kinesin
Moves along the microtubule.



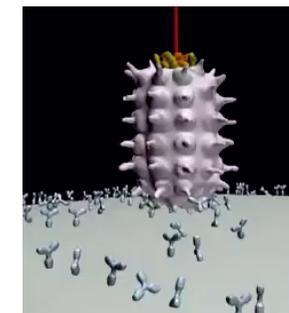
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Nucleic acid based motors

Ribosome
mechanoenzyme complex



Viral portal motor
DNS „packaging“

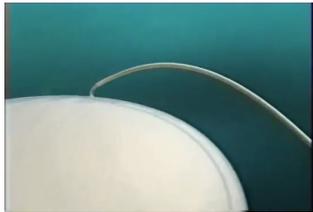
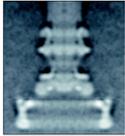


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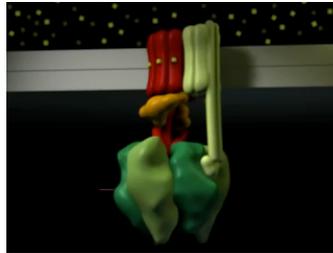
Rotatory motors

driving force: proton gradient

Flagellar motor
bacterial motion



F_1F_0 ATP synthase
reversible functioning



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Muscle biophysics

Cell and tissue specialized for movement.

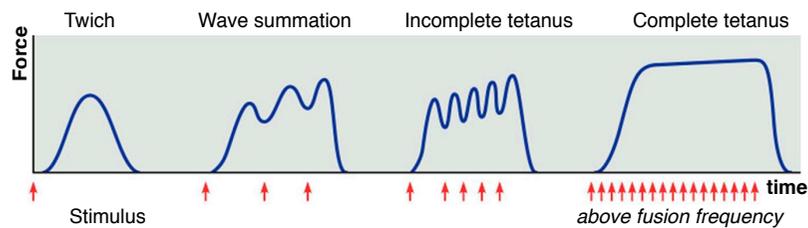
It can only pull, not push!



Machina Carnis

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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.

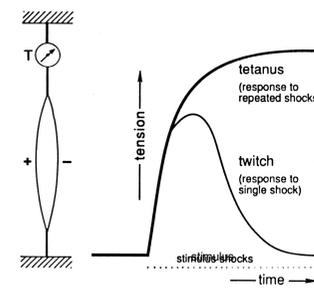
A sustained contraction that lacks even partial relaxation is known as **tetanus**.

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Basic phenomena of muscle function II.

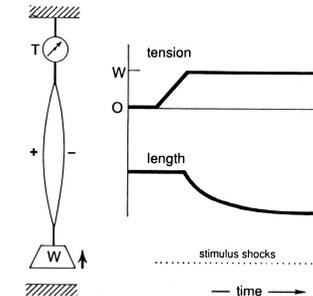
1. Isometric contraction

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)

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Basic phenomena of muscle function III.

1. Work and Power

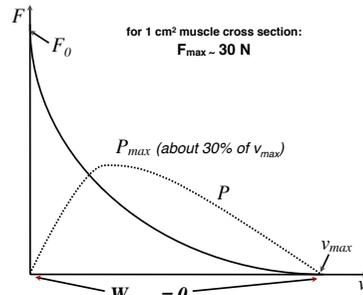
$$W = F \cdot s$$

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

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

If $v = \text{maximum}$, then $F = 0$

2. Force - velocity diagram



Hill equation:

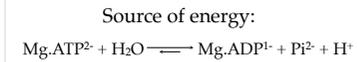
$$(F + a)(v + b) = (F_0 + a)b$$

F : force, v : shortening velocity
 a and b : constants
 F_0 : maximal isometric force $v_{\text{max}} = \frac{bF_0}{a}$

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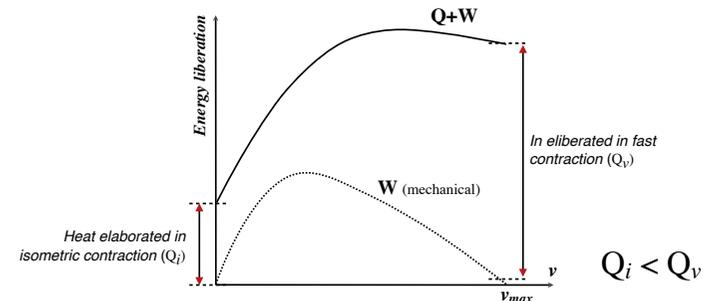
Energetics of muscle contraction

ATP hydrolysis, heat liberation



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.

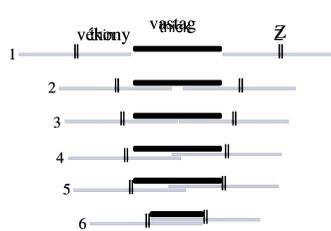
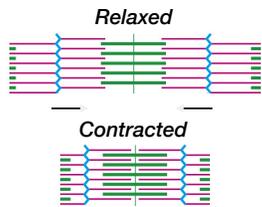
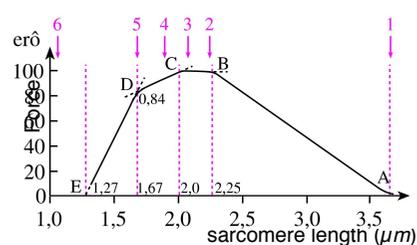
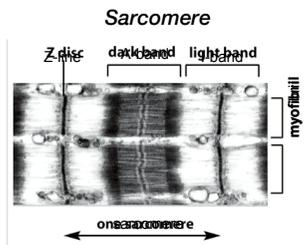
The majority of chemical energy used by the muscle is dissipated as heat



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The mechanism of muscle shortening

Phenomenological mechanism: sliding filament model

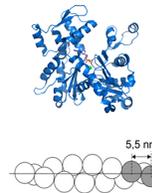


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Parts of contractile apparatus

Globular actin (G-actin)

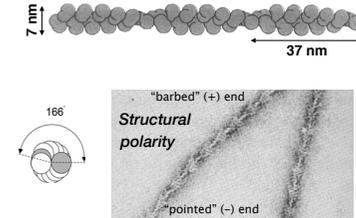
Monomer unit building up the actin filament



Bruno Straub
the discoverer of actin (1941)

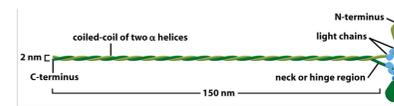
Actin filament (F-actin)

Cytoskeletal semi flexible biopolymer



Myosin II

Non-processive actin based motor protein



Thick filament

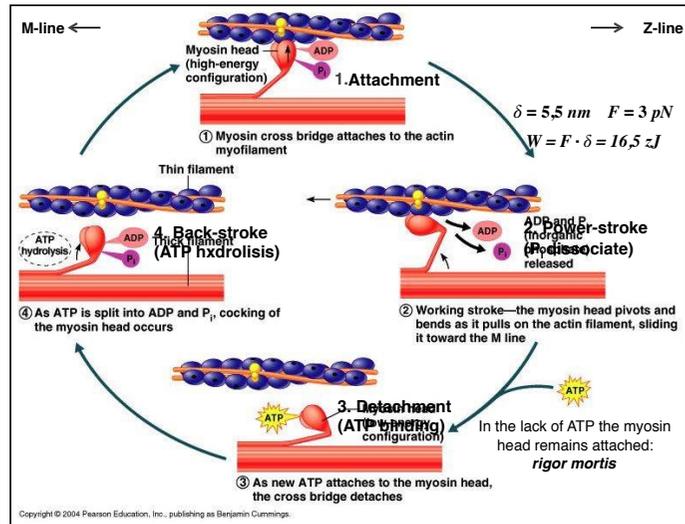
myosin heads (motor domains)



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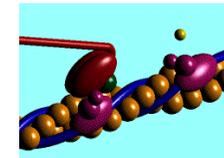
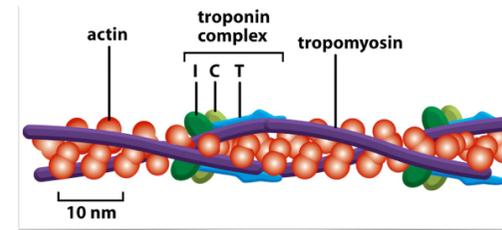
The myosin „cross-bridge“ cycle

Molecular bases of muscle contraction



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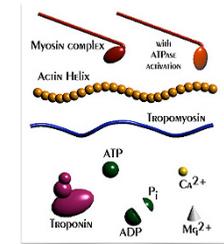
Contraction regulation in striated muscle



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

Tropomyosin: blocks myosin-binding site on the actin filament

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.



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