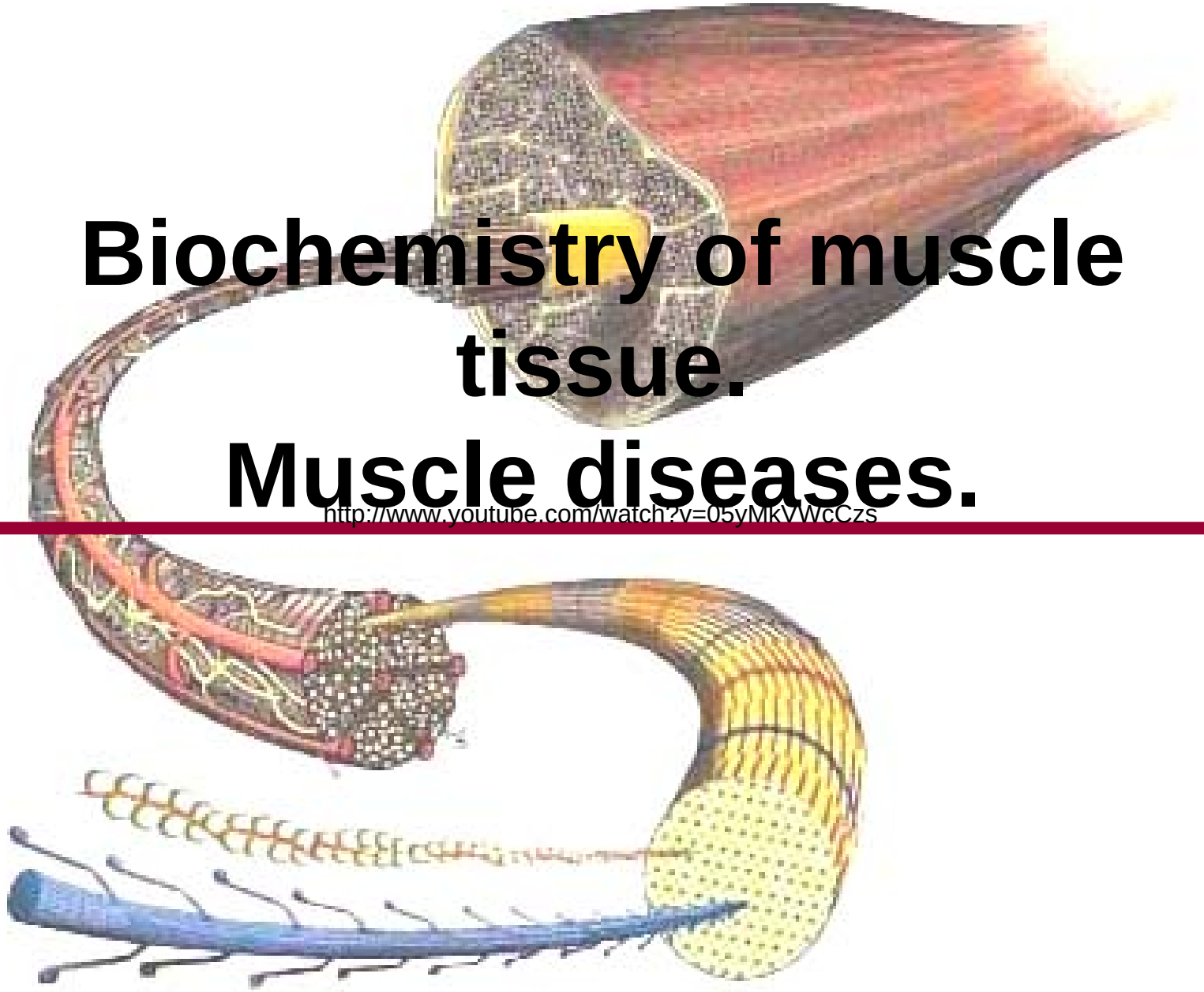
Biochemistry of muscle tissue.
Muscle diseases.

http://www.youtube.com/watch?v=05yMkVWcCzs



Muscle types

Smooth muscle

- slow
- no drawning
- internal organs
- involuntary
- no exhaustible
- extracellular Ca^{2+}
- single cells

Myocardial muscle

- fast
- striated

Skeletal muscle

- skeletal muscle
- is worked by knowledge
- exhaustible
- intracellular Ca^{2+}
- syncytium

Metabolism of the skeletal muscle

1.Slow oxidative muscles – red muscles

- constantly engaged muscles with low-intensity work (anti-gravity muscles)
- to be tired slowly
- high content of mioglobin and mitochondria
- so much capillaries
- not contain glycogen
- cover their energy by oxidation of fatty acids and ketone bodies

2. Fast glycolytic muscles – white muscles

- muscles with short periods of intense effort
- to be tired soon
- few content of mioglobin and mitochondria
- advanced sarcotubulated membrane system
- cover their energy by glycogen degradation

3. Fast oxidative and glycolytic muscles

- rapid rate of contraction
- fatigue tolerances better than the white muscles becauses of the mixed metabolism

The thick filaments - myosin structure

Myosin structure:

- Heavy chain: 230 kD
  - ✓ 2 chain in the helical arrangement
  - ✓ forms the tail part wich is150 mm long and diameter is 2nm tail
- Light chain: 20 kD
  - ✓4 light chains form the globular head part (4x11 nm)
  - ✓ contains the ATP-degrading active site location

Features of the thick filaments:

- myosin polymers - myosin molecules are held together by electrostatic interactions
- through the "hinge" region the myosin is capable of displacement in the direction of the tail portion
- the head parts form 6 lanes at the 2 end of the thick filament
- the myosin heads are repeated within 58 nm in a band

The thin filament – actin

- one of the most widespread protein
- G-aktin (globular): 42 kD, monomer
- F-aktin (fibrillar): polimer
- Types:
  - ✓ α-actin: contractile system of the myocardial-, skeletal- and smooth muscles
  - ✓ β-, γ-actin: system can be found in every cell's cytoskelet

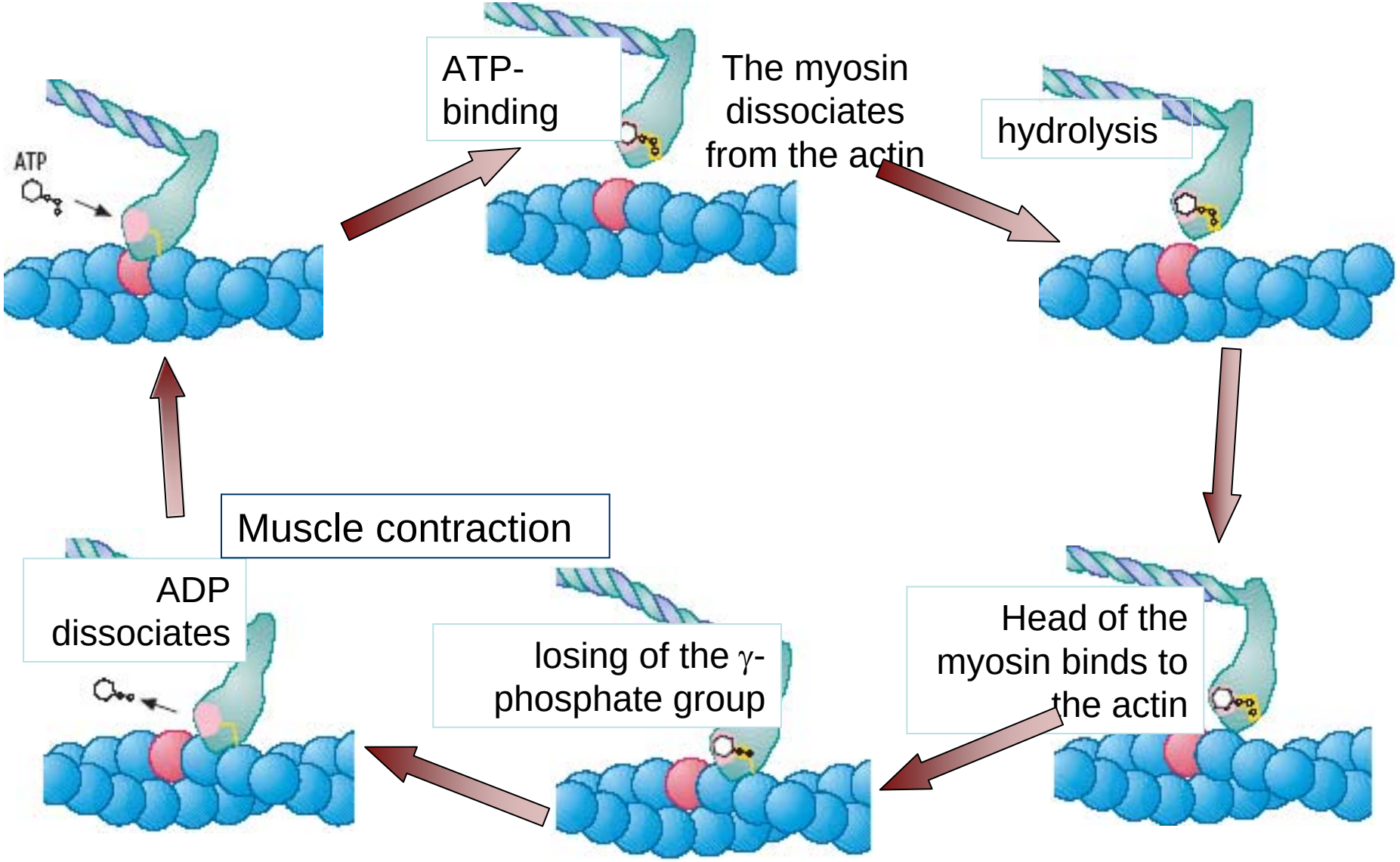
Tropomyosin (70 kD):

- cover the region with the cross bridge on actin's surface

Troponin complex:

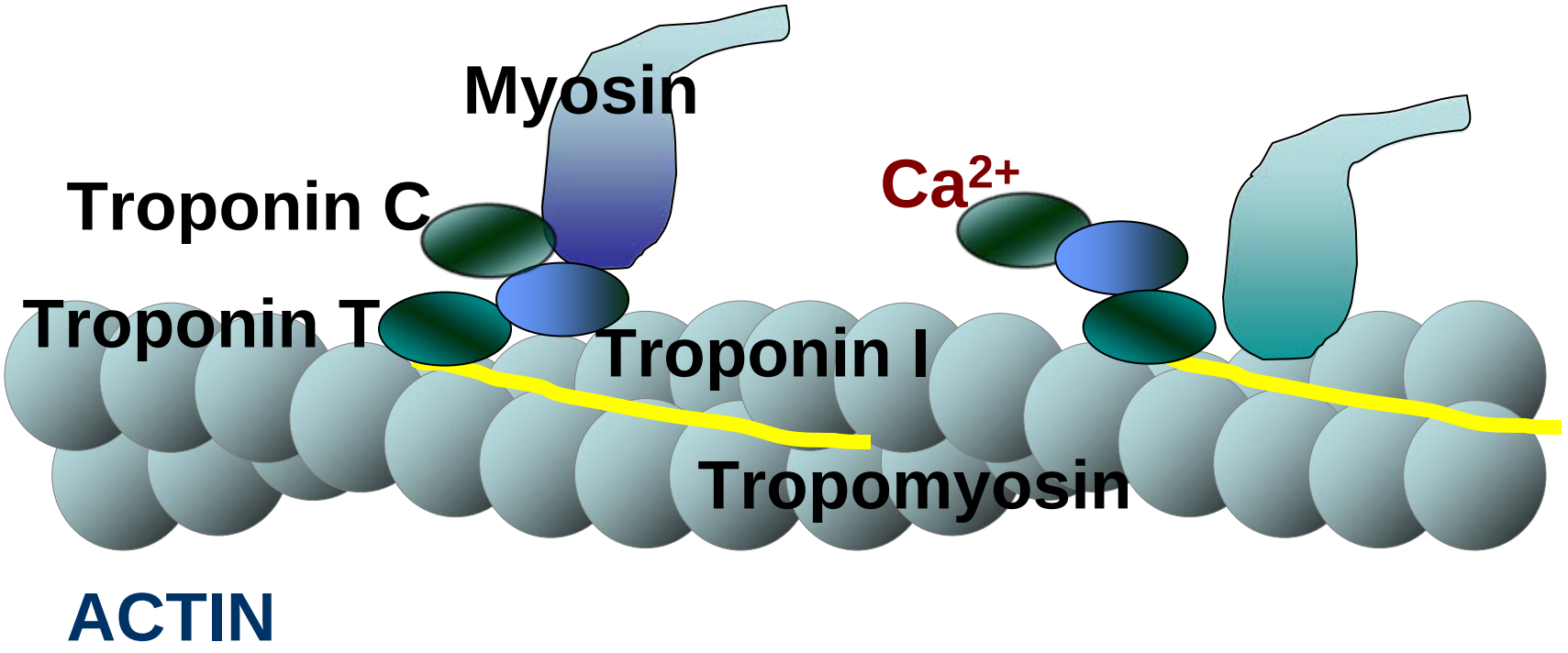
- troponin T (37 kD): connects to the tropomyosin
- troponin C (18 kD): contains the Ca-binding domain
- troponin I (24 kD): inhibitory subunit, interacts with the cross bindings

The mechanism of the muscle contraction

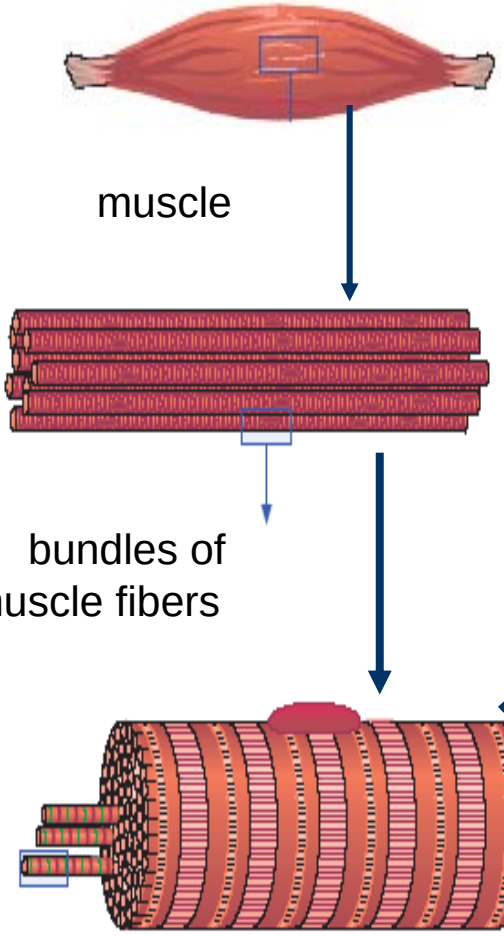


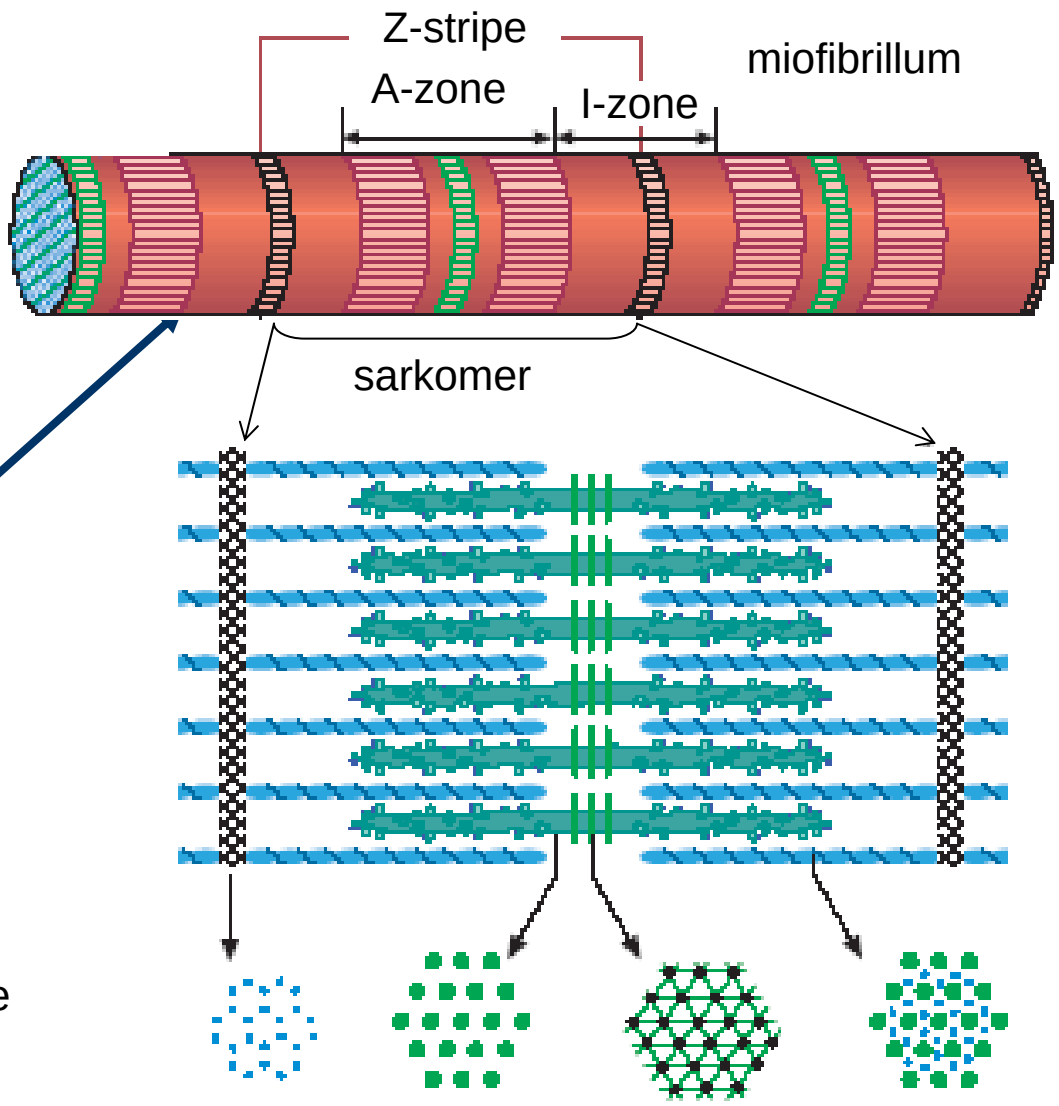
Regulation of the skeletal muscle's contraction-relexation

- ATP-as activity of the myosin is Mg-dependent
- if $[Ca^{2+}] < 10^{-6}$ M → TnC not binds Ca^{2+} → TnI overlies on the myosin-binding region of actin → **relaxation**
- if $[Ca^{2+}] > 10^{-6}$ M → TnC binds Ca^{2+} → TnI is putted over, can be formed the cross-bridge → **contraction**



Structure of the skeletal muscle





muscle fiber: unit of the skeletal muscle

Connection between the length and stretch of the skeletal muscle

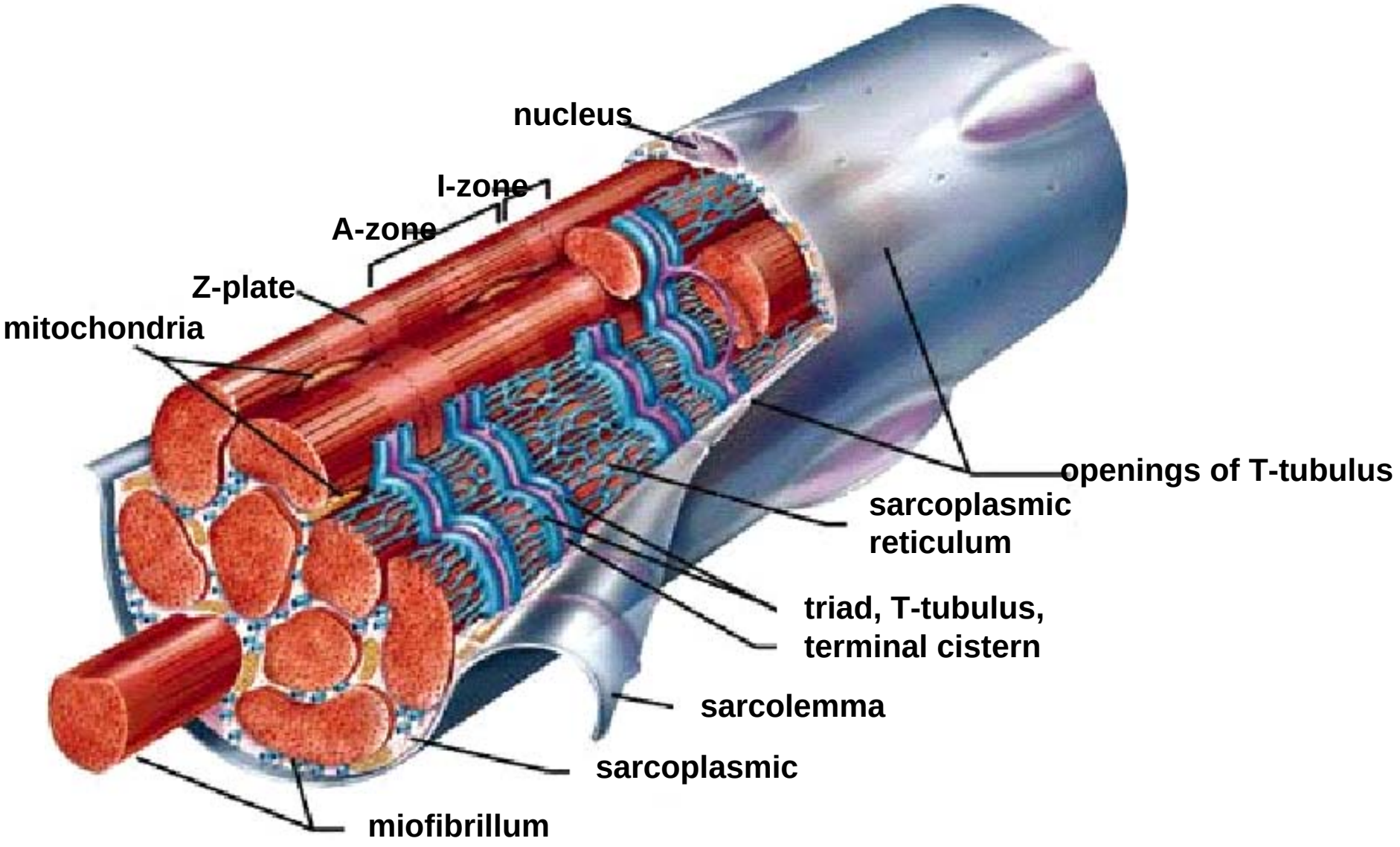
Stretch and effort capacity of skeletal muscle :

- depends on the sarcomer's length
- can be reach the maximum in case of 2,0 – 2,5 μm sarkomerlength
- if the sarkomerlength is > 3,5 μm v < 1,2 μm, muscle is not capable to do active tension

The effort of the muscle and the capable to do active tension is proportional with the cross-bridges

- the maximum shortening capacity of the muscle is the third part of resting length
- the maximum effort is proportional with functional cross-section

The structure of the sarcotubulated system



The excitation-contraction coupling

The regulator of the muscle contraction and relaxation is the change in concentration of the cytoplasmic free Ca^{2+}.

In skeletal muscle:

- Dihidropiridin-receptor (DHPR)= L-type Ca^{2+}-chanel
The change in conformation is enough the opening of rianodinreceptors (Ryr).

In cardial muscle:

- There is no directly mechanical relationship between DHPR and Ryr
- Ca^{2+}-indicated Ca^{2+}-release
- The cells of myocardial muscles can not be activated in the absence of extracellular Ca^{2+}

In smooth muscle:

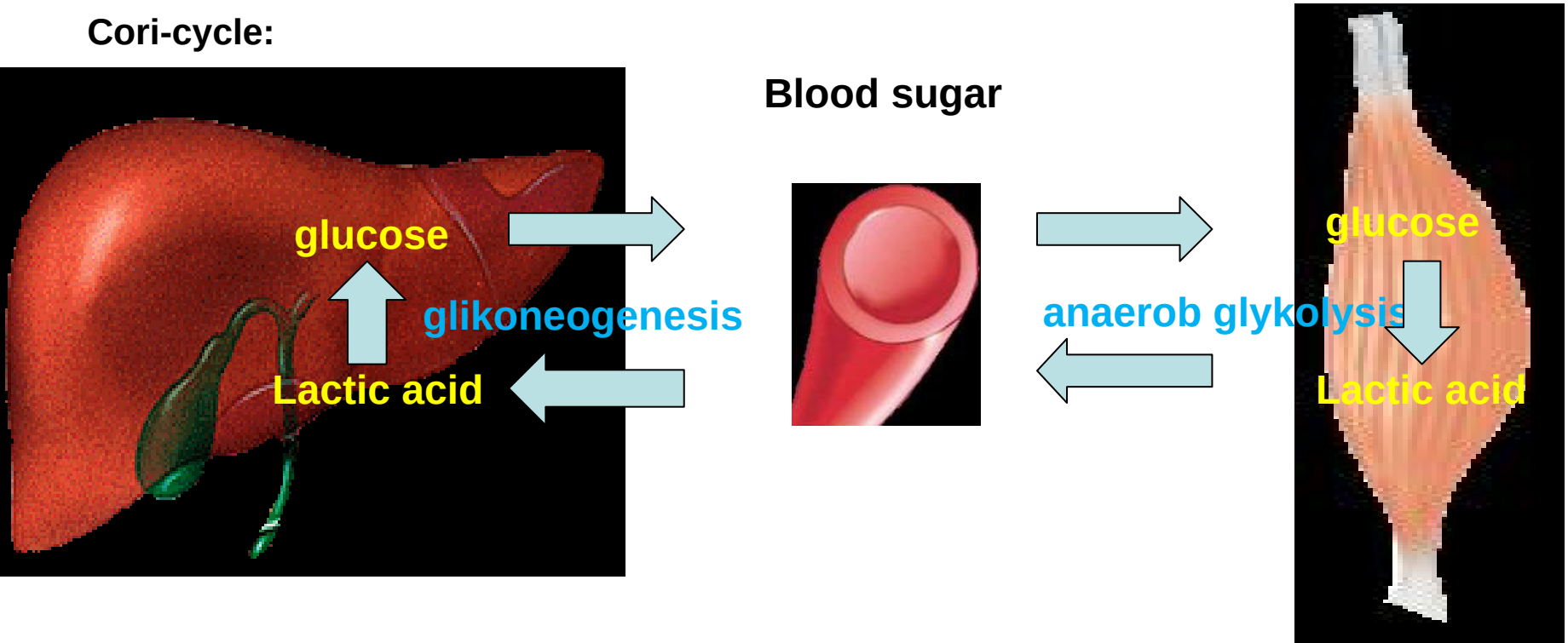
- slowly process
- Accessing of intracellular Ca^{2+} 's storage can be occured by inositol-triphosphate release and intracellular diffusion

The mechanism of Ca^{2+} reuptake

The relexation can be occured by the increase of the ionisated Ca^{2+}-concentration in the sarcoplasmatic place.

- SERCA (SR Ca^{2+}-ATPas): with the application of 1 ATP, 2 Ca^{2+}could be pumped to the lumen of sarcoplasmtaic reticulum
- Ca^{2+}-binding proteins in the lumen of SR: calsequestrin, calreticulin
- in cardial muscle: the dephosphorilated phospholamban connect to the SERCA, and decrease it's activity. Due to the effect of β-adrenerg stimulation the phospholamban will be phosphorilated and get isolated from the SERCA , so it's effort will be increased

Cori-cycle:



Tired muscle, muscle strain

Tired muscle: the force and/or speed of the muscle contraction is decreased.

Levels:

- excitation-contraction connection
- contractile system
- metabolic energy support
- Ca^{2+}-reuptace

In the tired muscle can be observed:

- the depletion of glycogen stores
- locally H + -, lactic acid and phosphate concentration increased, acidosis
- K^{+}-efflux
- water flow due to hyper-osmotic induced degradation products

Muscle strain:

- rough morphological damages,distortion of membrane elements and filaments, disintegration
- primarily observed during eccentric muscle work

Ion chanel diseases

1. **Malignant hyperthermia**
   - cause: point mutation of ryanodin receptor
   - by using of inhaled anesthetics
   - the muscle will be full with Ca^{2}
   - symptoms: hypercontraction, acceleration of metabolic process, increasing of temperature
   - life-threatening!
2. **States with miotonia**
   - defect of Cl^{-} or Na^{+}-chanels (such as: prolonged paralysis with hiper-, hypokalaemia)
   - symptoms: prolonged muscle relaxation
3. **Muscular disgenezis**: lack of dihidropiridin-receptor

Cytoskeletal structure of the muscle I.

Z-stripe:

- basic structure: α-aktinin (100 kD)
- here become fixed the F-aktin and the connected nebulin
- titin:
  - ✓ the most highest molecular weight protein (2,5 MD)
  - ✓ it is located between Z-stripe and thin filaments
  - ✓ functions: restitution of the original position of the thin and thick filaments after the overstreching, limitation of the streching

Intermedier filaments:

- desmin: specific for myocardial and sceletal muscles
- vimentin: in smooth muscle
- role:
  - ✓ control of muscle morphogenesis
  - ✓ structural settlement of the sarcomers, filaments, fibrillums

Cytoskeletal structure of the muscle II.

Cytoskeletal structure of the membran:

- role:
  - ✓ regulater of the diffusion of integral membranproteins, receptors, chanels
  - ✓ connenction with the internal cytoskeleton and extracellular matrix components
- distrofin: creates a connenction between cytoskeletal actin system and membran-built glycoproteincomplex
- utrofin: placement of theT-tubulus SR juncion and myoneural juncion

Duchenne-disease:

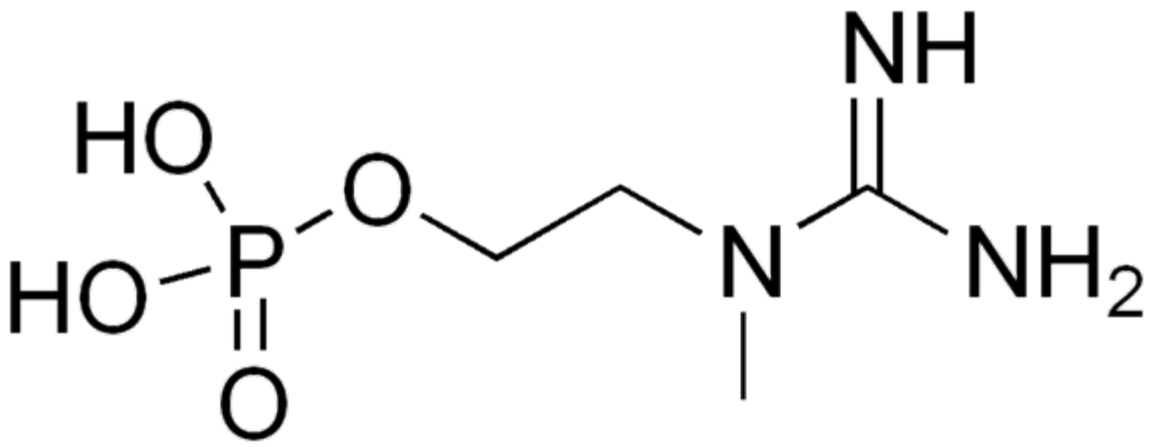
- X-linked inheritance
- Defect of the dystrophin gene
- repeated fiber necrosis
- Unable to walk at the age of 6-8
- early death due to respiratory muscle and heart muscle damage

Becker-muscle dystrophy

- milder form
- shorter, but even to some extent functional dystrophin synthesis

ATP synthesis in the muscle

- adenylate-kinase
- Fatty acid-oxidation
- creatin-phosphate
- glycogen breakdown



creatin-phosphate