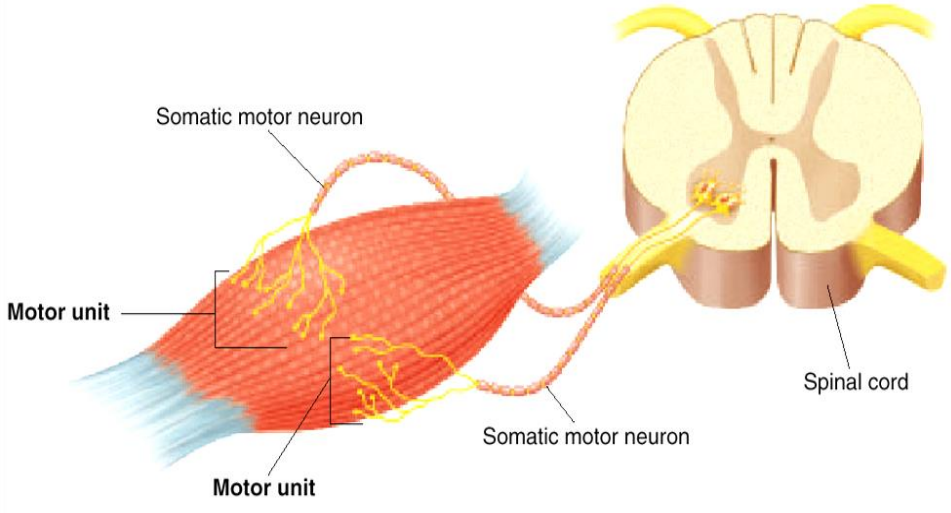
GOMEL STATE MEDICAL UNIVERSITY
Normal and Pathological Physiology Department

PHYSIOLOGY OF EXCITABLE TISSUES

PHYSIOLOGY OF MUSCLES



Lecturer:

Victor Melnik
Professor,
Doctor of Biological Sciences

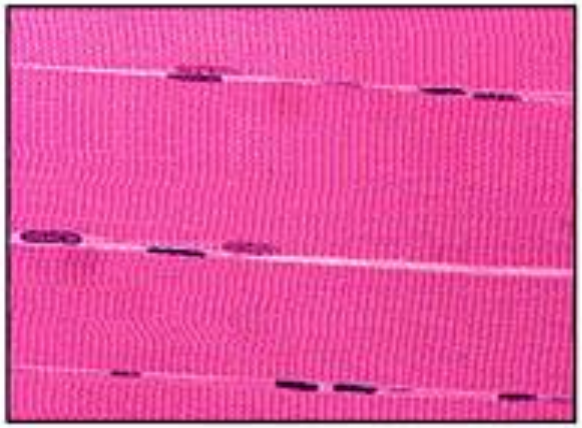
Lecture plan:

1. Forms and types of muscle contractions. Mode of muscle contractions.
2. Strength and work of muscle fiber.
3. Motor units. Composition (structure of muscles).
4. Structure of muscle fiber. Theory of muscle contractions (sliding of filaments).
5. Muscle fatigue. Hypertrophy and atrophy of muscles.
6. Smooth muscles.

1. Forms and types of muscle contractions

Muscle tissues in the human body are divided by structure and physiological properties into **3 types:**

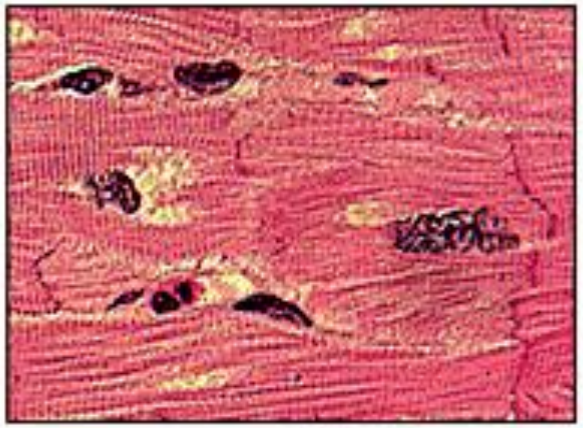
1. **Skeletal.**
2. **Smooth.**
3. **Cardiac.**



Skeletal Muscle
300 x

Nuclei

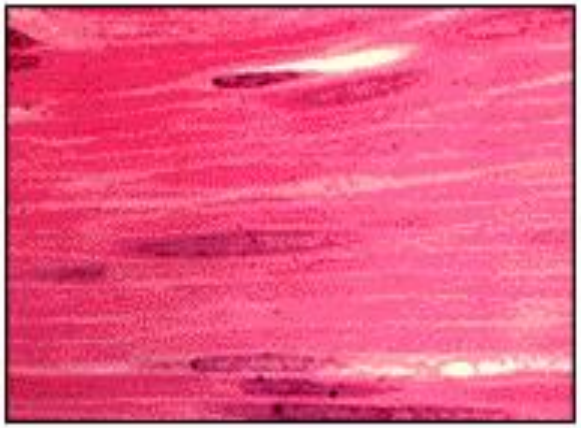
- Elongated cell
- Multiple peripheral nuclei
- Visible striations
- Voluntary



Cardiac Muscle
400 x

Nucleus

- Branching cell
- Single central nucleus
- Visible striations
- Involuntary



Smooth Muscle
1200 x

Nucleus

- Spindle-shaped cell
- Single central nucleus
- Lack visible striations
- Involuntary

All the types of **muscles** possess some **properties**:

1. Excitability.

2. Conduction.

3. Contractility, *— change of length or strain, — and ability to relax.*

In natural conditions the activity of muscles have the reflex character. The electric activity of muscles can be recorded by means of electromyography, which is widely used in sports medicine.

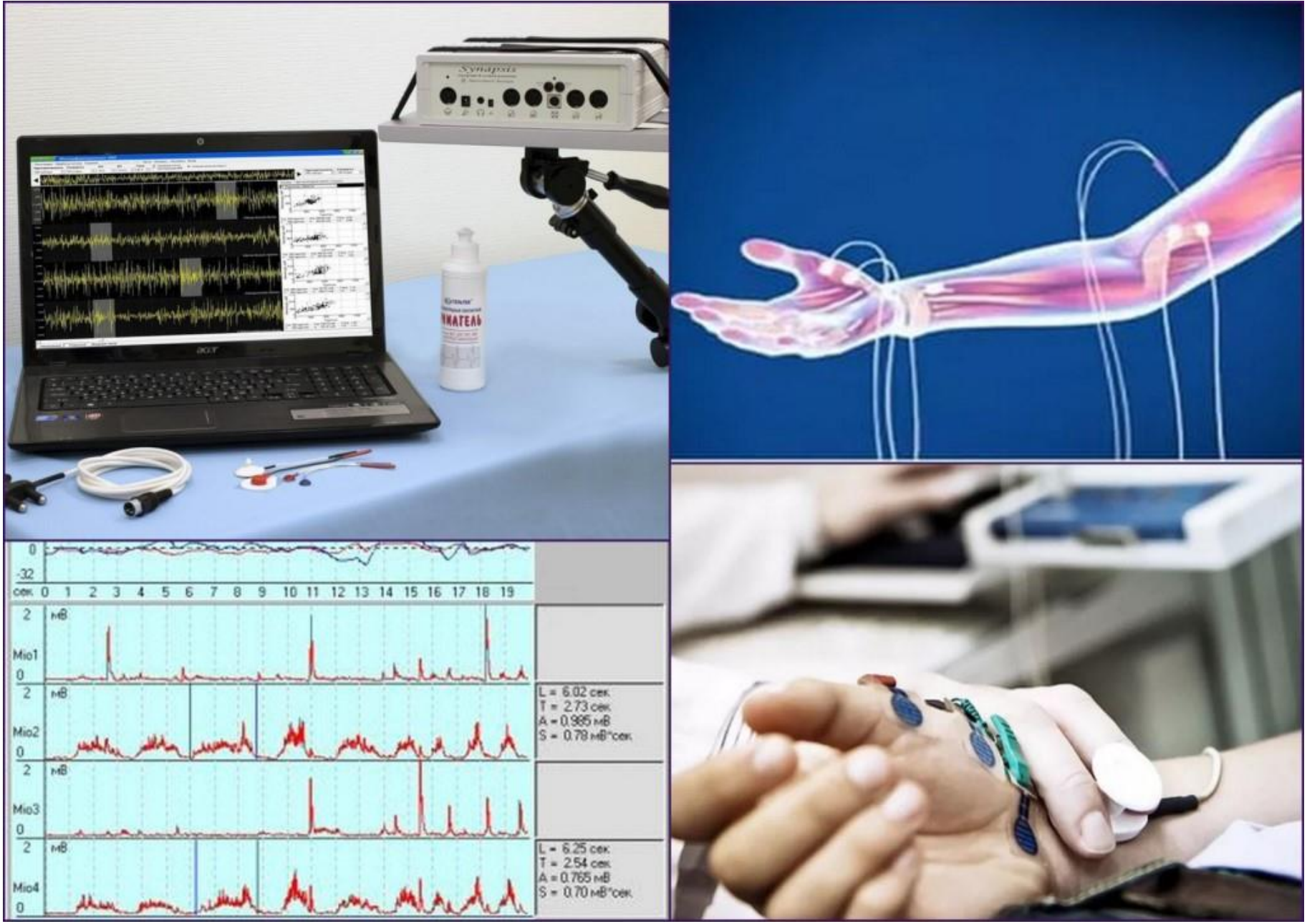


Figure — Electroneuromyography

There are several forms and types of muscle contractions.

1. *Dynamic form*. In this form of contractions the length of the muscle changes but its strain does not. This form includes two types:

a) *Isotonic*, or concentration type (the muscle is shortened but does not change its strain). E.g., walking.

b) *Eccentric type*. If a load on a muscle is higher than its strain, the muscle is stretched. E.g., lowering of a heavy object.

2. *Static form*. This form is observed during posture maintenance or overcoming of terrestrial attraction.

This form includes one type of muscle contractions — *isometric*, when the muscle changes its strain but does not change its length.

3. *Auxotonic or mixed*.

The division into forms and types of muscle contractions is conditional, since all contractions are mixed. However, one type predominates.

Mode of muscle contractions

The character or the mode of muscle contractions depends on the frequency of signals coming from motoneurons.

There are single and tetanic muscle contractions.

If a muscle is imposed by a ***single signal***, a single muscle contraction (Figure) appears and it has several **periods**:

1*. Latent period* — the time from the action of the stimulus till the beginning of a contraction.

2. *Shortening period* in isotonic contractions or *strain period* in isometric contractions.

3. *Relaxation period*.

Single muscle contractions are characterized by minor fatigability, yet the muscle is not capable to realize its capabilities.

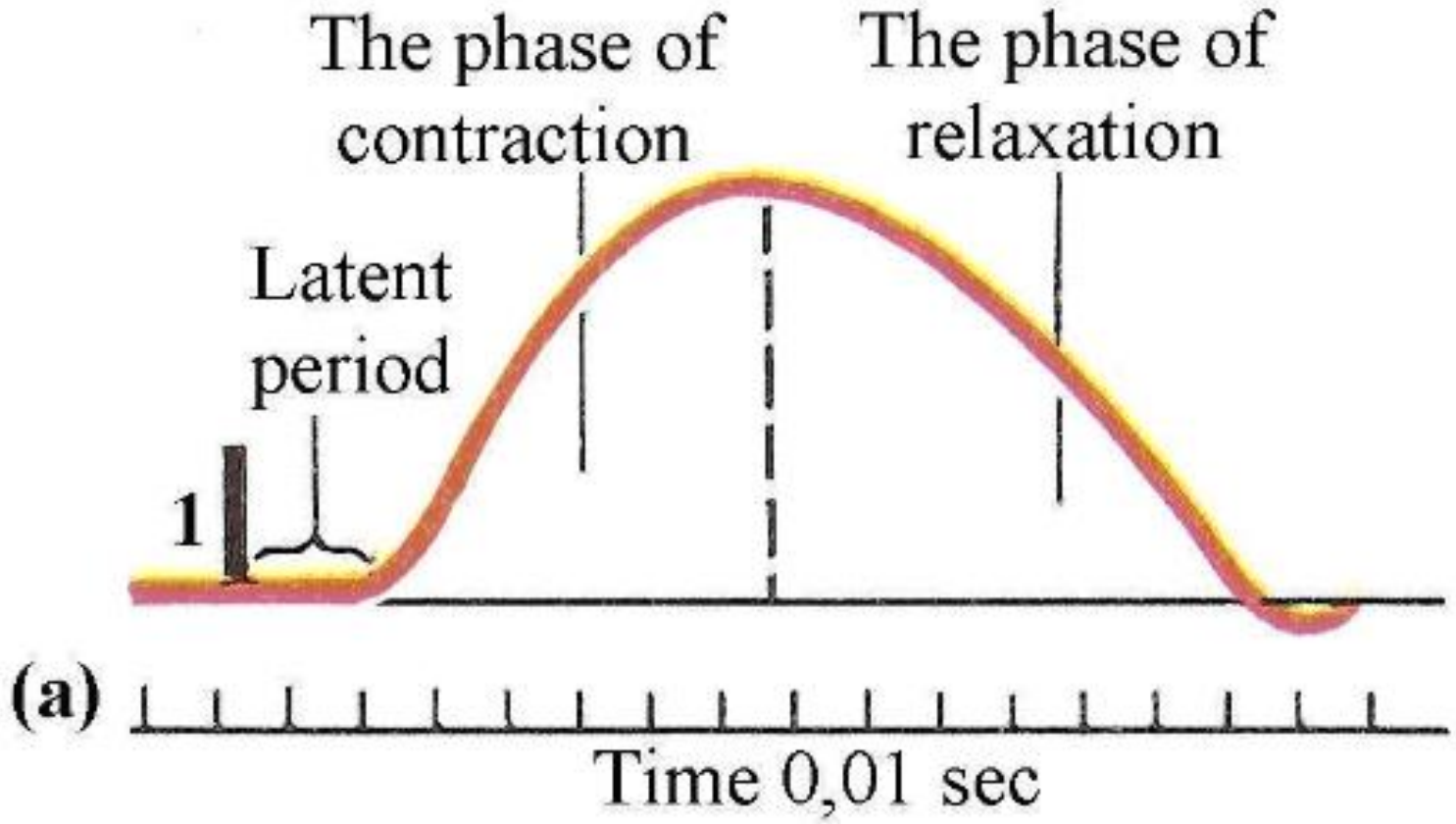


Figure — Single muscle contraction

Tetanic muscle contractions. If muscle fiber is influenced by two signals quickly following each other, contractions are overlapped to induce strong contractions.

The process when two signals following each other are overlapped is called ***summation.***

There are two types of summation (Figure):

1. If a second stimulus comes at the moment when the muscle starts to relax, the curve's peak is separated from the peak of the first contraction. This type of summation is called ***incomplete***.

2. If a second stimulus comes at the moment when the muscle contraction has not yet reached its peak, i.e. the muscle has not started to relax, both the contractions unite as a whole. This type is called ***complete***. Long and strong muscle contractions influenced by the rhythm of signals with consequent rapid relaxation are called ***tetanus***. In the human body tetanus can develop if signals come at a frequency of 50–70 sgn/sec.

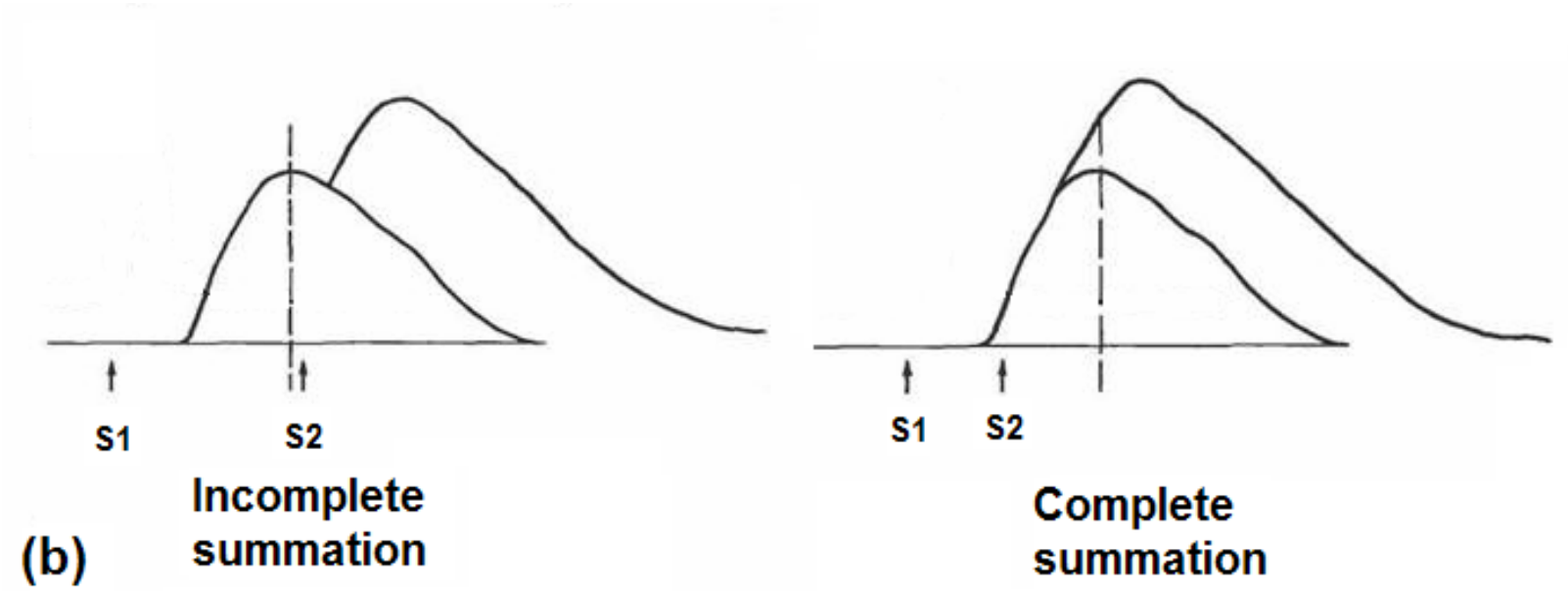


Figure — Summation

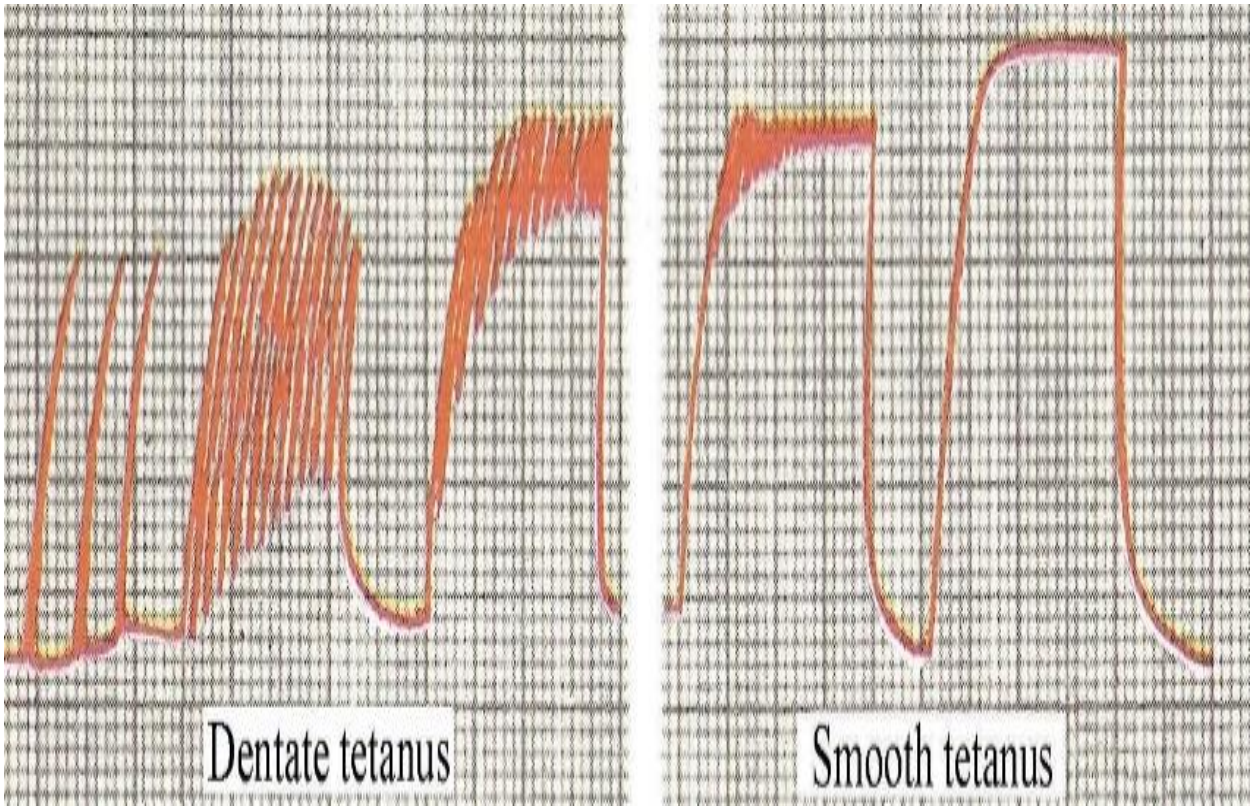


Figure — Tetanus

There are two types of tetanus (Figure):

1. *Dentate*, arising at a low frequency of signals (e.g. to 150 sgn/sec). It is formed due to the incomplete summation of muscle contractions)

2. *Smooth*, arising at a high rhythm of signals (e.g. 200 sgn/sec). It is formed due to the complete summation of muscle contractions.

There are optimal and pessimal rhythms of the work of muscles.

Thus, if the rate and strength of signals produce the maximal contracting effect, this is the ***optimal rhythm*** of the work. It is formed during the exaltation phase (i.e. supernormal).

If the rate of signals and strength of stimuli are higher than the optimal rhythm, it decreases the contracting force. This rhythm is called ***pessimal.*** This muscle work rhythm is formed during the absolute refractory phase.

Sometimes, steady continuous stationary reversible contractions of muscles with their strongly prolonged relaxation can be observed. These muscle contractions are called *contracture (cramps).* It differs from tetanus, as there are no action potentials extending along muscles.

There are 3 kinds of contracture:

1. *Potassium* contracture. It appears if the fluid surrounding muscle fiber accumulates many potassium ions.

2. *Caffeine* contracture. Influenced by a high concentration of caffeine, calcium ions come inside muscle fiber and induce long muscle contractions.

3. *Post-tetanic contracture*. This is the residual contraction of muscles after the action of stimuli. For example, if you carry a heavy bag for a long time not changing your hands, you cannot unbend your fingers instantly after you get rid of the bag.

2. Strength and work of muscle fiber

Muscular strength is the amount of force a muscle can produce in a single effort. **The force of contractions (muscular strength) depends on the morphological properties and physiological state of muscles:**

1. **Length of muscles**. Muscles create great forces. The force of a muscle contraction depends on the initial length of the muscle, or its length at rest.

2. **Cross-section (diameter) of muscles**. There are two diameters:

a) *Anatomical diameter* being the cross-section of muscles.

b) *Physiological* area of the section, i. e. of the perpendicular section of each muscle fiber. The more the physiological section is, the greater strength the muscle has (Figure).

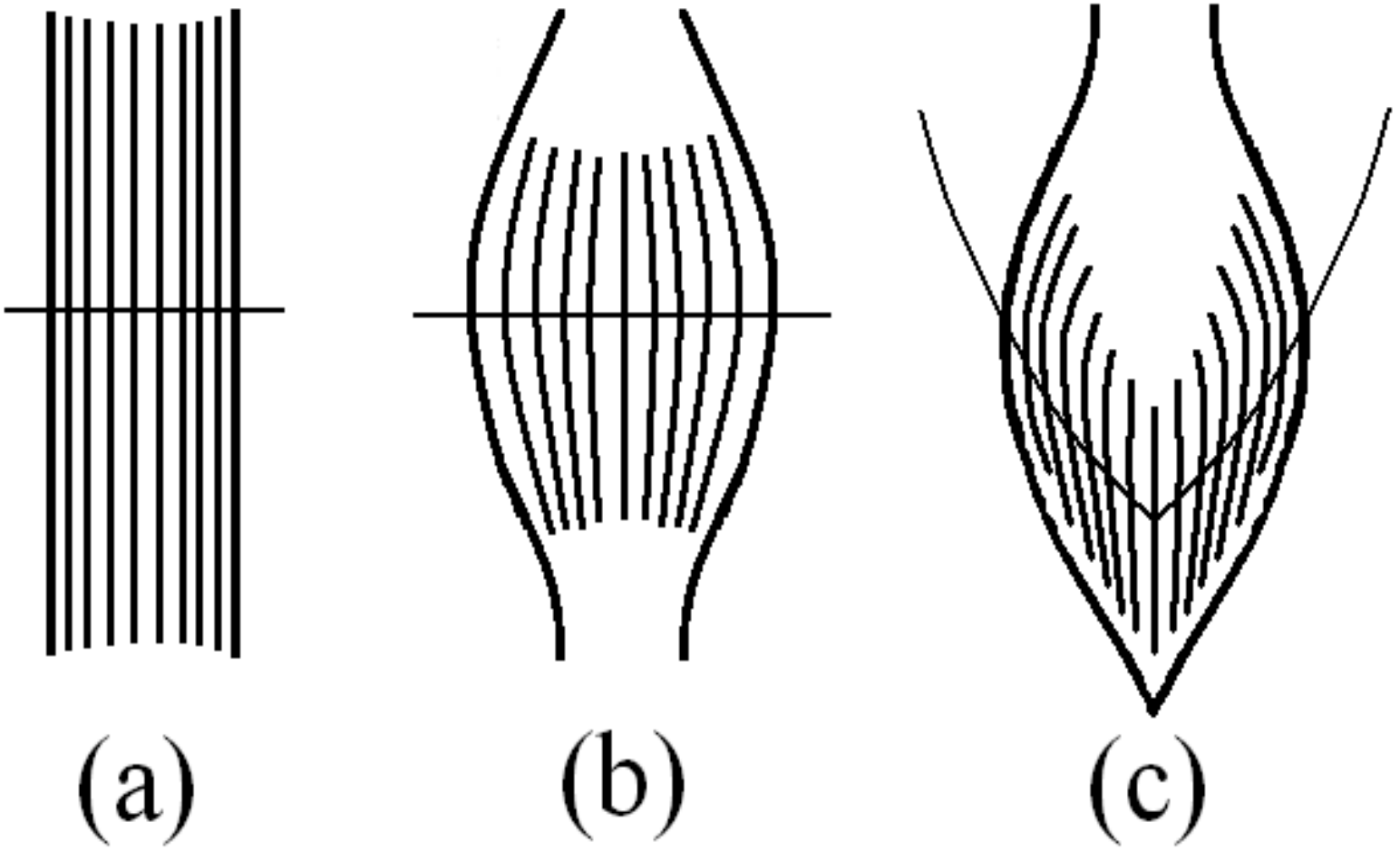


Figure — The structure of different types of muscles and their physiological cross section

Notes: (a) Sartorius muscle; (b) Biceps brachii; (c) Gastrocnemius muscle

The strength of muscles is measured by the maximal lifted weight. It is measured in kilograms or newtons. The method of the measurement of muscular strength is called dynamometry.

There are two kinds of muscular strength:

1. *Absolute strength* , which is the relation of the maximal strength to the physiological diameter.

2. *Relative strength*, *which is the* relation of the maximal strength to the anatomical diameter.

During contractions muscles are capable to perform their work. The muscle work is measured by multiplying the mass of the raised cargo and the height at which it is raised. The muscle work is characterized by its power. The muscle power is determined by the amount of work done per unit of time and is measured in Watts. The greatest work and power are reached in average loads.

3. Motor units. Composition (structure of muscles)

Muscle contractions depend on the frequency of signals coming from motoneurons. The axons of motoneurons can branch and innervate a group of muscle fibers (Figure). One axon can innervate from 10 to 3,000 muscle fibers.

A motoneuron and the group of muscle fibers innervated by it compose a *motor unit*.

There are motor units different in their structure and functions.

By their structure, motor units are divided into:

1. ***Small motor units*** which have a small motoneuron and a thin axon capable to innervate 10–12 muscle fibers. For example, facial muscles, muscles of fingers.
2. ***Big motor units***. They differ in the large body of a motoneuron, a thick axon which is capable to innervate more than 1,000 muscle fibers. For example, quadriceps.

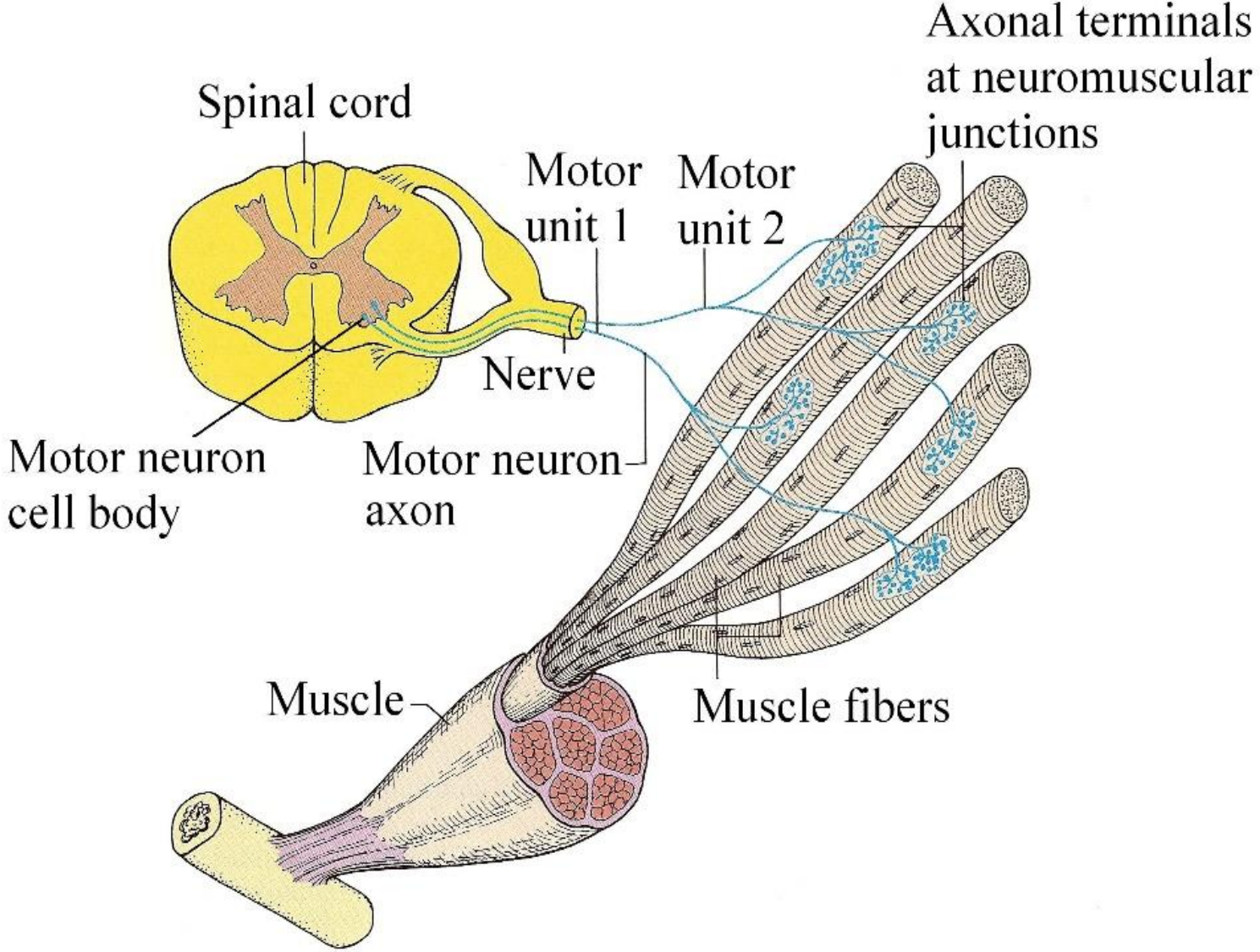


Figure — Motor units (schematic view of the parts of two motor units)

By their functional value, motor units are divided into:

1. *Slow motor units*. They include small motor units, and are easily excitable, characterized by the low velocity of the signal conduction, first involve into work but they almost never get tired, e. g., muscles of a marathon runner.

2. *Fast motor units*. They consist of big motor units, are badly excitable, have high-velocity signal conduction, high speed and strength of responses. E.g., muscles of a boxer.

These features of motor units are ensured by a number of properties.

Muscle fibers included into the motor units have similar properties and differences. **Slow twitch muscle fibers have:**

1. Rich capillary network.

2. They contain a lot of myofibrils.

3. They contain a lot of myoglobin (i.e. capable to bind large amounts of oxygen).

4. They contain a lot of fats.

5. They contain a lot of mitochondria.

Due to the above features, these muscle fibers have high endurance and are capable to contract continuously for a long time.

Due to the reddish color of myoglobin, these fibers may be referred to as red fibers.

The distinctive features of fast twitch muscle fibers:

1. They contain more myofibrils than slow twitch fibers.

2. They have a greater rate and strength of contractions.

3. They contain few capillaries.

4. They contain little myoglobin.

5. They contain few fats.

6. They contain a lot of glycogen.

Due to the lack of myoglobin, fast twitch muscle fibers can be referred to as white fibers.

Accordingly, these muscle fibers get tired rapidly but have great strength and high speed of responses.

The ratio of slow and fast twitch muscle fibers in different muscles is unequal and varies in individuals.

The interrelation of muscle fibers is genetically determined. Transition of fast twitch muscle fibers into slow ones and vice versa during life-time is impossible.

In natural conditions muscles are hardly ever relaxed, as they are at the state of normal tonicity. The ability of muscles for constant low-level activity at the normal state of balanced tension and minimum energy consumption is called muscle tone or muscle tonus. For example, the muscles of the neck maintain the head the whole day. In some disorders of the nervous system muscle tone can be affected.

4. Structure of muscle fiber

The average length of muscle fiber is 12–14 cm. It contains many nuclei. Its membrane is called the ***sarcolemma*** and it has flexures inside fibers (Figure). The cytoplasm of muscle cells is called ***sarcoplasm*** and consists of myofibrils, myoglobin, glycogen, sarcoplasmic reticulum (a system of longitudinal tubules and extended saccules containing calcium).

Myofibrils are grouped into bundles and pass through the whole fiber without interruption. They are divided into dark and pale bands. The dark bands are called *anisotropic*, the pale ones — *isotropic*. The pale bands at the center have the Z-membrane, the dark bands have the H-strip (Figure). The contractile unit of the myofibril between the two Z-lines is called the ***sarcomere***.

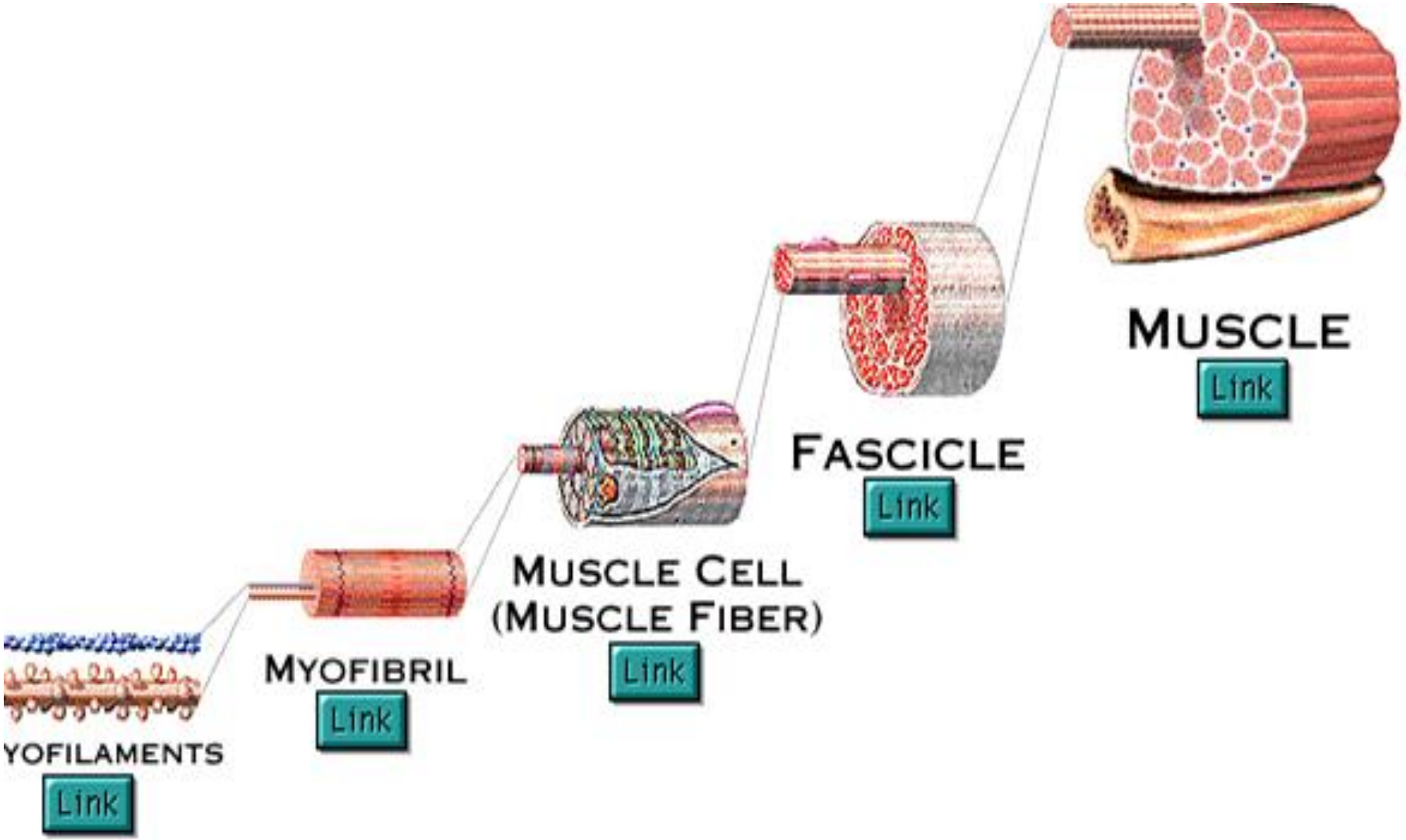


Figure — Levels of skeletal muscle organization

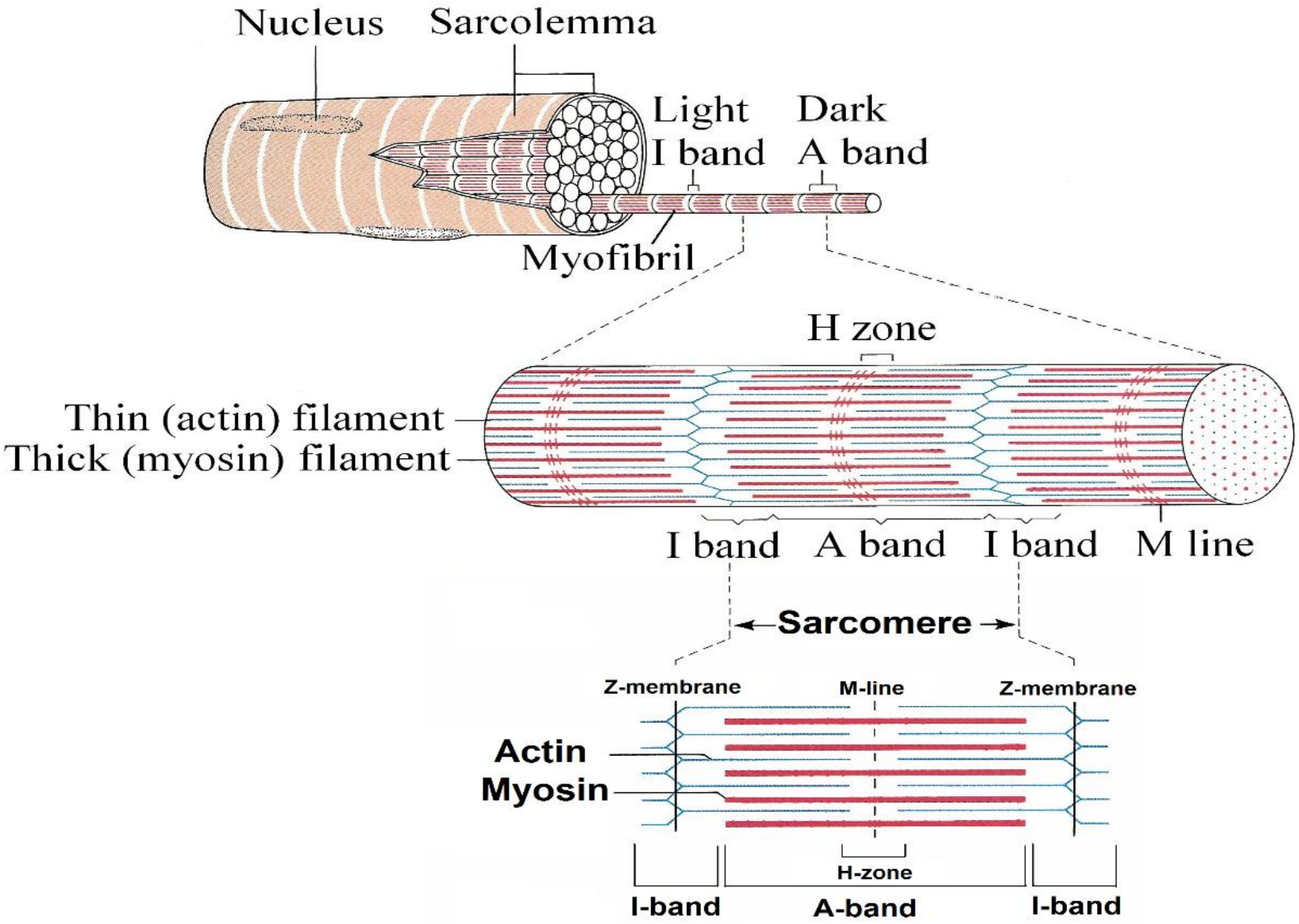


Figure — Structure of muscle fiber and sarcomere

Each myofibril consists of ***actin (thin)*** and ***myosin (thick) filaments***. The proteins *troponin* (has high affinity for calcium ions) and *tropomyosin* are located on the actin filaments. Each myosin molecule is composed of two long protein chains with a globular head at one end. The myosin head attaches to the binding site on the actin filament. (Figure).

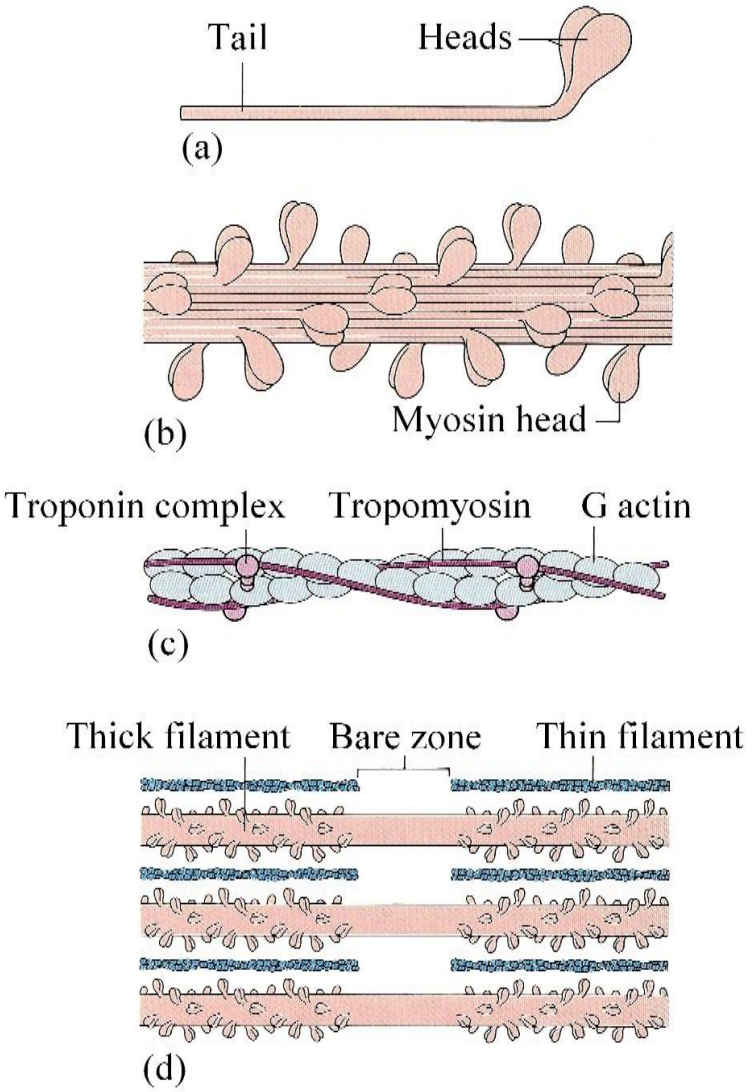


Figure — Myofilament composition in skeletal muscle

Theory of muscle contractions (sliding of filaments)

A muscle contraction is connected with the appearance of an action potential on the muscle fiber membrane. Then AP is distributed along the sarcolemma and enters the fiber.

To cause a muscle contraction, a current must penetrate deeply into the muscle fiber. This is achieved by the transmission of action potentials along transverse tubules (T tubules), which penetrate all the way through the muscle fiber. The action potentials of the T tubules promote a release of calcium ions from the sarcoplasmic reticulum. In the sarcoplasmic reticulum, there are voltage-gated calcium channels. As these channels open, calcium reaches the cytoplasm down the concentration gradient.

Cross-bridge cycling.

1. The muscle contraction cycle is triggered by **calcium ions released from the reticulum and binding to the protein complex troponin** (Figure). The troponin complex undergoes a conformational change, and tropomyosin molecules move more deeply into the groove between the two actin strands. As a result of this, the obstacle inhibiting the interaction of the actin and myosin filaments is removed. The active actin sites become uncovered for binding with myosin.

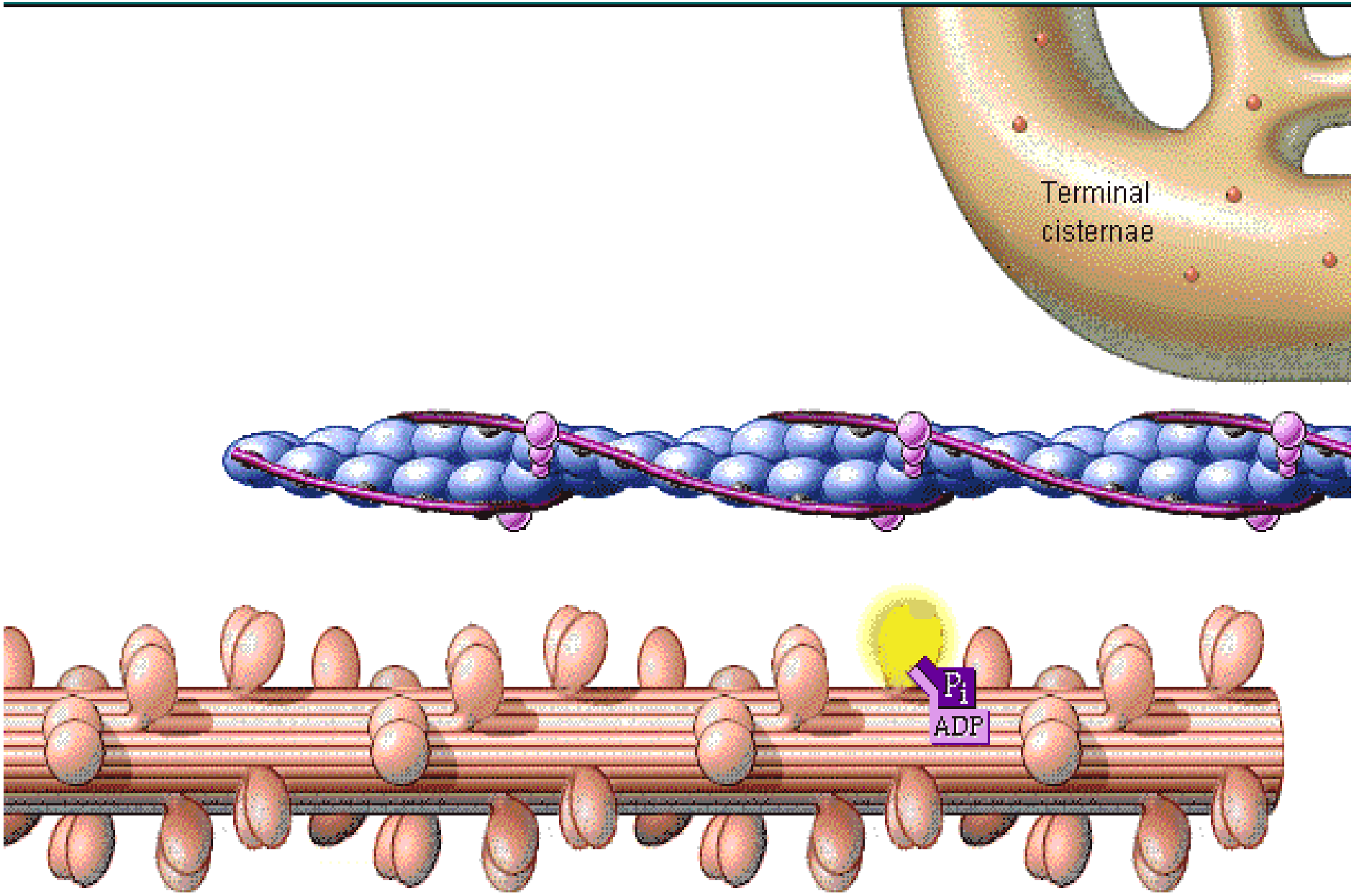
2. The high-energy myosin head bridges the gap and attach to the binding sites on the thin actin filaments, forming a cross-bridge. ATP is split, but ADP and phosphate ion are bound to the head.

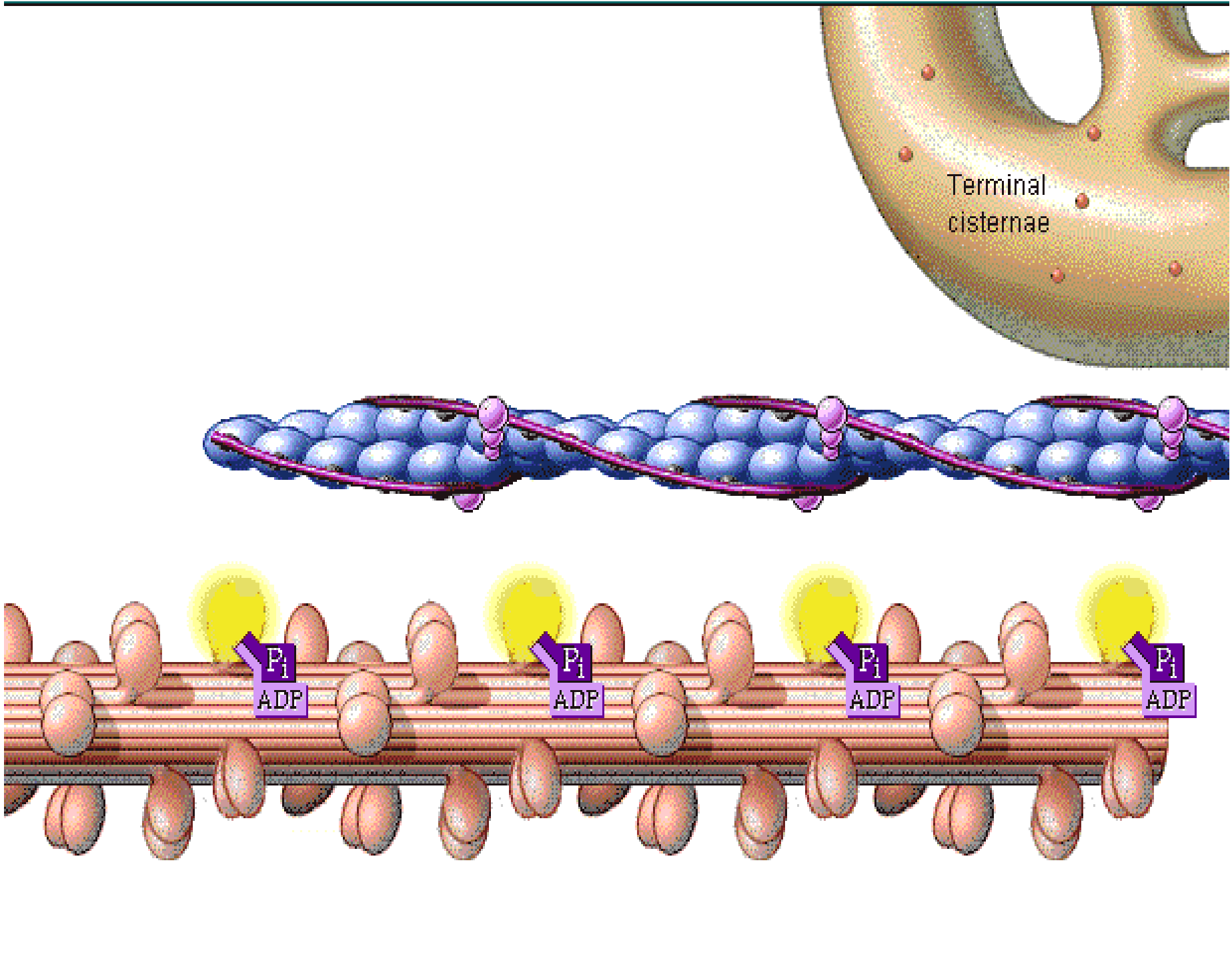
3. The heads of the myosin filaments perform a longitudinal pull. As a result, the sliding of the actin filaments between the myosin ones appears. The bond between the myosin head and the active actin site causes a conformational change in the head to a lower energy state, prompting the head to tilt. This provides the “power stroke” for pulling the actin filament. ADP and phosphate ions are released, but the cross-bridge is still in place.

4. ATP then binds to myosin, and the detachment of the myosin head from the actin active site takes place. The released energy is spent on breaking the connection of the actin-myosin cross bridge.

5. The ATP molecule is split (but ADP and phosphate ions are not released). **The initial conformational state of the myosin head is restored, which allows the cross-bridge cycle to start again,** leading to a new power stroke. Thus, these cycles can repeat till calcium ions and ATP are present in the sarcoplasm.

The calcium ions are pumped back into the sarcoplasmic reticulum. Calcium in the sarcoplasma activates CA^{2+} ATPase, which provides active transport of calcium into the sarcoplasmic reticulum. Thus, the tropomyosin-troponin complex covers the binding sites on the actin filaments and the contraction ceases.


Terminal
cisternae
Pi
ADP


Terminal
cisternae
Pi
ADP
Pi
ADP
Pi
ADP
Pi
ADP

5, Muscle fatigue. Hypertrophy and atrophy of muscles

Muscle fatigue is a temporal state of exhaustion or loss of strength and/or muscle endurance following strenuous activity which disappears after some rest.

Causes of muscle fatigue:

1. Accumulation of metabolic products (lactic acid) in muscles inhibiting generation of action potentials.

2. Oxygen starvation, i.e. muscles are deprived of adequate oxygen supply.

3. Energy exhaustion.

4. The central-nervous theory of muscle fatigue. According to this theory, the fatigue of nervous cells develops faster than that of muscles. The fatigue of synapses through which impulses are transferred to muscles also occurs.

On the whole, there is no first or last cause. All of them act simultaneously.

Hypertrophy and atrophy of muscles

Muscle hypertrophy involves an increase in the size of muscle fibers due to regular physical exercise. **There are two types of hypertrophy:**

1. *Myofibrillary type* develops due to static work (lifting of heavy objects). In this type of hypertrophy, the number of myofibrils increases and muscle strength is significantly enlarged, for example, in weight-lifters.

2. *Sarcoplasmic type* focuses more on increased muscle sarcoplasm storage (glycogen, phosphocreatine, myoglobin, number of capillaries). In this type of hypertrophy, muscle endurance develops, for example, in marathon runners.

Muscle atrophy develops due to low physical activity, e. g. it is common in those who wear a plaster bandage or are bedridden, or it may be caused when an injury or disease harms the nerve which attaches to the muscle (dissection of tendons, nervous disorders).

6. Smooth muscles

Smooth muscles are present in the walls *of the blood vessels, skin, and internal organs.*

Smooth muscles differ from transversal striated muscle fibers in irregular actin and myosin myofibrils. The junction of smooth muscles represents close continuous contacts between the membranes. These junctions are called ***nexuses***. Thus, they form a network acting as a whole.

Smooth muscles provide slow motions and continuous tonic contractions (e. g., pendulum-like and peristaltic contractions of the intestines). Smooth muscles provide the tonus of arteries and arterioles (Figure)/

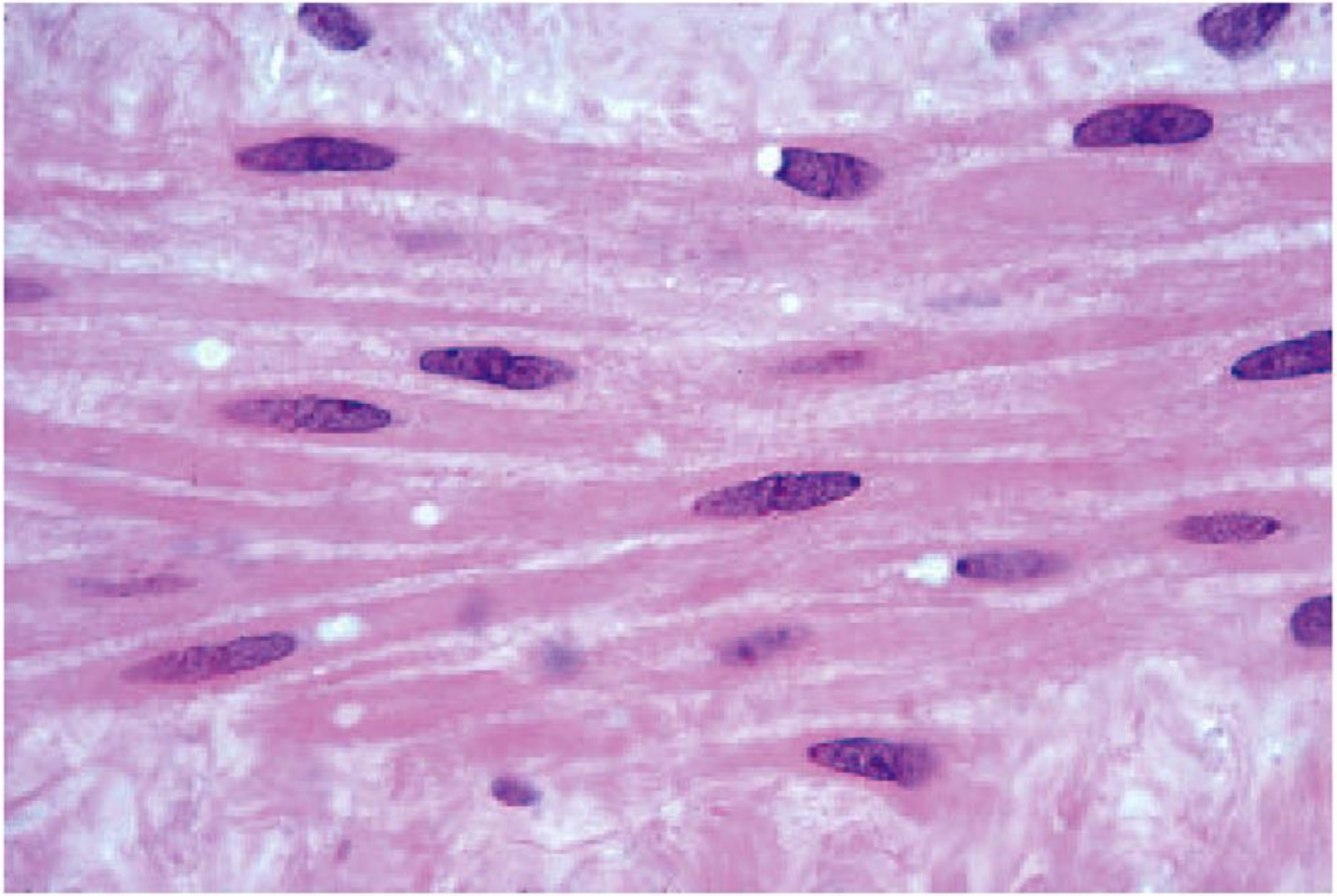


Figure — Smooth muscle cells

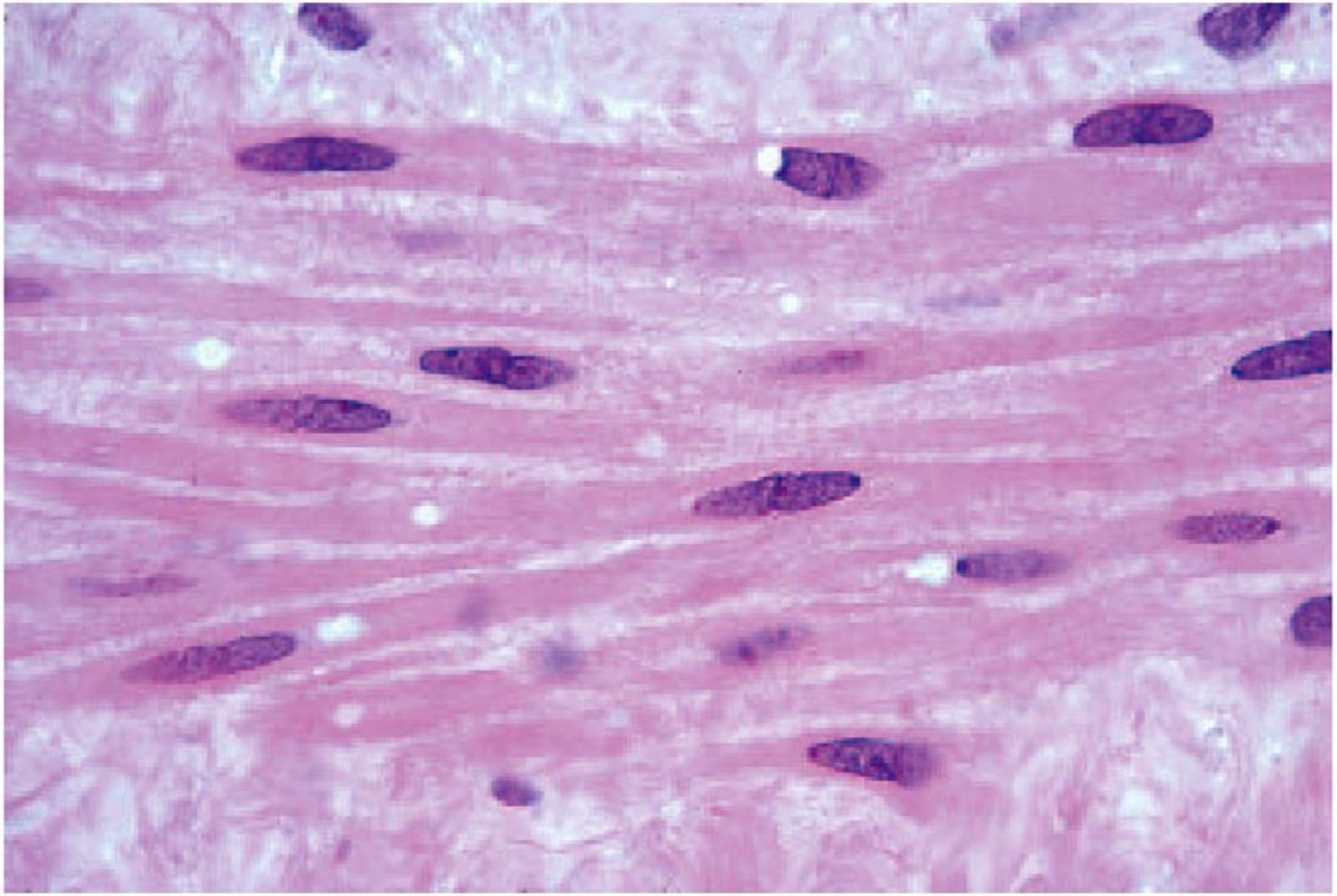


Figure — Smooth muscle cells

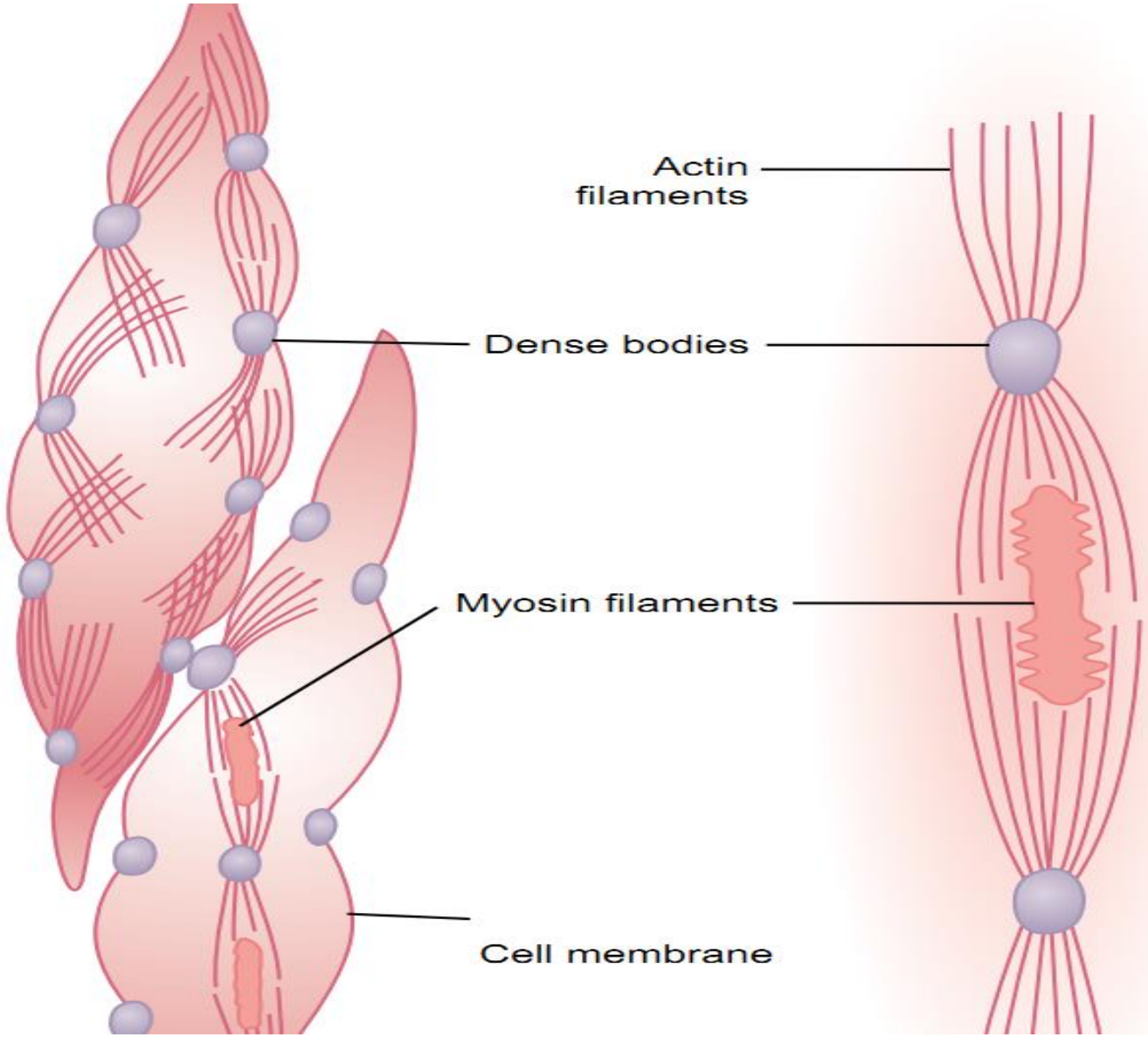


Figure — Structure of smooth muscle cells

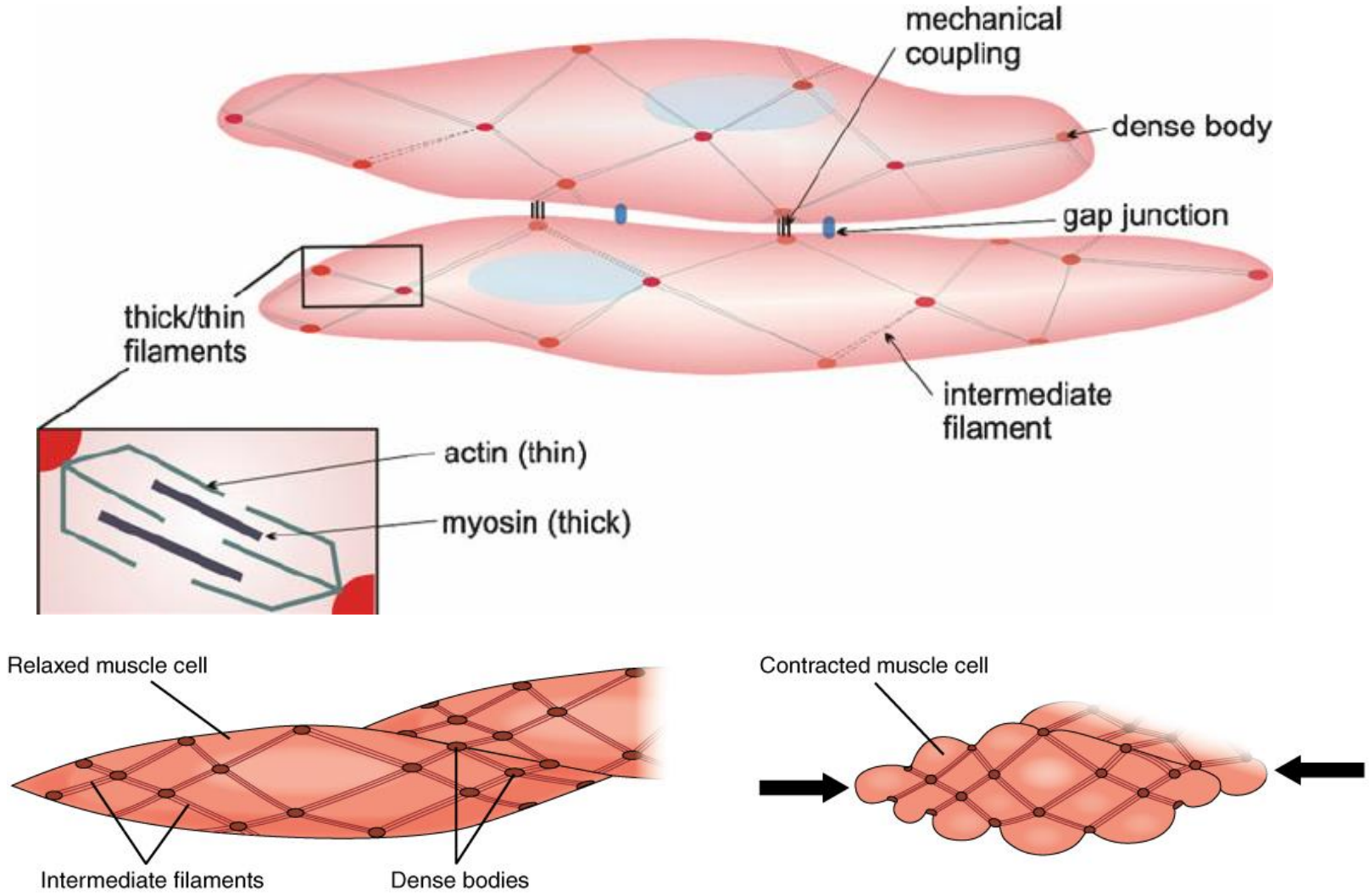


Figure — Structure of smooth muscle cells

Smooth muscle distinctive properties in comparison with the skeletal muscle are the following:

- **Contraction can be caused by various stimuli, not by nervous impulses only.**
- **The source of Ca ions for contraction is not only reticulum, but extracellular fluid as well**
- **It is innervated by autonomic nervous fibers, not by somatic ones.**
- **Some of the smooth muscle cells have the ability to auto-excitation.**

Structural distinctive properties of smooth muscle cell:

- Electrical coupling of cells by gap junctions
- Absence of T-tubules system
- Absence of troponin in the thin filaments
- Much less developed sarcoplasmic reticulum
- Much less of myosin filaments
- Presence of dense bodies instead of Z disks
- Presence of the specific kinase for myosin

By functional value, smooth muscles are divided into two types:

1. Unitary (*visceral, single-unit)* located in the gastrointestinal tract and urinary system.

2. Multi-unit, consisting of units containing a large number of muscle cells. Multi-unit smooth muscles are present in the walls of the blood vessels, in the pupil, lens, and skin.

The activity of smooth muscles is influenced by the sympathetic and parasympathetic parts of the autonomic nervous system.

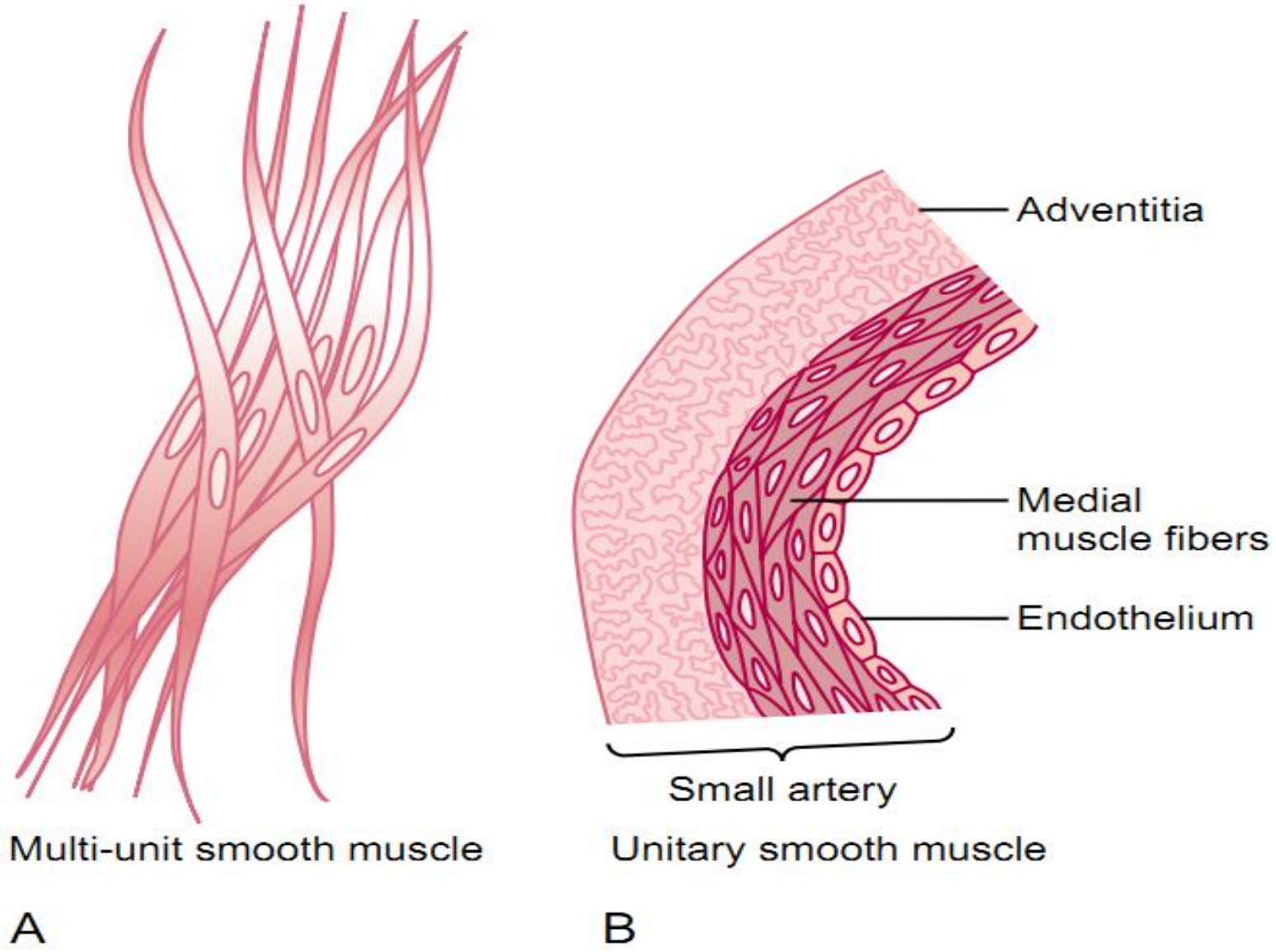


Figure — Multi-unit (A) and unitary (B) smooth muscle

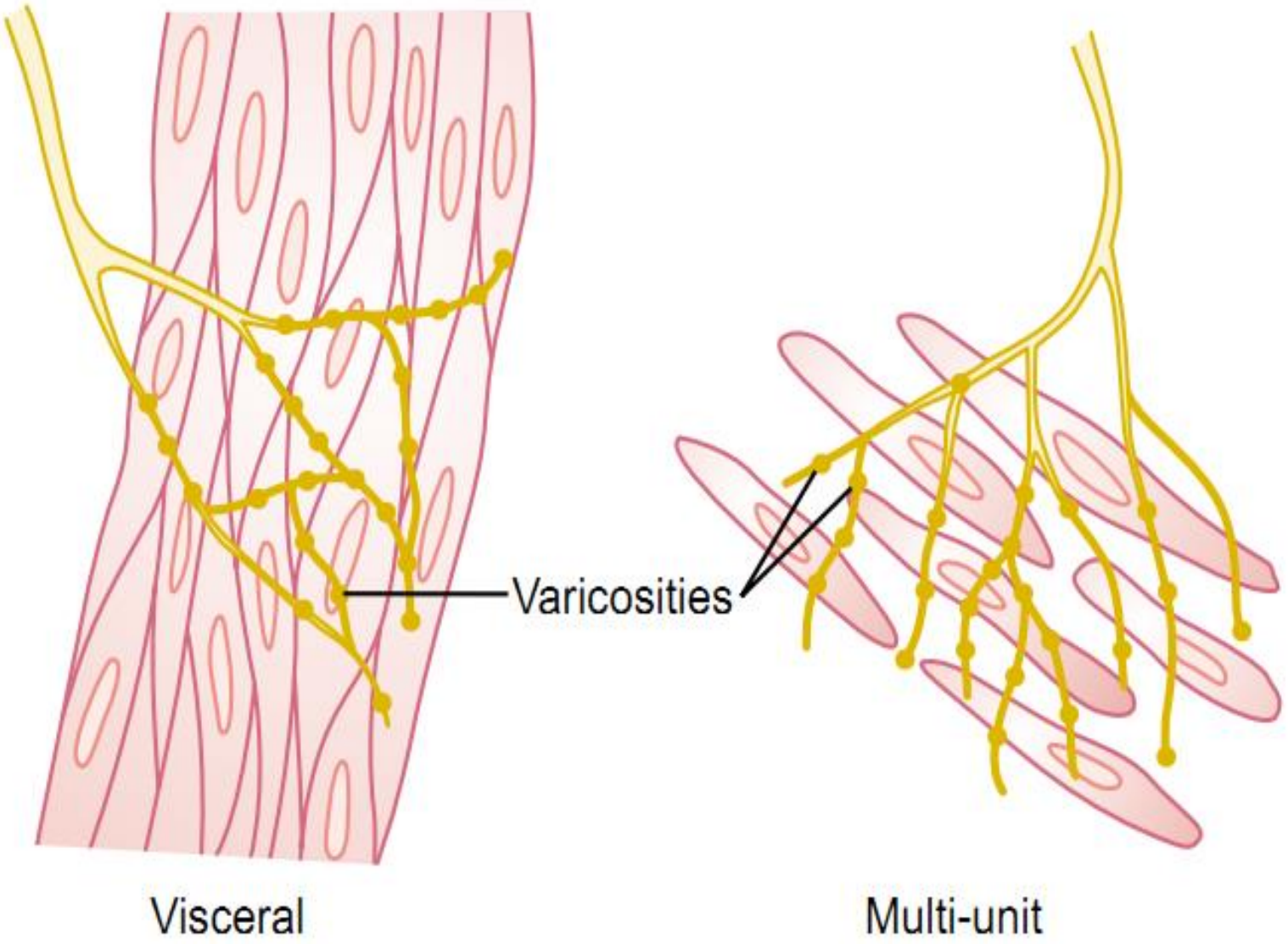


Figure — Innervation of smooth muscle

Multi-unit and unitary smooth muscles

- **Multi-unit smooth muscle is composed of separate smooth muscle fibers.**
- **Each fiber can contract independently of the others and often is innervated by a single nerve ending, as occurs for skeletal muscle fibers.**
- **Examples of multi-unit smooth muscle are the ciliary muscle of the eye, and the iris muscle of the eye.**

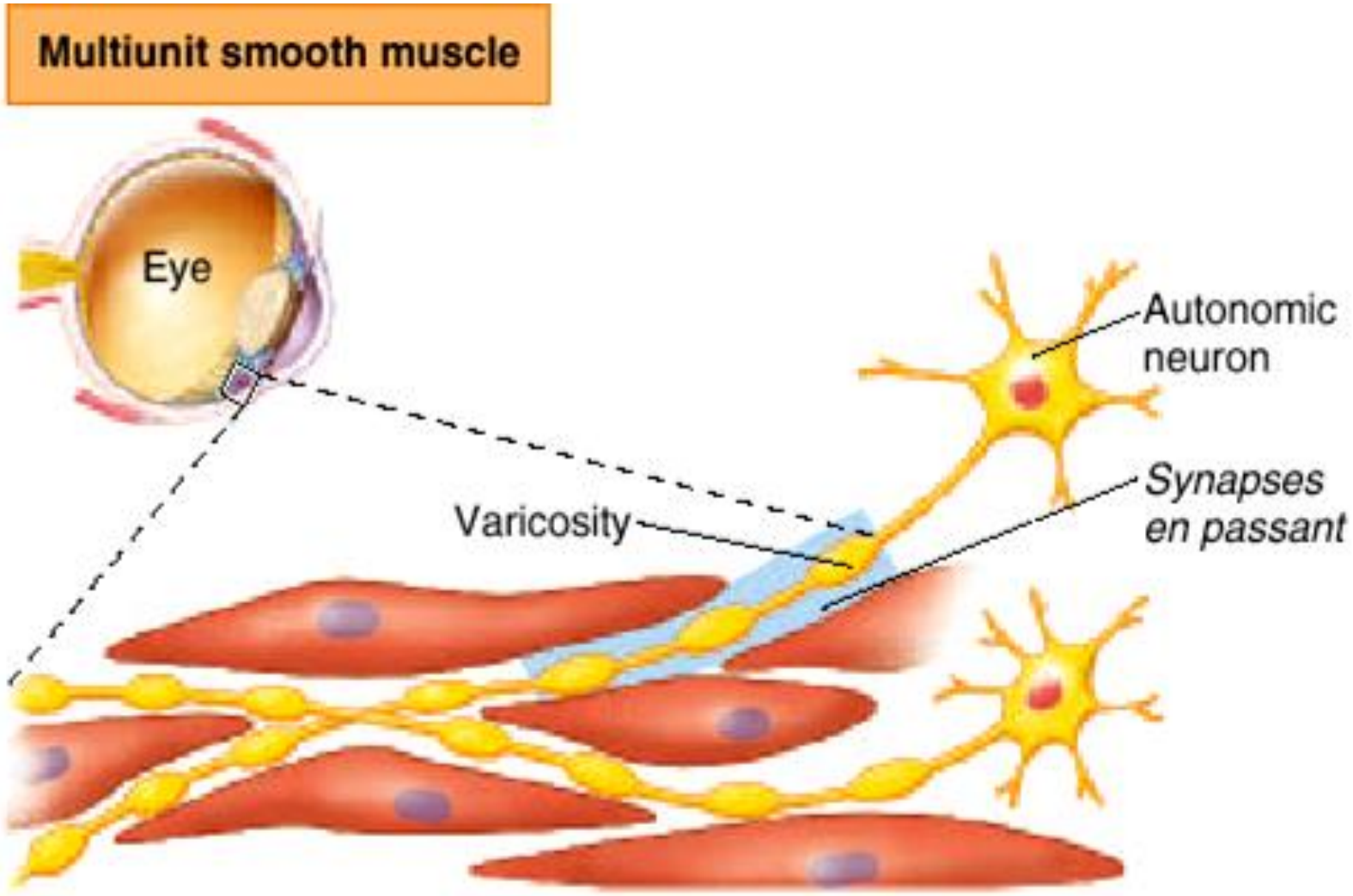
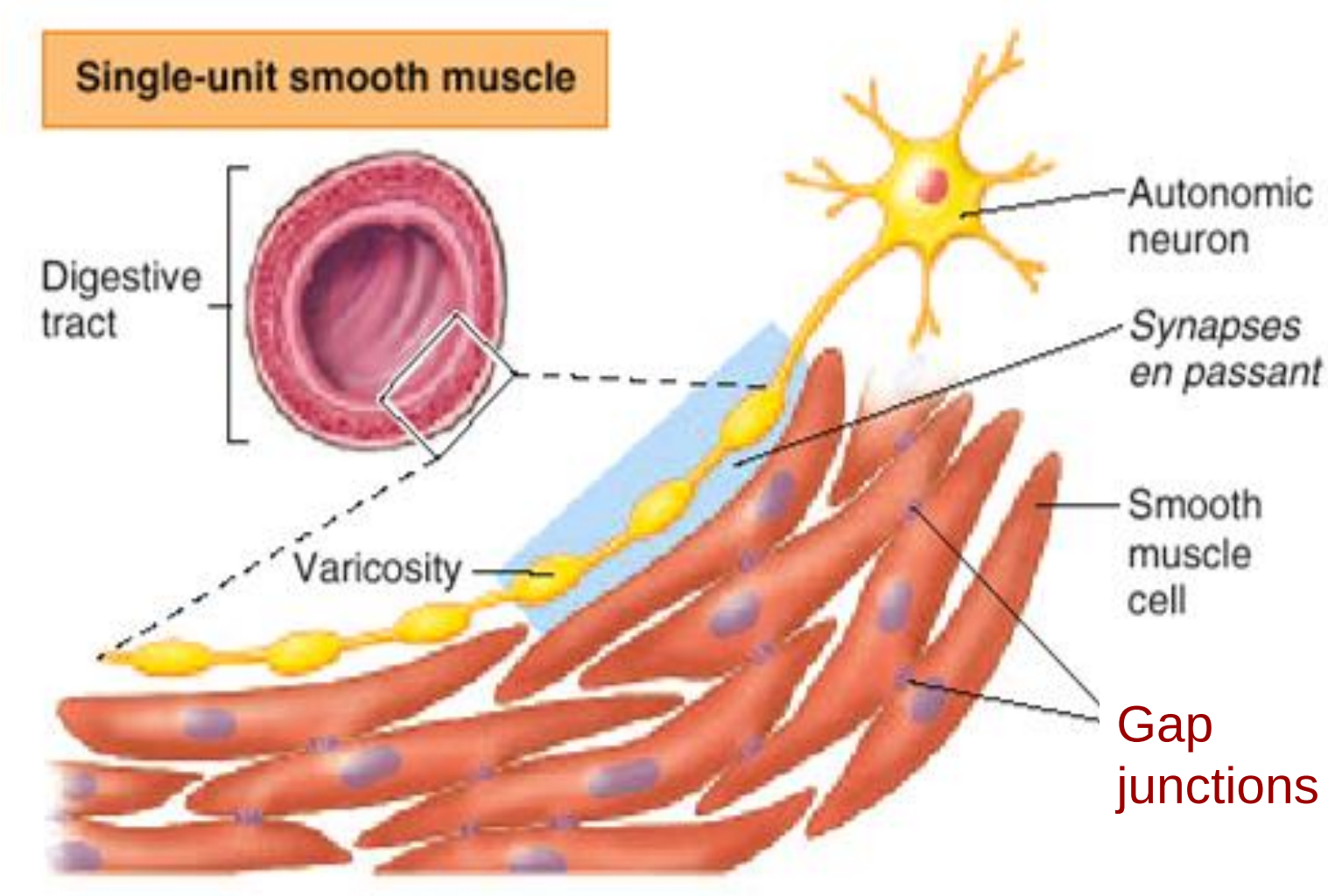


Figure — Multi-unit smooth muscle

Unitary smooth muscle

- **Unitary smooth muscle fibers contract together as a single unit.**
- **The fibers membranes are joined by numerous gap junctions making up the functional syncytium.**
- **Due to gap junctions depolarization can be passed from one fiber to the next and cause the muscle fibers to contract together.**
- **This type of smooth muscle prevails in the organism and is present in the walls of the visceral organs, including the gut, blood vessels and others.**

Figure — Single-unit (unitary) smooth muscle



Comparison of skeletal and smooth muscle

CHARACTERISTIC	SKELETAL MUSCLE	SMOOTH MUSCLE
Innervation	Somatic	Autonomic
Visible striation	Yes	No
Electrical coupling of cells	No	Yes, gap junctions
T-tubules system	Yes	No
Troponin	Yes	No
Sarcoplasmic reticulum	++++	+

CHARACTERISTIC	SKELETAL MUSCLE	SMOOTH MUSCLE
Source of Ca ions	Sarcoplasmic reticulum	Extracellular fluid and reticulum
Role of Ca ions	Exposure of actin binding sites	Initiating myosin heads phosphorylation
Speed of contraction	Fast	Slow
Energy consumption	High	Low
Auto-excitation	No	Yes
Effect of nerve stimulation	Excitation	Excitation or inhibition
Hormone regulation	No	Yes
Activation by stretching	No	Yes

Visceral smooth muscles are able to contract without direct nervous influences. The constant resting membrane potential in smooth muscles is absent, it continuously drifts and makes — 50 mV on the average. The drift is spontaneous, without any influences and, once the resting membrane potential has achieved the critical level, an action potential is generated, which induces a muscle contraction. The action potential lasts for a few seconds, therefore the contraction lasts for a few seconds, too. The excitation is distributed through the nexus to the next areas inducing their contractions.

The velocity of the signal conduction by the nerve fibers towards smooth muscles is 0.5–1 m/sec.

Spontaneous (independent) activity is connected with extension of smooth muscle cells and when they are stretched, an action potential is generated. The frequency of action potentials depends on the degree of fiber extension. For example, peristaltic contractions of the intestines strengthen because of the extension of its walls caused by the chyme.

Basically ***multi-unit muscles*** contract when they are influenced by nervous impulses, but sometimes spontaneous contractions are also possible. A single nervous impulse cannot induce a response. To induce a response, several impulses are required.

In all smooth muscles, the generation of excitation leads to the activation ***of calcium channels***, therefore in smooth muscles all processes go slower as compared with skeletal ones.

Humoral regulation of smooth muscle contractions. The force of smooth muscle contractions is influenced by *adrenalin*, which produces continuous contractions. Smooth muscles can respond to the action of the biological substances of blood. Opposite to them, skeletal muscles respond to the action of the substances only through synapses.

Smooth muscles consume little energy and possess *plasticity*. **Plasticity** is the ability of muscles to store the given length with the strain unchanged. This property is very important for the functioning of the urinary bladder.

The action of the biologically active substances on smooth muscles located in various organs is not similar. Thus, ***acetylcholine*** excites smooth muscles of the internal organs but inhibits those of the vessels; ***adrenalin*** is capable to relax the uterus in a non-pregnant woman but produces contractions of the uterus in a pregnant one.