

Pathophysiology of the cardiovascular system

3.1 Functional characteristics of the cardiac muscle structure

The basic unit of cardiac muscle is represented by **cardiac muscle cell – cardiomyocyte**. It is substantially larger than other nonmuscular cells of the heart. Cardiomyocytes are cylindrically shaped with several processes. By means of the cylindric ending and lateral processes they communicate with the neighbouring cells.

Regarding the contractile function of the heart, the most important cardiomyocyte organelles include: cellular membrane – sarcolemma, sarcoplasmic reticulum (SR), mitochondria and contractile proteins.

See fig. 3.1 on page 89 (the cell is characterized by its clubbed cylindrical shape and pronounced articulation in the intercallary disc area. Intercallary discs are situated also on the lateral side of the cardiomyocyte. According to Šimko et al., 1987), fig. 3.2 on page 89 (apparent are the T tubules which course mutually parallel, and perpendicular to the longitudinal axis of the myocyte - one arrow. Mitochondria (two arrows) are localized subsarcolemmally. Magnified 1000x. According to Šimko et al., 1987 fig. 3.3 on page 90 (ID – intercallary discs, M – mitochondria, Z – Z line of the sarcomere. Magnified 12 500x. According to Šimko et al., 1990) and fig. 3.4 on page 90 (Regular serial repetition of lighter and darker

bands forms the characteristic striation. Magnified 500x. According to Šimko et al., 1986)

Sarcolemma separates cells from the extracellular fluid and serves to transfer electric activity via cellular surface. Its semipermeable character enables a precisely regulated exchange of ions and metabolically active substances with the surroundings. The cellular surface is covered with **glycocalyx**. It is a chemically complex layer which to a great measure affects the cellular permeability for calcium. The sarcolemma is modified into the so-called **intercallary discs** in sites of mutual contact of myocytes. These areas have low electric resistance and enable a free flow of ions between cells. Hence the heart behaves as an electrically homogenous substance – electric syncytium. In some sites the sarcolemma invaginates deeply into the interior of cells thus forming the so-called **T-tubules**. The latter participate in transport of calcium ions.

Sarcoplasmic reticulum (SR) – comprises a system of cisternae and minute channels mutually interconnected. The cisternae represent "reservoirs" filled with calcium and the channels serve as "tunnels" via which intracellular transport of calcium takes place.

Mitochondria represent ATP producing "factories". The majority of metabolic processes take place therein. The cellular cytoplasm represents environment where sugar is metabolized – aerobic and anaerobic glycolysis. Practically all other energy producing events take place in mitochondria (breakdown of fatty acids, Krebs' cycle, oxidative phosphorylation).

Contractile proteins include actin, myosin, troponin and tropomyosin. Myosin filaments are comprised of a great number of club shaped molecules

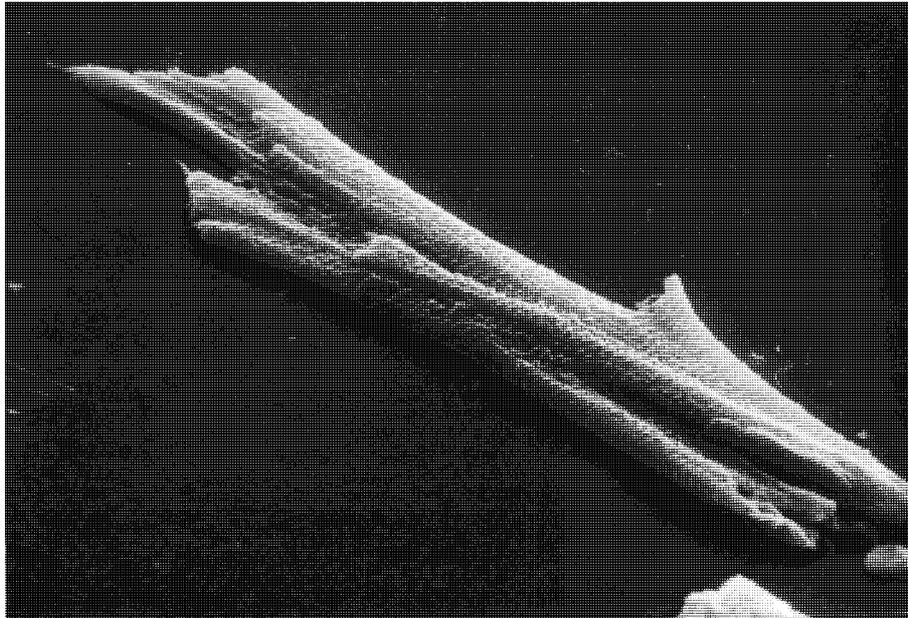


Figure 3.1: Isolated cardiomyocyte in scanning electron microscope

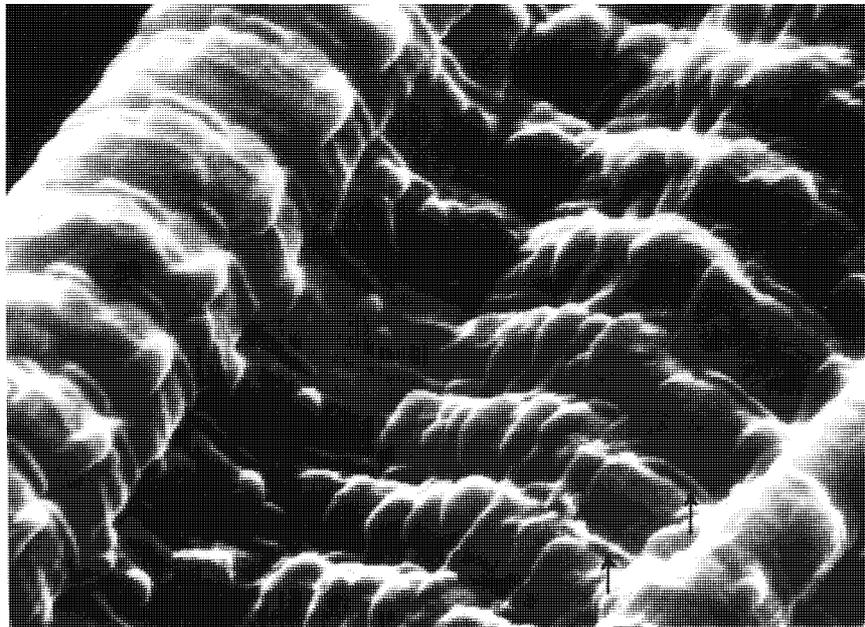


Figure 3.2: Surface of isolated cardiomyocyte in scanning electron microscope

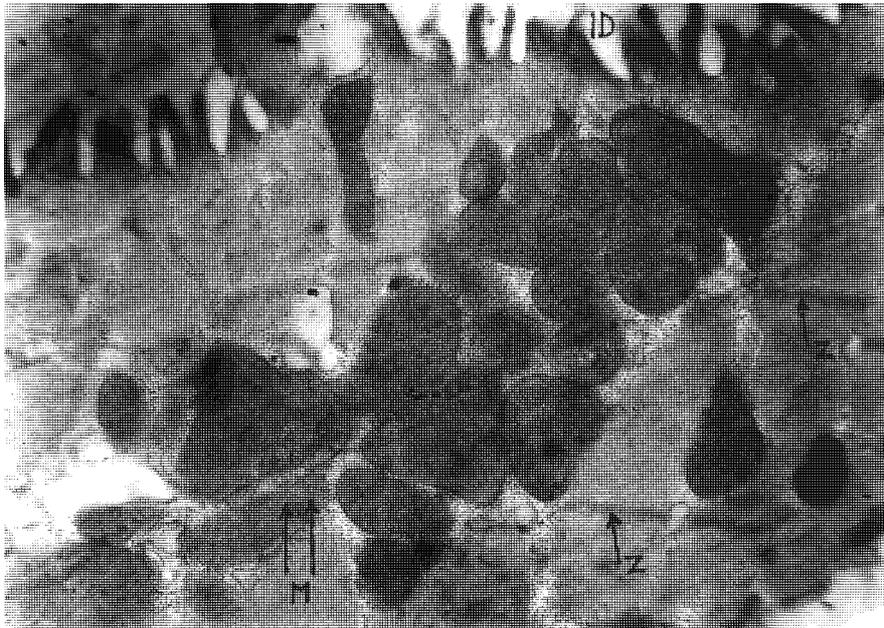


Figure 3.3: Isolated cardiomyocyte in transmissive electrone microscope

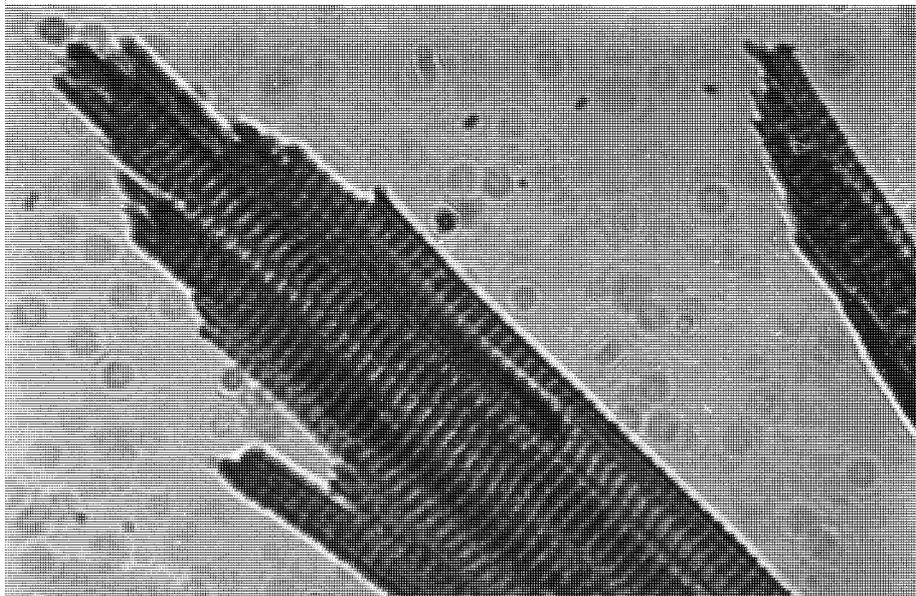


Figure 3.4: Intercalar disc of isolated cardiomyocyte in light microscope

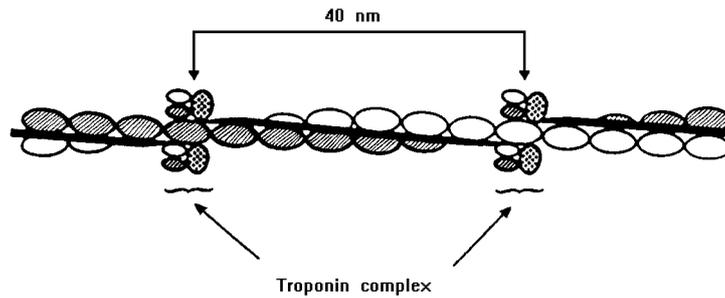


Figure 3.5: Contractile proteins

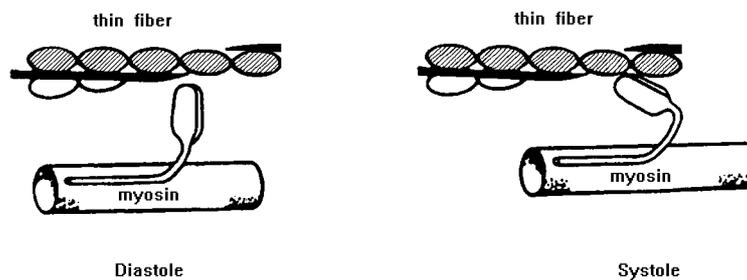


Figure 3.6: Interaction of thin (actin, troponin and tropomyosin complex) filament and myosin one during contraction of the heart

with a widened ending which contains myosin ATP-ase. Actin filaments are formed by two chains of small molecules which are mutually wound about each other thus forming a helix. See fig. 3.5 on page 91 (Scheme of protein arrangement in the thin actin filament. Two chains of actin molecules are mutually wound about each other thus forming a helix. The tropomyosin molecule is formed by a thin filament which is in contact with seven actin molecules of each chain. Troponin complex consists of three protein molecules which adhere to each of the tropomyosin molecular endings. According to Katz, 1992) and fig. 3.6 on page 91 (the scheme of spatial alterations between the thin and thick filaments during contraction. In consequence of mutual interaction of actin and myosin the myosin molecular orientation alters, which results in a longitudinal

movement of the thin filament. According to Katz, 1992). The tropomyosin molecule is of fibrous shape and spreads along seven actin molecules. A troponin molecule is bound to one of the tropomyosin molecular endings. The latter is tightly bound with the tropomyosin molecule and at the same time contains a binding site for calcium.

The ultrastructure of contractile proteins displays thick filaments of myosin, and thin filaments of tropomyosin. The arrangement of these thick and thin filaments results in formation of **myofibrils**. Myofibrils represent the basic functional elements of cardiac muscle cell and they run along it lengthwise. They are formed by regularly repeating structures – **sarcomeres**, which represent the basic contractile units.

The structure of sarcomeres is determined by the

specific arrangement of actin and myosin filaments which telescopically slide in between each other thus forming a number of characteristic lines and bands. Regarding the proper comprehension of function, the most important are the Z-lines. They issue thin actin filaments and at the same time demarcate the borders of sarcomeres. The distance between two Z-lines represents the length of the sarcomere. The diastolic length of the latter varies between 1,5–2,2 μm . Shortening of muscles is realized by the procedure of telescopic insertion of thin myosin filaments in between thick myosin filaments thus shortening the distance between Z-lines and the sarcomere itself.

Several myofibrils form one functional unit, in which the Z-lines of individual sarcomeres precisely align each other.

3.2 Metabolism of cardiac muscle cell

The contractile function of the heart is a process with extraordinarily high energy demand. Oxygen consumption in the beating heart depends on three main factors **wall stress**, **contractile state of myocardium** and **frequency of contractions**. Although the weight of the heart mass represents merely 1% of the body weight (in adults), the myocardium consumes app. 10% of the total body oxygen consumption. The heart is a typical aerobic organ with a minimal ability to work under oxygen debt. The amount of energy consumed during systole must be inevitably re-supplied during the diastolic recovery period. An adequate and fluent supply of cardiac muscle cells with oxygen and substrates is inevitable in order to replenish the consumed energy. It is to say, that already under rest conditions the extraction of oxygen from arterial blood is almost maximal. Therefore when heart activity increases, the augmentation of oxygen supply takes place almost exclusively by means of the increase of coronary blood flow.

During each cardiac revolution the energy expenditure takes place in three phases which are tightly bound (see fig. 3.7 on page 93):

1. energy production
2. energy storing
3. energy utilization

3.2.1 Energy production

Myocardium is able to produce energy from several substrates: fatty acids, glucose, lactate, pyruvate, ketone bodies and even aminoacids. Preference of individual substrates representing the particular sources of energy depends on their current concentration in both blood and cardiac muscle cells. This determines the concentration gradient of the given substrate on the level of cardiomyocyte membrane. Aside from the concentration gradient, the selection of substrates is also determined by natural capacity of particular enzymatic systems of the cardiac muscle cell, which limitates predominantly the utilization of atypical sources of energy also in case of their high concentration in blood.

If the oxygen supply is sufficient, the dominant fuel is represented by fatty acids which are predominantly utilised and they cover 50-70% of the total energy demands myocardium, and glucose which covers the remnant 30%. Lactate is utilized as an energy substrate under the condition of increased muscular activity, during which the lactate concentration in blood augments rapidly. Ketone bodies and aminoacids are utilized exclusively under special pathological conditions (e.g. in diabetic ketoacidosis). They participate in ATP production by more than 10%.

The process of the splitting of each of the mentioned substrates provides a common intermediate product – **acetyl KoA**. In the case of fatty acids it is formed by their splitting in the process of beta oxidation. Glucose is by means of glycolysis or pentose cycle converted to pyruvate and the subsequent oxidative decarboxylation converts pyruvate to acetyl-KoA. The latter is formed also during the processing of lactate, ketone bodies and aminoacids.

The common intermediate product of all these reactions, the acetyl - KoA, enters the Krebs cycle in mitochondria where it is split to CO_2 and hydrogen. The latter is subsequently processed in the process of **oxidative phosphorylation**. It is a sequence of reactions in which the cellular respiration (oxidation) is coupled with energy in form of ATP (phosphorylation). Cellular respiration represents the transfer of