

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  $\mu\text{m}$ . 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  $\text{CO}_2$  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

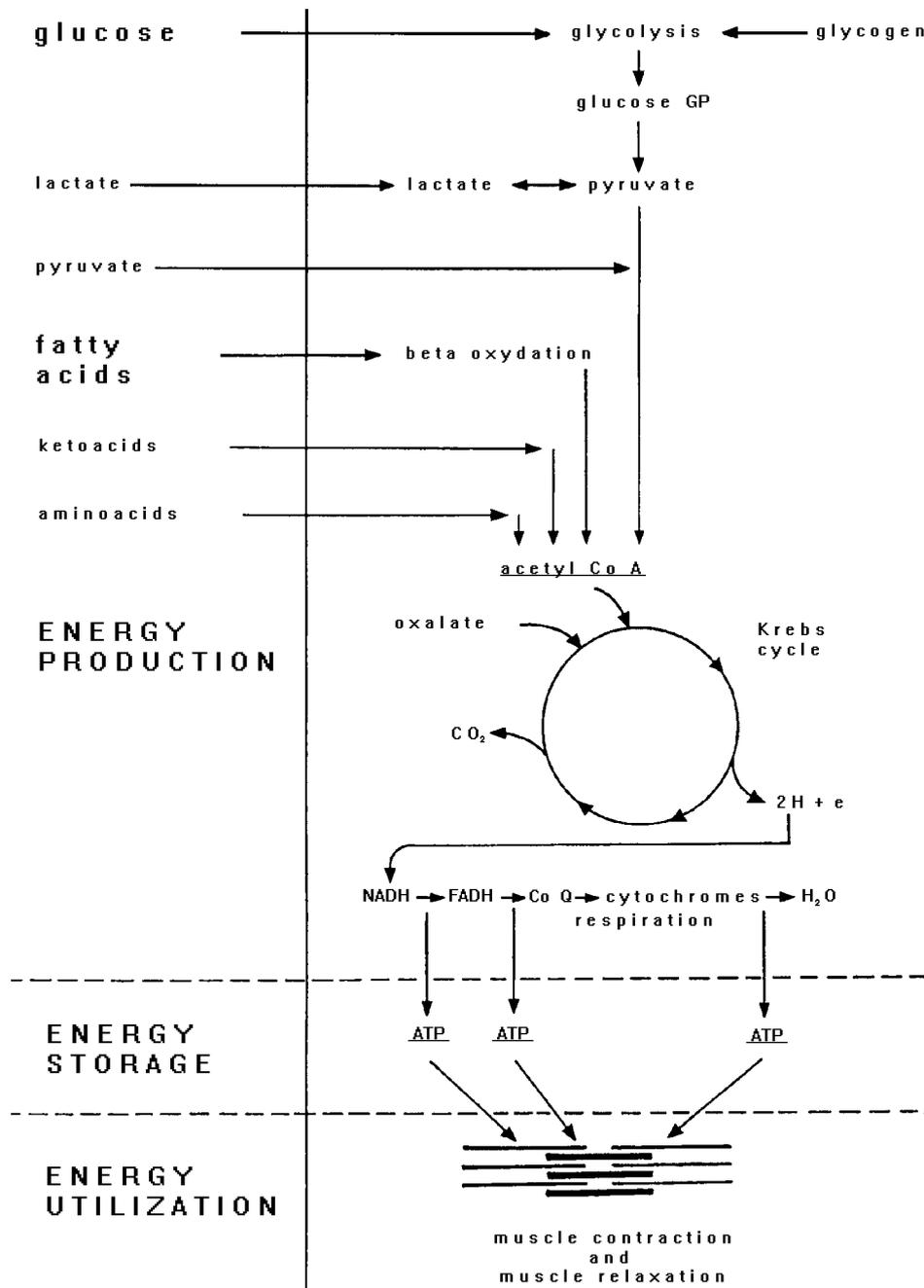


Figure 3.7: Metabolism of cardiomyocyte

hydrogen onto oxygen within the respiratory chain, thus forming  $H_2O$ . Simultaneously, phosphorylation is carried out, which means that energy produced by means of respiration and liberated in a cascade-like manner is being bound gradually by the conversion of  $ADP+P_i$  to ATP.

36 to 38 molecules of ATP are produced by processing of 1 molecule of glucose in the mentioned aerobic manner. Processing of 1 molecule of fatty acid results in a several-fold higher ATP production, the particular value of which depends on the chain length of the particular fatty acid.

### 3.2.2 Energy storing

The energy within heart muscle is stored in form of two basic macroergic compounds – adenosine triphosphate (ATP) and kreatin phosphate (KP). ATP serves as a prime energy donor for the process of contraction as well as for energetically dependent transportation membrane systems (ATP-ases). KP is a substance which stores energy. Under the condition of a fluent and sufficient supply with oxygen and substrates, the ADP and  $P_i$  formed by splitting are resynthesized to ATP and the energy necessary for this resynthesis is provided from kreatinphosphate. The ATP level is preserved while the cytoplasmic level of KP, representing a form of stored energy, decreases. When energetic situation improves, KP is replenished by energy from the respiratory chain.

The store of kreatinphosphate in the cardiac muscle is relatively small and can preserve the ATP level merely for a relatively short period of time. A severe ischemia finally implies a decrease of ATP and thus a decrease of cardiac muscle function.

Besides its store function, kreatinphosphate plays the role of a transporter of energy from mitochondria toward myofibrils. ATP, that is to say, originates in mitochondria, but is being utilized in other intracellular sites – predominantly in myofibrils.

### 3.2.3 Energy utilization

Energy is utilized in the process of contraction which is going to be explained in the following chapter.

---

## 3.3 Contraction-relaxation cycle

---

The most specific property of the cardiac muscle is the ability to contract.

**Contraction is a complex process which is represented by a precisely balanced interaction between contractile proteins (actin, myosin and tropomyosin), calcium ions, cellular transportation systems of calcium (sarcolemma, sarcoplasmic reticulum, mitochondria) and high energy phosphates (ATP, KP). The initial step in this complex reaction is the origin of action potential (excitation) and the resultant action is the shortening of muscular fibers (contraction).**

The thick filaments of myosin and thin filaments of actin are the proper elements of contraction. Troponin is firmly bound with tropomyosin thus forming one functional unit, troponin-tropomyosin complex. The latter participates in contraction as a regulatory protein. During diastole, the troponin-tropomyosin complex is firmly bound on actin and thus inhibits chemical interaction between actin and myosin. The surface of troponin contains a receptor which is able to bind calcium. Providing this site is not occupied by calcium ion, the troponin-tropomyosin complex is in a position which inhibits the chemical interaction between actin and myosin. Such a situation supervenes during diastole. During excitation (during the plateau period of action potential) which closely precedes the systole, the cytoplasmic concentration of calcium elevates. Calcium is bound with troponin. Thus the troponin-myosin complex is released from the binding with actin. In this way the inhibitory effect of troponin-myosin complex on actin is removed, and chemical interaction between actin and myosin takes place. The clubbed molecules of myosin after being bound with actin are leant thus shifting actin and myosin filaments propel in mutually opposite directions. According to the sliding theory the actin filaments slide telescopically between the myosin filaments while the length of either of filaments is not changed. This process is manifested as contraction. Hence, in this difficult process, calcium plays an important role of being the contraction inducer.