This chapter aims to provide an understanding of how our skeletal muscles contract based on the anatomical structures shown in the previous chapter.

The excitation of the muscle cell – the excitation-contraction coupling

To describe the process of muscle contraction, it is not sufficient to explain the mechanism at the cellular level. The movement to be performed must first be programmed in the brain. The corresponding afferent signal is then transmitted via the spinal cord to the alpha motoneuron that innervates several muscle fibers. At the myoneural junction (the synapse that transmits excitation from the nerve fiber to the muscle fiber), the signal ensures the release of acetylcholine into the synaptic cleft. The mechanisms in the nervous system and in the muscle fiber are interdependent and therefore difficult to separate, so that the initial situation in the muscles must first be explained before the processing of the afferent signal can be described. The coordination of the two processes, the transmission of the stimulus and the final contraction of the muscle fiber is called **“excitation-contraction coupling”**.

Like nerve fibers, muscle fibers are excitable and are characterized at rest by a so-called **resting membrane potential**. Various negatively charged particles (anions) and positively charged particles (cations) are distributed along the cell membrane. Extracellularly there is a higher concentration of **sodium** and chloride, but also some **potassium**. The intracellular concentration of potassium as well as negatively charged anions is comparatively higher, so that the intracellular space is negatively charged (-90mV) compared to the extracellular space. In addition, there is a concentration gradient due to the unequal distribution of the ions.

What happens now when acetycholine is released? The acetycholine binds to chemically-activated sodium channels (NaC), which become more permeable for sodium ions, so that they can enter the cell interior. When the positively charged sodium ions diffuse into the intracellular space, it becomes increasingly positive. If enough sodium channels open so that the **threshold of -55mV** is exceeded, voltage-sensitive sodium channels (NaV 1.4) are activated. The influx of sodium is thus suddenly accelerated, so that the cell can even reach a positive charge state for a short time (+20mV). This so-called **overshoot** only occurs when the **depolarization** by the chemically activated sodium channels exceeds the threshold value of -55mV. If this is not reached, the potential is not passed on (all-or-none law).

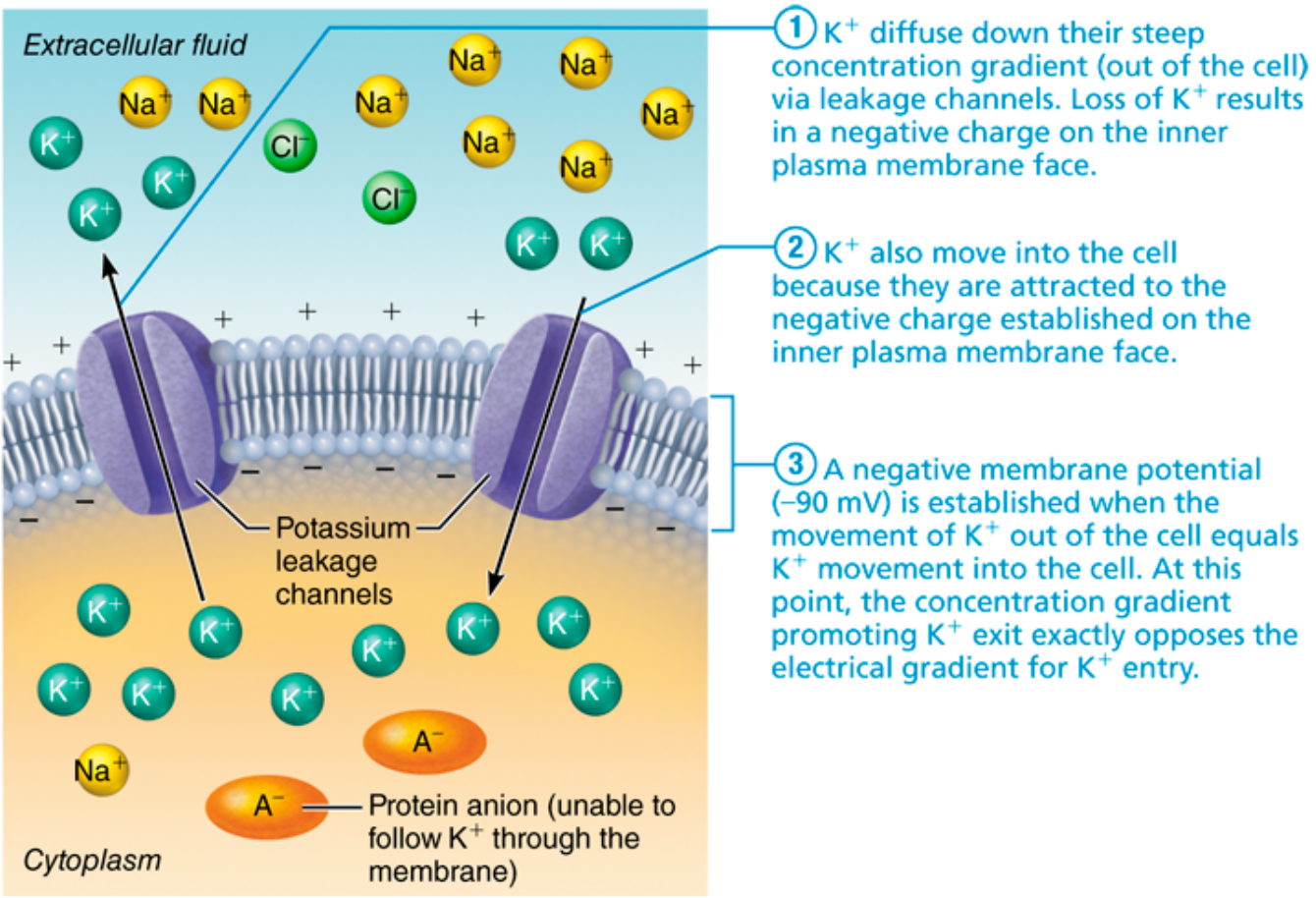

Figure 1 – Ionic basis of resting membrane potential.
https://quizlet.com/365660978/resting-membrane-potential-diagram/

The transmission of excitation takes place in two levels, once along the muscle fibre at the sarcolemma to ensure synchronous contraction of the muscles, and also into the depth of the muscle fibre via the T-tubule system. Along the membrane of the t-tubules there are voltage-dependent sodium channels, which enable the transmission of excitation. In the depth of the muscle fibre the action potential activates the voltage-sensitive dihydropyridine receptor (DHPR). By a conformational change of the DHPR, the ryanodine receptor opens, which regulates the calcium release of the sarcoplasmic reticulum. This release of calcium initiates the **cross-bridge cycle**.

The mechanics of muscle contraction

The cross-bridge cycle – the “mechanical” muscle contraction – begins with the rearrangement of troponin C by the calcium, so that the binding sites on the actin are released. The myosin head can now bind onto the free binding sites of the actin. The myosin heavy chains are loaded with ADP and a phosphate. The splitting off of the phosphate engages the **“power stroke”** that moves the actin filament relative to the myosin filament. In addition, the ADP is also split off so that the myosin head tilts more strongly and the Z-disks move closer together. In order for further “power strokes” to occur, the link between actin and myosin needs to be dissociated. This requires ATP, which attaches itself to the myosin head and lowers the affinity for the actin. ATP is hydrolysed, ADP and phosphate remain at the myosin, whereafter the initial position for rebinding of the filaments has been recreated (**“recovery stroke”**).

But how is the initial situation restored to make the cell excitable again?

Previously, potassium diffused into the extracellular space, whereas sodium was “lost” into the cell. This process is now reversed by the **sodium-potassium pump**. **Repolarization** occurs through the exchange of extracellular potassium with intracellular sodium. Through this process, which takes place with energy consumption, the resting membrane potential is restored. Within the muscle fiber, the calcium must be transported back into the sarcoplasmic reticulum in order to enable a new contraction. This process also costs energy, which is applied for the return transport by means of **sarcoplasmatic/endoplasmatic reticulum calcium ATPase (SERCA)**.Until these processes are completed, no new muscle contraction is possible.