ARTICLE TITLE

The Cardiac Conduction System: Generation and Conduction of the Cardiac Impulse

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KEY WORDS

4-8 keywords to direct and optimize search results

Action Potential, Cardiac Conduction System, Electrocardiogram, Automaticity

KEY POINTS

List 3 to 5 key points of approximately 25 words each that summarize the main points of the article. Key points appear beneath the article title and authors in print and online

- Contraction of the heart is based on the generation and conduction of the cardiac impulse.
- Pacemaker cells can generate an impulse without any external stimulation, due to changes in electrolyte concentration inside and outside the cell.
- The cardiac impulse is primarily generated from pacemaker cells in the SA node and spreads through the atria in a uniform manner.

- An impulse is conducted from the SA node to the AV node via internodal pathways.
- The impulse passes through the AV node to depolarize the ventricular myocardium through the Purkinje network.
- The conduction system of the heart is self-sustaining although it can be influenced by the nervous and endocrine systems.
- Changes in the ionic potential during the heartbeat can be recorded from the surface of the skin: this is known as the electrocardiogram.

SYNOPSIS

Provide a brief summary of your article (100 to 150 words; no references or figures/tables). The synopsis appears only in the table of contents and is often used by indexing services such as PubMed

The normal cardiac-conduction-system is responsible for the contraction of the heart muscle. Damage or irregular function of the cardiac conduction system can lead to serious and, in some cases, fatal clinical events. Every cardiac myocyte has the potential of contracting when stimulated with an adequate impulse. Electrical impulses are generated through changes in electrolyte concentration inside and outside pacemaker cells (a concentration gradient). The normal cardiac conduction system allows for, not only, the generation of this impulse but, also, its automatic propagation of it throughout the atrial and ventricular myocardium allowing for complete contraction of the heart muscle. In this paper we outline the key components behind the automated generation of the cardiac impulses and the effect these impulses have on cardiac myocytes. Also, a description of the key components of the normal cardiac-conduction-system is provided including the sinoatrial node, the atrioventricular node, the His Bundle, the Bundle branches and the Purkinje network. Other principles, including depolarisation and repolarisation of the myocardium and autonomic nervous system regulation, are also included. Finally, an outline of how each stage of the cardiac conduction system is represented on the electrocardiogram is described, allowing the reader to translate background information about the normal-cardiac conduction system to everyday clinical practice.

1 Introduction

Cardiac disease is the most common cause of mortality in the developed world, and, the number of patient-deaths from cardiovascular related disease rose by a third between 1990 and 2010[1]. This, coupled with a further projected increase in the prevalence of cardiovascular disease,[2] has led to the electrocardiogram (ECG) becoming one of the most used tools in clinical practice. To fully understand the ECG and interpret its results, an understanding of the normal conduction system of the heart is necessary.

The human heart contracts approximately 2.5 billion times during the average person's lifespan; this is accomplished by the cardiac conduction system[3]. The cardiac conduction system is a physiological system whereby the myocardium (heart muscle) is stimulated to contract without the requirement of any external stimulation. Contraction of a cardiac myocyte (heart cell) is initiated by an electrical impulse (the cardiac impulse) which propagates freely through the atrial and ventricular myocardium. This phenomenon occurs because cardiac myocytes are electrically coupled via, so called, gap junctions[4]. All of the myocytes within the heart have the capacity to conduct cardiac impulse; this means that a single stimulation of an atrial or ventricular myocyte can produce contraction of the entire myocardium. During normal activation of the heart, the cardiac impulse originates from pacemaker cells within the sinoatrial (SA) node and uniformly spreads through the atria. The cardiac impulse is then conducted to the atrioventricular (AV) node, via internodal pathways, where it spreads throughout the conduction system of the ventricles and the ventricular myocardium. Irregularities in the normal cardiac-conduction-system can cause cardiac arrhythmias and, as such, an

abnormal ECG. This paper outlines the key principles behind the normal cardiac-conduction-system including the generation of the cardiac impulse and propagation of this impulse from the atria through the normal conduction-system to the ventricular myocardium.

2 The Underlying Principles behind The Heartbeat

2.1 ELECTROLYTES AND CONCENTRATION GRADIENTS

To understand the cardiac conduction system, it is important to understand the way in which cells, in particular, pacemaker and normal cardiac cells, function. The human body is comprised of millions of cells, each cell enclosed by a fatty membrane and surrounded by extra-cellular fluid[5,6]. All components of the cell contain electrolytes. The electrolytic concentration gradient, along with the ability of the electrolytes to cross the cell membrane, allows the generation of an electrical current[7].

For contraction of a cardiac myocyte the most important electrolytes are sodium (Na), potassium (K) and calcium (Ca). The electrolytes are moved in and out of the cell through two main pathways: (1) pumps embedded in the cell membrane and (2) ion channels in the cell membrane[8]. The sodium potassium pump plays an important role in this process as it moves sodium out of the cell and pumps potassium in. A concentration gradient is created because the pump is continuously pumping potassium into the cell leading to a greater concentration of potassium inside of the cell than outside, resulting in a change in intracellular potential. In this process, the opposite is true for sodium as a greater sodium concentration is created on the outside of the cell with a lesser sodium concentration inside. The other method by which electrolytes move in and out of a cardiac myocyte is through ion channels[9]. Unlike the sodium potassium

pump, which allows multiple electrolytes to pass, ion channels are specific to a single electrolyte. Ion channels are voltage gated and allow for each specific electrolyte to move either in or out of the cell depending on the concentration gradient of that particular ion[10]. When potassium channels are opened potassium leaves the cell; when sodium channels are opened sodium enters the cell. It is these opposing reactions that result in an electrical charge across the cell membrane. This is therefore the underlying principle behind generation of the cardiac impulse.

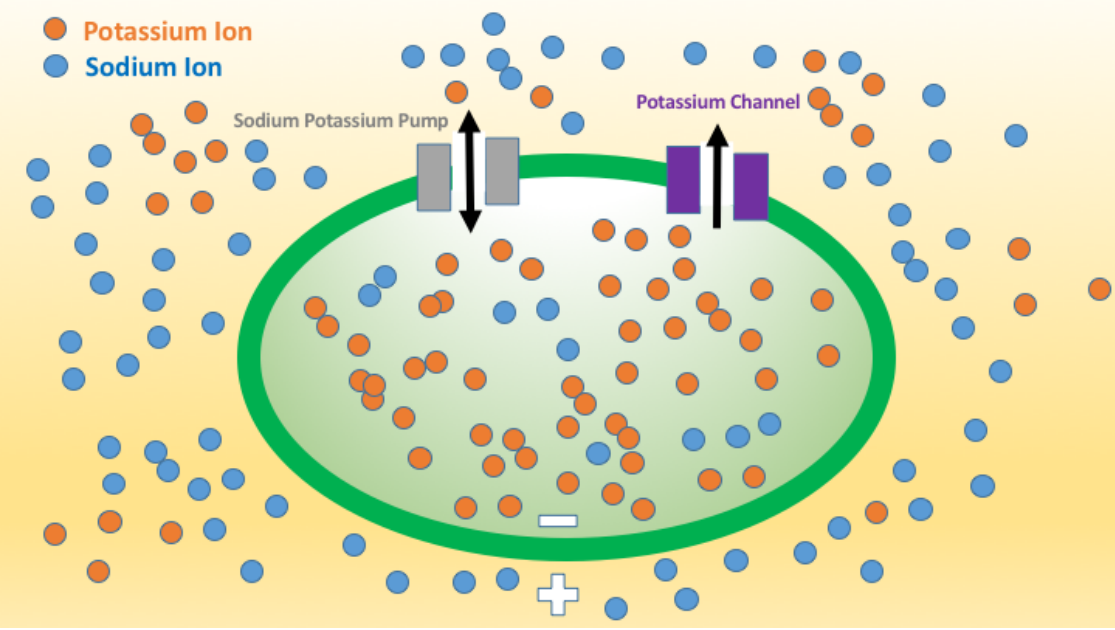

Figure 1. The main components of a normal cardiac myocyte.

2.2 DEPOLARISATION AND REPOLARISATION

Contraction, and subsequent relaxation of the heart, is achieved through depolarisation and repolarisation of all the cardiac myocytes. The change in cell membrane permeability directly affects the electrolyte concentration within and surrounding the cell, creating an impulse. This cardiac impulse propagates through surrounding tissues causing depolarisation of the entire myocardium. Depolarisation involves a surge of

electrical current across the cell membrane, which forces a change in the cells resting potential and generation of an action potential that spreads through the heart. Repolarisation is the process by which the cell returns to its normal resting state.

2.3 ACTION POTENTIAL OF A CARDIAC MYOCYTE

Action potential is a brief change in the voltage across the cell membrane of a muscle or nerve cell when an adequate stimulation is applied. The cardiac action potential is described in five, main phases (0-4). Phase four represents the cell at rest; at this time the cell has a potential of approximately -90mV[11]. An electrical current from a pacemaker cell or surrounding myocyte (muscle cell), then, stimulates the membrane opening the potassium sodium pump allowing sodium to enter, rapidly altering the potential of the cell from negative (-90mV) to positive (+20mV). This is known as phase 0 and is, commonly, referred to as the depolarization phase. Next, the calcium channels open allowing calcium to enter the cell creating a slight fall (Phase 1) and stabilization in the cell's potential (the plateau phase, Phase 2) at approximately +10mV and closes the sodium channel. Calcium is then released from intracellular stores increasing the concentration of calcium within the cell and causing mechanical contraction. In post contraction, Phase 3, the calcium channels close and potassium channels open causing the cell to repolarize and return to its resting potential of -90mV[10] . Once a cardiac myocyte experiences an action potential it rapidly spreads from cell-to-cell. However, once a cell is depolarized it becomes refractory for a short-period-of-time; this essentially means the cell cannot be stimulated again until its reaches its resting state. There are two stages to the refractory period: (1) the absolute refractory phase where no stimulation, no matter how great, will cause the cell to

contract and (2) the relative refractory phase where a large enough electrical current will cause the cell to contract. This prevents excessive rapid contraction of a cardiac myocyte and results in stable and continuous propagation of the electrical current throughout the entire myocardium.

2.4 ACTION POTENTIAL OF A PACEMAKER CELL

Pacemaker cells, unlike standard cardiac myocytes, coordinate the rhythm and pace of the heartbeat and, as such, have automaticity. Pacemaker cells are responsible for the generation of the cardiac impulse and, therefore, have a different action potential from that of standard, cardiac myocytes. Pacemaker cells do not actually contract and, as such, have no plateau phase in their action potential[7,10]. The action potentials of pacemaker cells also differ from that of the normal cardiac myocytes in that automatic cells have the ability to initiate an impulse or electrical current without any external stimulation[11]. In comparison, a normal cardiac myocyte can only contract when stimulated by an external impulse from an electrically coupled cell. The action potential of pacemaker cells is shown in comparison to the action potential of a normal cardiac cell in Figure 2.

Ionic currents play a key-role in the function of pacemaker cells. After repolarization an outward current is created by potassium ions. This is, then, followed by an inward current of sodium ions. These sodium ions are activated post repolarization and are followed by a slow inward current of calcium ions which are activated during depolarization of the cell membrane[9,11].

Pacemaker cells are fundamental to the contraction of the heart and are found in three areas: the SA node, AV node, and bundle of His. Although the cells found in these

areas are classified as automatic, the rate of depolarization does vary across all three types of automatic cells. The SA node has the shortest depolarization phase (phase 4) and, therefore, the quickest firing rate: approximately 60 to 100 times per-minute. The AV junction has a lower firing rate of between 40 to 60 times per-minutes and finally the Bundle branches and Purkinje fibers have a firing rate of less than 40 times per-minute[10]; thus the design is non-competitive.

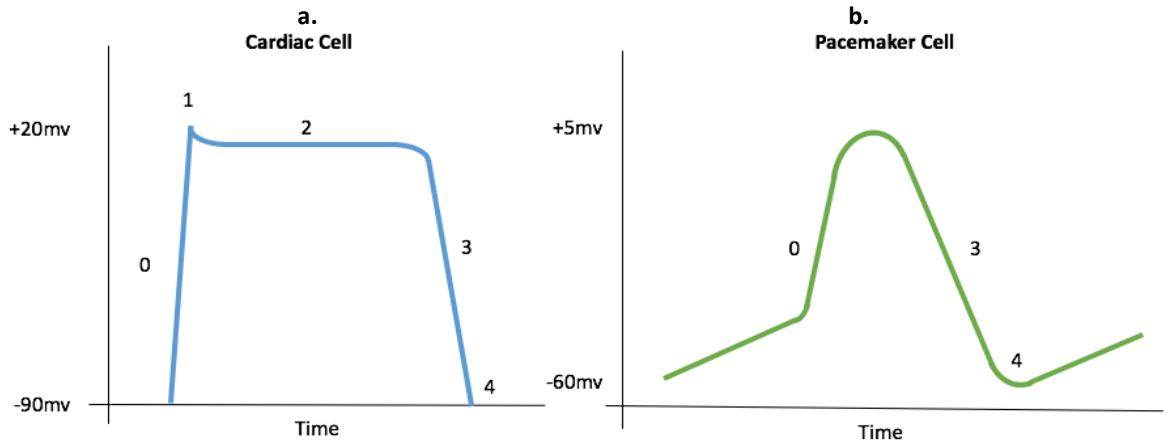

Figure 2. (a) Normal Cardiac Cell Action Potential (b) Pacemaker Cell Action Potential. The action potential of pacemaker cells do not contain a plateau phase, allowing for a much more rapid contraction of the cell.

3 The Conduction System of the Heart

Possibly, the most important aspect of the contraction of the heart is the cardiac conduction system. The conduction system ensures that an electrical impulse generated by pacemaker cells in the SA node can effectively travel throughout the entire atrial and ventricular myocardium, creating a consistent and timely contraction of the heart muscle. The cardiac conduction system is comprised of the SA node, the AV node, the bundle of His, bundle braches, and the Purkinje network. As mentioned

previously, the heartbeat originates from the SA node in the upper right atrium and has the primary responsibility for the heart's electrical activity.

4 Atrial Activation

Atrial activation begins with the generation of a stimulating electrical impulse from the pacemaker cells of the SA node[12]. This pulse propagates freely throughout the atrial myocardium causing contraction of the right and left atria. Sir Thomas Lewis from the united Kingdon, was the first to analyse contraction of the atria. He described it as follows:

"the excitation wave in the auricle may be likened to the spread of fluid poured upon a flat surface, it edges advancing as an ever widening circle, until the whole surface is covered; such variation as exists in the rate of travel along the varies lines in the auricle fully accounted for by the simple anatomical arrangement of the tissue". Sir Thomas Lewis 1908[13].

4.1 THE SINOATRIAL NODE

For years, many were baffled by the question, "How does the heart beat?" Until the electrica- conduction-system of the heart was fully accounted for by the discovery of the SA node by Keith and Flack in 1907[12].

The SA node is a group of specialized myocardial cells located at the junction of the superior vena cava and the right atrium close to the crest of the atrial appendage. The node consists of two types of myocytes: (1) the central nodal cells, arranged in a complex interdigitating manner with connective tissue and (2) the transitional myocytes that change gradually from the typical pacemaker cells to ordinary myocytes[14].

The location of the SA node was first described by Lewis[15] in 1910 and, later, confirmed on a canine model. In 1952, transmembrane potentials were first recorded from pacemaker cells of a frog heart.[14] This was closely followed by the mammalian heart in 1955[16]. These studies revealed that the most dominant feature of pacemaker cells is the spontaneous deploarisation of the cell-membrane. Further discoveries into the origin and function of pacemaker cells of the SA node occurred in 1963 when Trautwein and Uchizono[17] discovered dominant pacemaker cells in rabbits using microelectrode structures. They determined that the origin of the heartbeat occurred in a small area (approx. 0.3mm square) which contained about 5,000 pacemaker cells that fire synchronously[14].

4.2 INTERNODAL PATHWAYS

The impulse generated by pacemaker cells in the SA node is conducted through the atria via four main pathways in the atrium. Three of these pathways are found in the right atrium and one in the left atrium. These structures are known as internodal pathways as they carry the cardiac impulse from the SA node to the AV node. Internodal pathways consist of specialised myocytes, which run from the SA node to the AV node. Previously, internodal pathways were thought to consist of atrial myocytes alone; however, studies into the propagation speed of impulses from the SA node to the AV node found that the speed achieved was much greater than what is possible from normal atrial myocytes alone[18]. In fact, these internodal pathways have been shown to exhibit Purkinje fibre-like characteristics, meaning they have a much greater conduction velocity. However, much controversy still remains around this issue and the

characteristics of the cells, which conduct the cardiac impulse from the SA node to the AV node have not been conclusively defined[19].

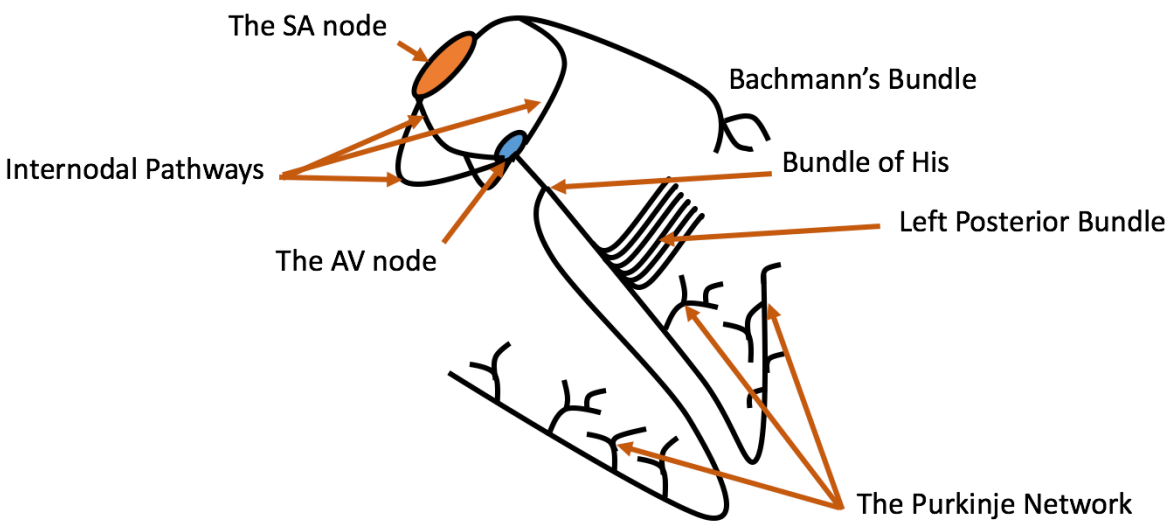

Figure 3. The cardiac conduction system.

5 Ventricular Activation

The atrial stimulus cannot be propagated throughout the ventricular myocardium because the atria and ventricles are separated by an electrically non-conductive cardiac-skeleton. The AV node instead causes contraction of the ventricular myocardium.

5.1 THE ATRIOVENTRICULAR NODE

The AV node coordinates the contraction of the heart by conducting the normal electrical impulse from the atria to the ventricles. The AV node delays the electrical impulse by approximately 0.12s[7]. This delay is vital as it ensures the atria have filled with blood before the blood is ejected from the ventricles and pumped throughout the

circulatory system. This ensure atrial-ventricular synchrony and allows for mechanical activity which is far slower than electrical activity.

In the presence of atrial arrhythmias such as atrial fibrillation (AF), te AV node is critically important because it actually blocks most of the many uncoordinated electrical impulses through[20]. AV conduction during normal cardiac activation occurs via two different pathways: (1) the first pathway has a slow conduction velocity but shorter refractory period and (2) the second pathway has a faster conduction velocity but longer refractory period[14].

5.2 THE BUNDLE OF HIS, BUNDLE BRANCHES AND THE PURKINJE NETWORK

From the AV node the impulse is conducted to the bundle of His which was discovered by Wilhelm His, a Swiss Cardiologist and Anatomist, in 1893[10]. The bundle of His is divided at the septum to provide the left and right bundle branches. These branches carry the cardiac impulse into both the left and right ventricles. The branches of the bundle of His end at a branching junction of the Purkinje system. The Purkinje system was discovered by the Czech physiologist Johannes Evangelist Purkinje in 1893. The primary function of the His-Purkinje system is to rapidly conduct the cardiac potential throughout the ventricles to ensure that the muscle contractions are in the correct order and blood is sufficiently ejected. The His-Purkinje system conducts action potentials much more rapidly than regular ventricular myocardium (2.3m/s vs. 0.75m/s)[14].

6 Factors which Influence the Cardiac Conduction System

6.1 AUTONOMIC REGULATION

Since pacemaker cells within the cardiac-conduction-system have automaticity[9] they do not require stimulation from the central-nervous-system. However, the heart is heavily influenced by the autonomic nervous-system because sympathetic and parasympathetic nerve branches run from the brain to the heart[21]. These branches of nerves regulate heart rate, speed of conduction, and contractility so that the heart can match cardiac output with the demands of the circulatory system during any given task. The sympathetic nerve supplies the SA node, AV node, atria and ventricles and is responsible for the fight-or-flight complex[7]. Although not in detail, briefly, the sympathetic nerve not only increases the heart rate but, also, alters the conduction and contractility of the heart. The sympathetic nerve has an increased activity during times of emotional excitement, exercise, and physiologiocal and pyscholgical stress. For example, pharmaceuticals such as beta blockers shield the heart from sympathetic nerve activity leading to a lower heart rate, blood pressure, and, as a result, a lower myocardial workload. The parasympathetic nerve supplies mainly the SA node and works in the opposite fashion to slow down the heart. The more activity there is from the parasympathetic nerves the slower the heart rate will become. Increased vagal tone is often associated with patients who suffer a myocardial infarction.

7 Abnormalities of the Conduction System

When there is damage to the normal conduction-system of the heart this can lead to severe clinical events. For example, patients suffering damage to the myocardium due to ischemic heart disease or bundle-branch-block can develop bradycardia[22] or defects such as complete heart block. In addition, abnormal electrical conduction in the atrium, such as AF is a leading cause of stroke events[23,24]. During AF the atria does not

contract effectively so blood begins to clot in the atria, particularly in the left atrial appendage.

Another example of abnormalities of the cardiac conduction stem is Wolf Parkinson White (WPW) syndrome. To maintain effective contraction of the myocardium there must be a substantial delay between atrial and ventricular contraction (0.12s). This allows the atria to complete its contraction and for the blood to effectively fill into the ventricles. If this does not occur, which is the case in some patients with arrhythmias, such as WPW syndrome, there is a reduction in cardiac output.

8 The Cardiac-Conduction-System and the ECG

The function of the cardiac-conduction-system can be recorded from the surface of the skin; this is known as the ECG. The ECG is a representation of the electrical activity of the heart and is one of the most widely used diagnostic tools in medicine. As the ECG is a measurement of the electrical activity of the heart, it can be used to monitor and detect abnormalities in the normal cardiac-conduction-system. The ECG is recorded through conductive electrodes placed on the surface of the skin which transduce the ionic current on the skin's surface to electrical current for analysis by electronic equipment.

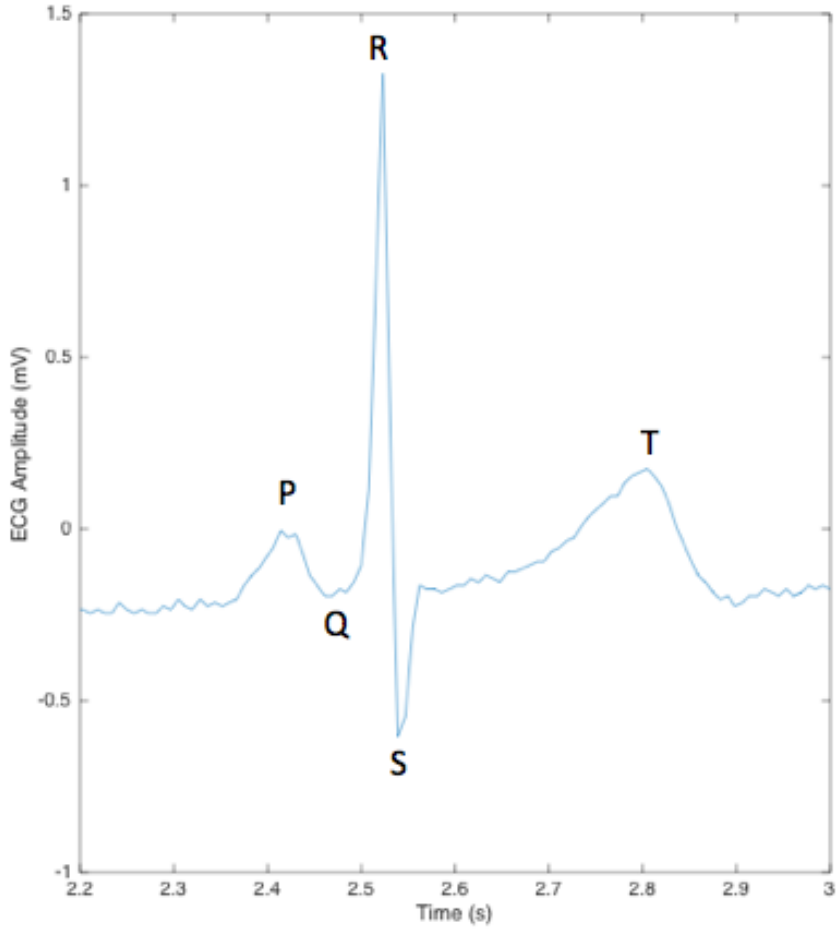

Figure 4. A normal ECG waveform recorded from a healthy patient (16272) taken from the MIT-BIH Normal Sinus Rhythm Database [22].

The most common form of ECG recorded in clinical practice is the 12-lead ECG which involves the placement of 10 electrodes on the body. Other ECG monitoring equipment, such as bedside monitors and telemetry systems. also record and analyse the ECG ; however, these methods of ECG monitoring are usually performed with a reduced number of electrodes, commonly two or three. The ECG consists of five main wave characteristics known as the PQRST complex. The P-wave reflects atrial depolarization (contraction). The P-Q interval is referred to as the period of atrial systole which corresponds to the time it takes for the impulse to travel from the SA node to the

AV node via the internodal pathways. The QRS complex refers to the conduction of the cardiac impulse through the AV node, the bundle of His, the bundle branches and the Purkinje network, and therefore represents depolarization of the ventricular myocardium. The T-wave represents repolarization of the ventricular myocardium; whereby, all cardiac cells return to their resting potential and the completion the heart beat is achieved.

9 Summary

The normal conduction system of the heart is a complex structure comprised of specialised cells, which allow for spontaneous initiation and conduction of an electrical impulse. These impulses are responsible for contraction of the myocardium in a synchronised fashion and maintenance of an adequate heart rate. However, if abnormalities are found in any of the components of the cardiac-conduction-system, this can lead to or dangerous heart rates and rhythms.

A fundamental principle of contraction of the heart is the spontaneous generation of an electrical impulse which occurs due to rapid changes in the permeability of the pacemaker cells. This electrical impulse is generated from pacemaker's cells, found in the SA node that are responsible for atrial activation. The impulse is then conducted to the AV node through internodal pathways. The impulse then enters the bundle of His where it is conducted to the Purkinje network and the complete contraction of the heart muscle is achieved.

The paper has provided a description of the key components of the cardiac-conduction-system and describes how each component functions in synchronicity to allow for the normal and sustained contraction of the myocardium. It also outlines some

abnormalities which can be found in the normal cardiac-conduction-system due to cardiovascular disease. An outline of the role of the sympathetic nervous system in regulating the function of the heart is also provided.

To conclude, this description of the fundamental principles behind the normal cardiac-conduction-system and how they relate to the origin and maintenance of the heartbeat should allow for a better understanding of the underlying physiology of the heartbeat and the ECG.

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