The College of Saint Rose

Mathematical Models for Cardiac Action Potentials

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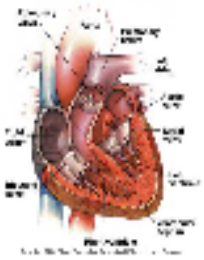
Abstract

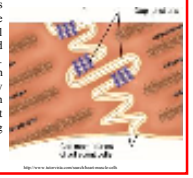
The heart is an amazing muscle that pumps five quarts of blood per minute throughout the entire human body. For the heart to do this, it must have a normal heart beat. A cardiac arrhythmia is basically the condition in which the heart's normal rhythm is disrupted. Cardiac arrhythmias continue to be an important clinical problem to diagnose and treat. They occur from the irregular formation or abnormal conduction of an action potential. An action potential is a rapid change in the electrical potential across a myocardial cell from negative to positive and back. To investigate the relationship between the cardiac action potential in cardiac arrhythmias, we have considered how mathematical modeling can be used to examine the behavior of an action potential. In this poster we explore the relationship between the spread of action potential across myocardial cells and heart arrhythmias and a present the Hodgkin-Huxley model for Cardiac Action Potential.

Background



How the Heart Works: The heart is a pump with four chambers, two upper and two lower. The upper, *atrium* chambers are small. The lower, *ventricle* chambers are larger. Oxygen-starved blood enters the right atrium via the superior and inferior vena cava veins. The right atrium pumps the blood to the right ventricle, which then pumps the blood to the lungs via the pulmonary arteries. After passing through the richly vascularized lung tissue, oxygen-rich blood return to the heart via the pulmonary veins and into the left atrium. The left atrium pumps the blood to the left ventricle, the launching pad that pumps the blood through the huge aortic artery and delivers blood to the rest of the body.

Myocardial Cells: Myocardial cells are what make up the muscle of the heart. The most important aspect of myocardial cells is the intercalated discs. Within the intercalated discs there are gap junctions. Without these gap junctions, the action potential would not have a way to spread smoothly across myocardial cells. Think of the gap junctions like open pathways between the cells that allow for the depolarization current to run smoothly from cell to cell without having to leave one cell before going to another.

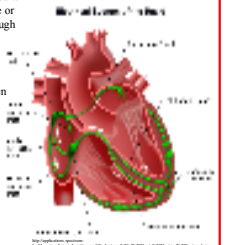


Introduction

Cardiac Arrhythmia : is a term for any of a large and heterogeneous group of conditions in which there is abnormal electrical activity in the heart. For instance, Brugada syndrome is a life-threatening disorder in which the structure of the heart is normal but the ion current on the cell membrane is altered. Ventricular fibrillation is the most typical arrhythmia that this syndrome causes. An electrocardiograph can be used to diagnose Brugada syndrome and an implantable cardiac defibrillator can be implanted so when the heart begins an arrhythmia the defibrillator can stop it and make the heart return to a normal rhythm.

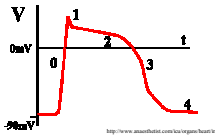
Cardiac Action Potential: The cardiac action potential is a specialized action potential in the heart, with unique properties necessary for function of the electrical conduction system of the heart. It differs significantly in different portions of the heart. This differentiation of the action potentials allows the different electrical characteristics of the different portions of the heart.

The action potential starts at the Sinoatrial node or SA node in the right atrium. It then travels through intermodal pathways across both atria until it reaches the atrioventicular node or AV node. There is then a 100 millisecond pause while the atria contract and push the blood into the ventricles. After this the action potential then moves through the AV bundle that is located in the septum (the tissue separating the two ventricles). When these fibers start to split apart they turn into Purkinje fibers. The action potential then runs through these fiber causing ventricular contraction.



Cardiac Action Potential Phases

Phase 0-1: First, the resting potential has to be around -90 mV, then a stimulus excites a muscle cell. This is when the voltage sensitive sodium channels open and sodium ions enter the cell. The sodium channels then close when the transmembrane potential reaches approximately +30 mV. These channels stay closed until the potential of the membrane reaches -60 mV.
Phase 2: The voltage sensitive calcium channels open and calcium ions move into the cell. The membrane potential remains relatively constant for an extended amount of time. This is known as the plateau.
Phase 3: The calcium channels start to close and potassium channels begin to open. Potassium ions rush out of the cell. As the membrane potential gets closer to -90 mV the potassium channels start to close. This is known as repolarization.
Phase 4: The membrane is at its resting potential at -90 mV. The membrane is now waiting for a new stimulus.



The Hodgkin-Huxley Model for Cardiac Action Potential:

- Is a model that describes how action potentials in cardiac myocytes are initiated and propagated
- The semi-permeable cell membrane separates the interior of the cell from the extracellular liquid and acts as a capacitor and is represented as a capacitance C_m
- It depicts the time and voltage–dependent sodium and potassium conductance, g_{Na} and g_k in terms of number of gating particles. These two voltages are independent from each other. A third, smaller conductance called "Leak" $g_{L\,is}$ independent of the membrane potential.
- The total ionic current flowing is the sum of the sodium, a potassium and the leak current is given by: $I_{total} = I_{ionic} = I_{Na} + I_K + I_{leak}$
- The electrochemical gradients driving the flow of ions are represented by batteries E_{Na}, E_k and E_l;
- The ion pumps and exchangers are represented by current sources I_C
- Figure 1 represents the The Hodgkin-Huxley model and shows that:
  - The potassium channel is modeled by a variable resistor g_k and a battery E_K;
  - The sodium channel is modeled by a variable resistor g_{Na} and a batter E_{Na}
  - The "leak" is modeled by a variable resistor g_{leak} and a batter E_{leak}
- At rest, the sodium and potassium conductances are zero, that is, the channels are closed and the flow of ions through the respective channels is turned off.
- The rate of change in membrane potential (V) over time is proportional to the sum of the currents in the circuit. This is given by the following equation (1):

$$\frac{dV}{dt} = \frac{-I_{total}}{C_m}$$

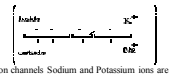
Where C_m is the membrane capacitance and I_{total} is the algebraic sum of ionic currents.

- The individual ionic current $I_i(t)$ are linearly related to the driving potential by (2):

$$I_i(t) = (V - E_i)g_i$$

Where E_i is the reversal potential of the i-th ion channel, and gi are the channel conductance.

Voltage-gated ion channels



Ion channels Sodium and Potassium ions are involved in action potential generation.

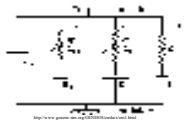


Figure 1: Basic components of Hodgkin–Huxley-type models: The lipid bilayer is represented as a capacitance (C_m). Two voltage-gated and leak ion channels representing the sodium (g_{Na}) and the potassium (g_k) channels and g_L respectively. The electrochemical gradients driving the flow of ions are represented by batteries E_K, E_{Na} and E_L and ion pumps and exchangers are represented by current sources (I_C).

The Hodgkin-Huxley Model for Cardiac Action Potential:

The membrane voltage V, is the same for each parallel branch of the circuit in Figure 1. Hence we can write:

For the Sodium branch: $V = E_{Na} + I_{Na}/g_{Na} \rightarrow I_{Na} = g_{Na} \cdot (V - E_{Na})$
For the Potassium branch: $V = E_k + I_k/g_K \rightarrow I_K = g_K \cdot (V - E_K)$
For the Leak branch: $V = E_L + I_L/g_L \rightarrow I_L = g_L \cdot (V - E_L)$

Using the Kirchhoff's law: the input current must balance the outgoing current:

$$I_C + I_L + I_K + I_{Na} = I_{in} \rightarrow I_C = -I_L - I_K - I_{Na} + I_{in}$$

Substituting the currents into the gives the first Hodgkin-Huxley equation for the membrane voltage:

$$C_m \frac{dV}{dt} = g_{Na}(E_{Na} - V) + g_K(E_K - V) + g_L(E_L - V) + I_{in}$$

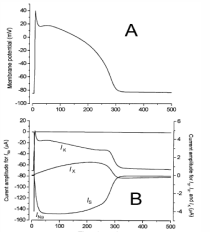


Fig. 1: Computed action potential in response to a 1-ms current pulse of 7-mA amplitude. The simulation was performed according to the B-R model for the ventricular cell. Panel A contains membrane potential on a 0–500 msec scale, whereas panel B shows the corresponding four types of ionic currents. The two inward currents were the fast current Na^+ (I_{Na}) and the slow secondary current labeled I_S. In this and the following figures, inward current was plotted downward. The outward currents, both of which are attributed to K^+, are the time-independent I_K, and the voltage- and time-dependent I_K.

Summary

- A Cardiac Arrhythmia is a condition in which the normal heart rhythm is disrupted.
- Cardiac Arrhythmias continues to be an important clinical problem to diagnose and treat
- The Hodgkin-Huxley Model can be used to describe Action Potential behavior has it is initiated and propagated in cardiac muscle cells.

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