C 2. Electrical properties of the heart

a. Explain the ionic basis of the spontaneous electrical activity of cardiac muscle cells (automaticity).

resting membrane potential (V_m)
- maintained by Na^+-K^+ ATPase pump and ion channels
- in [Physiol G](#)
- normally -90 mV

depolarization
- phase 0
    - m-gates open over 0.2 ms around V_m -65 mV, raising g_{Na} markedly
    - rapid influx of Na^+ (and Ca^{2+}), V_m rises to +30 mV
    - h-gates close over 1 ms and g_{Na} falls again
    - h-gates remain closed until repolarization (refractory period)
- phase 1
    - when V_m is positive in phase 0, K^+ efflux through i_{to} channels is increased due to electrochemical gradient
    - this is the i_{to} "transient outward current" of phase 1
        - i_{to} is pronounced in atrial cells which merge phases 1 and 3
- phase 2
    - plateau is maintained by Ca^{2+} influx through
        - L channels (predominant) open at V_m +30 mV
        - stay open to maintain plateau
        - T channels open briefly at V_m -20 mV
        - minor effect
    - Ca^{2+} influx is balanced by K^+ efflux
        - K^+ current through i_{K1} channels is *inwardly rectified*
            - g_K is high for inward currents and low for outward currents
        - g_K is low during phase 2 and the small K^+ current balances the Ca^{2+} current
    - Ca^{2+} channels slowly inactivate and i_K channels slowly open
- phase 3
    - delayed rectifier i_K channels finally open
    - i_{K1} current rises as V_m falls
    - outward K^+ current through i_{to}, i_{K1} and i_K repolarize cell
- phase 4
    - Ca^{2+} concentration is restored by Ca^{2+}-Mg^{2+} ATPase pump and Ca^{2+}/Na^+ secondary active transport
    - Na^+ and K^+ gradients are maintained by Na^+-K^+ ATPase pump
    - in automatic cells, specific Na^+ channels open with hyperpolarization to produce i_f, an inward current depolarizing the cell
    - when V_m becomes partly depolarized, Ca^{2+} channels open, initiating a rapid rise in V_m until an action potential is initiated

Many cardiac muscle cells display automaticity (spontaneous regular action potentials). The cells of the conducting system display the greatest automaticity; usually the SA node cells start the regular action potentials which spread to the rest of the myocardium.

The cells of the SA node have membranes which are relatively permeable to Na^+ and so have a resting membrane potential of only -55 mV to -60 mV. At this potential the fast Na^+ channels remain permanently closed and refractory. The gradual leak of Na^+ into the cell causes a progressive rise in the membrane potential until the slow Ca^{2+} channels are activated. The influx of Ca^{2+} and Na^+ generates an action potential for 100 to 150 ms before the channels close and the K^+ channels open, repolarizing the cell.

b. Describe the normal and abnormal processes of cardiac excitation.

The sinus nodal fibres fuse with the atrial cardiac muscle fibres, carrying the action potential throughout the atria. There are several condensation of muscle fibres which carry the action potential more rapidly: the anterior interatrial band and the internodal pathways which run to the AV node. The action potential reaches the AV node after 30 ms. Propagation of the action potential throughout the atria takes under 100 ms.

The AV node consists of transitional fibres from the internodal pathways, a node within the atrium and penetrating fibres connecting to the distal portion of the AV bundle in the ventricle. The fibres of the AV node conduct the action potential very slowly due to their low degree of polarization, small size and few gap junctions. This results in a delay in transmission of the action potential of about 130 ms. The AV node can conduct only one way in normal contraction.

Within the interventricular septum, the AV bundle joins the Purkinje fibres. These conducting cells are of a large diameter and have many gap junctions, transmitting the action potential rapidly throughout the ventricles. The transmission time for the entire Purkinje system is 30 ms. Propagation to the entire ventricular muscle takes another 30 ms, yielding a coordinated contraction.

Abnormalities of cardiac conduction
- accessory atrioventricular muscle bundle (WPW) may lead to recurrent arrhythmias or rapid conduction of AF or flutter.
- EAD
  - early after depolarization occurs in phase 3 at a slow heart rate
  - Ca^{2+} channels recover and can be reactivated before phase 4
- DAD
  - delayed after depolarization occurs in phase 4 at high heart rate
  - raised ICF $[Ca^{2+}]$ results from high rate and produces spontaneous Ca^{2+} release from sarcoplasmic reticulum
- ectopic pacemaker
  - AV node or Purkinje fibres or even muscle may generate action potentials at a higher frequency than the SA node and thus become the pacemaker
  - If transmission of action potentials is blocked, automaticity of more distal cells will produce a continued but slow rate of contraction
- fibrillation
  - if electrical activity in the atria or ventricles becomes uncoordinated because of high rate or abnormal conduction, a stable state of fibrillation may result
- abnormal cardiac may be terminated by external initiation of action potentials
  - overdrive pacing
  - DC reversion

c. Explain the physiological basis of the ECG.

The ECG is a representation of the net electrical potential detected at the skin from the electrical events taking place in the cardiac cycle. Depolarization moving towards the observed lead gives a positive deflection as the extracellular fluid becomes more negatively charged around depolarized tissue than around polarized cells. The P wave represents atrial depolarization, the QRS complex, ventricular depolarization and the T wave ventricular
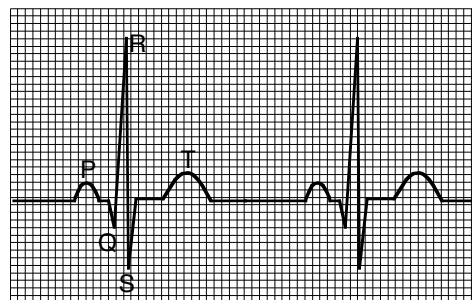
repolarization.

During the plateau phase of depolarization, there is little effect on the ECG as there is little flow of current. The initial depolarization of the ventricles produces the Q or R wave, the gradual reduction in membrane potential is represented in the ST segment and the repolarization produces the T wave.

Thus the PR interval represents the time between atrial and ventricular depolarization, usually 160 ms, and the QT interval is close to the period of ventricular contraction, about 350 ms.

The standard leads of the ECG are I, II, III, aVR, aVL, aVF and V_1 to V_6.

Depolarization of the atria proceeds from the SA node around the walls, giving a net vector at about 60°. Repolarization of the atria takes place in the same direction, but occurs at the same time as ventricular depolarization which obscures it on the ECG.

Because depolarization of the ventricles proceeds from the septum down to the apex and around the left and right ventricles, finishing with the superior part of the left ventricle, the net electrical vector during the QRS complex is initially towards the apex (60°), then swinging to the left (-60°). Repolarization proceeds from the apex and outer surface back towards the base of the heart, generating a net vector about 40° in the frontal plane.

The QRS axis may be altered by the position of the heart. LAD is seen in expiration and in short fat people and RAD in inspiration and in tall thin people. The normal range is 20° to 100°. Ventricular hypertrophy causes axis deviation towards the hypertrophied ventricle, because of the increased muscle mass and delay in depolarization. Bundle branch block causes a delay in depolarization of one ventricle and thus results in axis deviation towards the blocked side as well as widening of the QRS complex. Bundle branch block also causes repolarization of the blocked ventricle much later than the ventricle with normal conduction, causing the axis of the T wave to deviate away from the blocked side.

The size of the QRS complex is determined by the muscle mass of the ventricles and the effective conduction of electrical potentials to the skin. Thus it is increased in ventricular hypertrophy and reduced in pericardial effusion or COAD.

When part of the ventricle is acutely injured (usually infarcted) it remains constantly depolarized. This produces an electrical vector directed away from the infarct. As the point in the ECG during which no current flows is the start of the ST segment when the entire ventricle is depolarized (J point), the ST segment is elevated relative to the TP segment in the leads over the site of injury. This is because the ST segment remains the true baseline, while the TP segment is depressed by the vector produced by the infarcted muscle while the rest of the ventricle is polarized. With reperfusion or fibrosis, this effect on the TP segment diminishes over time.

Digoxin prolongs the period of depolarization of cardiac muscle, causing changes in the T wave and ST segment in overdose as well as impairing conduction at the AV node.

d. Describe the factors that may influence cardiac electrical activity.

Na^+
 gradient has little effect on resting membrane potential
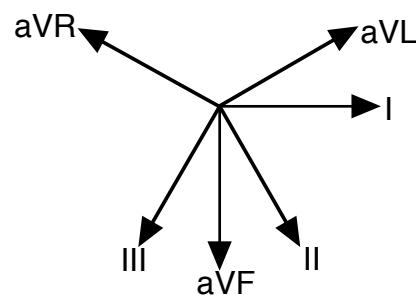 high ECF $[Na^+]$ is required for phase 0 V_{max}
 gradient required for secondary transport of Ca^{2+} out of the cell
K^+
 gradient is the major determinant of resting membrane potential
 low ECF $[K^+]$ is required for maintaining the electrical gradient which drives phase 0
 high ECF $[K^+]$ causes low V_{max} and slow conduction

Ca^{2+}

low ECF [Ca^{2+}] or blockade of Ca^{2+} channels increases the slope of phase 2 and reduces its duration, it also markedly reduces force of contraction

cycle length

i_K inactivates very slowly

rapid heart rate results in i_K being active in phase 2

increased slope and reduced duration of phase 2 (adaptive)

Activity of the SA and AV nodes is controlled by parasympathetic and sympathetic nerves. Vagal stimulation releases acetylcholine which increases membrane permeability to K$^+$ and thus hyperpolarizes the cells. This reduces the rate of discharge at the SA node and delays or blocks conduction in the small fibres of the AV node.

Sympathetic nerve stimulation releases noradrenaline which increases intracellular cAMP via G-protein-linked ß-receptors. A rise in protein kinase activity increases membrane permeability to Na$^+$ and Ca^{2+} as well as upregulating the Ca^{2+} uptake by sarcoplasmic reticulum. Increased Na$^+$ and Ca^{2+} permeability leads to more rapid depolarization of cells and more rapid uptake leads to quicker relaxation. These changes thus yield both chronotropic and inotropic effects.

e. Describe and explain the mechanical events of the cardiac cycle and correlate this with the electrical and ionic events.
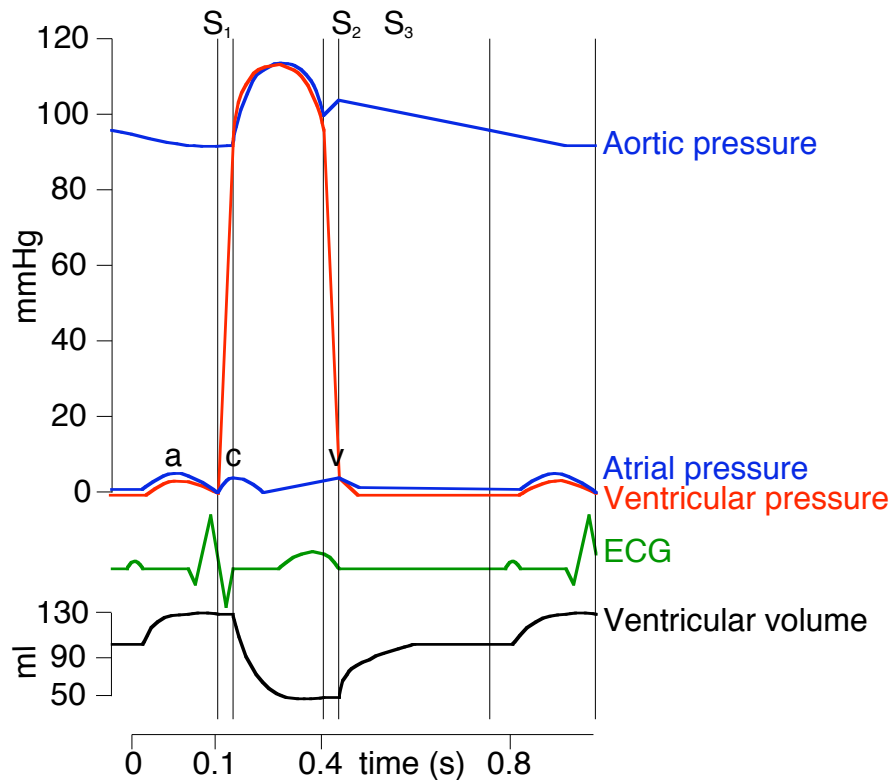
The cardiac cycle consists of diastole and systole. During diastole, the heart initially fills with blood passively from venous return. The SA node initiates the electrical activity which drives the cardiac cycle. This leads first to atrial depolarization, which produces the P wave of the ECG and contraction which increases the end diastolic volume of the ventricles about 25% and produces the venous a wave.

After a delay of about 160 ms, the conducting system of the ventricles and the ventricles themselves depolarize, generating the QRS complex, and contract, closing the AV valves (S$_1$) and producing the venous c wave. Intraventricular pressure rises rapidly (isovolumetric contraction), opening the aortic and pulmonary valves at around 80 mmHg and 8 mmHg respectively.

There is a period of rapid ejection in systole, followed by slower ejection and then closure of the aortic and pulmonary valves (S_2). During systole the atria have filled with venous blood, producing the v wave. Relaxation of the ventricles also coincides with the T wave of the ECG. The cycle then begins again with passive filling of the ventricles.