SIMULTANEOUS AMBULATORY CARDIAL AND OESOPHAGEAL MONITORING

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The contents of this thesis are based on my own research

Linda Hickey

ABSTRACT

A method for recording and analyzing patient signals is described. The electrocardiogram and the pH in the lower oesophagus are simultaneously monitored over a 24 hour period. Signals are recorded onto cassette tape for later analysis.

The pH record is analyzed for reflux episodes which are correlated with patient symptoms. The corresponding ECG episodes are checked for ischemia which appears as depression of the ST segment.

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CHAPTER 1 INTRODUCTION

1.1 OBJECTIVES

The aim of this project was to provide the instrumentation and analysis software for a medical trial to be conducted at a local hospital. The trial would investigate the relationship between angina and oesophageal reflux (or regurgitation). These two ailments are often discussed together, although one reflects a problem in the heart and the other a problem in the digestive tract. The reason is that both are felt as chest pain by the patient. This presents a problem for the doctor when he is making a diagnosis. However, the purpose of this trial was to establish a link between angina and oesophageal reflux - does one cause the other?

A portable recording device used to capture the electrocardiogram (ECG) was already available. It was adapted to simultaneously record the pH signal from an electrode placed in the oesophagus. The signals were recorded onto magnetic tape for later analysis. Software was written to transfer the analogue patient signals onto digital computer. The ECG and pH signals were analyzed using specially developed algorithms. The final stage was to correlate incidents of angina with oesophageal reflux.

1.2 THESIS OVERVIEW

A full description of the medical background to the project is given in Chapter 2. The first section discusses the physiology and in particular the electrophysiology of the heart. This facilitates an explanation of the electrocardiogram. We are particularly interested in angina, its cause and its effect on the ECG.

The oesophagus is also described, with an explanation of oesophageal reflux. Criteria for recognising angina in the ECG and reflux in the pH record can then be established.

The medical trial is then described with a review of background literature. Each patient must be carefully prepared to ensure a successful 24-hour recording.

Chapter 3 is devoted to a description of the hardware used in the project. There is a technical review of Holter (ECG) recording technology and pH monitors. The recorder we used is novel in that it stores a 24-hour record of both the ECG and the pH signals. It is described in detail, together with the playback unit which was used to replay patient tapes.

A description of ECG and pH analysis algorithms is given in Chapter 4. It is preceded by a comprehensive literature review of ECG analysis techniques. The analysis of the pH signal is more straightforward and involves calculating statistics based on the number and duration of reflux episodes. There is also a description of the analogue to digital conversion of the patient signals, i.e. transferring patient tapes onto computer.

The medical results of the clinical trial are presented in Chapter 5. Finally, the project is discussed in Chapter 6. Conclusions are drawn and recommendations are made for future work.

CHAPTER 2 THE MEDICAL BACKGROUND

2.1 THE NORMAL HEART

The heart is a hollow, muscular organ about the size of the owner's fist. It weighs about 255g (9 oz) in women and is slightly heavier in men. Its function is to pump oxygenated blood through the body and it can do this at a rate of 5.5 litres of blood per minute or 2,000 gallons per day. The heart lies between the lungs, slightly to the left of the sternum.

2.1.1 The Structure of the Heart

The heart is composed of three layers of tissue:

1. **The Pericardium:**

   The heart is enveloped by a double sac called the pericardium. The outer sac consists of fibrous tissue and the inner sac is a double layer of serous membrane (a membrane that lines a cavity which has no communication with the external air [1]). The outer layer of the serous membrane lines the fibrous sac, while the inner is attached to the heart muscle. The serous membrane is made up of cells which secrete serous fluid into the space between its two layers. This allows smooth movement between the layers when the heart beats.

2. **The Myocardium:**

   The myocardium is composed of specialised muscle tissue known as cardiac muscle. This muscle is found exclusively in the heart. Each cell has a nucleus and one or more branches (Figure 2.1). The ends of the cells are in very close contact with

adjacent cells. These joints are known as intercalated discs. Effectively cardiac muscle is a 'sheet' of cells and when an impulse of contraction is initiated, it can spread from cell to cell over the entire area of the muscle.

The myocardium is thickest at the apex of the heart and thins out towards the base. The atria and ventricles are separated by a ring of fibrous tissue. Consequently, when a wave of contraction passes over the atrial muscle, it can only spread to the ventricles through the conducting system.

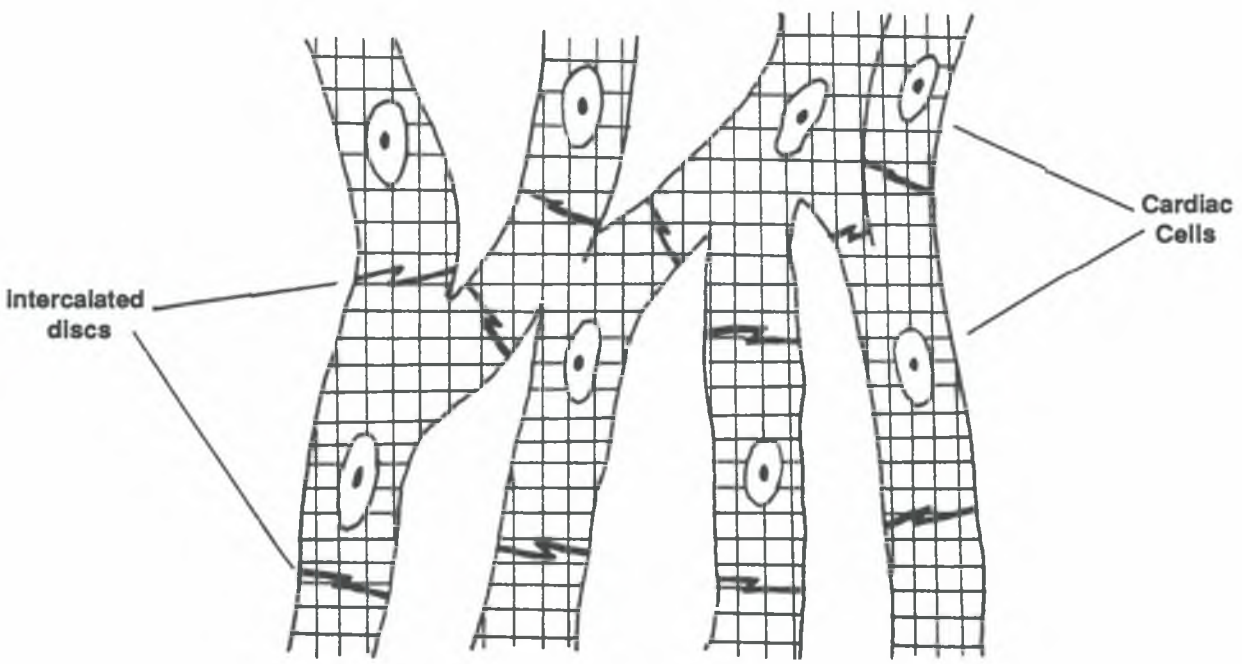


Fig. 2.1
Cardiac Muscle

3. **The Endocardium:**

This is the smooth inner lining of the heart.

2.1.2 The Interior of the Heart

The interior of the heart (Figure 2.2a) is divided into a right and a left side by a partition of muscular tissue and endocardium known as the septum. This gives rise to the right atrium (RA) and ventricle (RV) and the left atrium (LA) and ventricle (LV). The valves dividing the atria from the ventricles are formed by double folds of endocardium strengthened with fibrous tissue. These valves open and close as a result of changes in the pressure of blood within the chambers. Flow is always from the atria to the vertricles because the valves are prevented from opening upwards by the chordae tendinae (tendinous cords) which extend from the valves to the ventricle walls. (Figure 2.2b).

Although the chambers of the heart are full of blood, they cannot nourish the heart. The cardiac muscle receives its oxygen rich blood from a system of arteries known as coronary arteries. The name "coronary" comes from the fact that the arteries appear like a crown surrounding the heart.

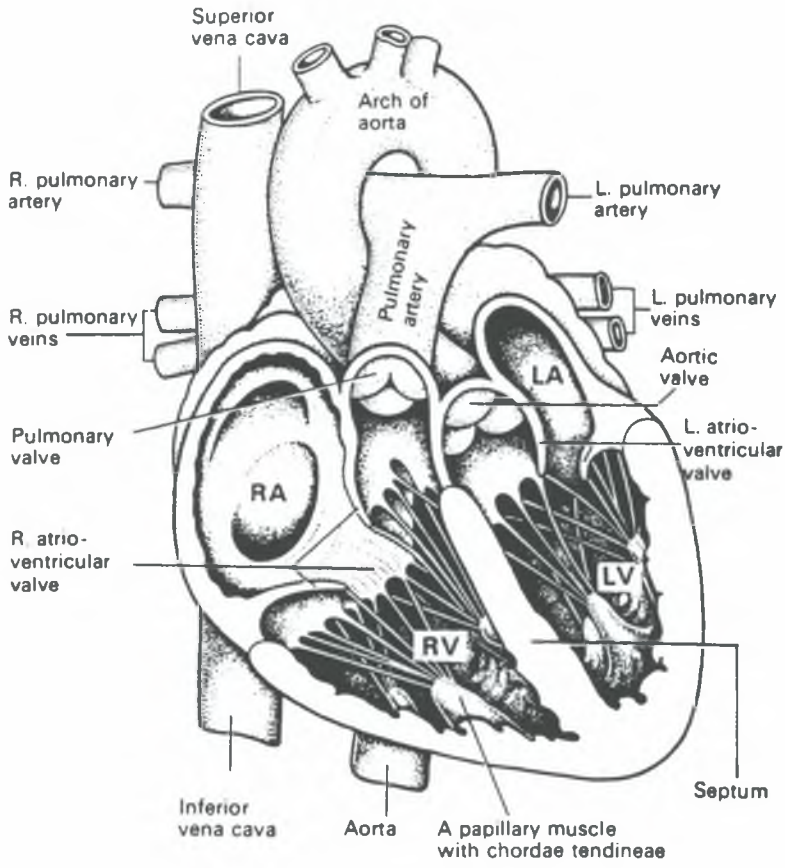


Fig. 2.2a

The Interior of the Heart [2]

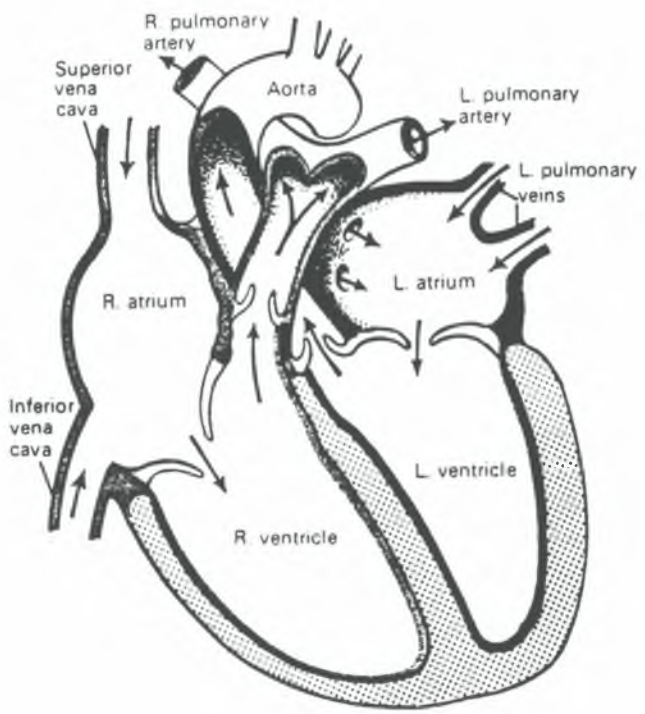


Fig. 2.2b

Flow of Blood through the Heart [2]

2.1.3 Electrical Properties of Cardiac Muscle

To understand the behaviour of cardiac muscle, we must first look at its electrical properties.

Each cardiac cell has a resting transmembrane potential with the interior negative relative to the exterior. This potential difference exists because the cell wall is semipermeable to ions, such as potassium, calcium and sodium. In addition the permeability of the cell wall can change with electrical stimulation. When a wave of depolarisation or action potential propagates through the cardiac muscle, each individual cell depolarises by allowing the ions to pass through the cell wall. This in turn initiates contraction and the result is a wave of contraction moving from the atria to the ventricles. After depolarisation the cell repolarises more slowly and the transmembrane potential returns to its resting value (Figure 2.3).

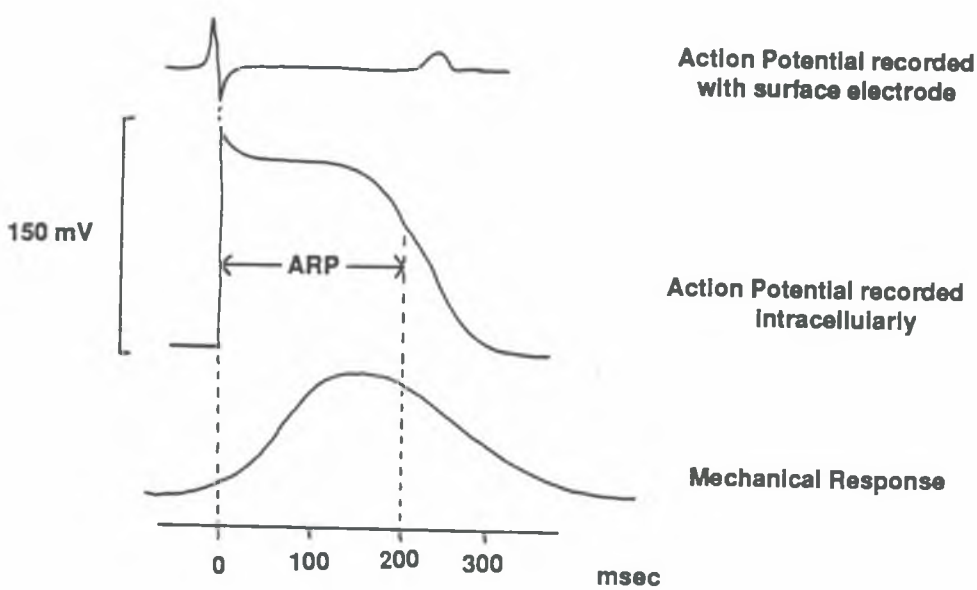


Fig. 2.3

Action Potentials and Contractile Response of Cardiac Muscle [3]

Depolarisation lasts about 2ms, but the plateau phase and repolarisation last 200ms or more. Repolarisation is therefore not complete until the contraction is more than half over. In the extracellular recording, the electrical events include a spike and a later wave which resembles the QRS complex and T wave of the ECG.

Changes in the external K^+ concentration affect the resting membrane potential of cardiac muscle, whereas changes in the external Na^+ concentration affect the magnitude of the action potential. The initial rapid depolarisation and overshoot are due to a rapid increase in Na^+ permeability and the plateau phase is due to a slower and more prolonged increase in Ca^{2+} permeability (Figure 2.4).

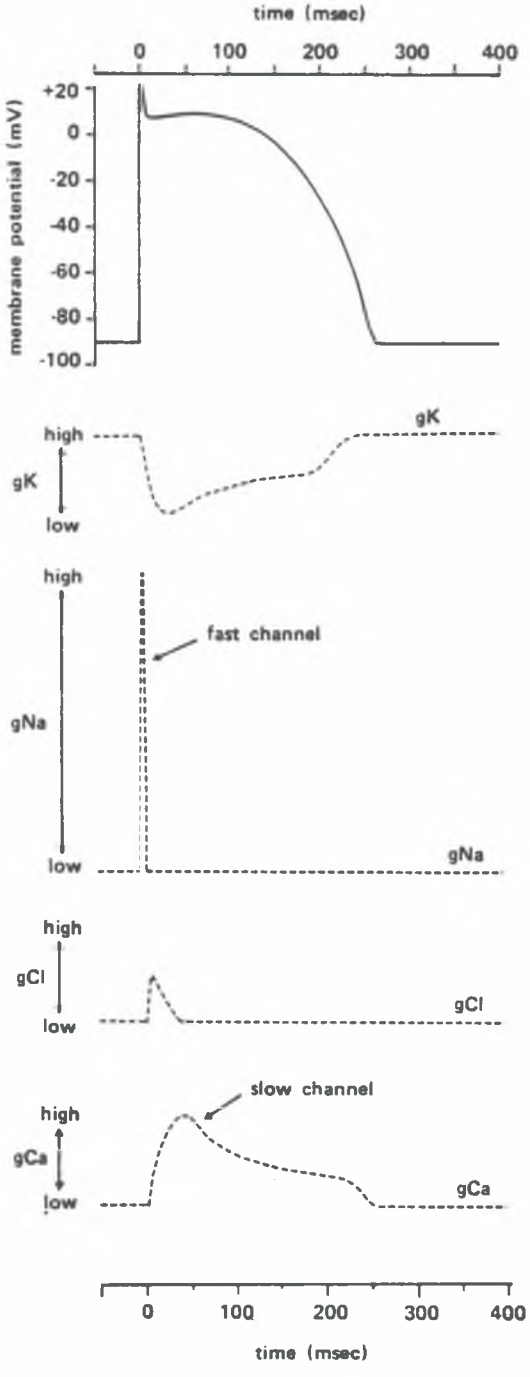


Fig. 2.4

Changes in Ionic Conductances during the Action Potential [3]

The third phase is the manifestation of a delayed increase in K^+ permeability. The ion movements responsible for cardiac action potential are as follows:

Ion	Movement	Current	Phase of Action Potential
Na^+	In	Inward	Depolarisation
Cl^-	In	Outward	Early Repolarisation
K^+	Out	Outward	
Ca^{2+}	In	Inward	Plateau
K^+	Out	Outward	
K^+	Out	Outward	Repolarisation

Table 2.1 [3]

2.1.4 The Mechanical Response of Cardiac Muscle

The contractile response of cardiac muscle begins just after the start of depolarisation and lasts about one and a half times as long as the action potential.

Responses of the muscle are "all or none" in character, that is the muscle fibres contract fully if they contract at all. Since cardiac muscle is absolutely refractory during most of the action potential, the contractile response is more than half over before a second response can be initiated.

2.1.5 Pacemaker Tissue

The heart continues to beat after all nerves to it are sectioned. Indeed, if the heart is cut into pieces, the pieces continue to beat. This is due to specialised pacemaker tissue that can initiate repetitive action potentials.

Pacemaker tissue is characterised by an unstable membrane potential. Instead of having a steady value between impulses, the membrane potential declines steadily after each action potential until the firing level is reached and another action potential is triggered. This slow depolarisation between action potentials is called the prepotential (Figure 2.5). The steeper the slope the faster the rate at which the pacemaker fires. The prepotential has been shown to be primarily due to a slow decrease in K^+ permeability. In atrial and ventricular muscle cells K^+ permeability is constant during diastole (the relaxation period of the cardiac cycle).

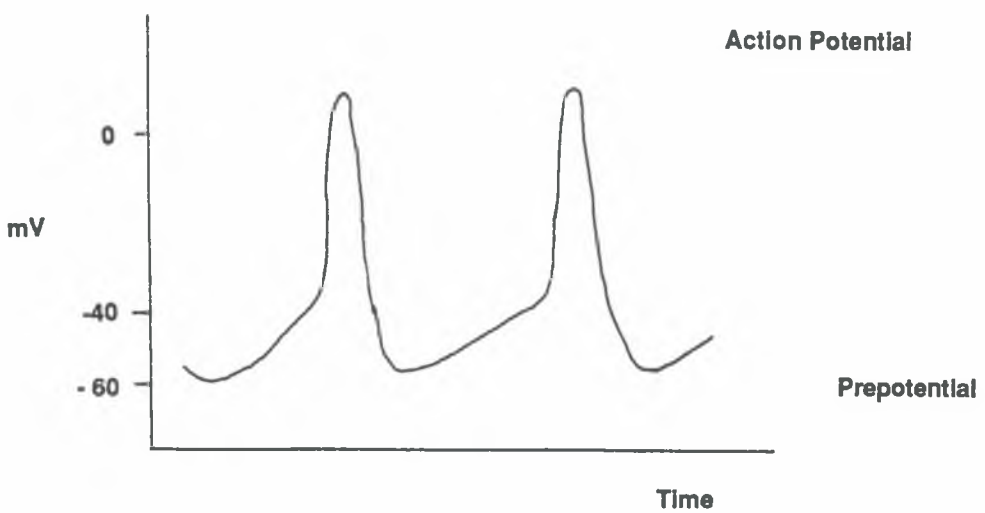


Fig. 2.5
Membrane Potential of Pacemaker Tissue

2.1.6 The Cardiac Cycle

Deoxygenated blood passes into the right atrium at the same time as oxygenated blood pours into the left atrium. The sinoatrial node (SA) acts as the cardiac pacemaker and emits an impulse of contraction (Figure 2.6). This stimulates the myocardium to contract by causing its cardiac cells to depolarise. The contraction spreads over both atria, pushing the blood through the atrioventricular valves into the venticles. When this wave of contraction reaches the atrioventricular node (AV) it is in turn stimulated to emit an impulse of contraction. Although the AV node also consists of pacemaker tissue, its rate is controlled by the more rapidly beating SA node. Excitation spreads to the ventricular muscle via the bundle of His and Purkinje fibres.

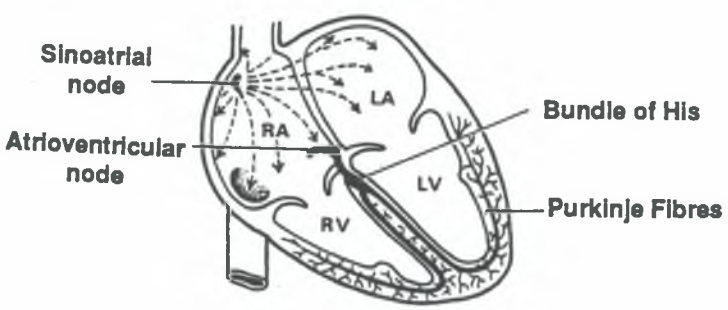


Fig. 2.6

The Conducting System of the Heart [2]

This results in a wave of contraction which sweeps upwards from the apex of the heart and pushes the blood into the pulmonary artery and the aorta. Atrial systole or contraction lasts 0.1s. and ventricular systole lasts 0.3s. The heart then rests for 0.4s. and this period is known as complete cardiac diastole.

2.1.7 Spread of Excitation

Depolarisation initiated in the SA node spreads radially through the atria converging on the AV node. Excitation then spreads to all parts of the ventricles via the rapidly conducting Purkinje fibres.

Depolarisation of the ventricular muscle starts at the left side of the septum and moves first to the right (Figure 2.7). It then spreads down the septum to the apex of the heart. Activation of the major portion of the ventricular myocardium proceeds from the inner surface of the heart outwards. Finally depolarisation spreads to the back of the left ventricle and the uppermost portion of the septum.

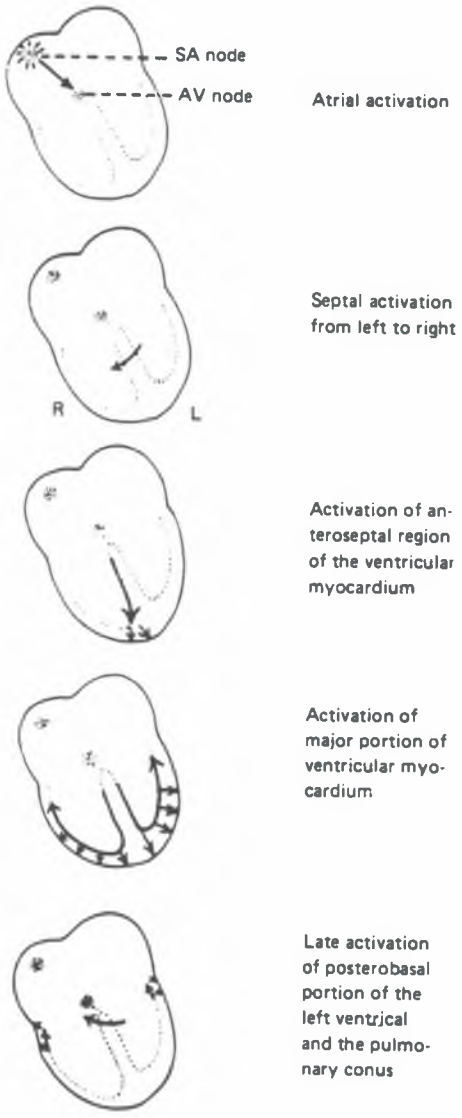


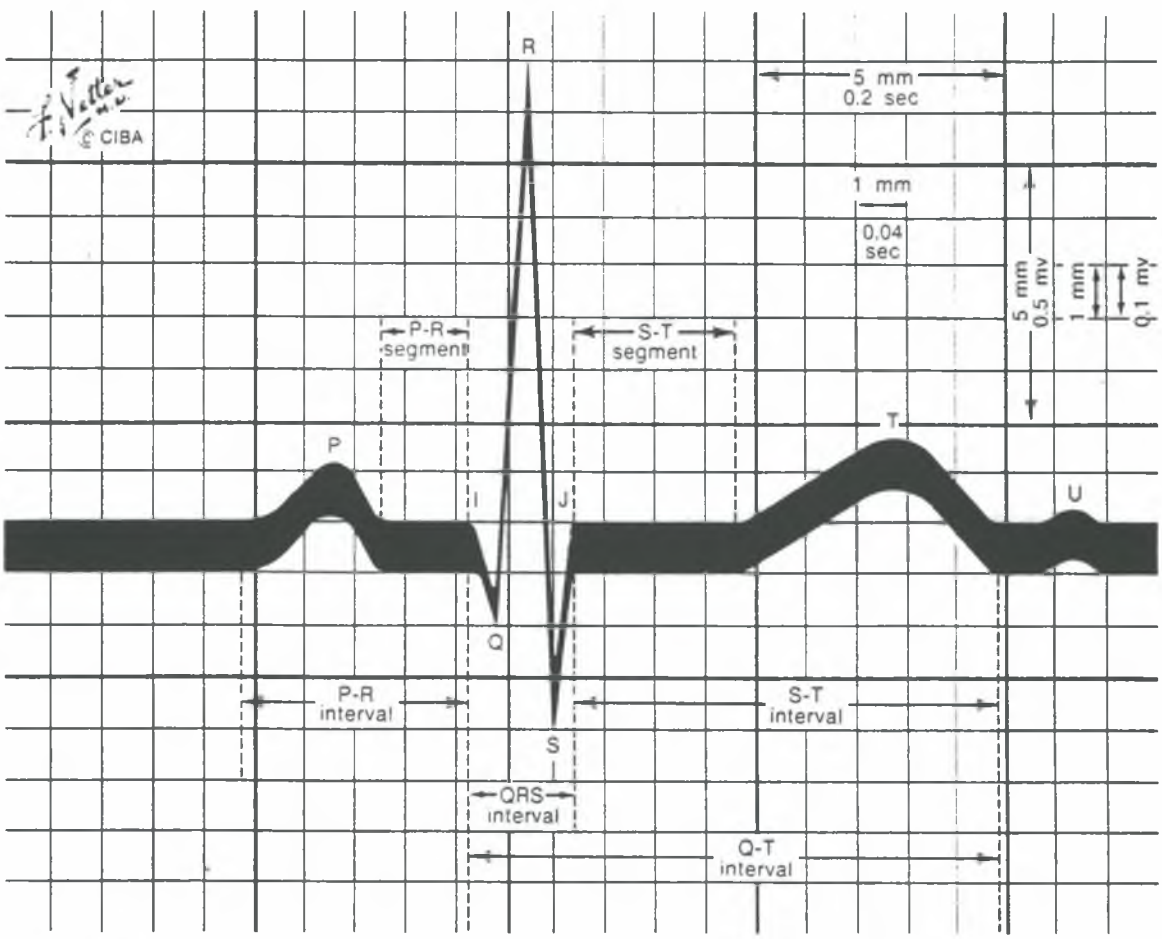
Fig. 2.7

Spread of Excitation through the Heart [4]

2.2 THE ELECTROCARDIOGRAM

The fluids of the body are good electrical conductors so changes in the potential of the myocardial fibres can be recorded from the surface of the body. Electrodes placed on the chest read variations of a few millivolts. Each beat of the heart gives a characteristic waveform known as the electrocardiogram (ECG). The individual waves of the ECG were named by Einthoven, a pioneer in the field of electrocardiography. He simply started in the middle of the alphabet with the letter P (Figure 2.8).

The cardiac cycle begins with atrial depolarisation which appears as the P wave. The Q wave marks initiation of ventricular depolarisation. The QRS complex represents complete ventricular depolarisation. Comparing the duration of the P wave with the duration of the QRS complex shows atrial depolarisation to be a lot slower than ventricular depolarisation. This can be explained by the efficient conducting system of the ventricles. The magnitude of the QRS complex is larger than that of the P wave which reflects the much larger relative mass of the ventricles. It is thought that atrial repolarisation is buried in the QRS complex. The ST segment is isoelectric, but not zero. It corresponds to all regions of the ventricles being equally depolarised, i.e. corresponding to the plateau of the cardiac action potential (2.1.3). Finally, the T wave represents ventricular repolarisation.



	P-R interval	QRS interval	Rate	Q-T interval	S-T segment
Normal ranges (Adults)	0.18 to 0.20 sec	0.07 to 0.10 sec	60	0.33 to 0.43 sec	0.14 to 0.16 sec
Normal ranges (Children)	0.15 to 0.18 sec		70	0.31 to 0.41 sec	0.13 to 0.15 sec
			80	0.29 to 0.38 sec	0.12 to 0.14 sec
			90	0.28 to 0.36 sec	0.11 to 0.13 sec
			100	0.27 to 0.35 sec	0.10 to 0.11 sec
			120	0.25 to 0.32 sec	0.06 to 0.07 sec

Fig. 2.8

The Normal Electrocardiogram [5]

In hospitals the ECG is recorded on graph paper with standard divisions (Figure 2.9). The voltage axis is divided into 0.1 mV divisions equal to 1mm of paper. This has led to doctors using millimetres to quantify shifts in the ECG and in particular the displacement of the ST segment from the baseline.

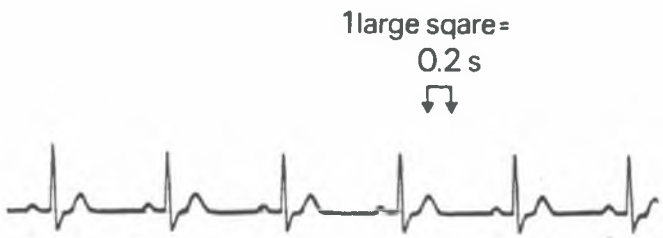


Fig. 2.9
Hospital Record of the ECG [6]

Depolarisation moving toward an active electrode produces a positive deflection, whereas depolarisation moving in the opposite direction produces a negative deflection. In Figure 2.10 we can see how the wave of depolarisation moving through the conduction system of the heart is reflected in the ECG recorded at the surface of the body. The first diagram shows the spread of excitation through the atria from the SA node to the AV node.

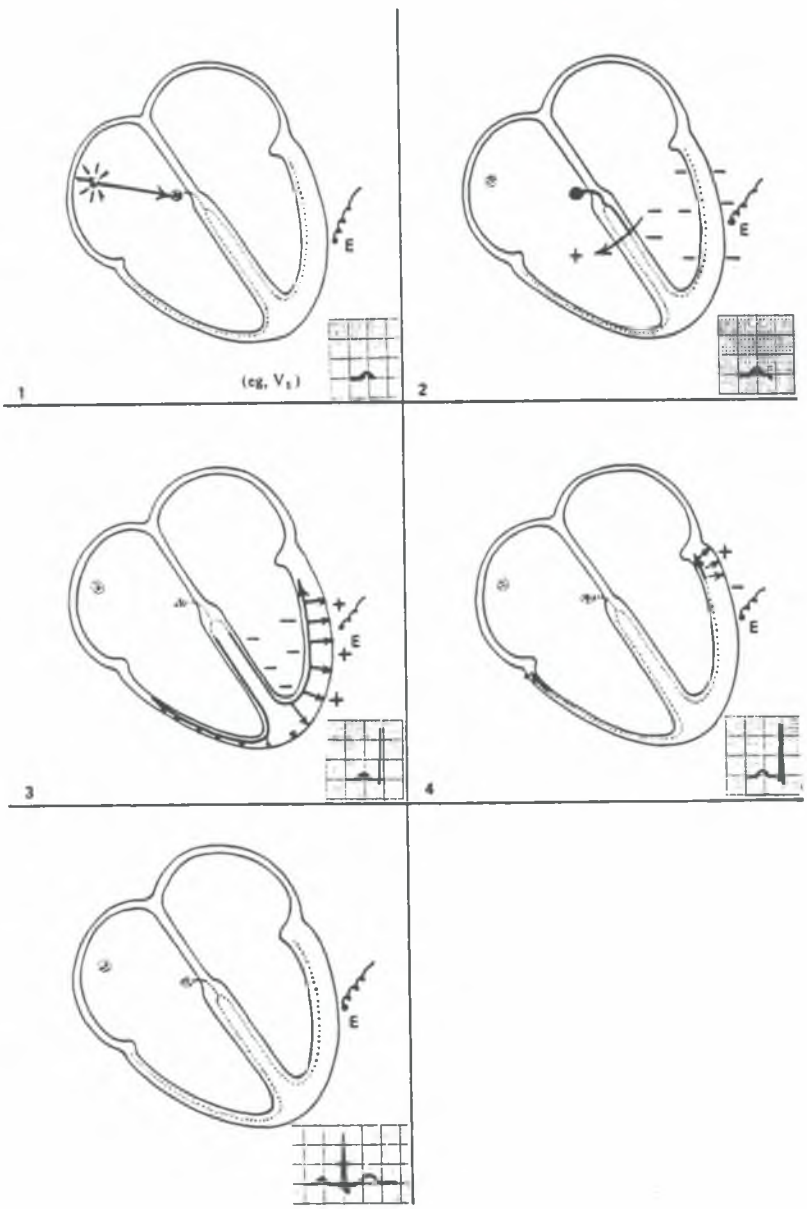


Fig. 2.10

Genesis of the ECG [7]

This is moving towards the electrode (E) so a positive P wave is produced. The impulse spreads across the septum from left to right away from the electrode producing a negative Q wave. Depolarisation spreads through the wall of the ventricles resulting in a large R wave. In diagram 4 we see that late activation of the back of the left ventricle gives the S wave. Finally, repolarisation of the ventricles produces the T wave.

The ECG is recorded using exploring electrodes with reference electrodes to give unipolar readings and between two active electrodes to give bipolar recordings. The magnitude and configuration of the individual waves of the ECG vary with location of electrodes.

2.2.1 The 12 Lead System

Unipolar Leads

There are nine standard locations: the six precordial or chest leads V1-V6 and three augmented limb leads aVR, aVL and aVF (Figure 2.11). If we view the body as a conductor we can see that the potential will remain roughly the same shape along the limb. So the exploring electrodes aVR and aVL can be placed on the wrist, and aVF near the ankle.

Bipolar Leads

Leads I, II and III are records of potential between two limbs. In lead I, the electrodes are connected so that an upward deflection is recorded when the left arm becomes positive relative to the right. In lead II, the electrodes are on the right arm and left leg, with the leg positive. In lead III the electrodes are on the left arm and left leg with the leg positive.

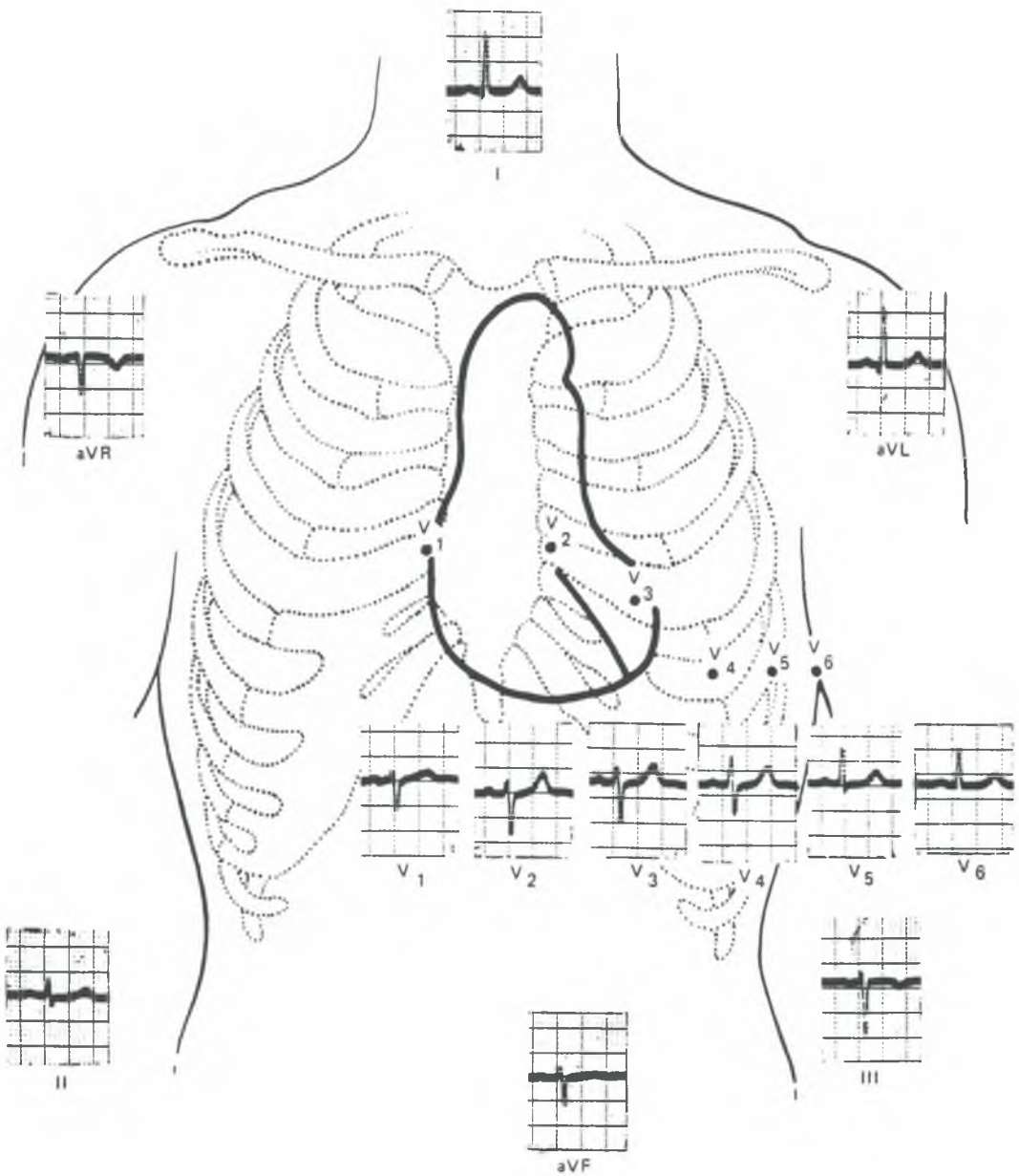


Fig. 2.11

The 12 Leads of the Electrocardiogram [8]

The sequence in which the parts of the heart are depolarised and the position of the heart relative to the electrodes are important considerations in interpreting the configurations of the waves in each lead (Figure 2.12).

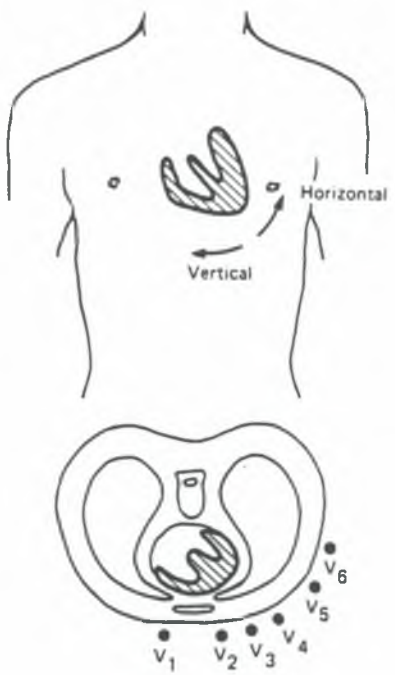


Fig. 2.12

The Position of the Heart in the Chest [4]

Thus aVR looks at the cavities of the ventricles. Atrial depolarisation, ventricular depolarisation and ventricular repolarisation move away from the exploring electrode, and the P wave, QRS complex and T wave are therefore all negative deflections. The remaining augmented limb leads aVL and aVF look at the ventricles and so the deflections are positive or biphasic. There is no Q wave in V1 and V2, and the initial portion of the QRS complex is a small upward deflection because ventricular depolarisation first moves across the mid portion of the septum from left to right towards the exploring electrode. The wave of excitation then moves down the septum and into the left ventricle away from the electrode, producing a large S wave. Finally it moves back along the ventricular wall towards the electrode, producing the return to the isoelectric line. Conversely in the left ventricular leads (V4-V6), there may be an initial small Q wave (left to right septal depolarisation), and there is a large R wave (septal and left ventricular depolarisation) followed in V4 and V5 by an S wave (late depolarisation of the ventricular walls moving back towards the AV junction).

There is considerable variation in the position of the normal heart since it can rotate on any of its 3 axes. These position changes affect the configuration of the ECG waves in the various leads [9]. So for 24 hour recording of the ECG it is important to know the approximate movements of the patient so that changes in the ECG are not confused with pathological events. Physique is significant in this context. Tall, thin people will have large waves in V1-V5, because the heart is more vertical.

Conversely, short, heavy people will have small waves in V1-V5 because the heart tends to be more horizontal. The age of the subject can also affect the ECG. Children have a relatively high R wave and a negative T wave. Depression of the ST segment is used to diagnose certain problems in the heart. Anxiety, hyperventilation, taking certain drugs or drinking coffee can also cause a downward shift. It is therefore important that a doctor or ECG technician knows certain details about a patient before he or she can properly analyze the ECG. The same is true for ECG analysis algorithms.

2.3 THE ISCHEMIC HEART

The patients studied in this project were chosen because they were known to suffer from coronary artery disease (CAD). The first stage of the disease is the onset of arteriosclerosis or hardening of the arteries. This is a build up of fatty deposits in the coronary arteries which ultimately harden to form yellow plaques called artheromas. If the plaques are close to each other or opposite one another, they can obstruct blood flow to the cardiac muscle. If this happens in conjunction with a thrombosis or blood clot, the oxygenated blood to part of the heart muscle will be interrupted and the patient is in danger of having an acute heart attack. In less severe cases blood supply to the heart is merely inhibited. The area of the heart muscle served by the partially blocked artery becomes injured and behaves differently to healthy tissue. The damaged tissue is said to be ischemic and suffers a loss in contractility. If the heart beats faster because the patient is exercising or perhaps under stress, the heart muscle's oxygen demand increases. However, the damaged artery is unable to meet this increase in demand and the patient experiences chest pain, commonly known as angina.

Cardiac chest pain is usually described as a heaviness, burning or tightness and is located in the mid-sternum. Usually it does not radiate, but if it does it will spread to the arms, neck and shoulders. The pain is generally mild in intensity and lasts only a few minutes. To the doctor it can be an early warning of damage to heart muscle.

2.3.1 ST Segment Depression

If a patient known to have CAD is made exercise while his ECG is being recorded, ischemia manifests itself as an apparent drop in the ST segment (Figure 2.13). One theory suggests that this is caused by a "current of injury". During diastole both membrane resting potential and the ECG baseline are at their normal levels. However, damage to ischemic cells results in a leakage of negative ions. This means that the extracellular potential of the injured cells is slightly more negative as compared to that of healthy cells. A current of injury flows from the healthy tissue to the injured tissue. The potential of the ECG signal rises, except for the ST segment which corresponds to

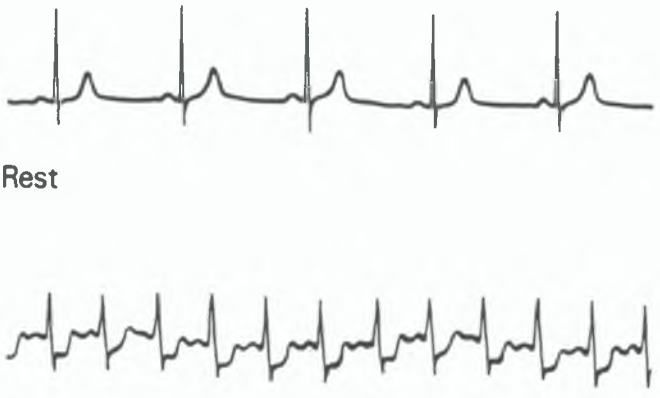


Fig. 2.13
Exercise Induced Ischemic Changes [6]

the ventricles being completely depolarised (Figure 2.14). When the cells of the ventricles are depolarised the potential difference between non-injured and injured regions is reduced and therefore no current of injury flows during this time. The ST segment remains at preinjury level, but when talking about the ECG we usually refer to ST depression.

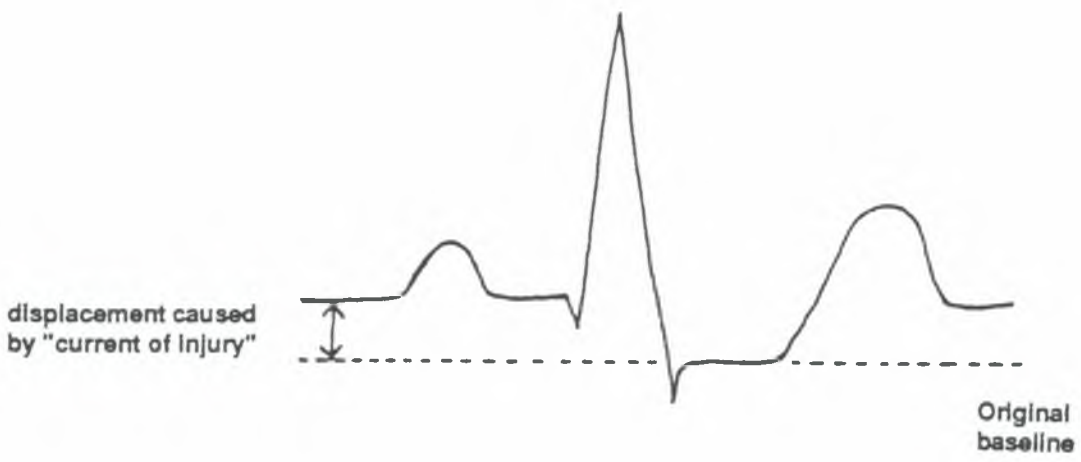


Fig. 2.14
ST SEGMENT DEPRESSION

For quantifying ST segment depression the zero or reference is taken as the isoelectric baseline between the P wave and the QRS complex. In myocardial ischemia it should be depressed by 0.1 mV (or 1mm measured on hospital graph paper) at a point 0.08s after the onset of the ST segment (J point). The character of the ST depression has major significance [7]:

1. Downsloping ST Segment - there is 1mm or more ST depression at the J point. and the ST segment continues downward for 0.08s or more. This finding yields the highest specificity (ability of a test to correctly identify individuals who do not have a specific disease) for the recognition of myocardial ischemia.

2. Horizontal ST Segment - 1mm or more depression at the J point continuing horizontally for 0.08s or more. Although this is considered to indicate ischemia. the incidence of false positive test results is approximately 15%.

3. Slow Upstroke of the ST Segment - this is defined as ST depression of 1mm or more at 0.08s after the J point and an upward sloping of the ST segment not greater than 1mV/s. The incidence of false positives exceeds 30%.

4. Rapid Upstroke of the ST Segment - there is 1mm or more J point depression. but the ST segment is rapidly upward and the slope exceeds 1mV/s. This is of no diagnostic significance.

Any of these criteria should last for more than 60s or approximately 72 consecutive beats.

2.3.2 The Exercise Test

Patients who present to their GP with chest pain are usually referred to hospital for an exercise or stress test. Since the ECG is normal in 25-40% of resting patients with angina, it was necessary to devise a test where the ECG was recorded during exercise. Various techniques have been used including Dr. Master's two steps test and bicycle ergometry. However, the most popular system today is the treadmill test using the Bruce Protocol which was used to test some of our patients.

As with other protocols, all 12 leads of the ECG are recorded. Since hyperventilation alone can produce ST changes that are indistinguishable from those of myocordial ischemia, a 60 second hyperventilation test is performed prior to test. Before the patient steps on the treadmill the target heart rate is calculated. This is generally taken as:

Target Heart Rate = 220 - (age in years)

If the heart rate reaches 90% of the target rate, the test is terminated.

The speed and gradient of the treadmill can be adjusted by the ECG technician. The patient is instructed to step on the treadmill and to commence walking:

1st Stage:	1.7 Miles per hour at	10% gradient
2nd Stage:	2.5 mph	12% gradient
3rd Stage:	3.4 mph	14% gradient
4th Stage:	4.2 mph	16% gradient
5th Stage:	5 mph	18% gradient
6th Stage	5.5 mph	20% gradient
7th Stage	6 mph	22% gradient

It is uncommon for patients with coronary artery disease to exercise past stage 5. A doctor and resuscitation equipment should be on hand to monitor blood pressure and physical symptoms. The test is continued through the stages until changes appear in the ECG or 90% of the maximum target heart rate is reached. If the patient begins to feel pain in his legs or general exhaustion the test will be terminated.

The ECG is monitored for at least 6 minutes after exercise or longer if abnormalities exist [7].

2.4 THE OESOPHAGUS

When food is swallowed it passes down through the oesophagus and into the stomach where it is digested. It is aided by waves of pressure in the oesophagus or peristalsis. The oesophagus is about 25cm long and is located behind the lungs and heart, just in front of the backbone [2].

The normal pH of salvia in the mouth is between 6.4 and 7.4. This is reflected in the oesophagus where the pH is also neutral. However, the pH of gastric juice is about 1.8. This highly acidic pH is maintained by hydrochloric acid secreted into the stomach by special cells in the stomach wall. Acid is prevented from entering the oesophagus by the lower oesophageal sphincter muscle (sphincter - a circular muscle, contraction of which serves to close an orifice [1]). The LES can be detected by manometry as a zone of 2-4cm in length with a resting pressure of 12 to 30mm Hg [10]. It maintains this high pressure most of the time, but relaxes when food is swallowed.

2.5 GASTRO-OESOPHAGEAL REFLUX

In our overweight and anxiety ridden population indigestion is a frequent complaint. This is usually an indication of gastro-oesophageal reflux. There are many theories as to its cause including problems with motility (the mechanism of swallowing [1]) or sensitive oesophageal mucosa (lining). The more traditional explanation is incompetence of the lower sphincter muscle which permits reflux of acid gastric contents into the oesophagus. The subsequent failure of the oesophagus to clear the acid from its distal or lower portion results in inflammation of the oesophageal wall [4] [11]. The resulting pain is described as a burning sensation referred to as heartburn. In more severe cases, it is a localised pressure or squeezing pain across the middle portion of the chest. The condition can be treated by avoiding irritating foods, taking drugs and if medication fails, surgery. Reflux tends to occur after meals or acidic drinks and during activities which involve bending or stooping. It is more frequent during daytime, but is more rapidly cleared. Episodes occurring at night tend to be fewer and longer in duration.

Oesophageal reflux occurs to some extent in the normal population but when pH in the lower oesophagus regularly drops below 4 for extended intervals, the reflux is said to be abnormal or pathological (Figure 2.15).

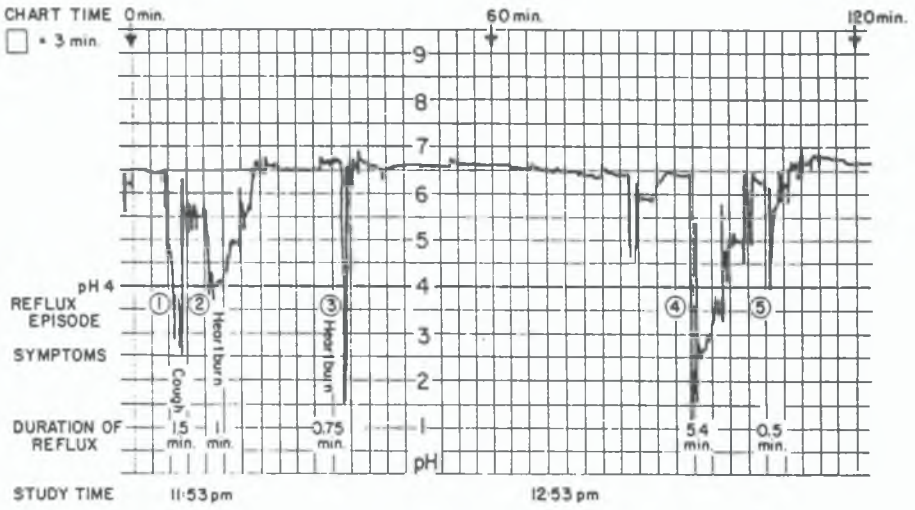


Fig. 2.15

Part of a 24 Hour pH Recording

Showing Reflux Episodes and Concomitant Symptoms [12]

2.6 MOTIVATION FOR THE CLINICAL TRIAL

Two separate causes for chest pain have been described. If a patient presents to his doctor with substernal pain, it may be cardiac pain or pain due to gastro-oesophageal reflux (The autonomic nerve supply of the oesophagus is similar to that of the heart, and oesophageal pain closely mimics cardiac pain [13]). The doctor can look to the patient's history for help with a diagnosis. Typically angina is brought on by exertion and relieved by rest. 'Oesophageal pain' can be

brought on by spicy foods and may go after taking antacid. However, there is a group of patients for which it is difficult to decide whether to refer them to a cardiologist or gastroenterologist [14] [15]. In fact there are many cases of reflux sufferers ending up in cardiology clinics. When all possible tests have been done they may then be referred to a gastroenterologist.

For some patients the diseases may coexist which further compounds the problem of diagnosis [16] [17] [18]. Recently one study described simultaneous 24 hour oesophageal pH and ECG monitoring to help decide the origin of the patients' pain [19]. In 5% of cases, simultaneous coronary insufficiency and pathological gastro-oesophageal reflux was noted.

Early research by Kramer et al [16] showed an interesting result. He inserted a balloon into the oesophagus of a number of patients. Pumping air into the balloon irritated the oesophagus and caused the patient to feel pain. One group of patients studied were angina sufferers. The test produced typical angina pain in some, but a different pain in others. In one case (out of nineteen) where the pain was dissimilar, ST segment depression accompanied the pain.

It was not until some years later that Mellow [20] [21] introduced the idea of oesophageal acid perfusion inducing myocardial ischemia. He used the Bernstein test of instilling hydrochloric acid into the lower oesophagus while recording the ECG. Twenty-five patients were suffering from coronary artery disease : 64% of these with no history of reflux, had a positive acid perfusion test, while 56% who developed pain during the test could not distinguish the pain from their usual angina.

Mellow concluded that in coronary disease, acid perfusion (and presumably reflux) resulting in chest pain causes an increase in the rate pressure product (an indication that the heart is working harder) and can trigger myocardial ischemia.

Does reflux in some way cause angina? Or does angina cause reflux?

The purpose of this study was to show a correlation between the incidence of oesophageal reflux and angina.

2.7 THE MEDICAL PROTOCOL

2.7.1 Choice of Patients

All patients had suffered from coronary artery disease detected by angiogram (a film demonstrating the arterial system by injecting an opaque medium into the arteries [1]) and/or exercise test. They all experienced frequent attacks of chest pain. The group was made up largely of older men. This reflects that arteriosclerosis is a disease of age and is traditionally more common in men than women.

2.7.2 Setting up the Recording

For each 24 hour recording a new tape and batteries were used. The test was fully explained to the patient and he was given a card to record the events of the day. In particular he was asked to write down when he went to bed, when he arose, any meals taken and any chest pain and when it occurred. Without this information the test would be invalid.

The first step was to place the pH probe in the oesophagus. Before this could be done manometry was used to locate the position 5cm above the lower sphincter where the pH electrode should be placed (Figure 2.16).

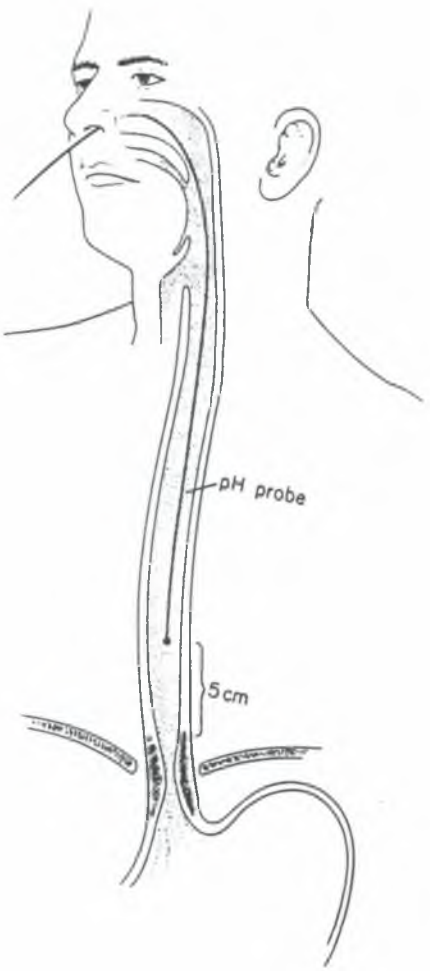
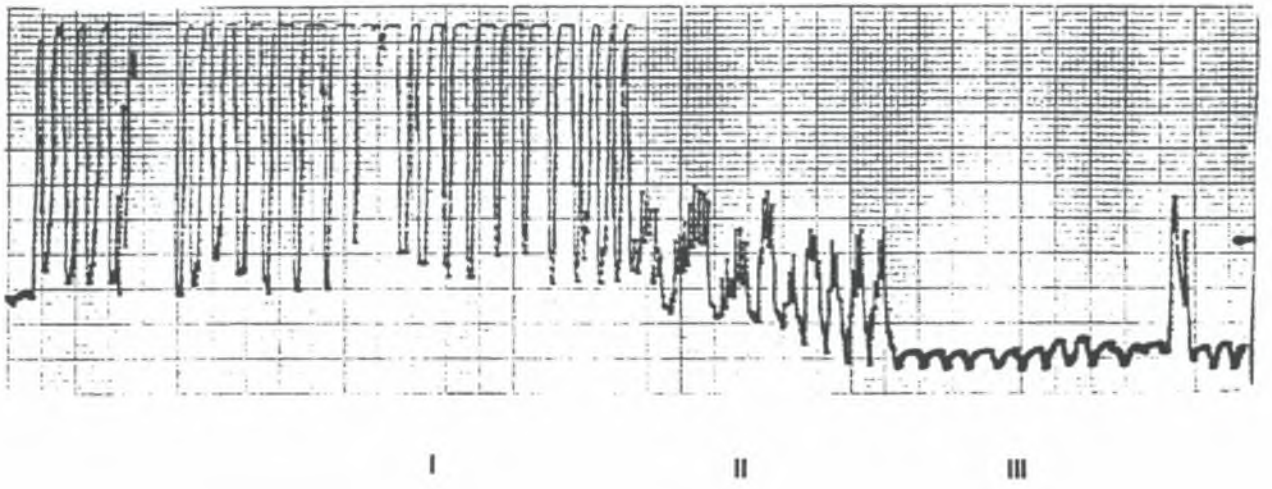


Fig. 2.16
Position of the pH Probe during 24 Hour Oesophageal Monitoring [12]

A tube is fed through the mouth into the oesophagus, down into the stomach. In the stomach it detects large pressure waves because the stomach muscles are constantly contracting and expanding as the diaphragm moves up and down (Figure 2.17). Slowly the tube is pulled upwards until the amplitude of the pressure waves decreases. This corresponds to the lower oesophageal sphincter. Again pressure is caused by movement of the diaphragm. Finally, there is a sharp decrease in pressure and the tube is in the oesophagus. The baseline of the pressure wave has become negative. This is because pressure in the oesophagus tends to be outwards because the lungs are continually collapsing and the chest wall is moving out. The tube is moved up 5cm and marked at the mouth - this is the distance the pH probe should be inserted. It is necessary to anaesthetize the nose before insertion of the probe. The reference electrode is attached securely to the right chest.

The next step is to take a full 12 lead ECG using the hospital monitor. The doctor asks the patient to stand, to sit and then to lie down. This establishes the effect of posture on the patient's ECG. It was also important to discover whether the patient has ST segment depression while at rest. If there was resting ST depression of 1mm, for example, then further depression of 1mm or more would indicate ischemia.

The 24-hour ECG recording is then started. Two Holter ECG leads (V2 and V5) were used for reasons which will be described later. Each has its own reference electrode so that if one should become loose, one ECG channel will still be recorded. The patient was advised not to entrap any part of the lead system under tightly fitting clothes. A 24-hour recording gives a good picture of how pH and ECG vary with daily activity and increases the possibility of finding a correlation between chest pain, angina and reflux.



I Gastric Pressure waves

II Lower Oesophageal sphincter

III Oesophagus

Fig. 2.17

Manometry of the Oesophagus

CHAPTER 3 24 HOUR AMBULATORY RECORDING OF THE ELECTROCARDIOGRAM AND OESOPHAGEAL pH

3.1 A REVIEW OF HOLTER RECORDER TECHNOLOGY

As early as 1947, physicist Normal J. Holter invented the first device for recording the ECG over extended periods of time [22] [23]. This consisted of just one ECG lead with a transmitter capable of broadcasting over a short distance. The equipment weighing 85 lb, was worn on the patient's back while pedalling a bicycle. The signal was picked up by a receiver standing close by.

With the advent of transistors the equipment was miniaturised and by 1961 Holter had condensed the equipment into a single recording device weighing 1 kg [24]. Today ambulatory monitors or Holters weigh as little as 14 oz. and are worn in a case strapped to the patient's waist. A photograph of the Holter used in this project is seen in Appendix 1.

The ECG signal is recorded onto commercially available magnetic cassette tape. The recorder runs at a slow speed (2mm/sec) so that recording lasts for 24 hours. The tape is played back at a faster speed, e.g. x25 or x60. Two ECG leads are recorded: usually V5 and either V1 or V2. It is important to fix the electrodes properly to the chest to minimise noise. Other precautions include not reusing old tapes and replacing the batteries after each run.

During the 24 hour period, the patient keeps a diary, noting any symptoms. If pain occurred with concomitant ST segment depression this would indicate myocardial ischemia (2.3.1).

Ambulatory ECG recorders have been in widespread use for 25 years now. There are many companies both in Europe and the United States manufacturing Holter recorders. Most designs are a compromise between low cost, wide bandwidth, speed accuracy, compact dimensions, reliability and cheap recording medium. Before running the clinical trial it was necessary to assess the reliability of Holters in reproducing shifts in the ST segment and in particular the performance of the Oxford Medical Holter (Mark 1) which we used.

3.1.1 Frequency Response

Originally Holter recorders were confined to investigating arrhythmias or disorders in heart rhythm [24]. However, more recently the recording of ST segments has aroused much interest as it provides a non-invasive method for assessing myocardial ischemia.

The frequency content of the electrocardiogram has been previously analyzed [25] [26]. In his study, Scher recorded the ECG of 17 normal and 8 abnormal subjects. The result of his work is shown in Figure 3.1. He concluded that frequencies above 100 Hz. do not contribute significantly to the ECG. Ideally, the bandwidth of the recorder and playback unit combination should include frequencies up to 100 Hz. and down to the inverse of the R-R interval.

Berson and Pipberger examined the affect of poor frequency response of direct-writing ECG monitors on the ECG. In their 1966 paper they describe simulating different low frequency characteristics using a variable high pass filter [27]. Input ECG signals were taken from magnetic tape, passed through the filter and analyzed. They were particularly interested in any distortions between the J point and the end of the T wave. Their results showed that abnormal ECG's were more

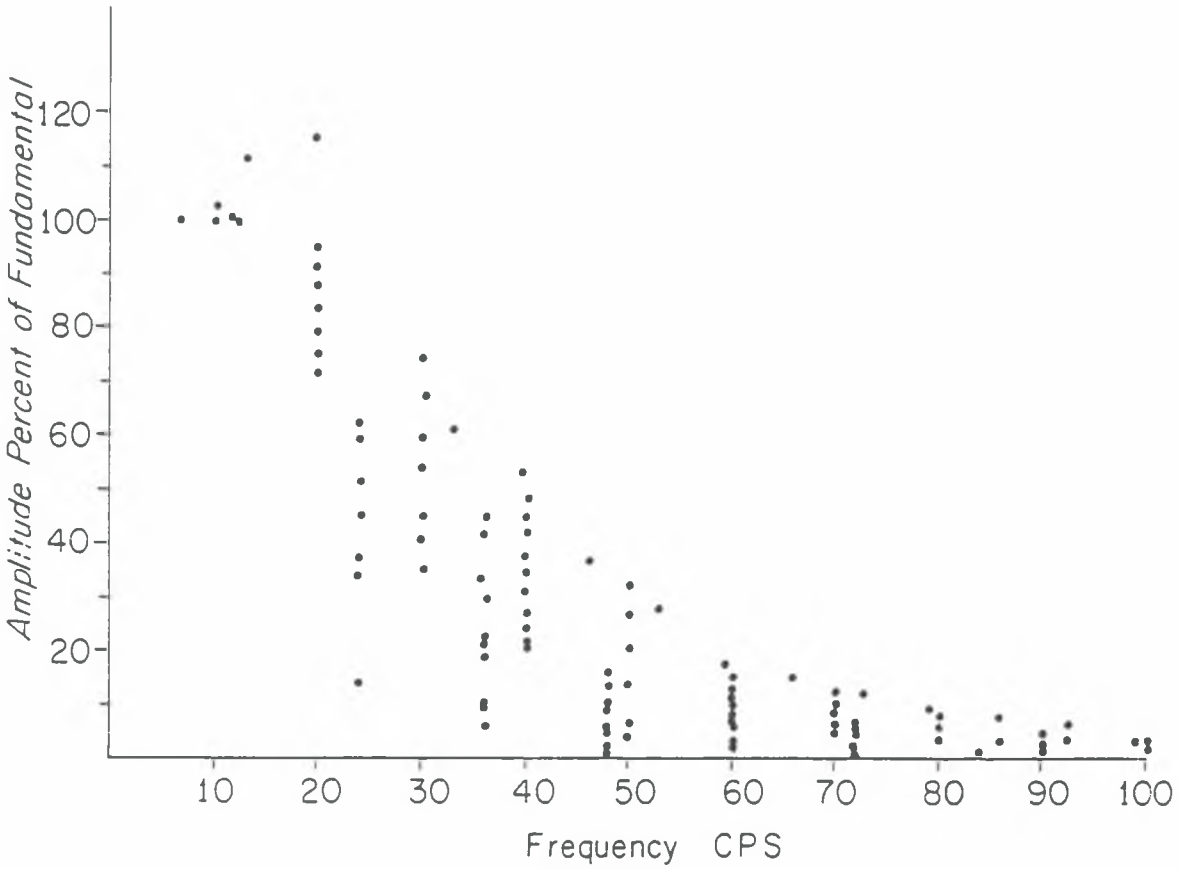


Fig. 3.1

Frequency Content of the Electrocardiogram [25]

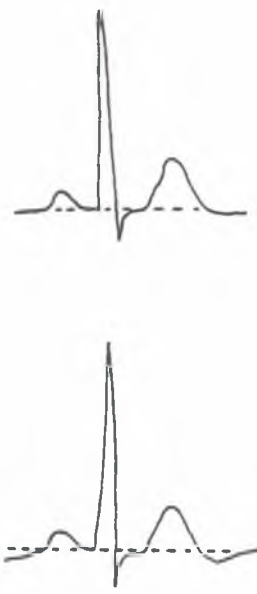
readily distorted. They also found that records having essentially monophasic QRS patterns (see lead V5 in Figure 2.11) were more readily distorted than records having biphasic QRS patterns (see lead V4 in Figure 2.11). In almost all cases, the distortions that did occur showed up as depressions at the J point and gradually became less depressed as time increased, reaching zero and sometimes becoming elevated in the T wave area.

The amount of distortion depended on cutoff frequency and rolloff. They recommended a low cutoff frequency of 0.05-0.08 Hz. and a roll off of 6 db per octave.

In their 1967 paper, Berson and Pipberger passed ECG records through a low pass filter to investigate the high frequency response of ECG monitors [28]. They found that a poor high frequency response reduced the magnitude of the Q, R and S waves. Also, if the cutoff frequency is less than 60 Hz. the QRS complex will be widened. They recommended a cutoff frequency of at least 100Hz. to reduce amplitude errors below 0.1mV.

Soon after, Hinkle et al investigated the bandwidth of a commercially available Holter and Scanner [29]. They found the effective frequency range to be between 0.5 and 50 Hz. The amplitude of the R wave was reduced by the poor high frequency response (Figure 3.2). In addition the poor low frequency reponse caused the ST segment to be artificially depressed and the signal 'sagged' after the T wave.

A few years later Stern and Tzivoni attempted to validate the Holter Avionics recorder by comparing 3 normal and 3 abnormal traces recorded with this system [30]. They concluded that it was reliable for reproducing ST segment changes. This study has been used as justification for using several of the currently available machines for ST-segment recording.



Bandwidth 0.05-2000 Hz.
(ECG Monitor)

Bandwidth 0.5-50Hz.
(Holter Scanner System)

Fig. 3.2
Distortion of a Simulated ECG Complex
Produced by an Early Model Recorder [29]

One of the most frequently referred to publications in recent years is a report by Bragg-Remschel et al [31]. She examined the frequency response and reproducibility of ST segment shift for equipment from eight manufacturers. An important observation she made was that manufacturers claimed a low frequency cutoff of 0.05Hz for their equipment. However, closer examination of the technical literature revealed that the specifications apply to the recorders amplifiers and not to the entire recording and playback system. In addition, the manufacturers do not report the degree of flatness of the amplitude versus frequency curve. The first test involved recording a 0.5mV sine

wave for frequencies in the range 0.05-100 Hz. The Oxford Mark II FM recorder had a flat frequency reponse curve and was the only recorder with a low frequency cutoff of 0.05 Hz. All the direct recording systems (including the Oxford Mark I with the PB2 playback unit) had gains of 1.4 to greater than 2 at some point on the frequency curve. In the case of the Mark I, the gain was greater than 1 in the range 0.2 to 1 Hz. with a peak at 0.4 Hz. This was also reported by Tayler and Vincent where they claimed that this was due to the mechanical design of the replay heads [32]. Another test described by Bragg-Remschel involved recording an ECG signal from a simulator. A plot of ST segment depression in the input ECG waveform versus that for the output waveform was plotted for the eight recording systems. The Oxford Mark I system consistently amplified any depression at the J point. She claimed that this was linked to the excessive gain of 1.6 at 0.4 Hz. She concludes that while a low frequency cutoff greater than 0.05 Hz. may be acceptable, using the Oxford Mark I and playback unit for ST segment studies may be unwise. However, her measurement of ST segment depression was taken only at the J point. According to Berson and Pipberger distortion is greatest at this point [27]. To properly evaluate the ST segment, it is necessary to look at both depression at the J point and ST segment slope. Bragg-Remschel claimed that the Mark I distorted the shape in some cases, but made no attempt to quantify this error.

Research in Europe also indicated that the Mark I was less effective than other recorders for reproducing ST segment [33]. Bala Subramanian looked at both depression at the J point and the slope of the ST segment for patients during exercise. He found maximum differences of 1.2mm (or 0.12 mV) as compared with J point depression of the standard. Measurements of ST slope differed from the standard by more than 1.0

mV/s in all recordings. However, Bala Subramanian used the CASE replay system manufactured by Marquette Electronics. He gives no indication of the bandwidth of the CASE playback unit so his study can not be used as an absolute measure of ST segment distortion by the Oxford Mark I.

A group of researchers in the Netherlands produced a report on six Holter systems available in Europe [34]. They claimed that the Oxford Mark I distorted the ECG, but did not say how they came to this conclusion. They did say, however, that the Mark I was relatively light in weight and was well constructed both mechanically and electrically. It was the cheapest of all the recorders and was the only 4 channel recorder. Multichannel recorders have an advantage over 1 or 2 channel recorders because they can be used for simultaneous recording of the ECG and another signal such as blood pressure [35].

3.1.2 Phase Response

In her study, Bragg-Remschel used square waves at different frequencies to plot the phase response of the eight recording systems [31]. She found that for the Oxford Medical system (Mark I recorder and PB2 playback unit) there were large phase shifts at lower frequencies - the phase shift went from 0° at 1 Hz. to 90° at 0.1 Hz. So the lower frequency content of the ECG including the ST segment, was being delayed relative to the rest of the signal. Tayler and Vincent used an all pass filter with a low frequency delay to assess the affect of poor low phase response on the ECG [32] [36]. They found ST changes resembling myocardial injury. This was due to low frequency components in the QRS complex being delayed [37]. The Oxford Mark I was one recorder they singled out as having a poor phase reponse. They used a phase compensating network after the replay amplifier, but found only

some improvement in the signal. Playing the tape backwards, however, greatly improved signal quality. Low frequency components that suffered delays in recording were being similarly delayed in the opposite direction on replay. In one of their papers Tayler and Vincent comment that simple analogue filters produce phase distortion at frequencies up to 10 times greater than those at which significant amplitude attenuation occurs [32]. So although there are no components in a normal ECG lower than 0.5 Hz., a low frequency cutoff of 0.05 Hz. is necessary to ensure minimal phase distortion.

The American Heart Association brought out a special report in 1985 dealing with standards in ambulatory electrocardiography [38]. They covered all aspects of Holter recording. The frequency reponse should fall within the limits shown in Figure 3.3 and the phase response should be linear for the entire range of 0.05 Hz. to 60 Hz. Clearly there are no commercially available recording systems that meet these standards.

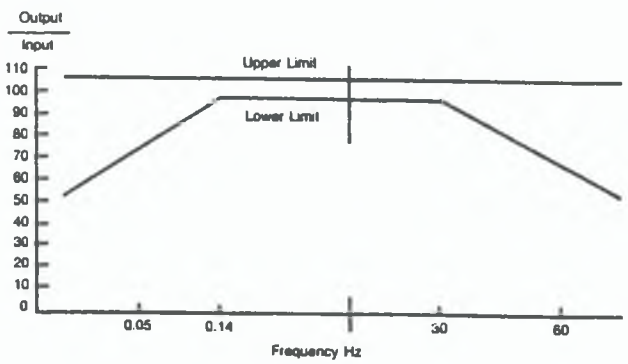


Fig. 3.3

Recommended Bounds to the Frequency Response of Ambulatory Recorder and Playback Systems [38]

3.1.3 Artefact

It is important to take great care in setting up a 24 hour recording. Signal quality can be reduced by excessive electrical noise and the recording has to be repeated.

The potential at the surface of the body is taken as the reference potential. This voltage varies slowly with time and produces a baseline drift in the ECG signal. However, it has been shown that the effect of baseline drift is greatly reduced by fixing the electrodes firmly to the skin [33] [39]. Another cause of low frequency noise is respiration.

Noise is also present at the higher frequencies of the ECG. Muscle tremor due to the electrical activity of muscles increases with activity. Interference at 50 Hz. can also be seen. This noise is in the passband of the Holter recorder and replay system so it cannot be filtered out.

Errors can also arise if the batteries are run down. This will cause the ECG signal to be weaker and ST segment shift will be underestimated. Intermittent battery failure can mimic an increase in heart rate [40].

Reusing old tapes is common practice in many public hospitals. Traces of old recordings can confuse interpretation of the ECG [40].

Sometimes it is the technician and not the equipment that causes the error. The tape may be inserted the wrong way. When it is played back the larger T wave will precede the QRS complex. Another common error is mixing up the ECG leads. Although the electrodes are colour coded the active and reference electrodes may be switched causing the signal to be inverted.

3.1.4 Leads

In general two leads are recorded. V5 is an obvious choice because it has been proven to be the single most sensitive lead for the detection of ischemic ST segment depression [41]. V2 is a good second choice because it is placed over the sternum and is less susceptible to noise from muscle movement [42].

The positioning of these electrodes is very important. Leads in close proximity can produce different wave morphologies (V4 and V5 in Figure 2.11). Hurst reports a study which investigates the placement of lead V2 [43]. The position varied by 10cm vertically and 8cm horizontally.

Before placing the electrodes the skin should be carefully prepared. First the area is shaved, then it is cleared and the skin abraded. Disposable, pre-gelled electrodes are commercially available to which the leads can be attached [38] [41].

Using two leads greatly reduces the loss due to single channel malfunction [38]. It also improves the detection of P wave and ST segment shifts [44] [45].

3.1.5 Medical Evaluation

In the early seventies manufacturers claimed that Holter recorders could be used for detecting ischemic heart disease because of significant improvements in the low frequency reponse. This has prompted many technical evaluations as already discussed. However, Holter recording has also been widely compared with other medical tests.

Two medical doctors tested 20 patients with postive evidence of coronary artery disease [46]. Each patient underwent 24 hour ambulatory monitoring and a stress test. The results were concordant in 10 cases; ST segment depression greater than 1mm occurred both during treadmill exercise and during continuous ECG monitoring. The remaining patients had either a positive exercise test or a positive Holter test. In the same year Wolf, Tzivoni and Stern did a similar trial and found a fairly good correlation between exercise testing and ambulatory ECG monitoring [47]. A further test by Stern et al compared ambulatory ECG monitoring with coronary angiograms which are used to show up blocked arteries [48]. They found good correlation between the results from both tests.

However, a few years later Crawford et al subjected 70 patients to coronary angiograms, exercise tests and ambulatory ECG monitoring [49]. They found a relatively high number of false positives and false negatives for Holter recording and criticized methods used by Stern et al [48].

A more interesting test was reported by Tzivoni et al in 1985 [50]. One hundred and forty four patients underwent a Bruce protocol treadmill exercise test (2.3.2) with simultaneous 2-channel Holter recording. In 96% of patients the results were concordant. The severity of the ST segment depression was identical on both recordings. Their work strongly indicates that ambulatory monitoring can reliably reproduce the ST segment. They also comment that Wolf, Stern and Crawford only used a single lead which is less effective for diagnosing ischemia than two leads (3.1.4).

3.1.6 The Future of Holter Recording

Twenty-four hour tape recorded ambulatory ECG monitoring has become a widespread diagnostic tool over the past 25 years. Over this time a plethora of Holter monitoring systems have been developed and marketed.

The traditional recording medium is cassette tape which facilitates a complete 24 hour record of the ECG. In recent years two types of solid state recorder have been developed. The first is activated by the patient in response to chest pain. This recorder used only a single ECG channel and has limited memory. If the patient experiences chest pain his first reaction will be to reach for his nitroglycerin which will ease the pain and not to trigger the recorder. This meant that early recorders missed significant events. However modern recorders have a delay circuit so that up to 2 minutes of ECG data preceding patient activation can be captured.

The second form of solid state recorder analyzes the ECG signal in real-time and stores examples of suspected abnormalities. As the real-time analysis is performed immediately after the signals enter the Holter device, the problems which may arise from mechanical and electronic limitations of the magnetic heads in the tape recordings are circumvented. However, it has been found that frequently the real-time analyzer could not distinguish between noise and ECG signal [51] [52].

The disadvantage of the two solid state recorders described is that they do not provide a full 24 hour record of the ECG. They are also more expensive than conventional tape recording systems.

Oxford Medical Ltd. have produced a dual tape recording and real-time analysis system [53]. Two ECG signals are recorded onto tape and are also digitized for real-time analysis. Elfner et al found that the system was accurate for detecting arrhythmias but they did not investigate its performance in detecting ST segment shifts.

In a later publication Silber et al validated digital Holter ST segment analysis [54]. They used the Oxford Medilog 4000 similar to that described above. Two ECG signals were recorded onto two channels of the cassette tape. The third channel was used to record the results of real-time arrhythmia analysis and ST segment measurements. A timing signal was recorded on the fourth channel. There was a 32 kB memory available : 16 kB was needed to store the program and 16 kB was available for ECG analysis. The frequency response of the digital system was 0.07-70 Hz.

They compared digital Holter recordings with reference electro-cardiograms and found a good correlation between ST segment measurements.

The future of Holter recorders lies in solid state memories capable of storing 24 hours of ECG data and performing sophisticated real-time analysis.

3.2 A REVIEW OF AMBULATORY pH-METERING

In the treatment of patients with gastro-oesophageal reflux complaints it is very important to obtain information about frequency and duration of the episodes during which the oesophageal walls are exposed to gastric acid. The determination of the pH in the distal part of the oesophagus has become a standard technique in clinical practice and medical research. Long-term monitoring of the distal oesophagus is the best single test available for the assessment of gastro-oesophageal reflux [55].

3.2.1 The pH Electrode

The method involves inserting a pH probe through the nose into the oesophagus (Figure 2.16). A reference electrode is placed externally on the surface of the skin. The pH electrode generates a millivolt signal proportional to the pH. According to the Nernst equation a 59.1 mV change in potential is expected for every pH unit [56]:

$$E = E_o + \frac{(RT)}{F} (2.3026) \log [x]$$

E_o = the emf for standard ion concentration
E = the emf for other ion concentrations
R = Universal Constant = $8.3144\ JK^{-1}\ mol^{-1}$
F = The Faraday Constant = $96{,}485\ Cmol^{-1}$
T = Temperature 25°C. or 298K
[x] = ion concentration, i.e. pH = log[x]

Multiplying out the constants gives:

$$E = E_o + (59.1\ mV) \log [x].$$

Glass pH electrodes are sometimes used but in our study we used a Synectics monocrystalline antimony pH electrode with an Ag/AgCl reference electrode [57].

3.2.2 pH-Metering Systems

In a 1984 publication, Breedijk and Akkermans described their own oesophageal pH monitoring system [58]. The pH signal was frequency modulated and recorded onto cassette tape. The recorder they used was the Oxford Medilog Mark I.

It is more usual nowadays to store pH data in a solid state memory. Stokkel et al describe a digital recorder capable of storing 24 hours of pH data in a 16 kB RAM [59]. Their circuitry includes a pH amplifier stage and an analogue to digital converter which converts input voltage to hexadecimal numbers. The system is controlled via a microprocessor. One mean pH value is stored in memory every 6 seconds giving 14400 bytes of data over a 24 hour period. There is a liquid crystal display indicating current pH readings.

The Digitrapper system developed in Sweden also stores pH data digitally [60]. Subsequent analysis provides a pH score which includes the total number of reflux episodes and the longest reflux episode. The score can be compared with normal values.

3.2.3 The Future of Ambulatory pH Monitoring

At present ambulatory oesophageal pH monitoring is widely used clinically. Its advantages over other tests has been acknowledged.

Evans used ambulatory pH monitoring for recording gastric pH and intestinal pH [61]. He claims that with these new applications, ambulatory pH monitoring is a rapidly expanding technique.

3.3 SIMULTANEOUS RECORDING OF THE ELECTROCARDIOGRAM AND OESOPHAGEAL pH : OUR SYSTEM

Twenty-four hour ambulatory monitoring of the electrocardiogram and oesophageal pH is well established. However, to the authors knowledge simultaneous monitoring of both signals has been reported only once. In their study Marianeschi et al use a Holter recorder and an ambulatory pH meter to aid diagnosis in patients with ambiguous chest pain [19]. We discarded this possiblity because of the unnecessary discomfort to the patient of carrying two recorders.

Oxford Medical manufacture a tape recorder conventionally used to record the ECG [Appendix 1]. There is a four-way recording head which facilitates recording of four signals. Two channels were used to record the ECG, one channel was used to record a timing signal and we used the fourth to record oesophageal pH. The ECG and timing signal were recorded directly onto the tape, while it was necessary to modulate the low frequency pH signal using pulse width modulation. The advantage of this method is that all patient records are stored on a single cassette tape.

3.3.1 **Recording the Electrocardiogram**

The Holter recorder used in this study was the Oxford Medical 4-24 Mark I recorder. A list of specifications is given in Appendix 1. It is described as being rugged but light in weight. The tape runs at 2mm/sec. so that 24 hours of data can be recorded on conventional 120 minute tape. Details of signal amplifier circuits and the tape speed control circuit are also included in Appendix 1.

In choosing the Holter Recorder we were confined to a multi-channel recorder to facilitate two ECG channels and one pH channel. Oxford Medical manufacture two such recorders. The Mark I is a direct recording device and the Mark II is an FM recorder.

The Mark II has a flat frequency response and reproduces the ST segment with no detectable distortion [31] [33]. It is not widely used in hospitals however, because it is more expensive than other recorders. The Mark I was made available to us by the Mater Hospital.

To test the performance of the recorder a 1 mV pulse was recorded at 1 Hz. Replay showed distortion of the peak of the signal and artefactual depression of the baseline (Figure 3.4). This result was also recorded by Bala Subramanian et al [33].

The frequency response of the recorder and playback system was also tested (Figure 3.5). A 0.5mV sine wave was recorded onto a blank TDK D120 tape. There was a peak in the frequency response between 0.1 and 1 Hz. However, the peak was significantly narrower than that reported by Bragg-Remschel [31]. The 3dB bandwidth was found to be 0.14-74 Hz. To convince ourselves of the Oxford Mark I's ability to reproduce the ECG and in particular the ST segment we subjected patients to a simultaneous ambulatory monitoring and Bruce Protocol exercise test. A medical doctor compared the results from both tests and found that the ST segment was faithfully reproduced. This concurs with findings published by Tzivoni et al [50].

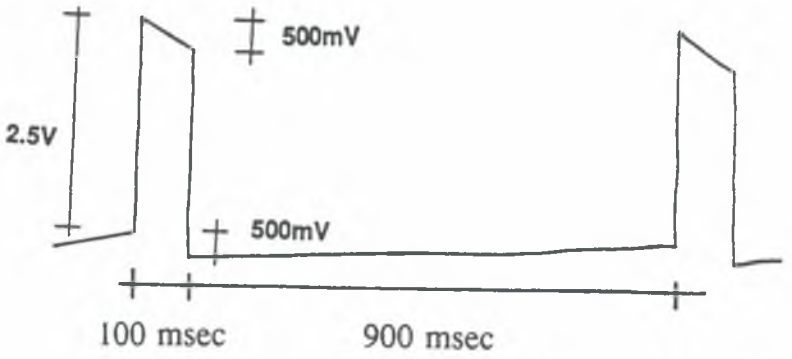


Fig. 3.4

Response of the Oxford Mark I Recorder

to a 1mV Square Wave Calibration Signal

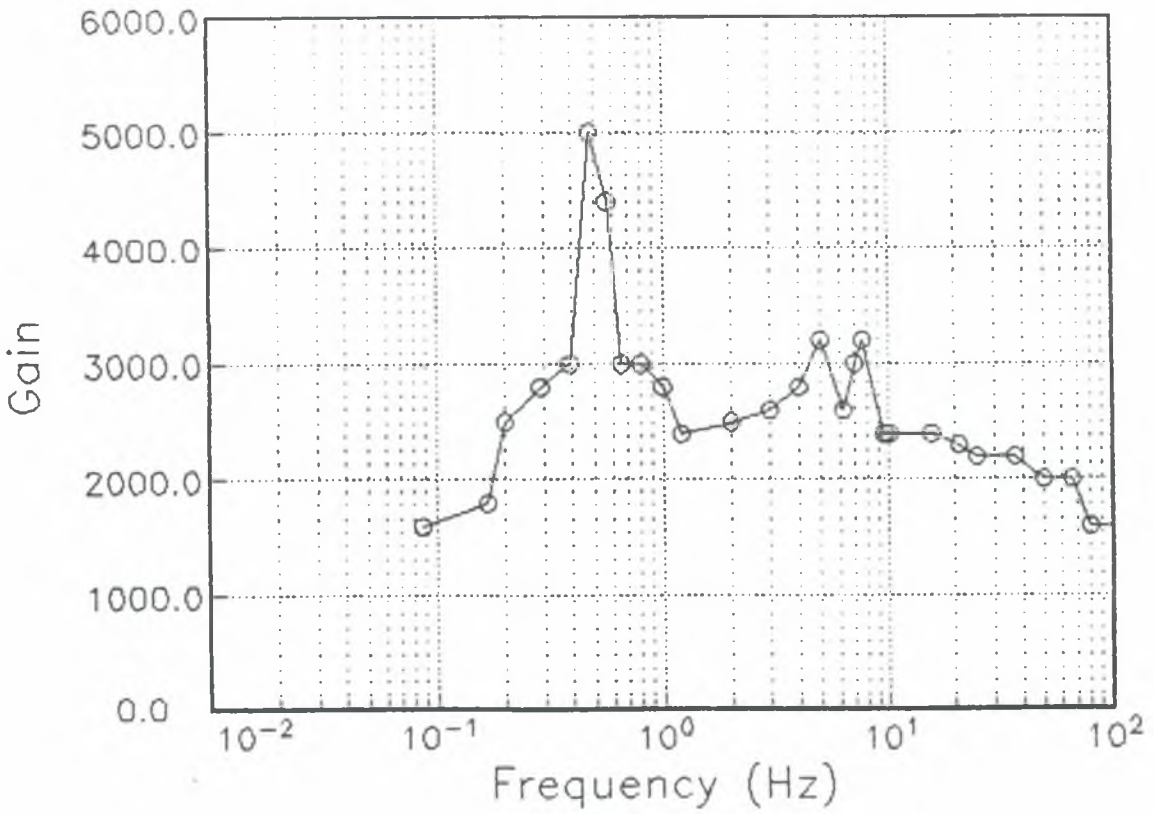


Fig. 3.5

Frequency Reponse of the Oxford Medical Mark I

Holter and Playback System

3.3.2 Recording Oesophageal pH

The first stage was to calibrate the Synectics pH probe discussed in Section 3.2.1. Two pH solutions of 7.01 and 1.07 were available from the manufacturers. The results of calibration at room temperature are given in Figure 3.6. As pH is temperature dependent, a new graph was calculated for 37° C., the temperature in the oesophagus. A correction factor was necessary to take the reference electrode into account. It is applied to the skin which is at 32° C., with a chloride gel : temperature correction of +5mV, junction potential factor = 6mV and chloride ion concentration in gel = -26mV, which gives a total correction of -15mV [62].

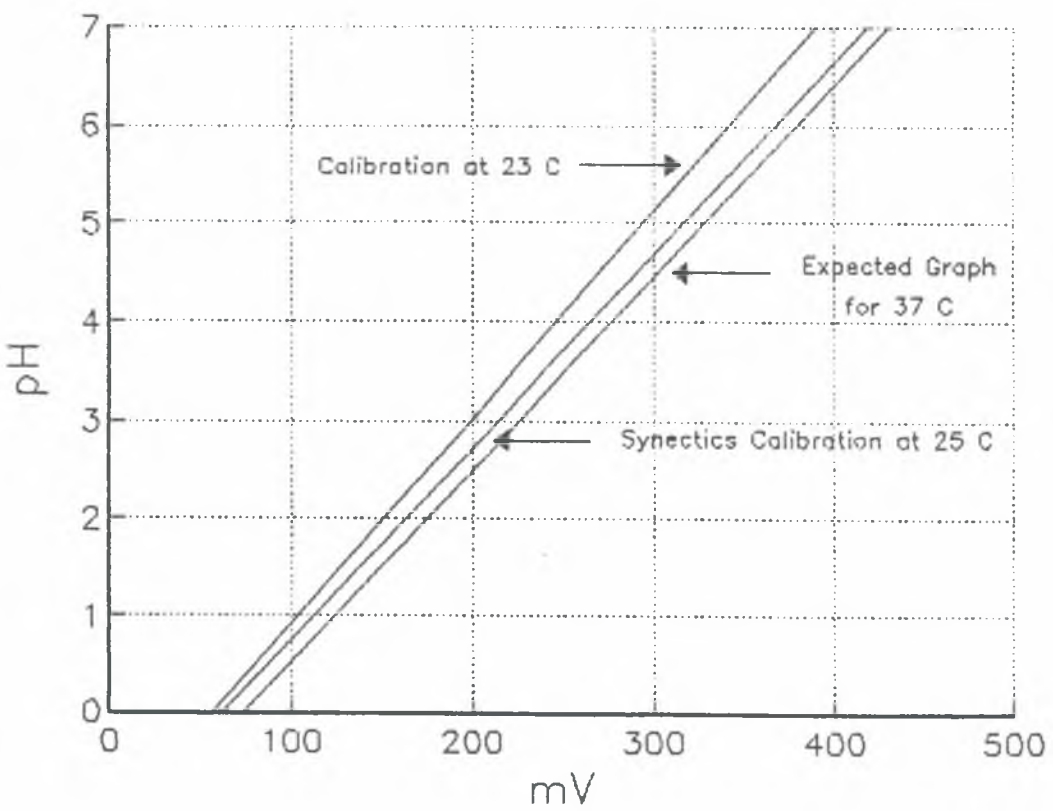


Fig. 3.6

Calibration of the Synectics pH Probe

The pH probe was tested while in the oesophagus of a volunteer patient. We used manometry to position the electrode (2.7.2). The potential difference between the probe and the reference electrode was 438mV which corresponds to a pH of 7.15, as expected (Figure 3.6). Pushing the pH probe a further 1cm into the nose gave a reading of 200mV or a pH of 2.49 because the probe was now in the stomach. This test also validated the use of manometry to find the position 5cm above the lower oesophageal sphincter where the probe should be placed.

The pH signals varies slowly with time and is modulated before being recorded onto cassette tape. Using pulse width modulation for this purpose has been previously described [63]. Oxford Medical manufacture a PWM circuit (referred to as the AM3) which can be slotted into the Mark I recorder. Details of the AM3 are included in Appendix 1.

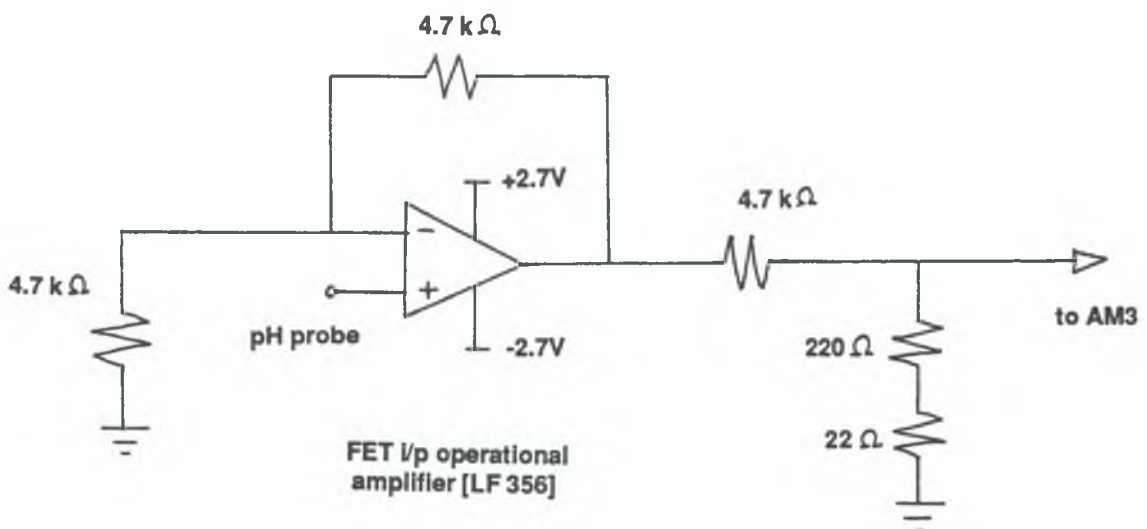


Fig. 3.7

High Impedance Input Stage for the pH Signal

The pH signal was buffered using a FET input operational amplifier (Figure 3.7). A potential divider was included at the output so that the input voltage range to the AM3 was 5-50 mV as required. A graph of the recorded input pH of the oesophagus versus the output voltage of the playback unit is given below.

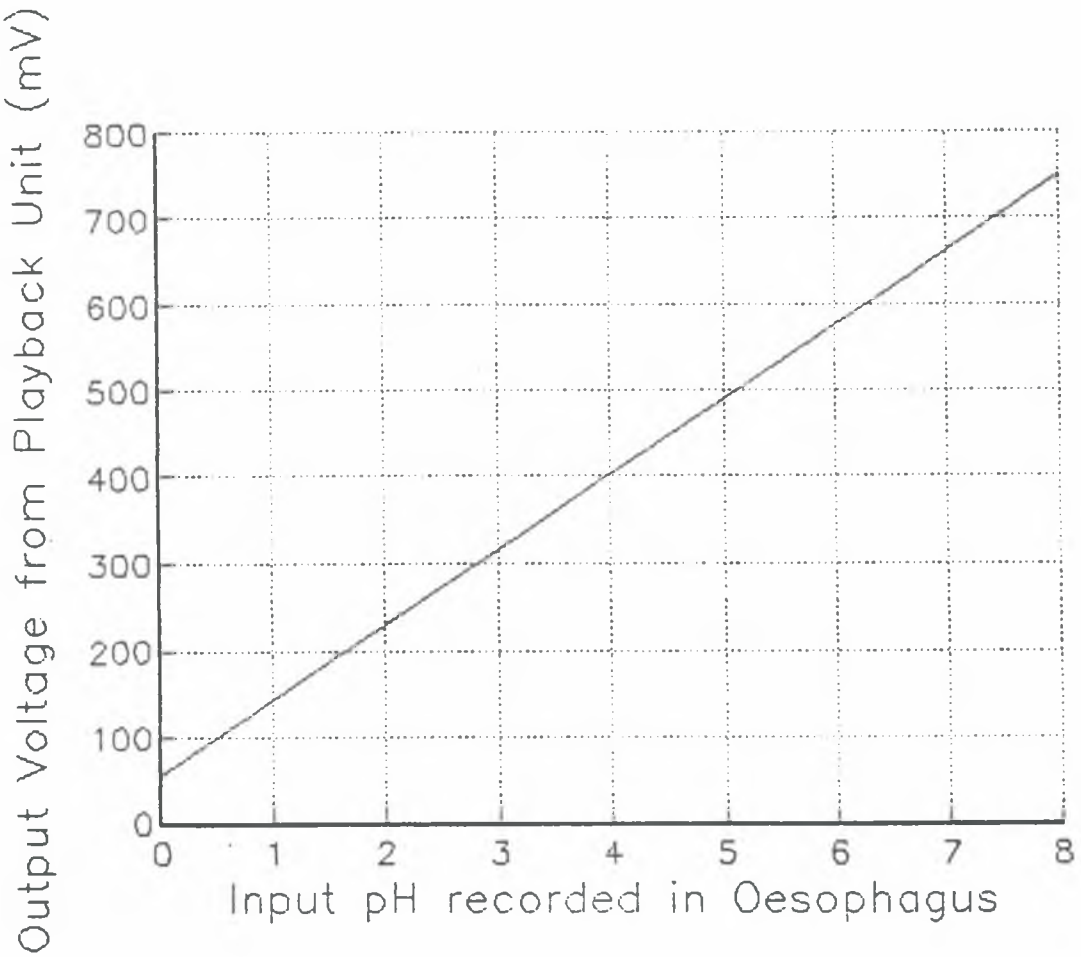


Fig. 3.8

3.3.3 The Timing Signal

A 60Hz. sine wave is generated by a crystal controlled circuit and recorded onto the fourth channel of the Holter recorder. A circuit diagram of the ATE-1 is included in Appendix 1.

3.4 THE PLAYBACK UNIT

The replay unit we used was the Oxford PB3 compatible with the 4-24 recorder. The PB3 is identical to the PB2 except there is no 24 hour time display (the PB2 was used in Bragg-Remschel's study, 3.1.1). Details of the PB3, including circuit diagrams are contained in Appendix 2.

We acquired this equipment from a medical service company and some repairs were necessary. A new tape deck was mounted on top of the unit, but the existing 4-way recording head was retained. This meant that the original playback speed of 60 x recording speed could not be attained. With some adjustment the playback speed was set at 32.59 x recording speed.

Two PD2 amplifiers compatible with the AD20 were used to amplify the ECG signals. The PM3 was used to demodulate the pH signal. An LED indicates the presence of a carrier. The PD2 is also compatible with the ATE-1 timing circuit.

The frequency response of the PD-2 is given as 12Hz-6kHz in the specifications. The manufacturers claim an overall flat response. To get the frequency reponse in real time we divide by the replay speed factor mentioned above. This gives a bandwidth of 0.37 - 184.13 Hz.

CHAPTER 4

SOFTWARE ANALYSIS OF THE ELECTROCARDIOGRAM AND OESOPHAGEAL pH

4.1 pH ANALYSIS

The pH signal from the oesophagus normally varies between 6 and 7 pH units. During a reflux episode however, the acidic contents of the stomach are released into the oesophagus and the pH drops to values below 4. When recording the oesophageal pH over a 24-hour period, it is necessary to define a scoring system which will indicate the degree of a patient's reflux problem.

4.1.1 A pH Scoring System

The pH scoring system used in this study was taken from a report by Johnson and DeMeester [64]. It was first developed 15 years ago, but its logic and scoring principles are consistent with new concepts that concern the pathophysiology of gastro-oesophageal reflux disease.

Reflux of the acid gastric contents into the distal oesophagus was defined as a drop in pH to a value below 4. The authors give several reasons for choosing this figure. They refer to a previous study which linked the onset of heartburn with pH <4. Another study showed that it best discriminated between symptomatic patients and controls. The end of a reflux episode was defined as a rise in pH to a value of >5 for at least 18 seconds.

As mentioned previously, the pattern of reflux episodes is dependent on posture (2.5). Episodes of reflux which occur during the daytime tend to be frequent, but are rapidly cleared. When the patient is supine (lying down [1]) reflux is less frequent and less rapidly cleared. It is therefore important to divide the 24-hour period into time spent upright and time spent lying down.

Johnson and DeMeester describe 6 parameters for their scoring system. They have based their system on clinical observations and on an understanding of gastro-oesphageal reflux:

1. Percentage Acid Exposure while supine (<1.2%)
2. Percentage Acid Exposure while upright (<6.3%)
3. Percentage Acid Exposure for the total 24-hour period (<4.2%)
4. Total number of reflux episodes (<50)
5. Number of reflux episodes longer than 5 minutes (<= 3)
6. The single longest reflux episode (<9.2 min.).

Reflux also occurs in asymptomatic patients, so it was necessary to calculate normal values for these six parameters (listed in parentheses after each parameter).

4.2 ECG ANALYSIS

Analysis of the electrocardiogram was originally confined to detecting cardiac arrhythmias. In recent years, Holter recorders which have a sufficient bandwidth to accurately record the ST segment have been developed (3.1.1). Consequently, algorithms for ST segment analysis have been introduced.

Computer processing of the ECG has two principal advantages. Firstly it can analyze vast amounts of data which would not be practical otherwise. In modern hospitals 24 hour ECG tapes are processed in less than an hour by an ECG technician interacting with a computer. Secondly, computer algorithms standardise ECG analysis which eliminates error due to interobserver variability.

4.2.1 Noise Reduction

Holter recording is susceptible to noise (3.1.3). Respiration causes low frequency drift, while 50 Hz interference and muscle artefact constitute higher frequency noise superimposed on the ECG. As the spectral content of these forms of noise overlap that of the ECG, filtering is not possible without introducing distortion.

In 1962 Steinberg et al reported using least square parabolic smoothing to remove noise before detecting all waves of the ECG [65]. They found that a moving average did not eliminate as much of the background noise as desired without degrading the signal.

Sheffield et al used a 29 point parabolic filter subroutine to smooth the ECG [66]. They claim that it reduced muscle artefact. After obtaining the first derivative of the signal, they used a 17 point moving average filter to remove 60 Hz. interference (the mains frequency in the United States) and other noise. The filtration reduced the R wave peak amplitude by about 10 per cent.

Weisner, Tompkins and Tompkins described a real-time ST-segment analyzer for use in an operating room [67]. One design requirement for the analyzer was the ability to handle electrosurgical noise during cardiac surgery. They used a Hanning digital filter to smooth data before getting the derivative:

$$y[n] = (1/4)\ [x(n+1) + 2\,x(n) + x(n-1)]$$

The use of a notch filter to remove 60 Hz has been previously reported [68]. Reisman and Yang describe two FIR filters with bandwidths of 0.5-55 Hz. and 65-100 Hz [69]. Again the most obvious manifestation of the distortion caused by such filters is a decrease in R wave amplitude.

MacFarlane and Lawrie used two low pass digital filters to remove frequencies above 50 Hz. [70]. The moving average filter removed irregularities in the waveform but attenuated the R wave peak. The recursive filter required less calculations, but distorted ECG wave amplitude and duration. The smoothed data was used to locate wave onsets and offsets. Then the unsmoothed data was used for measurement of the peak amplitude within these limits.

Clearly the filtered ECG can only be used for detecting abnormalities of rhythm in the heart. Filtering can however be used to aid the detection of the QRS complex (for example) if the unfiltered data is then used for more exact amplitude measurements.

4.2.2 QRS Complex Detection

The QRS complex can sometimes be quite difficult to detect. Its morphology or shape can change due to physiological factors or technical problems. The ECG signal may have a low signal to noise ratio or it may be difficult to distinguish the QRS peak from large P or T waves.

One method described by many researchers in the past is the use of a bandpass filter to exclude all but the QRS complex. The low frequency cutoff is chosen so as to minimise the influence of large P and T waves. The high frequency cutoff is chosen so as to suppress motion artefacts, but not narrow QRS complexes [71]. An analogue bandpass filter with a centre frequency of 17 Hz. and Q = 3.3 was used by Thakor [72]. It was followed by a thresholding circuit which registered the R wave peak. A five step digital filter was described by Okada [73]. The output of the filter was a series of square waves easily detectable in software.

A popular method for detecting the R wave is to find the maximum negative first derivative which corresponds to the downslope [66][70][74][75][76]. MacFarlane and Lawrie used 3 orthogonal ECG leads and were able to combine the first derivatives of these three signals to give the spatial velocity:

$$S = \sqrt{\frac{\Delta x^2}{\Delta t^2} + \frac{\Delta y^2}{\Delta t^2} + \frac{\Delta z^2}{\Delta t^2}}$$

The maximum value of S indicated the QRS peak. A value equal to 50% of this maximum was used as a threshold to detect the next QRS complex. Using multiple ECG leads is clearly superior to using just a single channel. One reason for this is that aberrant beats are sometimes low in amplitude in one channel, but are larger in another channel. Only by using a combination of these channels will the aberrant beat be detected. The disadvantages of analyzing a few channels are the increased volume of data to be stored and a longer computation time.

Ruiz and Duch suggested that a certain number of samples in the first derivative (or spatial velocity) must be below the threshold so that noise such as impulse artefact was not included. Also adaptive thresholding is superior to using a fixed threshold as QRS amplitude and morphology can change drastically during a short time. An inherent property of most detectors is their restrictive use of information available from the pattern of preceding R-R intervals. Even though a regular rhythm has prevailed for a long time, the next QRS to be detected is treated as if it could occur almost anywhere in the observation interval. Pahlm and Sornmo suggest an "eye-closing" period from the end of the QRS complex up to the approximate end of the T wave [71]. Their method was successful in excluding large T waves, but there was a risk of missing early QRS complexes (premature ventricular

contractions or PVC's). The eye-closing period was chosen in the interval 120-200 msec. Pahlm and Sornmo describe another method for QRS complex detection where complexes are detected in order of magnitude and not in temporal order. Eye-closing periods of equal length are applied both before and after each detected beat. The threshold is updated allowing the detector to find QRS complexes, even when a sudden decrease in amplitude occurs.

Nicklas, Lee and Jenkins report a novel method for QRS detection based on convexity [77]. They use the Convexity Operator to provide information about the sharpness of the indentation or protrusion at a point:

$$C_i^L = 2Lx_i + \sum_{J=-L,\, J\neq 0}^{L} W_j\,(x_{i-Nj} + x_{i+Nj})$$

where x_i is the ith sample value, W_j is the weighting factor, L is the number of points to be considered and N is the operator window size. By appropriately choosing these parameters, it is possible to make the convexity operator sensitive to QRS complex peaks alone while ignoring very sharp, noisy peaks and wide premature beats. The parameters are found empirically. Nicklas et al chose N=5, L=3 and $W_j = 1$ for an ECG sampling rate of 250 Hz. They found that the convexity operator always gave pronounced peaks for the Q, R and S waves and was insensitive to noise.

4.2.3 Pattern Recognition

Pattern recognition of the P, QRS and T waves of the ECG has been widely described. However, only delineation of the QRS complex is important for ST segment analysis. The reference level for ST measurements is estimated from an interval just before QRS onset. ST levels are then measured at certain time intervals from the end of the QRS complex.

The number of leads monitored greatly influences the accuracy of QRS delineation. In the single lead case. it may be difficult to achieve accurate delineation since initial depolarisation can be very small in the selected lead. The Q wave amplitude may, furthermore, change from beat to beat due to body movements causing the wave to vanish in certain beats. Another problem is the determination of the QRS end in beat morphologies with no distinct transition between the S wave and the ST segment.

Stallmann and Pipberger noticed that the signal to noise ratio of the ECG was high for frequencies below 60 Hz., but low for frequencies above 60 Hz [78]. This led them to design a filter which passes only frequencies below 60 Hz. They found that filtration did not disturb wave onsets and offsets. The spatial velocity was calculated for 3 orthogonal leads. For a given cardiac cycle the maximum spatial velocity was first detected. In cases where there were two maxima, the first was used. The spatial velocity was traced both backwards and forwards until values below 3μV/msec were found. These points were defined as the beginning and end of the QRS complex, respectively.

They compared computer delineation of the QRS complex with visual interpretation. QRS durations calculated by the computer tended to be longer. Stallmann and Pipberger claim that their method is only accurate enough for large scale statistical studies.

Wartak, Milliken and Karchmar describe a computer program for ECG pattern recognition rather than exact wave delineation [76]. The first derivative of the ECG cycle is calculated. The maximum positive slope corresponds to the upslope of the R wave or in some cases, the S wave. Similarly the maximum negative slope corresponds to the downward slope of the R wave or S wave. Maxima and minima indicate a change from positive to negative slope or vice versa. A maximum corresponds to the peak of the R wave while minima correspond to the Q and S troughs.

Corners are defined as points located between a slope and a flat portion. A flat portion is said to be present if among 6 adjacent points at least 3 first differences equal to zero are found. Corners will correspond to the onset and end of the QRS complex. The search region is taken as 80 msec before the maximum positive slope and 80msec after the maximum negative slope.

Pahlm and Sornmo report that QRS delineation is generally based on thresholding a function such as spatial velocity [79][80]. Another method involves cross correlating the ECG with a set of QRS functions which have been manually delineated. An improvement to this method would be to create a template for each subject at the start of analysis.

These methods sometimes fail during exercise due to excessive noise. Therefore some programs employ a delineation function at rest only. During exercise they suppose that onset occurs at the same time before the fiducial point as at rest and similarly the offset occurs at the same time after this point. The fiducial point is estimated by summing the envelope signals from the individual leads and finding the maximum.

Finally, Balda et al report a method which defines search windows for detecting the QRS onset and offset [81]. Three ECG channels are taken from a hospital monitor. Based on the fact that the most outstanding characteristic of the QRS complex is its dynamic properties, they define the waveform boundary indicator. This is an algebraic combination of the first and second derivatives of the ECG:

$$WBI = C_1 \sum_{i=1}^{3} |f_i'(k)| + C_2 \sum_{i=1}^{3} |f_i''(k)|$$

where k is the kth discrete time increment and i is the ECG measurement from the ith channel. The derivatives are calculated as follows:

$$f'(k) = f(k+1) - f(k-1)$$
$$f''(k) = f(k+2) - 2f(k) + f(k-2)$$

The WBI worked quite well in practice except that it tended to be somewhat narrower than the QRS. To correct this problem a second WBI called the WBIF was computed from the same data after digital filtering. The filtered data was obtained by convolving the raw ECG data, f(n) with the impulse response. The result is a waveform boundary indicator wide enough to cover the entire QRS interval. Subtracting the WBI from the WBIF results in two search regions. Analysis returns to the original signal to find the QRS onset and end.

The program described by Balda et al also uses a method to determine if an ECG signal contains too much contamination. Each waveform has a "signature" defined in terms of its critical points, such as maxima, minima and zero crossings and those of its derivatives. If this signature does not fall within the acceptability range, the data is preprocessed by smoothing with an adaptive filter. A quadratic polynomial least squares technique is used to smooth both raw data and the derivatives. After filtering, the signature is recomputed and analyzed if within the acceptable limits.

4.2.4 Detection of Ectopic Beats

An ectopic heart beat indicates that depolarisation of cardiac muscle has originated in an abnormal place. The result is premature contraction of the ventricles. Any QRS complex detection algorithm is based on a trade off between including normal beats and excluding aberrant ones.

Feldman et al described the characteristics of an ectopic beat [82]. It arises prematurely, before the next expected discharge of the dominant pacemaker of the heart. A longer interval or compensatory pause follows. The time interval between the normal beat preceding and succeeding the ectopic is approximately twice the average R-R interval. The shape of the ectopic beat is abnormal compared to the patients usual QRS complex.

The algorithm used by Feldman et al first checks whether an R-R interval is less than 90% of the running average. When this condition is true there is a check for the compensatory pause. For each beat a normalized cross correlation coefficient is computed between the beat and a beat which the computer selected earlier in the run and stored as a standard normal beat. If the waveform is judged to be abnormal it is also correlated with a stored version of the first beat that the computer detected as being premature. The purpose of this latter test is to discover episodes of multiple PVCs.

Geddes and Werner agreed that PVCs differ from normal complexes in that they are detectably premature and invariably of abnormal shape [83]. They added that ectopics are usually of increased duration. For regular rhythms the standard R-R interval is calculated as:

$$\frac{2\,(\text{R-R avg}) \;+\; (\text{R-R last})}{3}$$

Where (R-R avg) is the previous standard and (R-R last) is the R-R interval immediately preceding the cycle under consideration. A complex falling at the end of an R-R interval of less than 90% of the standard is considered premature. If this test is false a further check on the QRS duration is made. A width more than 40 msec above the average is considered abnormal. A final check is made on the shape of the complex by comparing it with a normal morphology determined earlier by the computer.

A more stringent definition of abnormal QRS complex duration is given by Pipberger [84]. His computer algorithm finds the median QRS duration and complexes deviating from this value by more than 12 msec are eliminated as outliers.

Fentem et al reported their computer program to identify the occurrence of an ectopic beat by the negative duration of adjacent pulse intervals [85]. The program steps through the data progressively, examining ratios within each sequence of 4 beat intervals (Figure 4.1).

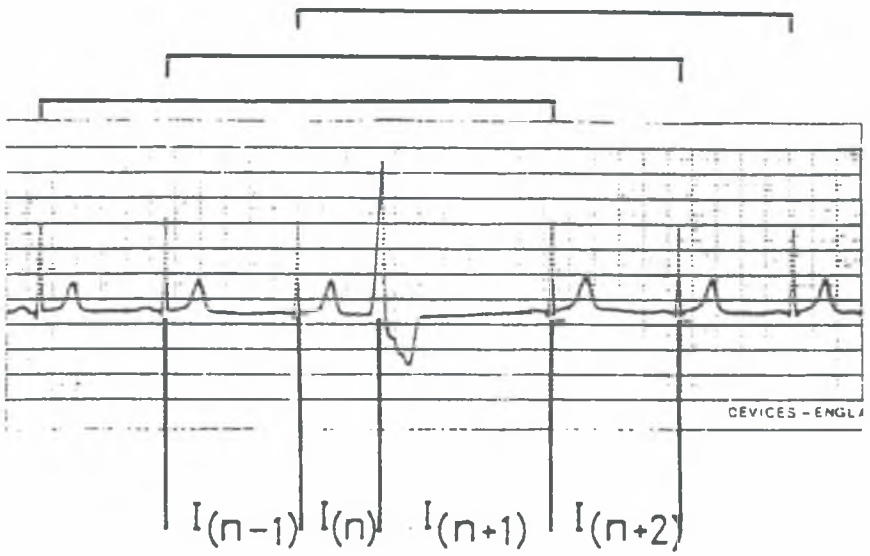


Fig. 4.1
Definition of Successive Intervals Surrounding the Ectopic Beat [85]

a. Each interval must be in the range 250 msec - 2000 msec. This limits further examination of spurious intervals in noisy records.

b. The ratio I(n)/I(n-1) must be less than 0.9. When this condition is satisfied the presence of a short interval in the sequence is established.

c. The ratio I(n)/I(n+1) must be less than 0.9. This indicates a short interval followed by a long interval.

d. Finally the ratio [I(n) + I(n+1)]/2I(n+2) must lie between 0.7 and 1.1. This condition distinguishes an ectopic sequence from interval changes associated with the onset of cardiac acceleration.

When all four criteria are satisfied an ectopic beat is recorded. Their program was validated by manual counting. One limitation was that ectopics could not be detected when they occurred in runs of 2 or more. They found that this did not lead to a serious underestimation in the 18 patients included in the study.

Abboud and Sadeh used cross-correlation to reject ectopic beats [86]. Prior to the correlation procedure each of the ECG waveforms was filtered through a non-recursive digital bandpass filter (30-250 Hz). They showed that when normal ECG waveforms were correlated, the normalized cross correlation factor had a maximum value of 0.9. When a normal ECG waveform was correlated with a PVC however, the normalized cross correlation factor had a maximum value of 0.49. The routine is designed for use in a cardiac care unit. Accurate detection is very important as a ventricular premature beat may be the forerunner of catastrophic electrical seizures of the heart known as ventricular fibrillation which can result in sudden death.

4.2.5 The Isoelectric Level

The isoelectric level is the reference level from which the ST segment is measured. Accurate evaluation of ST change depends upon finding the true isoelectric level.

Wartak et al recommend the flat portion before the QRS complex as the reference level [76]. There might be a small error in this measurement due to atrial repolarisation. The isoelectric level could be taken between the T and P waves. Again this measurement is subject to error because the T and P waves may overlap or there may be an extra wave in the ECG, called the U wave following the T wave. In this case the error would be unpredictable.

Some years later, Clark et al defined more precisely detection of the isoelectric level [87]. It is defined as the average voltage of 6 consecutive points whose first differences are minimal in the 56 msec prior to QRS onset. Weisner et al described their algorithm which searches between the P and Q waves for a 30msec period with zero slope [67]. The signal was smoothed using a Hanning digital filter before the first derivative was calculated.

Pahlm and Sornmo recently described their criterion for establishing the reference level [71]. After the QRS complex has been delineated, a few samples are taken in a short interval (6-10 msec) just before the onset. These samples are then averaged to give the isoelectric level.

4.2.6 Removal of Baseline Wander

Baseline wander is the name given to low frequency noise caused by respiration and body movement. If the ST segment is continually on an upsloping ECG, the error could lead to a false negative result. However, correction of baseline wander can lead to distortion of the low frequency components of the ECG, including the ST segment.

In 1981 Clark et al described a baseline drift adjustment technique which preceded ST segment analysis [87]. The first step was to detect the onset of successive QRS complexes and then join these points with solid lines. Dashed lines drawn horizontally from the onset points were used as piecewise baselines to which inter-QRS sample points were adjusted according to the slopes of the solid lines. The piecewise baselines were then merged to a common baseline level.

Pahlm and Sornmo also suggest the method of subtracting a linear slope from each beat [79]. The slope is estimated from two short segments separated by an R-R interval. This method can be inaccurate as the beats included in the estimate do not necessarily occur on linear slopes. MacFarlane and Lawrie showed how this error can arise and suggested a different approach [70]. The raw ECG is low pass filtered to remove the P, QRS and T waves and leave the wandering baseline. This signal is then subtracted from the original ECG signal. They claim that this method is more accurate.

In their algorithm Wartak et al determine the isoelectric level in two successive beats [76]. If the difference is greater than 0.4mV in amplitude, the first QRS complex of the pair is eliminated. If the amplitude difference is less than or equal to 0.1mV, the histogram method is used. Otherwise the ECG is corrected to a straight line. The histogram method involves determining the most 'popular' amplitude in an R-R interval. This is used as the baseline and all data points are normalized with respect to it.

Ruiz and Duch also used the amplitude histogram [75]. If baseline wander is present, the peak of the histogram will be less showing a wider dispersion of amplitudes. This enabled them to quantify baseline drift and thus establish a criterion for accepting or rejecting a certain segment of the ECG. They also comment that comparing successive QRS onsets as a means of detecting drift is not always adequate. Take the case of baseline wander which is at the same frequency as the heart rate. There will be little or no difference between successive isoelectric levels, but the ECG between the QRS complexes may be subject to excessive baseline wander. This would only be seen by calculating the amplitude histogram.

In the same year Riedl et al described their method for baseline wander removal used in the Siemens program [68]. The first stage was to take every 20th sample from the raw ECG data which was sampled at 250 Hz. Samples which deviated from the average by more than 0.3mV were corrected. Parabolic smoothing and interpolation follow to give a baseline signal with the P, QRS and T waves removed. This signal is subtracted from the original ECG data.

Watanbe et al reported the PR cubic spline technique [68]. Using this method, PR segments are fitted using a polynominal equation that is then subtracted from the wandering ECG signal. They claim that this can result in a smoothing of the baseline without any ST segment distortion.

More recently van Alste et al discussed real-time reduction in baseline wander for the exercise ECG [89]. The first method considered was the estimation and subsequent removal of the drift using polynominal splining techniques. However, splining methods are dependent on measuring the level of the PR segment as this is supposed by definition, to be the baseline level. If the PR segment is not well

defined then this method fails. Another method discussed was digital high pass filtering. The low frequency cutoff was taken as the inverse of the heart rate. This technique caused distortion of the ST segment.

Finally, Marques de Sa described a digital filter capable of passing frequencies corresponding to baseline drift [90]. Narrowband FIR filtering using a cascade of decimating and interpolating stages was used. The frequency characteristic could be specified by the user, but they suggested a bandwidth of 0.375-1.5Hz. Their system has several advantages over the method of curve fitting and classical filtering. Curve fitting has an unspecifiable frequency response while classical filtering is too time consuming and introduces long delays. Their filter showed only a very small amplitude distortion for the low frequency components of the P and T waves.

4.2.7 Signal Averaging

Averaging is a common technique for removing noise. Successive beats are aligned and analysis is performed on the averaged beat. It provides excellent improvement in signal quality because noise is random and is therefore averaged out. However, there is a difficulty in preventing aberrant beats from being included and degrading the average. Misalignment can result in a prolonged QRS complex and diminution of the Q, R, S and T waves.

The algorithm described by Clark et al first checked for 11 consecutive normal beats [87]. The outer 2 beats were then discarded as these may succeed or precede an ectopic beat. Intervals of 256 msec preceding and 504 msec following the R wave peak were averaged to give a threefold improvement in the signal to noise ratio. The disadvantage of this method is that ST segment changes which occur in an episode contaminated with ectopics will be missed.

MacFarlane and Lawrie used cross correlation techniques to align heart beats [70]. This is considered more accurate than aligning with respect to a peak amplitude. Their algorithm takes 9 second episodes and checks for noise. If the noise level of the ECG is below a critical value of 30 μV in all leads, one representative complex is selected for analysis. If not, the averaging procedure is used.

Pahlm and Sommo discussed two approaches to signal averaging: blockwise processing and recursive processing [79]. When averaging blocks of ECG data the choice of interval length is important. Analysis should reveal changes in the ST segment while at the same time include sufficiently many beats in the estimate in order to achieve efficient noise reduction. If the interval is too long there will be an underestimation of ST segment change. A length of 10-15 seconds seemed to be a reasonable compromise.

There are two possible methods of averaging. The sample mean and the sample median both operate on a point by point basis. Sample means provide better suppression of muscle noise. On the other hand, sample medians are naturally less sensitive to outliers caused by baseline shifts, spikes or included aberrant beats. Accurate removal of baseline wander is especially critical when using sample medians. In general, outliers are few in number so a trimmed mean could be the most suitable method.

Recursive processing involves calculating a running average. The estimate of the kth sample is given by:

$$x_k(\ell) = x_k(\ell-1) + \propto (r_k(\ell) - x_k(\ell-1))$$

where ℓ is the number of the beat under consideration, and α is the weighting factor which determines the extent of the influence of the most recent sample $r_k(\ell)$. If $r_k(\ell)$ corresponds to an outlier then the expression in brackets will be large. It is desirable to reduce the influence of such values. Pahlm and Sommo suggest using an "incremental averaging" technique where a fixed value is added or subtracted, independent of the magnitude of the residual:

$$x_k(\ell) = x_k(\ell-1) + \alpha \, \text{sign}\,(r_k(\ell) - x_k(\ell-1))$$

$$\text{sign}\,(x) = \begin{cases} 1 & x>0 \\ 0 & x=0 \\ -1 & x<0 \end{cases}$$

and α is a positive scalar. While this is a robust technique, response to fast changes in the ST segment may not be acceptable. This response could be speeded up by using a larger increment, but this results in less efficient noise reduction.

Filtering and averaging have been well described in literature because in general, the resultant signal is adequate for arrhythmia analysis. There is a good improvement in signal quality, but possible distortion of the ST segment.

4.2.8 Analyzing the ST Segment

The classical criterion for diagnosing ischemia from the exercise test is horizontal or downsloping ST depression of 0.1mV or more at the end of the QRS complex [79]. The specificity of this criterion is high but the sensitivity is low. It is improved if certain types of upsloping ST depressions are also classified as abnormal, e.g. ST segment depression of 0.1mV or more 80msec after the QRS end.

Gallino et al stated that horizontal or downsloping ST segment depression greater than 0.1 mV should last for at least one minute to be considered pathological [91]. Episodes occurring after each other in rapid succession were considered as separate ischemic events when the ECG had returned to baseline level for at least 2 minutes.

Before the ST segment can be measured its start and end points must be defined. The ST segment onset or J point is the first inflection point after the S point or may be the same as the S point in certain ECG complexes. There is a difficulty in defining the exact point where the ST segment ends and the T wave begins. In fact gradual upsloping may start right after the QRS end. Most researchers measure the x point or ST segment end at a fixed time interval after the J point.

The J point occurs at the end of the QRS complex and can be detected using the second derivative (4.2.3). In their 1970 publication, Wartak et al used J + 120 msec to delineate the ST segment [76]. This interval was further subdivided into 3 intervals for analysis. Modern ST analysis routines favour an interval of J + 80msec for low heart rates. When the heart rate exceeds 105 beats per minute J + 64 msec is used to avoid falling within the T wave range [92]. Bala Subramanian et al recognised that the length of the ST segment varied the heart rate and used the following equation to calculation the x point [33]:

$$x = 1/8 \text{ (R-R interval) after the J point}$$

Clark et al took the ST segment as the interval from J + 6 points (sampling rate of 250 Hz.) for a length of n points [87]:

$$n = \max [4, (200 - \text{Heartrate})/16]$$

A starting point of J + 6 avoided inclusion of small J point notches. ST deviation was measured from the baseline to the point on the ST segment closest to the baseline. It was expressed as a percentage of the height of the averaged QRS complex. The ST slope was taken as the slope of the linear least squares line of best fit through n points of the ST segment.

Weisner et al suggested a novel approach for their ST segment analyzer used during surgery [67]. They defined the T point as the point which marked the beginning of the T wave. The first step was to find the T wave peak which was the maximum absolute value relative to the isoelectric voltage between J + 80 msec and R + 400 msec (or less if the heart rate exceeds 100 beats/min).

If the T peak was not present or undetectable due to noise then the search limit point was used as the T peak. The T point was then found by looking for a 35msec period with sampled filtered values within one sample voltage unit of each other on the R side of the T wave. If no apparent T wave was present, J + 120 msec was used instead. Two end points were used to define a search window: J + 20 msec and the T point. The algorithm then searched for the point of maximum depression. This method automatically compensates for variations in conduction times and erroneous measurements due to very fast heart rates.

McHenry noted that noise could lead to an error in calculation of the ST slope [93]. Many researchers including Weisner et al measure the ST area to overcome this problem [66][67]. All the sampled points between the J and T points were summed after subtracting the isoelectric level from each.

Yet another parameter called the ST index is sometimes used [67]. It is defined as:

$$\text{ST Index} = \text{ST Segment Level} + 1/10\ \text{ST slope}$$

The index is abnormal if negative and normal if positive. This parameter was discovered by Dr. Paul McHenry and has an overall sensitivity of 92%.

In 1986 Skordalakis published his algorithm for recognition of the shape of the ST segment [94]. It was based on the idea that the ST segment is supposed to be a straight line or a parabolic segment. The ST segment is difficult to delineate exactly so Skordalakis overcame this problem by taking a larger segment with some constraints. Firstly it should incorporate the ST segment. Secondly that its onset and end can be reliably calculated and finally that it can be divided into subsegments in such a way that one of them is the ST segment. The first and second criteria are satisfied if the beginning of the segment is taken as the peak of the S wave (or if the S wave is missing, the peak of the R wave) and the end as the peak of the T wave. This will give three subsegments which can be detected by their different slopes. The middle subsegment is the ST segment. A routine for determining ST shape follows.

In 1984 Kortas introduced a new approach to qualifying the ST segment [95]. He acknowledged that horizontal and downsloping ST segments are precisely analyzed. However, there was a problem with interpretation of ST segment depression with upsloping morphology. He described the ST index as a heuristic rule created from examination of a limited amount of data and is without any theoretical background. The important properties of the ST segment are:

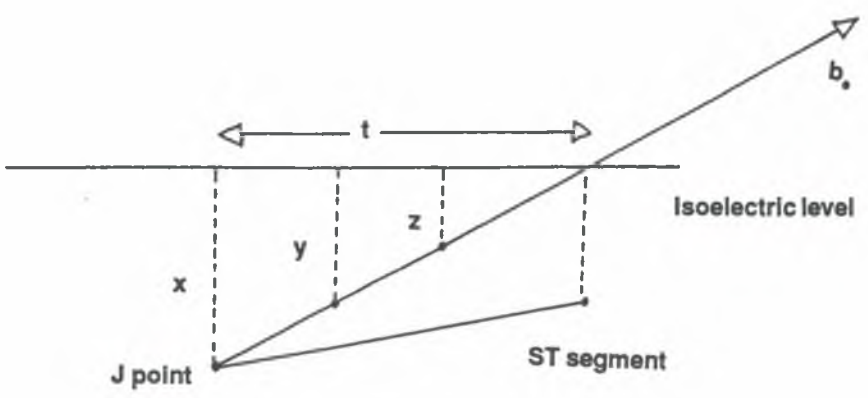
1. J point depression is normal and can be caused by a variety of factors, including ischemia.

2. The depressed J point does not return to the isoelectric level instantaneously.

3. Depression at the end of the ST segment is abnormal.

Rules 1 and 2 suggest that a certain amount of depression should be considered normal.

The existence of a normal component of ST segment depression requires the use of a new baseline called the effective baseline (Figure 4.2). The time taken by normal J point depression to return to the isoelectric baseline is given by 't'. There is no information available about the length of 't' so it is taken as the normalized duration of the ST segment. X, y and z are normal depressions.



b_o is the effective baseline

Fig. 4.2

In the case of constant J point depression and varying slope, the integral to calculate area works well (Figure 4.3a). However, in the case of constant x point depression and varying J point depression, the ST integral is in sharp conflict with clinical knowledge (Figure 4.3b). Its value will decrease while significance for ischemia increases. Pathological changes in ST area reflect an increase in the effective area, A_e or a decrease in the normal component of area, A_n (Figure 4.4). Kortas proposes $(A_e + A_n^{-1})$ as an indicator of the possibility of coronary artery disease and $(A_n + A_e^{-1})$ as an indicator of normality. He defines the effective ST segment as:

$$ST_e = (A_e/A_n).ST = \frac{ST^2}{J}$$

and ST* is defined as the optimum discriminant value between $(A_e + A_n^{-1})$ and $(A_n + A_e^{-1})$.

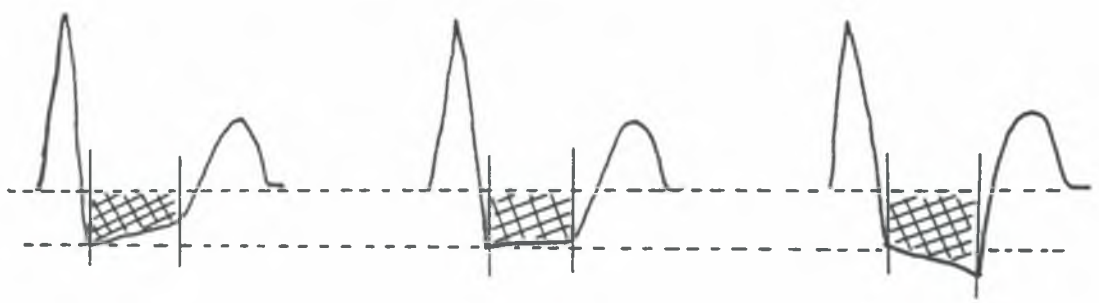


Fig. 4.3a

Constant J Point Depression, Varying ST Slope

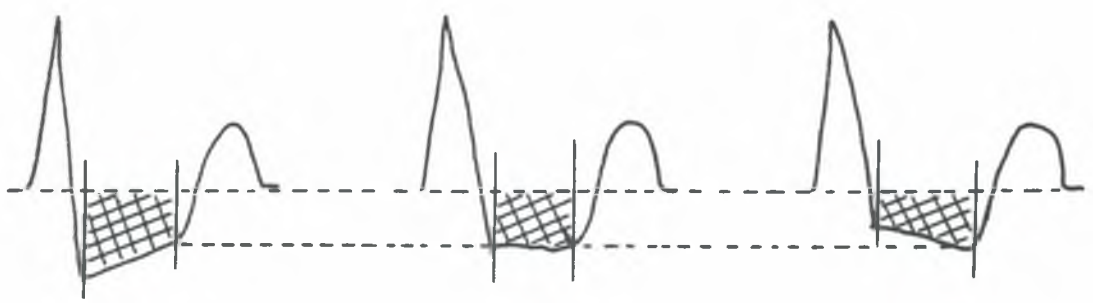


Fig. 4.3b

Constant x Point Depression, Varying ST Slope

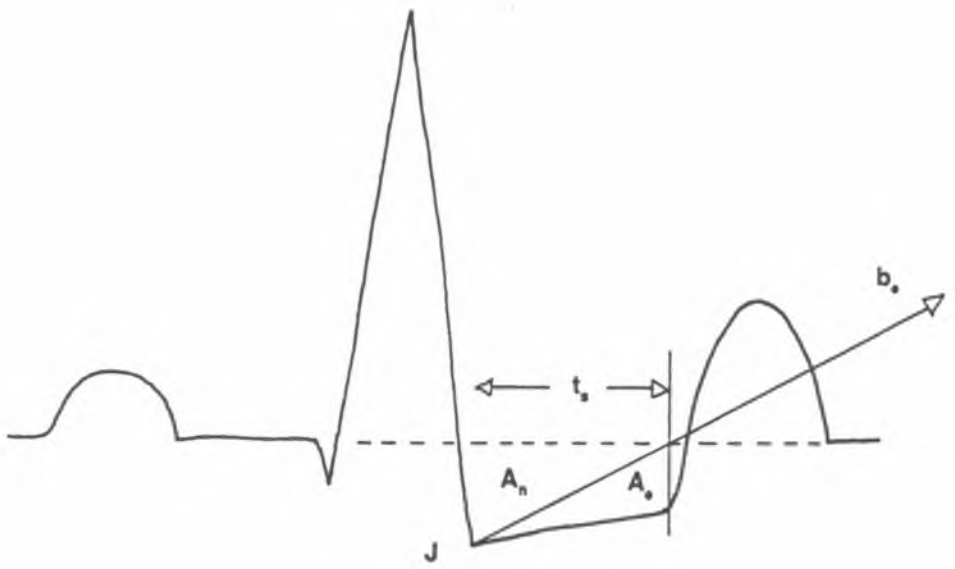


Fig. 4.4

Normal and Effective ST Area

This leads to a classification criterion. If ST_e is greater than or equal to ST* then the heart beat is ischemic. If not, the heart beat is labelled normal. A clinical trial consisting of a study of 42 exercise tests gave a sensitivity of 88% and a specificity of 94%.

Pitas et al introduced another novel approach to the classification of ischemic and normal beats [96]. First the signal was preprocessed to suppress incidentals, noise, etc. Then the WBIF was calculated (4.2.3) and convolved with a function, h_n:

$$h_n = \frac{1}{K}\left(1 - \frac{n-K}{K}\right) \text{ if } 0 < n < 2K-1$$

$$0 \quad \text{Otherwise}$$

$$g_n = h_n * f_n$$

where f_n is the WBIF. The autoregressive model of the waveforms {g} is given by:

$$g_n + a_1 g_{n-1} + \ldots\ldots + a_p g_{n-p} = E_n$$

Where E_n is a white noise process. Normal and ischemic sequences $\{g_n\}$ were separated by a difference in corresponding AR model coefficients $\{a_1, a_2 \ldots\ldots a_p\}$. Pitas et al took $p = 2$ and plotted a_1 against a_2. Normal and abnormal waveforms formed two distinct clusters.

4.2.9 Automatic versus Semiautomatic Analysis

The medical profession tend to be sceptical of automatic ECG analysis. They demand "full disclosure" so that they can check the accuracy of the computer. This usually takes the form of a printout of 24 hours of ECG data in miniaturised analogue form [97].

Many modern systems provide semiautomatic analysis, e.g. the Reynolds Pathfinder. These systems are based on audio visual superimposed ECG presentation (AVSEP), described by Norman J. Holter in 1961 [24]. Signals appear successively superimposed on the screen. The R wave is used to trigger the display. Up to 80 ECGs are superimposed and when an abnormal wave shape is encountered, it is easily seen.

The semiautomatic system described by Stein et al first classifies ECG beats into clusters [98]. The operator examines examples of beats from each family and places electronic markers on the isoelectric baseline, the J point and the ST segment end. The x point is usually placed either 60 or 80 msec from the J point. He can also set the threshold for detection of ST segment changes: normally depression of 1 mm, lasting one minute. As the observer sees a few example beats from each family there is less chance of abnormal beats being included in ST analysis.

Gallino et al developed a computer program for ST analysis [91]. They compared their program with 3 other methods of analysis:

1) Visual analysis from a television screen.

2) Semiautomatic analysis where the operator selected the isoelectric baseline and the J point. The difference was stored and used to plot the J point trend.

3) Visual analysis of a compressed beat by beat printout.

All systems used the same criteria for ischemia. After a careful comparison of the results achieved by automatic analysis and the other techniques, the former was discovered to be most accurate for detection of transient ischemic ST changes.

Pisani and Eggeling et al performed similar tests [99][100]. In particular Eggeling et al determined automatic analysis combining measurements of the J point and the x point, was superior to both visual analysis and automatic analysis of the J point only. They claimed that manual interaction is unnecessary.

Automatic analysis appears to be superior to visual analysis because it standardises the analysis process. Willems found inter- and intra-observer variability in determining wave recognition points [101].

4.2.10 The Future of ST Segment Analysis

Traditionally the ECG is analyzed in the time domain. However, frequency analysis of the exercise ECG has been reported by Abboud and Sadeh [86]. Two groups of patients underwent an exercise test. One group consisted of patients suffering from ischemic heart disease (IHD) while the second group had no clinical evidence of IHD. The digitized ECG waveforms were aligned, averaged and bandpass filtered between 150 and 250 Hz. The difference in morphology or wave shape between the high frequency complexes before exercise and during the recovery phase was examined using cross correlation analysis. They found that the difference was significantly lower in patients without IHD (correlation coefficient = 0.83) than in patients with ischemic heart disease (c.c. = 0.66). They conclude that exercise induced changes in the morphology of the QRS complex can be detected by the high frequency content of ECGs and may represent a sensitive early indicator of coronary artery disease.

Nikias et al describe a method for detecting and locating acute myocardial ischemia in dogs [102]. This is an important study because early detection means the process of damage to the cardiac muscle will be arrested. They used a monopolar electrocardiogram and focussed on cardiac activation rather than repolarisation as in conventional analysis. They found that the spectral content of these waveforms changed noticeably when ischemic heart disease was present.

Despite these studies, sophisticated ECG analysis has not yet been used commercially. It was mentioned earlier that the future of Holter recorders lies in solid state memories. If this is the case then work will be concentrated on producing accurate and efficient algorithms for real time analysis.

4.3 ANALOGUE TO DIGITAL CONVERSION

The software was developed on an Ericsson Personal Computer. Programs were written principally in 'C' language and compiled on a Microsoft 'C' compiler. Graphics software was written using GraphiC subroutines.

4.3.1 Sample Rates

Before writing the analogue to digital conversion software there were two important considerations: the choice of sampling rate and precision level. Berson and Pipberger considered the precision to be crucial because it affects the storage space [103]. Their study looked at 12, 10, 8, 7 and 6 bit resolution and found that as the precision was reduced, the errors increased and amplitude values tended to be larger. They also found discrepancies in wave duration measurements.

The choice of sample rate is governed by two factors. On one hand there is a shortage of memory space on the P.C., but on the other hand there is a need to capture an accurate representation of the signal.

In their semiautomatic ECG analysis software, Stein et al used a sampling rate of 102.4 Hz. [98]. Silber et al reported a sampling rate of 128 Hz. for their digital Holter recorder [54]. However, their recorder used a small solid state memory which may account for the low sample rate. Pisani et al recommended a sample rate between 100 and 200 Hz. [99]. Their program was used for 24-hour ST segment analysis.

Researchers who were not restricted by data storage limitations have used higher sample rates. Cox et al claims that the American Heart Association recommend 500 Hz., but the sampling rate can be anywhere in the range 200-1000 Hz. with 8-12 bit precision [74]. Steinberg et al used 625 samples per second presumably because they were primarily concerned with pattern recognition of the ECG [65]. A sampling rate of 500 Hz. was used by Tranesjo et al in their exercise ECG analysis program [104].

The most popular sample rate used by researchers who wish to analyze the ST segment in 24-hour recordings is 250 Hz. [87][105][106]. Joseph et al reported using this sampling rate with a resolution of 10 bits. However, Geddes and Warner reported using a lower sampling rate of 200 Hz. for their CCU ECG monitor [83].

According to Scher frequencies above 100 Hz. do not contribute significantly to the ECG (3.1.1). It was therefore decided that a sampling rate of 200 Hz. should be used for our program. The tape was replayed at 32.59 times real time so the ECG signal was sampled at 6.5 kHz (= 200 Hz x 32.59).

The pH signal was sampled at a much lower rate than the ECG as it is a slow varying signal. The Synectics solid state recorder takes one sample every 4 sec [60]. Breedijk and Akkermans sampled the pH signal at a rate of 1 every 7.2 sec. while Stokkel et al used a rate of 1 every 6 sec. [58][59]. The former resulted in 12,000 data points representing 24 hours of oesophageal pH.

A sample rate of 2.73 Hz. was used in our program. The average was then calculated over 10 consecutive data points. This corresponds to a rate of 1 sample every 3.66 sec. in real time. As the tape was replayed 32.29 times faster than real time, the pH signal was actually sampled at 88.96 Hz. (= 2.73 Hz. x 32.59).

4.3.2 A/D Hardware

The MetraByte DASH-8 high speed A/D converter was used. It can sample signals from 8 channels in the range -5V to +5V with a resolution of 2.44mV. Each 12 bit sample can be obtained in 25 μsec.

An 8253 programmable counter provides periodic interrupts for the A/D converter. The user can choose the interrupt level (between 2 and 7) and can program the 8253 to the required sample rate. The DASH-8 includes status and control registers to enable interrupt handshaking (Figure 4.5).

4.3.3 A/D Software Development

It was decided that the full 24 hour record of pH data would be sampled but only significant 10 minute episodes of ECG would be captured. This was a convenient way of avoiding the large amounts of data contained in the ECG record (a single channel 24 hour record of ECG is equivalent to 17 MegaBytes - a high density floppy disk stores only 1.2MB and the average PC hard disk stores 20MB). The medical doctors involved felt that this method was adequate for their purposes as they were attempting to correlate ST segment depression with reflux episodes in the pH signal.

As this is the first stage in software development only one ECG channel was used. The timing channel was included initially, but it was found to be unnecessary for our purposes.

The A/D programs were written in 'C' language. MetraByte provided BASIC subroutines for controlling the DASH-8, but these were not used as they could not be called from a 'C' language main program.

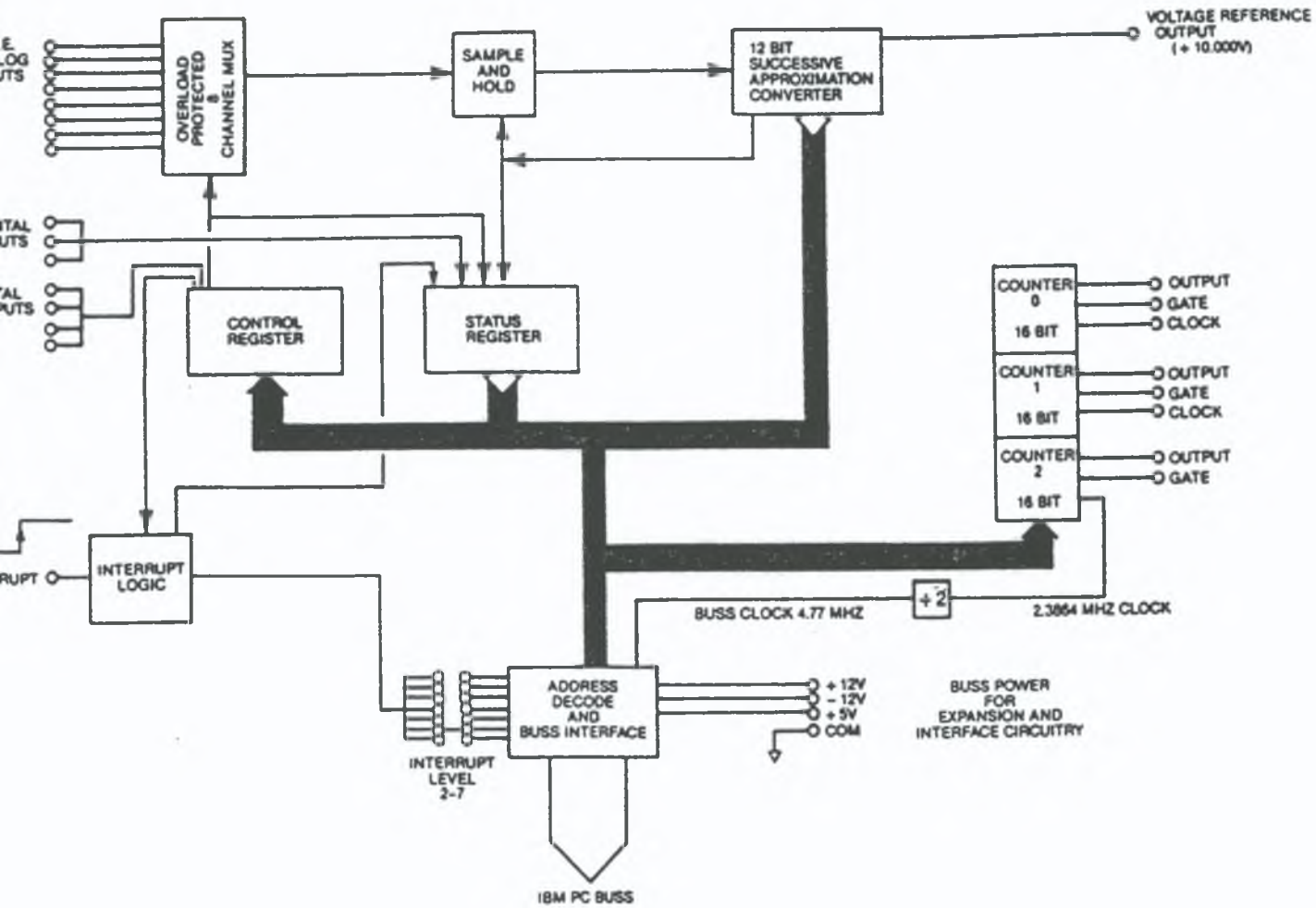


Fig. 4.5

Block Diagram of DASH-8

The interrupt service routine was written in 8086 assembler as 'C' was found to be too slow for this purpose. Flow diagrams of the pH sampling program and interrupt service routine are shown in Figures 4.6a and 4.6b.

The ECG sampling program and interrupt routine are similar. However, a third program is provided for converting 'raw' ECG data to voltage units.

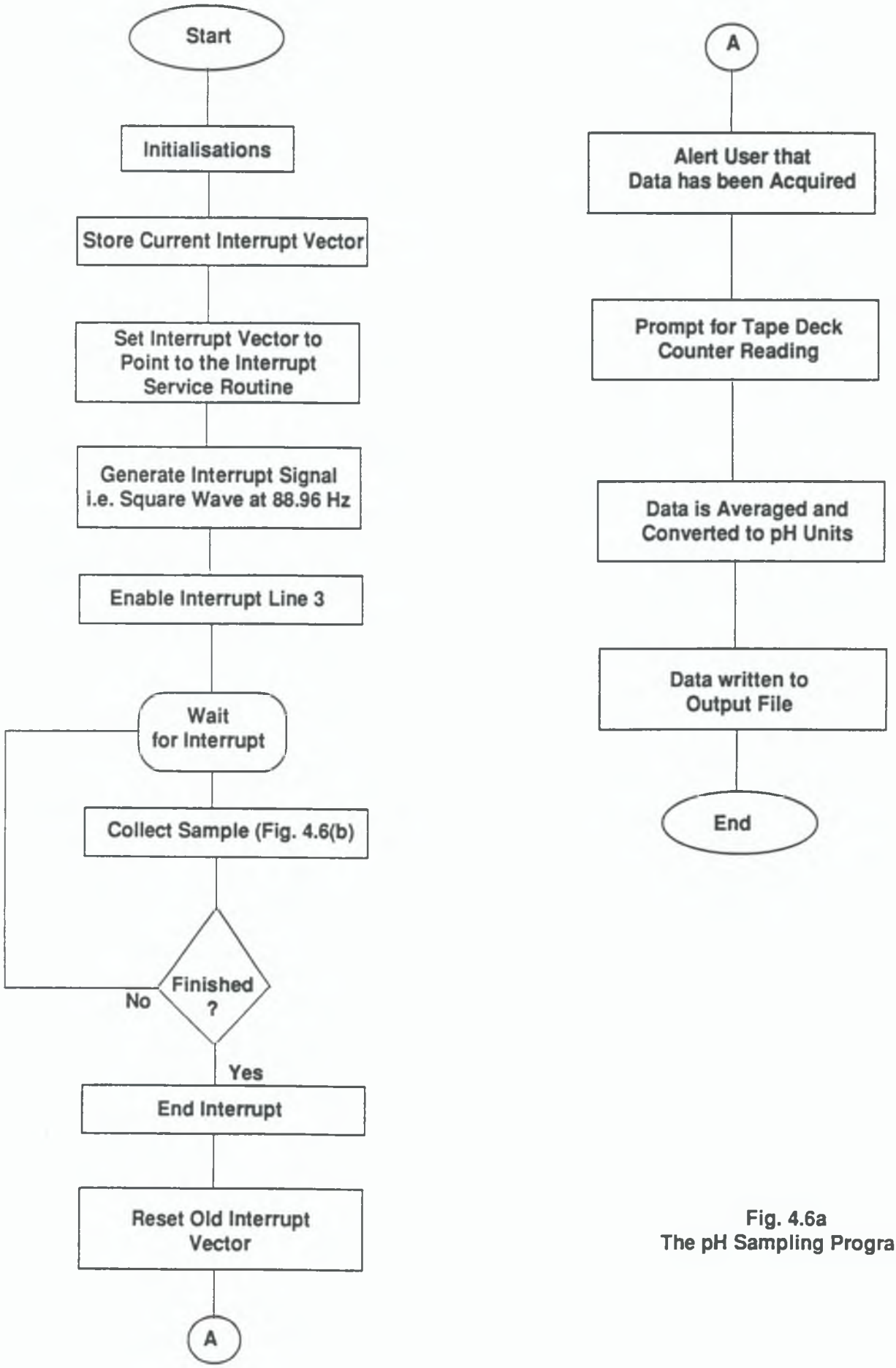


Fig. 4.6a
The pH Sampling Program

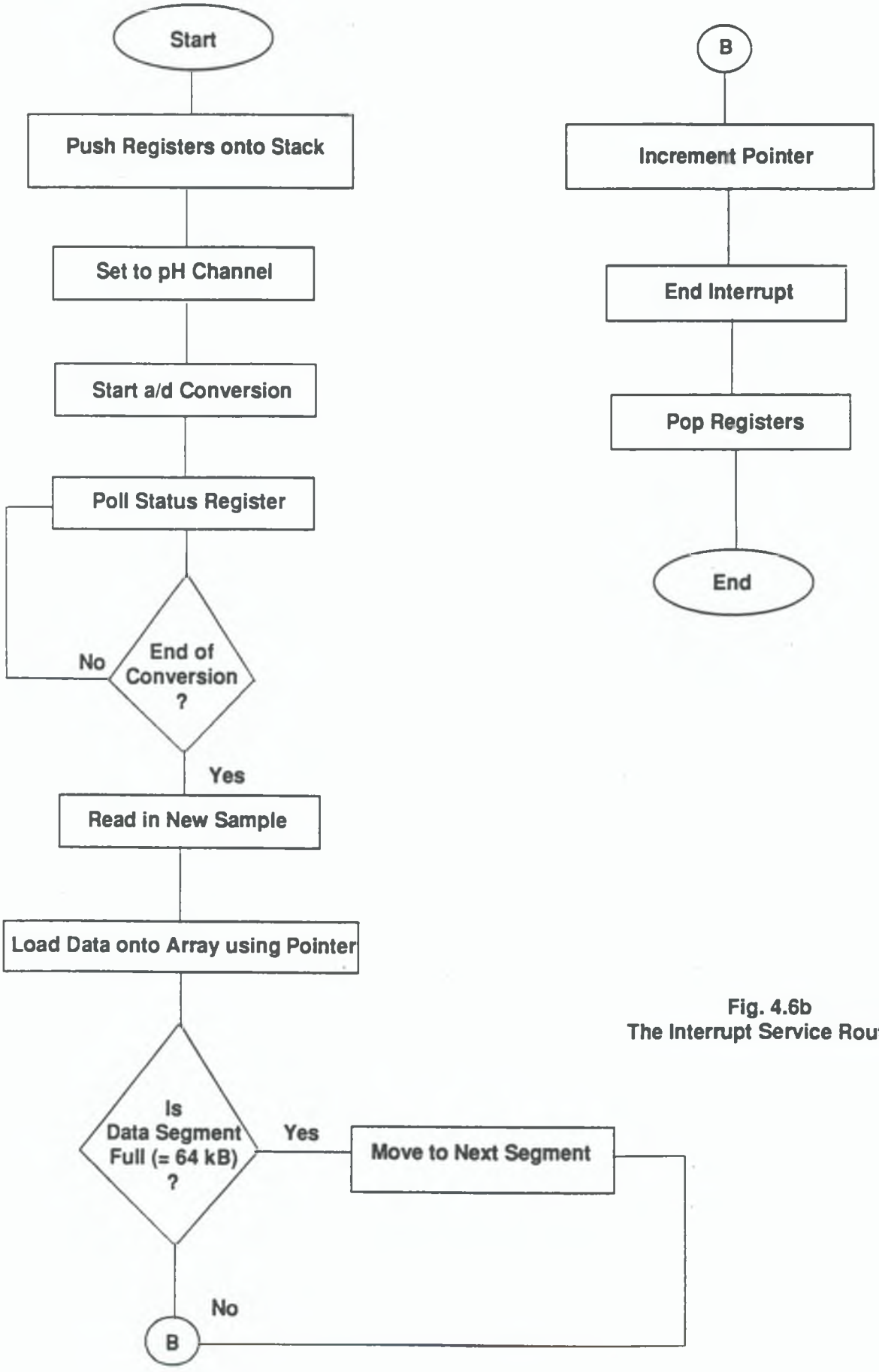


Fig. 4.6b
The Interrupt Service Routine

Graphics routines were written so that both the pH and ECG signals may be viewed on the computer screen. Printouts were also available.

A guide to using these and other programs is given in Appendix 3.

4.4 PROCESSING OF THE pH DATA

After analogue to digital conversion is complete, the pH data is analyzed. The first step is to load details from the patient diary into the computer. The user is prompted for the time the recording started, meal times, times at which pain occurred and the time that the recording ended. This information is stored for later use by the pH analysis programs.

The pH data is then checked for reflux episodes. A list of the reflux episodes, when they occurred and whether the patient was upright or supine is written to the output file. The pH score (4.1.1) is calculated and may be compared with normal values. A medical doctor can decide whether the patient's reflux is pathological based on this information.

The next stage is to discover which reflux episodes are post prandial, i.e. occurring up to 1 hour after a meal. Pain is then correlated with reflux episodes. Ideally we would have liked to check all of the reflux episodes for angina, but this would have been too time consuming. Instead a doctor selected particular intervals for ECG analysis : post prandial episodes, especially those occurring after the main meal and painful episodes occurring within 10 mins. of a reflux episode.

4.5 DEVELOPMENT OF THE ECG ANALYSIS SOFTWARE

A single 10 minute ECG episode contains 120,000 sample points. When this data has been loaded onto the computer it is converted to voltage units and stored in data files.

The first stage in the analysis is to correctly detect each beat. Abnormal beats are excluded and the average heart rate is continually updated. For each beat, depression of the ST segment is measured. The result is an ST trend graph with corresponding heart rate for the 10 minute episode.

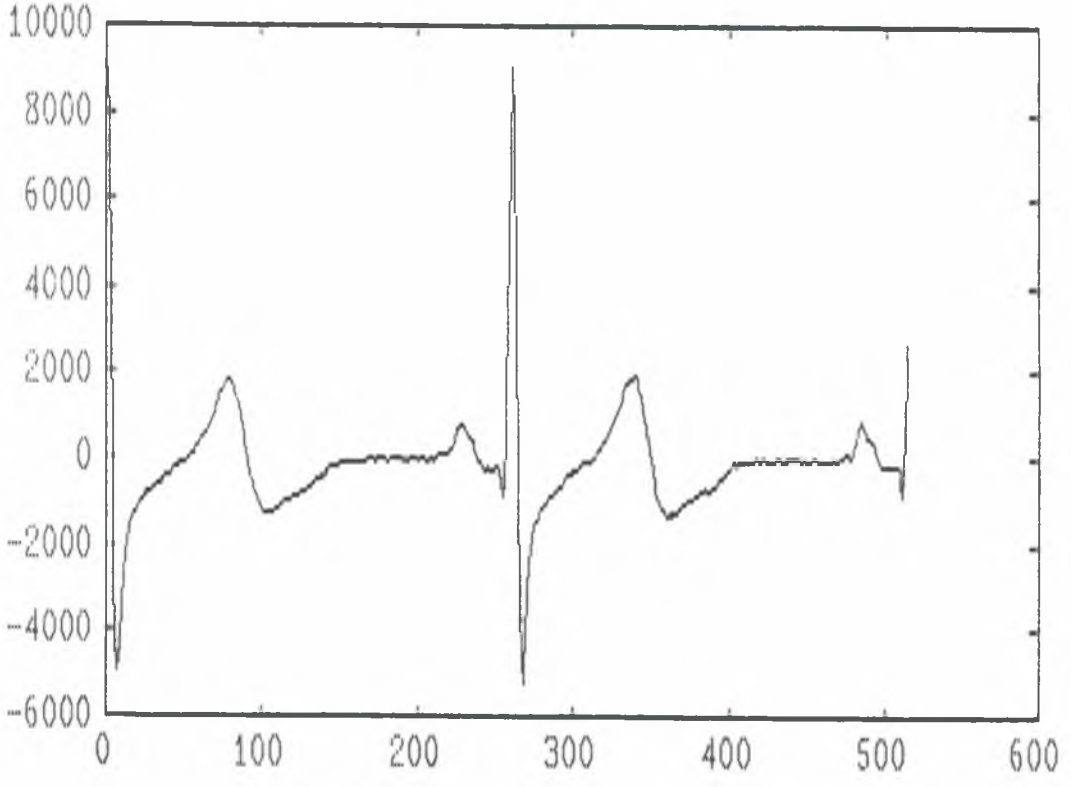
4.5.1 R Wave Detection

Initially a direct approach was taken. Observations showed that the R peak was the tallest wave in lead V5 of the ECG. Therefore, when the ECG voltage went above a certain threshold the algorithm searched for the R wave peak.

The threshold was calculated for each patient. It was taken as 60% of the maximum voltage located in the first 200 sample points. These values were purely empirical, but worked well for different patients. One example of this is shown in Figure 4.7. However, when the algorithm was tested on sample exercise ECGs, the tall T wave was mistaken for an R wave in a number of cases.

A review of current literature showed that the most popular method for R wave detection is searching for the maximum negative slope (4.2.2). The first stage is to calculate the first derivative of the entire ECG file (Figure 4.8). A threshold is set at 35% of the minimum slope found in the first 200 sample points. This minimum should be less than -0.23 mV per sample interval (-46 mV/sec) to distinguish between normal and ectopic beats. When the first derivative goes below this threshold, the algorithm searches for a negative peak corresponding to

the downslope of the R wave. The peak of the R wave is located by searching backwards through the data for the latest zero crossing. This method was checked for a number of patients and was found to be robust.



Calculations:

R Wave Peak	Baseline	J Point
8906.0	-195.0	-1957.0
9028.0	-211.3	-1882.0

(As this was only a test program the units have not been corrected to mV).

Fig. 4.7

ECG Analysis I (using Averaged Beats)

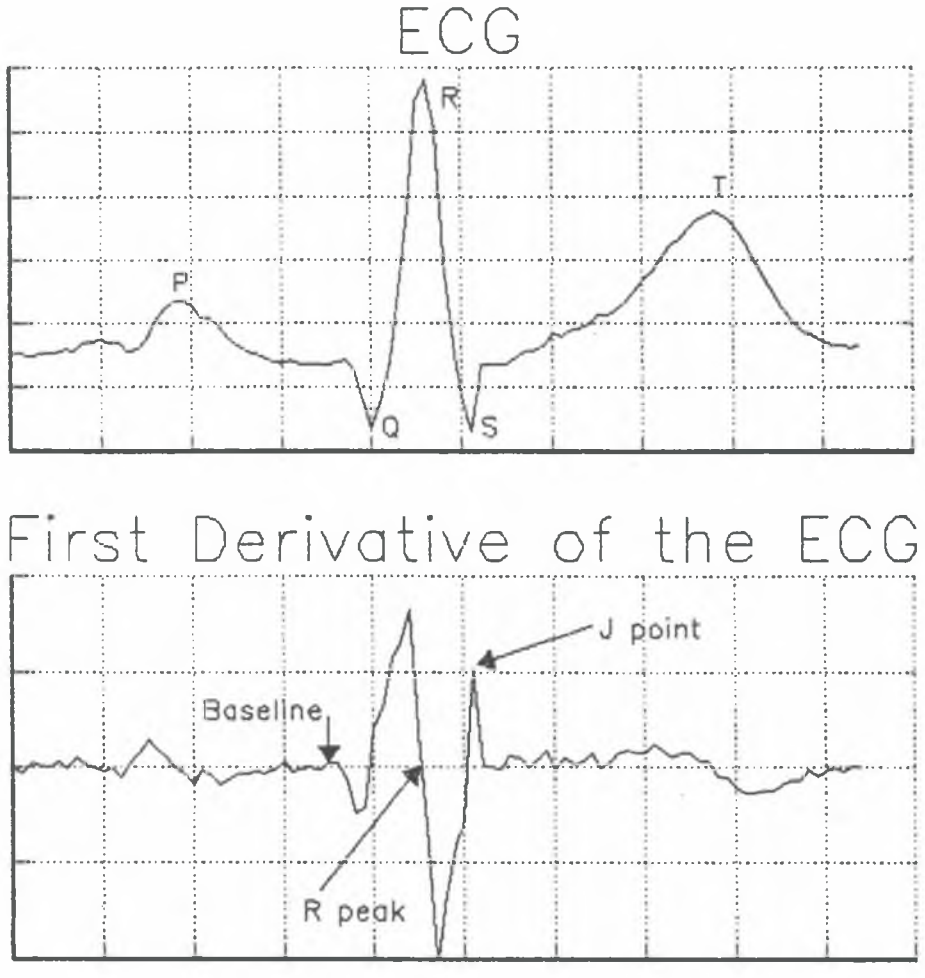
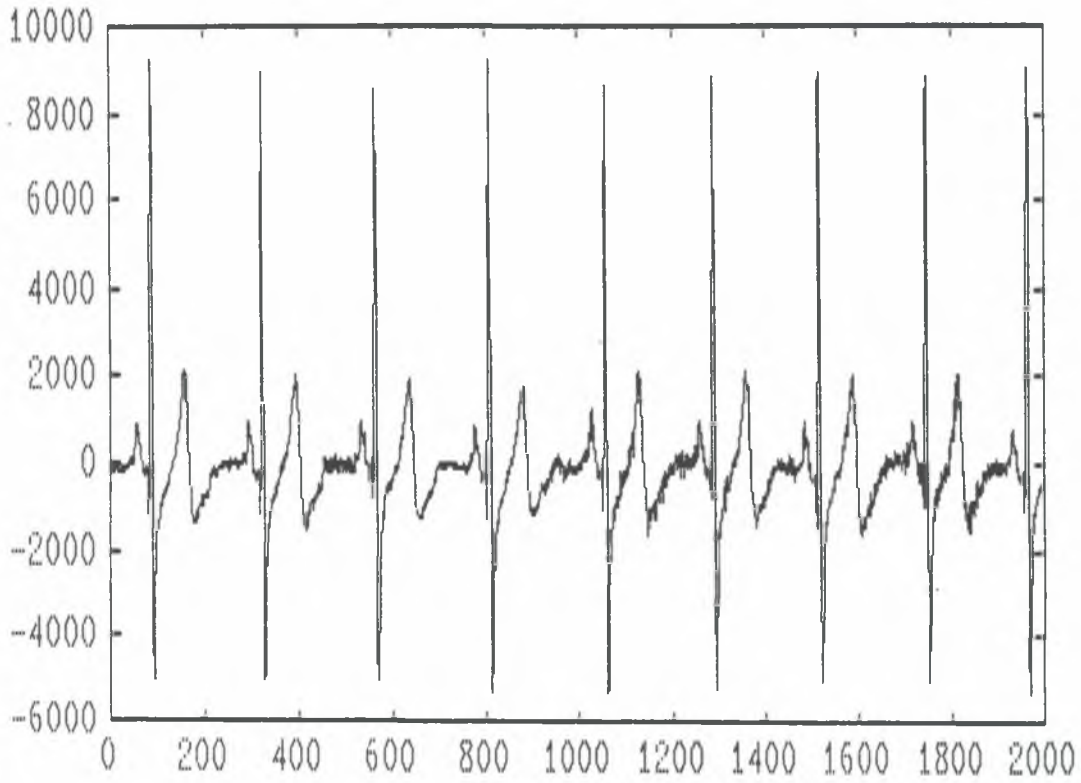

ECG
R
T
P
Q
S
First Derivative of the ECG
J point
Baseline
R peak

Fig. 4.8



Calculations:

Beat	R Wave Peak	Baseline	J Point
1	9264.0	-288.0	-1392.0
2	8960.0	-224.0	-1312.0
3	8512.0	+128.0	-1456.0
4	9200.0	-352.0	-1440.0
5	8672.0	-288.0	-1392.0
6	8848.0	-352.0	-1664.0
7	8960.0	-304.0	-1344.0
8	8832.0	-176.0	-1328.0
9	9056.0	-336.0	-1296.0

(As this was only a test program the units have not been corrected to mV).

Fig. 4.9

ECG Analysis II (using the Original ECG Data seen in Fig. 4.7)

The results for one particular patient are given in Figure 4.9. The accuracy of this method could be improved by combining the first derivative of 2 ECG channels to give the spatial velocity. The threshold below which the algorithm searches could be continuously updated as the shape and magnitude of the R wave changed.

The waveform boundary indicator method described previously (4.2.3) was also tested. It involves calculating the WBI and the WBIF which are combinations of the first and second derivative of the 'raw' ECG and the filtered ECG, respectively. Subtracting WBI from WBIF results in two search regions, one containing the QRS onset and the other, the QRS offset. The constants C_1 and C_2 were taken as equal and the optimum value of N, the number of points in the low pass filter, was 53 (Figures 4.10a and 4.10b). Note that in Figure 4.10b both the P and T waves are detectable in the WBIF. Although it proved to be a reliable method for delineating the waves of the ECG, it was not used because of the large number of additional calculations.

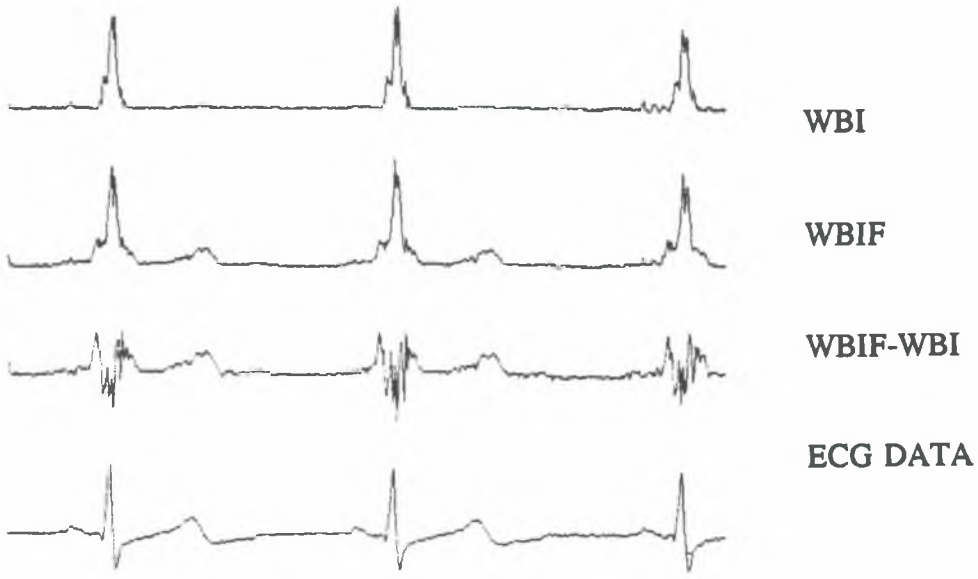


Fig. 4.10a

N = 17

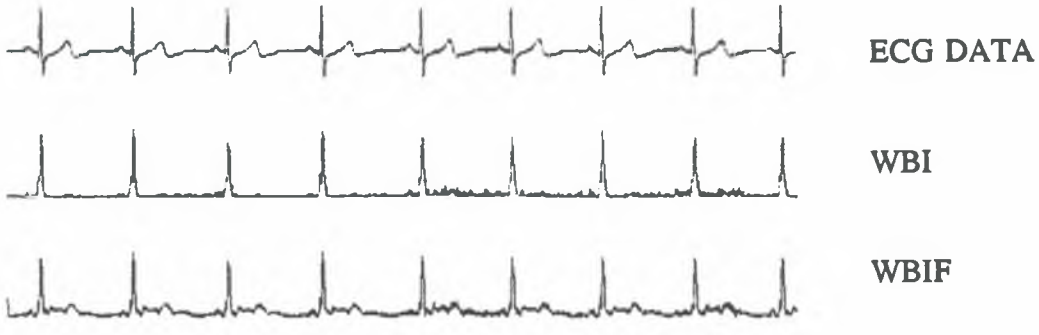


Fig. 4.10b

N = 53

4.5 ECG AVERAGING

ECG averaging is a method used to reduce random noise (4.2.7). Successive beats may be aligned in a number of different ways. It was decided here that consecutive R-R intervals would be superimposed. The number of samples in the first R-R interval was counted and all other intervals adjusted to contain this number of samples.

Initially 8 beats were averaged. There was good reduction in noise, but the magnitude of the T wave was reduced (Figures 4.11a and 4.11b). Increasing to an average over 10 beats caused both the P and T waves to diminish and in one patient the U wave (a small wave following the T wave, only present in some people) completely disappeared (Figures 4.12a and 4.12b). Further increasing the number of beats included showed no noticeable improvement in noise reduction (Figure 4.11c).

It was decided that this method would not be used in the final program because of the possibility of ST segment change being averaged out. There was also a danger that abberant beats might be included in the average.

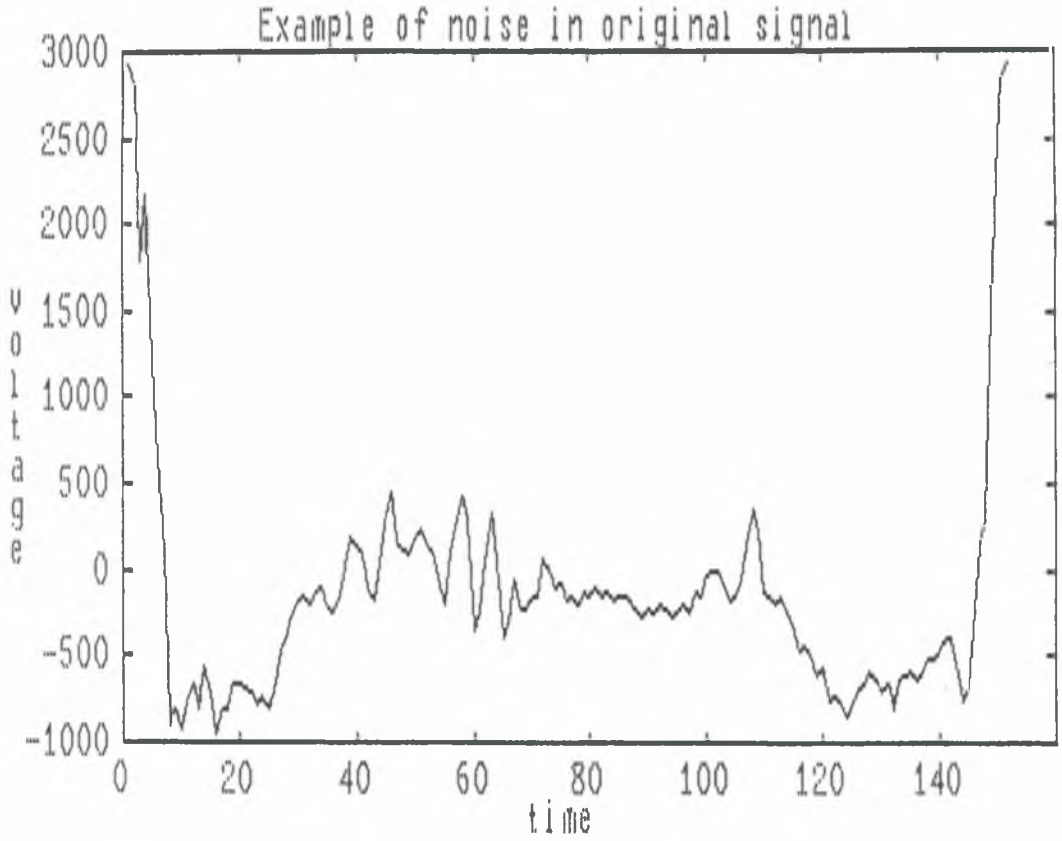


Fig. 4.11a

(One R-R Interval)

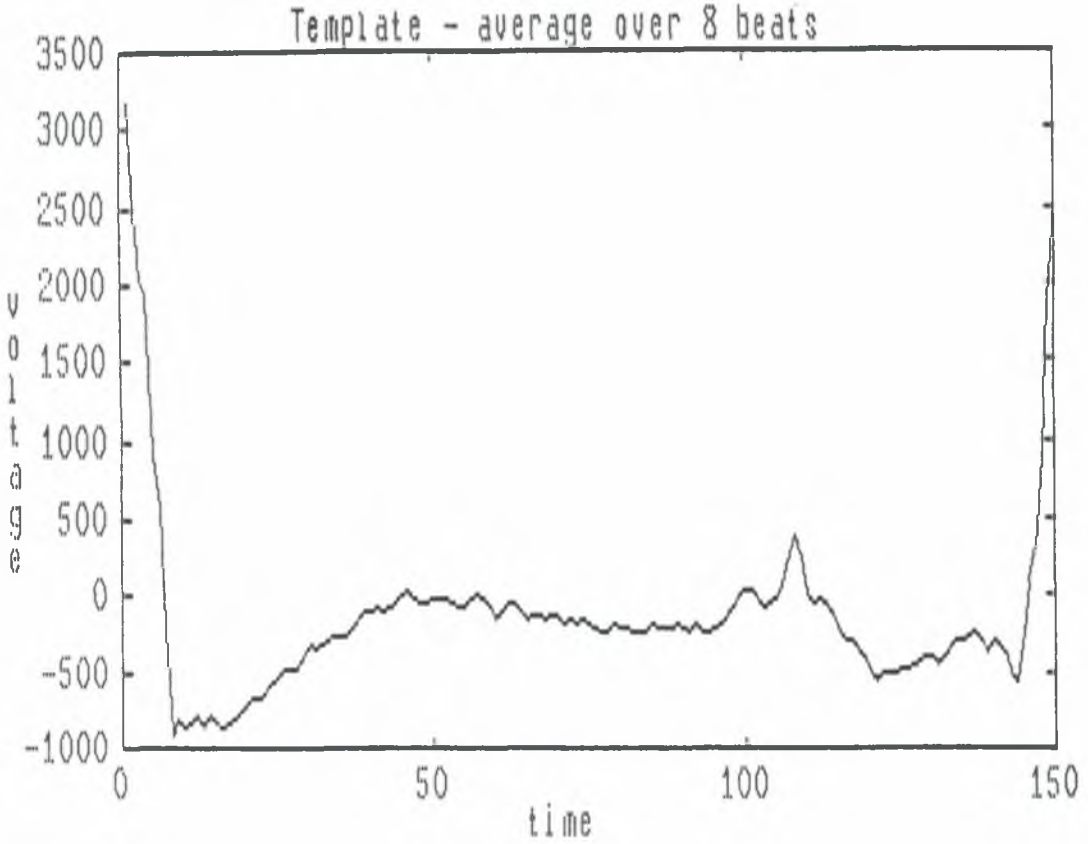


Fig. 4.11b

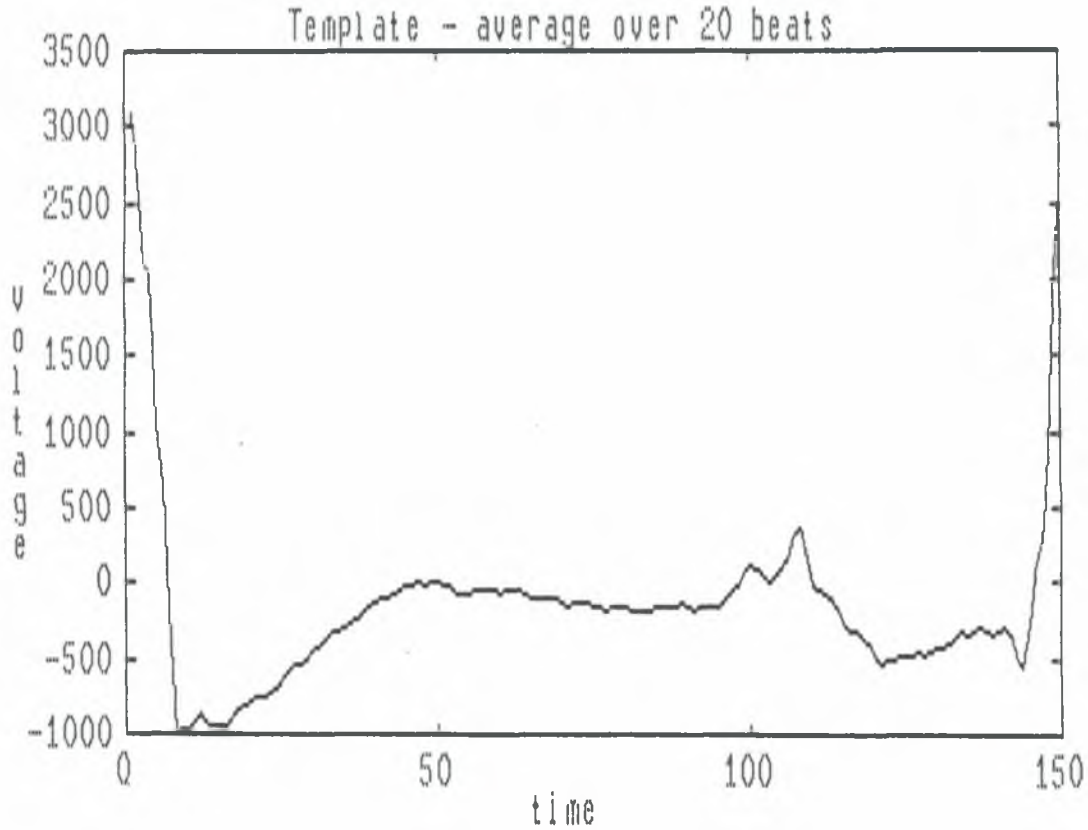


Fig. 4.11c

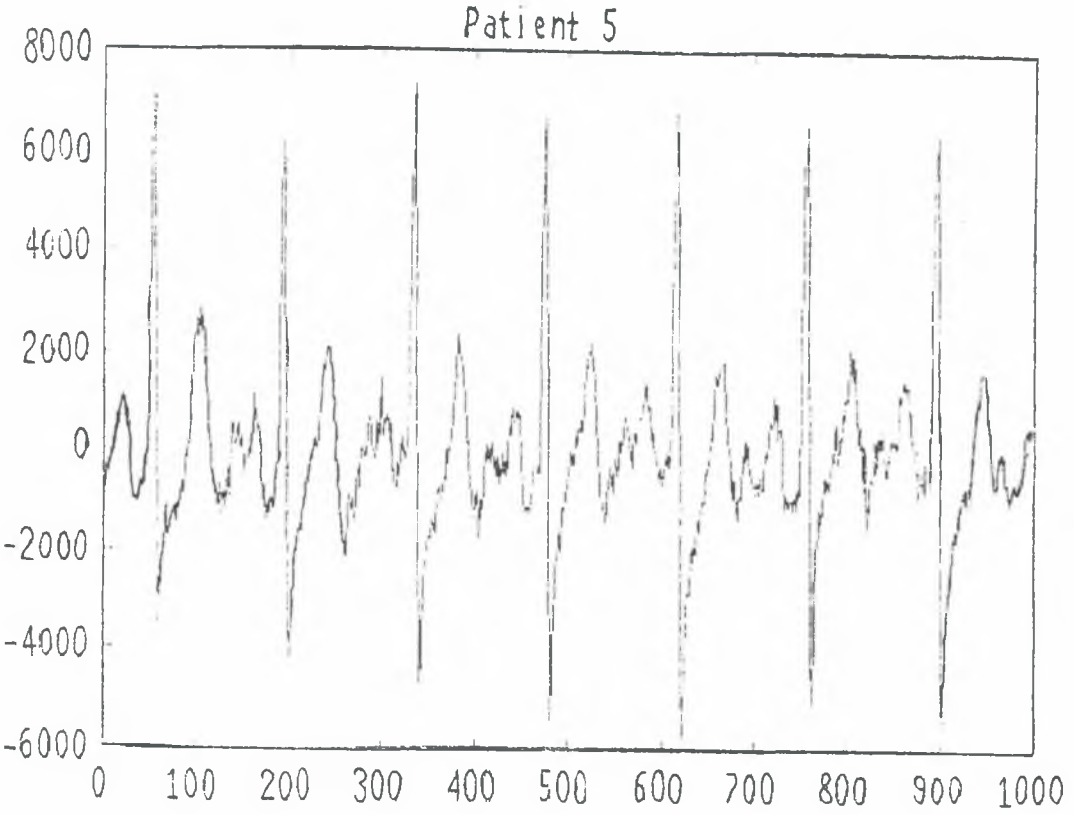


Fig. 4.12a

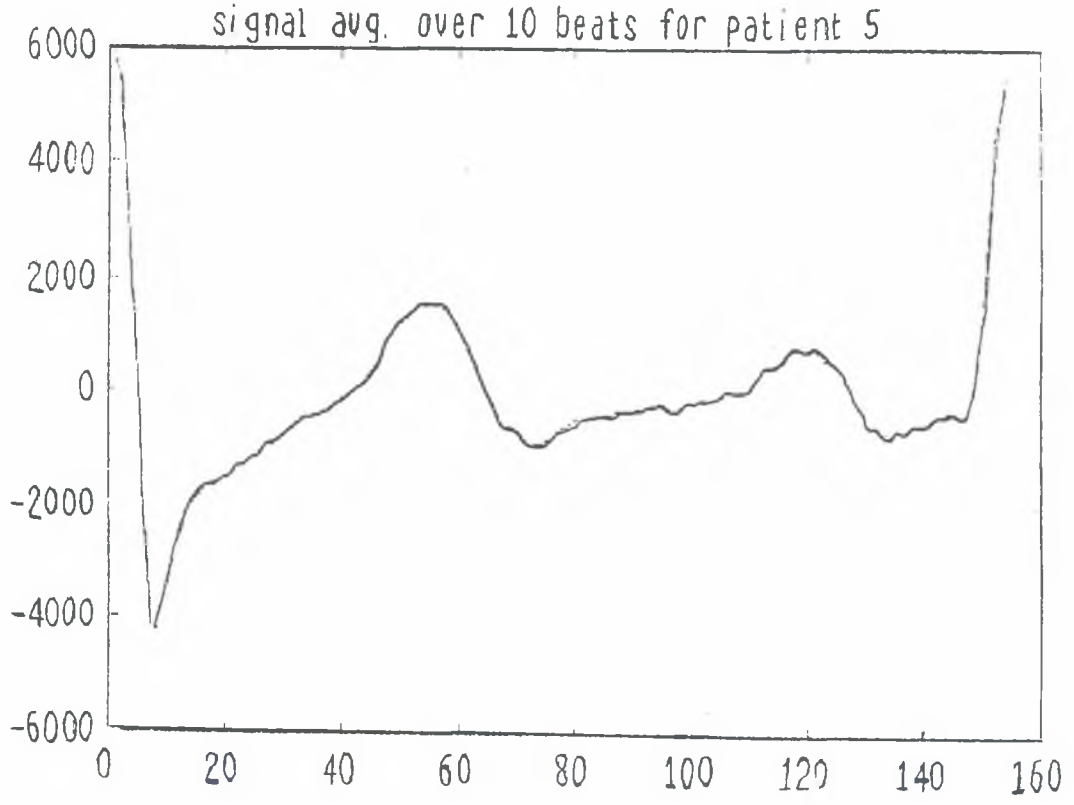


Fig. 4.12b

4.5.3 The Isoelectric Baseline

The ST segment is measured with reference to the isoelectric baseline which is generally taken between the P and R waves (4.2.5). The first attempt at detecting the baseline simply analyzed the original ECG data. After the R peak had been located, the algorithm searched backwards through the data for a change in slope, i.e. the Q wave. The slope was calculated for the next 14 sample points and the point at which the sign changed became the baseline level. This method worked well on averaged beats, but is not robust enough to work in a noisy environment (Figure 4.7).

The first derivative of the ECG was already calculated for the R wave detection algorithm. It may also be used for establishing the isoelectric level (Figure 4.8).

The location of the R peak is passed to the subroutine and the first step is to move backwards through the data searching for a change in sign which corresponds to the upslope of the R wave. When the next zero crossing is found (Q wave), the algorithm continues to search backwards for a ratio between successive slopes which lies between 0.7 and 1.3, i.e. a flattening of the signal. This method was quite successful, as seen in Figure 4.9.

As the ECG is susceptible to noise, further improvement was necessary. In the last stage, the first derivative is averaged over five points before the ratio is calculated. This ensured that baseline detection was immune to high frequency noise.

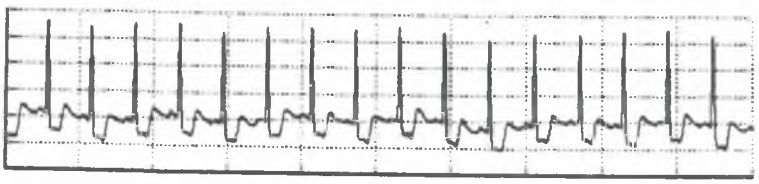
4.5.4 Detecting the J Point

Again the first derivative of the ECG signal can be used. The J point is defined as the point where the S wave ends and the ECG becomes flat. It corresponds to a positive peak in the first derivative (Figure 4.8). This method was successful for the patients studied. However, it presupposes the existence of an S wave and could not be used indiscriminately.

It was decided that the J point would be taken at 80 msec after the R wave peak. This worked quite well in practice (Figure 4.9).

4.5.5 The ST Segment

The ST segment begins at the J point and ends at the x point. As previously mentioned, the x point is difficult to determine exactly, so it is generally taken at a fixed time interval after the J point. In this case it was taken as J + 60 msec. Examples of x point measurements are given in Figure 4.13a and Figure 4.13b. Note that in the first case the ST segment is slightly downsloping which is reflected in the results. In the second case it is upsloping and this is correctly shown in the results.



x axis : 1 division = 1 second

y axis : 1 division = 0.5 mV

Key to table
Rpk - the height of the R wave followed by the last period
Baseline - the height of the isoelectric baseline
and the time at which its measured
J pt - the depth of the J pt followed by time its measured
STseg - J point depth relative to the baseline
x - the depth at J+x again relative to the baseline
Slope - the slope of the ST segment

Beats	Rpk	Period	Base	t	Jpt	t	STseg	x	Slope
2	1.7	0.59	0.02	1.1	-0.37	1.2	-0.39	-0.43	-0.04 I d,h
3	1.8	0.59	-0.03	1.7	-0.30	1.8	-0.27	-0.30	-0.04 I d,h
4	1.8	0.60	0.08	2.3	-0.24	2.4	-0.32	-0.39	-0.07 I d,h
5	1.6	0.60	-0.07	2.9	-0.40	3.0	-0.33	-0.34	-0.01 I d,h
6	1.7	0.59	0.00	3.4	-0.29	3.6	-0.29	-0.30	-0.01 I d,h
7	1.8	0.60	0.10	4.1	-0.23	4.2	-0.33	-0.38	-0.05 I d,h
8	1.7	0.59	-0.02	4.7	-0.31	4.8	-0.29	-0.35	-0.06 I d,h
9	1.8	0.60	0.03	5.2	-0.23	5.4	-0.26	-0.29	-0.03 I d,h
10	1.7	0.60	0.03	5.9	-0.37	6.0	-0.39	-0.44	-0.05 I d,h
11	1.5	0.60	-0.10	6.4	-0.50	6.6	-0.40	-0.40	-0.00 I d,h
12	1.7	0.60	-0.03	7.0	-0.34	7.2	-0.31	-0.31	0.00 I u
13	1.7	0.60	0.04	7.6	-0.33	7.8	-0.36	-0.40	-0.03 I d,h
14	1.7	0.59	-0.05	8.2	-0.40	8.4	-0.34	-0.36	-0.02 I d,h
15	1.8	0.60	0.04	8.8	-0.31	9.0	-0.35	-0.36	-0.01 I d,h
16	1.7	0.59	0.01	9.4	-0.43	9.6	-0.44	-0.47	-0.03 I d,h

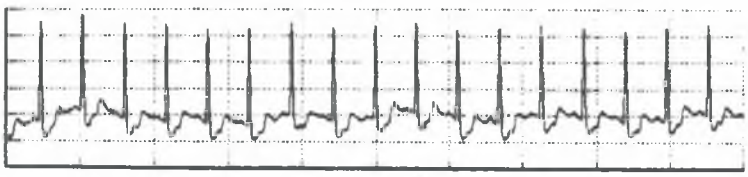
All results in mV

I d,h : Ischemia, ST downsloping or horizontal

I u : Ischemia, ST upsloping

Fig. 4.13a

ECG Analysis III



x axis : 1 division = 1 second

y axis : 1 division = 0.5 mV

Key to table
Rpx - the height of the R wave followed by the last period
Baseline - the height of the isoelectric baseline
and the time at which its measured
J pt - the depth of the J pt followed by time its measured
STseg - J point depth relative to the baseline
x - the depth at J+x again relative to the baseline
Slope - the slope of the ST segment

Beats	Rpx	Period	Base	t	Jpt	t	STseg	x	Slope		
2	1.9	0.56	0.13	0.9	-0.19	1.1	-0.33	-0.16	0.17	I	u
3	1.7	0.56	-0.03	1.5	-0.37	1.7	-0.34	-0.17	0.17	I	u
4	1.7	0.56	-0.10	2.1	-0.39	2.2	-0.29	-0.13	0.15	I	u
5	1.6	0.56	-0.11	2.7	-0.46	2.8	-0.35	-0.20	0.15	I	u
6	1.6	0.56	-0.16	3.2	-0.45	3.4	-0.29	-0.15	0.14	I	u
7	1.8	0.56	0.05	3.8	-0.24	3.9	-0.29	-0.25	0.03	I	u
8	1.7	0.56	-0.09	4.4	-0.38	4.5	-0.29	-0.19	0.10	I	u
9	1.7	0.57	-0.01	4.9	-0.30	5.1	-0.28	-0.17	0.12	I	u
10	1.7	0.56	0.09	5.5	-0.23	5.6	-0.32	-0.21	0.11	I	u
11	1.6	0.57	-0.03	6.1	-0.43	6.2	-0.40	-0.27	0.13	I	u
12	1.6	0.57	-0.09	6.6	-0.42	6.8	-0.33	-0.22	0.11	I	u
13	1.7	0.56	0.00	7.2	-0.27	7.3	-0.27	-0.15	0.12	I	u
14	1.7	0.56	-0.01	7.7	-0.32	7.9	-0.30	-0.17	0.14	I	u
15	1.6	0.57	-0.09	8.3	-0.36	8.5	-0.26	-0.17	0.09	I	u
16	1.6	0.56	-0.09	8.9	-0.30	9.0	-0.21	-0.07	0.14	I	u
17	1.7	0.56	0.08	9.5	-0.20	9.6	-0.28	-0.17	0.10	I	u

All results in mV

I u : Ischemia, ST upsloping

Fig. 4.13b

ECG Analysis III ctd.

A plot of the x point was drawn for each 10 minute ECG episode together with the heart rate (Figure 4.14). Each trend was examined for a 0.1 mV (or 1mm) drop lasting 1 minute or more.

As already seen in Figures 4.13a and 4.13b a full listing of the measurements taken from each ECG beat in the record is also available. If the J point is depressed by 1mm or more and the ST slope is horizontal or downsloping, then the beat is labelled ischemic (I u,h). If the ST slope is upsloping, then the J point must be depresed by 2mm or more to be considered ischemic.

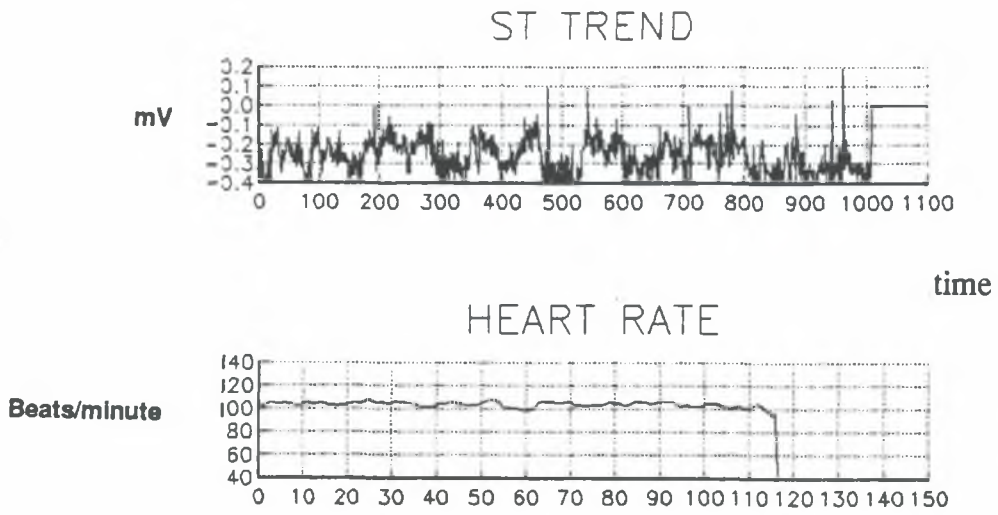
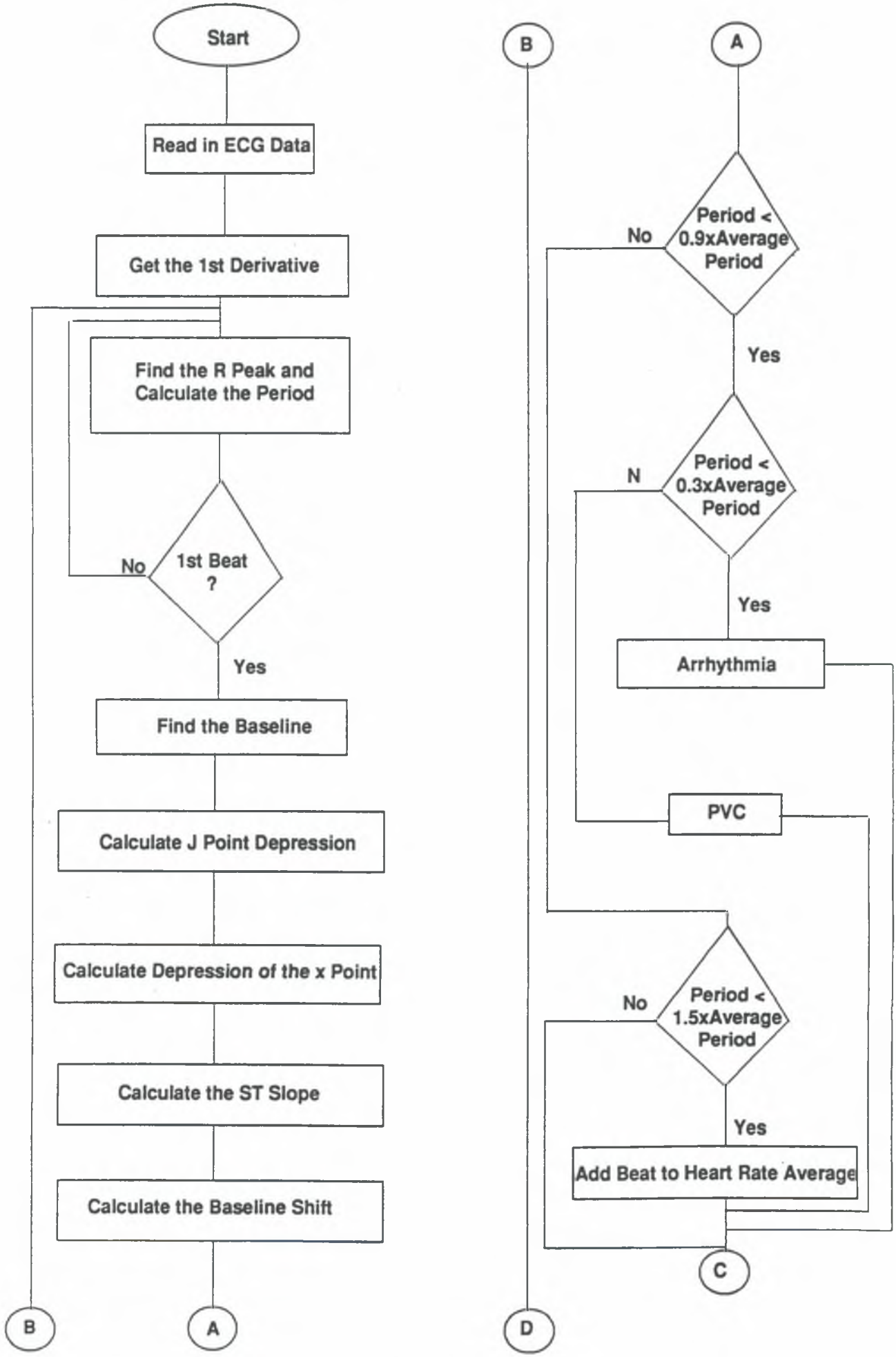


Fig. 4.14
ST Trend for a 10 Minute Interval
(For Examples of the ECG during the 10 Minute Interval See Figures 4.13a and 4.13b)

A flow diagram of the analysis program is given in Figure 4.15. After the initial parameters have been calculated, the beat is checked. If the period is less than 0.3 of the average (corresponding to a heart rate greater than 200 beats per minute) then the beat is classified as arrhythmic and is ignored. Alternatively if the period is between 0.3 and 0.9 of the average, the beat is said to be ectopic or a PVC (4.2.4). Beats with a normal period are included in the heart rate calculation. A final check is made for excessive baseline wander. If the baseline shifts by 0.4 mV or more between successive beats, then the last beat is ignored. The analysis routine is repeated for all beats of the ECG record.


Start
Read in ECG Data
Get the 1st Derivative
Find the R Peak and Calculate the Period
No
1st Beat ?
Yes
Find the Baseline
Calculate J Point Depression
Calculate Depression of the x Point
Calculate the ST Slope
Calculate the Baseline Shift
B
A
B
A
No
Period < 0.9xAverage Period
Yes
N
Period < 0.3xAverage Period
Yes
Arrhythmia
PVC
No
Period < 1.5xAverage Period
Yes
Add Beat to Heart Rate Average
C
D

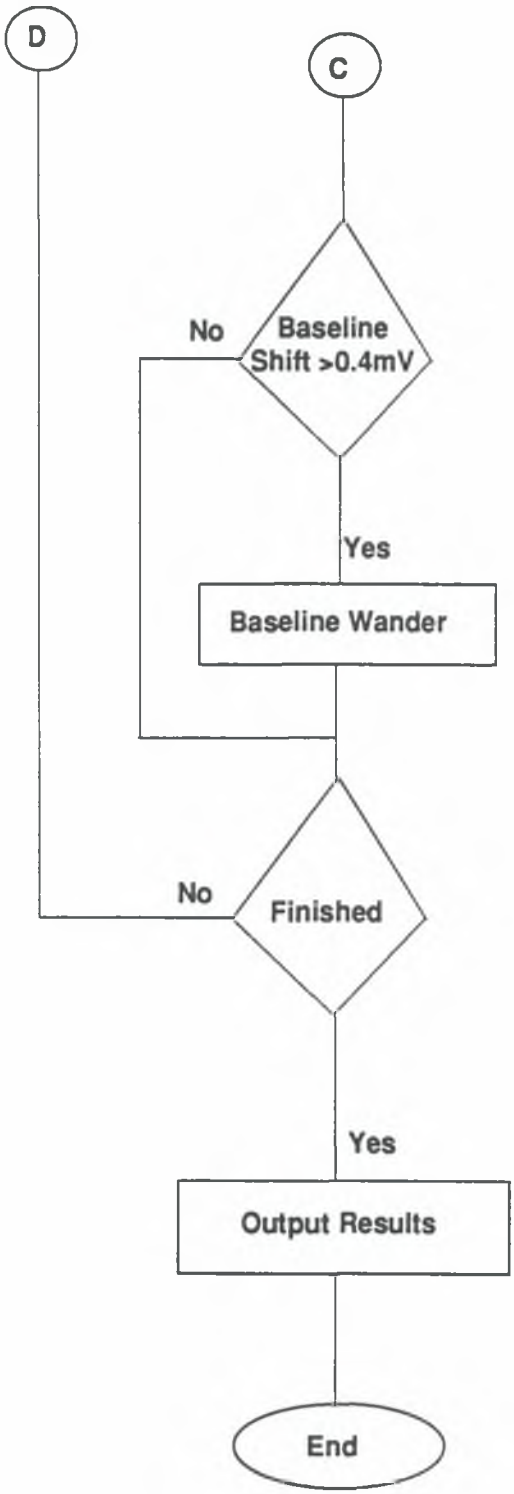


Fig. 4.15
The ECG Analysis Program

CHAPTER 5 MEDICAL RESULTS

5.1 THE STUDY OF 24-HOUR OESOPHAGEAL pH

The first stage in the study was to analyze the 24-hour pH record for each patient. An example of the first 4 hours of one patient's tape is shown in Figure 5.1. The analysis routine detects reflux episodes and decides whether they occurred post prandially. In this case the patient eats his tea 10 minutes after the recording started.

The pH score was calculated for all five patients. This showed an interesting result: all pH scores were abnormal, whereas only one patient had a history of reflux oesophagitis. The results are shown in Table 5.1. Note that it is not necessary for all six parameters to be abnormal. In the case of patient PB, only parameters 5 and 6 are above normal. However, they indicate abnormally long reflux episodes which reflect the inability of the oesophagus to clear gastric contents.

5.2 ANALYSIS OF THE ECG

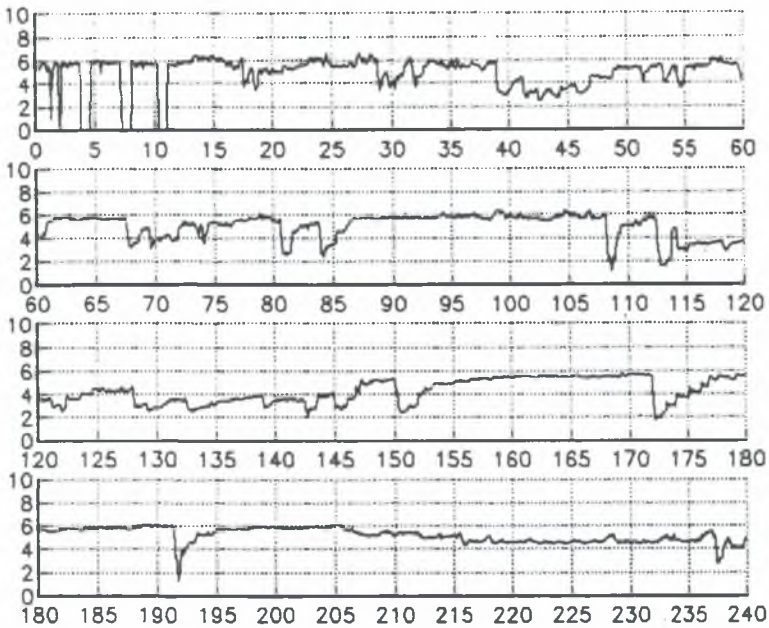
We analyzed two sets of 10 minute ECG intervals for each patient:

1. Those for which reflux was associated with pain.
2. Those for which reflux occurred after a meal (post prandial).

5.2.1 **Episodes of Reflux with Pain**

Only two patients experienced symptomatic episodes of pain during the 24-hour period. Another patient (BS) suffered pain all of the time so could not be included in this part of the study.

Episodes of reflux were correlated with symptoms of pain. We found that pain tended to precede reflux. This may reflect carelessness on the part of the patient in filling out the diary. Reflux and pain occurring up to 8 minutes apart was considered significant.



x axis : minutes

y axis : pH units

Reflux :	Start		Finish	(mins)	Post Prandial ??
1	1.3	-	1.5		
2	2.0	-	2.2		
3	3.8	-	4.8		
4	7.3	-	8.2		
5	10.4	-	11.2		pp
6	17.6	-	19.2		pp
7	28.9	-	31.0		pp
8	32.0	-	32.7		pp
9	39.1	-	48.9		pp
10	51.4	-	51.9		pp
11	53.3	-	53.8		pp
12	54.5	-	55.0		pp
13	60.3	-	60.8		pp
14	67.7	-	72.1		pp
15	74.0	-	74.4		
16	80.7	-	82.5		
17	83.9	-	86.1		
18	108.2	-	110.4		
19	112.4	-	147.8		
20	150.2	-	155.0		
21	171.9	-	176.9		
22	191.4	-	193.2		
23	237.3	-	242.2		

Fig. 5.1

4-Hour pH Record for Patient BS with a Listing of Reflux Episodes

Patient / Parameter	PB	JF	BG	JN	BS	Normal
1	2.5%	11.8%	6.9%	9.9%	51.0%	<1.2%
2	3.0%	17.3%	11.7%	17.7%	31.0%	<6.3%
3	2.8%	15.4%	9.8%	14.6%	36.5%	<4.2%
4	28	34	18	14	54	<50
5	6	18	10	12	19	<=3
6	40.2 min.	113.7 min.	70.3 min.	59.7 min.	203.5 min.	<9.2 min.

Key:

1. % Acid Exposure while Supine
2. % Acid Exposure while Upright
3. % Acid Exposure for the Total 24-Hour Period
4. Total No. of Reflux Episodes
5. No. of Reflux Episodes longer than 5 Mins.
6. The Single Longest Reflux Episode.

Table 5.1

pH Score for the 5 Patients

The ST trend was obtained for each 10 minute ECG episode. The results are shown in Table 5.2. In each case only 3 painful episodes correlated with reflux. The values listed for ST depression each lasted for 1 minute or more. Patient PB had an ST shift of 0.1 mV (or 1 mm) for the second ECG episode which was borderline for clinical significance (Figure 5.2).

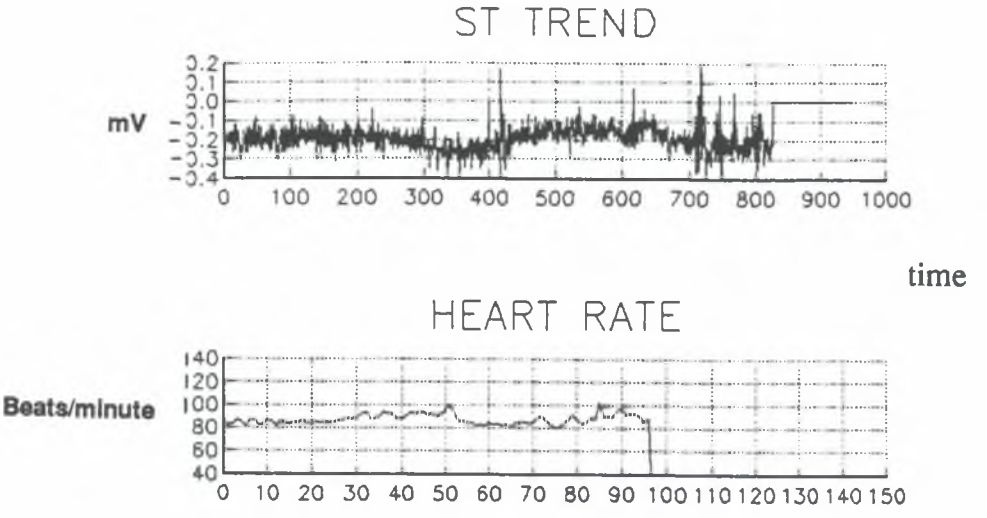


Fig. 5.2

ST Trend for Patient JF (Pain and Reflux occurred half way through the 10 Minute Interval)

	PB	JF
No. of Symptomatic Events	6	4
ST Depression (mV) for painful events correlating with with Reflux	0.1 0.1 - 0.15 0.1 - 0.15	0.17 - 0. 0.15 - 0.25 0.2

Table 5.2

Symptomatic Episodes

5.2.2 Post Prandial Reflux Episodes

We were also interested in analyzing the ECG for episodes of reflux which occurred after a meal. The results are shown in Table 5.3. Again patient JF had an ST shift of 0.1 mV (Figure 5.3). Patients BG and BS experienced ST segment shifts of 0.05 mV.

The results were inconclusive. However, we only had time to investigate reflux episodes occurring after the main meal of the day. If it were possible to look at all of the post prandial episodes and perhaps increase the number of patients tests, ST segment shifts greater than 0.1 mV may be found.

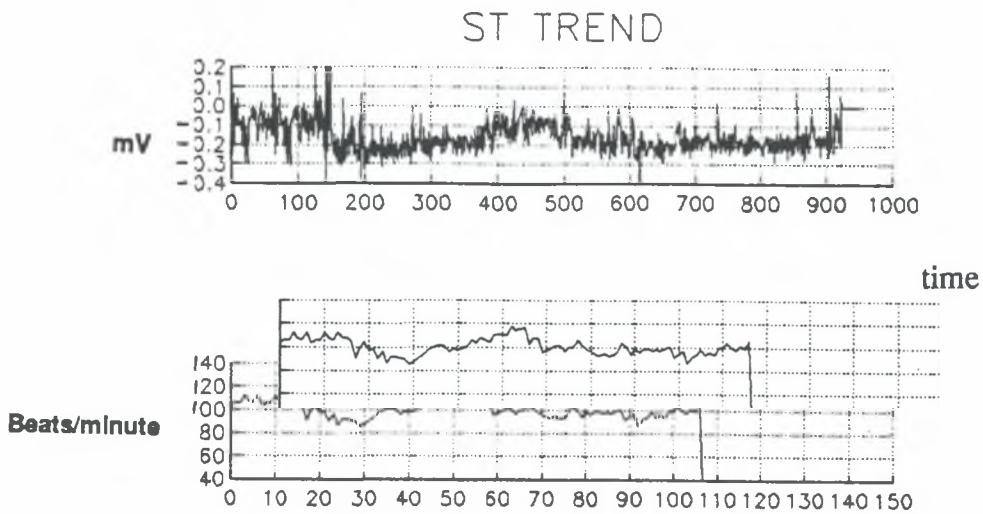


Fig. 5.3

ST Trend for Patient JF

(Post Prandial Reflux occurred after 1.5 minutes)

Patients	PB	JF	BG	JN	BS
ST Depression (mV)	0.12 0.12	0.15 - 0.2 0.15 0.1 - 0.2	0.1 - 0.15	0.35 0.35	0.3 - 0.33 0.3 0.3 - 0.35 0.35

Table 5.3

Post Prandial Reflux Episodes

CHAPTER 6
DISCUSSION, CONCLUSION AND FUTURE DEVELOPMENTS

6.1 DISCUSSION AND CONCLUSION

The aims of this project were laid out in Chapter 1. These have largely been achieved. A complete system to record and analyze patient signals is now fully operational.

6.1.1 The Hardware

Two types of Holter recorder were available in the hospital. Both used amplitude modulation to record the ECG. However, the Oxford Medical Mark I was chosen because it facilitated the addition of pulse width modulation circuitry to record oesophageal pH. The frequency response of the Mark I has been questioned previously [31]. Its non-flat response curve and poor low frequency response is said to cause distortion of the ST segment. We found that our recorder caused artificial depression of the J point. This is due to the associated poor phase response which causes low frequencies in the QRS complex to be delayed and to appear in the ST segment. The affect of this is also seen after large T waves (Figure 4.9). Kortas argued that distortion was principally at the J point or the start of the ST segment, and minimal at the x point or the end of the ST segment [95]. So if we evaluate the ST segment by looking at the x point and the ST slope as opposed to the J point, the error will be minimal.

When we analyzed patients ECG records we discovered that they all appeared to have resting ST segment depression. In a few cases it was evident on the patients hospital ECG record, but tended to be less severe. We recorded the ECG of a normal person and found no ST segment shift as expected (Figure 4.8). Does the Mark I amplify depression?

This could be a result of the abnormal gain of the system at low frequencies as claimed by Bragg-Remschel (3.1.1).

The playback unit consisted of a tape deck and 4 amplifiers. As already mentioned, the Oxford Medical tape deck had to be replaced with a commercially available audio tape which ran at half the speed (3.4). The low frequency cutoff was given as 12 Hz. When this figure was divided by the replay speed factor (x32.59), the result was a cutoff of 0.37 Hz. in real time. If we had used the Oxford tape deck the replay speed factor would have been x60. This would have given a lower frequency cutoff which would have improved reproducibility of the ST segment.

While patient tapes were being replayed, the ECG and pH signals could be viewed on an oscilloscope. This was an important facility for doctors using the system. If necessary the 24-hour patient tape could be viewed in 45 minutes.

6.1.2 Analysis of Patient Signals

Analysis of the pH signal was relatively straightforward. Episodes of reflux were easily detected and they were labelled 'supine' or 'upright', depending on the patient's posture and 'post prandial' if the patient had just eaten. A set of statistics were calculated based on the result. Four hour episodes could be viewed on the computer screen.

Analysis of the ECG signal was more complex. Each beat had to be located and analyzed. Several algorithms were developed and tested with patient data. The final calculations of ST segment were reasonably accurate (Figures 4.13a and 4.13b). There was good rejection of ectopic beats and of baseline wander. A graph of the ST trend was available for each 10 minute ECG episode analyzed. It was also possible to check the measurements from each ECG beat. Plots of ECG data were available so that the ST shift could be measured manually.

However, there are limitations to the present system. At present only 10 minute ECG episodes may be analyzed. This represents a large amount of data to the computer which takes time to process. It was impractical to look at more than 4 or 5 ECG intervals per patient.

6.1.3 Medical Discussion

It was clear from the study that all five patients suffered from ischemic heart disease and pathological reflux. We attempted to correlate ischemia with reflux to show if they were linked. ST segment shifts up to 1mm (the threshold for clinical significance) were noted. Although the study was probably too limited to be medically significant, it allowed us to examine the performance of the recording equipment and analysis software. We were satisfied that both worked well, but admitted improvements could be made.

The question remains: how could gastro-oesophageal reflux cause angina?

The answer may lie in a new study of the nerve system in the rat [107]. Originally it was thought that the nerve supply from the arm and the heart to the brain were separate. It has now been shown using fluorescent tracers that the 'nerve paths' meet at a common neuron and share a common path to the brain. Perhaps the nerve supply to the heart and the oesophagus also share a neuron. This would mean that pain from the oesophagus travels to the neuron which could then signal the coronary arteries to go into spasm, causing angina.

One reason for investigating a link between reflux and angina is that cardiac drugs are known to predispose to reflux. The drugs may be indirectly making the heart problem worse. This would imply that all cardiac drugs should be prescribed with a drug which suppresses reflux.

The recording equipment was developed for examining reflux and angina where they coexist. However, when a patient presents to his doctor with chest pain, our system might also be used to differentially diagnose one or other of the conditions.

6.2 FUTURE DEVELOPMENTS

This project will be continued in the future. It is therefore important to take a critical look at the work that has been done and to suggest any improvements which can be made.

6.2.1 Hardware Improvements

Clearly the Oxford Mark I recorder introduces an error into the ST segment measurement. It would be interesting to examine in more detail the affect of poor low frequency response on a variety of ECG morphologies. If it is decided that the Mark I is unsatisfactory, it could be replaced with the Mark II. This is an FM recorder with a flat frequency curve and a superior low frequency response (3.1.1).

One important alteration to the present Holter would be calibration before each patient recording. A 1 mV pulse could be recorded prior to fixing the leads to the patient's chest. The analysis software would then use this as a reference before processing the ECG. This is an important adjustment because we hope to detect voltage changes less than 0.1 mV and any error could affect the medical result.

It may also be necessary to replace the playback unit and in particular the tape deck. If the playback speed was increased the system low frequency cutoff would be reduced. This would improve the quality of the reproduced ECG.

6.2.2 Algorithm Development

Although the algorithms used for ST analysis worked well for the five patients tested, improvements could be made. Special attention should be given to removing noise and baseline wander, detecting arrhythmias and ST segment measurement. Several methods were already discussed in Section 4.2. It is important to test any new algorithms with a wide variety of patient ECG tapes.

At present only one ECG channel is analyzed, but in fact two channels are available. Including the second ECG lead would improve detection of the QRS complex and would provide a backup if lead V5 was contaminated with noise. However, the use of a second channel did not appear necessary based on the work done in this study.

The personal computer had two basic limitations: speed and memory space. This caused a problem when loading and analyzing the ECG data. A new, more powerful computer could be purchased with a faster system clock and a memory twice the size of the Ericsson we used. As the data is loaded onto the computer, it may be stored on cassette tape (or floppy disks) in digital form so that it may be easily accessed in the future. The ECG sampling rate could be reduced by up to 50%. The data would then have to be passed through a low pass filter to avoid aliasing. At present each data sample contains 12 bits which must be stored in two 8 bit memory locations with 4 redundant bits. This precision level could be reduced to 8 bits which would effectively halve the storage space required in memory.

6.2.3 Further Medical Work

Extending the study to a full 24 hour correlation between angina and reflux would greatly help doctors to analyze the medical results. At present we only know that significant ischemia did not occur within a few minutes of a reflux episode. It would be interesting to know whether ischemia occurred at all over the 24 hour period.

In the future it is hoped to study a larger patient group. Also looking at less severely ischemic patients may improve the sensitivity of the study.

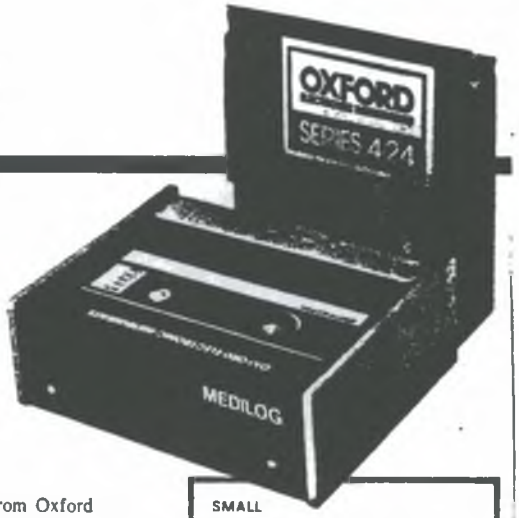
It may also be necessary to study the mechanism of pain in reflux. Does it occur before, during or after the reflux episode? This would help find a criterion for establishing a correlation.

Finally, an anatomical study may be done to investigate the nerve theory proposed earlier (6.2).

APPENDIX 1

THE OXFORD MEDICAL RECORDER

OXFORD
MEDICAL SYSTEMS



MEDILOG
Monitor/Recorder

Today's choice for Ambulatory Monitoring the world over!

The MEDILOG MONITOR/RECORDER, from Oxford Electronic Instruments, represents todays state-of-the-art in the field of ambulatory monitoring. This rugged, miniaturised, analog magnetic tape recorder is an ideal physiological data acquisition system.

A continuous 24-hour electrocardiogram on unrestricted ambulatory patients provides accurate measurements, during everyday stress and activity as well as during periods of sleep. The MEDILOG monitor is an invaluable aid to the physician in the differential diagnosis of many unexplained symptoms (dizziness, syncope, palpitations).

MEDILOG provides accurate data for evaluation of drug therapy, artificial pacemakers, status of myocardial infarction, stress testing and research programmes.

SMALL

The recorder is very small, 4¼" x 3¼" x 1½" (112 x 86 x 36mm), and is easily concealed under a coat, sweater or jacket.

LIGHTWEIGHT

Total weight of the unit, fully loaded with carrying case, is 14 ounces (400gms) making it ideal for pediatric, elderly, outpatients and stress lab. applications.

ACCURATE

Baseline stability of the unit combined with a continuous 24-hour recording of data, plus an exclusive and unique tape speed servo system ensures fidelity and accuracy of all measurements, including time of day.

RELIABLE

This very rugged, solid state instrument with low power consumption is ideally suited for out-patient operation and other non-laboratory environments.

SIMPLE OPERATION

This recorder utilises a standard C-120 casssette with only one on/off switch. It incorporates inexpensive, disposable mercury cell batteries with colour coded patient cables for fast and accurate patient hook-up.

FLEXIBLE

Four channel recording capability provides for cross correlation of physiological data previously only possible in laboratory environments using costly and sophisticated equipment.

The original equipment cost, plus day to day operational expenses for supplies are significantly less than competitive systems. There are no expensive optional items such as a battery charger to purchase.

Fig. A1.1a

Medilog Series 4-24 and 4-2

from Oxford-the data retrieval specialists

Oxford Electronic Instruments offer two versions of the Medilog Recorder - Model 4-24 for long-term studies and Model 4-2 for short-term experiments requiring data replay in normal time, speech annotation, or higher frequency response.

Both types utilise miniaturised, plug-in amplifiers to cope with most types of signal, resulting in the smallest and lightest data collection system currently available.

TYPE 4-24 RECORDER

for 24-hour continuous monitoring of ECG, EEG, EOG, EMG, blood pressure, temperature, and other parameters, with data replay in accelerated time (normally X25 or X60).

General Specification:

Size: 112 x 86 x 36mm
(4½ x 3½ x 1½ inches)

Weight: 400 gms. (14 ounces)

Operating Temperature Range: 0-40°C.

Signal to Noise Ratio: Better than 30 dB record/replay.

Tape Speed: 2mm/sec.

Speed Stability: ±2% overall.

Record Time: > 24 hours.

Batteries: 4 x Mallory RM-1N TR134 Burgess HG1 or equivalent.

Power Consumption: Less than 25 mA.

Battery Life: At least 24 hours.

TYPE 4-2 RECORDER

for applications with data replay in either normal (X1) or accelerated time (X5).

General Specification:

Specifications are as for Type 4-24 with the following exceptions:

Tape Speed: 25mm/sec.

Record Time: 2 hours.

Power Consumption: Less than 50 mA.

Battery Life: At least 4 hours.

4-24 COMPATIBLE RECORD AMPLIFIER MODULES

Type	Application	Record Method	Specification
AD-2	ECG, EOG, EMG.	Direct	0.15 - 100 Hz (X60). Input sens. adj. 1-3 mV pk. Input Imp. 100 KΩ. Compat. Replay Amp. PD-2.
AD-4	As AD-2. For active subjects. LF response restricted.	Direct	As AD-2 except frequency response 0.5 - 100 Hz. (X60 replay). PD-2.
AM-3	Slow varying DC parameters. Temperature, respiration for X60 replay.	PWM	Freq. Resp. (-3dB) DC -3Hz. Input Imp. 500 KΩ. Input Sens. adj. 5-25 mV pk. Linearity 2%. Compat. Replay Amp. PM-3.
AM-4	DC parameters - including BP, Temp. Resp. for X25 replay.	PWM	As AM-3 except frequency response DC-10 Hz.
AT-1	Time marking.	Direct	Frequency 1 Hz. Stability ±0.3% Compat. Replay Amp. PD-2.
AT-2	Time marking - to establish the base on replay.	Direct	Frequency customer specified 1 - 100 Hz. Stability ±0.3%. Compat. Replay Amp.
ATE-1	Crystal controlled time marking and event marking - used to generate time of day display at replay.	Direct	Frequency 60 Hz. Stability ±0.001%. Compat. Replay Amps. PD-2 or PE-2
AR-1	Resistance Measurement— Temperature, etc.	PWM	Max. Res. ~ 10 KΩ. Min. Res. ~ 1 KΩ. Resolution 3% of span. Span - Adjustable.
AR-2	Resistance Measurement— Specially calibrated to suit YSI Thermistor Temp. Sensors. For X60 replay.	PWM	Temperature Range 37°C ±2°C Resolution 3% of Range.
AR-3	As AR-2	PWM	Temperature Range 15°C ±10°C.
AR-4	As AR-2	PWM	Temperature Range 25°C ±10°C.

4-2 COMPATIBLE RECORD AMPLIFIER MODULES

AD-5	Speech Annotation, Vibration data, etc. Suitable microphone systems can be supplied at extra cost.	Direct	Frequency Response: 30 - 300 Hz (X1 replay) 10 - 500 Hz (X5 replay) Input Sens. 1 - 3 mV pk. Input Imp. 100 KΩ. Compat. Replay Amp. PD-2.
AM-5	Carrier Record Amplifier for DC parameters. ECG (with preamplification), BP, Temperature.	PWM	Frequency Response: -3dB DC-50 Hz. Input Imp. 500 KΩ. Input Sens. 5 - 50 mV pk. Carrier frequency 200 Hz. Compat. Replay Amps:- PM-3-250 (X5 replay). PM-3-100 (X1 replay).
AR-5	Resistance. Customer specified ranges. Strain, temperature, etc.	PWM	Max. Res. ~ 10 KΩ. Min. Res. ~ 1 KΩ. Resolution 3% of span. Span - adjustable. Carrier frequency 200 Hz Compat. Replay Amp. as AM-5.
AR-6	Temperature measurement— specially calibrated to suit YSI 400 series thermistor temperature sensors.	PWM	As AR-5 Temperature 37°C ±2°C. Resolution 3% of range. Compat. Replay Amp. as AM-5.
AR-7	As AR-6	PWM	As AR-6 Temperature 15°C ±10°C.
AR-8	As AR-6	PWM	As AR-6 Temperature 25°C ±10°C.
AT-1	Time marking.	Direct	Frequency 1 Hz. Stability ±0.3% Compat. Replay Amp. PD-2.
AT-2	Time marking - to establish the base on replay.	Direct	Frequency - customer specified 1 - 100 Hz. Stability ±0.3%. Compat. Replay Amp.

Fig. A1.1b

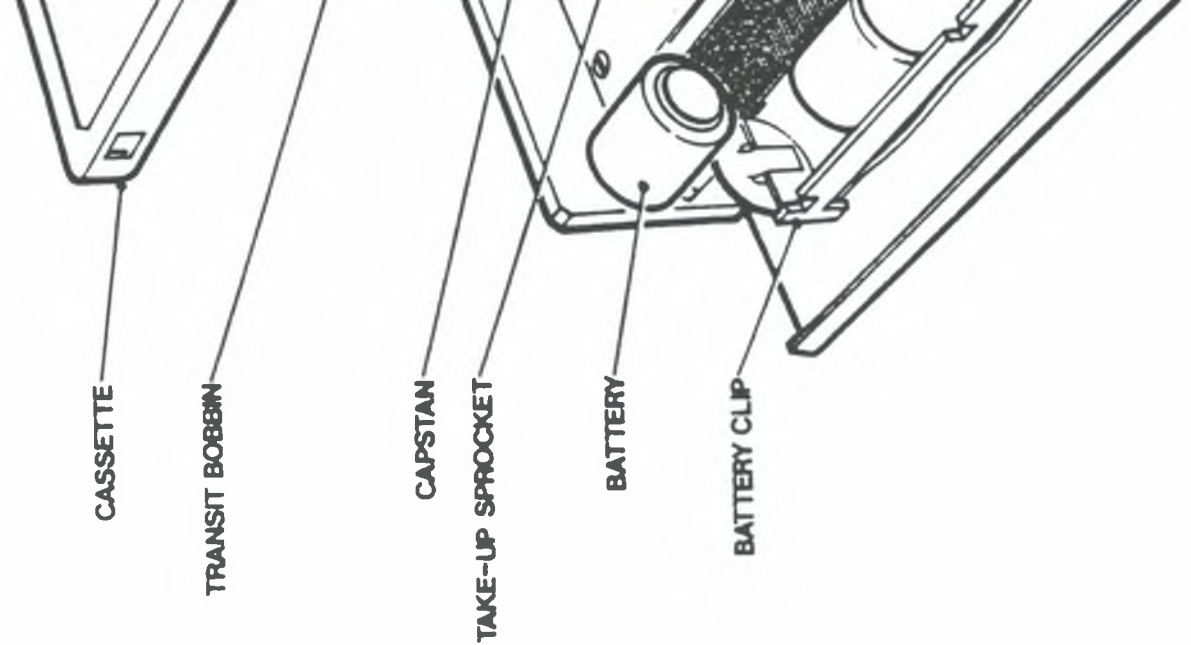
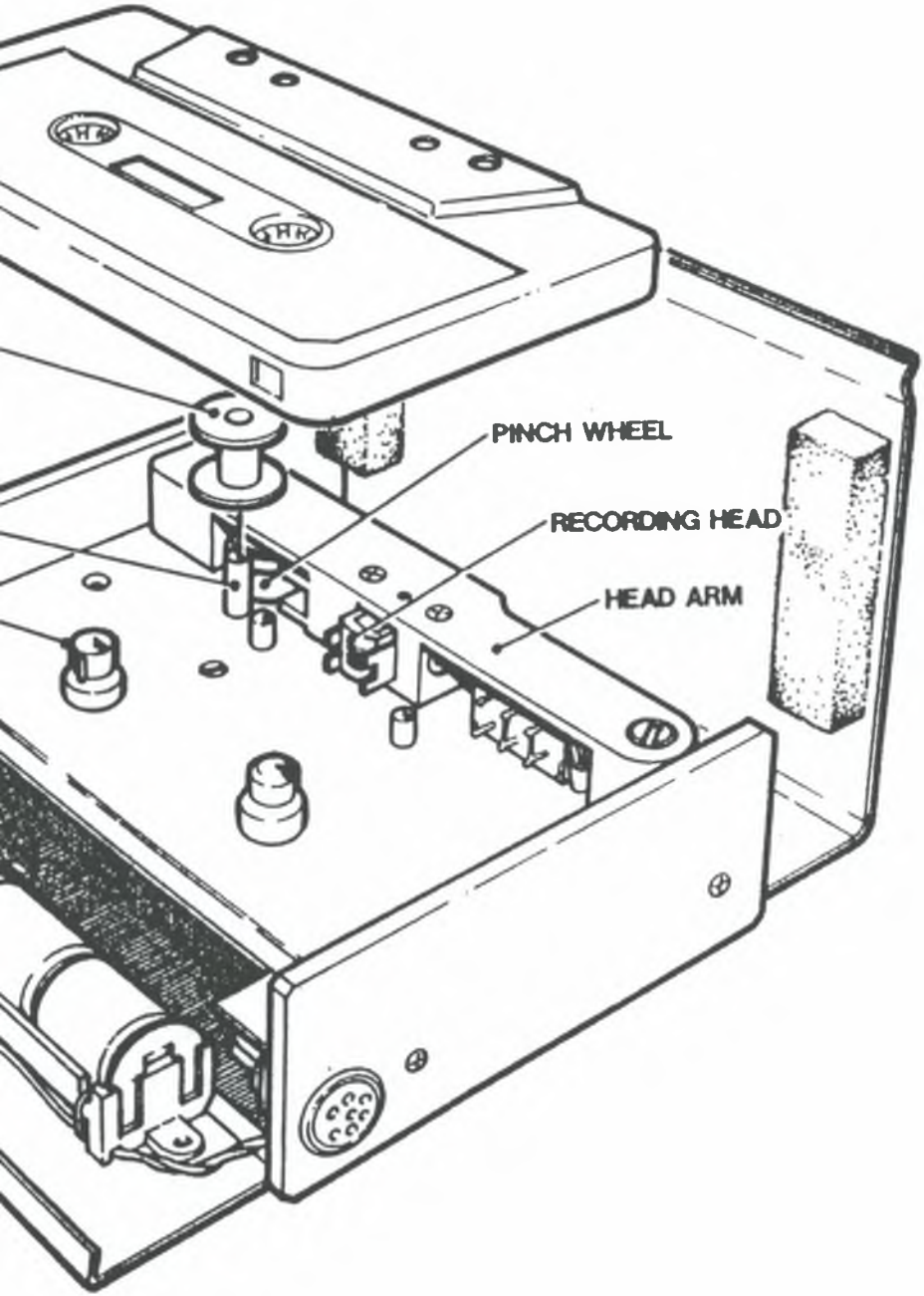

CASSETTE
TRANSIT BOBBIN
CAPSTAN
TAKE-UP SPROCKET
BATTERY
BATTERY CLIP

Fig. A1.2a


PINCH WHEEL
RECORDING HEAD
HEAD ARM

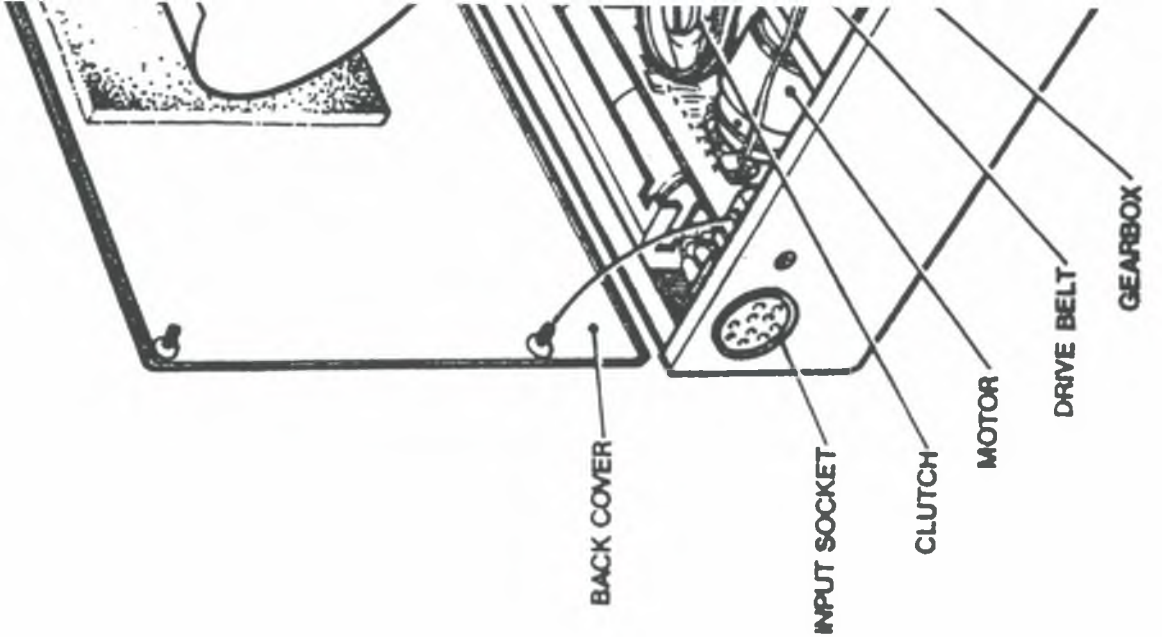
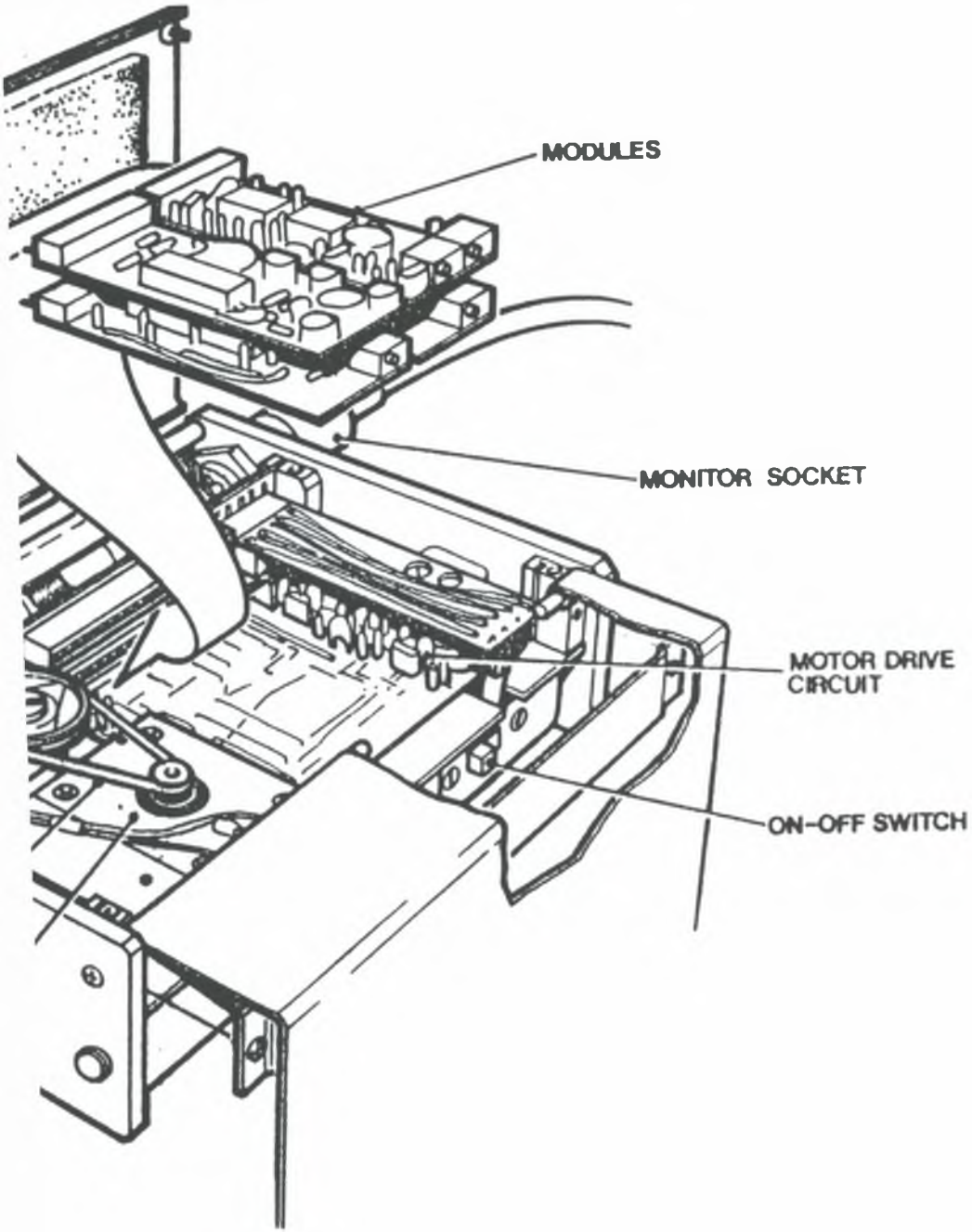


Fig. A1.2b


MODULES
MONITOR SOCKET
MOTOR DRIVE CIRCUIT
ON-OFF SWITCH

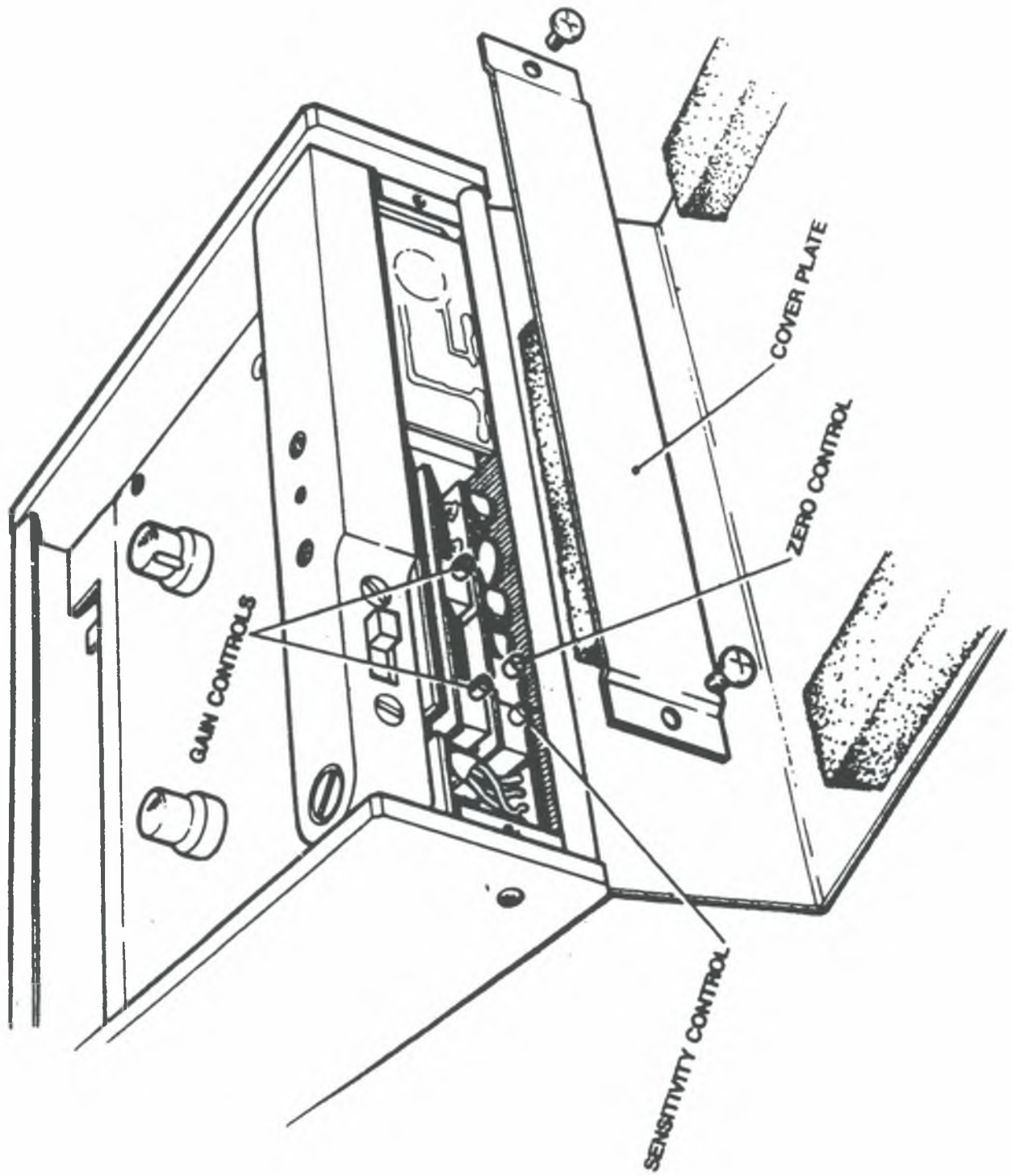

COVER PLATE
ZERO CONTROL
GAIN CONTROLS
SENSITIVITY CONTROL

Fig. A1.2c

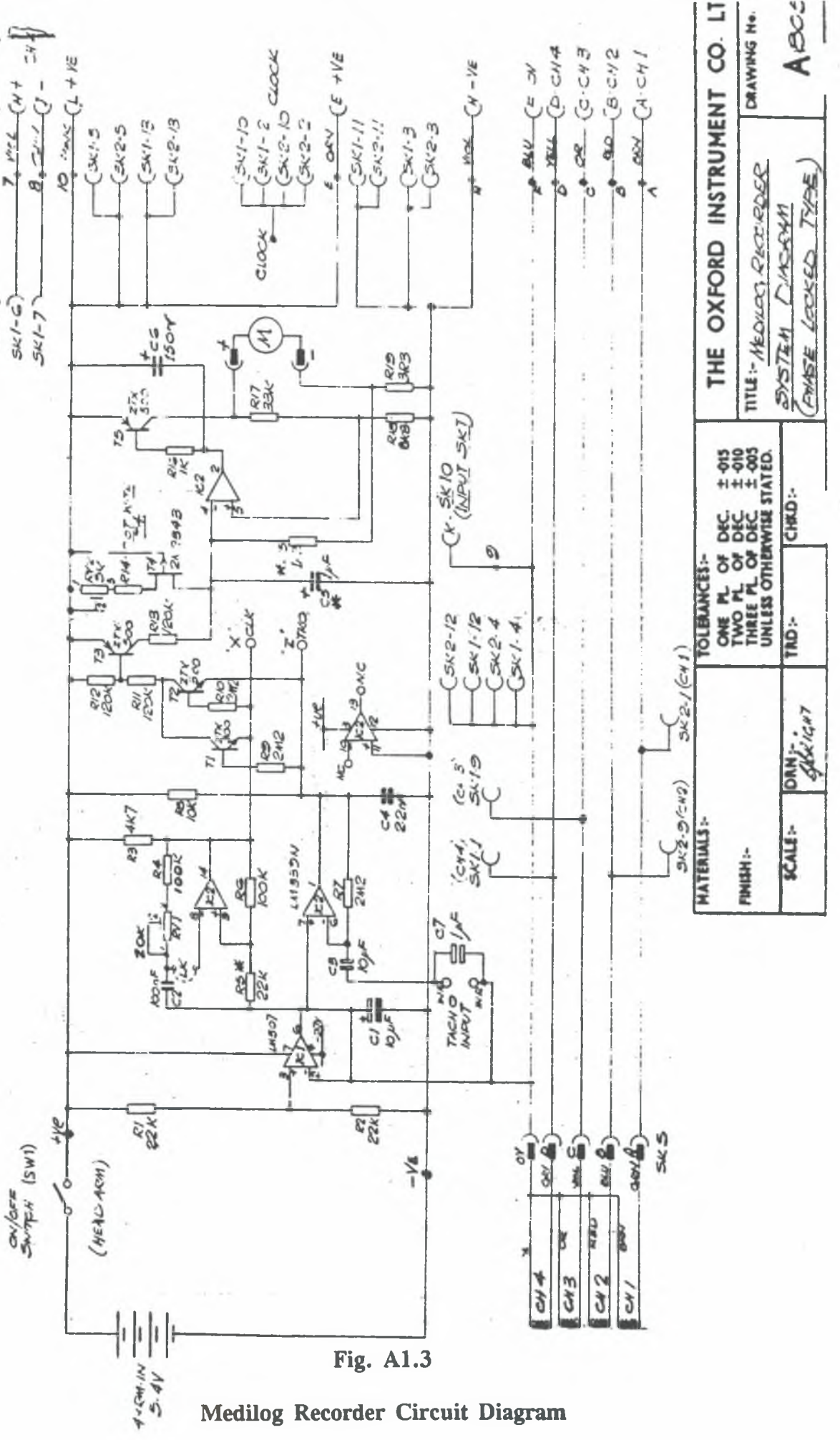
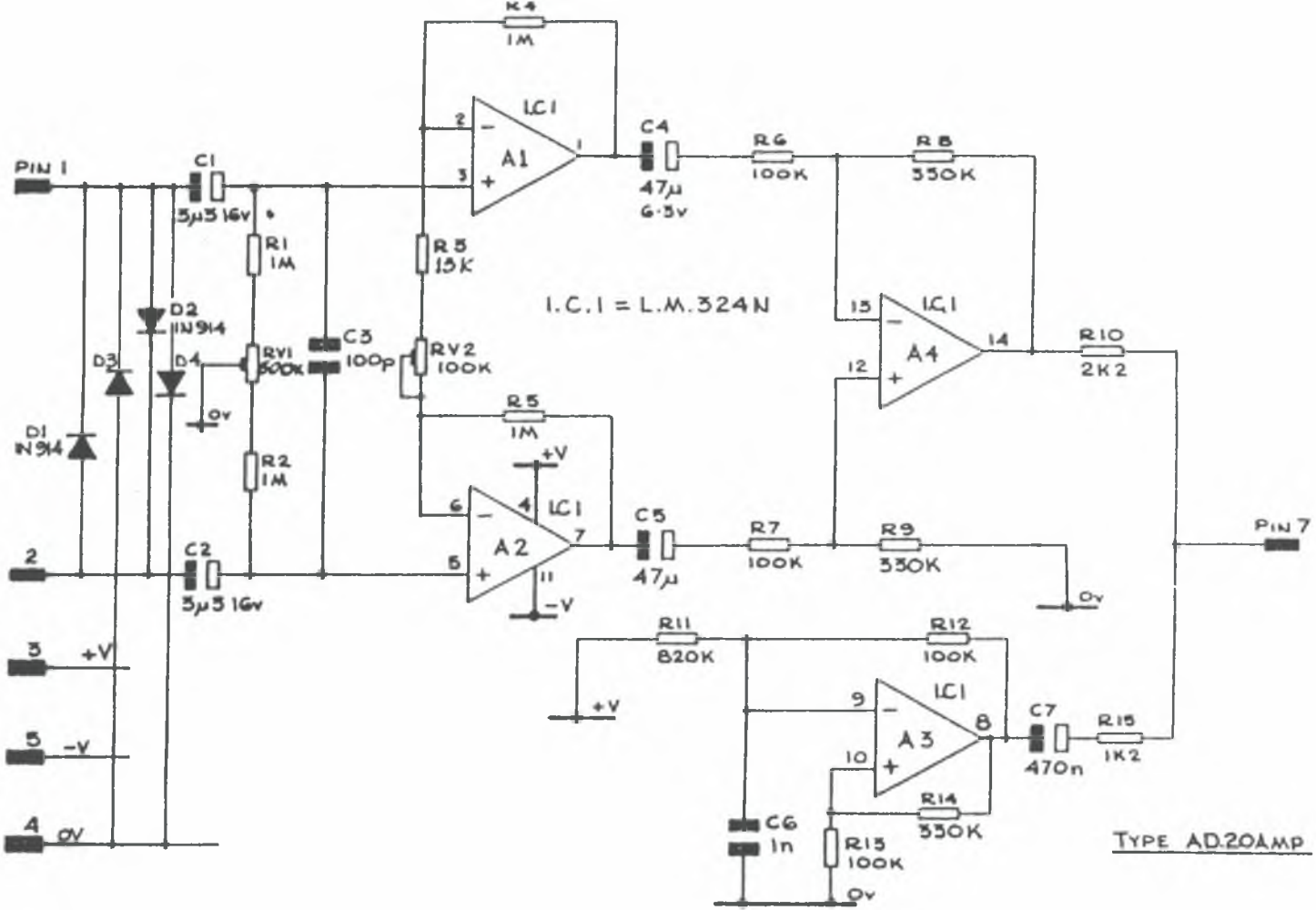


Fig. A1.3

Medilog Recorder Circuit Diagram



MATERIALS:-		TOLERANCES:- ONE PL. OF DEC. ± ·015 TWO PL. OF DEC. ± ·010 THREE PL. OF DEC. ± ·005 UNLESS OTHERWISE STATED	THE OXFORD INSTR
FINISH:-			TITLE - A.D.20AMP
SCALE:-	DRN:- D.J.	TRD:-	CHKD:-

Fig. A1.4

AD20 Amplifier

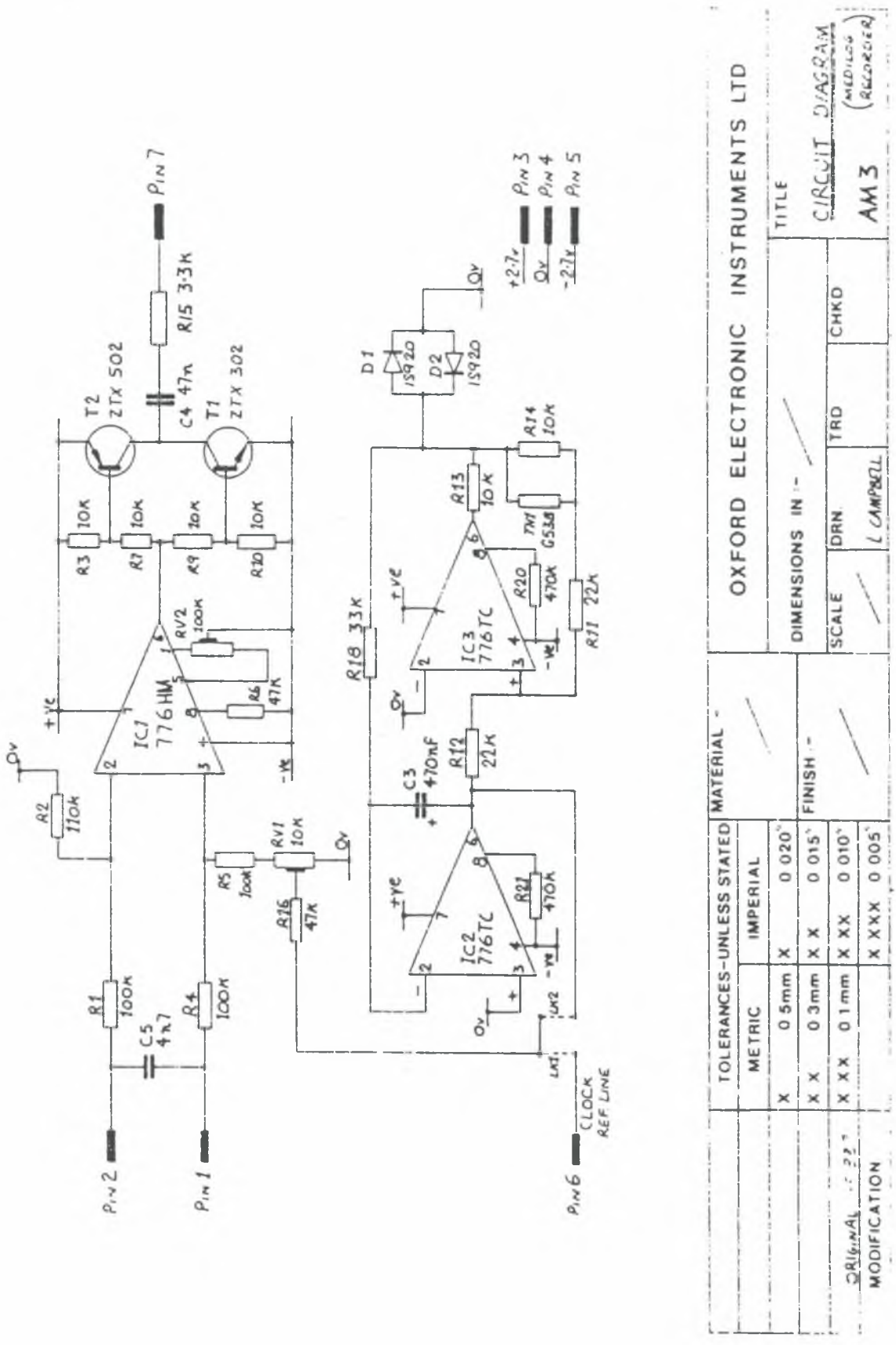


Fig. A1.5

AM3 Pulse Width Modulation Circuit

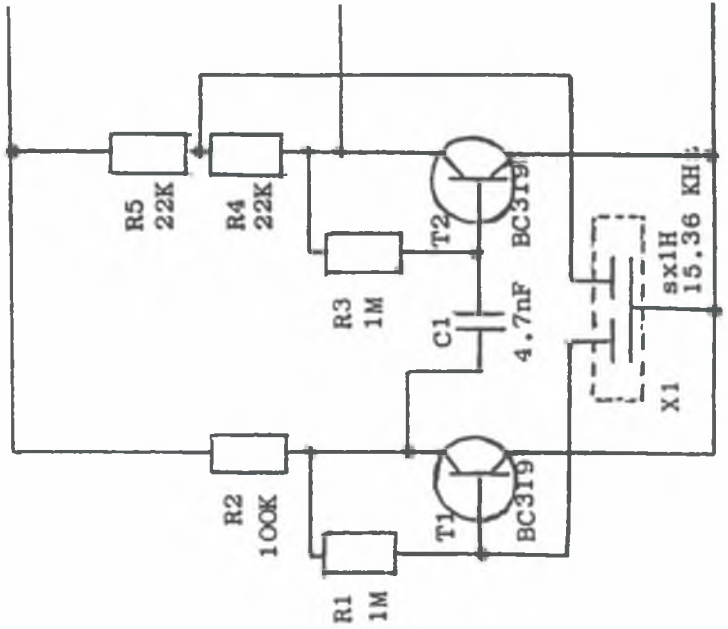
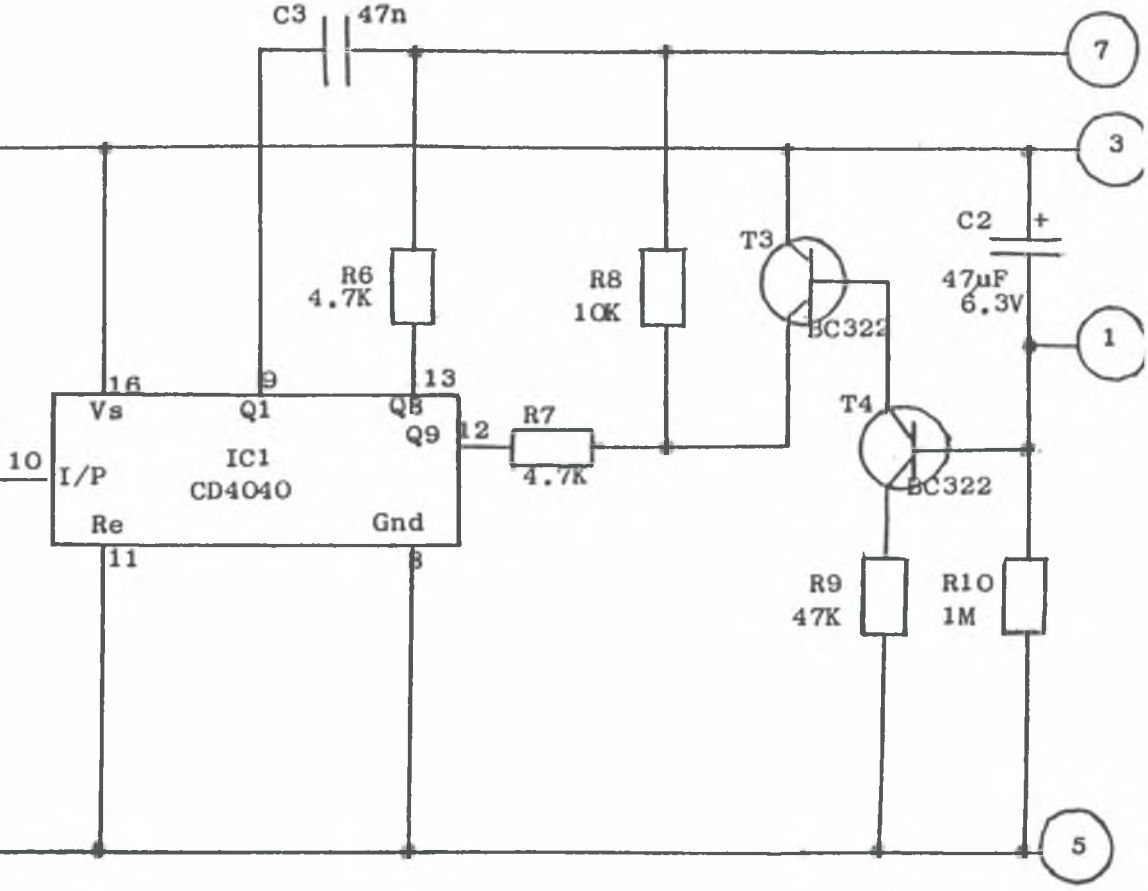


Fig. A1.6

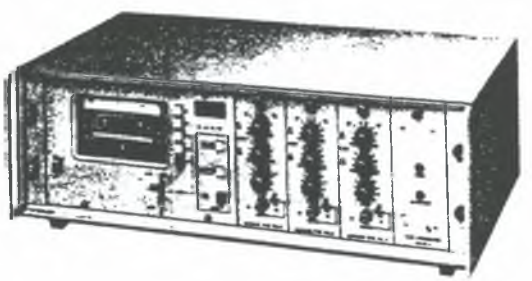
ATE-1 60Hz. Clock Module


C3
47n
7
3
C2
+
47uF
6.3V
T3
BC322
R6
4.7K
R8
10K
1
16
Vs
9
Q1
13
Q5
Q9
12
R7
4.7K
T4
BC322
10
I/P
IC1
CD4040
Re
Gnd
11
8
R9
47K
R10
1M
5

APPENDIX 2

THE OXFORD MEDICAL PLAYBACK UNIT

MEDILOG
High speed Replay Unit



The Medilog replay unit is designed to replay information recorded with MEDILOG 4-24 and 4-2 recorders on standard C-120 cassette tapes.

When used to handle 24 hour ambulatory electrocardiograms recorded on the 4-24 recorder, the unit replays tapes in 24 minutes and is designed to operate in conjunction with MEDILOG ECG ANALYSIS SYSTEMS to provide a rapid scan and analysis of the recorded ECG.

In other applications tapes are replayed at high speed, normally 60 times recording speed for 24 hour tapes and 5 times recording speed for 2 hour tapes, and the replay amplifiers provide high-level analogue signal outputs for connection to data processing or recording systems.

The replay unit is supplied in two versions:

The PB-2 which incorporates a Digital Time-of-Day Display in hours and minutes driven either from a clock track recorded on tape or from the replay tape transport.

The PB-3 which is a basic replay unit identical to the PB-2 except that the Time Display is omitted.

The replay comprises two sub-units, the tape transport and the amplifier bay.

The tape transport contains the mechanisms for driving the cassette tape, the tape head preamplifiers, power supplies and, in the case of a PB-2 replay, the digital time display.

The amplifier bay provides a housing for up to four replay amplifiers with simple, plug-in sockets to provide power supplies and signal interconnections.

Outputs are provided on the rear of both the tape transport and the amplifier bay to enable the unit to be remotely controlled and for signal connections to other devices.

Specifications for Medilog PB-2 and PB-3 Replay Units.

Tape Transport

Cassette: Standard C-120 cassette.

Standard Replay Speeds: 120mm/sec (x60 for 4-24 recorder), (x5 for 4-2 recorder).
50mm/sec (x25 for 4-24 recorder).
24mm/sec (x1 for 4-2 recorder).

Speed Stability: ±2%.

Fast forward and reverse wind: Approximately 1 minute to rewind C-120 cassette.

Push Button Controls: Forward play, Reverse play, Fast forward wind, Fast reverse wind, Stop, Mains on/off.

Rear Connections: Three pin mains output, 15-way control, 37-way analogue data output.

Time Display (PB-2 version only)

Display: 4 digit display of Hours and Minutes.

Push-button controls: Individual push-button on each digit to set start time, Time off tape/capstan select switch, 24 hour/2 hour display select, Zero reset.

Amplifier Bay

Housing to accept four, plug-in replay amplifiers. Sockets provide power supplies and signal interconnection.

General

Power requirements: 50VA.

Mounting Options:
Horizontal case: (Suitable for rack-mounting): 490 x 170 x 355mm (19½ x 6¾ x 14 in.)

Vertical case: 280 x 310 x 325mm (11 x 12¼ x 12¾ in.)

Weight: 12kg (26.4lb) without amplifiers.

Fig. A2.1a

Replay Amplifiers compatible with 4-24 Recorder

TYPE	APPLICATION	SPECIFICATION
PD-2	Replay of AD direct record amplifier information.	**Output level:** 4V pk nominal at maximum gain for fully modulated tape. **Bandwidth:** 0.15-100Hz (x60 replay) referred to recording. **Signal/Noise:** 30dB overall system response with fully modulated tape, LF filter set at 5. **Controls:** Gain, HF cut, LF cut, signal invert. **Output Connector:** BNC front panel, 37-way on amplifier bay.
PM-3-250	Replay of AM and AR carrier record amplifier information.	**Output level:** ±0.5V nominal at maximum gain for fully modulated tape. **Bandwidth:** DC-3Hz (x60 replay) referred to recording with AM-3 amplifier. DC-10Hz (x25 replay) referred to recording with AM-4 amplifier. **Signal/Noise:** Better than 30dB overall system with fully modulated tape. **Controls:** Gain, offset (preset), filter. **Output Connector:** BNC front panel, 37-way on amplifier bay.
PM-3-500	Replay of AM and AR carrier record amplifier information.	As PM-3-250 except: **Bandwidth:** DC-8Hz (x60 replay) referred to recording with AM-4 amplifier. **Signal/Noise:** 30dB overall system response with fully modulated tape.
PE-2	Detection of Event signal recorded by ATE-1.	**On event signal:** LED illuminates, logic level output.
PE-21	Detection of Event signal recorded by ATE-1 with replay stop facility.	**On event signal:** LED illuminates, logic level output, replay stops. **Controls:** Switch to select indicate/stop, push-button to restart replay after event.
PIT-2(60)	R-R interval measurement. Operates on output of adjacent PD-2 on left.	**Outputs:** 1) DC Voltage proportional to instantaneous R-R interval variable by preset gain control on front panel. 2) 5V Positive Pulse for each R wave detected. **Controls:** Trigger level, gain (preset) **Internal Calibration Switch:** 50bpm/Off/100bpm. **Output Connectors:** 1) BNC socket on front panel. 1) & 2) 37-way on amplifier bay.
PIT-2(25)	R-R interval measurement. Operates on output of adjacent PD-2 on left.	As PIT-2 (60)

Replay Amplifiers compatible with 4-2 Recorder

PD-2	Replay of AD direct record amplifier information.	As for 4-24 recorder except: **Bandwidth:** 10-500Hz (x5 replay) referred to recording. 30-500Hz (x1 replay) referred to recording.
PM-3-100	Replay of AM and AR carrier record amplifier information at x1 record/replay ratio.	As for PM-3-250 (4-24 recorder) except: **Bandwidth:** DC to 50Hz (x1 replay) referred to recording with AM-5 amplifier. **Signal/Noise:** 30dB overall system response with fully modulated tape, filter at position 1.
PM-3-250	Replay of AM and AR carrier record amplifier information at x5 record/replay ratio.	As for 4-24 recorder except: **Bandwidth:** DC to 50Hz (x5 replay) referred to recording with AM-5 amplifier.

OXFORD MEDICAL SYSTEMS

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CAT. NO. X63 PRINTED IN ENGLAND

Fig. A2.1b

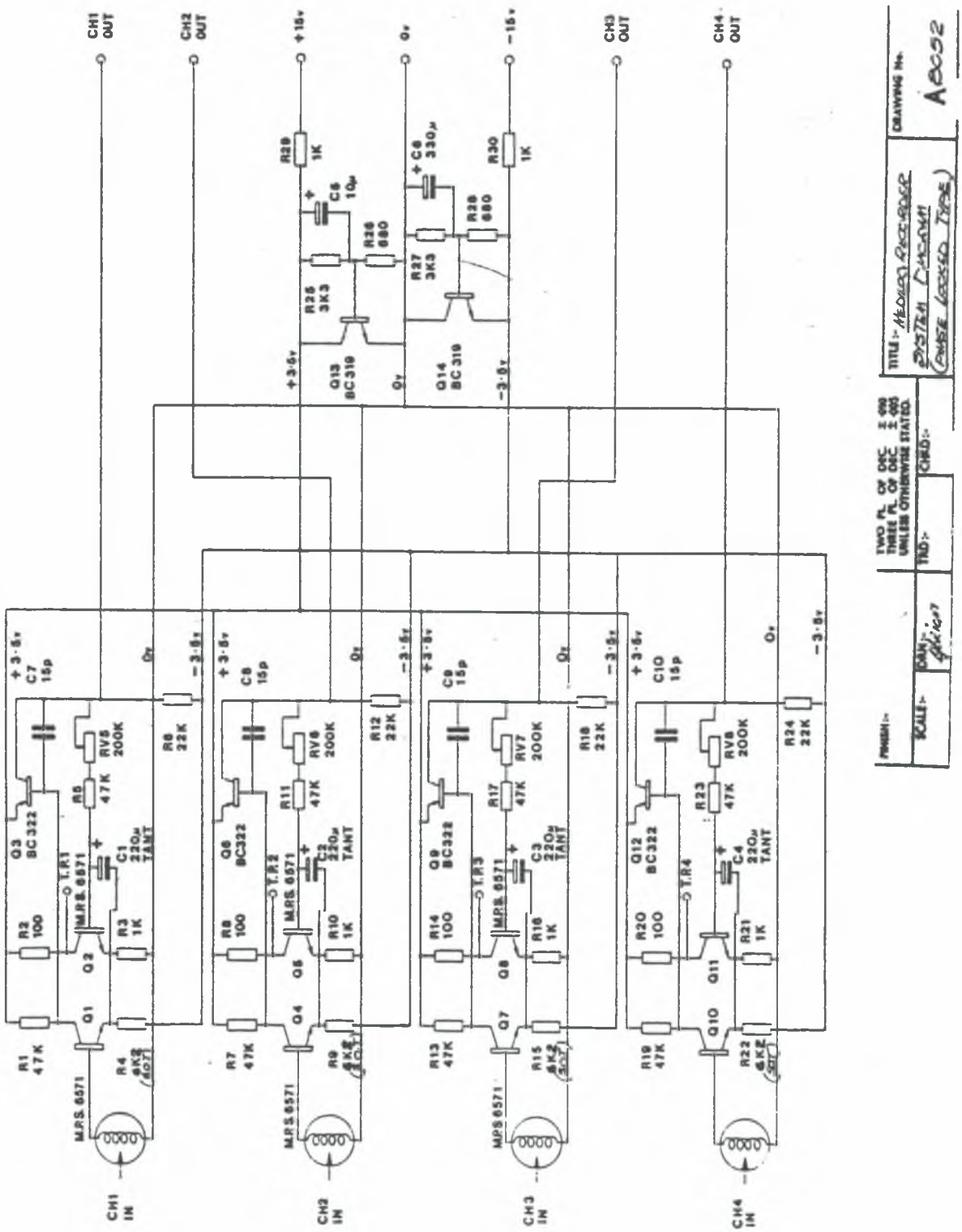

Fig. A2.2

Pre-Amplifier

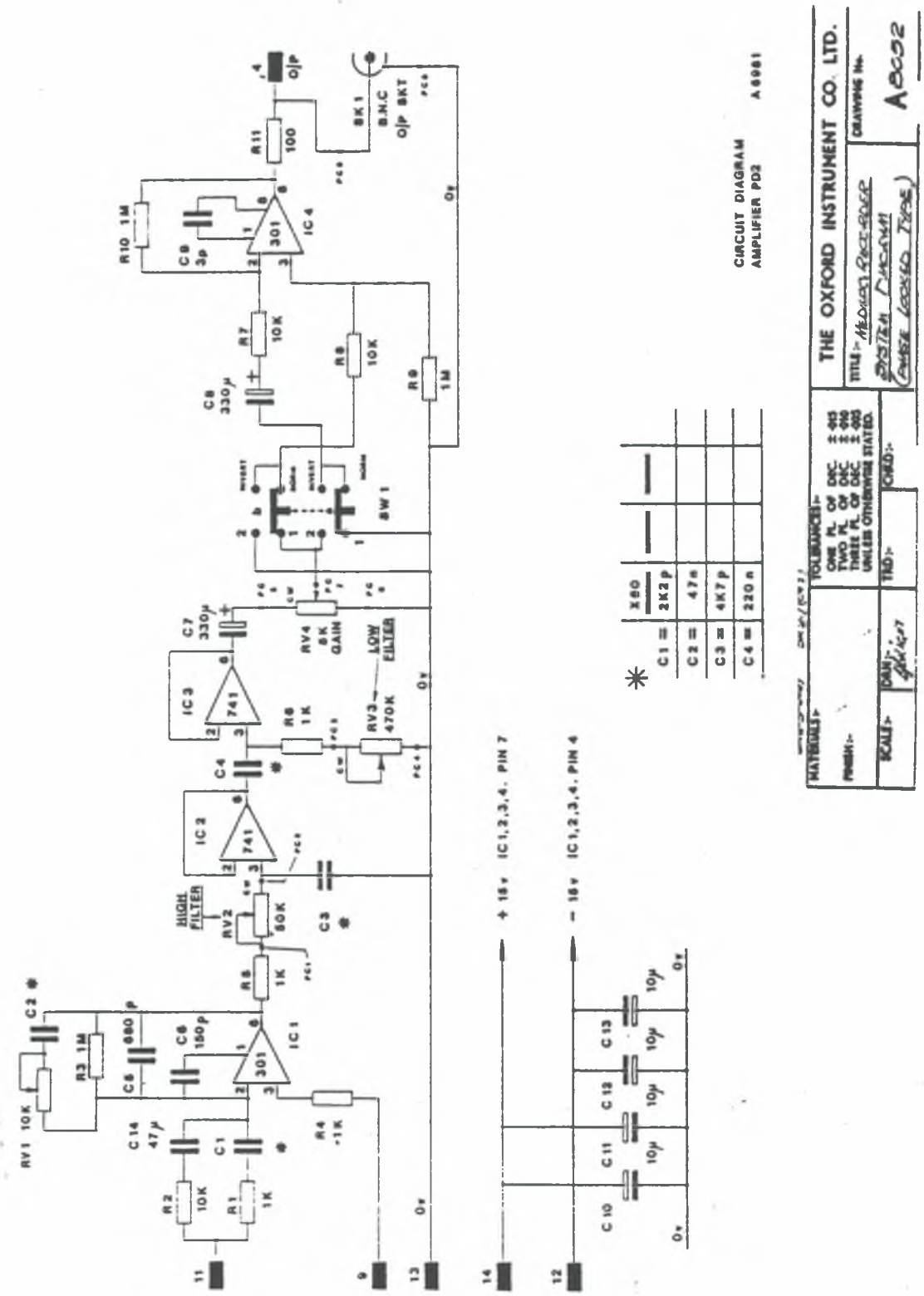

Fig. A2.3

PD2 Amplifier

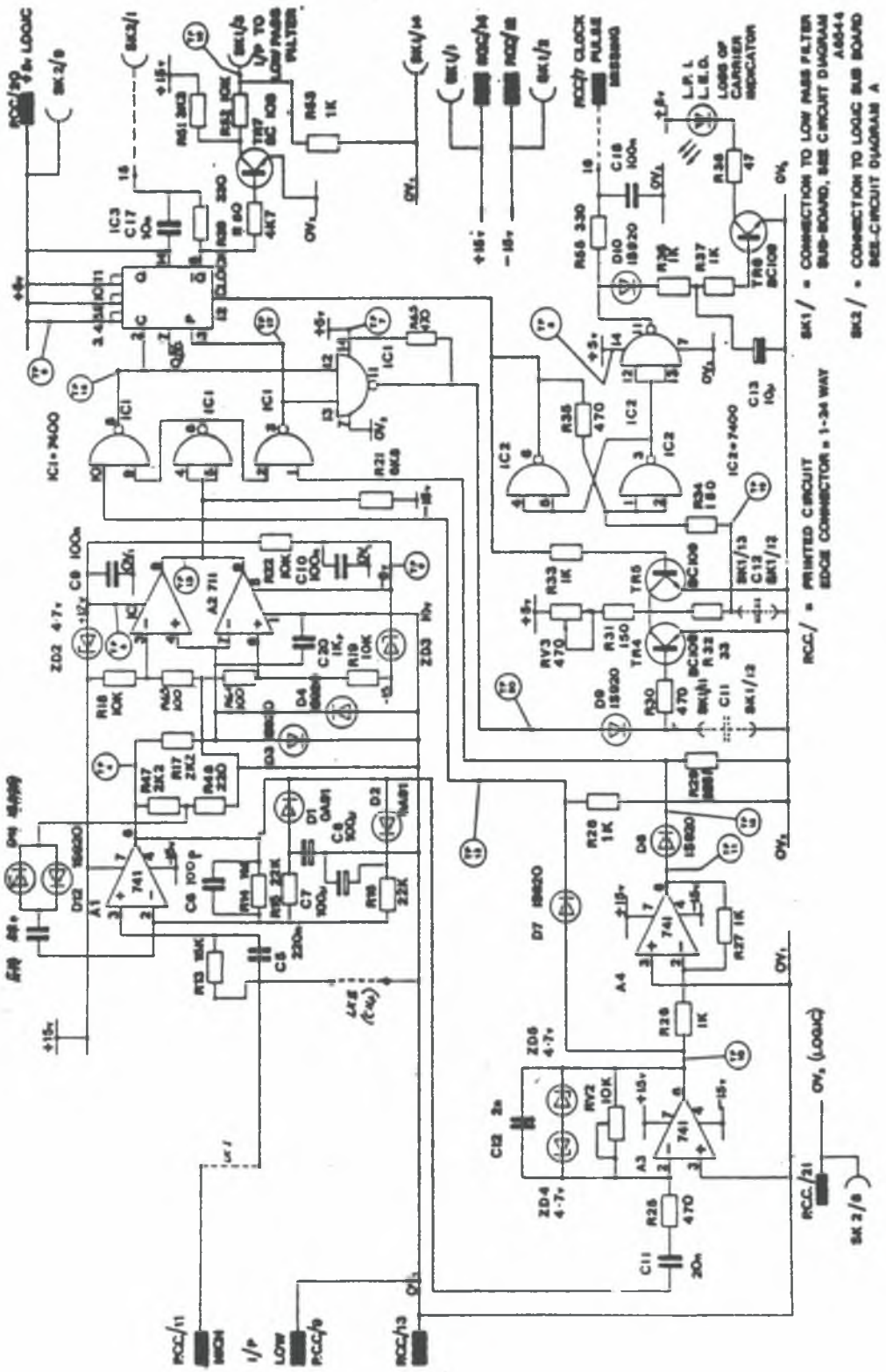

Fig. A2.4a

PM3 Pulse Width Demodulator

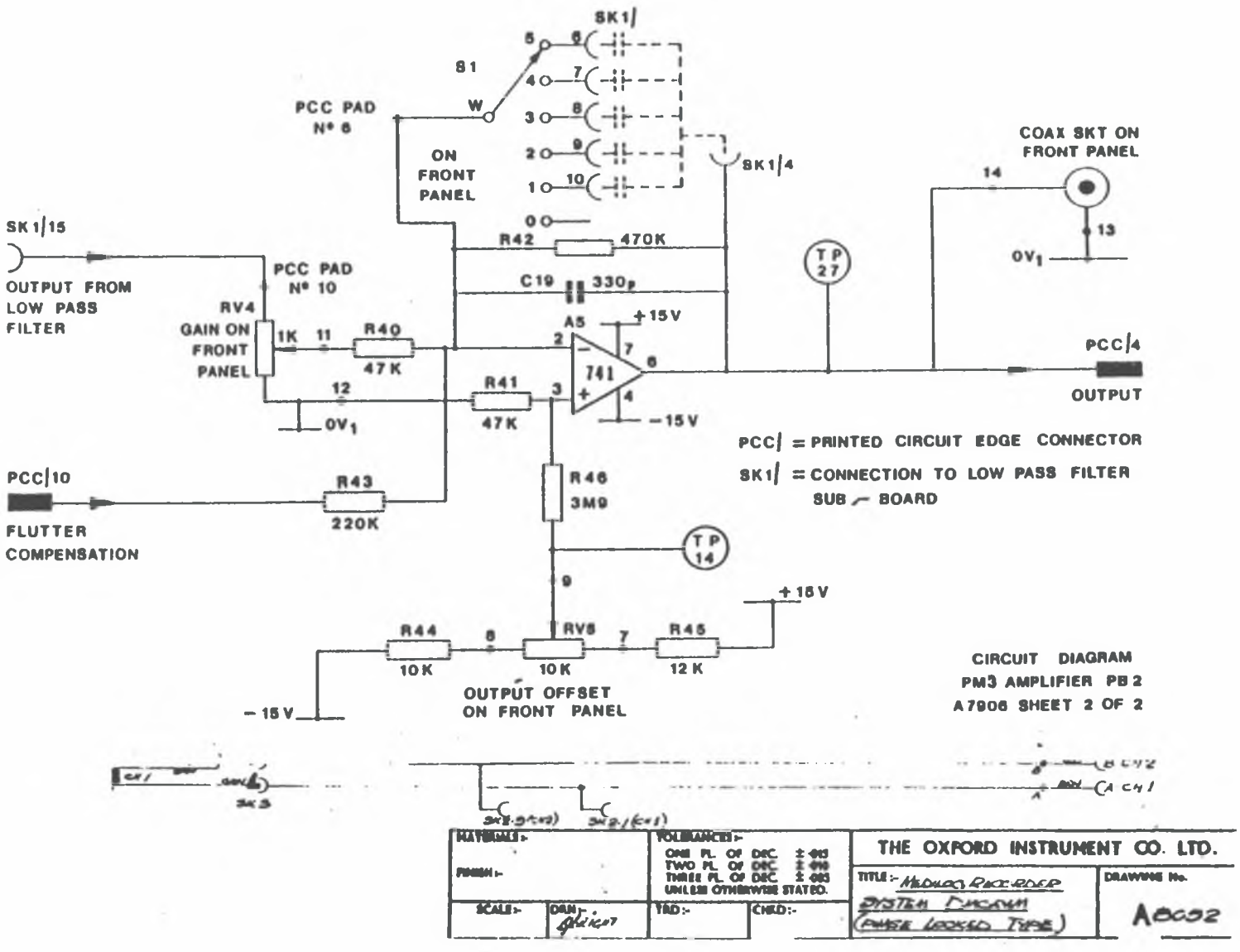

Fig. A2.4b (Contd.)

APPENDIX 3

USER GUIDE TO SOFTWARE

pha2d in directory c:\a2d

This program loads 24 hours of pH data from the patient cassette tape to the computer.

Instructions:

Insert cassette tape with the patients name sticker showing.
Rewind to start, then play until the beginning of the magnetic tape has just passed the roller.
Zero the tape deck counter.
Type in "pha2d" into the computer and press enter.
Type in 0, the counter reading and at the same time start the tape.
When the program has finished you will be alerted by a bleep.
Type in the tape deck counter reading (e.g. 787) and press return.
The program then writes the data to the output files rawph1.dat, rawph2.dat .... rawph6.dat. Copy these files to the patient's sub-directory.

NB

There is an LED on the front of the playback unit which turns off when it detects the pH signal. If it does not turn off when the tape is played, readjust the position of the tape head.

plotphh in c:\a2d

This program enables you to plot 4-hour episodes of the pH signal.

Instructions:

Type in "plotphh" and press enter.

The 24-hour period has been divided into six 4-hour intervals starting at the beginning of the recording. You will be prompted as to which 4-hour episode you wish to see.

Type any number between 1 and 6 and press return.

The graph is plotted using GraphiC software and when the plot is complete, you will hear a tone.

Press the space bar.
The plot is quickly redrawn.
Press the space bar again.

A menu will appear which enables you to get a printout of the graph (e.g. press shift 'm').

If you type in 6 (see above), you will be prompted as to how many hours you want. Check the diary for the length of the recording. If it was 22 hours 45 mins. long for example, then you will want to see 23 hours of pH data. The sixth episode contains only 3 hours, so type in "3".

data in c:\a2d

This program is used to gather information from the patient diary.

Instructions:

After typing in "data" and pressing return, you will be prompted for the starting time of the recording, the finishing time, meal times (breakfast, dinner and tea) and the times at which pain occurred.

NB

All times must be converted to the 24-hour clock and entered in the form 13 56. Press return after each entry.

process in c:\a2d

This program searches through the pH data files (rawph1.dat etc.) for episodes of reflux. The reflux episodes are listed in the output file with information as to whether the patient was upright or supine. The pH score is calculated and normal values are given for comparison.

Instructions:

Simply type "process" and press return.

correl8 in c:\a2d

This program lists reflux episodes and indicates those which happened up to 1 hour after a meal, i.e. post prandial. It then correlates reflux episodes with symptoms, usually pain.

Instructions:

Type "correl8" and press return.

Results are written to corrout.dat which may also be printed out.

After completing the above, change the names of files results.dat and corrout.dat. e.g. for patient PB : pbresult.dat and pbcorr.dat and save these files in the patient's sub-directory.

You are advised to delete rawph1.dat, rawph2.dat .... rawph.dat6, results.dat and corrout.dat as these files are now all stored in the patients sub-directory and are no longer needed. It will save memory space and stop confusion when the next patient is analyzed.

The next step is to choose significant episodes of reflux and therefore define 10 minute ECG intervals which you want to analyze, e.g.

360 - 370 mins. (all episodes are measured from the beginning of the recording).

Divide 360 by 32.586, the tape replay speed factor to give 11 mins. The tape is then played for 11 mins. before loading the ECG data.

ecga2d in c:\a2d

This program loads 10 minute episodes of ECG data and writes the data into output files rawecg1.dat, rawecg2.dat.... rawecg5.dat.

Instructions:

Rewind the tape and set up as before.

Start the clock and the tape simultaneously. Type in "ecga2d10", press return and type in 0. When the clock reaches the start of the ECG interval (e.g. 11 mins) press return.

prepecg in c:\a2d

This program takes the data from rawecg1.dat, rawecg2.dat... rawecg5.dat and converts it to the normal ECG voltage range. The data is further subdivided into 15 files: ecg1.dat .... ecg15.dat.

Now transfer the ecg data files to the directory c:\linda with the command:
> copy ecg*.dat c:\linda.

main in c:\linda

The program main together with subprograms analyzes the data for ST segment depression. Each of 15 data files is analyzed individually.

Instructions:

Type "main" and press enter. You are prompted for the data file number. Type in a number between 1 and 15 and press return.

It is suggested that you work through the 15 data files sequentially.

A comprehensive listing of the beats analyzed is given in output1.dat... output15.dat. Measurements taken at the x point are stored in st1.dat... st15.dat and average heart rates are stored in hr1.dat .... hr15.dat.

ischemia in c:\linda

This program takes the 'st' and 'hr' files which have just been created and amalgamates them into two files st.dat and hr.dat. It also counts the number of data points in each file.

plotst in c:\linda

A plot of the ST trend from data stored in st.dat together with a plot of heart rate from hr.dat is drawn by this graphics program.

Instructions:
Simply type "plotst" and proceed as for plotphh.

Before repeating 'ecga2d10' it is recommended that you delete the following files: rawecg*.dat, ecg*.dat in directory c:\a2d and ecg*dat, st*.dat, hr*.dat, output*.dat in directory c:\linda where * indicates all possible numbers.

Before starting analysis of a new patient also delete the following files in directory c:\a2d: rawph*.dat, beginend.dat, meals.dat, exercise.dat, pain.dat and posture.dat.

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