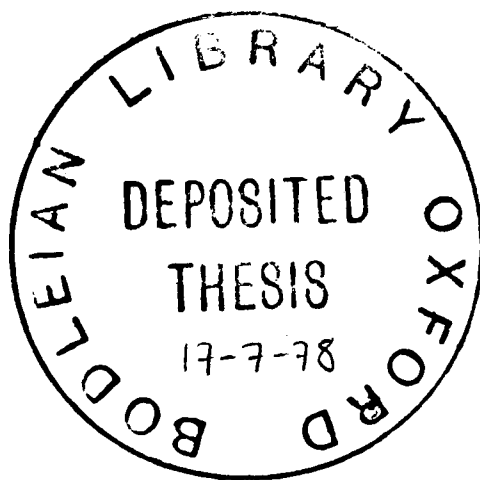


CARDIAC MONITORING IN AMBULANT SUBJECTS

by

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To

URSULA

ABSTRACT

Miniature magnetic tape recorders permit physiological data to be collected from ambulant subjects. During 24 hours the signals from some 100,000 heart beats can be registered but the analysis of this amount of information poses technological problems.

Monitoring of an oscilloscope display of the signal replayed from tape was an early method. A record-replay speed ratio of 25:1 enabled a tape to be scrutinised in one hour but was a tedious task. Digital computers were being used to analyse standard ECGs of short duration but were expensive and complex.

It appeared that a comparatively simple semi-automatic analyser based on analogue techniques would be practical, given the limited objective of identifying ventricular and supraventricular extrasystoles, ventricular and supraventricular tachycardias, bradycardia, gaps or short periods of asystole and change in QRS wave-form.

Commercial systems using variations in width or area of the QRS complex as criteria for classifying ventricular extrasystoles proved to be unsuccessful in real time analysis and seemed unlikely to be suitable for adapting to high speed operation.

It appeared possible that the QRS wave-forms from ventricular extrasystoles might contain a higher proportion of low frequency components than those from contractions arising in the atrium and that they might be segregated by a method based on this hypothesis.

No information could be found on this subject in the literature, so measurements were made which showed that ventricular extrasystoles contain a high proportion of frequencies around 2.8 to 3.8 Hz, whilst for sinus beats the predominant frequencies are near 13 Hz.

This being so, an analyser using analogue filters was developed to exploit the discovery.

In validation tests on 51 recordings the incidence of false positive or false negative detection of premature beats ranged from 0% to 5.8%, whilst misclassification of ventricular and supra-ventricular premature beats occurred with a frequency of 0% to 1.5%. No errors occurred in the classification of tachycardias, bradycardia or gaps.

Subsequently the analyser has been used in a survey of the 24-hour ECG of 100 normal subjects, in a study of the diurnal variation in the incidence of ventricular extrasystoles and in several drug trials.

Et homine ante mortem habitu utcumque melancholico, et admodum vigili, et pulsu praedito miris sane modis inaequali et vario, quique arteriae contractionem manifeste ostendebat. Ita enim multis mensibus ante mortem (quum tamen alioquin veluti sanus obambulare) pulsus aut arteria potius contrahi visa fuit, ut trium aut quatuor pulsationum ictuum've intervallo contracta maneret velutque expulsionem moliretur.

Andreas Mesalius 1514 - 64

De Fabrica Humani Corporis 2nd edition, 1555.

This man was, before his death, in a persistent melancholic and somewhat wakeful state, his pulse being really astonishingly unequal and changeable, manifestly demonstrating the contraction of the artery. For, during many months before death (though he walked about generally as a fit person), it was observed that the pulse - or, more accurately, the artery - was contracted, and remained constricted during the interval of three or four pulsations, or beats, as if labouring upon the expulsion of blood.

Translated by Leibowitz, Medical History VII, 1 p.259.

London, 1963.

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FOREWORD

When attempting the description of a system for categorising cardiac arrhythmias it is unfortunate that there is no agreement on the description of that most common cause of arrhythmia, the extrasystole.

The term "extrasystole" appears to have been first used by Engelman (1897) and to many it has an archaic sound. Purists may argue that the term is only correctly used to describe interpolated beats. If, however, the word "extra" is used as a prefix, in the sense of being situated outside something, then the term "extrasystole" becomes synonymous with "ectopic" and can legitimately have wider application.

The three other terms in common use, "premature contractions", "premature beats" and "ectopic beats" also fail to be entirely accurate. For example, in sinus arrhythmia an extrasystole may not be premature, whilst in atrial fibrillation prematurity cannot be defined.

The third term, "ectopic beat", is unsatisfactory on two counts. Firstly, escape beats have ectopic origins but are produced in a quite different manner from that of extrasystoles and, secondly, the probably rare sinus extrasystole obviously does not arise in an ectopic focus.

Fashion may be a factor in the selection and use of technical terms in cardiology as in other branches of science

but a brief survey of the literature of the last sixty years shows little evidence of this.

As examples, Mackenzie (1913) used "premature beat" and "extrasystole" synonymously. Lewis (1918) used "premature contraction" and "extrasystole" in the same fashion. Cowan (1939) used "extrasystole" whilst Berliner (1946), perhaps reflecting the then current American usage, referred to the arrhythmia as "premature extrasystoles".

Den-Boer et al (1954) provide an example of European (Dutch) usage in which "premature beat" and "extrasystole" are used as synonyms as they had been nearly forty years earlier. In Britain, Somerville (1960) was using "ectopic beat" and "premature beat" to describe the same phenomenon and Friedberg (1966) showed a catholic taste and employed "premature beat", "ectopic beat" and "extrasystole" interchangeably.

Wood (1968) adhered to "ectopic beat". Oram (1971) was using "ectopic beat" and "extrasystole" but at the same time categorically expressed his belief that the prefix "extra" in extrasystole should be used in the sense given earlier, that of being situated or arising outside, and not as indicating an extra number of beats.

These examples, although not exhaustive, may give some impression of the dilemma facing those who seek an accurate but concise description of this common disturbance of cardiac rhythm.

In this thesis I have, in common with more eminent writers, chosen to follow the definition given by Scherf & Schott (1973) which is "contractions of the whole heart, or parts of the heart,

due to impulses which are abnormal, either regarding their site of origin - ectopic - or their time of occurrence - premature - or both, interfering with or replacing a dominant rhythm, whereby in the electrocardiogram the abnormal beats are accurately coupled to the preceding beat and in many though by no means all cases have constant shape".

There are occasions, nevertheless, when even these authors felt justified in using the other two terms "premature beat" and "ectopic beat", indicating perhaps, that the semantic problem is still unsolved.

CHAPTER 1

AMBULATORY MONITORING - EVOLUTION OF DATA ACQUISITION

1) The development of the electrocardiograph

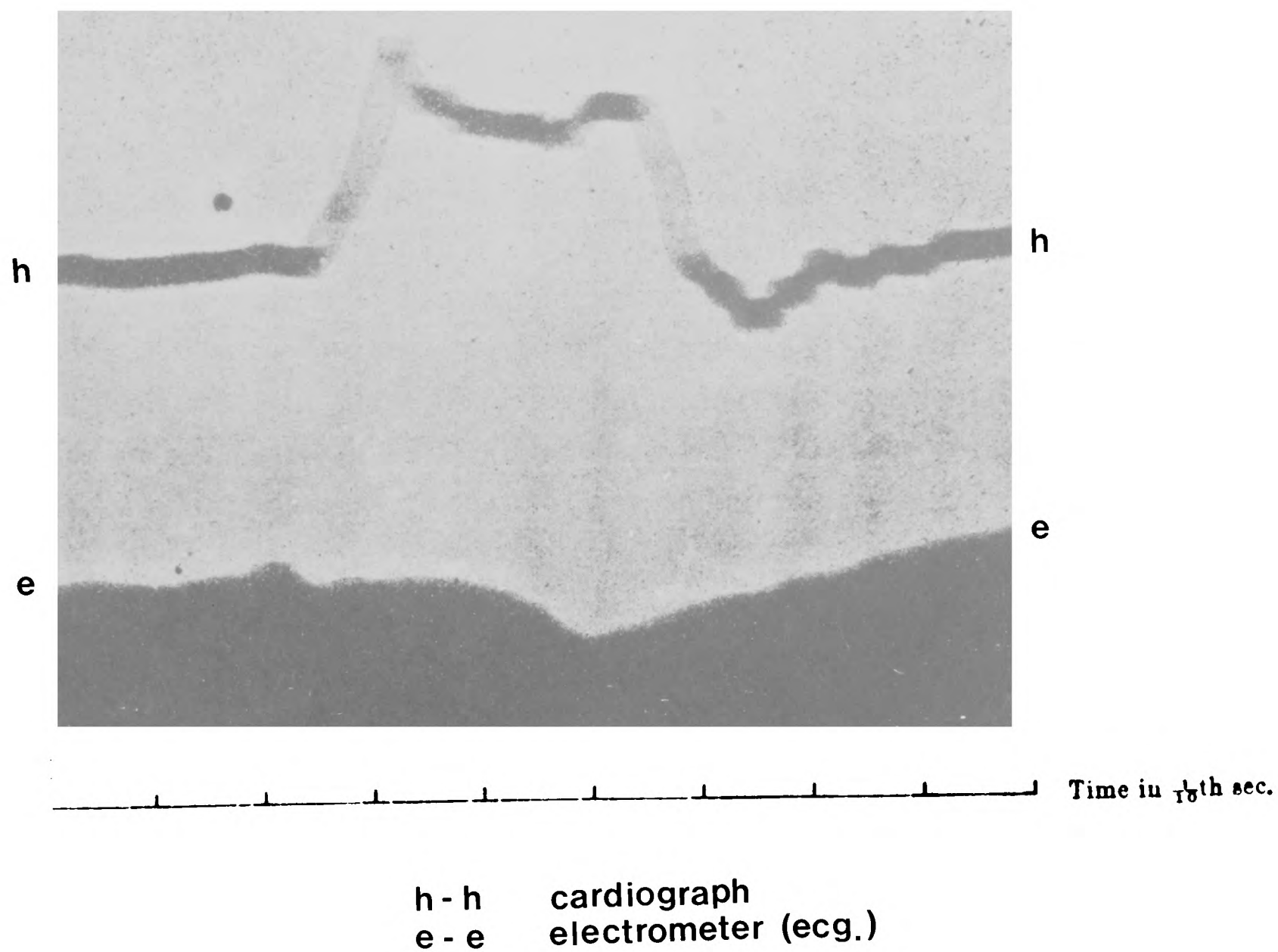
Nearly 120 years ago Kölliker and Müller (1856) showed that heart muscle activity was accompanied by small changes in electrical potential. A.D. Waller (1887) used the Lippman capillary electrometer to record the electrical activity of the intact heart in man and in dogs. (Fig. 1). In 1888 he read before the Royal Society a paper entitled "On the electromotive changes connected with the beat of the mammalian heart and of the human heart in particular". (Waller, 1890). He must also be credited with introducing the term "electrocardiogram" to describe the record of electrical potential associated with the action of the heart. (Barron, 1952).

The capillary electrometer consisted of a glass capillary tube containing mercury and immersed in dilute sulphuric acid. Electrical connections were made to the mercury and to the acid and changes in potentials applied to these connections caused the meniscus at the mercury/acid junction to move in the capillary. Records of this movement were obtained by projecting a magnified image of the meniscus on to photosensitive paper. (Fig. 2). Although the electrometer was extremely sensitive and could detect changes in potential of as little as 250 micro-volts, it was not an ideal instrument for electrocardiography, mass and friction seriously limiting its frequency response.

In May 1887 Einthoven was present at St. Mary's Hospital, London, when Waller demonstrated the human electrocardiogram. Subsequently he used the instrument himself in Holland and attempted to correct mathematically for the shortcomings of the capillary electrometer. At



Augustus Desiré Waller and "patient"



First human electrocardiogram

1887

Fig. 2

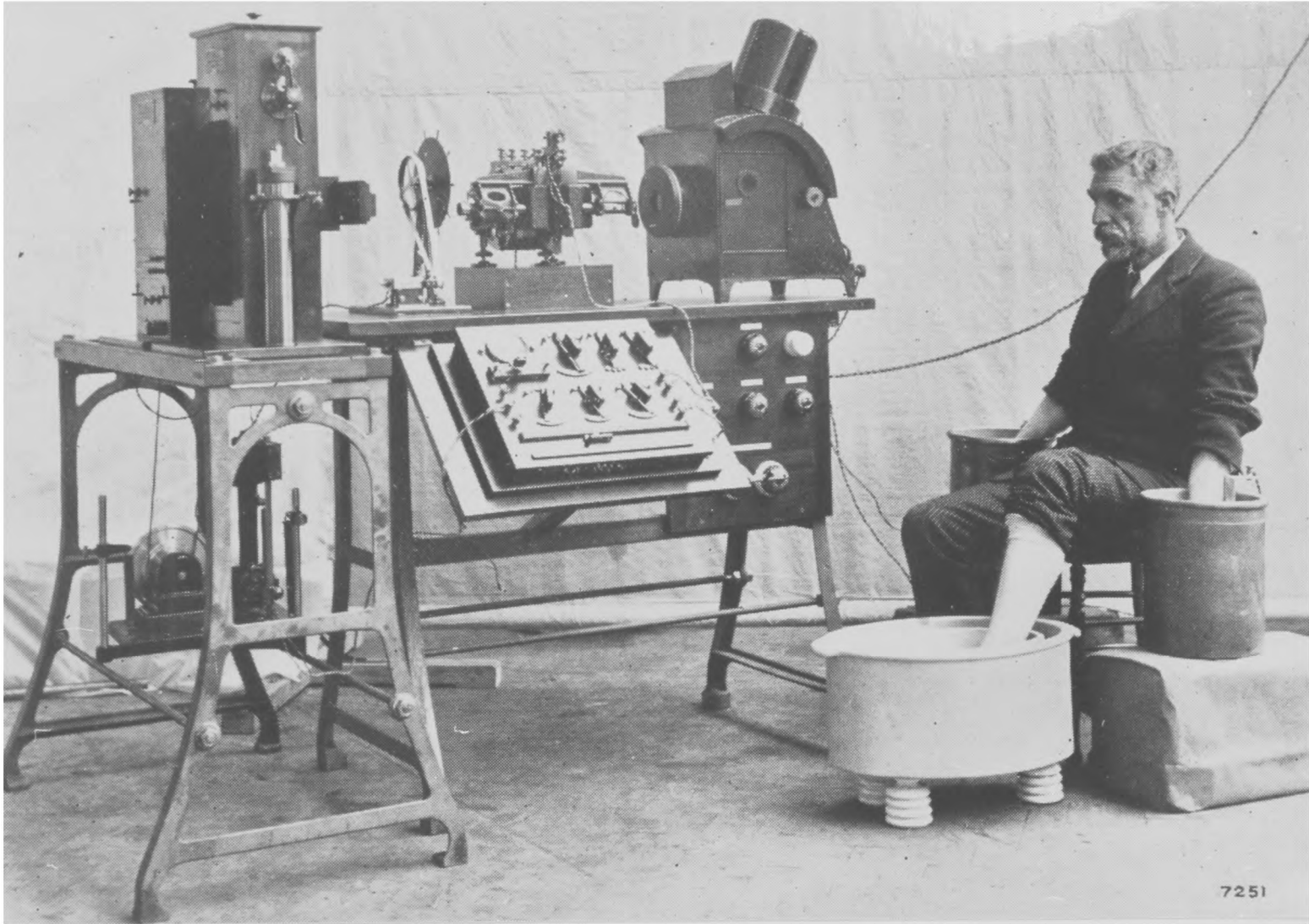
the same time he introduced the designation, P, Q, R, S, T, to describe the component waves of the electrocardiogram.

The second half of the 19th century was a period of intensive activity in the field of telegraphic communication and progressively more sensitive equipment was being developed for detecting weak electrical signals. Ader (1897) described "un nouvel appareil enregistreur pour cables sous-marins".

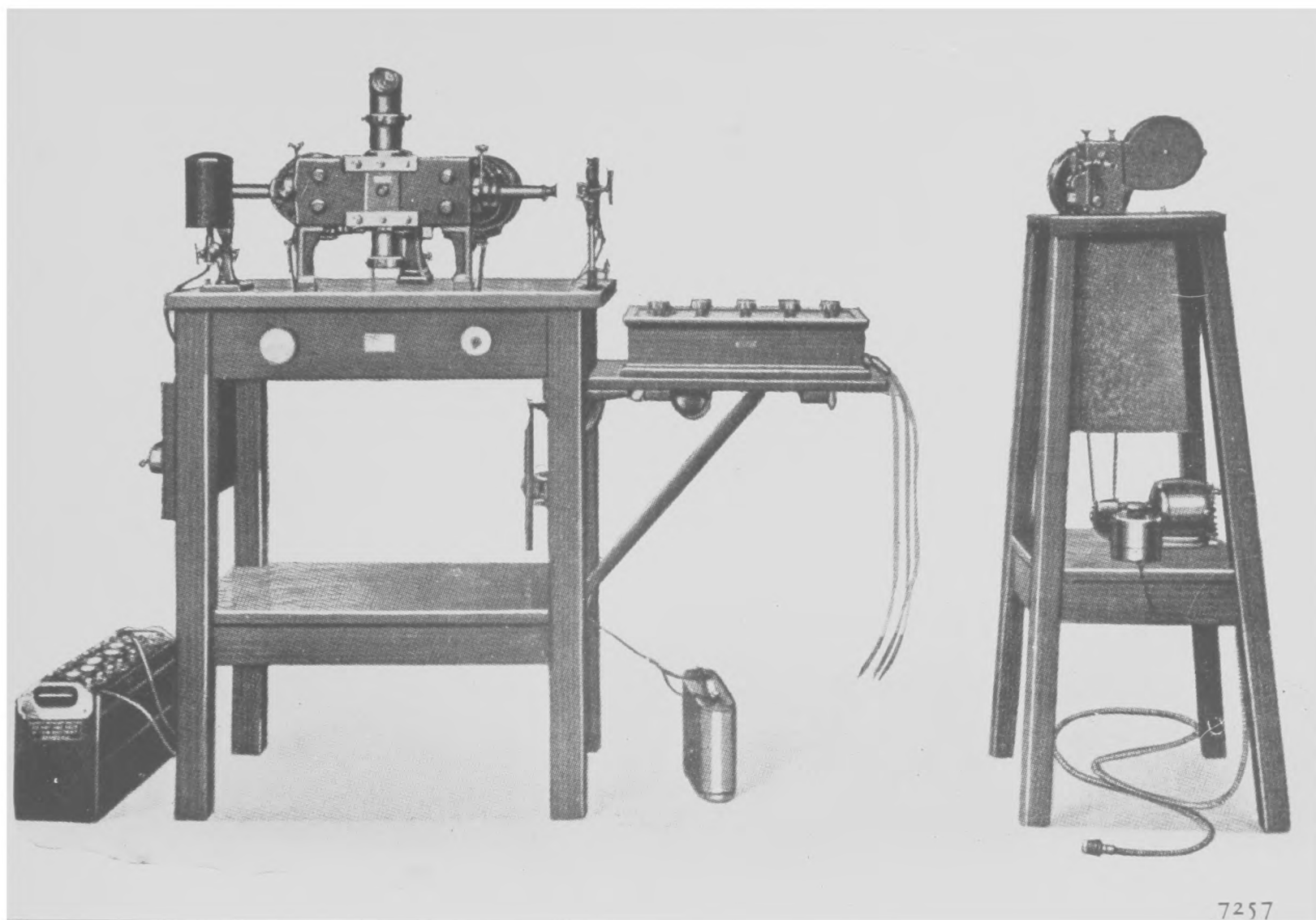
A frequency response of 1600 Hz could be achieved with Ader's galvanometer which basically consisted of a very fine wire suspended in a powerful uniform magnetic field. Potentials applied to the wire caused a current to flow in it, which in turn induced a circular magnetic field around it, the strength of this magnetic field being proportional to the current and at right angles to the field. The field around the wire interacted with the uniform field in which it was suspended and the wire was deflected at right angles to its long axis. The sensitivity of this instrument was such that it was used to detect telegraphic signals transmitted by submarine cable across the Atlantic from Brest to Saint Pierre off the coast of Newfoundland.

This advance in technology in a branch of science remote from medicine and physiology was to influence electrocardiography for half a century.

Einthoven, then Professor of Physiology in the University of Leiden, had with the technical assistance of Dr. Berghansuis been attempting to find a replacement for the capillary electrometer. Adaptations of many contemporary galvanometers were tried but ultimately Einthoven and his co-workers saw the solution in a modification of Ader's instrument. For telegraphy, qualitative detection of signals was sufficient, so the fact that the sensitivity of Ader's galvanometer varied with temperature changes was unimportant, as was the very low input resistance of the instrument. Einthoven, however, needed to make quantitative measurements



Electrocardiograph as used by Sir Thomas Lewis 1912



Hindle electrocardiograph

U.S.A.

1918

Fig. 4

and also to match the input resistance of the galvanometer closely to the electrical resistance of his subjects. Fortunately C.V. Boys (1887) devised a curious but effective method of producing extremely fine filaments of glass by attaching a lump of molten quartz to the tail of a light wooden arrow and shooting this with a crossbow. The quartz was drawn out into a thread in the region of 90 feet in length and 0.004 mm. in diameter which was collected by winding it on a sticky wooden frame. Originally these filaments were made electrically conductive by chemically plating them with silver. It was, however, difficult to control the thickness of the metallic deposit and consequently its electrical resistance. Einthoven substituted electro-plating for the chemical method and produced a more robust and predictable result. Gold was later substituted for silver in a commercial version of the process which was used until the mid 1950s. These electro-plated filaments, or fibres as they were described by Boys, met both of Einthoven's requirements.

The quartz substrate gave dimensional and thermal stability and the very thin metallic coating provided the necessary high electrical resistance in the regional of 2000 to 3000 ohms. The movements of the fibre were optically magnified 600 times and projected on to moving photo-sensitive material in much the same fashion as in the capillary electrometer. Einthoven made a careful comparative study of the new "string" galvanometer and the capillary electrometer, publishing his results in the classical paper (Einthoven, 1903). After this the new instrument was unchallenged in the field of electrocardiography and, later, phonocardiography.

During the first quarter of this century Einthoven (1905) and later Lewis (1925) used the string galvanometer to record the electrocardiogram (Fig. 3) (Barron, 1952) and to begin the analysis of cardiac arrhythmias. Throughout this period the maximum useful continuous recording time for the ECG was some six to ten seconds. Concurrently, Hindle in the U.S.A. (Fig. 4), Huth and Siemens Halske in Germany and Boulitte in France

(Barron, 1952), produced instruments with continuous recording times of several minutes but some were unreliable, some cumbersome and some both! None achieved the success of the instrument used by Lewis. All needed a static patient from whom to record.

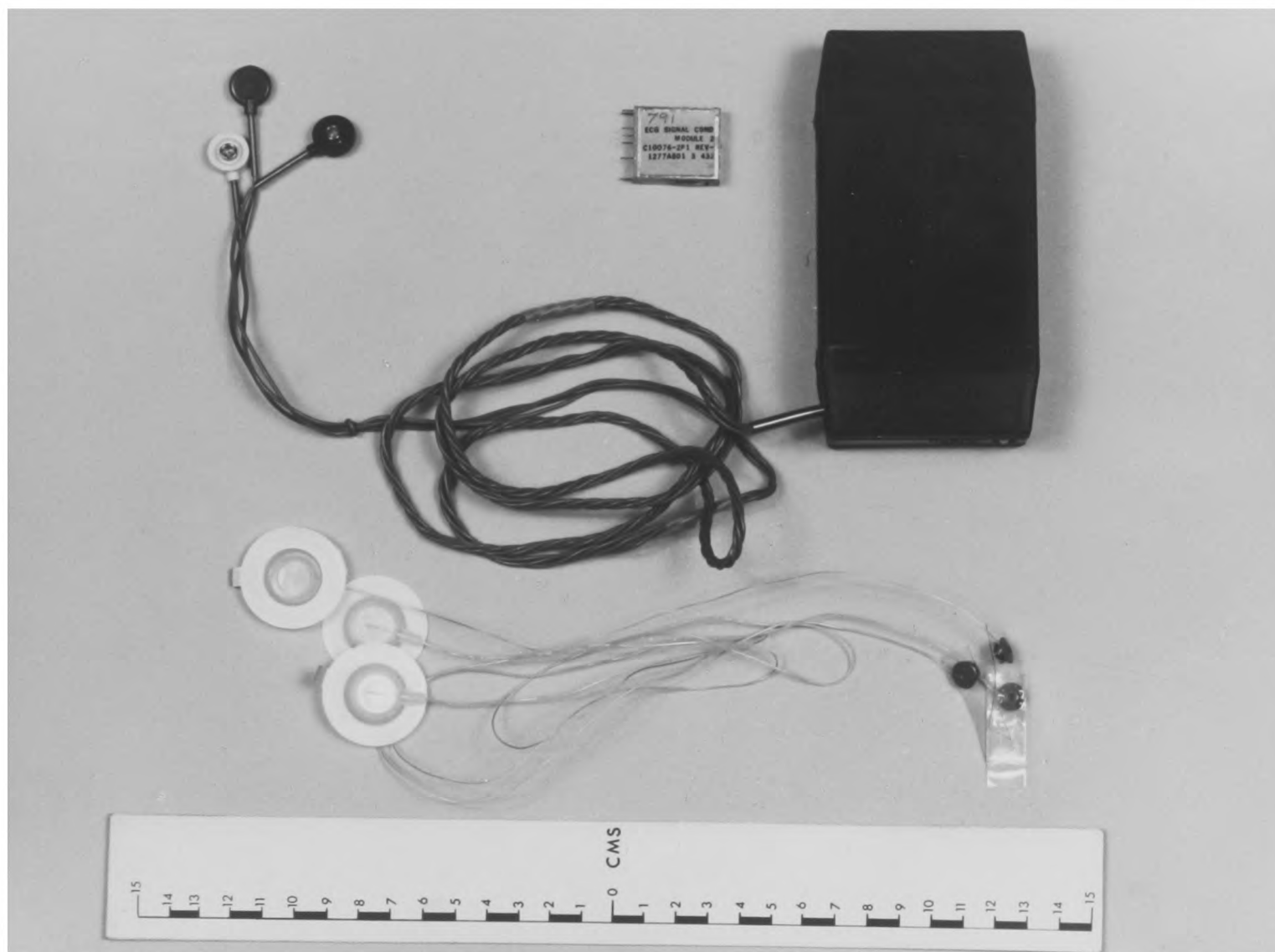
Asher and Hoecker (1938) devised an instrument in which the light beam from a mirror galvanometer was directed on to a slowly moving band of ciné film which had been coated with zinc sulphide. A fluorescent tracing was produced which persisted for a second or two and could be monitored in subdued light but there was no provision for producing a permanent record.

The first truly long-term recording of the electrocardiogram was described by Likoff et al (1944). Using a mirror galvanometer whose movements were projected on to a 16 mm. film they were able to record the electrocardiogram continuously for more than 26 hours. The patient was, however, still static.

2) Radio telemetry of the electrocardiogram

The very rapid development of electronic technology during the 1939-45 war meant that by the mid-forties it was feasible to record the ECG from ambulant subjects, using the technique of radio telemetry. The first reported ambulatory monitoring of biological data was by Breakell and Parker (1949) who described a series of radio transmissions of the ECG and EEG which they had carried out during the previous two years. All these recordings, however, were made within the hospital premises so, although the term ambulatory monitoring could be justified from the point of view of semantics, the clinical advantages were limited.

Parker, Breakell and Christopherson (1953) developed their system of radio telemetry to the extent that they could now record the ECG and EEG from the truly ambulant subject going about his normal activities, within limits! The transmitter was mainly valve-operated



Four-channel radio transmitter for telemetry of physiological data
ECG amplifier/transmitter module shown in top middle of illustration
1975

Fig. 5

which necessitated a heavy and bulky power supply and was only capable of providing four hours' recording time. In the U.S.A. Gengerelli and Holter (1941) had been studying the possibility of stimulating remotely the brain of the intact animal and of transmitting the EEG and ECG by radio. MacInnes (1954), using the facilities of Holter's laboratory, developed an apparently unique form of radio telemetry. The ECG of an ambulant subject was transmitted some 200 metres and displayed on a television screen which was photographed to give a permanent record. The experiment was more of a feasibility study of electronics than a clinical trial and the technique was not developed.

Holter and Glasscock (1958), however, were to discard simple radio telemetry as a means of ambulatory monitoring and develop a hybrid system in which radio telemetry was combined with magnetic tape recording of the ECG. Taggart et al (1967) (1969) and Somerville et al (1968) also used a combination of radio telemetry and magnetic tape recording to obtain the ECG from motor car drivers in London traffic and on the racing circuit. In these specialist studies the equipment was carried in the same motor vehicle so the bulky receiver, 26 x 16.5 x 10 cms. and conventional reel to reel tape recorder, Uher 4000 Report/1, presented few problems.

Although Holter had found the limited range and sensitivity to electrical interference of radio telemetry to be serious disadvantages, many workers continued to use this method, taking advantage of the miniaturisation and comparative immunity to interference possible with transistorised and later integrated circuit transmitters. A typical example of commercially available equipment is seen in Fig. 5.

Radio telemetry is claimed to be helpful in recording the ECG during effort tests in which either the Masters two-step or the riding of a stationary bicycle is used. Many examples are reported by Bellet et al (1962a) using both normal patients and those suffering from angina pectoris (Bellet et al, 1962b). The authors stress the advantage of being able to

record during effort when they consider that the effects of myocardial ischaemia are most pronounced. It seems unlikely that this facility is unique to radio telemetry for in many laboratories perfectly satisfactory recordings during strenuous effort are made using conventionally "tethered" patients, providing common sense precautions are taken in the routing of connecting leads between the subject and the recorder.

The present general use of the Masters test or a stationary bicycle or treadmill in preference to comparatively non-reproducible tests such as climbing stairs, has limited the ambulatory aspect of effort testing to such an extent that there seems little point in using radio telemetry. Later, in fact, Bellet et al (1968) were using a tape recorder and not radio telemetry for continuously recording the ECG during car driving. The instrument, which had been developed by the Biomedical Electronics Section of the Division of Cardiology at Philadelphia General Hospital, weighed 14 lbs!

Opinion appears to be divided concerning the suitability of radio telemetry for ECG recording during effort tests. Cerkez et al (1965) considered it offered little advantage over conventional recording whilst Sandler (1967) makes the curious statement that the radio-cardiograph is more sensitive to ST depression than the conventional recorder. Any such difference in performance must surely have been due to the frequency response of the system rather than the mode of signal transmission between patient and recorder.

All radio telemetry systems for electrocardiography use frequency modulation techniques to transmit the signal. The ECG is fed to an amplifier which incorporates automatic gain control to compensate for changes in amplitude which may be caused by alterations in electrical axis of the heart due to postural changes or to changes in orientation between the transmitter and receiver aerials. The amplified ECG modulates the carrier frequency which is generated by an oscillator within the

transmitter and the resulting variable frequency signal undergoes further power amplification.

Typical frequency bands for biological radio telemetry are 102 to 105 MHz in Britain, 150 to 160 MHz in Canada (Woodwark et al, 1970) and New Zealand (Hunter et al, 1973), whilst in the U.S.A. the 450 to 470 MHz Business Frequency Band is often used (Craven et al, 1973). The higher band offers the advantage of smaller components and hence smaller overall size of transmitter but this can be offset by shorter range of transmission. This incompatibility has led some workers to use a combination of both systems; a small lightweight transmitter with a range of only a few hundred metres whose output is received and relayed by a much more powerful fixed transmitter operating in a different frequency band.

Using this approach, Woodwark et al (1970) transmitted ECGs over a range of 720 miles. If sufficient co-operation and finance are available, much more dramatic feats can be achieved; for example, Monnier et al (1965) transmitted the ECG over 1000 miles from the s.s. "France" to Paris and to New York using radio transmission via the Early Bird Satellite 22,300 miles above the coast of Brazil.

In Britain the constraints imposed by the Home Office Radio Regulatory Department on Medical and Biological Devices, Class II, in particular with respect to transmitted power (limited to 5 milli-watts if oscillating continuously or 1 milli-watt if pulsed) preclude the use of radio telemetry over distances greater than 200 metres. The amendments to this specification which came into force at the beginning of 1976 affected only the allocated frequency band (102.2-102.4 MHz to 104.6-105 MHz) and not permitted power.

From the foregoing it is evident that, in the majority of circumstances, radio telemetry is not the method of choice for the transmission of the ECG from ambulant subjects. The one possible exception

is the military use in monitoring the state of aircrew and manned space flights (Roman, 1965a) (Roman, 1965b), where high cost and complex equipment are apparently acceptable.

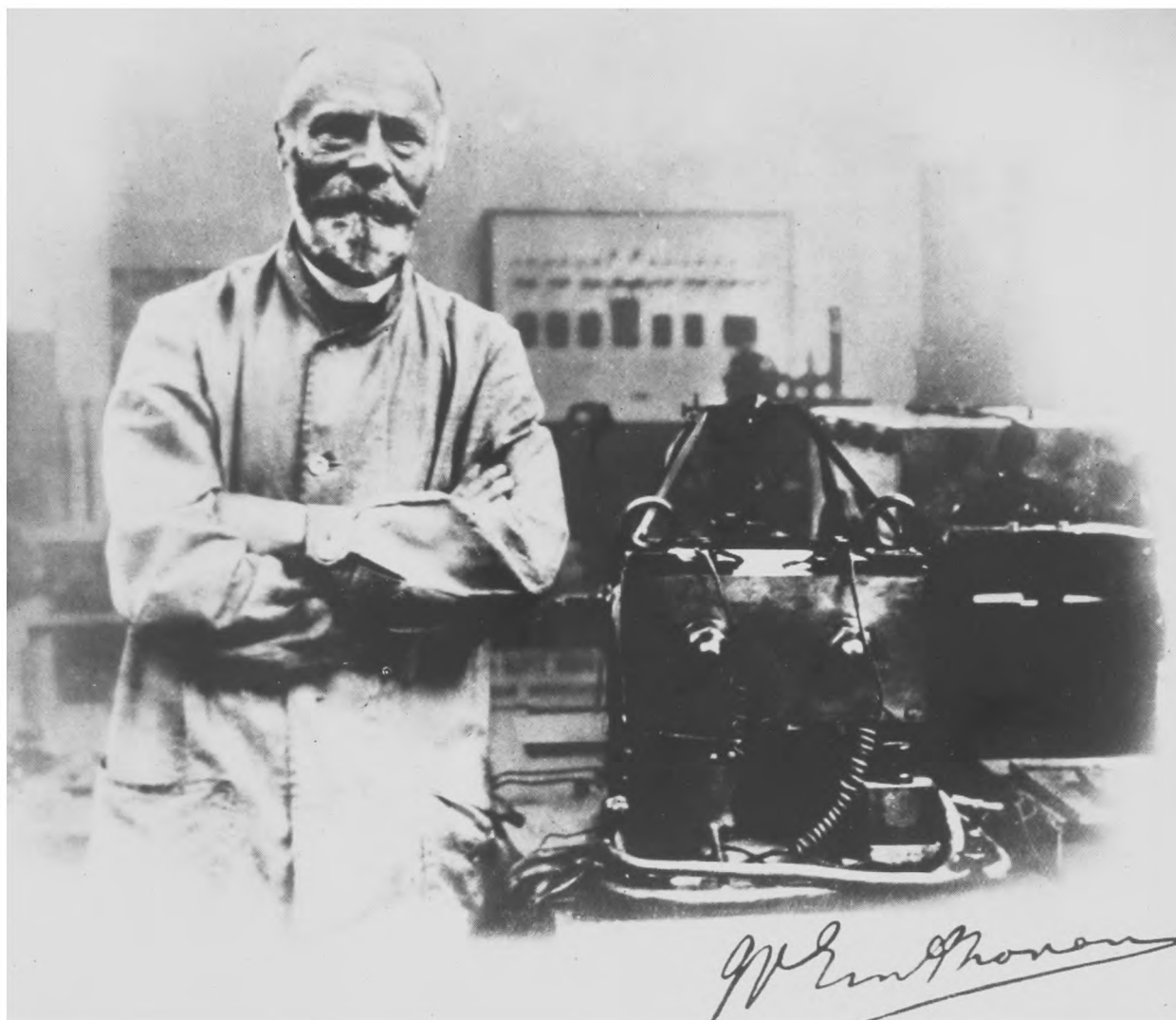
3) Electromechanical recording of heart rate

At the other end of the scale of complexity and cost was probably the most elementary example of ambulatory monitoring of cardiac action, described by Rowley et al (1959) and Glagov et al (1970). This was by means of a device measuring only 7.5 x 5.0 x 1.0 cm. in which the ECG signal from two precordial electrodes was first filtered electronically to minimise the comparatively low frequency T-wave and respiratory artifact and enhance the QRS complex and then fed to an amplifier with automatic gain control which coped with variations in QRS amplitude. From this a constant amplitude output pulse for each heartbeat was generated by a multi-vibrator circuit. This pulse drove an electromagnetic relay which, in turn, released the escapement mechanism of a watch and advanced the hands of the watch 0.4 secs. for each heartbeat, so that 1 minute on the watch dial corresponded to 150 beats; readings were made at intervals which varied from half an hour to several hours and average minute rates calculated.

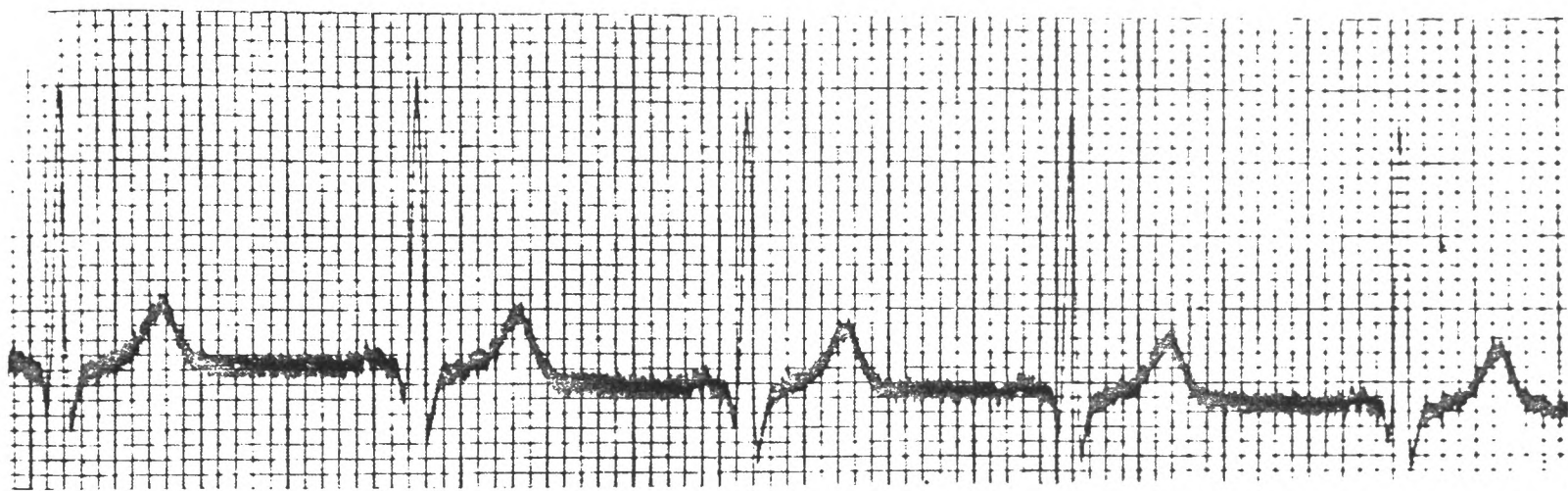
This device certainly permitted ambulatory monitoring of the heart rate but it could not identify abnormal ECG complexes nor indicate instantaneous heart rate.

4) Transmission of the ECG by telephone

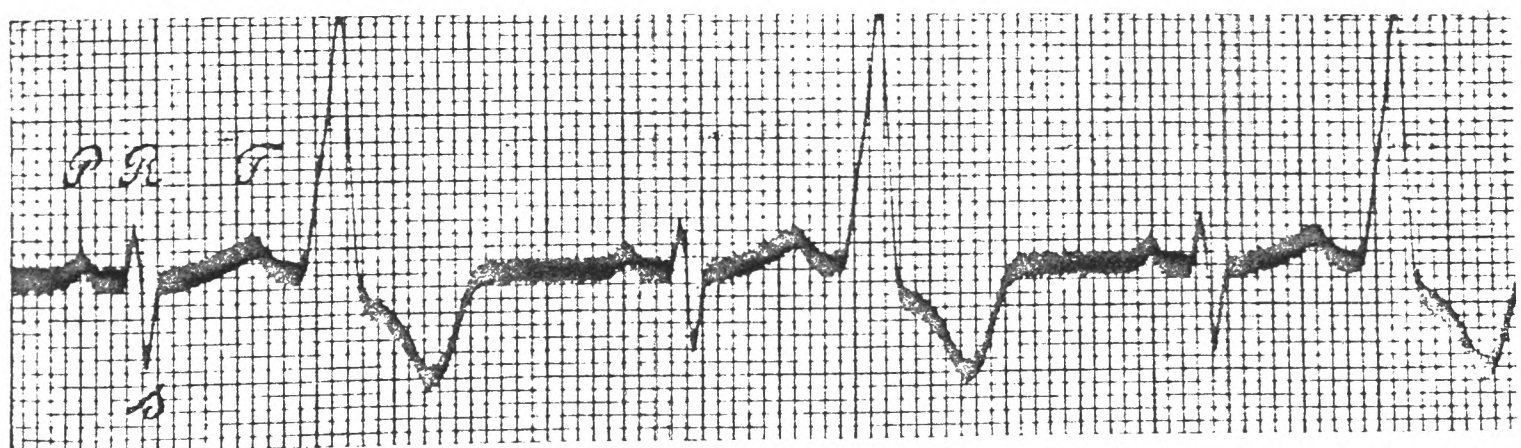
Another approach to finding a solution to the problem of recording the ECG from ambulant subjects is to use the telephone system. This is not a new technique and some writers have claimed that Einthoven used it in 1905. In fact he only used the wires of the telephone system and not the telephones themselves (Einthoven, 1905).



Professor Willem Einthoven in laboratory



First "télécardiogramme" transmitted 1.5 km. over telephone wires
22nd March 1905



Télécardiogramme from a subject with "permanent slow pulse"
1905

Fig. 7

Einthoven's instrument was decidedly not mobile; it weighed 3 cwt. occupied two rooms and needed five people to operate it! (Fig. 6). (Goulding, 1962). Professor Bosscha of Leiden University suggested linking the hospital of the university with the physiological laboratory where Einthoven's electrocardiograph was installed, hoping thereby to record the ECG of patients who were too ill to be transported. Many technical problems had to be overcome, including a tendency for the insulation of the wires to drop markedly in damp weather. Nevertheless satisfactory recordings were obtained over a distance of 1 mile (Fig. 7). (Mathewson et al, 1954).

Nearly half a century was to pass before the telephone system was used as a means of providing what might loosely be termed ambulatory monitoring. In a country such as the U.S.A. with vast distances between areas of sparse populations, the public telephone system was a long-established means of communication between patient and physician, and physician and colleague. It needed only a modest advance in electronics for it to be possible to transmit the ECG by a telephone circuit. Obviously a signal such as the ECG, composed of frequencies from some 0.1 Hz to 50 Hz, could not be transmitted over a system designed to operate over a limited section of the audible range, typically 200 Hz to 2.50 KHz. With the post-World War II development in electronics it became simple to design an oscillator which could be frequency-modulated by the unamplified voltage of the ECG. A basic frequency in the mid-band of the telephone system could be chosen: for example, 1250 Hz, and frequency modulated $\pm$ 200 Hz. (Dimond et al, 1953).

The oscillator generated a variable audible tone which was acoustically coupled to the standard telephone hand-set by placing the F.M. oscillator output speaker close to the mouthpiece. At the receiving

end the frequency modulated voltage was amplified and fed to a discriminator which converted the frequency variations to amplitude variations which, in turn, drove an electrocardiograph.

This technique could obviously be used equally well on internal telephone systems and the writer developed a transmitter/receiver system capable of relaying the ECG from ward to department. Like all early acoustically coupled systems, it was susceptible to extraneous noise and it may have been this failing which made the British Post Office look with disfavour on the technique. Perhaps it was coincidence that they were developing their own MODEM system for transmitting non-audible signals over telephone systems!

In the U.S.A. the Bell Telephone Company and others developed the "Dataphone" system for transmitting biological data over telephone systems (Levine et al, 1964). In Britain, Macfarlane et al (1970) used a combined radio and telephone system developed by Dynatel Data Systems to transmit the ECG from a coronary care unit to a computer for analysis. To avoid the use of a telephone for each patient, the ECG signals from three patients were fed to a single radio transmitter where they were summed and transmitted some 30 metres as a single combined signal. At the receiver the signal was converted into audio form, transmitted again by telephone, after which the separate analogue signals were recovered by band pass filters and demodulated.

Although telephone transmission of the ECG does not provide true ambulatory monitoring, it is approached in the technique described by Peter et al (1973) in which patients with palpitations, "dizzy spells", or with newly implanted lithium-iodide powered pacemakers whose rate needed to be checked regularly, were supplied with miniature amplifier/transmitter units which could be acoustically coupled to the telephone hand-set. No separate electrodes were needed, the amplifier case having built-in electrodes which needed only to be pressed against the chest. The transmitted signal was processed in

virtually the same manner as previously described and either displayed on an oscilloscope, recorded on an electrocardiograph or stored on magnetic tape.

5) Magnetic tape recording of the ECG

As mentioned previously, Holter (1961) discarded the use of pure radio telemetry for ambulatory monitoring and switched to a combination of radio telemetry and magnetic tape recording.

"Electrocardiocaster" was the name he coined for a miniature radio transmitter small enough to be worn in the breast pocket of a suit and with a range of a few tens of metres. The ECG was transmitted to a combined receiver/tape recorder which could be left nearby if the subject was stationary but had to be carried by him in a large brief case when he was ambulant. This technique had obvious limitations, especially as Holter was hoping to make prolonged ECG recordings from swimmers and broncho riders in action!

The next step in the work of Holter and his associates was the development of the "electrocardiocorder", a portable reel to reel tape recorder combined with an appropriate ECG amplifier, oscillator and mixer circuits to enable the low frequency ECG to be recorded on magnetic tape. The unit weight 1 Kg. and measured 19.5 x 9.8 x 4.6 cms. It operated at a tape speed of 7.5 inches per minute and could record two channels continuously for 10 hours. Here was the first system for enabling long-term recording of the ECG from ambulant subjects. Five hours' recording could be obtained using 1.5 mil. standard tape. To achieve ten hours a thinner tape had to be employed with the risk of introducing small speed variations.

In 1964, the Holter recorder became available commercially and the need for such a system is apparent by the mass of work on continuous ambulatory monitoring which followed.

Not unnaturally a new technique often produces new problems and the Holter system was no exception, although many of the problems were comparatively innocuous. Hinkle et al (1967) reported a very detailed study of the performance of the types of recorder in use at that time and their findings showed that the early models (350 A) had maximum tape speed variations between 6% slow and 10% fast with $\pm 2\%$ jitter and the later model (350 C) 1% slow and no fast deviation and with a maximum jitter of $\pm 2.4\%$.

The earlier models had a cumulative time error (defined as 'true elapsed time divided by indicated elapsed time expressed as a percentage') in the range $+14.3\%$ to -7.9% , mean error $+1.3\%$ and standard error of $\pm 4.6\%$. In the later models the figures were in the range 3.7% to -0.7% , mean error 2.1% and standard error $\pm 0.7\%$, all figures based on 6-hour recordings. Frequency response was found to be -3 dB at 0.2 Hz and at 50 Hz which corresponded closely to the manufacturers' specifications, although it was somewhat inferior to the Recommendations of the American Heart Association 1966, which set the minimum desirable frequency response of direct writing electrocardiographs as flat to within ± 0.5 dB from 0.14 Hz to 50 Hz. Overall reliability, judged by the number of "technically adequate" six-hour records obtained, was found to have been 93% originally, rising to 97%. This advance was thought to have been due to improvements in the tape drive and take-up mechanisms.

Malek (1972) reported artifacts simulating a tachycardia of 300 beats a minute and bizarre complexes superimposed on T-waves, both of which phenomena had occurred in Holter-Avionics recordings. The former artifact was due to a worn tape drive mechanism; the latter was caused by incomplete erasure of a previous recording and could not be attributed to failure of the recording system. Errors in tape speed,

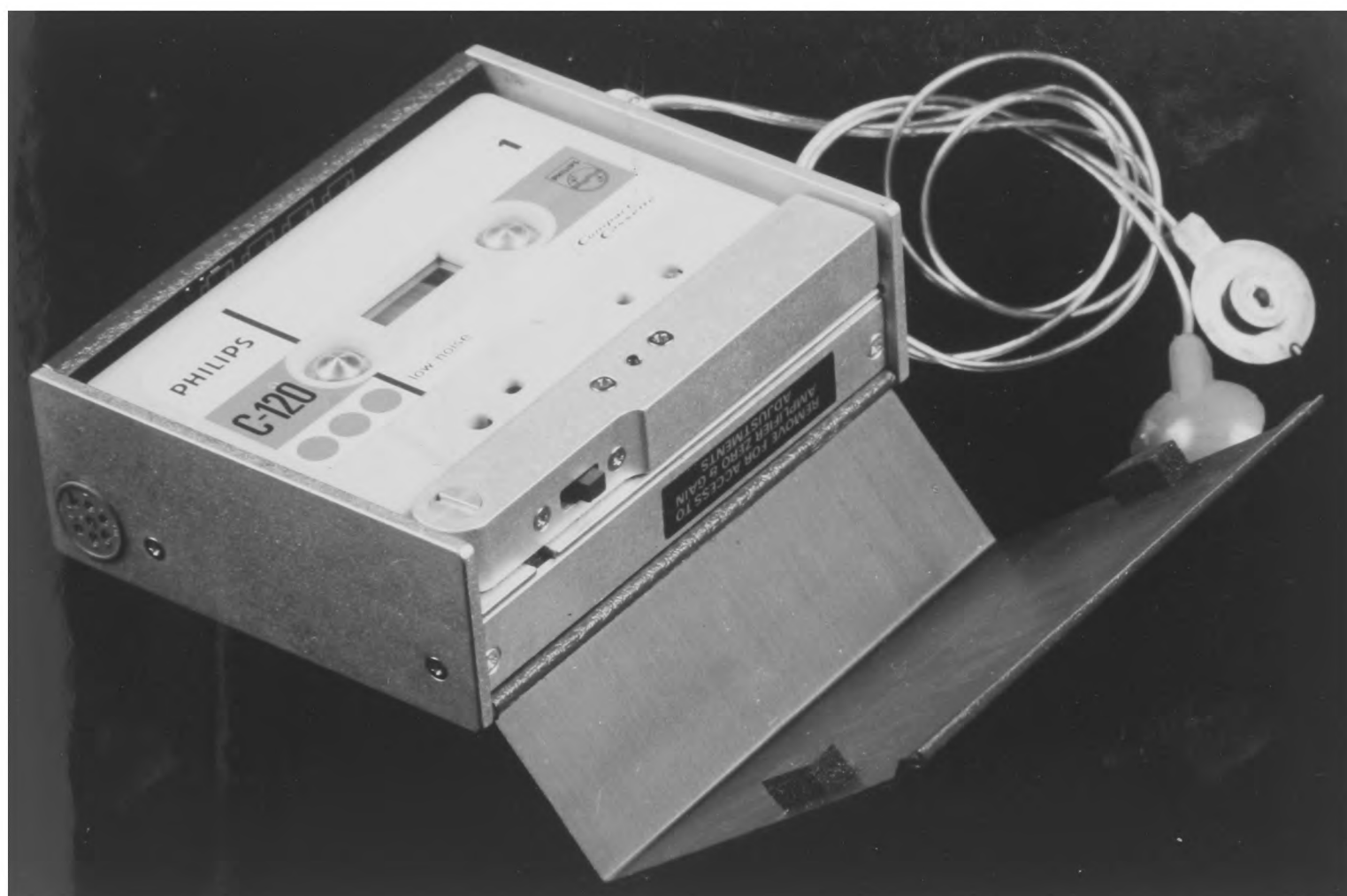
even if they cannot be entirely eliminated, can be recorded quantitatively by a simple method which will be discussed in a later section.

The success of the Holter system was doubtless a factor in the development of other tape recorders for physiological monitoring. Military laboratories, such as that mentioned by Roman (1965), produced a six-channel recorder weighing 4 lbs. but small enough to fit into the pocket of a flying suit. It had a maximum recording time of 1 hour 45 minutes; this was adequate for the purpose for which it was designed, that of monitoring physiological parameters from a pilot during a single flight, but not suitable for development for civilian use.

The Irish Institute of Industrial Research and Standards, in co-operation with the Irish Heart Foundation, designed and developed a "Cardiotape" machine described by Sterling (1972). It was, however, too large, 280 x 240 x 80 mm. and somewhat heavy, 3 Kg, to be used for ambulatory monitoring. Likewise its maximum recording time of 1 hour imposed serious restrictions. Graham et al (1975) reported its use by general practitioners who recorded the ECG from patients either as a routine investigation or in cardiac emergencies. For routine use the cassette was posted to the nearest hospital equipped with transcribing facilities, whilst in emergencies the recording was transmitted by telephone as a frequency modulated tone off tape.

Several commercial recorders are in limited use, mainly in the U.S.A. where they are manufactured by Delmar Engineering Laboratories of Los Angeles; Clinical Data Services of Brookline, Mass; and Medcraft of Dallas, Texas. The only recorder manufactured in the U.K. at present is the Medilog unit, which is the result of a joint development effort between Dr. F.D. Stott of the Medical Research Council, Clinical Research Centre, Northwick Park, Harrow, and Oxford Instruments Ltd.

The decision to explore the possibility of using magnetic tape



4-channel tape recorder

Fig. 8

for long-term physiological recording followed a series of studies of hypertension which had involved 12-hour recordings of arterial pressure from ambulant patients. (Bevan et al, 1969). A miniature single-channel clockwork-driven photographic recorder had been developed for this work by Stott (1966) but the very slow recording speed of 6 inches per hour and single-channel facility imposed by the need for miniaturisation led to a search for a new recording technique.

6) The Medilog recorder

It is with the Medilog recorder that the data and results to be described later were obtained. It was first available commercially in 1967 and has since undergone a series of electronic and mechanical improvements. It is comparatively small, 110 x 86 x 36 mm. and weighs 0.4 Kg. (Fig. 8). It has a maximum continuous recording time of 24 hours on standard C.120 magnetic tape cassettes. Four channels of data can be recorded simultaneously: for example, ECG, EOG (electro-oculogram), respiration rate and skin temperature whilst, with an additional plug-in unit for increased amplification, the EEG can also be recorded.

Different techniques are required for recording different parameters, the governing factor being the frequency band of the signal; only that appropriate to the ECG will be described. The technique necessary for recording blood pressure is described by McKinnon (1974) and, from the clinical aspect, by Littler et al (1972).

To record for 24 hours continuously on a C.120 cassette requires a very slow tape speed which, in the case of the Medilog, is 2 mm. per second. This imposes both mechanical and electronic problems which, in the former, are aggravated by miniaturisation.

It is customary to refer to short-term tape speed variations as "wow" and "flutter", the former referring to fluctuations with a frequency below 1 Hz and the latter to those from 1 Hz to 10 Hz. Long

term changes in speed are described as "drift".

In a conventional tape recorder, tape drive is maintained at a constant speed by the flywheel action of the large mass of the capstan. In the Medilog, the tape capstan is a spindle with a diameter of 2 mm. and, as this has an inertia too small to be of use in maintaining a constant speed, it was necessary to employ electronic speed control of the motor.

In the earlier Medilog recorders, the combined speed variations amounted to 2% overall. Recently (1977) a redesigned electro-mechanical speed control was introduced. This incorporates a phase locked loop circuit in which a transducer placed around the motor spindle generates an alternating signal whose frequency is dependant on the motor speed. The frequency of this signal is compared with a constant frequency generated within the phase locked loop integrated circuit. Any difference between the two frequencies generates in turn a control voltage which alters the motor speed to compensate for the original speed variation. This development has reduced the speed variations to 0.5% overall.

The motor drives the capstan directly through a gearbox and tape take-up is by means of a slipping clutch which is belt-driven from the gearbox. The slipping clutch mechanism is required to cope with variations in diameter of the take-up spool of the cassette as tape is wound on to it.

The accuracy of the alignment of the 4-track recording head is crucial at such slow recording speeds where a skew of 1 degree would be equivalent to the length of an ECG complex. In use, however, it has been found unnecessary to adjust the alignment of the recording head unless the recorder has been ill-treated.

The electronic problems in design have been less difficult to overcome. The earlier amplifiers used discrete transistors and the later versions integrated circuits, whilst the passive components remain

virtually unchanged. Developments in technology have tended to result in better performance as described above rather than further miniaturisation. The ECG is recorded on tape, using the signal plus bias method, often referred to as "direct recording" as distinct from "carrier recording" in which the incoming signal modulates an internally generated signal. When the Medilog is used in the direct-recording mode, the A.C. bias signal is used conventionally to minimise the non-linear distortion which would otherwise occur due to the shape of the initial magnetisation curve of the tape which departs further from linearity at its origin than at its mid-point.

CHAPTER 2

AMBULATORY MONITORING OF THE ECG - EVOLUTION OF DATA PROCESSING

1) Analogue and digital computers

Automatic ECG analysis is a facility unknown before the late 1950s and, indeed, unnecessary until techniques were available for the long-term recording of the ECG. The fact that some 100,000 beats are recorded in 24 hours makes the need for some form of automatic analysis essential.

Just as the ability to make long-term continuous recordings of physiological data had to await the development of electronic technology, so did the appearance of automatic analysis. From the very beginning there have been two basic approaches to the problem of imitating the cardiologist's ability to interpret the ECG. These are the digital and the analogue, plus of course combinations of the two.

An analogue computer is one in which the variables, such as the ECG wave-form, are represented by voltages or currents and mathematical operations such as addition, subtraction, multiplication, division, integration and differentiation, can be carried out. With combinations of these functions equations can be solved.

Digital computers, in basic form, consist of an input unit, memory unit, arithmetic unit, control unit and output unit. At the input, the analogue signal is converted into a series of numbers representing x-y co-ordinates. In the case of the ECG this sampling takes place at from 200 to 1000 times per second. Once this conversion or digitisation has been performed the subsequent processes depend on the "power" or complexity of the computer.

To generalise, the choice is between comprehensive and comparatively expensive methods, using digital techniques, and the

more limited but less expensive methods using analogue. The method to be described later is of the latter type but evidence will be presented to support the belief that although the approach is simple it performs a clinically useful task.

The digital computer, in its present form, was born in the second half of the 1940s, some time between ENIAC (Electronic Numerical Integrator and Calculator) designed and built at the University of Pennsylvania in the early 1940s and EDVAC (Electronic Discrete Variable Computer) described by von Neumann (1945) but not finished until after another device, EDSAC (Electronic Delay Storage Automatic Calculator), based on von Neumann's design had in May 1949 performed at Cambridge University the first stored program computation. ENIAC had 18,000 thermionic valves and, statistically, one of these was liable to fail each hour.

Even in the early 1960s major computers had a mean time between expected failures of only minutes. It is not surprising, therefore, that early attempts at automatic arrhythmia analysis were made using analogue methods.

Probably the first worker to use a computer of any type to process ECG data was McFee (1950). His apparatus comprised two sub-computers designed to calculate $(e_1^2 + e_2^2)^{\frac{1}{2}}$ and $\frac{\text{Arc Tan } e_2}{e_1}$ where e_1 and e_2 consisted of two of the components of the VCG and were the inputs to the first sub-unit together with the third component of the VCG. The output of the second sub-computer was $\frac{\text{Arc Tan } e_2}{e_1}$. McFee's computer could solve this equation 2000 times per second with an accuracy of 5% but by no stretch of the imagination could these processes be said to have aided automatic analysis of the ECG. As Pipberger^{et al.} (1960) stated, the newly obtained records had to be interpreted in much the same fashion as the originals.

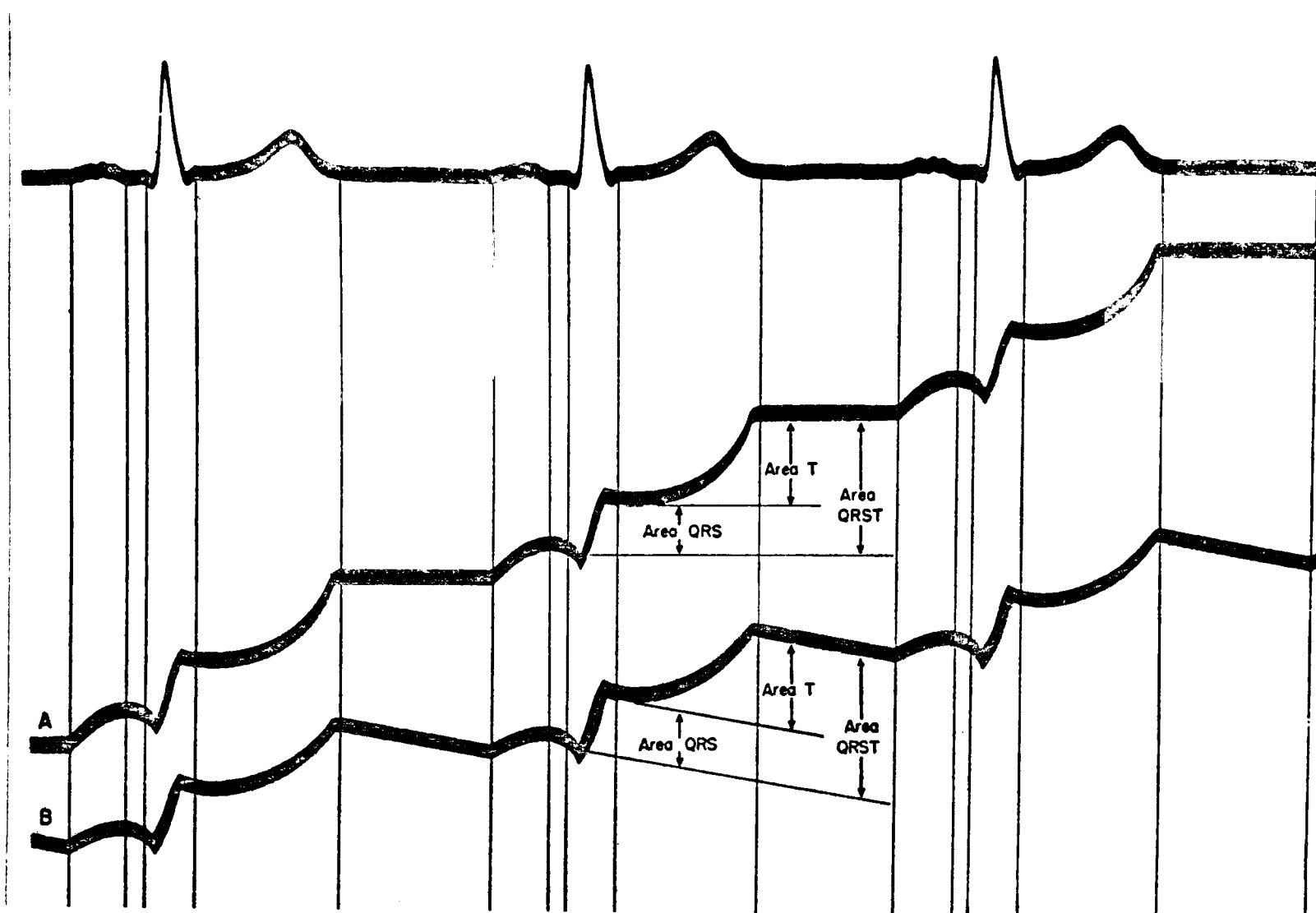


Fig. 9 Integration of the electrocardiogram

A An ideal case

B Integrator drift causes false slope during T-P interval
but areas can still be accurately measured

2) Estimation of the ventricular gradient by analogue computer

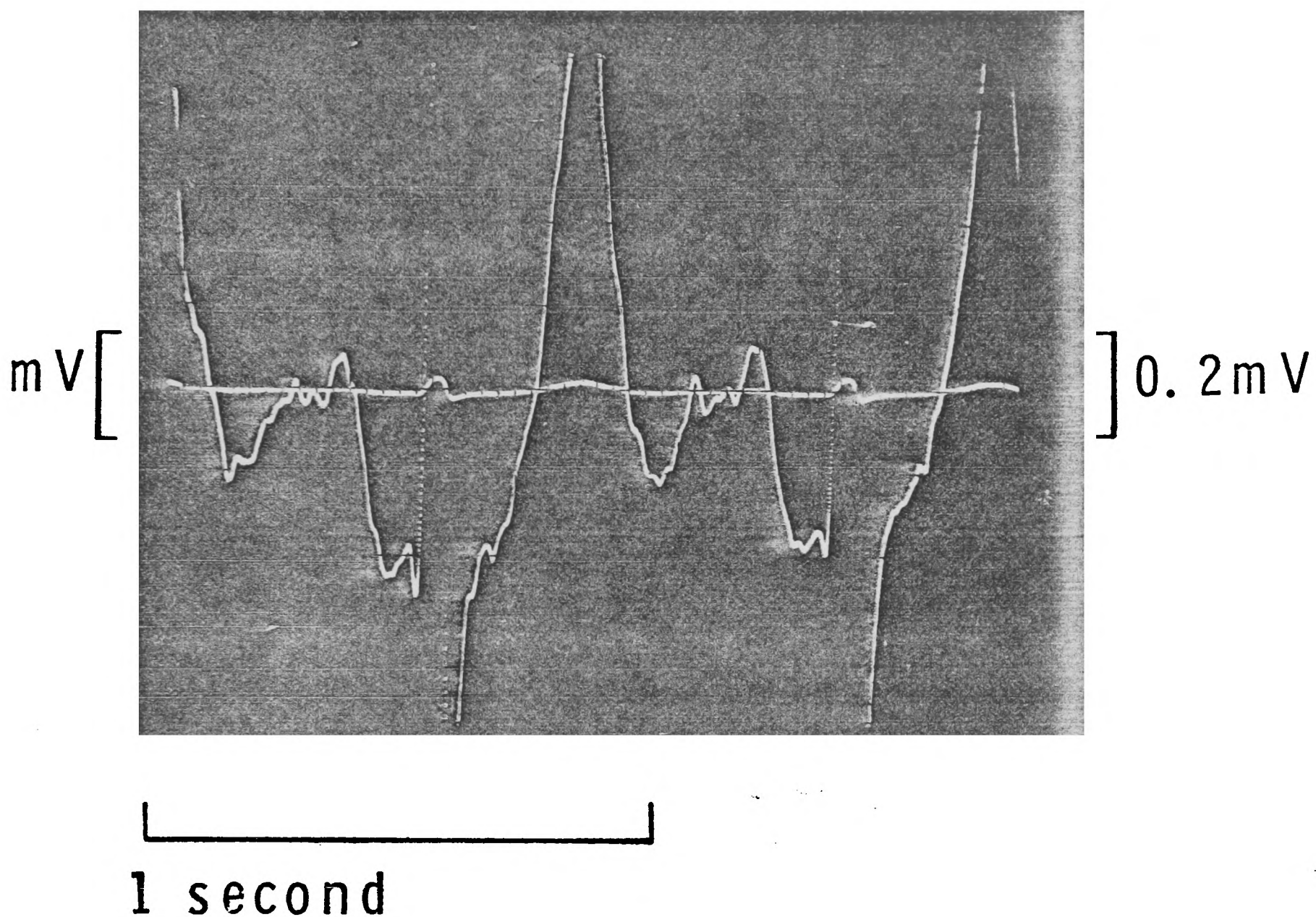
At about the same time, Johnston et al (1950) applied to the ECG the ability of analogue circuits to integrate. Wilson, Macleod and Barker (1931) had introduced the concept of estimating the ventricular gradient from the areas of the QRS and T waves in standard ECG limb leads. This was an obvious task for a device which could integrate. Johnston's circuit was valve-driven and suffered from drift; the bane of all early integrating circuits with long time-constants.

Base-line shift in the ECG itself was another problem as the integrator could obviously not discriminate between this and slow changes between S and T-waves. In the illustration (Fig. 9), (A) shows the ideal case and (B) shows that the QRS, T and QRST areas could still be measured in the presence of drift, as shown by the downward sloping segment of the integrating signal between T and P.

Although the system facilitated the then popular estimation of ventricular gradient it, like the previous example of the analogue approach, did little for automatic analysis of the ECG. Some ten years were to elapse before either analogue or digital methods were applied to what might truly be regarded as automatic analysis.

3) Identification of the P, Q, R, S, and T-waves by digital computer

Haber (1959) described a system which operated in real time and could detect tachycardias, bradycardias, widened QRS complexes or asystole. To detect variations in rate the system compared the frequency of the amplified QRS complex with a reference variable frequency oscillator. Differences in rate triggered alarms and could also start a recording of a conventional ECG on paper. Changes in QRS width were recognised by comparison with a variable width square wave generated within the



Absence of iso-electric baseline in ECG

ECG recorded simultaneously at sensitivities of 0.2 mV/cm and 10 mV/cm

Fig. 10

instrument. Clinical use of this system in patients with acute myocardial infarction is described by Spann et al (1964).

The medical world, particularly in the U.S.A., was surprisingly quick and enterprising in enlisting the digital computer to aid ECG analysis. In spite of the problems with early systems, investigators such as Taback et al (1959), Stallman et al (1961) and Pipberger et al (1960) were laying the foundations on which, in some cases, impressive edifices were built.

In any form of detailed analysis of the ECG the first task is to identify the components that comprise the wave-form: the P, Q, R, S and T, the U-wave generally being ignored. Taback, Stallman and Pipberger and their co-workers used orthogonal 3-lead systems while collecting their ECG data for processing as it was believed to vary less than the conventional bipolar and unipolar leads in the presence of physiological rotation of the heart on its axes. All used Schmitt's SVSC III system (Schmitt et al, 1955) while Stallman additionally used that of Frank (Strong, 1970). All analyses were conducted in real time and were digitised at a rate of 1000 samples per second per lead, a rate which is still considered adequate to resolve all significant characteristics of the analogue signal (Sherwood, 1973).

At first sight it might be thought practical to identify the component waves of the ECG wave-form by measuring their heights above the iso-electric baseline and perhaps identifying the largest positive signal as the R-wave. In fact, the concept of an iso-electric baseline is false and is founded on the low, 1 millivolt per 10 mm. sensitivity at which the ECG is conventionally recorded. If this sensitivity is increased, it will be seen (Fig. 10) that the baseline varies continuously and provides no datum from which to measure.

Taback's method for identifying the P, Q, R, S and T-waves was first to filter the incoming signal to remove 60 Hz mains hum, somatic tremor artifacts, etc. This he did by successively averaging 40 samples

taken at 1 millisecond intervals and using this average to represent the signal level at the first millisecond point. Thus the average of intervals 1 to 40 gave the value of interval 1, the average of intervals 2 to 41 gave the value of interval 2, the average of intervals 3 to 42 gave the value at interval 3, and so on. Each value obtained from this process was compared with the minimum accepted value of a P-wave. If none of the sample values reached this level an absence of P-waves was recorded.

If a difference was found, sampling continued until this reached a maximum value and then decreased for three successive intervals. When this happened the sampling process retraced its path until a minimum difference was again found and that point was defined as the beginning of the P-wave in that lead. The process was repeated for the other two orthogonal leads and the earliest point of the three accepted as the reference zero point from which all timings were measured. The remaining components of the ECG were identified in a similar fashion although the filtering was discontinued for the remainder of the calculations.

Stallman et al (1961) and Pipberger et al (1963) also filtered the incoming signal to remove "noise" and they found that this filtering did not significantly affect the accuracy with which the components of the ECG wave-form could be measured. They discovered that, in the orthogonal leads, the spatial velocity of the ECG during the T-P, P-R and S-T intervals did not often exceed 3 micro-volts per millisecond and was usually between 2 and 5 micro-volts per millisecond. When a greater value than these was detected it was accepted as indicating one of the component waves. The maximum value of spatial velocity indicated a point in the QRS complex and initiated a search for the beginning and end of the QRS as indicated by spatial velocities of less than 5 micro-volts per millisecond.

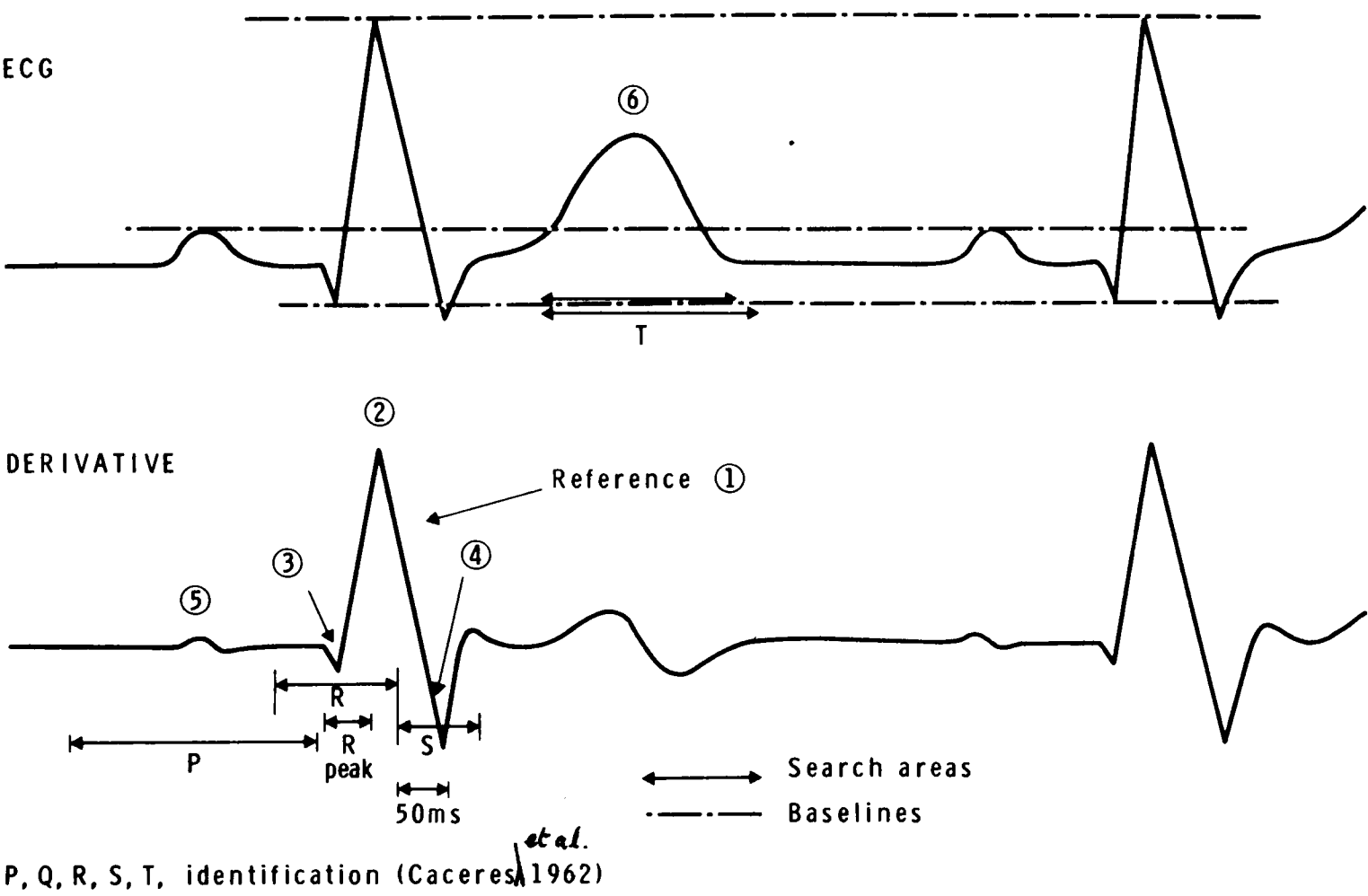
P and T-waves were identified in a similar fashion, using limits

of 2 micro-volts per millisecond which had to be exceeded for 16 milliseconds in the case of the P-wave and 32 milliseconds in the case of the T-wave. This avoided errors due to short artifactual variations in the ECG which may have occurred at frequencies which escaped the filtering process.

Because the identification of the PQRSW-waves is so fundamental to the production of a comprehensive system of automatic analysis, it is perhaps justifiable to consider a further approach to the problem. Caceres et al (1962) used ECG leads II and V_3 as data sources for their program to identify the PQRSW-waves by digital computer. In common with other workers, Caceres and his colleagues initially filtered the incoming signal. Then, seeking some reference point which would be constant from subject to subject and lead to lead, they chose the point of greatest negative rate of change in the ECG wave-form which they obtained from its first derivative. This point is between the R and S-waves. (Fig. 11).

The R-wave was found by searching for the first derivative value greater than 9.375 micro-volts/millisecond within 12.8 milliseconds of the maximum negative value. If this was found, the R-wave peak was located at the point of maximum amplitude within 6.4 milliseconds of the reference point. The S-wave was searched for by checking for a first derivative greater than 3.75 micro-volts/millisecond within 12.8 milliseconds after the reference point. If this was found the peak of the S-wave was the maximum negative amplitude within 80 milliseconds of the reference point. The Q-waves were identified as peaks in the interval 8 to 56 milliseconds before the R-wave peak with a velocity less than 1.875 microvolts/millisecond. The interval 86.4 to 313.6 milliseconds before the reference point was searched for the P-wave peak and the maximum and minimum values of the first derivative was estimated at 1.6 millisecond intervals.

All values within 25% of the maximum positive and maximum negative were found. Only values from successive intervals in which the



- (1) Reference area where 1st derivative has maximum negative value
- (2) R-wave peak
- (3) Q-wave
- (4) S-wave
- (5) P-wave

(N.B. ECG and derivative not vertically aligned in time)

Fig. 11

derivative changed polarity were retained as these would indicate a local peak. Any peaks separated by more than 9.6 milliseconds were discarded as not being part of the P-wave.

The remaining maxima and minima define the type of P-wave present, e.g. positive, negative, bifid, etc. and the greatest value indicates the position of the peak. The onset of the P was defined as that point in the interval 32 to 12.8 milliseconds before the peak where the velocity was less than 1.875 micro-volts/millisecond for 1.6 milliseconds.

The T-wave was located in the filtered ECG, not the derivative, and using time and amplitude as the criteria. The maximum amplitude, positive or negative, in the interval 99.2 to 331.2 milliseconds after the S-wave peak, if this was present, otherwise 150.4 to 350.4 milliseconds after the R-wave peak.

To overcome the problem of measuring amplitudes when, as has been shown earlier, no iso-electric line exists to be used as a reference, Caceres constructed a reference baseline by linking with a straight line the beginning of the P-waves in two successive complexes. (Fig. 11) If P-waves were not present, successive Q-waves or R-waves were linked to provide the baseline. The onset and end of the S-wave (the former also being the end of the R-wave), the end of the P and T-waves and the start of the Q-wave, if present, were determined by satisfying the two criteria of (a) the wave-form crossing the baseline reference and (b) a first derivative velocity not greater than 1.875 micro-volts/millisecond.

This description of the analytical processes involved in the program, though of necessity simplified, may give some idea of the complexity involved when the digital computer is required to simulate a cardiologist's analytical processes.

When the components of the ECG complex have been identified and their durations and amplitudes measured, it is a comparatively simple matter to calculate the values of the R-R, P-R and Q-T intervals.

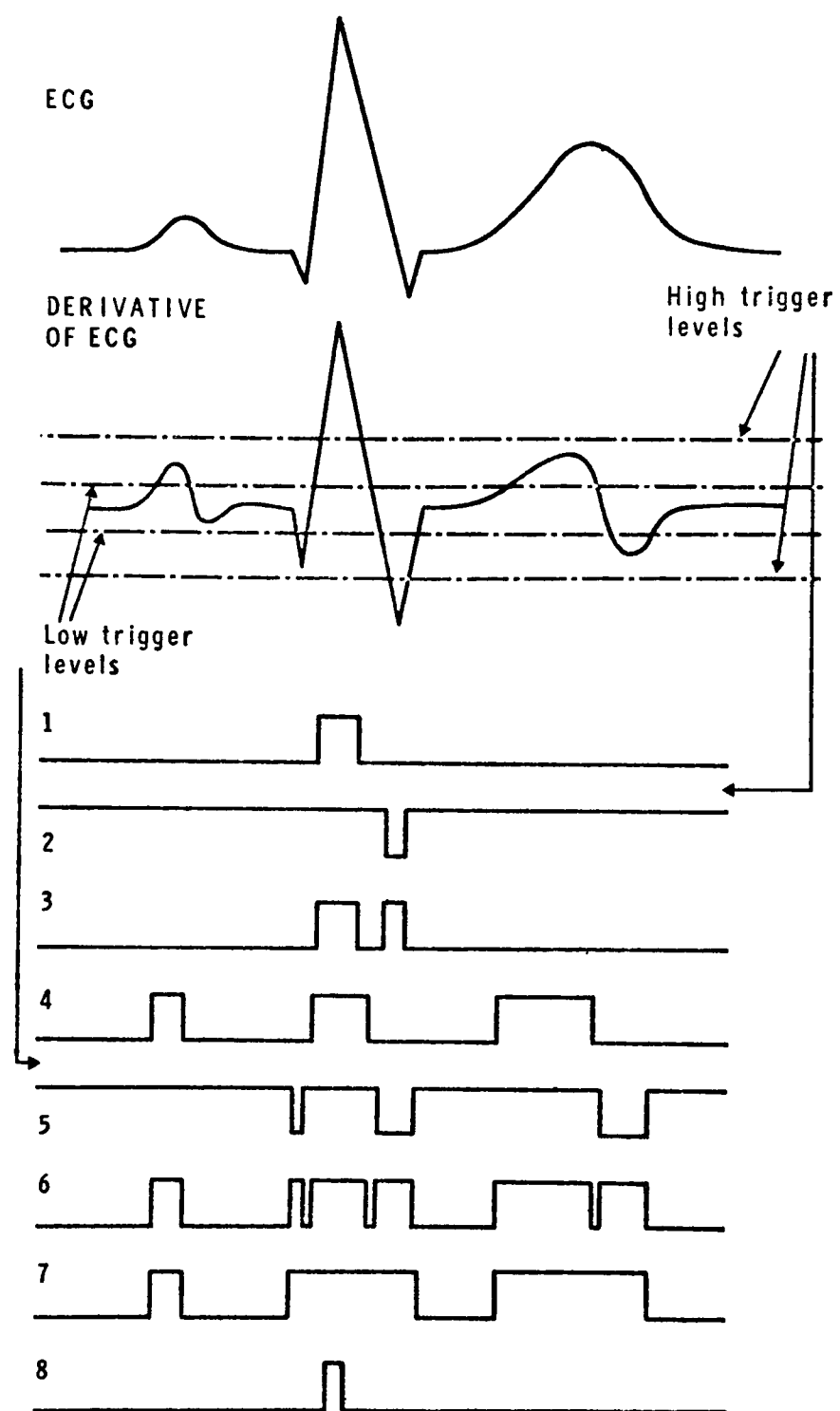
This part is generally termed the measurement section of the computer program, whilst a second section comprises the interpretation logic and defines the criteria by which an arrhythmia is classified. Although the absolute values will depend on the computer in use, the measurement process occupies, typically, three times as much time as the interpretation sequences in an entirely digital system (Bonner, 1973).

Many of the procedures in the measurement section have remained acceptable for more than ten years, which is quite remarkable in such a changing atmosphere as that which surrounds the digital computer world. As an example of such surprising stability, Leblanc et al (1975) continued to use the same reference point when estimating the relationships between the ECG wave-form components as did Caceres in 1962. This may, of course, merely emphasise how far-sighted Caceres was.

4) Analogue pre-processing of the electrocardiogram

The comparatively high proportion of operating time which is spent by a digital computer in performing the measurements involved in ECG analysis has lead several groups of workers to develop in recent years forms of analogue pre-processing methods which effect a substantial degree of data reduction.

As mentioned earlier, one of the fundamental requirements in automatic ECG analysis is to identify the QRS complex. This is a time-consuming procedure when digital techniques are used but a relatively simple task for an analogue system. A basic but effective approach is to filter the ECG through a band-pass active filter whose characteristics are such as to attenuate strongly 50 Hz and somatic interference at the top and the T-wave at the bottom and yet pass normal and abnormal QRS complexes without loss. The reason for attenuating the T is to avoid abnormally large T-waves being confused with QRS complexes. A filter with centre frequency 10 Hz and with a theoretical attenuation of 24 dB per octave (reduced to 12 dB per octave actual, due to component tolerances) has been found to be effective and forms part of the system to



P, Q, R, S, T, identification (Kimura 1973)

Fig. 12

be described later. The filtered ECG signal is full-wave rectified so that it operates irrespective of the polarity of the incoming QRS complex and drives a trigger circuit which generates a constant width, constant amplitude pulse. A passive filter system performing a somewhat similar function was described by Mogensen et al (1965).

In more recent years, the falling cost of integrated circuits has made it possible to use them quite lavishly to construct active filters, differentiators, integrators and Schmitt trigger circuits whose performances are much more stable and predictable than those using thermionic valves or individual semi-conductor devices.

5) Identification of the P, Q, R, S, and T-wave by analogue methods

Kimura et al (1973) of the Department of Internal Medicine, Nippon Medical School, Tokyo, used the ubiquitous filter circuit to remove noise, followed by a differentiator and two Schmitt trigger circuits operating at different levels. (Fig. 12). The higher level trigger generated a positive or negative square wave for each component of the differentiated QRS complex. The negative square waves were inverted and summed with the positive square waves to form a single pulse, using a short delay circuit to superimpose the unsynchronised pulses.

Large amplitude P or T-waves could occasionally confuse the analyser, so a peak level detector was used to identify the differentiated QRS wave-form and generate a reference signal. This was compared with the square wave pulses and whichever of the latter coincided with it was judged to be the QRS. The low level Schmitt trigger initiated a similar process for the P and T-waves.

The system has the advantage of being capable of indicating the duration of each component of the ECG in addition to its timing but it does so at the cost of considerable complexity. For example: to be

certain of detecting the P-wave, six ECG leads, plus the differentiated ECG, plus the square wave ECG, have to be treated in parallel! Results do, however, show an agreement of 91.5% with the physician interpretation in 318 cases.

6) Identification of the QRS complex by analogue methods

Sandman et al (1973) describe an analogue pre-processor which had the limited objective of measuring the R-R interval and width of the R-wave. To enhance the certainty of detecting the R-wave in the presence of large T-waves, the first derivative of the R-S wave was inverted and added to the original ECG wave-form. R-R interval was measured by generating a triangular wave whose duration and hence height was controlled by successive trigger pulses derived from the R-waves.

To provide some immunity from noise and fast transient artifacts such as might occur when the ECG was transmitted over a telephone line, the triangular pulse generator was prevented from re-cycling for an adjustable minimum time after the previous trigger pulse. The R-wave width was determined by measuring the time elapsing between the moments when the upstroke and downstroke crossed the mean D.C. level of the complete wave-form. Batches of 128 R-R intervals and the associated R-wave durations from the pro-processor were fed to an Elliott 903 digital computer.

Hacke et al of the Department of Intensive Care, State University of Ghent (1974) used a further permutation of the familiar building blocks (filter, differentiator, comparator) to construct a QRS detector/pre-processor which was simple and inexpensive but did not sub-divide the QRS complexes into normal and abnormal. At detecting QRS complexes per se, however, it achieved a success rate of 98% which was similar to that of the three commercial systems with which it was compared. These were the

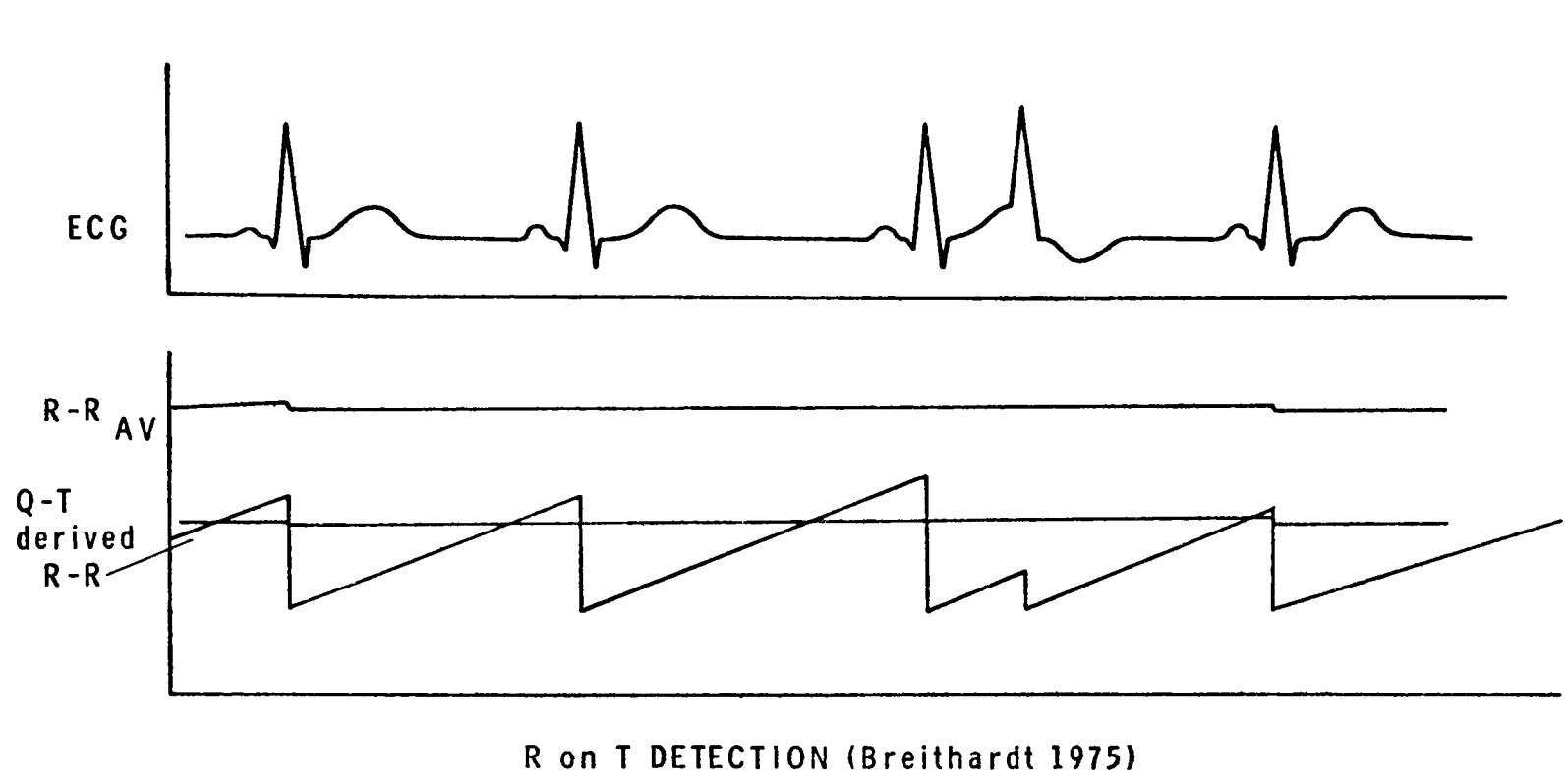


Fig. 13

Simonsen & Weel EAC 804 ECG arrhythmia computer, the Hewlett Packard model 7822A arrhythmia monitor and the Neilson arrhythmia computer.

A system of similar capabilities and based on virtually the same techniques was described by Swenne et al of the Institute of Medical Physics in Utrecht (1974). In a trial analysis of 10,937 QRS complexes from 12 different patients, the incidence of false positives was 0.28% with no false negatives. The systems and results of these last two groups of workers show that basic detection of the QRS complex can be accomplished very successfully in real time by comparatively inexpensive and simple analogue circuitry.

7) Detection of the R on T phenomenon by analogue methods

Finally, an example of the extension of basic analogue techniques by a little applied mathematics: Ashman (1942) demonstrated a relationship between the duration of the normal Q-T interval and the heart rate, which could be expressed by the formula

$$QT = K \times \log_{10}(R-R + 0.07)$$

with the R-R interval expressed in seconds. Lown et al, among others, showed that the degree of prematurity of an ectopic beat could be given by the quotient $\frac{R_{ES} - Q_N}{T_N - Q_N}$ where the subscript ES indicates a component of the abnormal beat.

Breithardt et al (1975) of the Medical Clinic B, Dusseldorf, applied these two relationships in the development of an analogue circuit for the automatic detection of the R on T phenomenon. In this circuit QRS complexes were detected in a conventional manner and from these the R-R interval was calculated. The Q-T interval was estimated from the R-R value using Ashman's formula and averaged over ten seconds to give an almost steady D.C. level (Fig. 13). This level was compared with the peak height of a ramp function which was generated during the R-R interval.

The peak height of the ramp was proportional to the R-R interval and therefore the relative values of this and the steady level derived from the averaged Q-T intervals could be used to indicate a premature beat. The value of K in Ashman's formula was estimated for each patient at the beginning of a recording by measuring from a triggered ECG display on an oscilloscope. The variation of K during 16 to 24 hours was also investigated and a mean relative standard deviation of 3% was found in patients in sinus rhythm, rising to 3.9% in one case of atrial fibrillation, neither value being large enough to invalidate the basic assumption.

CHAPTER 3

DEVELOPMENT OF DATA PRESENTATION

1) The need for data compression

Whichever methods of data collection and data processing are employed in the context of recording the ECG from ambulant subjects, some degree of data compression must be accepted if the results are to be presented in a manageable form.

All investigators instinctively fight shy of discarding information, which may have been collected with a degree of patience, not to say ingenuity. In the case under consideration, however, information will not be irretrievably lost. Even if it does not appear in its entirety when the data are displayed, it can always be recovered from the original recording medium.

A 24-hour ECG recording containing 100,000 complexes will also contain 99,999 R-R intervals and it is obvious that a tabulation of the values of these correct to, say, three decimal points, whilst feasible for a digital computer to generate, would serve little clinical purpose! On the other hand, some graphical presentation showing the variation in R-R interval over a period of possibly four, or twenty-four, hours could well be useful.

Many of the examples of data analysis which have previously been described include the facility for producing a voltage proportional to the R-R interval and it is a simple matter to display this variable on a recorder so that 24 hours of real time can be compressed into 50 cms. of chart and yet still indicate overall variations in heart rate during this period.

Fig. 14 shows an example of this form of presentation.

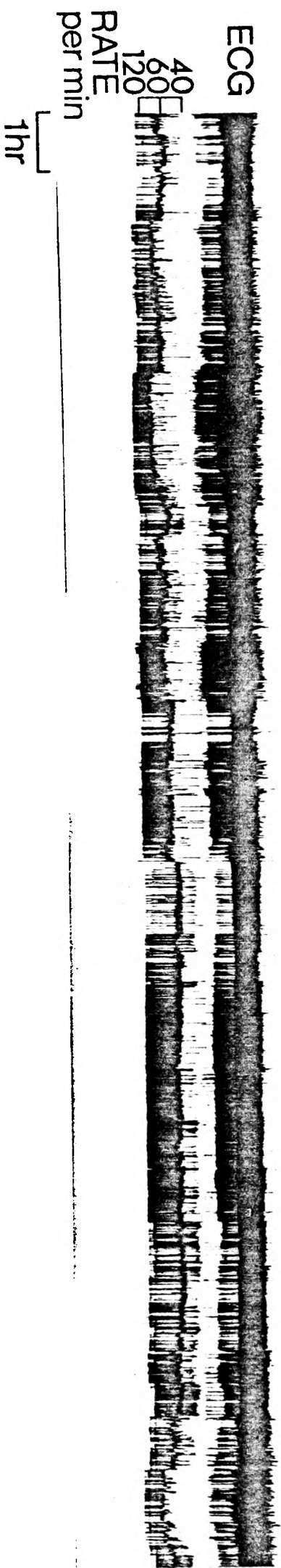
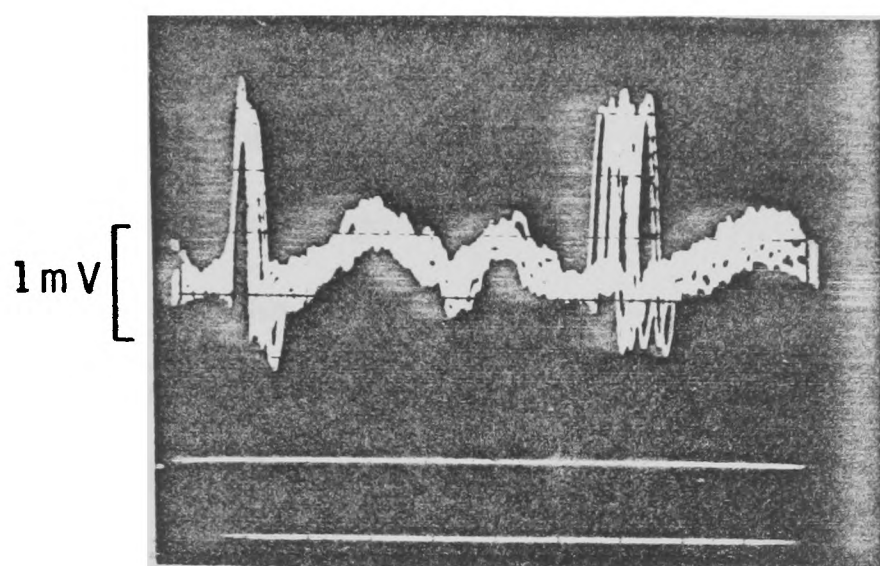
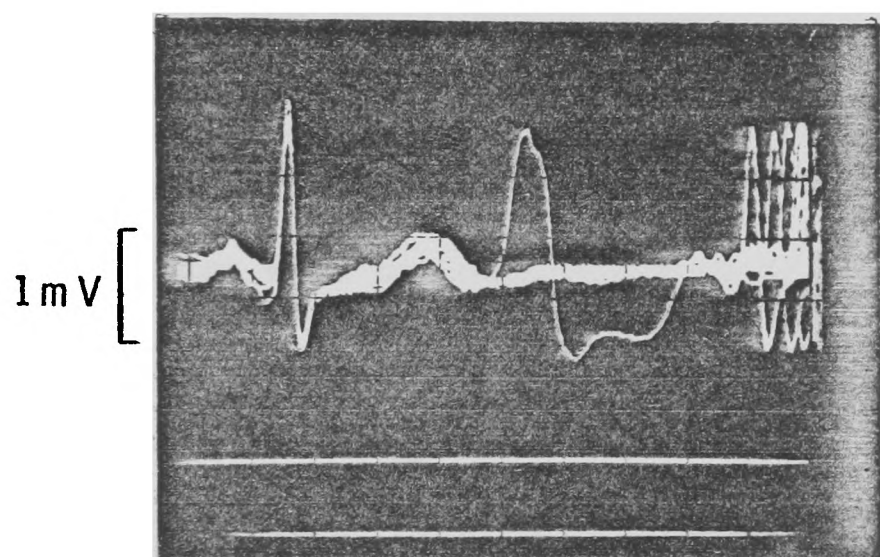


Fig. 14

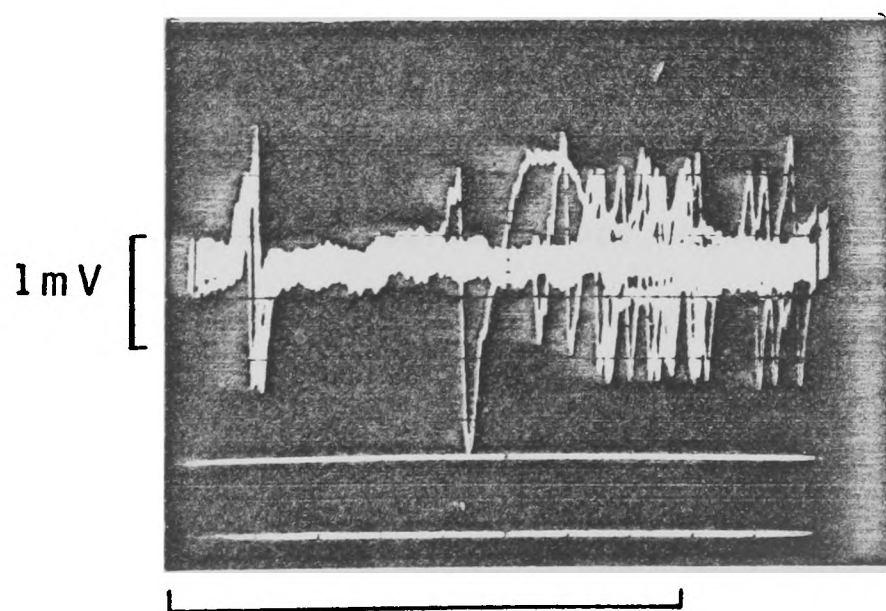
24 hour record of heart rate



SINUS RHYTHM



SINUS RHYTHM
WITH PVB'S



AF WITH
PVB'S

1 second

HOLTER AVSEP PRESENTATION

Fig. 15

2) Audio-visual presentation of data

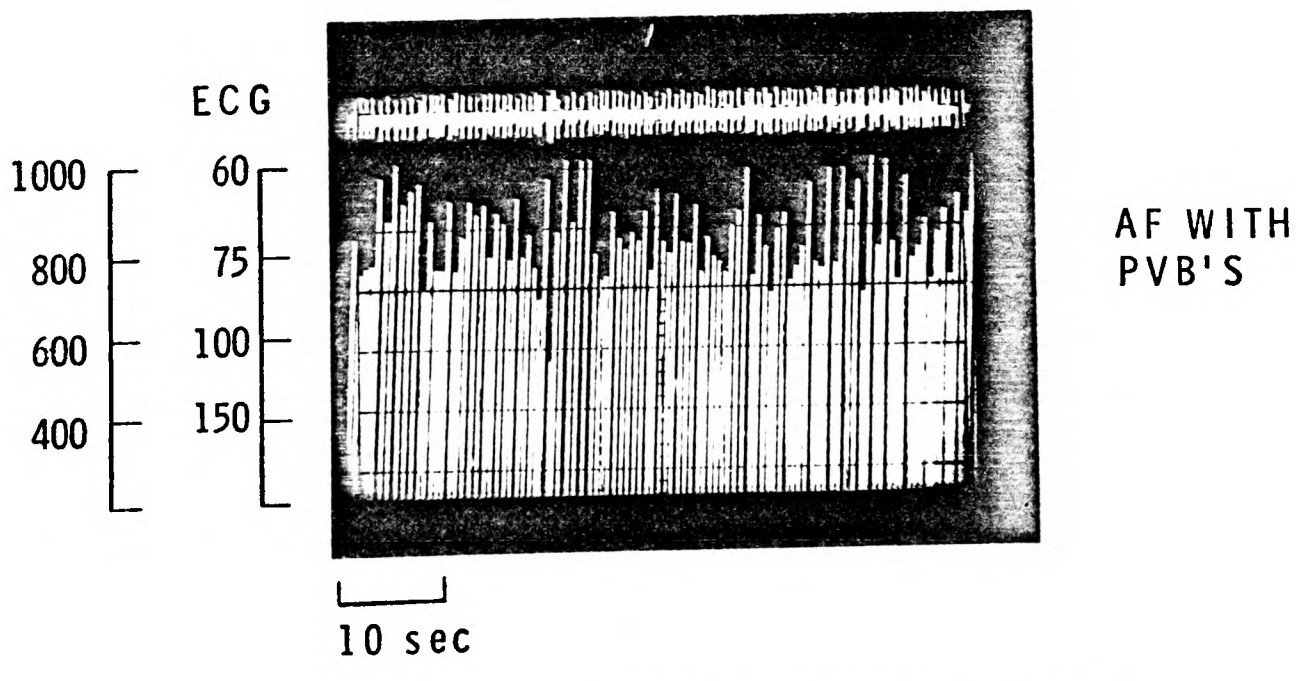
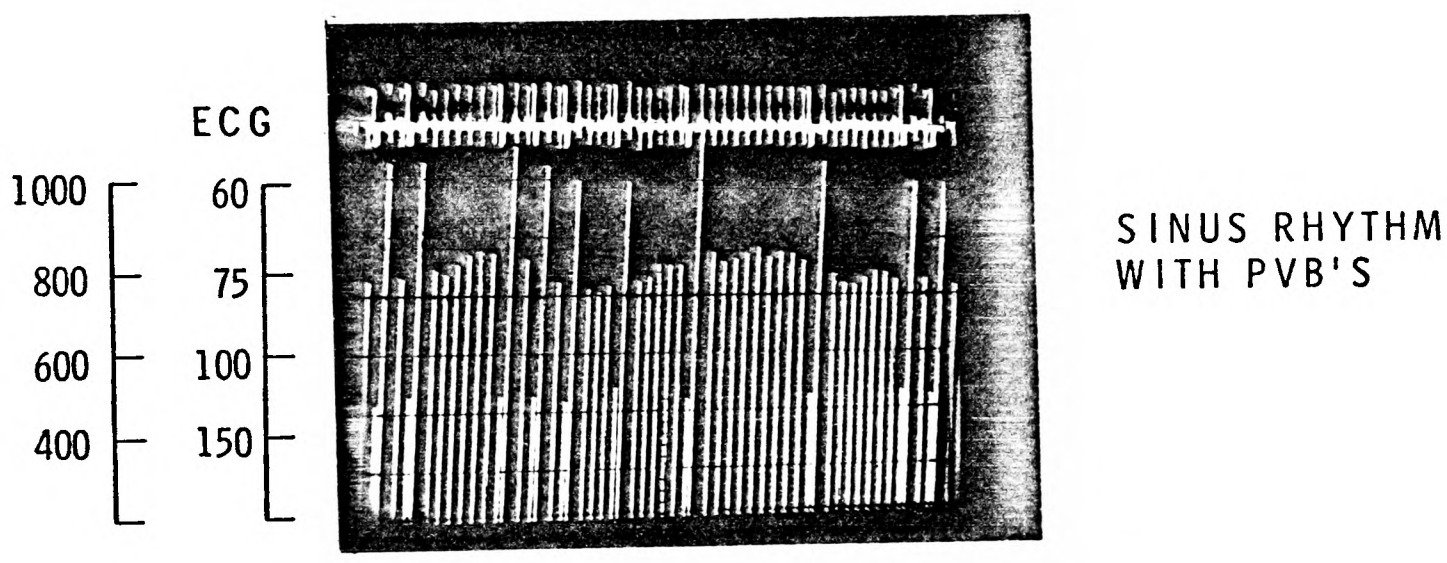
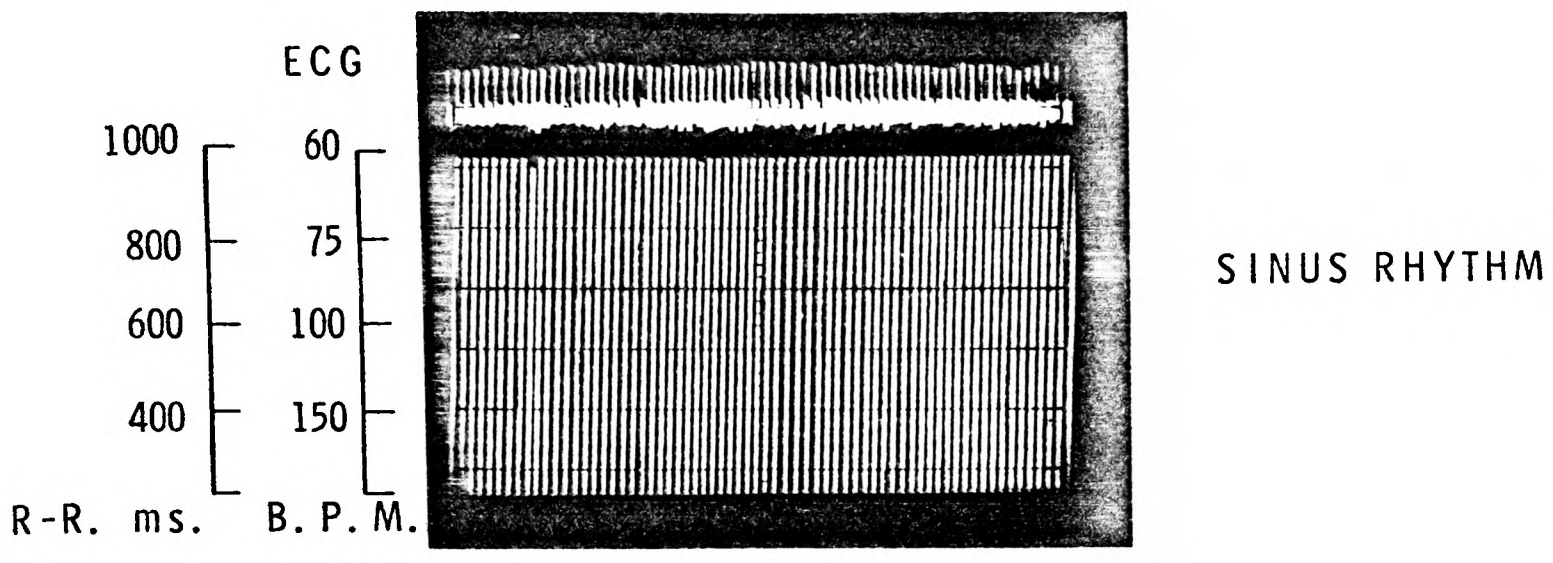
The AVSEP, or Audio Visual Superimposed Electrocardiogram Presentation (Holter, 1957) and "Arrhythmiagraph" (Holter, 1958) were two early methods of data compression. In the former, the ECG replayed at 60 x real time is displayed on an oscilloscope so that successive complexes are superimposed.

As mentioned earlier, Holter recorded two channels of ECG virtually simultaneously but in fact slightly asynchronously due to the displacement of the two recording heads in the tape recorder. The output of one channel was used in the AVSEP to provide sufficient delay in the oscilloscope time-base so that the entire ECG complex could be displayed although the trigger was derived from the R-wave. Variations in R-R interval and in wave-form were apparent if successive complexes were not completely superimposed.

Examples of the 'visual' part of Holter's AVSEP type of presentation are shown in Figure 15. The 'audio' part, which he described as a "noisy growl", must be left to the imagination!

Ciné photography of the oscilloscope face enabled abnormal episodes to be re-examined in detail but was rather a cumbersome and expensive process. From experience, Polaroid photographs are useful for only a relatively short sequence of complexes, say 20 to 30. Except in subjects with a more or less constant rate of sinus rhythm, the Polaroid traces resemble tangled knitting if more than some thirty complexes are superimposed.

In the "Arrhythmiagraph" successive R-R intervals were displayed on an oscilloscope as a series of vertical lines whose heights were proportional to the R-R durations. This form of presentation makes it quite easy to identify premature beats and sudden changes in heart rate but, again from experience, it does not seem feasible to display more than 100 intervals simultaneously.



ARRHYTHMIOGRAPH PRESENTATION

Fig. 16

Although a series of displays can be automatically triggered to appear successively, the sense of continuity is lost. Fig. 16 shows the arrhythmograph type of display.

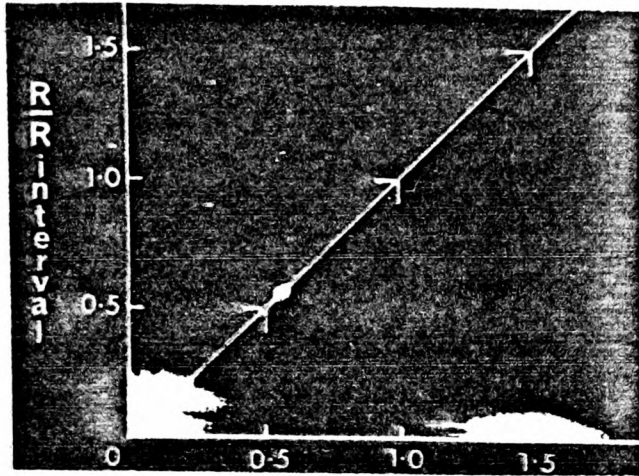
3) X-Y display of R-R intervals

A form of data presentation which does not suffer from an inability to display more than a short sequence of events is that which has been described as the Joint Rate Histogram by Rowlands et al (1970) and as the Scattergram by Stinton et al (1972). Others, for example Goldstein et al (1967) used the phrase "joint distribution function" and ten Hoopen et al (1969) "joint probability density function".

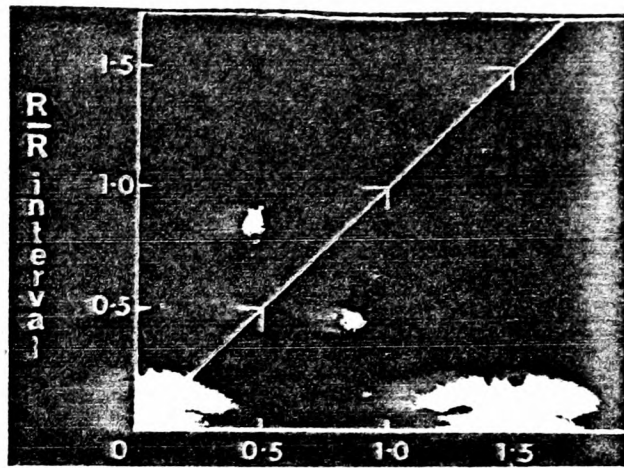
These last two terms doubtless indicate the increasing influence of the statistician in medicine. Both derive their data from ECG recordings made in real time but the former system displays the data retrospectively whilst the latter operates in real time. Both methods require the generation of a square-wave pulse from each QRS and for the measurement of successive R-R intervals.

Various methods for performing these functions have already been described, probably ad nauseam, and will not be repeated. Suffice it to say that the co-ordinate formed when the n th R-R interval is measured on the X-axis and the $n + 1$ th on the Y-axis is displayed on an oscilloscope. This graph is continuously updated with the $n + 2$ interval going on to the abscissa, the $n + 3$ on to the ordinate, and so on. If a storage or memory type of oscilloscope is used the information can equally well be seen and photographed.

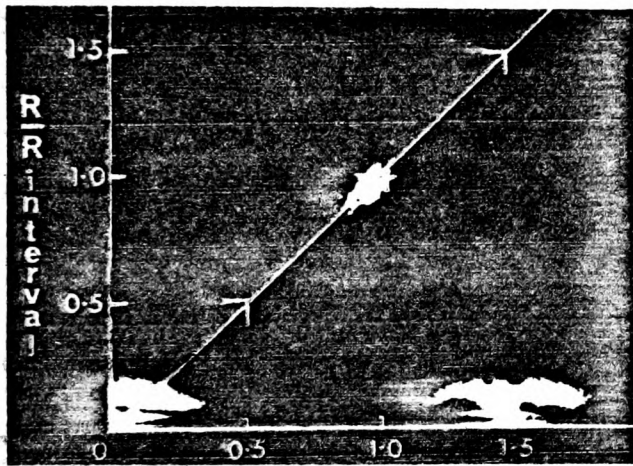
Rowlands et al (1970) used a digital computer to generate their joint-rate histogram from data supplied from paper tape. To indicate variations in density at any co-ordinate, they used eight symbols which were readily available from the computer. This



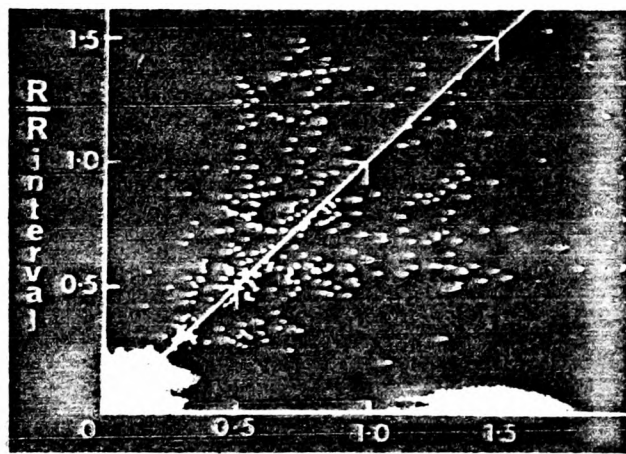
(a)



(c)



(b)



(d)

The Scattergram

- (a) Sinus tachycardia
- (b) Sinus rhythm
- (c) Coupled beats
- (d) Atrial fibrillation

Fig. 17

quantitative expression of density was not possible in the simpler system used by Stinton and his co-workers. Rowlands et al used 100 or 1000 pairs of R-R intervals from which to construct their joint-rate histograms. This implied that each display represented a maximum of some 25 to 30 minutes' monitoring. Stinton found that 15 minutes was a convenient period from which to build a scattergram. In 1972, however, some limitation was imposed by the inadequate performance of storage type cathode ray tubes and the relatively high cost of digital storage. Representations of the scattergram are shown in Figure 17.

4) The R-R interval histogram

In his study of the influence of digitalis on heart rate Arnoldi (1927) tabulated his data in a form from which a histogram could readily be drawn. Horan et al (1961) studied the R-R histogram in 17 patients with atrial fibrillation. They measured by hand some 10,000 intervals to an accuracy of 10 milliseconds and then manually plotted histograms. Moe et al (1964) calculated the R-R intervals in surface leads from the myocardium of dogs in atrial fibrillation. This group measured some 1000 intervals per subject. Simborg et al (1966) were more fortunate than the previous groups. Initially they had to measure the R-R intervals by hand but had the services of a computer to construct their histograms; latterly the entire sequence was automated and an hour's recording could be processed in two minutes.

Vachon et al (1972) used a multichannel analyser to convert R-R intervals into histograms in a study of an anti-arrhythmic drug and a histogram generator is a sub-unit of the arrhythmia analyser to be described.

Crook et al (1976) used an analogue pre-processor to produce the measurements of R-R intervals from which a minicomputer constructed the histogram. They also described an extension of the technique: the

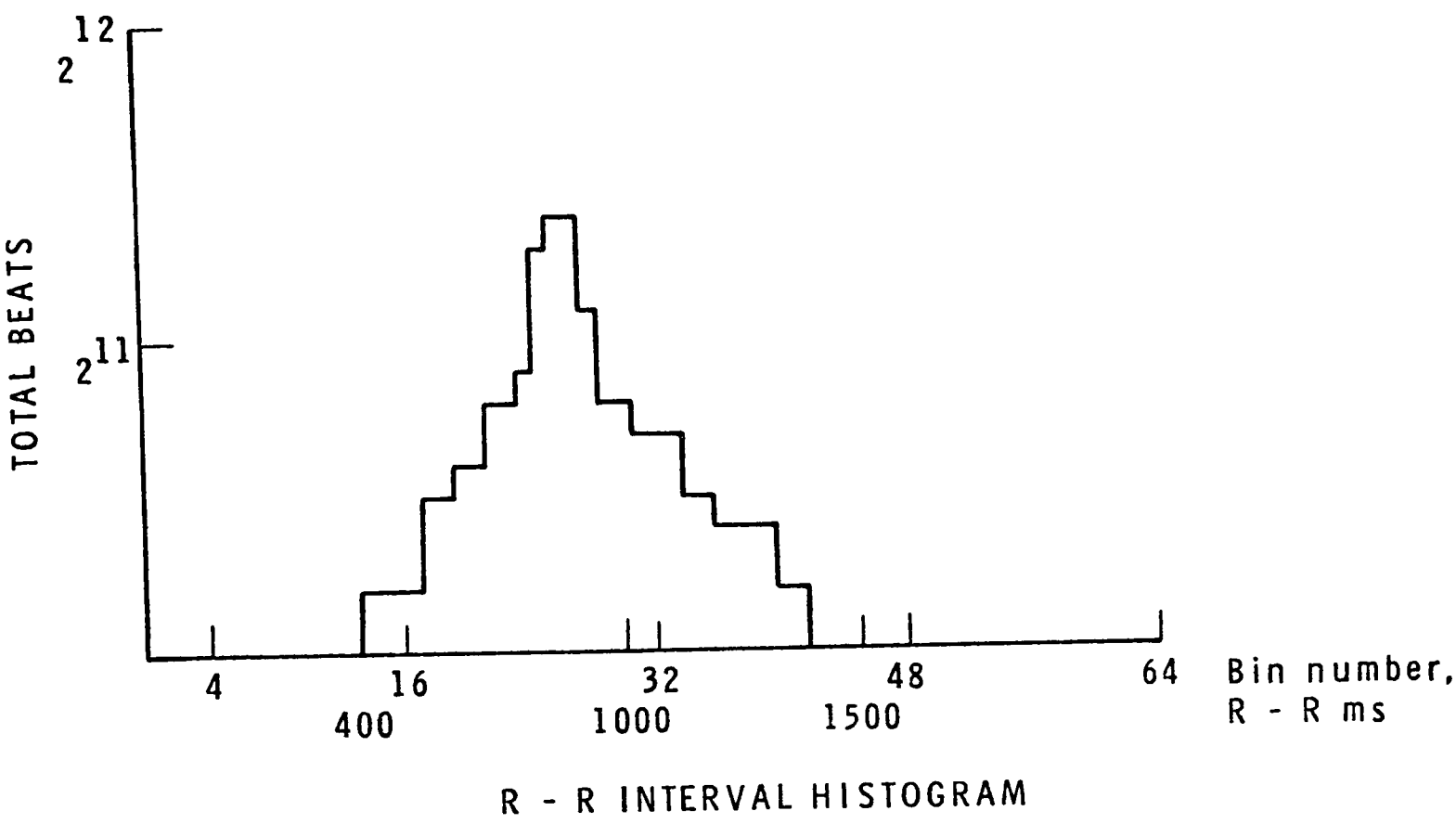


Fig. 18

R-R difference histogram. In this form of presentation it is the difference in the duration of successive R-R intervals which is calculated and sorted into batches. The interval difference histogram does not supplant the interval histogram but rather it is complementary to it. For example, if the latter is collected over a period during which the subject wakes from sleep, a bimodal histogram will be produced from the sleeping and the waking heart rates. The interval difference histogram, however, will show a single peak and help to differentiate the physiological bimodal histogram from that due to sino-atrial disease. (Cashman, 1977).

Horam, Moe, Simborg, Crook, Cashman and their colleagues all chose to divide the base of their histograms into 20 millisecond units whilst in the arrhythmia analyser histogram, for economic reasons, the units or bins, to use current terminology, are 30 milliseconds wide and cover a useful range of 200 to 2000 milliseconds in real time, equivalent to heart rates of 30 to 300 beats per minute. Because, when dealing with electronic circuits, it is easier to design for R-R intervals than the associated heart-rate, the histogram is scaled linearly in milliseconds and consequently as an inverse function with respect to rate. (Figure 18). Nevertheless bins corresponding to the usual range of heart rates occupy the centre half of the X-axis.

Each bin has a capacity of 4096 R-R intervals after they have been digitised. At first it might seem that this would only permit an hour or so of recording before a bin overflowed. In practice, few heart rates are so nearly constant that all intervals fall into a single bin. For example, a clinically insignificant change of heart rate from 75 per minute to 73 per minute will move the count to the next bin. There is, in most cases, enough variation in heart rate to provide accommodation for some six hours of recording. A notable exception to this is the patient with an artificial pacemaker in which almost all

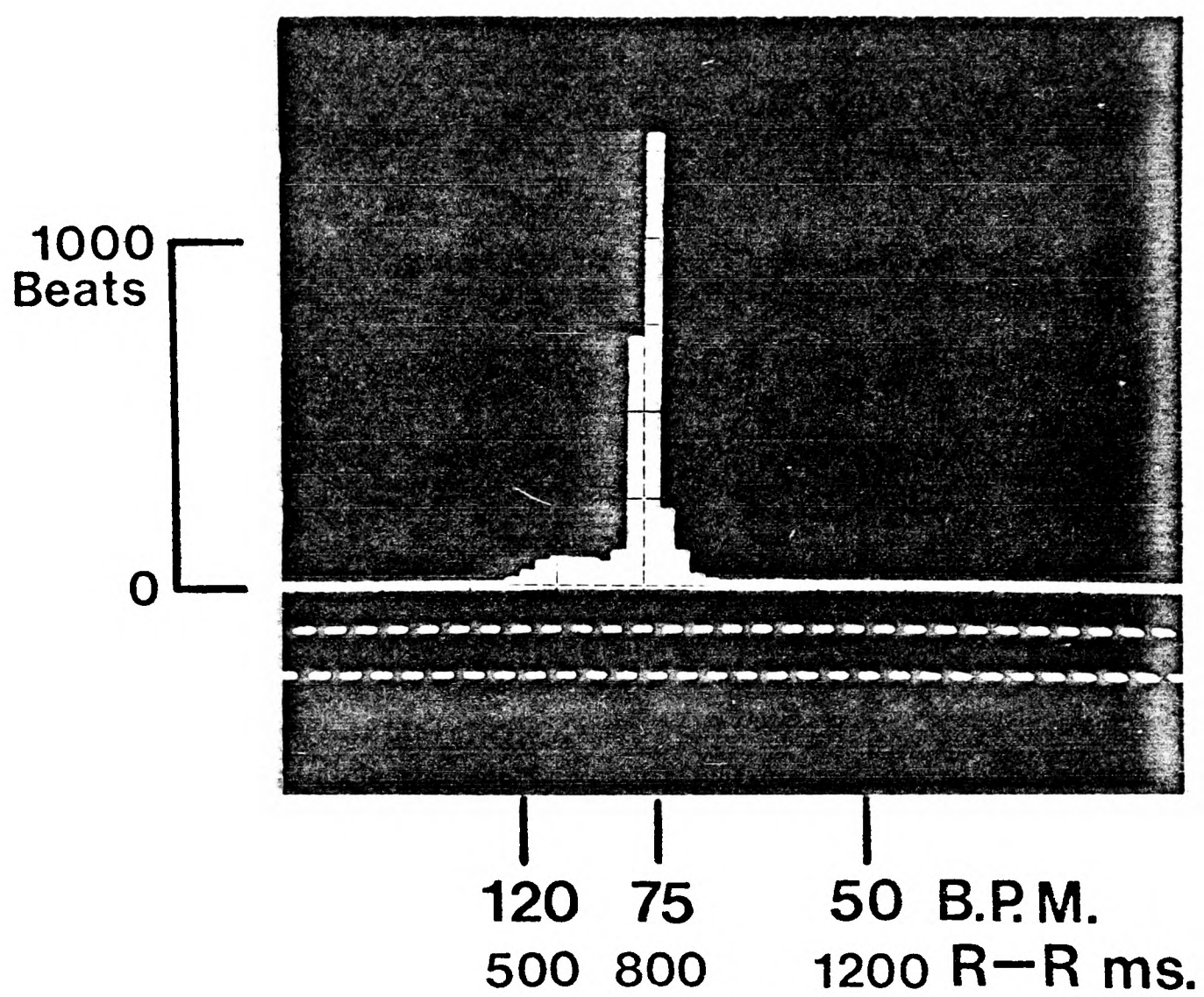


Fig. 19 R-R interval histogram from subject with artificial pacemaker

E.B. Episode A

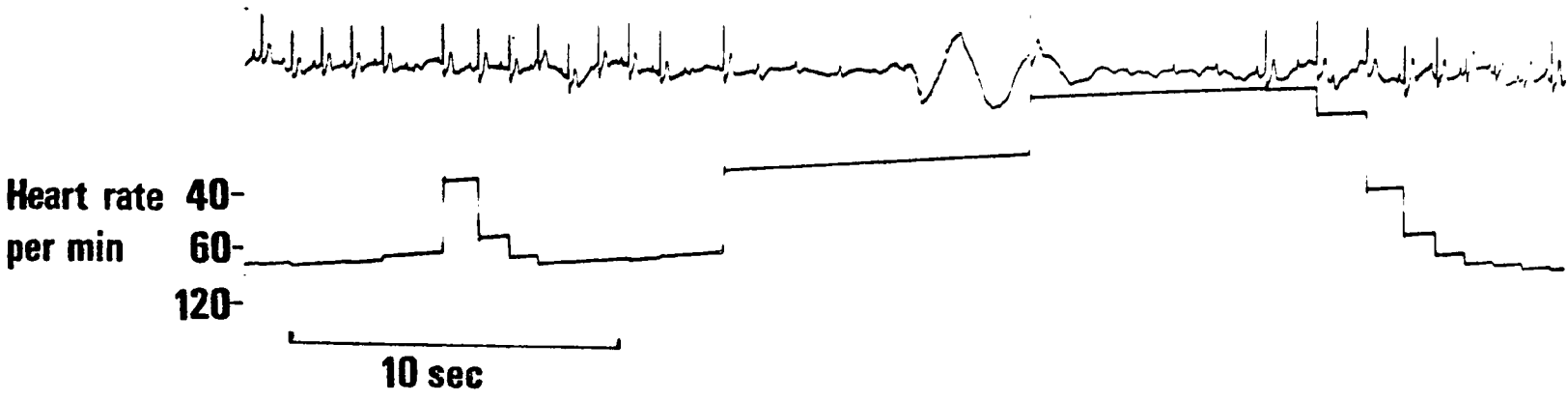


Fig. 20 A brief episode of arrhythmia

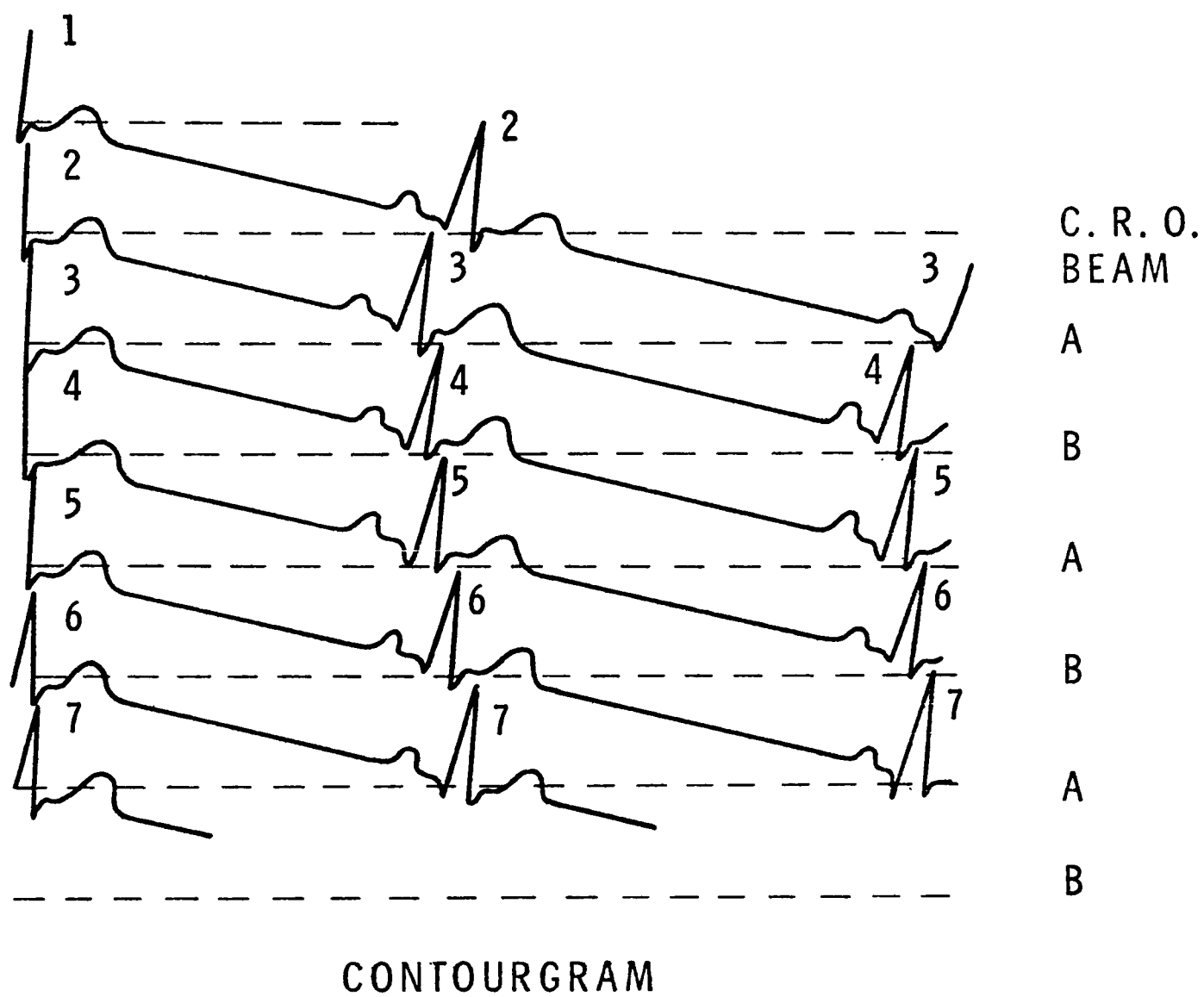


Fig. 21 Slope and vertical spacing of ECG trace exaggerated for clarity of illustration

all beats go into the same bin (Figure 19). It is possible to 'trade off' bin capacity against resolution of variations in R-R duration but to date the above relationship appears to be a clinically acceptable compromise.

Episodes lasting only a few seconds or a few minutes are better displayed by a strip recording of the ECG and R-R interval than by a histogram. (Figure 20).

5) The Countourogram

One final form of data presentation which may be considered in connection with ambulatory ECG monitoring is the Countourogram. Its use in cardiology was first suggested by Webb (1965) and it provides a useful degree of data compression. In this system a complete single ECG complex is displayed across a cathode ray tube in much the same fashion as in the Holter AVSEP. (Figure 21). The fundamental technique is, however, somewhat different.

Holter recorded two ECG channels asynchronously and used the earlier R-wave to trigger the oscilloscope time-base. Webb used a twin-beam oscilloscope, triggered the upper trace with the earliest R-wave (R_1) and displayed the complete second ECG complex on this channel. The second R-wave (R_2) triggered the second channel on which complex three was displayed. Thus successive complexes were displayed in their entirety from a single channel recording.

In 1964 Webb did not have the advantage of digital electronic storage. In his system the intensity of the trace was modulated by the ECG signal and the oscilloscope photographed by a camera in which the sensitive recording material was driven parallel to the Y-axis.

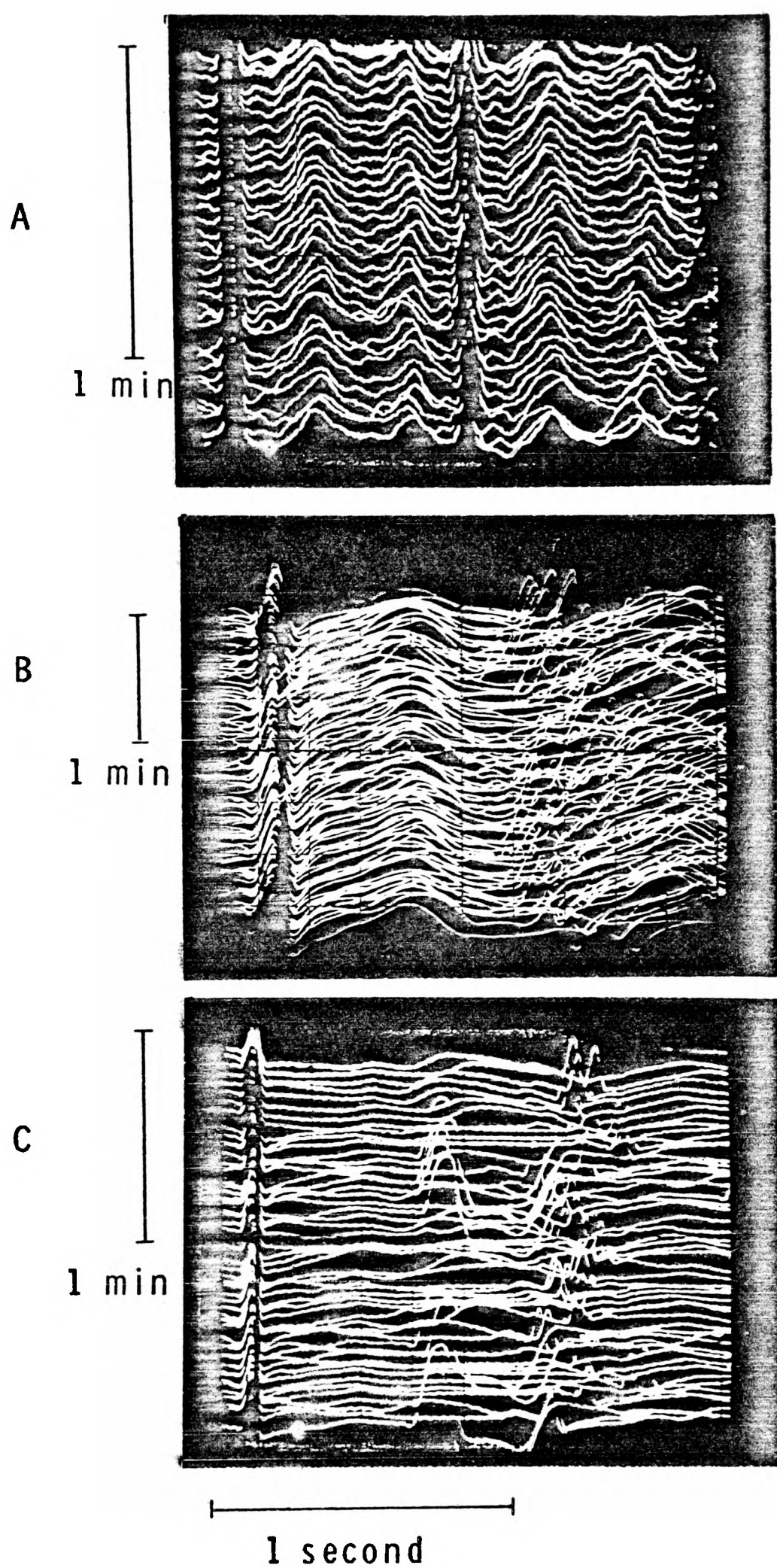


Fig.22 Simulated Contourogram

A Sinus rhythm

B Atrial fibrillation

C Ventricular extrasystoles

Using this technique continuous recordings of more than one hour were made; longer recordings could produce an embarrassing amount of paper. Cashman (1974) used coutourographic recordings made at a speed of 0.1 inches per second or 30 feet per hour.

Figure 22 gives an impression of a coutourogram but the characteristics of the oscilloscope tube and the circuitry which was available do not show this mode of presentation to its best advantage.

6) Summary

In conclusion, it appeared that no single form of data presentation was suitable for all requirements. Those which had high resolution were frighteningly prolific in their generation of 'waste' paper. Those which achieved high data compression, not surprisingly, did so with loss of detail.

For ECG rhythm analysis the histogram appears to be a useful compromise, whilst for ECG wave-form analysis of the S-T segment, the coutourogram successfully combines data compression with adequate resolution.

CHAPTER 4

METHODS FOR HIGH-SPEED SEMI-AUTOMATIC IDENTIFICATION OF EXTRASYSTOLES1) Identifying ventricular extrasystoles

The foregoing survey of the development of ambulatory ECG monitoring seemed to indicate that there was a vacant niche in the evolutionary chain of ECG rhythm analysers. There were complex, highly sophisticated, expensive and moderately successful packages based on digital computers. There were, at the other end of the scale, simple systems capable of producing relatively simple-minded analysers. In particular there appeared not to be any inexpensive device which could differentiate in accelerated time between premature ventricular ectopic beats and those arising from other foci.

Discussion with clinical colleagues indicated that a system which included this facility would be a useful clinical tool.

At the time, 1973, large scale integration (L.S.I.) techniques were in their infancy and microprocessors were not commercially available. Consequently, if the constraint of low cost was to be observed, then digital techniques and analysers dependant on them had to be ruled out.

Visual inspection shows the ECG of ventricular extrasystoles to have certain obvious differences from beats arising in the sino-atrial node or other sites in the atria. Ventricular extrasystoles are generally accompanied by ECGs which have comparatively large amplitude QRS complexes with a duration greater than 80 milliseconds and often with notches on some of the component wave. The T-wave is generally also abnormal as would be expected if the ventricular repolarisation process had followed an aberrant route. P-waves are generally absent but may be buried in the QRS. Of the entire ECG wave-form the QRS complex or its components have attracted most attention from those investigators seeking a method of

automatically identifying ventricular extrasystoles.

It would not be logical to consider variations in atrial activity in the context of the detection of extrasystoles arising in the ventricles. The P-wave can therefore be ignored. Although variations in T-waves do occur in ventricular extrasystoles the onset and end of this wave is often ill-defined and the variations less specific than those which occur in the QRS complex.

2) Limitations of commercial systems

In 1973 available information indicated that all methods which could identify ventricular extrasystoles with any useful degree of success operated in real time, unless they incorporated a digital computer. Of the commercial systems, the Hewlett Packard 7822C based its detection of V.E.S. on QRS width and prematurity. An increase of at least 15 milliseconds over normal QRS duration and a preceding R-R interval of no more than 80% of average were judged to indicate a V.E.S. In the Simonsen and Weel EAC 804 arrhythmia computer variations in another parameter, the QRST area, was added to those of the Hewlett Packard system.

An optional arrhythmia analyser was available for the Avionics Model 660 Electrocardioscanner and provided counts of ventricular and supraventricular extrasystoles. Details of the criteria which were used in the segregation have, however, not been disclosed.

Finally, there was the Neilson, R.M.E. Arrhythmia Computer which was then only available as a real-time system. In this instrument the QRS complexes of normal beats and extrasystoles were superimposed and the area not common to the two types were measured. When this area had a magnitude greater than a preset figure, a

ventricular extrasystole was counted.

The performance of the first two of the above commercial systems was poor and unlikely to be useful for high-speed analysis. Reports on the performance of the third system indicated a high level of frustration amongst its users. The basic theory employed in Neilson R.M.E. equipment required circuitry of such complexity that if it were to be used for high-speed analysis the fundamental requirement of low cost could not be met. This has been confirmed now that a high-speed version is available on the market. Having ruled out the systems then available, it remained to find an alternative.

3) The frequency spectrum of the electrocardiogram

Fourier in 1929 discovered that any wave-form could be synthesised from a combination of sine waves of appropriate frequencies and amplitudes and that such a wave-form could be expressed as a double series of sine and cosine terms. With this in mind, it seemed feasible that the longer duration of the QRS complex from a ventricular extrasystole compared with that of a normal beat might signify that the former was composed of lower frequency components, or that it contained a large proportion of low frequency components. However, if spectral analysis of a discrete signal such as the QRS complex were to be attempted, care would be necessary to exclude components contributed by the repetition rate of the signal.

There was considerable interest in the 1950s and early 1960s in America concerning the frequency response limitations of the then new direct-writing electrocardiographs and some information concerning the frequency content of normal and abnormal ECG wave-forms can be found in the literature of the period. The most prolific writer on the subject at this time was Langner of the Hospital of the University of Pennsylvania (1952, 1953), (Langner et al, 1960).

Langner and his co-workers estimated the relative frequency content of ECGs by passing them through a variable frequency bandpass

filter and comparing the amplitude of the transmitted signal with that of the original. They came to the conclusion that the QRS complex contained a significant proportion of frequencies at least as high as 1000 Hz, that the P-wave included frequencies up to 100 Hz but the T-wave had no significant frequencies higher than 20 Hz.

The variable filter technique used by Langner produces data for the construction of an amplitude spectrum of the ECG when a power spectrum might be considered preferable. It is common practice to express the performance of amplifiers, attenuators and filters by the ratio of power output to power input.

The conversion without modern computing facilities would have been tedious and would have needed the estimation of the root mean square values of the transmitted signals. Scher et al (1960) did not accept the significance of Langner's results and used an ingenious method to collect their own data concerning the frequency content of the QRS complex. They had the advantage of an electronic wave-form analyser but instruments of this type need to be supplied with repetitive identical signals while they build up the frequency spectrum. This presents no difficulty when closely controlled wave-forms from, for example, an oscillator, are being analysed but certainly the technique does not prove successful with the variations in successive ECG wave-forms and their coupling intervals.

To overcome this problem Sher and his colleagues recorded the ECG on an instrument known to have a frequency response in excess of 10 KHz. The record was enlarged photographically so that the QRS complex was about 80 mm. wide. This enlargement was attached to the tube face of a cathode ray oscilloscope whose image was focused on to a photo cell. The photo cell output varied as the oscilloscope trace started to pass behind the image of the QRS complex attached to the tube face. This change was amplified and fed back to the Y-amplifier of the oscilloscope in such a way that the oscilloscope trace was deflected around the outline of the QRS. The rate at which this sequence of events occurred was controlled by the

repetition rate of the oscilloscope time-base. Thus the input to the oscilloscope repeatedly duplicated the QRS wave-form and this signal was fed to the wave-form analyser. The results from this system indicated that the fundamental frequencies of normal QRS complexes were in the range 6.6 to 12 Hz but unfortunately no figures were given for QRS complexes from ventricular extrasystoles.

The effort needed to ascertain the frequency content of the ECG wave-form, in the days before computers were as versatile as they are now, is exemplified by the work of Thompson (1962) of the U.S.A.F. Medical Research Foundation, California. In this study the ECG wave-form was displayed on an oscilloscope and photographed at a film speed such that each cardiac cycle occupied 40 ft. of film! 1000 ordinates were measured corresponding to 1000 intervals on the X-axis. These values were transferred to punch cards which were processed by a Remington Rand 1103A computer to produce a Fourier analysis of the complete ECG wave-form. As far as can be judged from small reproductions of the spectra, strong harmonics occur between 5 and 10 Hz but their sources could be anywhere in the entire ECG wave-form.

Other workers and groups have employed spectral analysis of the ECG wave-form. Fusco (1965) at the University of Naples concluded that there was a deficiency in low frequencies in the ECG of incomplete bundle branch block. Curtis et al (1972) of A.E.R.E. Harwell studied possible "signatures" in the frequency spectra of normal and abnormal ECGs and the possibility of classification by spectral shape. Nikitine et al (1973) of the Université Louis Pasteur, Strasbourg, considered the same possibility. Golden et al (1973) of N.A.S.A. Manned Spacecraft Centre, Houston, Texas, were concerned to discover the minimal bandwidth required to transmit ECG wave-forms accurately. None of these studies provided the necessary information on the frequency content of the QRS complex in ventricular extrasystoles.

Although Langner's conclusions concerning the high-frequency content of the ECG have not been generally accepted, his report on the P and T-wave frequency characteristics appear to have catalysed a series of investigations in Sweden. These, in turn, stimulated the development of the arrhythmia analyser with which the data presented in this thesis was collected.

4) Identification of the P, QRS and T-waves by selective filtering

Nordgren of the University of Uppsala Hospital (1969) utilised the fact that the P-wave is composed of frequencies considerably higher than those in the T-wave to design a P-wave detector based on a band-pass analogue filter with low frequency cut-off at 25 Hz and a high frequency cut-off at 45 Hz. This heavily attenuated the T-wave which had been shown to have no significant content of frequencies higher than 20 Hz. A high pass filter with a cut at 25 Hz would have been equally effective at revealing P-waves but the high frequency cut was added to reduce A.C. mains interference. No attempt was made to interpret automatically the significance of the detected P-waves. Rather it was an attempt to replace oesophageal or intracardiac leads as a means of detecting atrial activity.

From this study, Nordgren (1970) concluded that it might be possible to detect aberrant QRS complexes by selective electronic filtering. Band-pass filters were chosen, apparently empirically, with centre frequencies 12 Hz and 25 Hz and the amplified ECG passed through each in parallel. The filtered signals were squared, integrated and a running average of the difference between them was derived electronically. This produced a more or less steady D.C. voltage in the presence of a run of normal QRS complexes but altered when an abnormally wide QRS complex occurred. This system operated in real time with inputs from patients in coronary care and intensive care units.

In the light of experience, the characteristics of the filters were altered to have centre frequencies of 8 Hz and 20 Hz. (Karlsson et al, 1970). The 8 Hz value was chosen to increase the transmission of lower frequency components and the 20 Hz to give increased rejection of muscle artifacts.

Extending the range of the lower frequency filter introduced the risk that components of the T-wave might be transmitted. Therefore a modification was made to the system so that the outputs of the filters were sampled 150 milliseconds after the beginning of the QRS complex, thus avoiding the T-wave.

In recordings from six patients, the success rate for detection of aberrant complexes ranged from 100 to 88.5%.

5) The application of selective filtering to high-speed ECG analysis

It was during a chance visit to the University Hospital, Uppsala, in 1973 that the writer first became aware of the work of Nordgren, Karlsson and their colleagues. Discussions then, and subsequent correspondence suggested that the fundamental concept of segregating normal and aberrant beats by means of their different frequency spectra could be adapted for the fast analysis of ECG tape recordings.

The Oxford Instruments MATR tape recorder (forerunner of the Medilog recorder previously described) had become available with an associated play-back system operating at 25 x real time. It was, therefore, logical to design the proposed analyser to be compatible with this equipment.

Consultation with clinical colleagues confirmed that an analyser which could detect and register the presence of the following cardiac rhythm abnormalities for 24-hour ambulatory tape recordings

would be useful in both routine clinical and research studies:

- 1 Sinus tachycardia
- 2 Sinus bradycardia
- 3 Asystole
- 4 Paroxysmal ventricular tachycardia
- 5 Paroxysmal supraventricular tachycardia
- 6 Premature ventricular extrasystoles
- 7 Premature supraventricular extrasystoles

Wide QRS complexes was added later.

It was considered important that the criteria of rate and prematurity be adjustable over a range to suit clinical requirements.

CHAPTER 5

PERFORMANCE TESTS OF RECORDER/REPLAY SYSTEM1) Routine tests of recorder, replay unit and pulse interval timer

Any form of analyser would be dependant for its success on the performance of the tape recorder, the playback deck and the associated amplifiers and pulse interval timer. It was therefore necessary to check the performance of these before designing the analyser.

The significant specifications of the commercial equipment were:

<u>MATR recorder</u>	Tape speed accuracy within 0.2% of preset value Frequency response 1 to 100 Hz
<u>Playback unit</u>	Tape speed accuracy within 0.2% of preset value
<u>Pulse interval timer</u>	None given

It was envisaged that performance testing could be divided into that which would be carried out on new apparatus, or after major overhaul, and that which could be performed regularly as a routine procedure. In the latter case it was desirable for the test to be as simple as possible, yet comprehensive.

For the routine test, the recorder, replay unit and pulse interval timer (P.I.T.) are treated as a single system. The P.I.T. is intended to generate a voltage proportional to heart rate. Therefore, if a constant frequency signal is to be recorded and replayed into the P.I.T., a steady voltage of appropriate level should be generated. Thus the three units can be checked with one test. Admittedly, if the test shows a poor overall performance the source of the problem cannot necessarily be located immediately for it could be in any of the three units.

Substitution of individual items and subsequent test recording could resolve the matter and, although this can become tedious and time-consuming, it can be done with available test equipment and be carried out by the relatively unskilled.

A Servomex type LF.141 low frequency wave-form generator was

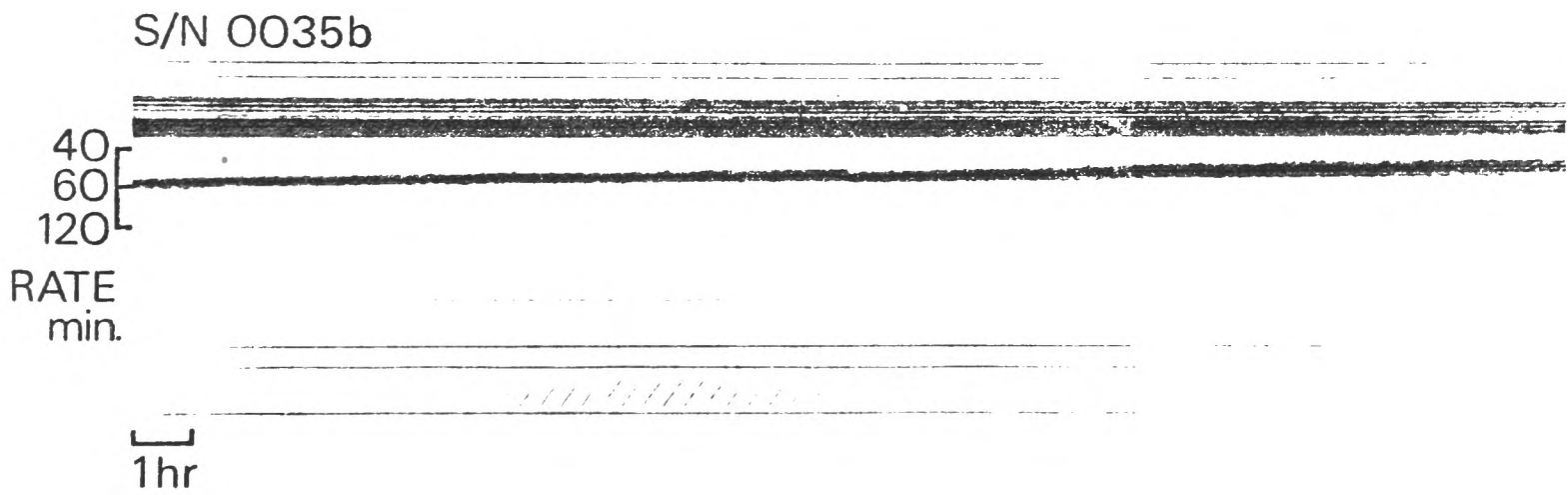
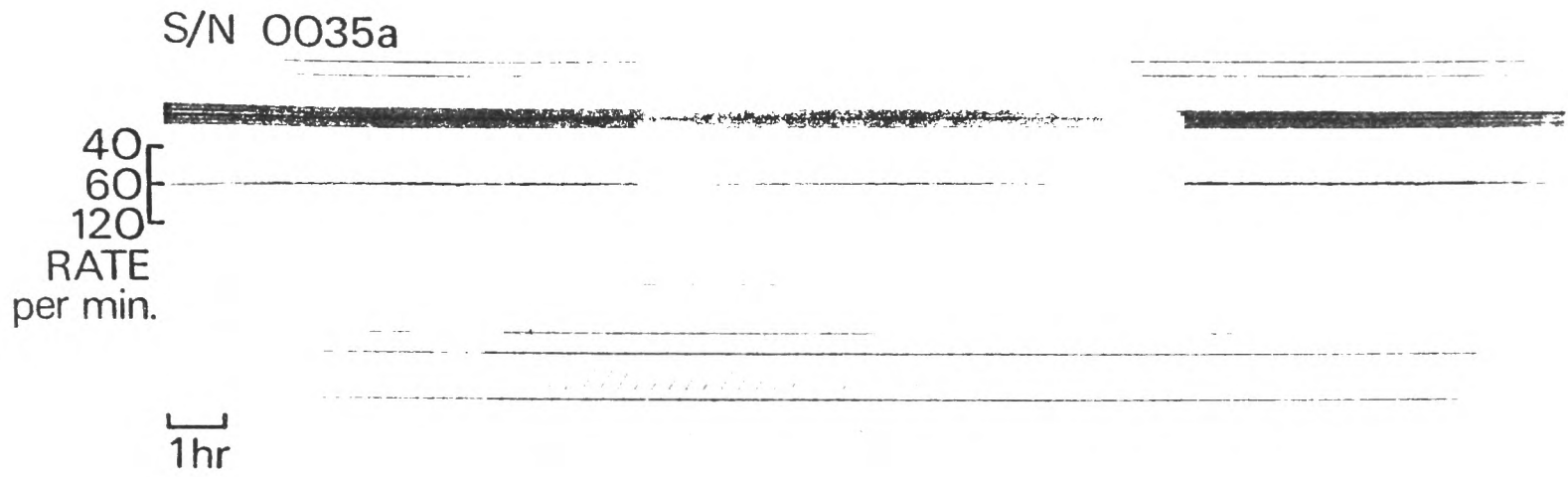


Fig. 23 24 hour recordings of simulated ECG
 Upper record shows constant satisfactory output of
 Pulse Interval Timer
 Lower record shows drift and fluctuations in rate

selected to generate a positive, symmetrical triangular pulse, 80 milliseconds wide, with an amplitude of 2 millivolts, at a rate of 60 per minute. These characteristics were chosen to approximate, within the limitations of the generator, to an R-wave complex. The specification of the LF.141 gave an accuracy of $\pm 3\%$ of the frequency selected and it was, therefore, comparable with what was considered to be a clinically insignificant variation in heart rate. In fact a calibration check of the individual instrument used showed it to have an error of 3.2% at 60 per minute but this variation was not thought to be significant. The long-term stability of the LF.141 was not given in the specification.

The frequency was therefore monitored over 24 hours, using a Racal timer/counter type 9837 which has an accuracy of ± 8 parts in 10^6 . Observed variations were $\pm 0.02\%$, which is equal to ± 0.12 beats per minute and consequently could be ignored with a clear conscience!

Figure 23 illustrates the output of the playback unit and P.I.T. made under the described test conditions. The upper record shows a satisfactory performance, whilst the lower is from a recorder in which there was tape flutter and long-term speed variation. These tests confirmed that the recorders were capable of a satisfactory mechanical performance after optimum adjustment.

Another method of tape speed monitoring is by incorporating in the recorder an oscillator generating 1 per second pulses. These are recorded on a separate channel and tape speed fluctuations detected by variations in the pulse rate on play-back.

2) Frequency response - tests of recorder and replay unit

The frequency response of recorder and play-back system were considered as a single function and measured as such. A Wavetek Model 144 HF sweep generator was used as a source of sine waves at frequencies from 0.1 to 100 Hz. These were swept automatically in three ranges,

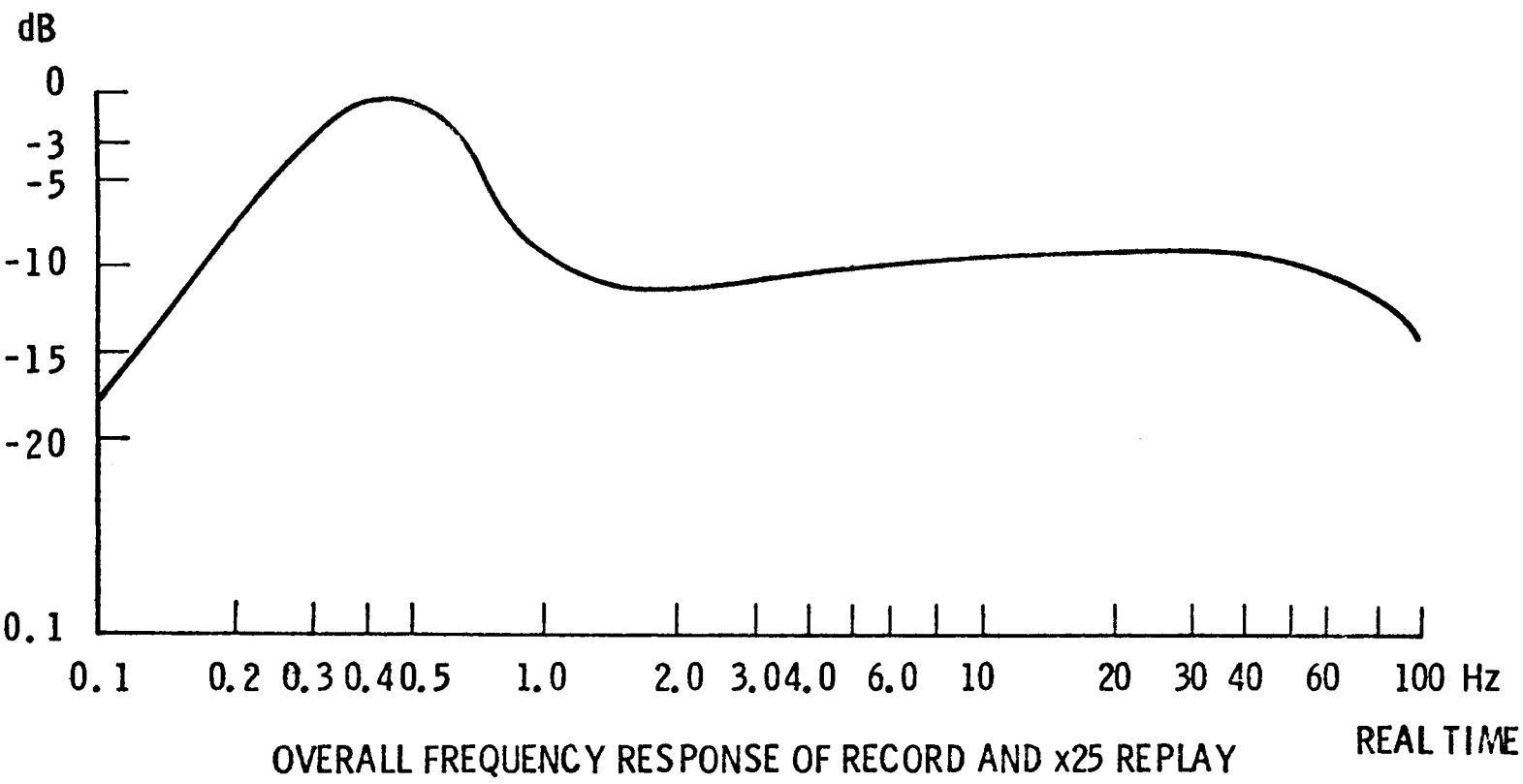


Fig. 24

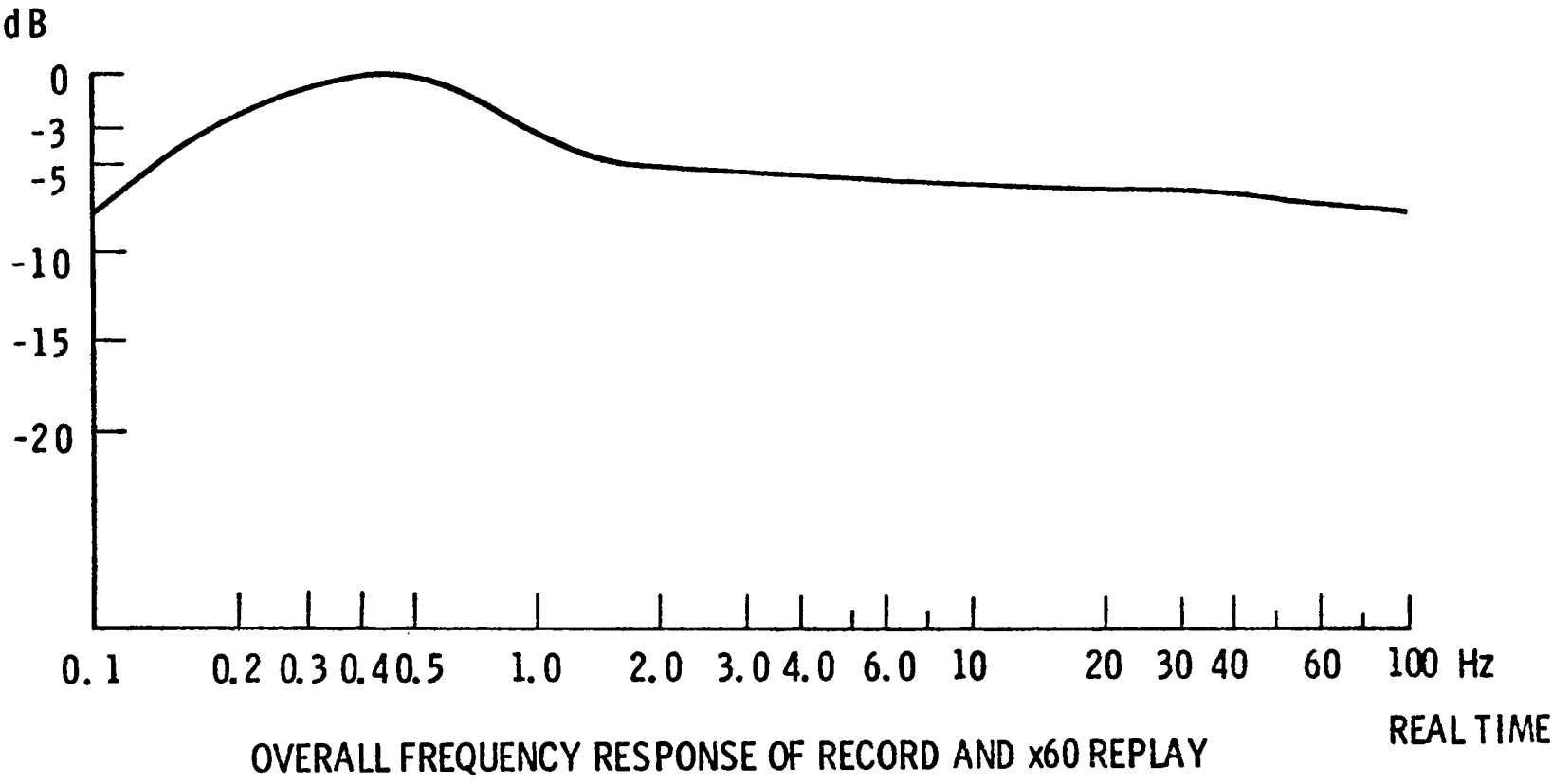


Fig. 25

0.1 to 1.0 Hz, 1.0 to 10 Hz and 10 to 100 Hz, and fed to the record amplifier of the MATR at an amplitude of 2 millivolts peak to peak.

The amplitude stability of the sweep generator was monitored on a Tektronix Model 5103N storage oscilloscope fitted with a type 5414N plug-in unit of $\pm 2\%$ accuracy, acting as a Y-amplifier. The playback unit was adjusted to replay the tape at 25 X real time. Therefore all frequencies would appear at the output at 25 X the recording value; that is, in the range 2.5 to 2500 Hz. For the output recording, and hence the frequency response measurements to be accurate, the permanent record needed to be made on an instrument capable of responding faithfully within this range.

The equipment used was a S.E. Laboratories (E.M.I.) Model 3006/DL oscillograph fitted with type S.E. 4910 amplifiers having a frequency response quoted as flat from D.C. to 5000 Hz. The type A.3300 galvanometer is described as having a response which is flat to 2000 Hz. This is an engineer's euphemism to indicate that there is probably 3 dB attenuation. This may have been a contributory factor in the fall-off in frequency response beyond 70 Hz which is illustrated in Fig.24.

In late 1976, the record-replay ratio was increased to 60:1 which raised the test-signal frequencies on replay to a maximum of 6000 Hz. This was beyond the capabilities of the galvanometers in the oscillograph so a modified test procedure was introduced in which the test frequencies were varied manually and not swept automatically, and on replay the output of the replay amplifier was fed to a Tektronix Model 5103N oscilloscope containing a type 5414N plug-in unit as a Y-amplifier. The frequency response of this oscilloscope extends to "not less than 1.0 MHz" and hence could display the replay test signals to within the overall $\pm 2\%$ accuracy of the Y-amplifier. Polaroid photographs were made at each test frequency and the overall frequency response of the record-replay units is shown in Fig. 25.

It will be seen that the low frequency response is enhanced

at the higher record-replay ratio. At both replay speeds, however, the overall frequency response is adequate for the purpose of identifying arrhythmias although it fails to satisfy the requirements of the American Heart Association (Pipberger et al, 1966) in respect of low frequency response and hence is incapable of accurately registering S-T segment deviation.

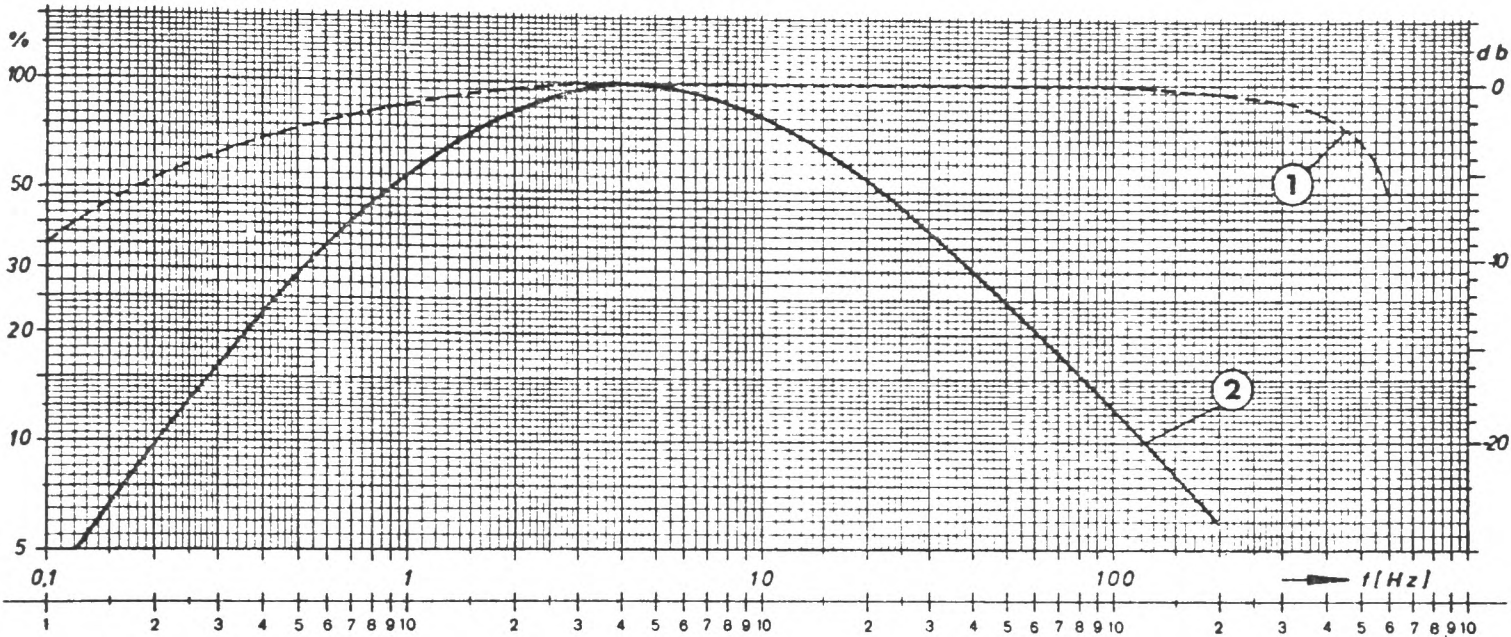
3) Measurement of tape speed variation in recorder

Apart from the frequency response of the system, analogue recordings on magnetic tape can be distorted by variations in the speed of the tape transport mechanisms. It was therefore necessary to include the measurement of such variations in the test procedures.

As mentioned earlier, it is customary to classify these variations according to frequency although there is no exact demarcation line. All generally accepted tests for quantifying tape speed variations have been devised for instruments used in the audible range of frequencies and the international standard test frequency is 3150 Hz.

It is obviously impossible to record such a frequency on the MATR but it is possible to take advantage of the record-replay ratio to provide the required frequency. If a sine wave at a frequency of 126 Hz is recorded on the MATR and replayed at 25 x recording speed, the output frequency will be the necessary 3150 Hz. Although the recorder is comparatively insensitive at 126 Hz it is possible to obtain a measurable output voltage. At a 60:1 record-replay ratio the input frequency becomes 52.5 Hz, which is well within the range of the recorder.

This technique, however, only permits the measurement of the combined speed variations in the recorder and the replay unit and it was thought preferable to measure the error in each unit separately. If the tape replay were to be made on an instrument which was devoid of any tape speed errors it would be possible to attribute any variations to



Peak voltage with and without weighting
1 Unweighted 2 Weighted according to DIN-/IEC-/ANSI-Standards

Fig. 26

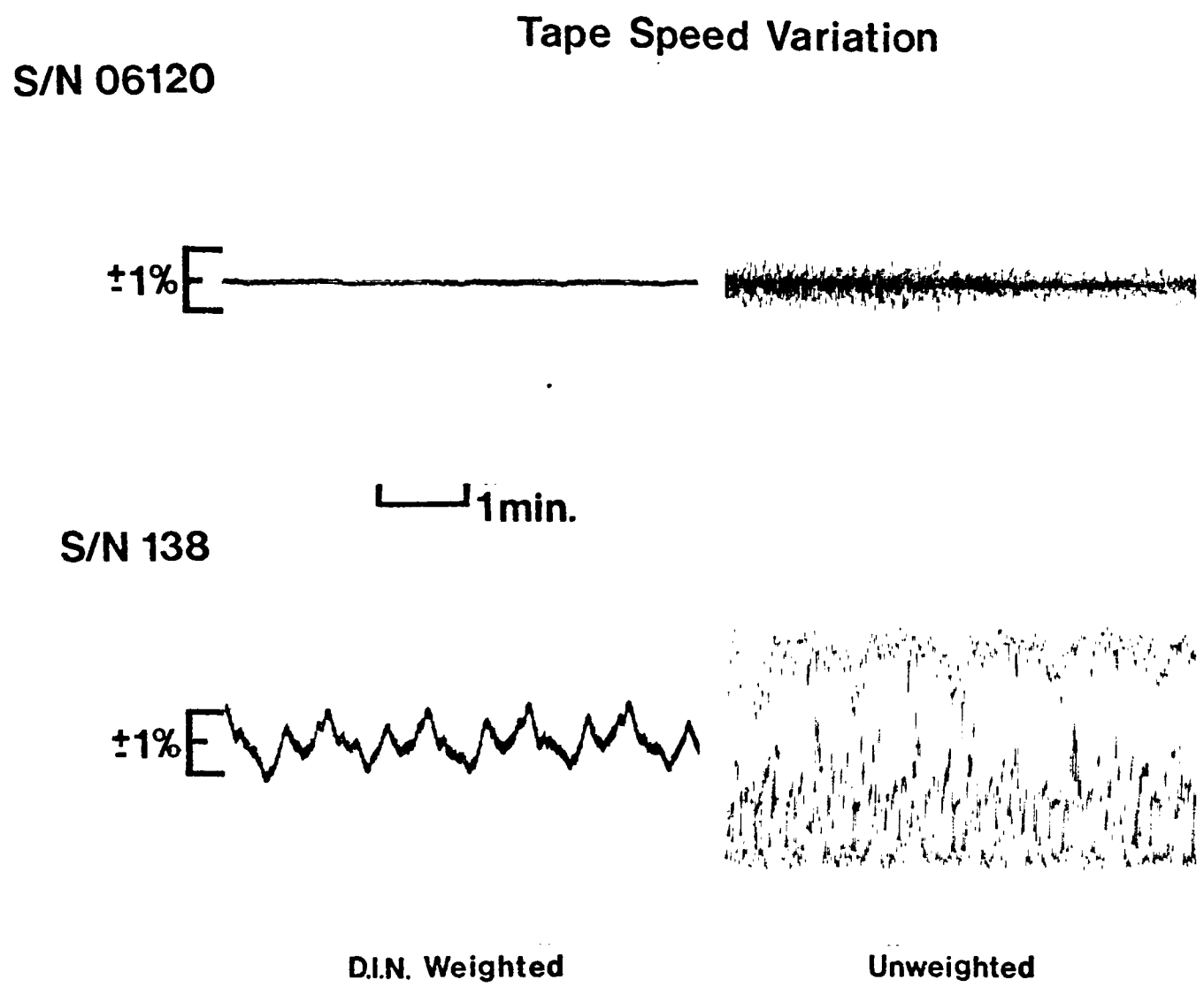


Fig. 27

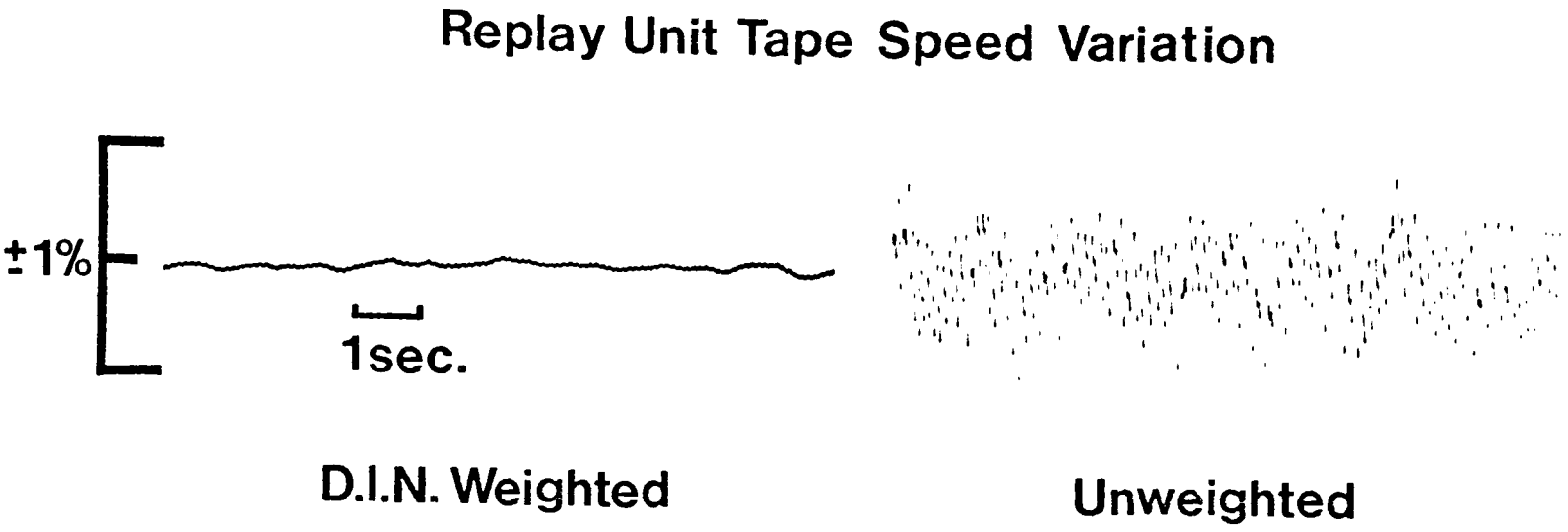


Fig. 28

the mechanism of the recorder. Unfortunately, the perfect replay unit does not exist, but it is possible to approach perfection in this context.

Through funds made available to the writer under the N.H.S. Locally Organised Research Scheme it was possible to use as a replay unit the NEAL Model 103 transcription cassette recorder which has a negligible tape speed variation of less than 0.09% R.M.S. This instrument operates at the standard tape speed of 1.875 inches per second, or 47.63 mm. per second. Replay on this unit gives a record-replay ratio of 23.8:1. Therefore, to generate the 3150 Hz required by international standards, the input frequency to the MATR needs to be approximately 132.5 Hz.

To generate this signal, a Levell type TG 66A decade oscillator which has an accuracy of $\pm 0.3\%$ at 132.5 Hz is used. A sine wave at 132.5 Hz is recorded on the MATR and then replayed on the NEAL 103 tape recorder. To quantify the tape speed fluctuations, the output of the NEAL 103 is monitored by a Woelke Magnetband Technik type ME 102C wow and flutter meter, which was also purchased with funds from the N.H.S. Locally Organised Research Scheme.

This equipment is primarily intended for use in the testing of recording equipment operating in the audible range of frequencies. Tape speed variations within two frequency bands are measurable. In the 'unweighted' mode the band covered is 0.5 to 500 Hz (-3 dB) whilst in the 'weighted' mode the range complies with the Deutsche Normen (DIN) 45507 standard of 2.0 to 15 Hz (-3 dB). (See Fig. 26). Although these ranges are not entirely appropriate to electrophysiological signals, they do however enable useful comparisons of recorders to be made as will be seen in Fig. 27. The upper traces are from a series 6000 Medilog recorder which is a development of the MATR, from which the lower traces were obtained.

4) Measurement of speed variation in play-back unit

To measure tape speed variation in the play-back deck is a relatively simple matter. If a 3150 Hz sine wave can be made available at the output of the play-back amplifier, this can be monitored by the wow and flutter meter in the manner described for testing the MATR. By making a recording on the NEAL 103 tape recorder a "master tape" with negligible wow and flutter can be produced. If this is replayed on the Oxford Electronics Instruments Company replay unit, virtually all of any detected wow and flutter will be attributable to variation in the tape speed of this unit.

As mentioned earlier, the NEAL 103 recorder operates at 47.63 mm/sec. whilst the Oxford Electronics Instruments Company unit is driven at either 50 mm/sec. (25:1 record-replay ratio) or 120 mm/sec. (60:1 record-replay ratio). If a frequency of 3000 Hz or 1250 Hz respectively is recorded on the master tape, this when replayed will provide the requisite 3150 Hz test frequency. Using this method a typical result is shown in Fig. 28. There was virtually no tape speed variation in the DIN 'weighted' mode.

5) Linearity test of Pulse Interval Timer

Unlike the recorders and the play-back unit, the P.I.T. contains no mechanical parts susceptible to wear. Consequently, apart from an initial calibration test, the P.I.T. does not need routine checks.

For calibration purposes, a simulated R-wave of 1 volt amplitude and 3 milliseconds duration was generated by the Servomex LF.141 wave-form generator whose performance has previously been described (Chapter 5.1). Pulses at repetition rates of from 16.6 Hz to 100 Hz were generated corresponding to 25:1 record-replay ratio to heart rates of from 40 to 240 beats per minute. These were fed to the input of the P.I.T. whose output was measured on a Keithley Model 168 digital multimeter, which has

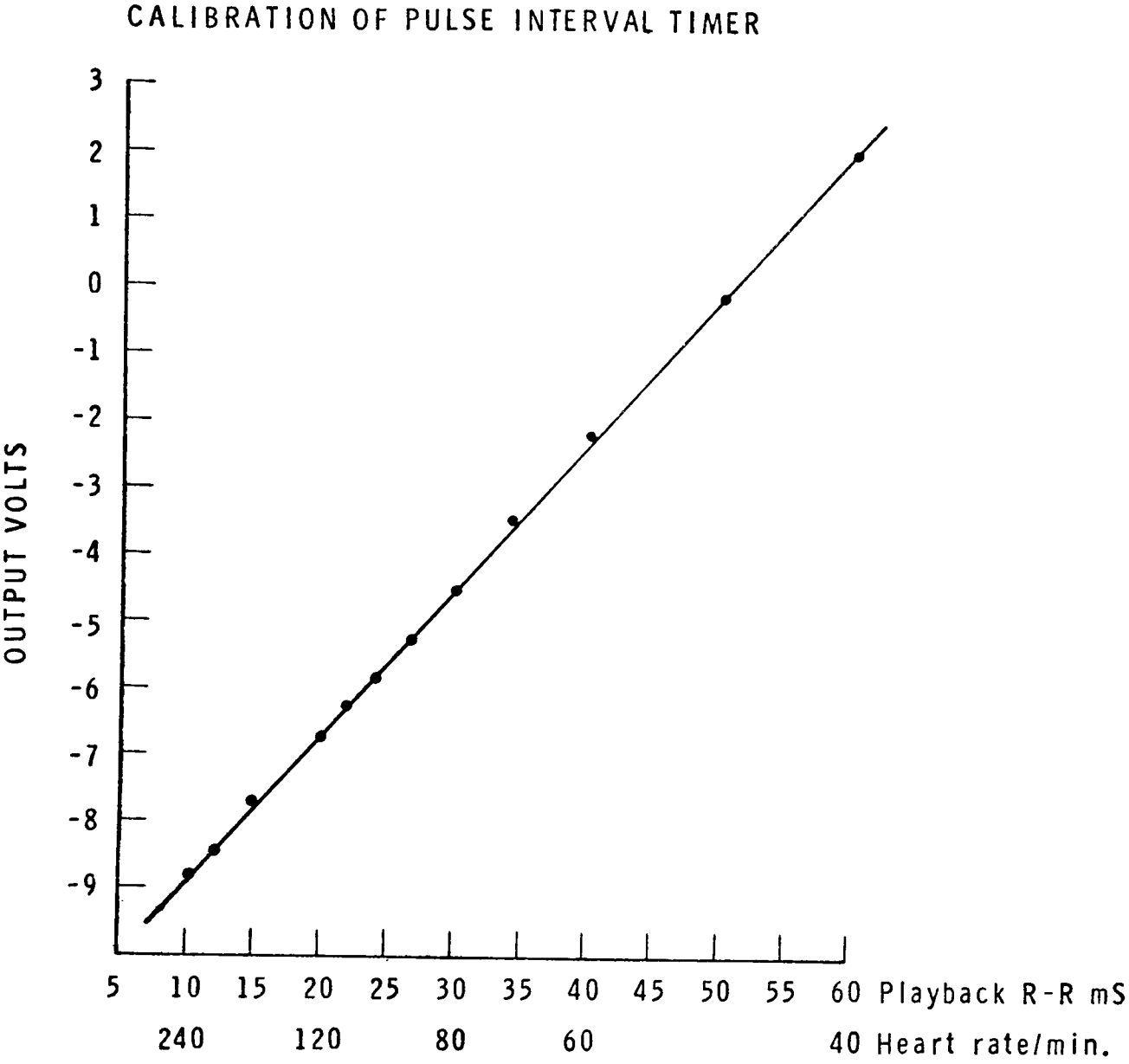
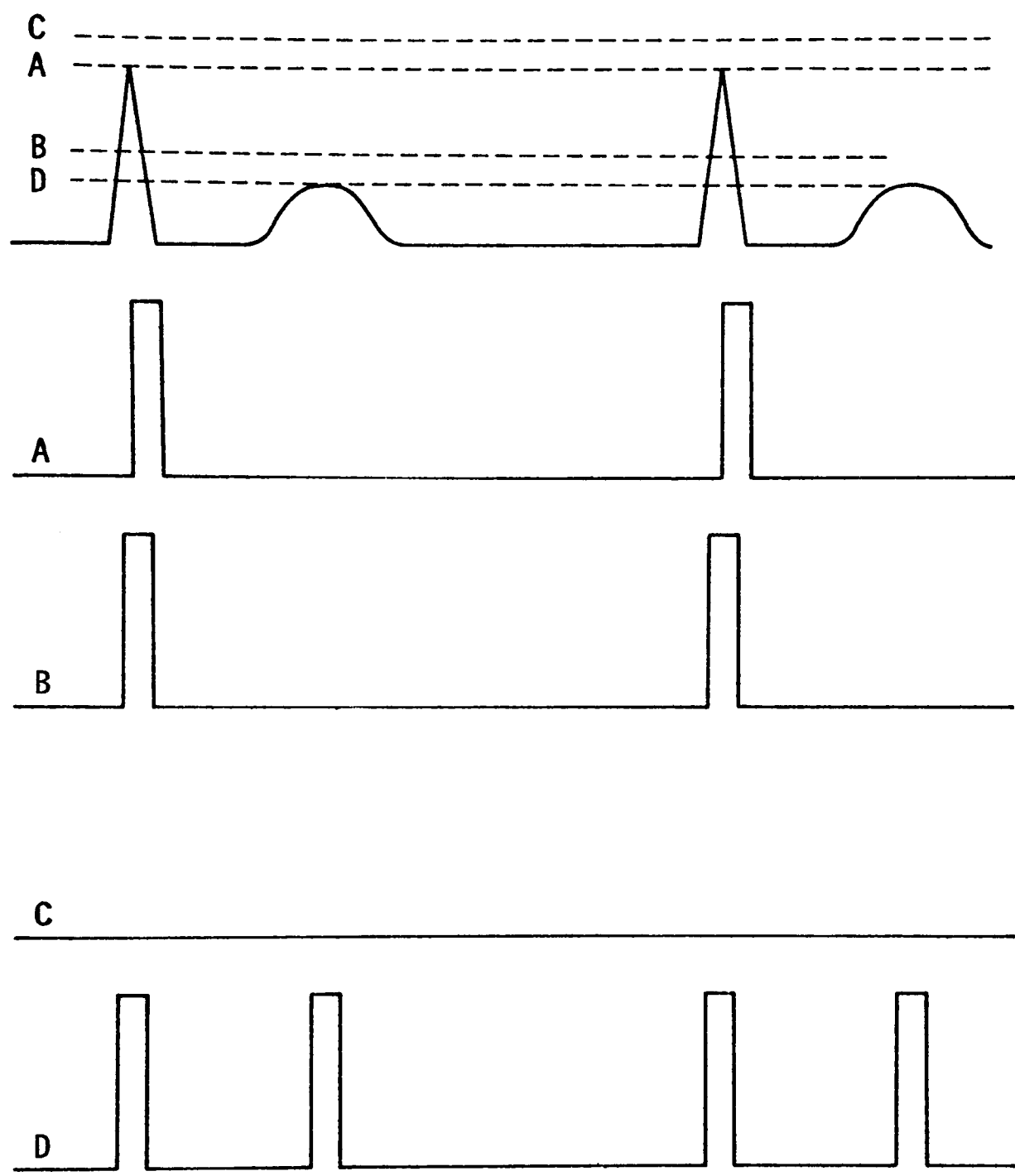


Fig. 29



Pulse interval timer trigger pulses

A, B, C, D indicate different trigger levels and the corresponding generation of trigger pulses

Fig. 30

an accuracy of $\pm 0.1\%$ of recording the range. The results of this test are shown in Fig. 29.

Subsequently the record-replay ratio of the system was raised to 60:1 and a new, non-commercial pulse interval timer was designed and built. The calibration graph of this unit is given in Appendix A with the circuit diagram.

It may appear pedantic to have subjected the recorder and play-back system to these tests. The reason was that the requirements of the proposed analyser could make more stringent demands on them than the designers would have anticipated.

6) The effect of trigger level on P.I.T. accuracy

In the pulse interval timer, each QRS complex generates a constant amplitude trigger pulse which, in turn, controls the operation of the analyser circuits as described in Appendix A. A trigger pulse is produced whenever the amplitude, positive or negative, exceeds a preset level. To accommodate a range of QRS voltage, this preset level is adjustable by an external control.

An obvious possible source of error in such a simple analogue approach is that, if the preset level is too low, the trigger pulse will be generated before the peak voltage of the QRS (Fig. 30). To have adopted the more elegant and sophisticated approach of, for instance, using the value and sign of the first derivative of the QRS as previously described (Caceres et al, 1962) would have been incongruously expensive and complex for a system whose main claim to be of value is based on simplicity and low cost.

Because the analyser was to be an interactive one in which the operator would adjust the controls to suit the input characteristics of each incoming record, it was necessary to include the operator in any

test of the accuracy of the pulse interval timer. For clinical purposes an error equivalent to ± 2 beats per minute at a heart rate of 75 beats per minute was thought to be acceptable. This is equivalent to approximately ± 22 milliseconds variation in R-R interval which, in turn, at 25 x real time replay $\approx \pm 1$ millisecond. At a heart rate of 120 beats per minute, the equivalent values at replay would be $\approx \pm 8$ milliseconds and ± 0.3 milliseconds respectively. Therefore any measurement of the performance of the pulse interval timer would need to be capable of resolving these values.

Ideally, a series of QRS complexes and the associated trigger pulses would be recorded at high speed on some permanent medium and the corresponding intervals compared. Unfortunately, the only high-speed recorder available, the S.E. Laboratories (E.M.I.) model 3006/DL, previously described, has a maximum recording speed of 1250 mm/second, which is equivalent to 50 mm/second at 25 x replay speed.

If it is accepted that one could not measure intervals to an accuracy of less than one millimetre, this would imply that measurements of less than 20 milliseconds would not be practical. Whilst these figures would be adequate at heart rates of 75 beats per minute, or less, they would not suffice at higher rates.

The only other method available was that of displaying the QRS and trigger pulses on an oscilloscope and taking Polaroid photographs of the trace. A Tektronix type 5103N storage oscilloscope was used with time-base running at the maximum calibrated speed which would enable two QRS complexes to be displayed, dependant on the heart rate. This was generally either 2 or 5 milliseconds per centimetre. The Polaroid photograph gave a reduction ratio of 0.8:1 but it was still feasible to measure to an accuracy of ± 5 milliseconds at heart rates of around 120 per minute. The tolerance of 2% on the accuracy of the time-base

calibration of the oscilloscope was not sufficient to affect the calculations significantly.

Method Twenty-five tape recordings were selected at random from departmental files, every tenth cassette being replayed on to the oscilloscope after the trigger level had been adjusted to its optimal level by the operator. All the records were from patients basically in sinus rhythm with heart rates ranging from 62 to 110 beats per minute. In seven cases premature ventricular extrasystoles were recorded and one showed atrial extrasystoles. The R-R interval and the interval between the upstrokes of the corresponding trigger pulses were measured by eye, aided by optical magnification.

Within the limits of accuracy mentioned previously, no difference could be detected between the duration of the R-R interval and that between trigger pulses. This applied both when the interval was between two sinus beats or between a sinus beat and an extrasystole.

From these results it was concluded that when the trigger level was adjusted by a competent operator, the interval between trigger pulses reflected the corresponding R-R interval with an accuracy adequate for clinical use. There was sufficient tolerance in the preset trigger level for the operator to be aware of any significant maladjustment. Too high a trigger level would manifest itself by erratic generation of trigger pulses whilst too low a level would cause trigger pulses to be initiated by T-waves.

CHAPTER 6

MEASUREMENT OF THE FREQUENCY SPECTRA OF NORMAL AND ABNORMAL QRS COMPLEX1) Problems with physiological wave-forms

Electrical signals composed of different frequencies can be separated by filter-circuits. The accuracy of the segregation is, however, dependant mainly on the frequency spectra of the electrical signals and the characteristics of the filters. Using modern integrated circuits, filters can be constructed to almost any specification but any attempt to use them to separate ventricular extrasystoles from sinus beats would be hindered by the extremely sparse amount of information available concerning the frequency content of the former. It was, therefore, felt essential that some measurements of this parameter be attempted before the arrhythmia analyser was built.

The frequency content of electrical signals is generally measured by either a wave analyser or a spectrum (Fourier) analyser; the former is virtually a tuned voltmeter which measures the energy present in a given wave-form within specific frequency bands. The second type of analyser sweeps through a series of frequency bands covering the range of the signal being studied and displaying on an oscilloscope how the energy present in the signal is distributed as a function of frequency.

The resolution in either method is dependant on the width of the frequency band of the analyser; the narrower the band the better the resolution but the greater the number of steps required to sweep through the frequency range of the signal and to complete the analysis.

Obviously the signal must be present at the input of the analyser throughout the duration of the analyses which may be many times

longer than one cycle of the signal. Most analysers are intended to deal with repetitive, constant signals where this requirement presents no problem. Unfortunately, from the point of view of frequency analysis, extrasystoles occur more or less at random and are interposed amongst complexes with different frequency characteristics. Only in paroxysmal ventricular tachycardia might the same wave-form persist long enough for the analyser to build up the frequency spectrum.

The only alternative method of using equipment available at the time (1974) would have been to carry out the Fourier analysis "by hand". A method was devised by which QRS complexes from conventionally recorded ECGs would be enlarged photographically and their duration normalised to represent 1 second from the true values of possibly 80 to 150 milliseconds. This normalisation would enable the subsequent constituent harmonics to be expressed in Hz. To cover an adequate range of harmonics some 100 X-Y co-ordinates would have had to be measured across each QRS complex - a daunting prospect, even with a Hewlett Packard programmable calculator available to process the data. The idea of repeating the process on perhaps 100 to 200 complexes was too intimidating to be considered.

By 1975 a short-duration digital store had been built as a prototype sub-unit for the proposed arrhythmia analyser. This was used experimentally to store a single ECG complex whose R-wave was, in turn, used to trigger a variable delay circuit which was able to isolate a portion of the next ECG complex.

Using this facility, attempts were made to store an isolated QRS complex on magnetic tape and to recycle it through a spectrum analyser and so satisfy the requirements previously mentioned.

Numerous problems became evident. Firstly, it was difficult to avoid discontinuities in the base-line at each side of the isolated complex. These artifacts were seen by the analyser as square waves which

converted into a series of harmonics as might have been expected from Fourier's theorem. The extraneous contributions were often quite dominant and made the interpretation of the frequency distribution unreliable.

A second difficulty was encountered when non-standard tape recorder record-replay ratios were needed to effect the normalisation referred to earlier.

2) The empirical approach

The empirical approach of constructing filters whose characteristics would be based on intelligent guesswork appeared to be the only solution even though this was unsatisfactory from the scientific point of view. The assumptions of Karlsson et al (1970) had apparently produced an effective real-time system, so it was decided to design two band pass filters with centre frequencies at approximately 8 Hz and 20 Hz real-time; that is, at 200 Hz and 500 Hz for a system which would analyse at 25 x real time.

To retain the concepts of cheapness and simplicity, it was decided to use, in cascade, high and low pass active filters based on the type 741 operational amplifier. An ideal filter would be one which transmitted 100% of the frequencies in its pass band and 0% of all other frequencies. This can never be realised in practice with analogue filters and consequently it is customary to describe such filters by the frequency or frequencies at which the transmission has dropped to 70% of its maximum. The rate at which the attenuation changes with frequency is also generally given. Attenuation is often measured over a range of 10,000:1 so it is less cumbersome to use a logarithmic unit to express the value. The original unit, the "bel", is large and has been replaced by one 1/10th the size, the decibel (dB). In all the references to the dB in this thesis it represents $20 \times \log_{10} \text{Voltage out} / \text{Voltage in}$. The rate of attenuation is also generally expressed using the dB, either as dB/octave

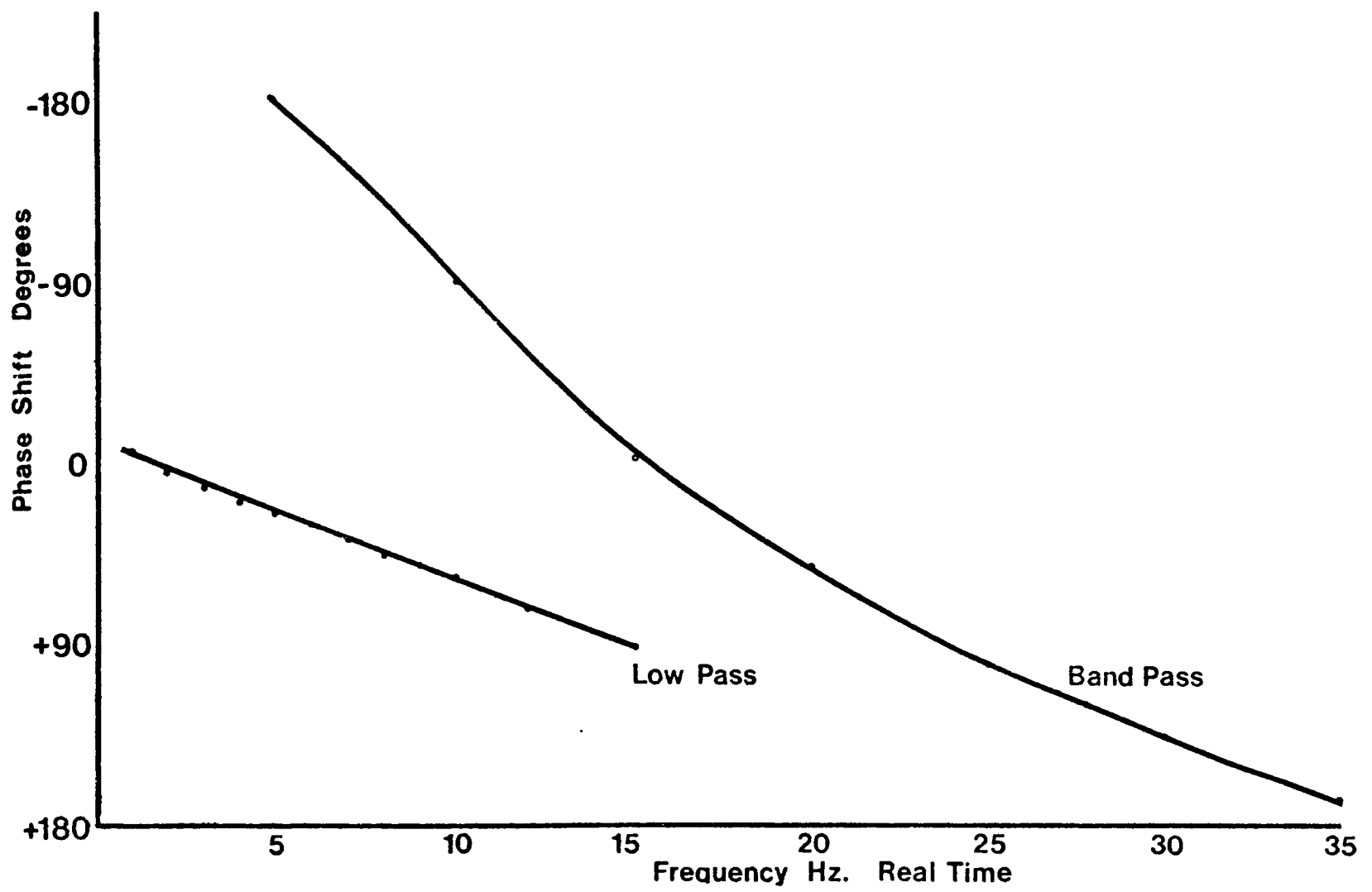


Fig. 31 Phase shift of QRS analyser filter (3)

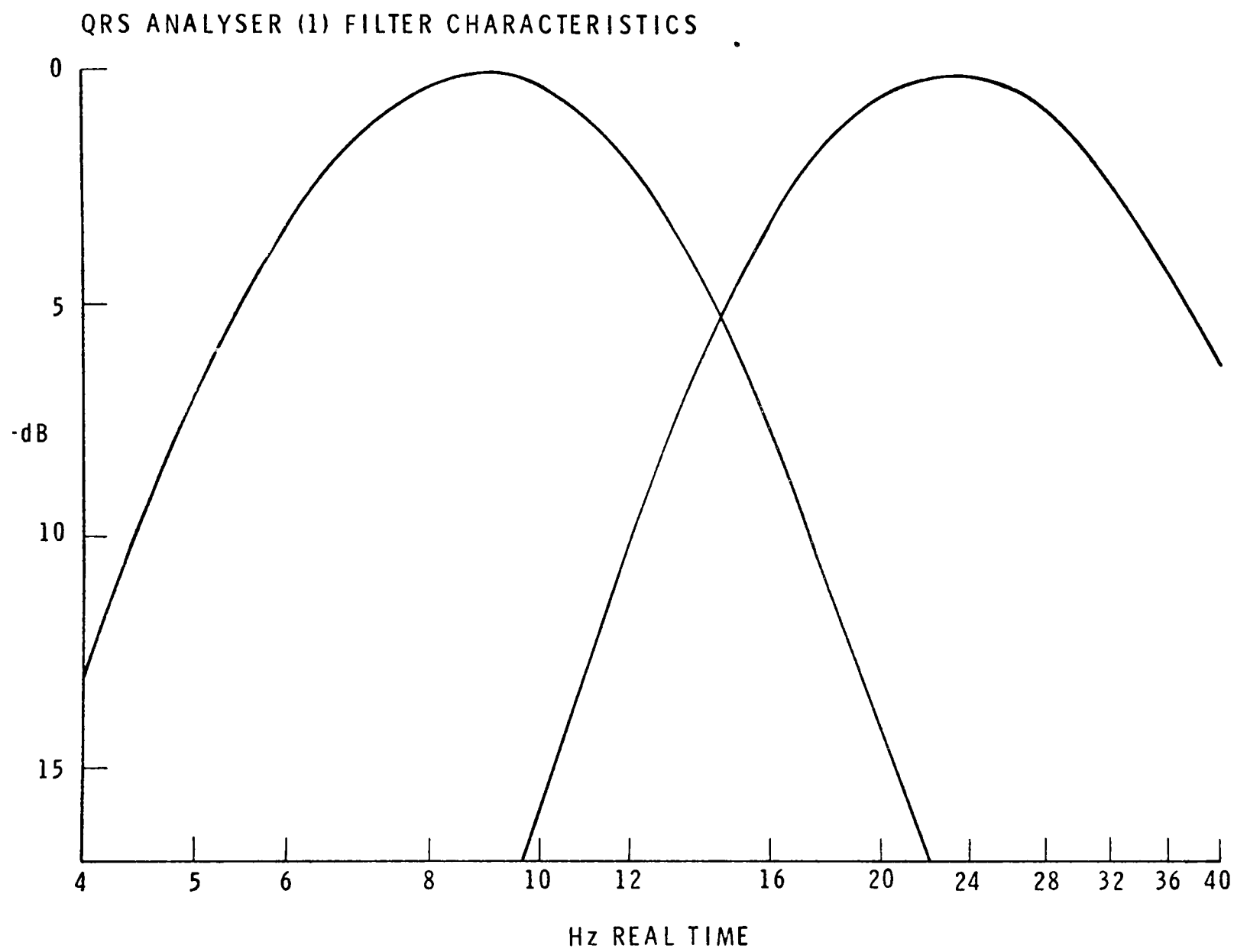


Fig. 32

or dB/decade. The former is used throughout this thesis.

The basic filter "building brick" used throughout the analyser is derived from the second order version of the circuit described by Sallen and Key (1955), which has a gain of unity within its pass band and a theoretical attenuation of 12 dB/octave beyond the cut-off frequency. Due to tolerances in component values, however, the full rate of attenuation may not be achieved in practice. There are two main active filter derivatives of the Sallen and Key method, those of Butterworth and Chebyshev. The former has the advantage of a flat amplitude response within its pass band, the latter the advantage of a more rapid rate of attenuation at increasing frequency but the disadvantage of considerable cyclical variations in amplitude within its pass band.

The Butterworth version was chosen because, whilst an increased rate of attenuation could be achieved by using a pair of second order filters of this type, in series, the amplitude variations inherent in the Chebyshev design could not be overcome.

The phase shift produced by the filter has not been found to be a problem in practice. The phase shift characteristics of the filters described in Appendix A are shown in Fig. 31. These were measured on a Philips type GM 5639 X-Y oscilloscope which is designed for phase shift measurement and has an inherent phase shift of not more than 2° between its X and Y amplifiers. Test frequencies were provided by the Servomex LF.141 wave-form generator described in Chapter 5.1.

The first version of complete filter for the analyser was composed of two band pass filters, each comprising two second order high pass filters and two second order low pass filters in series. The frequency response of this compound filter is shown in Fig. 32 and the circuit is given in Appendix A. Ironically, this filter was never to be used. Before the remainder of the analyser had been designed and built

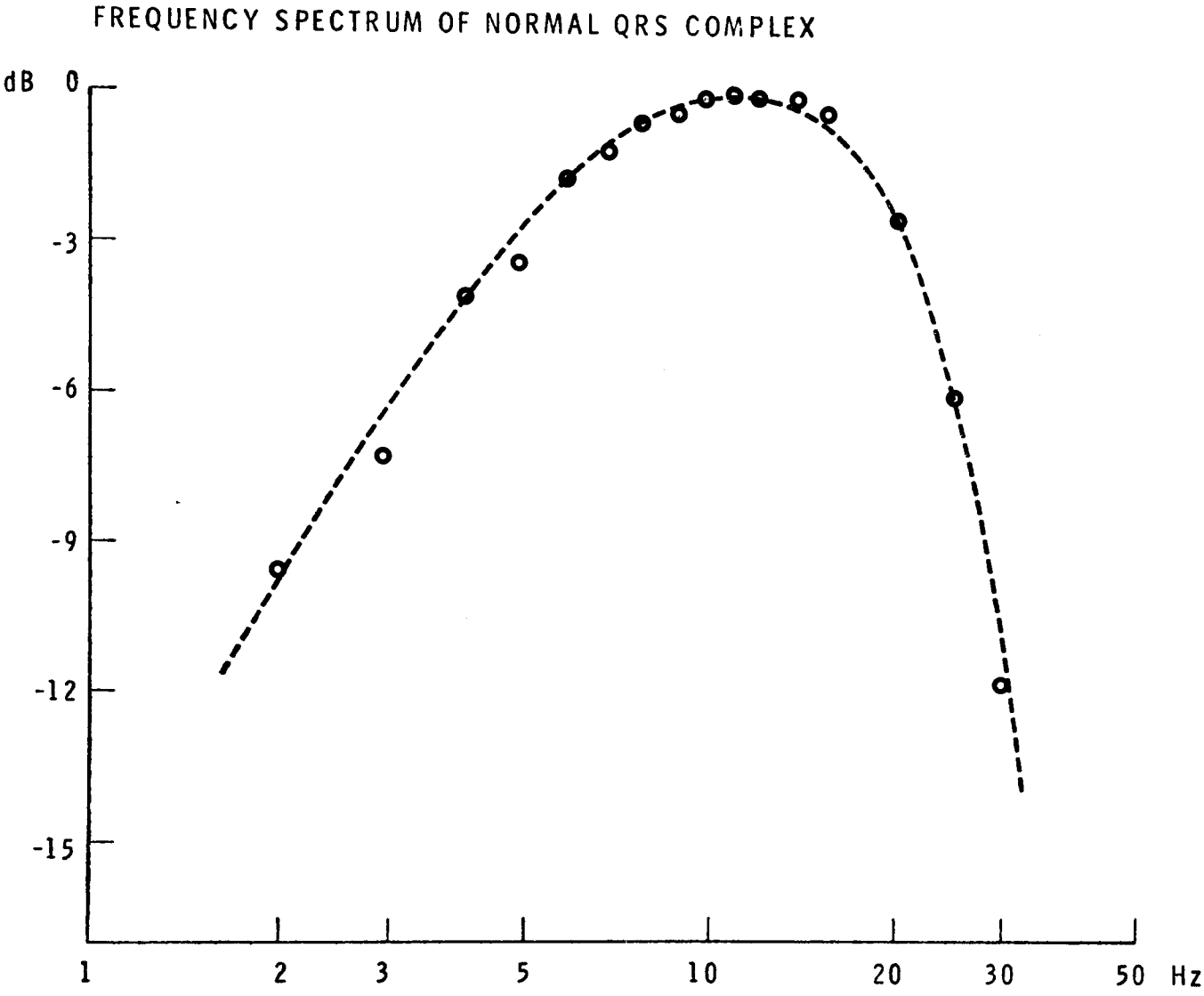


Fig. 33

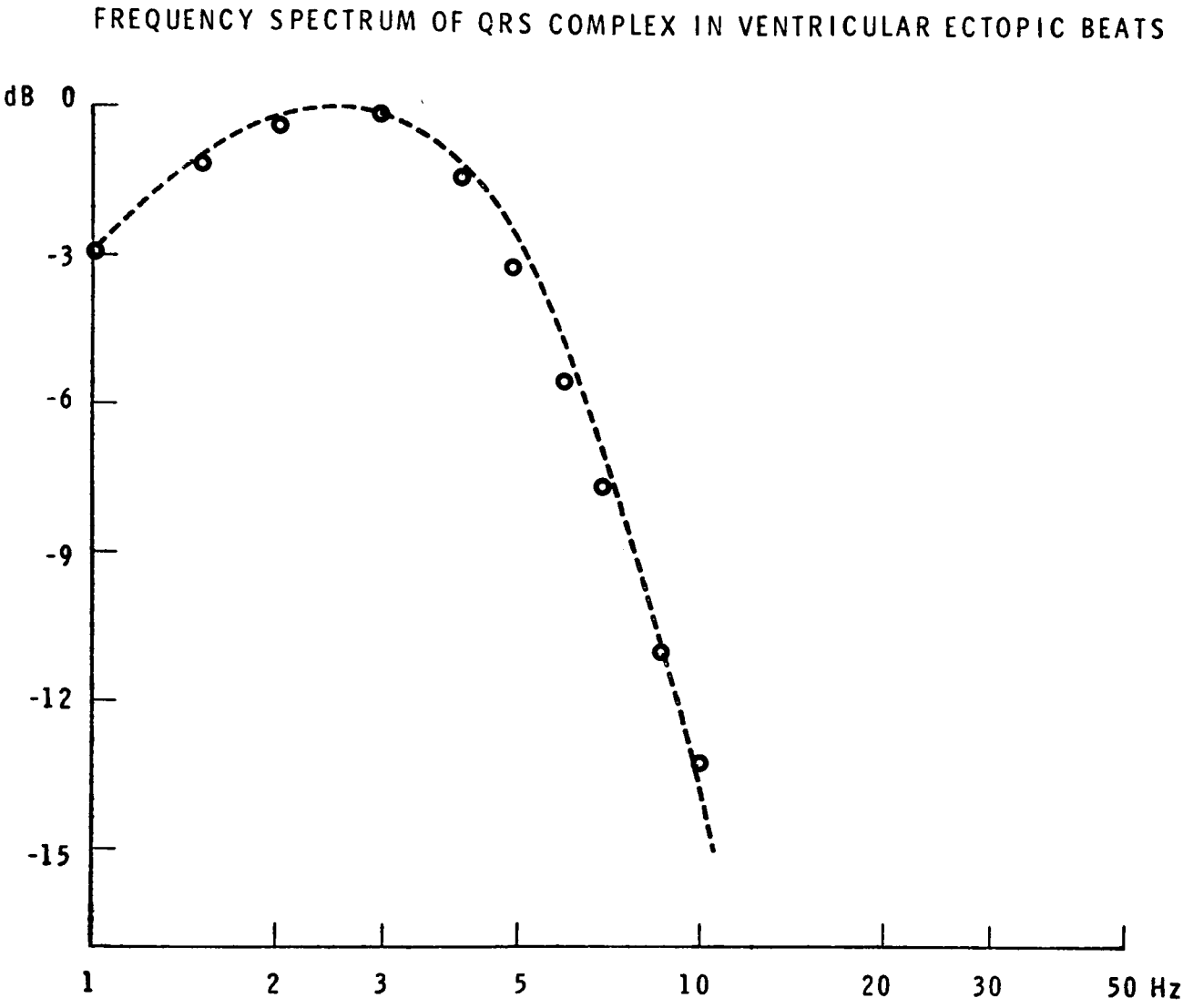


Fig. 34

an opportunity occurred to collect more information concerning the frequency content of normal and abnormal QRS complexes.

3) Computer analysis of the frequency spectrum of the QRS

The work of Curtis et al (1972) at the Atomic Energy Research Establishment in which they had studied the frequency spectrum of the complete ECG complex had produced little of clinical use. They had searched for spectra which could be linked uniquely with various cardiac rhythms but had been unsuccessful. There was, however, in the description of their methods much to indicate that these could be adapted to provide the elusive information about QRS complexes. The possibility of using the Harwell technique was discussed with Dr. Curtis and his colleagues and it appeared that their computer software and peripherals could be used to isolate the QRS from the complete ECG complex and perform a Fourier analysis of this section.

Through the courtesy of Dr. Gardener, of A.E.R.E. a series of normal beats and ventricular extrasystoles from ten subjects was analysed on a P.D.P.8/I computer. The problem of base-line discontinuity was again encountered but the speed of the Fast Fourier Transform Program made it possible to discard spectra which contained artifacts due to discontinuity but still retain a sufficient number of usable records from the subjects. Due to limited time, however, only two or three complexes, including an extrasystole, from each subject could be analysed. The results of this exercise were averaged and the frequency spectra are shown in Figs. 33 and 34.

These indicated that the QRS complexes from ventricular extrasystoles have a frequency spectrum with a peak at 2.8 Hz and that the QRS complexes in normal sinus beats have a frequency spectrum with a peak at 12.9 Hz. The ECGs from which these data were collected were

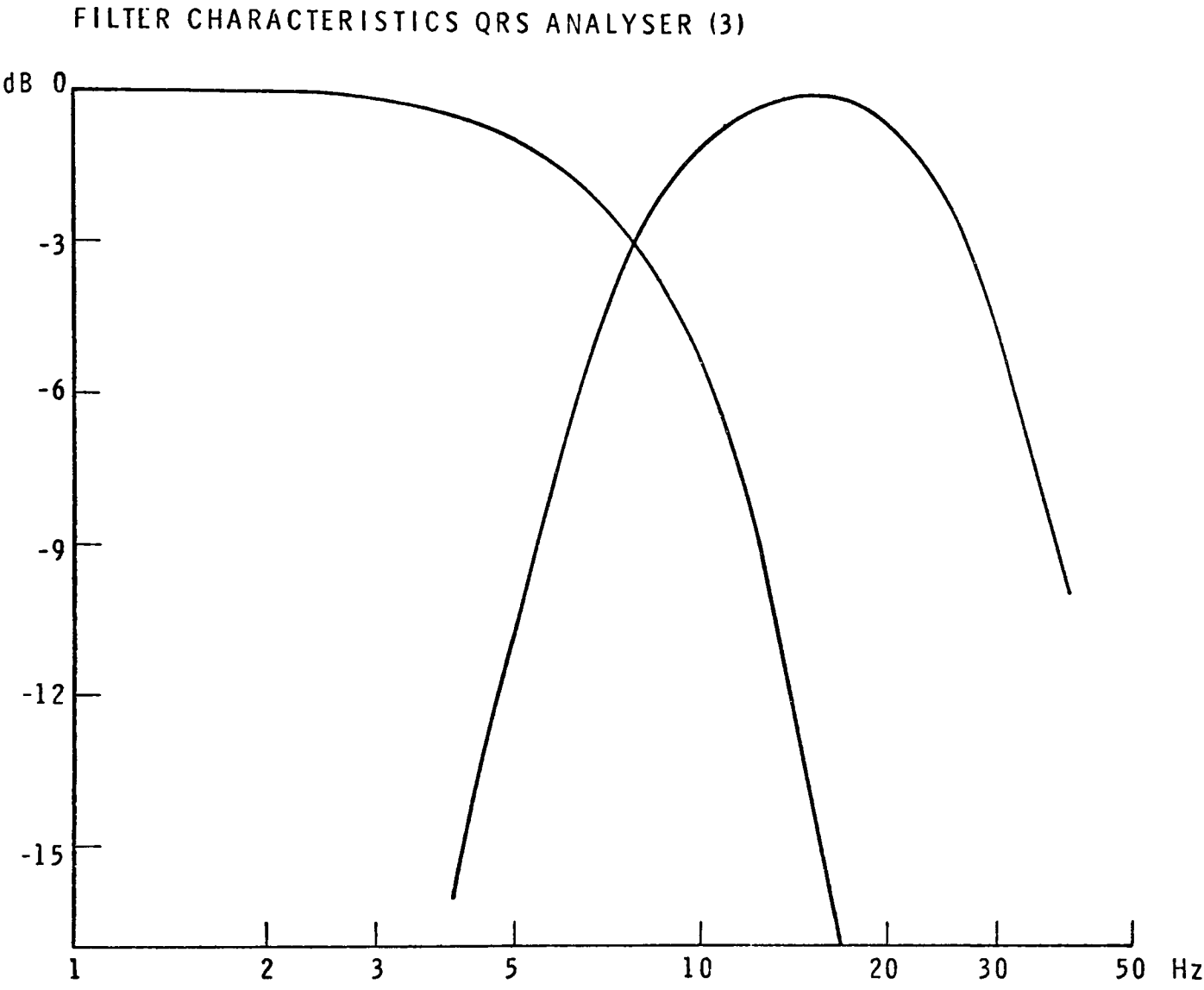


Fig. 35

recorded with an Oxford Instruments Medilog system whose frequency response has been given earlier. From this it seems likely that the recorder will have attenuated frequencies at the top and bottom of the frequency range; that is, below 0.4 Hz and above 40 Hz. Neither of these ranges, however, is within the significant portions of the two QRS frequency spectra. With these results available it was decided to modify the characteristics of the original filter. (Fig. 35).

4) Analysis of the frequency spectrum of the QRS using an analogue filter

The limited size of the sample which had been analysed by the Harwell computer made it seem desirable to augment it by a further study, especially as the data which had been obtained appeared to contain new information.

As further computer time on a suitable system was not forthcoming, it was necessary to search for another method. A variable dual channel analogue filter (Rocklands Systems Corporation model 452) had become available and it seemed possible that this could be used as a rather crude but possibly adequate spectrum analyser which would not have the need for a continuous input signal as described previously.

The Model 452 filter is composed of two identical sections, each of which can act as a high or low pass filter having an attenuation of 24 dB/octave. A band pass filter can be formed if the two sections are connected in series with the first operating in the high pass mode and the second in the low pass mode. A filter with the narrowest pass band is achieved when both sections are turned to the same frequency. If the centre frequency of the pass band is termed f_0 then signals with frequencies $\frac{1}{2}f_0$ and $2f_0$ will be attenuated by 24 dB. With Model 452 operating in this mode there is an additional overall attenuation (termed insertion loss) of 6 dB. As this affects all frequencies identically it

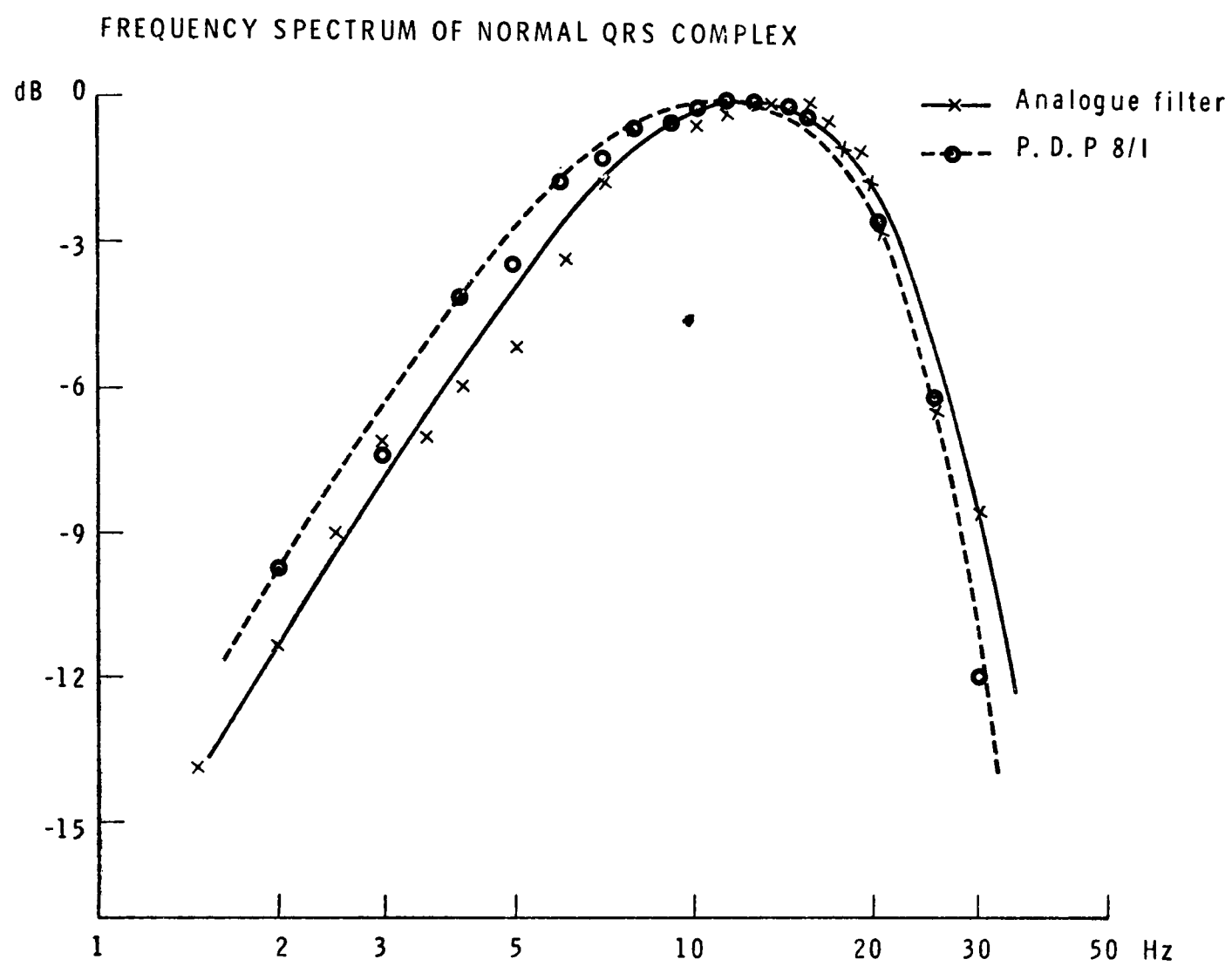


Fig. 36

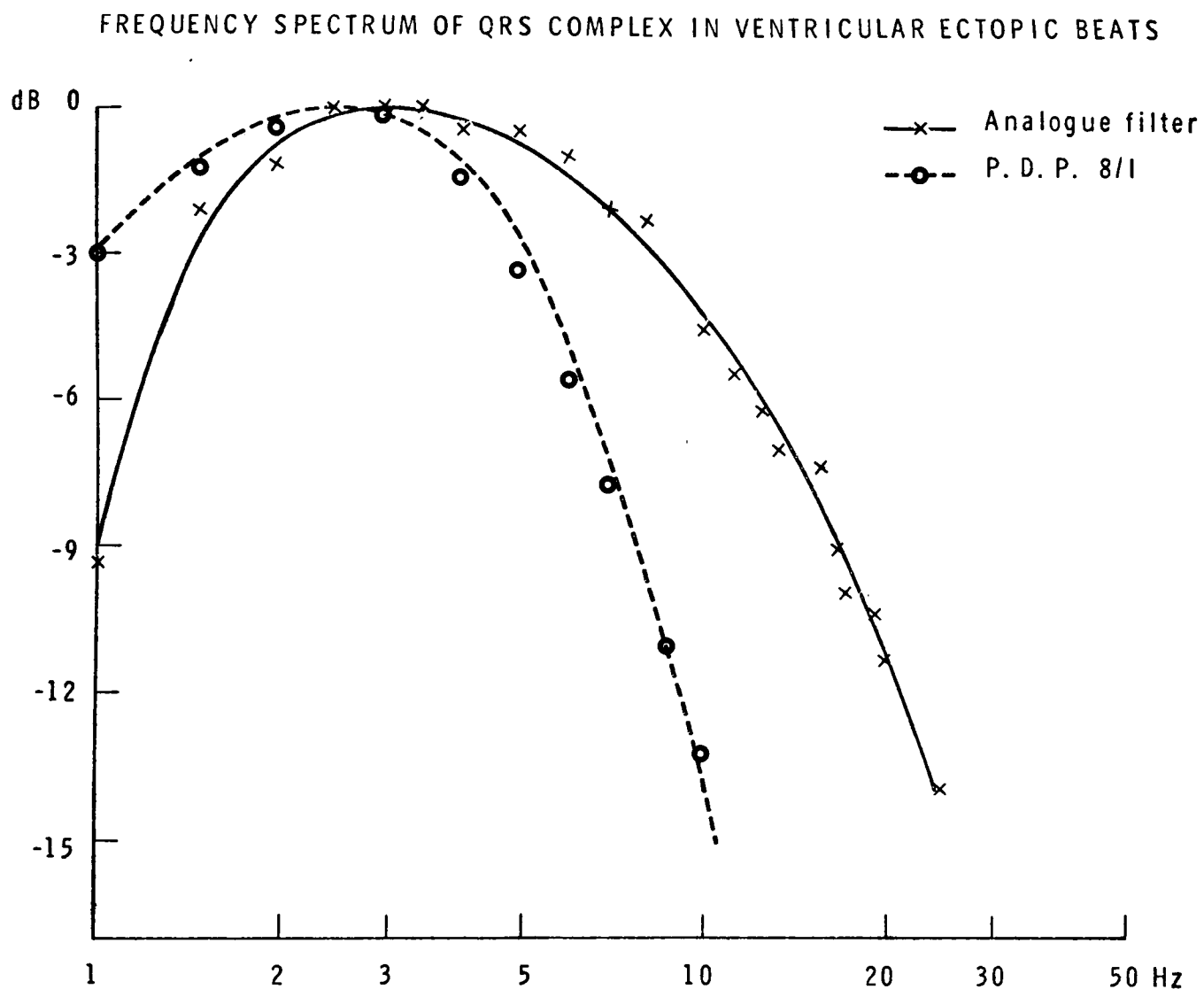


Fig. 37

does not contribute to the filter action and can be compensated for by additional amplification.

If a tape recording of the ECG were to be replayed on to a chart recorder via the filter there would be selective attenuation of the component frequencies present in the ECG. If the process were to be repeated with different values for the centre frequency of the filter pass band, termed f_0 , the varying degrees of attenuation of the QRS complex would indicate the frequencies present in this wave-form. A graph of relative amplitude of wave-form against f_0 would produce a frequency spectrum which it was hoped would supplement the data obtained with the P.D.P.8/I.

Tape recordings of the ECG from 20 subjects who were known to have frequent ventricular extrasystoles were selected at random and were replayed at 25 x real time into the Model 452 filter operating as described above. The value of f_0 was increased in steps over the range 0.5 Hz to 30 Hz real time, in increments of 0.5 Hz from $f_0 = 0.5$ Hz to $f_0 = 5$ Hz, in increments of 1 Hz from $f_0 = 5$ Hz to $f_0 = 15$ Hz and in increments of 5 Hz from $f_0 = 15$ Hz to $f_0 = 30$ Hz. With each subject the same series of four sinus beats and four extrasystoles was recorded via the filter at all values of f_0 .

At a replay speed of 25 x real time the frequency range of the ECG is approximately 2.5 Hz to 1.5 KHz. Therefore, to avoid any spurious attenuation of the recorded output of the filter, it was necessary to use a high frequency oscillograph and amplifiers. The system used was the S.E. Laboratories (E.M.I.) type 3006 DL fitted with A.3300 galvanometers which have a flat response $\pm 5\%$ from D.C. to 2.0 KHz and a natural frequency of 3.3 KHz. The galvanometers were driven by type S.E. 4910 D.C. medical amplifiers having a flat response from D.C. to 5.0 KHz.

The amplitude of each of the sinus and extrasystole QRS complexes was measured and an average found for each subject and at each f_0 . The values were normalised and composite graphs constructed for sinus beats and for ventricular extrasystoles. (Figs. 36 and 37).

The peak frequency present in the QRS for sinus beats was estimated to have a mean value of 13.1 Hz (S.D.=1.77 Hz) whilst for ventricular extrasystoles the values were 3.8 Hz (S.D.=1.41). The equivalent values obtained from the computer analysis were 12.9 Hz (S.D.=1.24) and 2.8 Hz (S.D.=1.59) respectively.

CHAPTER 7

THE ARRHYTHMIA ANALYSER - BASIC CIRCUIT DESCRIPTION

1) Bradycardia, tachycardia, gap and prematurity detection

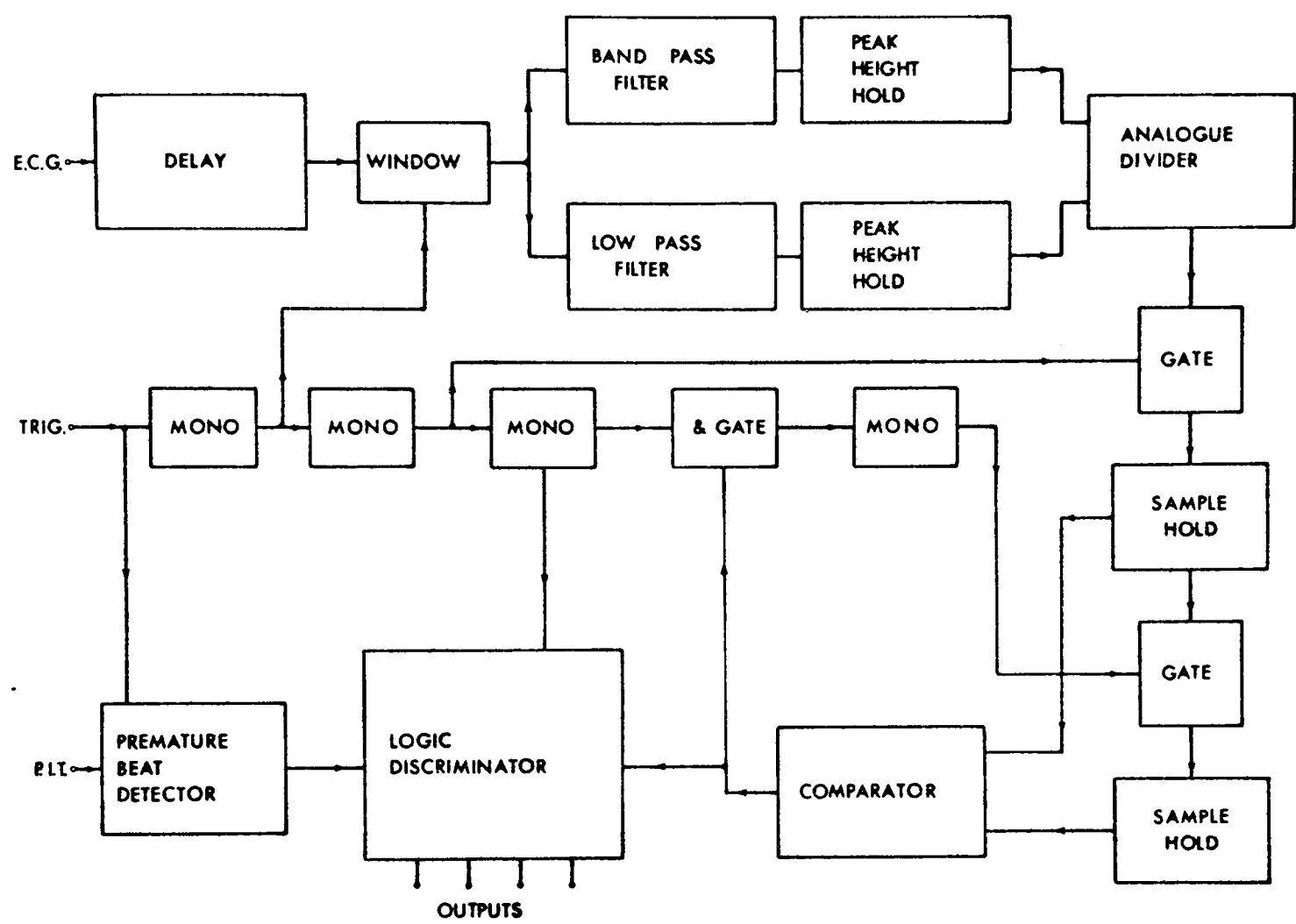
Circuit diagrams of the complete analyser, with a detailed account of its function, are given in Appendix A but a brief description of the sub-units and a block diagram are given here. (Fig. 38).

To ensure an inexpensive system it was decided to use standard, readily available components. The ubiquitous type 741 integrated circuit operational amplifier is used wherever possible and is the active component in the bradycardia, tachycardia, gap and prematurity detectors.

In the case of the tachycardia detector, the varying D.C. output of the pulse interval timer is fed to the non-inverting input of a type 741 operational amplifier and compared with a preset voltage applied to the inverting output. The preset voltage is calibrated to represent heart rate and is normally set to a value representing 100 beats per minute (b.p.m.) but can be adjusted to suit clinical requirements. Tachycardia is indicated when the input voltage from the P.I.T. exceeds the preset level.

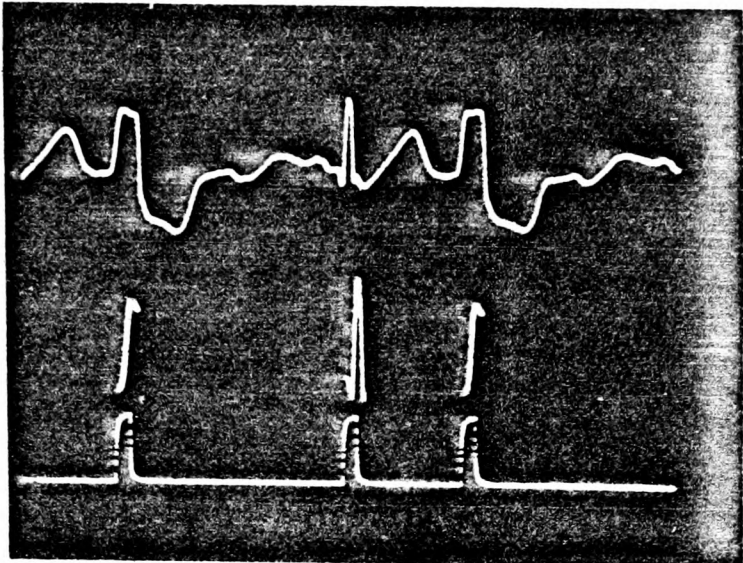
To detect bradycardia, a similar circuit is used but the P.I.T. output and preset voltages are applied to the inverting and non-inverting inputs of the operational amplifier respectively. A heart rate of less than 50 b.p.m. is the standard value used to represent bradycardia but, here again, it can be adjusted to suit clinical requirements.

The premature beat detector uses a type 741 operational amplifier to compare a running average of the P.I.T. output with D.C. level which represents a degree of prematurity adjustable from 10% to 30%.



ECTOPIC BEAT ANALYSER.

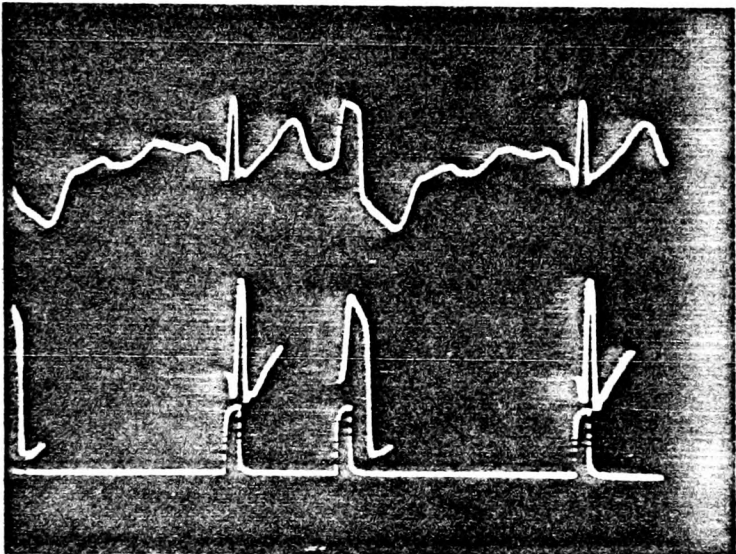
Fig. 38



ECG

Window

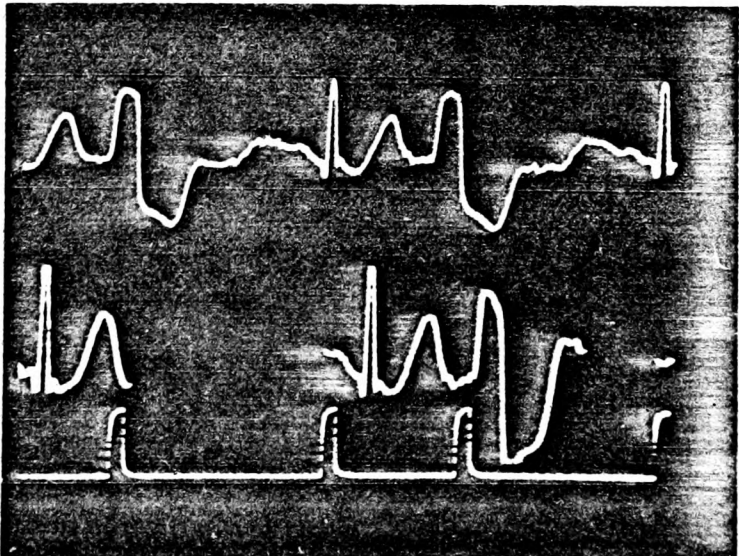
Trigger



ECG

Window

Trigger



ECG

Window

Trigger

Variable "Window"

Fig. 39

To detect gaps, or short periods of asystole, the P.I.T. is used to generate a ramp voltage whose peak height is proportional to the R-R interval. This peak voltage is compared with an adjustable D.C. level by the operational amplifier of the gap detector.

2) Normal and abnormal QRS discrimination

The circuit of the ventricular/supraventricular discriminator is considerably more complex but, again, is composed in the main of inexpensive components and consequently relies upon analogue and not digital filtering to perform the segregation.

Three input signals derived from the play-back unit are fed to this circuit: an amplified ECG; a trigger pulse which occurs at the peak of the R-wave; and a variable D.C. voltage output from the P.I.T.

The amplified ECG is fed to a delay unit and from this to a switching circuit at the input to the analogue filter section. The switching circuit is indicated as "window" in the block diagram and is opened by the trigger pulse applied to the first monostable which is a dual unit and can generate a variable width output pulse. Adjustment of length of the output pulses from the monostable controls which portion of the QRS complex is able to enter the filter circuits (Fig. 39).

The outputs of the filters are full wave rectified and the peak voltages will be dependant on the frequency content of the incoming QRS complexes. For example, if there is a high proportion of low frequency components, as in a ventricular extrasystole, then the peak voltage from the low pass filter will be high with respect to that of the band pass filter. The two peak voltages go to the inputs of the analogue divider whose output is the ratio of the two inputs and will vary in the presence of QRS complexes which contain an abnormally high content of low frequency components.

The output of the divider goes to a sample hold circuit

where it is stored, the route being via an analogue gate which opens briefly in response to the trigger pulse delayed by two monostable circuits in series. The delay ensures that sampling does not take place until the divider output is stable.

There are two outputs from the sample hold circuit, one going to an input of a comparator, the other to another analogue gate. This latter is "opened" by the output voltage of the comparator via a feed-back path including an AND-gate and yet another monostable. The effect of this arrangement is to enhance the discrimination between normal and wide (low frequency) QRS complexes. When such a complex reaches the comparator after a series of normal wave-forms, the effect is to cause the output of the comparator to inhibit the opening of the final gate circuit. Therefore the influence of the wide complex does not reach the comparator which "sees" normal and wide complexes at one input and only normal at the other.

Controls are available to enable minor variations in QRS frequency content to be transmitted to both inputs of the comparator. These are used to cope with variations from subject to subject. The final part of the circuit is the logic discriminator which receives inputs from the premature beat detector and the comparator and classifies each beat on the basis of whether or not it is premature and whether or not it has a normal QRS wave-form. A further input from the tachycardia detector can be accepted so that the discriminator can indicate the presence of ventricular or supra-ventricular tachycardia.

CHAPTER 8

VALIDATION OF THE ANALYSER

1) Introduction

All arrhythmia analysers are attempting to perform a task which would otherwise be undertaken by a trained human observer. It is logical, therefore, that the performance of the former should be judged with reference to the findings of the latter. In this context a hard copy (printed record) of the ECG input to the analyser and its classification is preferable to the transitory display of the same data on an oscilloscope. It permits a closer inspection of the incoming ECG but, what is perhaps more important, it enables errors to be attributed to the appropriate sources.

The optimum form of the validation and the size of sample is uncertain. From the literature it appears that other workers on this theme have found a wide range of procedures acceptable.

The question of sample size can be sub-divided into "how many subjects?" and "what duration of recording from each?". A range of from 4 subjects (Karlsson et al, 1970) to 34 subjects (Oliver et al, 1971), with an average of 17 is given in eight reports which have been examined. Recording times of from "at least one minute" in 26 patients (McLean et al, 1975) to more than 17 hours from 2 patients (Karlsson et al, 1970) are given in the same series of reports. All workers agree on the need for random selection of the subjects with the single exception of Karlsson whose small series would have made this approach farcical.

The term "random selection" does need some qualification in this context. If the population from which the selection is made were

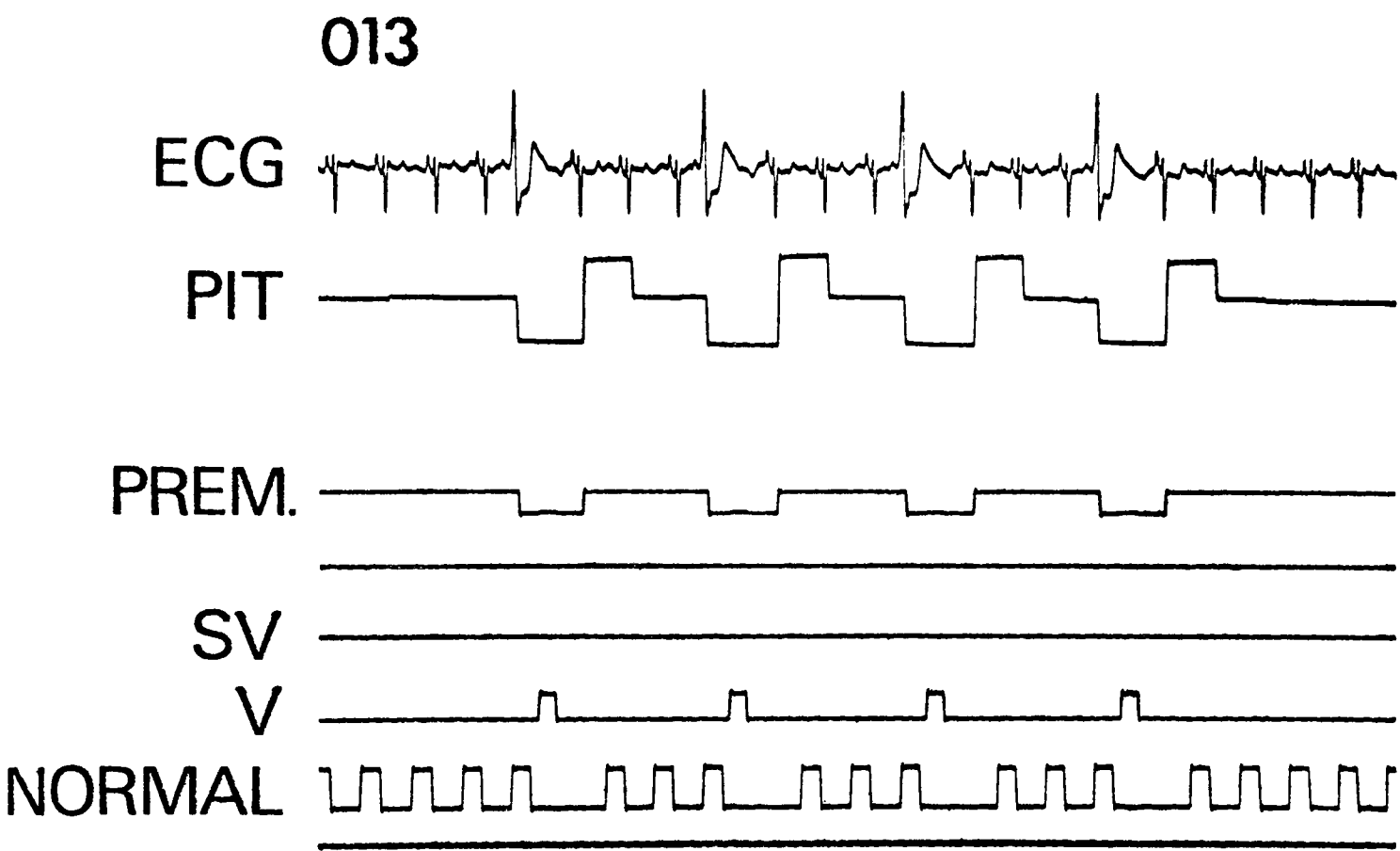
itself to be composed of randomly selected subjects then there is a strong probability that the recordings from many would not contain a significant number of extrasystoles with which to assess the performance of an analyser. For example, if the record contained one abnormal beat which was correctly classified, then a 100% success could be claimed for the system. Conversely, if the analyser were to be foiled, a 0% success rate would have to be accepted.

Finally, in those systems which incorporated parameters that could be adjusted for individual patients, the controls were set for optimum performance.

2) Material and methods

The material used to measure the accuracy of the analyser described in this thesis was obtained from tape recordings of the ECG of 51 subjects, all in sinus rhythm. Forty-nine of these were selected at random by colleagues in the laboratory, from recordings which they judged would contain some premature beats. This technique was adopted to avoid the problems mentioned above. That this was not entirely successful is shown by the results for Study No. 8 (see Table I) which contains only one premature beat, successfully categorised! Because of this, the number of subjects was increased from the fifty originally planned to fifty-one. The remaining two recordings were contributed by another laboratory in which the evaluation of a computer-based arrhythmia detector was in progress.

Instead of basing the duration of each sample on time, it was decided to base it on a standard 1000 beats. This meant that each subject would make an equal contribution to the overall result, regardless of his or her heart rate. In the trial, the duration of



(The unlabelled channel would indicate the occurrence of wide QRS complexes which are not premature)

Fig. 40

the recordings varied from approximately 10 minutes to 16 minutes per subject, depending on heart rate. The two recordings supplied from outside the laboratory did not follow the 1000 beat plan, so a thousand-beat sample was taken from each of these.

Each 1000 beats was replayed from magnetic tape on to a high-speed multi-channel S.E. Laboratories (E.M.I.) recorder, the details of which have been given previously. (Chapter 6.4)

A paper speed of 250 mm/second or 500 mm/second was used, which at the 25 x real time play-back speed of the tape recording gave a real time equivalent speed on paper of 10 mm/second or 20 mm/second respectively. These speeds were found to be high enough for the details of the ECG complex to be resolved satisfactorily and yet did not produce an unmanageable amount (30 metres) of recording paper.

In addition to the ECG, each recording displayed the output of the P.I.T. and the four outputs of the analyser. Fig. 40 shows a typical section of a tracing used for the validation exercise. Due to the limited number of categories into which the ECG complexes could be separated by the analyser, the task of checking the records, although tedious, was not too demanding.

The presence of any premature beats was confirmed by a cardiologist, the recording was then divided into units of 50 beats and the occurrence of the premature beats tabulated. Classification by the analyser was next listed and in the case of error, an attempt was made to identify the reason for the mistake. At the end of each recording the percentage of total premature beats, ventricular premature beats and supraventricular premature beats were calculated, as was the percentage of false counts. This last category was subdivided into false positive and false negative. A relatively infrequent error by

Age range of subjects used in validation analyses

6 subjects in age range 25-34 years					
4	"	"	"	35-44	"
18	"	"	"	45-54	"
12	"	"	"	55-64	"
<u>11</u>	"	"	"	65-74	"
51					

Premature ventricular beats occurred in:	4	subjects	within	25-34	age	range
	4	"	"	35-44	"	"
	18	"	"	45-54	"	"
	6	"	"	55-64	"	"
	7	"	"	65-74	"	"
	39					

Supraventricular beats occurred in:	2	"	"	25-34	"	"
	0	"	"	35-44	"	"
	8	"	"	45-54	"	"
	7	"	"	55-64	"	"
	8	"	"	65-74	"	"
	25					

Both types occurred in:	1	"	"	25-34	"	"
	0	"	"	35-44	"	"
	6	"	"	45-54	"	"
	2	"	"	55-64	"	"
	4	"	"	65-74	"	"
	13					

the analyser resulted in ventricular premature beats being classified as of supraventricular origin and vice versa. Errors of this type were listed as mis-classified.

Finally, the total error from all sources was estimated. Details of the source material are given in Table I.

A summary of the material follows:-

Total number of subjects:	51	
Total number of beats:	51,000	
Number of subjects with premature ventricular beats:	39	
Number of subjects with premature supraventricular beats:	25	
Number of subjects with both types:	13	
Total number of premature beats:	7212	
Number of premature ventricular beats:	5281	73.23% of total
Number of premature supraventricular beats:	1931	26.77% of total
Incidence of premature beats	40.6 to 0.1%	mean 14.14% S.D. 11.63%
Incidence of premature ventricular beats	40.6 to 0%	mean 10.36% S.D. 12.40%
Incidence of premature supraventricular beats	32.2 to 0%	mean 3.79% S.D. 7.31%

3) Results

The performance of the analyser in detecting and classifying premature ventricular and supraventricular beats was as follows:

	% range %	mean %	standard deviation %
False positives	5.8 to 0	1.11	1.43
False negatives	2.7 to 0	0.22	0.53
Sum of false positives and negatives	5.8 to 0	1.33	1.54
Mis-classification	1.5 to 0	0.13	0.33
Total error	6.0 to 0	1.46	1.63

Sources of Error:

Source	No. of studies	% range	% mean	% S.D.
Movement artifact	19	3.9 to 0.1	0.82	0.97
Incorrect triggering	18	3.7 to 0.1	1.34	1.19
Less than 20% prematurity	11	3.8 to 0.2	1.05	1.23
Frequency content of V.E.S. complex similar to sinus beat	8	1.0 to 0.1	0.45	0.35
Change in QRS wave-form during recording	1	6.0		
Interpolated premature beat causing succeeding beat to be classified as premature	2	1.5 & 0.1		
Paired V.E.S. with second classified as 'wide'	1	1.5		
Early sinus beat after premature beat, classified as S.V.E.S.	1	1.7		
Unclassifiable	12	1.5 to 0.1	0.45	0.45

4) Comparison with other systems

In a recent comparison of four commercial arrhythmia analysers,, Kùhn et al (1976) of the University Cardiology Clinic, Vienna, introduced two equations by which the performance of such analysers can be expressed:

Equation 1: $\text{Sensitivity \%} = \frac{\text{number of abnormal complexes detected}}{\text{actual number of abnormal complexes}} \times 100$
 $= \frac{\text{total abnormals detected} - \text{false positives}}{\text{actual number of abnormal complexes}} \times 100$

Equation 2: $\text{Specificity \%} = \frac{\text{number of normal complexes detected}}{\text{actual number of normal complexes}} \times 100$
 $= \frac{\text{number of normal complexes} - \text{false positives}}{\text{actual number of normal complexes}} \times 100$

Using these equations and the data from the validation exercise, the following results are obtained:

$\text{Sensitivity \%} = \frac{7212 - 565}{7212} \times 100 = 92.17$
 $\text{Specificity \%} = \frac{(51,000 - 7212) - 565}{51,000 - 7212} \times 100 = 98.71$

The performance of the analyser would appear to be comparable with that of other analysers in the context of detecting and classifying premature beats. ' It should be noted, however, that some of the other systems have capabilities which, although not pertinent to this comparison, may justify their greater complexity and cost.

A general comparison of the performance of the analyser with that of other systems follows. Strict comparison is not justified as full details of the validation techniques are not available. (Fozzard et al, 1976).

System	Computer	V.E.S. Detection
Washington University	System 7 and special hardware	89%
U.S. Air Force	Hybrid	Inadequate
Edinburgh	Hybrid	96%
Stanford	PDP.12 and special hardware	98%
Cardio-Dynamics	Special purpose	Inadequate

Kühn et al, (1976)

Apparatus	Sensitivity	Specificity
Hewlett Packard arrhythmia monitor 7822	48.3	98.7
Neilson arrhythmia computer	90.9	98.5
Päsel't arrhythmia computer	36.6	100.0
Siemens Cardalarm S.2	92.9	72.4

5) Clinical significance of errors

Although it is important to have information on the performance of the analyser as a detector and classifier of premature beats, it is possibly more important to have some indication of the

clinical significance of the errors it may perpetrate. To provide such information is not, however, simply a matter of mathematics. Yanowitz et al (1974), then from the Department of Medicine and the Biomedical Computer Faculty, University of Chicago, attempted such an evaluation. Cases were divided into four groups, based on the frequency of premature ventricular beats (P.V.B.) as follows:

- (1) Very frequent more than 12 per minute
- (2) Moderately frequent 6 - 12 per minute
- (3) Borderline 3 - 6 per minute
- (4) Occasional less than 3 per minute

Patients in the first two groups were judged to need antidysrhythmic drug therapy, whilst those in the third group were considered "close to the clinical criterion for antidysrhythmia drug administration".

Of the 51 recordings in this validation exercise, 39 were from subjects with premature ventricular beats. Of these, 13 showed more than 12 P.V.B. per minute, 10 showed 6 - 12, 3 showed 3 - 6 and 13 showed less than 3 per minute. On the basis of the analyser's findings alone, six cases would have been wrongly categorised, as follows:

Study No.	Source of Error	Change in Grouping
4	False positives	2 to 1
19	" "	3 to 2
20	" "	2 to 1
27	" "	2 to 1
46	" "	4 to 3
50	False negatives	1 to 2

6) Summary

Arrhythmia analysers, as a group, can be divided into those which are fully automatic and the semi-automatic which can be, and often need to be, adjusted to give optimum performance from each subject. The latter has the drawback of needing a trained operator to make the necessary initial adjustments but, at the present time (1977), does yield higher success rates. (Yanowitz et al, 1974) and (Hulting et al, 1976).

The sources of error can also be broadly divided into those due to an inadequacy of the instrument and those which can be attributed to a human failure in the operator.

Failures due to similarities in the frequency content of sinus beat QRS complexes and those of V.E.S. are undoubtedly in the former category as are those due to changes in the morphology of the QRS during recording, and those associated with interpolated and paired V.E.S. The errors due to less than 20% prematurity in extrasystoles can be overcome by adjusting the analyser to classify as premature those beats with less than 20% prematurity.

Such adjustments, however, cannot be extended to include less than 15% prematurity without the concurrent risk of false positive counts being initiated by physiological variations in R-R intervals. Incorrect triggering can arise both from the instrument and its inability to deal with a range of QRS amplitudes, or from incorrect initial adjustment by the operator. In this exercise the operator was the culprit more often than the instrument!

The greatest source of error was movement artifact. This can be minimised by careful placing of the electrodes to avoid muscle potentials, by securing electrode leads to the skin to minimise microphony

and the careful selection of electrodes.

False positive errors were five times as frequent as false negatives, the majority being due to movement artifact or mistriggering. The worst case of positive error (Study No. 4, Table I) was due to change in morphology of the QRS soon after the start of the analysis and could probably have been reduced if the criteria of the analyser had been re-adjusted and the analysis repeated.

Footnote

The R-R interval and difference histograms have been mentioned earlier (Chapter 3 (4)), when the limitations of "hard wired" inflexible units were discussed. Until recently a bin capacity large enough to accommodate, say, four hours of data would have had a resolution of around eight R-R intervals and hence could not show the infrequent rhythm abnormality.

Programmable histogram generators based on a microprocessor can, however, be easily adapted to suit the requirements of individual recording. The increased availability accompanied by lowering in cost of microprocessors have made histograms a very attractive form of data presentation in the context of high speed arrhythmia analysis.

It is hoped that a microprocessor and associated peripherals which have recently (1978) been made available to the writer and colleagues through a British Heart Foundation research grant will enable them to demonstrate the versatility of the method.

TABLE I

STUDY NO.	TOTAL PREMS.	PREM. V.	PREM. SV.	FALSE +ve.	FALSE -ve.	SUM FALSE +ve & -ve.	MISCLASSIFIED	TOTAL ERROR
1	262	262	0	1	0	1	0	1
2	183	183	0	9	0	9	0	9
3	399	399	0	0	0	0	0	0
4	148	144	4	58	0	58	2	60
5	384	384	0	1	1	2	1	3
6	89	0	89	4	0	4	1	5
7	4	4	0	12	0	12	0	12
8	1	0	1	0	0	0	0	0
9	4	0	4	2	0	2	0	2
10	10	8	2	4	0	4	0	4
11	40	11	29	0	1	1	1	2
12	70	70	0	38	3	41	6	47
13	151	151	0	5	4	9	0	9
14	285	285	0	0	0	0	0	0
15	16	8	8	0	3	3	0	3
16	37	36	1	1	2	3	1	4
17	174	5	169	3	0	3	0	3
18	396	396	0	7	0	7	0	7
19	69	60	9	28	1	29	2	31
20	186	143	43	28	12	40	0	40
21	213	213	0	1	1	2	15	17
22	26	0	26	5	1	6	0	6
23	170	0	170	0	3	3	0	3
24	323	323	0	2	0	2	1	3
25	406	406	0	8	0	8	0	8
26	125	0	125	4	22	26	0	26
27	130	130	0	24	0	24	8	32
28	100	100	0	38	0	38	0	38
29	232	232	0	9	0	9	10	19
30	176	176	0	19	2	21	0	21

continued

TABLE I (continued)

<u>STUDY</u> <u>NO.</u>	<u>TOTAL</u> <u>PREMS.</u>	<u>PREM.</u> <u>V.</u>	<u>PREM.</u> <u>SV.</u>	<u>FALSE</u> <u>+ve.</u>	<u>FALSE</u> <u>-ve.</u>	<u>SUM FALSE</u> <u>+ve & -ve</u>	<u>MISCLASSIFIED</u>	<u>TOTAL</u> <u>ERROR</u>
31	13	0	13	2	0	2	0	2
32	78	0	78	0	0	0	0	0
33	89	89	0	35	0	35	0	35
34	138	16	122	0	0	0	1	1
35	313	312	1	5	1	6	0	6
36	88	88	0	9	0	9	0	9
37	322	0	322	11	27	38	0	38
38	268	0	268	0	1	1	2	3
39	6	6	0	1	0	1	0	1
40	16	16	0	0	0	0	0	0
41	120	120	0	39	0	39	0	39
42	190	10	180	2	0	2	0	2
43	183	0	183	0	0	0	0	0
44	68	11	57	12	6	18	0	18
45	23	23	0	10	3	13	0	13
46	26	26	0	27	0	27	0	27
47	97	97	0	25	0	25	0	25
48	139	139	0	4	2	6	0	6
49	25	0	25	1	2	3	0	3
50	156	154	2	20	15	35	14	49
51	45	45	0	51	0	51	0	51
7212	5281	1931	565	113	678	65	743	

CHAPTER 9

DATA COLLECTION - PRACTICAL REQUIREMENTS1) Single or dual channel ECG recording

Both human and electronic ECG analysers need the maximum amount of accurate information if they are to arrive at a satisfactory interpretation. When analysing a conventional electrocardiogram a cardiologist is presented with twelve channels of data: three standard bipolar limb leads, three unipolar limb leads and six unipolar chest leads. In ambulatory monitoring, however, much less information must be accepted if the recording equipment is to be compact enough to be socially acceptable. In fact, the limited low frequency response of many recorders used at the present time (1977) for ambulatory ECG monitoring restricts their use to the detection of arrhythmias to the exclusion of ischaemic episodes in which accurate measurement of S-T segment changes would be required. In this context much of the information in a twelve-lead recording would be redundant even if it were possible to record it.

Currently it appears from the literature that, in the vast majority of cases, only one ECG lead is recorded in ambulatory monitoring but that this may be due to feasibility rather than desirability.

It would, in most cases, be possible to record two ECG leads simultaneously but to analyse two channels of data would mean either a duplication of equipment or two consecutive analyses. It is logical to expect more information from twice the amount of data and several workers have commented on the advantages and disadvantages of single and double channel recording. Bleifer (1976) has recently started using a new recorder with a frequency response which is flat from 0.005 Hz to 100 Hz

and consequently can faithfully record S-T segment shift. It is in this context that he found that a left ventricular lead and an inferior one are preferable to a single left ventricular lead. He also found that two leads are advantageous in differentiating between true ventricular ectopic beats and supraventricular ectopics with aberrations. The problems of replay and analysis were such, however, that at the time (May 1975) he had reverted to using the second channel of the recorder as a clock to allow accurate correlation between symptoms and electrocardiographic changes.

Pool et al (1976) also reported the use of two-channel ECG recordings in ambulatory monitoring. In this case, however, it was in the hope of obtaining "at least one noise-free recording" and no comments on the problem of replay were made.

It is the view of the writer that, given

(1) a recorder with limited low-frequency response

(3 dB attenuation at more than 0.005 Hz),

(2) an objective of solely arrhythmia analysis and

(3) an analyser operating at near-full capacity,

then a single lead ECG recording is the best compromise for ambulatory monitoring.

2) Choice of electrodes

If one accepts a single lead recording, then it is essential that the maximum amount of accurate information can be extracted from it; that is, the data must be there and not obscured by artifact which, in turn, is mainly dependant on the construction of the electrodes and their position.

An electrode which is to remain attached to the subject must be non-irritant, non-toxic, and capable of transmitting the biological signals

without distortion. Self-adhesive, disposable electrodes are most suitable for 24-hour ECG monitoring; they have a low profile, need no straps or suction to hold them in place and, if produced by a reputable manufacturer, can be relied upon to be non-irritant. The ability to transmit signals without distortion is dependant upon the metal from which the electrode is constructed.

The electrical link between an ECG electrode and the skin is complex and capacitative in nature. When two electrodes are placed upon the skin they behave in much the same fashion as if they were immersed in an electrolyte, and in both cases a potential difference can be measured between them.

The magnitude of this potential difference is mainly dependant on the position in the electro-chemical series of the metal from which the electrode is made. Some examples are given below of metals likely to be used in the manufacture of biological electrodes (Strong, 1970):

Metal	Electrode potential V
Aluminium	- 1.66
Zinc	- 0.76
Iron	- 0.44
Lead	- 0.12
Copper	+ 0.34
Silver	+ 0.80
Platinum	+ 0.86

In electrophysiology the difference in potential between two electrodes is generally referred to as offset potential and is approximately half the difference in the electrode potential of the metals used in the electrodes. In theory two electrodes made of similar metal would produce no offset potential but in practice slight differences in the metal produce sufficient offset potential to distort the biological signal.

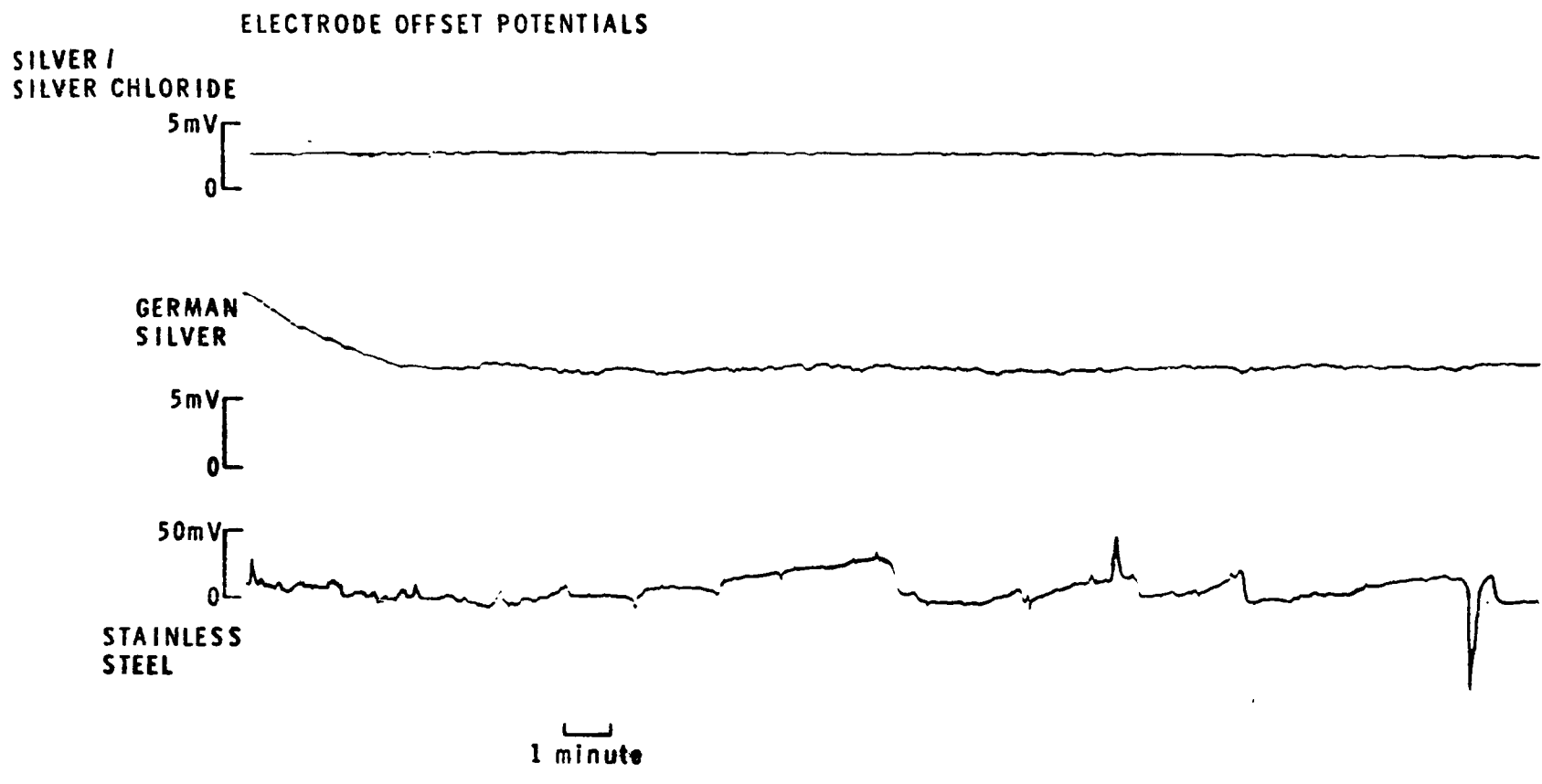


Fig. 41 Electrode offset potential
 Long term stability - drift

ELECTRODE OFFSET POTENTIALS

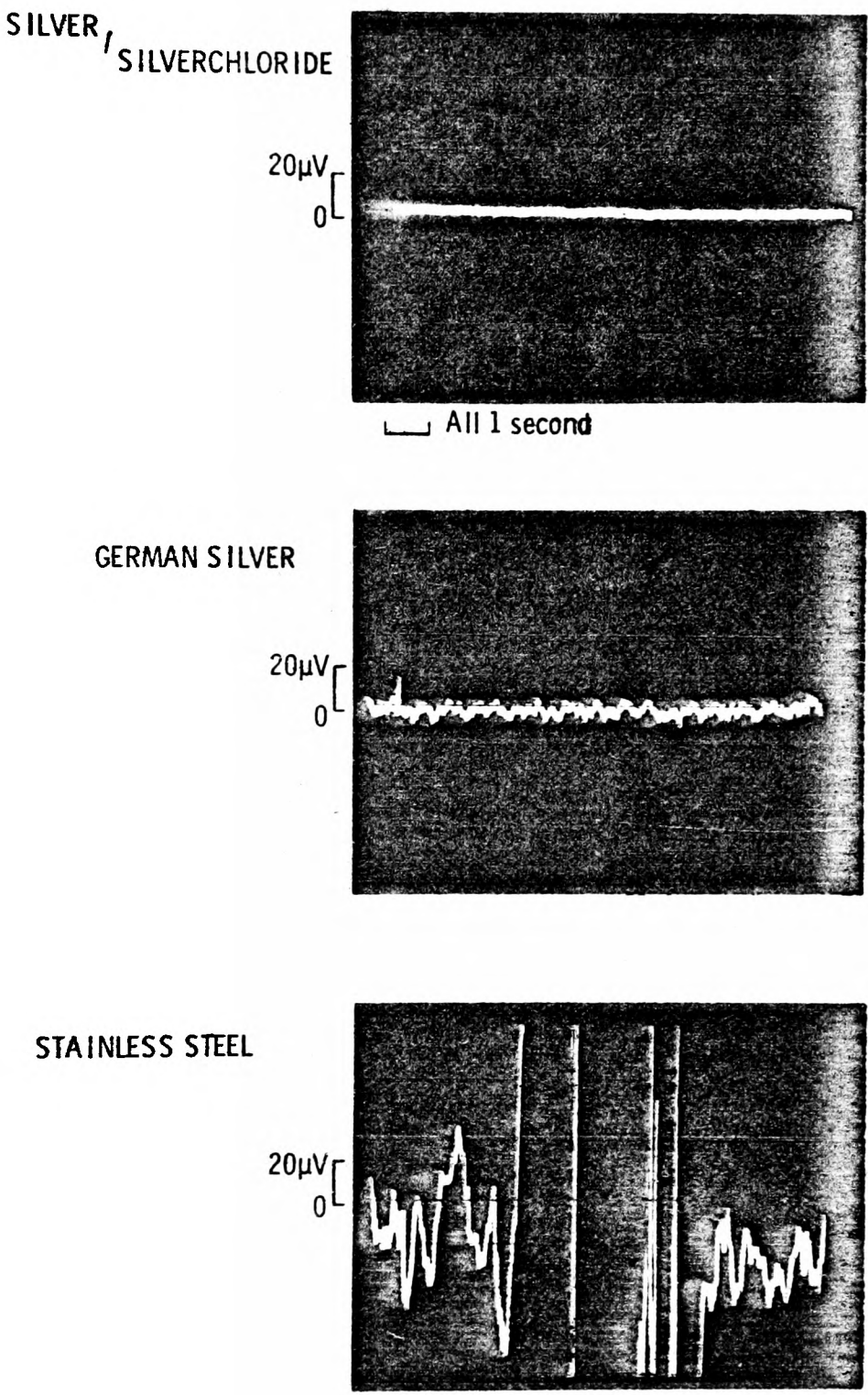


Fig.42 Electrode offset potentials 1 Hz - 100 Hz
Short term stability - noise

One way to overcome the problem of offset potential is to use electrodes made of silver/silver chloride, either in the form of metallic silver coated with silver chloride or as a compressed mixture of silver powder and silver chloride powder. The silver chloride prevents the build-up of two layers of ions of opposite sign which causes the electrode potential to form. Zinc/sinc sulphate electrodes are equally effective but are toxic. Fig. 41 shows long-term variations in electrode potential which manifests itself as base-line drift on an ECG recording. Fig. 42 shows short-term variations which appear on the recording as noise.

Although the ECG amplifiers used in the Oxford Medilog recorder are A.C. coupled, the time constant is sufficiently long to give little protection against drift.

3) Choice of electrode position

The second factor which influences the value of the data obtained from a single channel ECG recording is the position of the electrodes. When the project described in this thesis was started, in 1974, the available amplifiers had limited sensitivity so that the first pre-requisite for a satisfactory recording was to detect the largest possible signal.

For this reason one electrode was placed over the apex with the other in the first right intercostal space, one inch from the mid-line. Although there has been some improvement in the sensitivity of ECG amplifiers, it was decided to retain the same electrode positions until the end of the present studies in order to preserve the ability to compare earlier records with those made recently.

The main shortcoming of the lead position just described

is that it is not effective in differentiating between ventricular extrasystoles and those of supraventricular origin but with aberrant ventricular conduction. Lewis (1918) used the adjective "aberrant" to describe "beats which, propagated from supraventricular impulses, are distributed in a partial or faulty fashion" and he attributed the phenomenon to "difficult conduction in the main divisions of the bundle or along certain tracts of the junctional tissue".

Lewis also noted that aberration tended to appear if the premature supraventricular beats occurred early in the diastole of the preceding beats. Langendorf (1950) stressed the clinical importance of recognising aberrant ventricular conduction, especially in paroxysmal tachycardia. He also underlined the difficulties in the absence of a demonstrable P-wave, as in atrial fibrillation, but found that a considerable pause tends to follow an ectopic ventricular beat but not an aberrant beat.

Sandler and Marriott (1965) compared 100 records of ventricular ectopic beats having right bundle branch block (R.B.B.B.) pattern in lead V_1 with (a) 100 records of sinus beats showing R.B.B.B. and (b) 100 examples of aberrant ventricular conduction which showed a definite pattern of either right or left bundle branch block. Of the ventricular extrasystoles 92% showed a monophasic or diphasic pattern in V_1 whilst 6% showed a triphasic pattern. In contrast, 67% of the R.B.B.B. records and 70% of aberrant ectopic beats showed the triphasic wave-form.

In addition it was discovered that in 44% the initial vector, over an interval of 0.02 seconds in aberrant beats, was the same as in normally conducted beats whereas in ventricular ectopic beats the value was only 4%.

These findings provided very useful guidelines for separating

ABERRANT CONDUCTION v VENTRICULAR
ECTOPIC FOCUS

QRS_{V1} WAVE-FORM

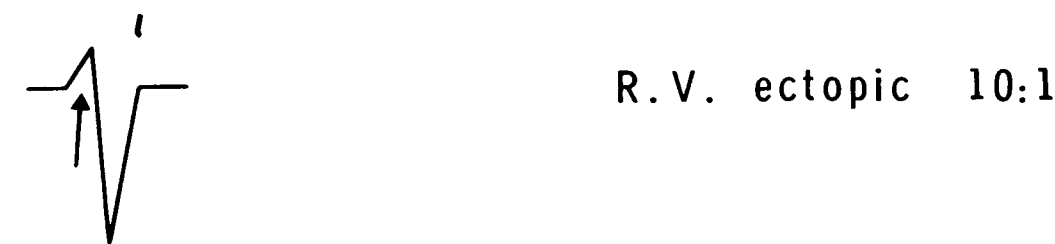
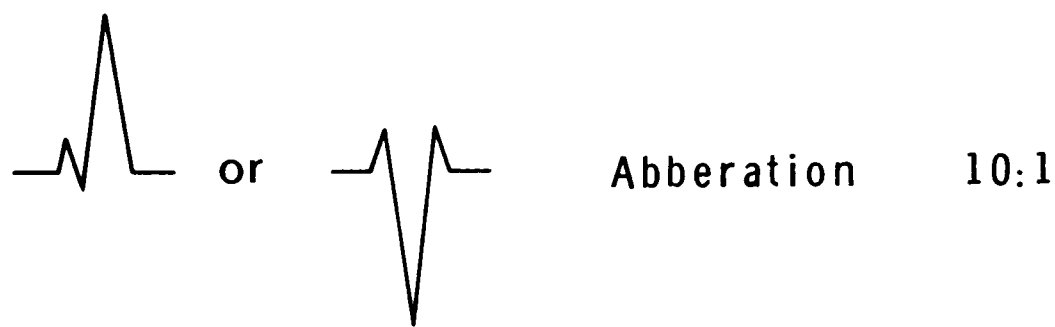


Fig. 43 QRS wave-form and probability of site
of origin of premature beat .

beats of ventricular ectopic origin from those arising in supraventricular sites but having aberrant conduction. Even so, there remain a few perverse forms of abnormal contractions which defy accurate description unless one has recourse to His bundle electrography, not a practical proposition in ambulatory monitoring.

Marriott and Nizet (1967) refer to one example of this problem, that form of A-V junctional extrasystole which is sometimes termed "main stem" extrasystole. These arise from a site above the bifurcation of the bundle of His, do not disturb the basic sinus rhythm and have a compensatory pause. If there is aberrant ventricular conduction it is not possible to differentiate such a contraction from one of ventricular origin. The phenomenon is probably rare but one cannot be sure.

Marriott and La Camera (1968) reported preliminary findings following a short series of studies in which they artificially produced ectopic beats from the right and left ventricle during cardiac catheterisation. A summary of this and previous investigations is shown in Fig. 43.

Marriott and Fogg (1968) criticised the generally haphazard manner in which electrodes were positioned for recording the ECG in coronary care units. They suggested that lead V_1 produced the most informative recordings and was the best for distinguishing between ventricular ectopic beats and supraventricular ectopic beats with aberration. This lead required the connection of the three limb electrodes which would be inconvenient in the C.C.U. and even more so in ambulatory monitoring. They therefore suggested the use of a modified version of lead CL_1 , long since outmoded in conventional electrocardiography. They proposed that the exploring electrode be placed normally in the fourth right intercostal space at the junction with the sternum and that the indifferent electrode be placed just below the outer third of the left clavicle. If a third lead should be needed for earthing purposes this would be placed on the right shoulder.

4) Comparison of QRS amplitude in two-lead systems

In view of the reported superiority of the modified CL_1 lead in distinguishing between aberrant ventricular conduction and ventricular ectopic beats, it was decided to compare the absolute amplitude of the QRS complexes derived from this lead and from the currently used lead.

As mentioned previously, the limited sensitivity of the available amplifiers made it highly desirable to detect the maximum amplitude QRS complex.

It seemed likely that the apparent superiority of the CL_1 lead in elucidating aberrant conduction might be offset by a low voltage QRS wave-form. To compare the performance of the two leads, both were recorded from twenty-five patients who came to the department for 24-hour ambulatory electrocardiograms. No selection was made unless the additional time needed for the extra recordings was inconvenient for the patient, in which case they were omitted from the series. Fifteen of the patients were considered by their physicians to have a normal cardiovascular system and were participants in a separate study. The remaining ten had been referred from outpatient clinics as possible cases of transitory arrhythmias. Eleven were male, fourteen female and their ages ranged from 27 to 62 years. The recordings in all cases were made on the same electrocardiograph, Siemens Mingograph type 34, and all patients were seated during the recordings. In all cases the amplitude of the QRS in the CL_1 was less than that obtained with the apical electrode, the proportion being 0.1 to 0.76, with a mean value of 0.39 and a standard deviation of 0.19.

The amplitude of any component of the ECG wave-form is dependant, other factors being equal, on the spatial relationship between the axis of the lead in which it is recorded and the mean electrical axis

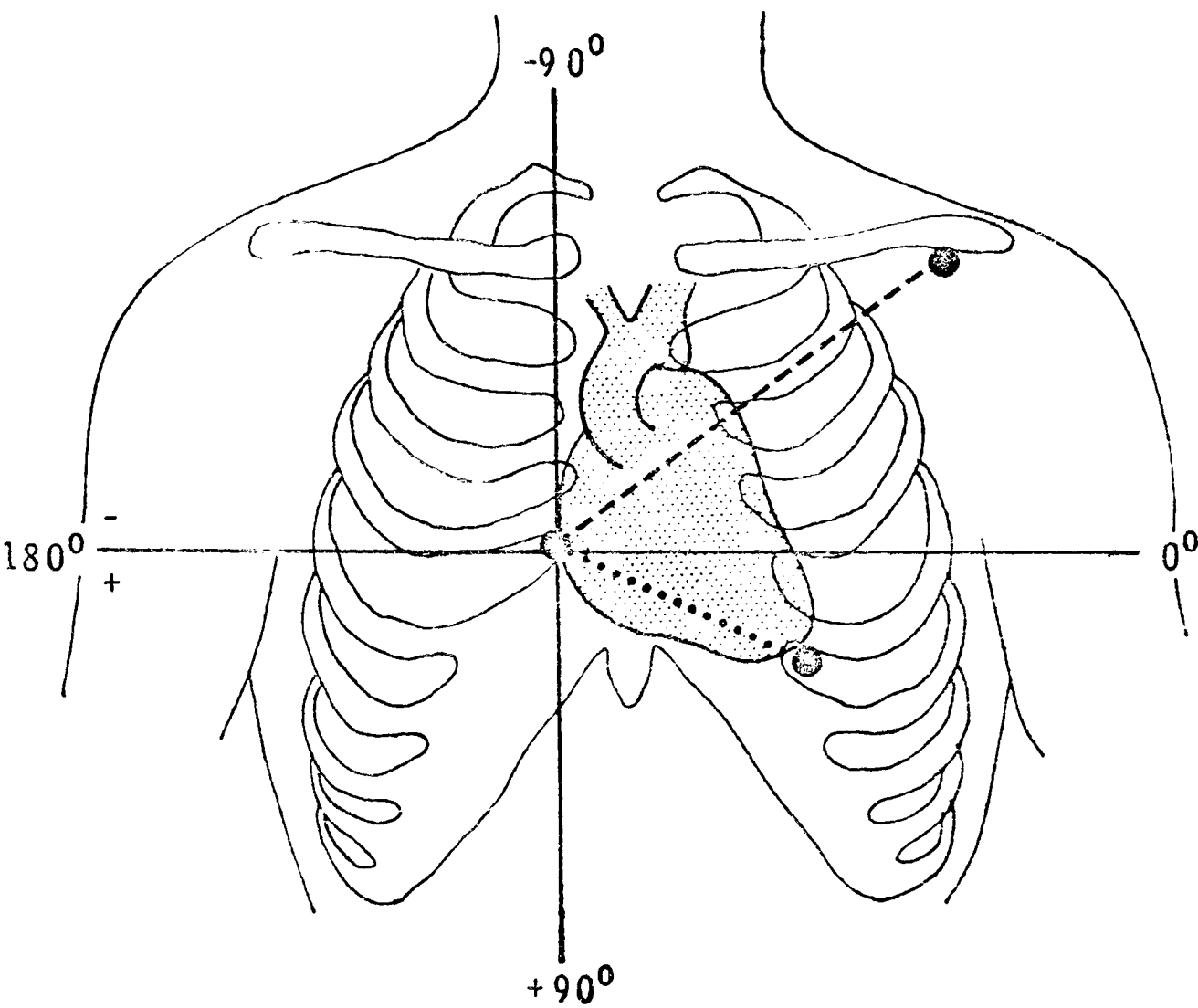


Fig. 114 Axis of Marriott modified CL_1 lead -----
Axis of apical lead

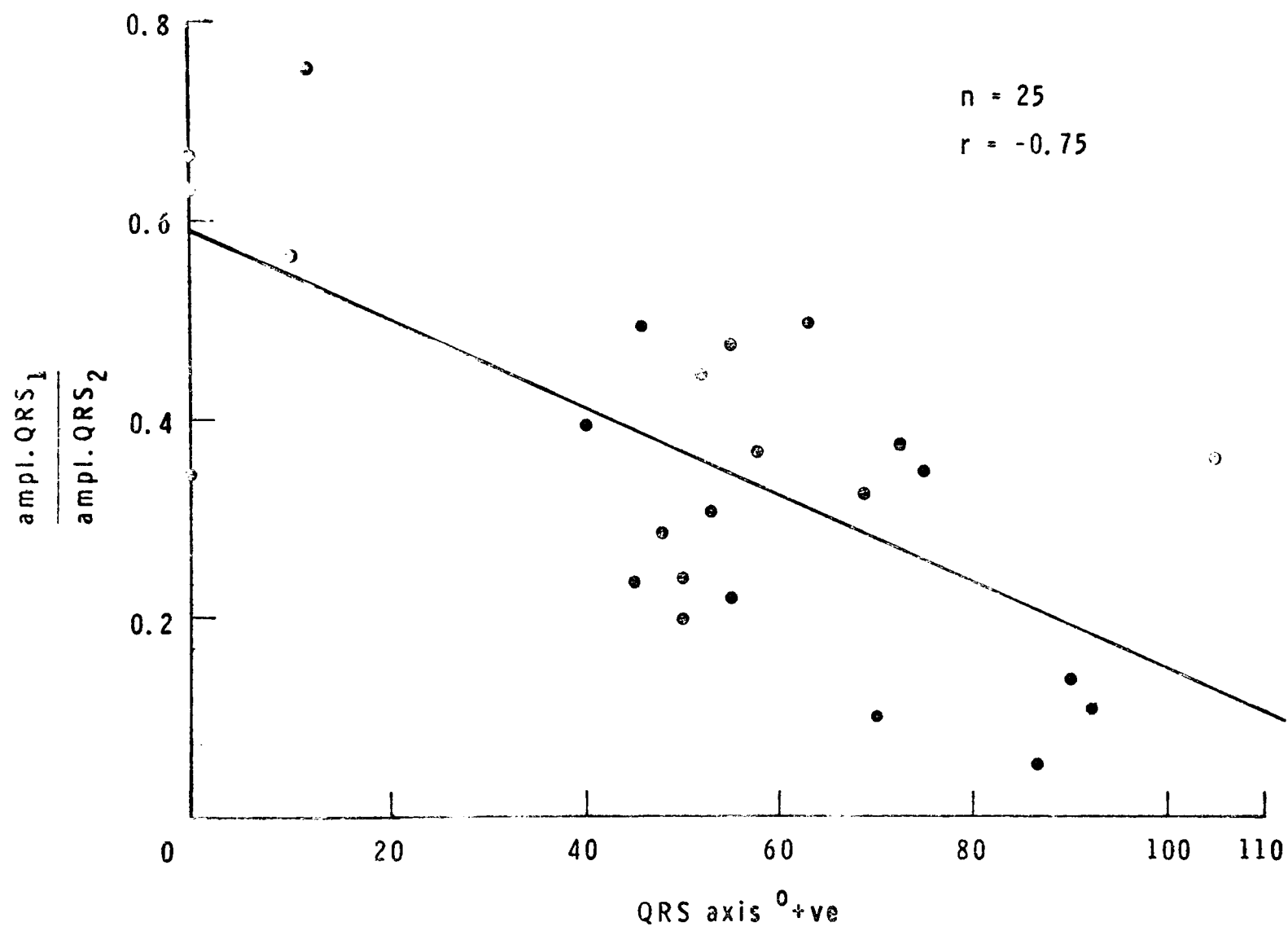


Fig. 45 Relative maximum QRS amplitude v Frontal plane mean QRS axis
QRS₁ from apical lead
QRS₂ from modified CL₁ lead

of the heart during the corresponding part of the cardiac cycle. In the case of the QRS wave-form this would be the period of ventricular depolarisation. The axes of the modified CL_1 lead of Marriott and that of the apical lead are markedly different (Fig. 44), so it seemed likely that the ratio of the amplitudes of the QRS complexes in the two leads could be related to the electrical axis of the heart.

It was not felt justifiable to detain patients, many of them normal subjects, for the additional time needed to record a conventional triple-plane vectorcardiogram. Instead, the frontal plane mean electrical axis of the QRS complex was derived from the scalar leads. For this purpose Dieuaides Chart was used with the algebraic sum of the QRS in lead I plotted on the ordinate, that of lead III plotted on the abscissa and perpendiculars dropped from each point. A line joining the centre of the chart to the intersection of the perpendiculars gave the mean electrical axis of the QRS complex on the frontal plane.

The range of this axis was 0° to 105° with a mean of 47.5° and standard deviation of 30.36° . Only one value, that of $+105^\circ$, was outside the generally accepted normal range of 0° to $+90^\circ$.

In Figure 45, the relative maximum amplitude of the QRS complex in the two leads is plotted against the frontal plane mean electrical axis of the QRS. The values give a correlation coefficient of -0.76 which, with $n=25$, gave $t = 5.61$ (p less than 0.001).

It would seem from these results that the modified CL_1 lead would be unlikely to provide adequately large QRS complexes for the present amplifiers, except perhaps from patients with left axis deviation (axis less than 0°) where the relationship between lead axis and cardiac electrical axis would be favourable.

Chapter 10

PRACTICAL APPLICATION OF THE ARRHYTHMIA ANALYSER: A STUDY OF THE 24-HOUR ECG IN NORMAL AMBULANT SUBJECTS

1) Introduction

Ambulatory monitoring during a continuous 24-hour period is an appropriate method for use in a study of a group of subjects who might be expected to have only transitory disturbances of cardiac rhythm. Wolff, (1976) has likened the task of making a diagnosis on information derived from short duration measurements, such as a routine electrocardiogram or blood pressure measurement, to attempting to work out the result of a Cup Final football match from evidence given by two photographs taken at random during the play.

One of the earliest attempts at ambulatory monitoring, that by Gilson et al (1964), was limited by technical considerations to a duration of 5 hours. In a study of 55 normal subjects they found ventricular extrasystoles occurred in 6%, although these were not apparent in the conventional 12-lead ECG taken immediately before the ambulatory monitoring period. Hinkle et al (1969) were limited to recordings lasting 6 hours for their study of ambulatory monitoring.

Subsequently, as has been described in Chapter 1, it became possible to extend first to 10 hours, then to 12 hours, and now 24 hours is the most commonly used period.

In a study of normal subjects who can be expected to gain little from the investigation it is desirable to reduce to the minimum the inconvenience they may experience. If a comparatively short recording time could produce reliable information it would obviously be preferable.

It would seem logical, however, that if the recording time is increased the probability of detecting an abnormality will increase also. Should the abnormality be infrequent, as is to be expected in normal subjects, then the increase in probability of detection with the longer recording time is likely to be even more enhanced. Studies by other workers confirm this hypothesis.

Lown (1971) reported that the standard ECG, which can be considered equivalent to one minute of monitoring, will show some ventricular extrasystoles in almost 8% of patients with coronary heart disease. If the period is increased to 3 minutes, about 14% show this arrhythmia and, after 12 hours of monitoring, 61.8% of the recordings show ventricular extrasystoles. If, however, the recording time was limited to 1 hour, only 70% of those found in the 12-hour period would have been detected.

Hinkle et al (1972) extended their recording time from 12 hours to 24 hours "when it became evident from other studies that important phenomena of heart rate, rhythm and conduction might occur in the evening and during the course of sleep".

Schroeder et al (1975) compared the success rates obtained in 12-hour and 24-hour recordings from 72 subjects known to have arrhythmias. They found that in 16% of the cases the arrhythmia was detected for the first time in the second 12-hour period. Ryden et al (1975) studied 52 non-ambulant C.C.U. patients, all of whom had either a confirmed or suspected myocardial infarction. Records of 1 minute, 2 minutes, 5 minutes and 3 hours' duration were made from each patient and the incidence of ventricular extrasystoles in each period compared. They found that in subjects with frequent extrasystoles a one-minute record detected the abnormality in 50% of the cases in which it was found in the 3-hour

recording, whilst the equivalent figure for a 5-minute recording was 80%. They found that the short recordings detected the extrasystoles very poorly but did not quantify the terms 'frequent' and 'infrequent'. Lown et al (1975) had similar results from subjects with frequent ventricular extrasystoles and found that in a 5-minute recording they detected the arrhythmia in 75% of the cases in which it was present.

Lipski et al (1976) studied a group of 55 patients with syncope, palpitations or dizziness in whom routine ECGs on several occasions had disclosed nothing of significance. 24-hour ambulatory monitoring showed significant arrhythmias in 30 patients. In six of these there were episodes of sinus arrest of up to five seconds.

There appears to be little published work on the comparative effectiveness of the routine ECG and 24-hour ambulatory monitoring in uncovering cardiac arrhythmias in normal subjects.

Raftery et al (1976) describe the results of 24-hour ambulatory monitoring on 53 normal subjects whose ages ranged from 20 years to 70+ years, and found arrhythmias in 28% although all had previously had normal 12-lead ECGs. No atrial fibrillation, atrial flutter, ventricular tachycardia or ventricular fibrillation was detected. Isolated supraventricular extrasystoles were the commonest arrhythmias.

Clarke et al (1976) performed two 24-hour ambulatory monitoring studies on each of 86 normal subjects aged 16 to 65 years, all of whom had been screened by conventional electrocardiography and biochemical and haematological tests. Arrhythmias, including frequent or multifocal ventricular extrasystoles, R-on-T, bigeminy and ventricular tachycardia, were detected in 12% of the subjects but supraventricular extrasystoles were excluded from the results as they had proved to be difficult to identify correctly. If the incidence of supraventricular tachycardia, infrequent ventricular extrasystoles, junctional rhythm and second degree

heart block are included, most of the subjects showed some arrhythmia.

It is difficult to explain the high incidence of arrhythmias found by this group of workers but they feel that it may be due to their "rigorous and time-consuming quality control programme" and "to long hours of skilled and careful analysis".

2) Material and methods

Since a "normal" population might comprise people with subclinical disease it seemed of interest to compare groups drawn from both urban and rural communities, although any conclusions which might be drawn would be limited by the relatively small size of the samples.

The members of a general practice in Oxford City were approached and asked if they would be prepared to help in the proposed study by selecting at random fifty patients whom they considered to be free from cardiovascular disease or hypertension. They chose equal numbers of males and females in each of five decades from 25 years to 74 years of age. A similar selection was made from a general practice in rural Oxfordshire.

Methods for the random selection of patients are often the object of criticism (Gore et al, 1977). In this study the method adopted was simple but acceptable to a statistician who was consulted. It was as follows: the records of every fifth patient on the files of the practice were scrutinised for a cardiac history, or hypertension. The records of unsuitable patients were returned to the file and the next fifth patient record examined, until the necessary numbers in each group were obtained.

A letter was sent to each person asking if they were willing to co-operate in a study of the normal ECG. The letter, in addition to

explaining the background of the study, stressed that it was being undertaken with the full support of the patient's own doctor. Care was also taken to emphasise that it was a strictly non-invasive procedure! Accompanying each letter was a form on which the volunteer was asked to indicate the times at which it would be most convenient for them to come to the hospital and also whether or not they could be reached by telephone. Those who had to make one or more special journeys to the hospital in connection with the survey were offered reimbursement for their travelling expenses.

Many of those who lived in villages remote from Oxford could not be expected to make long journeys to take part in a study from which they were unlikely to benefit directly. For these, arrangements were made for them to attend a hospital near their homes.

Before each 24-hour ECG study a standard 12-lead ECG and blood pressure were recorded. The occupation, smoking habits and details of any regular medication were also noted and diary sheets provided to enable them to record meal-times, the approximate period during which they were asleep and the timing of any episodes of particular activity. (Fig. 46).

All recordings were made on the Medilog 4-24 miniature tape recorders, previously described in Chapter 1. Silver/silver chloride disposable electrodes were used and these were placed, wherever possible, in positions from which large positive monophasic QRS complexes and comparatively small T-waves could be recorded. The amplitude and wave-form of the ECG were checked with a monitor unit (Oxford Instruments type M.1) and a Tektronix miniature battery powered oscilloscope type 204.

Because the volunteers were expected to be normally active during the 24-hours of recording, the adhesive of the electrodes

themselves was supplemented by hypo-allergenic adhesive tape. The electrode leads were similarly secured to avoid movement-induced artifacts.

Individuals who would have found it inconvenient to return to the hospital at the end of the 24 hours were shown how to disconnect the recorder and remove the electrodes. In those cases arrangements were made for the equipment to be left at nearby Health Centres or general practice surgeries from which they were returned by various methods.

The recordings were examined semi-automatically by the arrhythmia analyser previously described in Chapter 7, for the presence of ventricular and supraventricular extrasystoles, non-premature beats with wide QRS complexes, episodes of coupled beats, tachycardia, bradycardia and asystole or gaps.

Hourly counts were made of extrasystoles, "wide" beats and sinus beats, (wide beats being defined as those which, like ventricular extrasystoles, contained an abnormal proportion of low frequency components; unlike V.E.S. they were not premature).

A permanent recording was also made of any abnormality.

3) Results

A total of 169 invitations were sent to prospective volunteers, 85 to the urban group and 84 to the rural group.

From the former, 63 (74%) accepted and from the latter, 58 (69%) accepted. Definite refusals were uncommon: 3 (3.5%) in the urban group and 5 (6%) from the rural group. 32 invitations were not answered: 18 (21%) and 14 (17%) respectively. No attempt was made to investigate this lack of response. Specific reasons for not participating were given as follows: moved from the area, 6; found to be outside the age range, 1; sudden family illness, 1; envisaged having problems with the recorder during work, 1.

A total of 113 recordings was eventually made to achieve the sample of 100: 58 from the urban group and 55 from the rural group. The 13 which were discarded from the survey included the following: one subject (male!) investigated the operation of the recorder too thoroughly and caused the tape drive mechanism to jam; one disconnected the encumbrance prematurely because of social commitments. The remaining 11 recordings contained movement artifacts which, although generally of a minor nature, would have made the hourly count inaccurate. Surprisingly, this did not appear to be associated with the more active occupations.

In the following description of the arrhythmias detected the subjects have been divided into the two groups: city and country (Table II and Table III). Thirty-six of the recordings (36%) showed one or both of the extrasystoles classifiable by the analyser, i.e. ventricular extrasystoles (V.E.S) and supraventricular extrasystoles (S.V.E.S.) Neither ventricular tachycardia (V.T.) nor supraventricular tachycardia (S.V.T.) was detected. In addition to the semi-automatic analysis, each tape was scrutinised for other possible arrhythmias but no atrial fibrillation, atrial flutter, ventricular fibrillation or a-V block was detected. Of the arrhythmias present in the 36 recordings, five were trivial and consisted of a single V.E.S. (1 case) and a single S.V.E.S. (4 cases). In twelve cases the incidence of extrasystoles was greater than 1:1000 (0.1%) and of these eight were ventricular in origin; one (D.L.932) showing extrasystoles from two foci in the ventricles (0.25%) and a high incidence of S.V.E.S. (4.3%); and in one case (J.B. 709) an episode of coupling from S.V.E.S. was detected (Fig. 47).

The greatest incidence of V.E.S. and S.V.E.S. was found in the highest age group.

From Tables II and III it is apparent that the incidence of S.V.E.S. was highest in the age group 65-74 years. This applies to both the urban and rural groups although it more marked in the former. Since it is necessary to be cautious when interpreting the results of a relatively small sample, further studies with follow-up will be required to give information as to whether or not this increased incidence is due to occult coronary artery disease.

The significance of the comparatively high incidence of V.E.S. in age-group 35-44 of urban dwellers, where it is similar to that of the 65-74 age group, is also unclear. It is possibly a sampling problem which, again, will need a follow-up study.

Table II

Arrhythmias detected in Group I (urban)

Normal subject	Sex	Sinus beats	S.V.E.S.	V.E.S.
<u>25-34 years</u>				
J.B. 725	F	114,109	1	0
P.V-D. 863	F	111,406	0	551
G.T. 914	M	104,562	0	8
<u>35-44 years</u>				
N.G. 739	M	112,448	0	2
N.S. 861	M	114,306	0	265
H.C. 851	F	92,073	0	247
P.S. 860	F	108,158	0	82
<u>45-54 years</u>				
J.C. 718	M	93,425	0	3
J.B. 709	M	103,054	1073*	0
P.L. 744	M	98,893	0	75
S.S. 903	M	130,325	164	2
<u>55-64 years</u>				
E.F. 724	F	90,871	1	0
J.H. 822	F	115,848	0	132
R.Q. 899	F	130,129	0	10
M.S. 848	F	131,601	0	22
L.I. 909	M	93,239	0	57
<u>65-74 years</u>				
A.P. 940	F	89,011	2268	0
M.H. 912	F	131,572	0	64
R.W. 823	M	117,472	4720	0
H.S. 891	M	106,105	0	106
D.L. 932	M	88,278	3998	232**
* including episodes of coupling				
** from two foci				

Table III

Arrhythmias detected in Group II (rural)

Normal subject	Sex	Sinus beats	S.V.E.S.	V.E.S.
<u>25-34 years</u>				
J.E. 971	M	92,480	0	74
<u>35-44 years</u>				
E.S. 754	F	140,082	0	1
F. 871	F	105,125	0	6
<u>45-54 years</u>				
A.S. 818	F	131,208	0	9
L.S. 773	M	110,356	0	377
R.O. 945	M	107,167	0	9
<u>55-64 years</u>				
D.W. 1249	F	110,984	10	0
H.K. 746	M	89,990	0	655
T. 782	M	100,930	0	2
L.L. 953	M	117,263	1	0
<u>65-74 years</u>				
F.C. 1246	F	104,707	1	7
F.S. 1270	F	107,247	1	0
A.H. 1267	F	132,318	120	0
A.C. 783	M	94,380	0	20
A.B. 1237	M	105,310	2530	3519

JB 709 49 yrs. Male

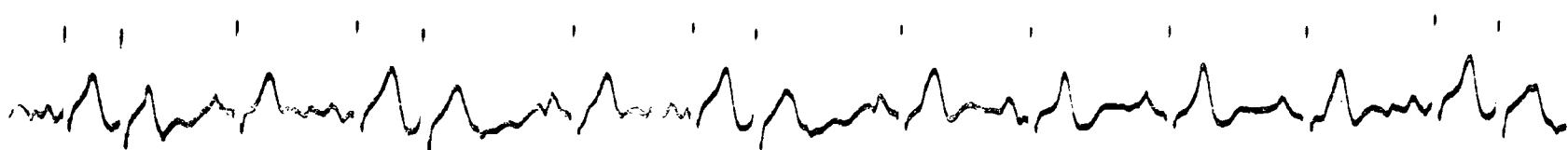


Fig. 47

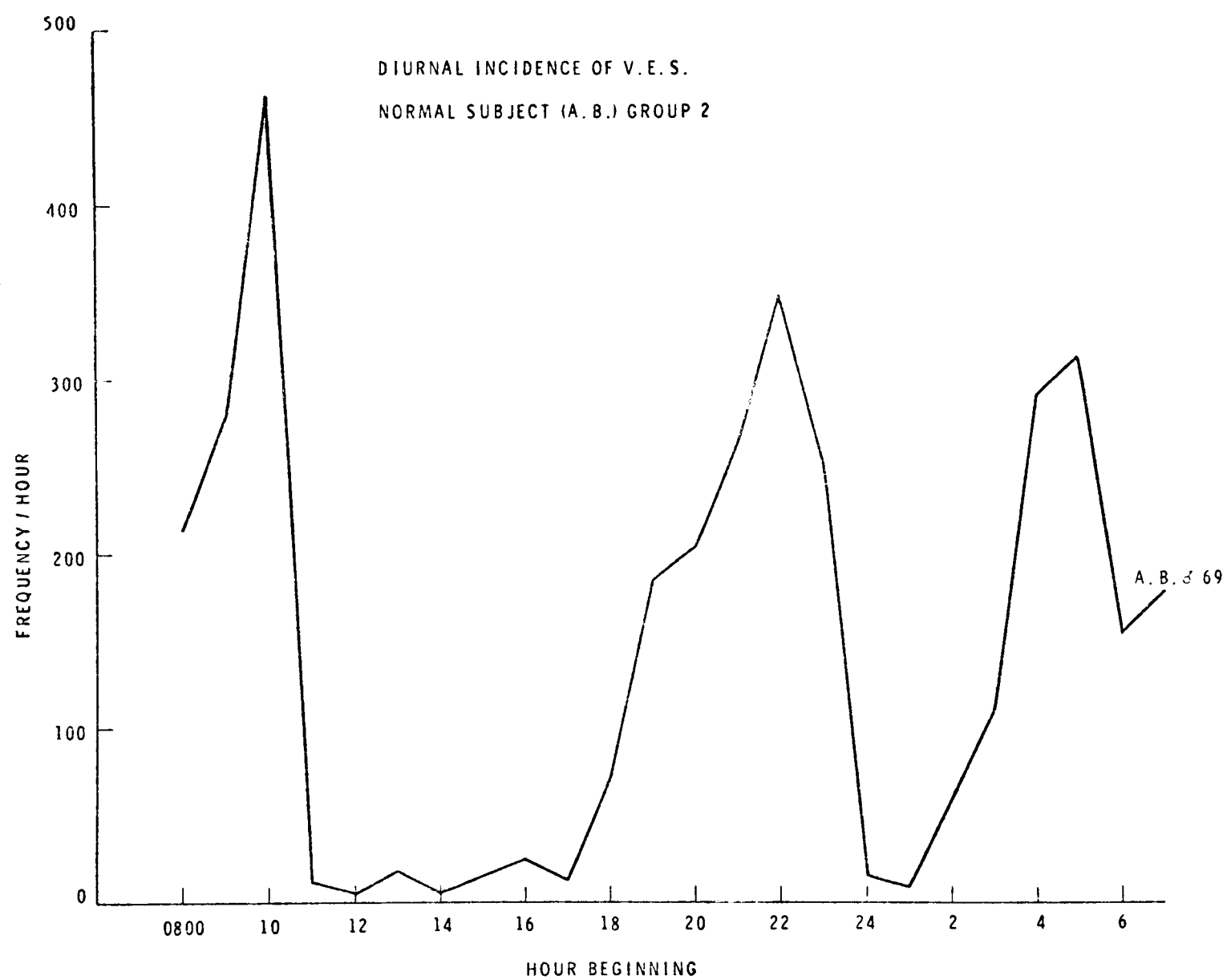


Fig. 48 Diurnal incidence of V.E.S.
Normal subject (A.B.) Group 2 (Rural)

DIURNAL INCIDENCE OF V.E.S.
NORMAL SUBJECTS GROUP 1

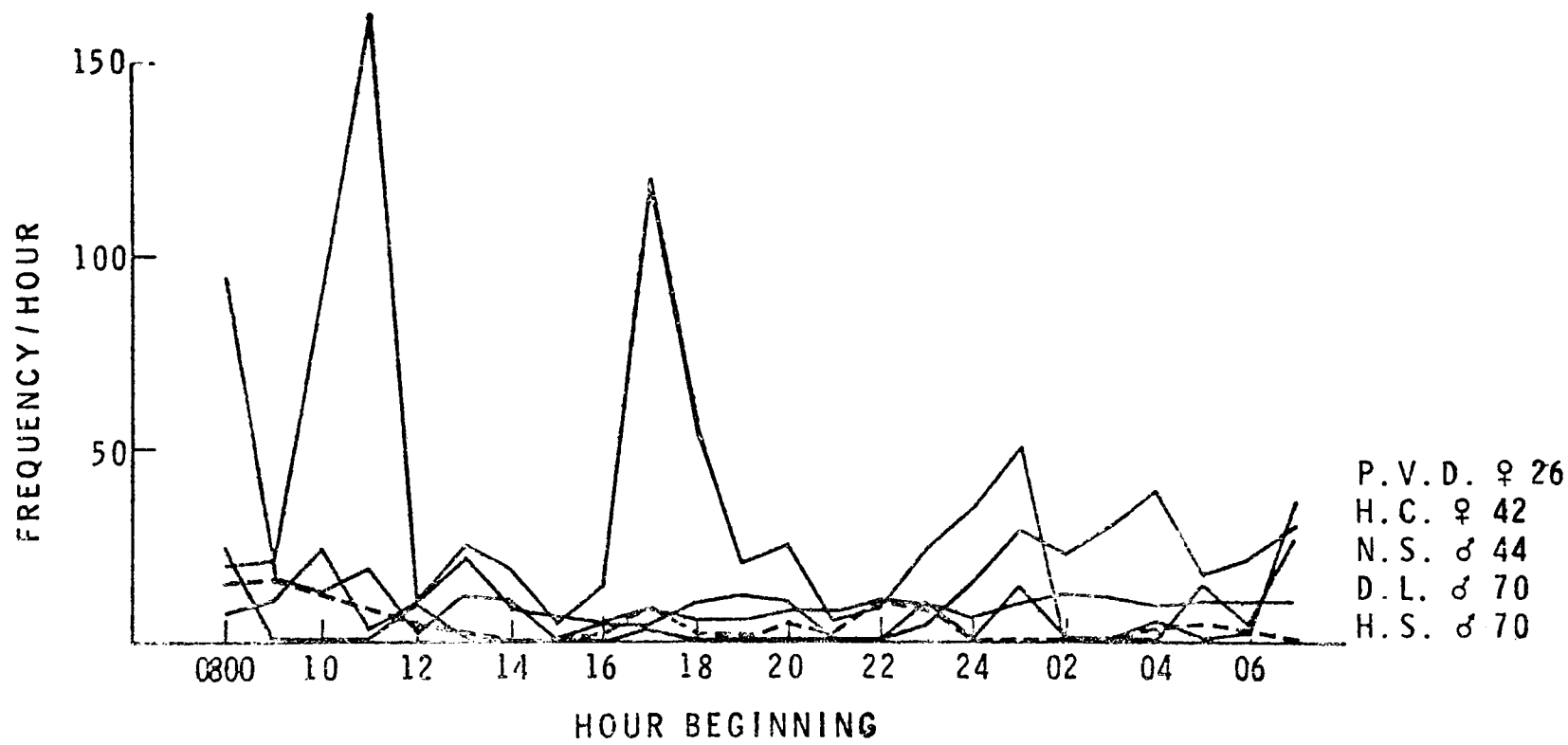


Fig. 49 Diurnal incidence of V.E.S.
Normal subjects Group 1 (Urban)

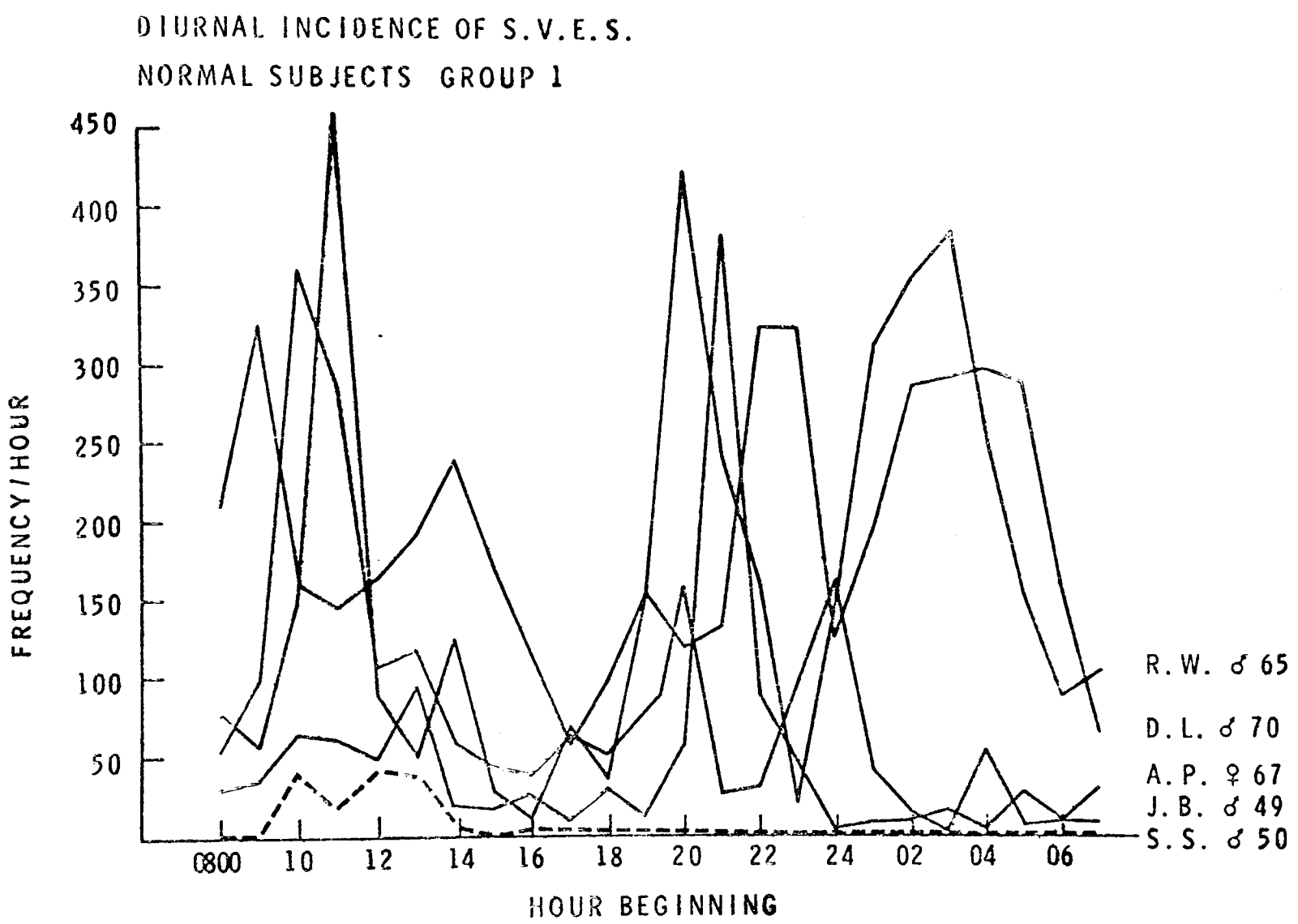


Fig. 50 Diurnal incidence of S.V.E.S.
Normal subjects Group 1 (Urban)

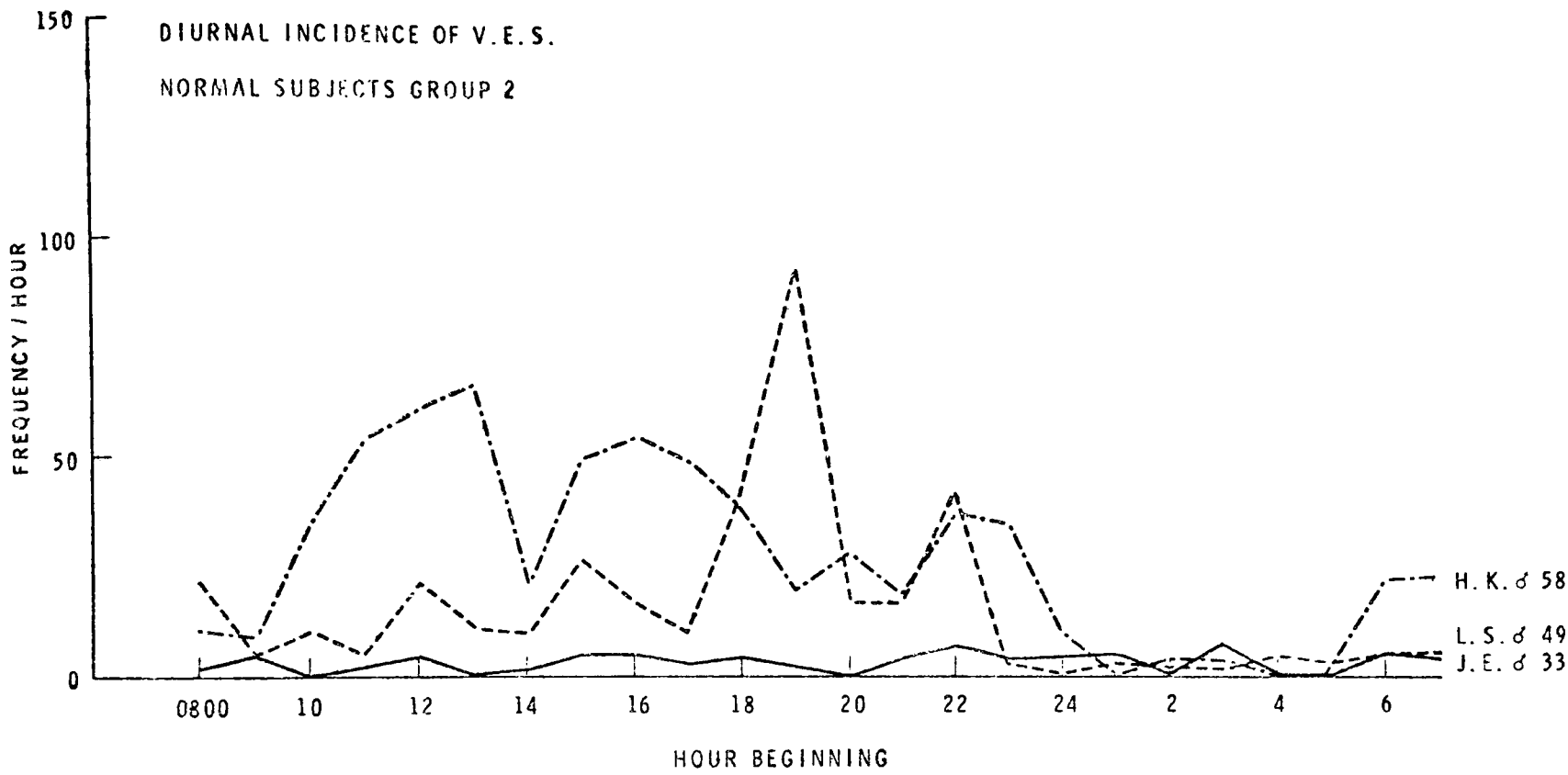


Fig. 51 Diurnal incidence of V.E.S.

Normal subjects Group 2 (Rural)

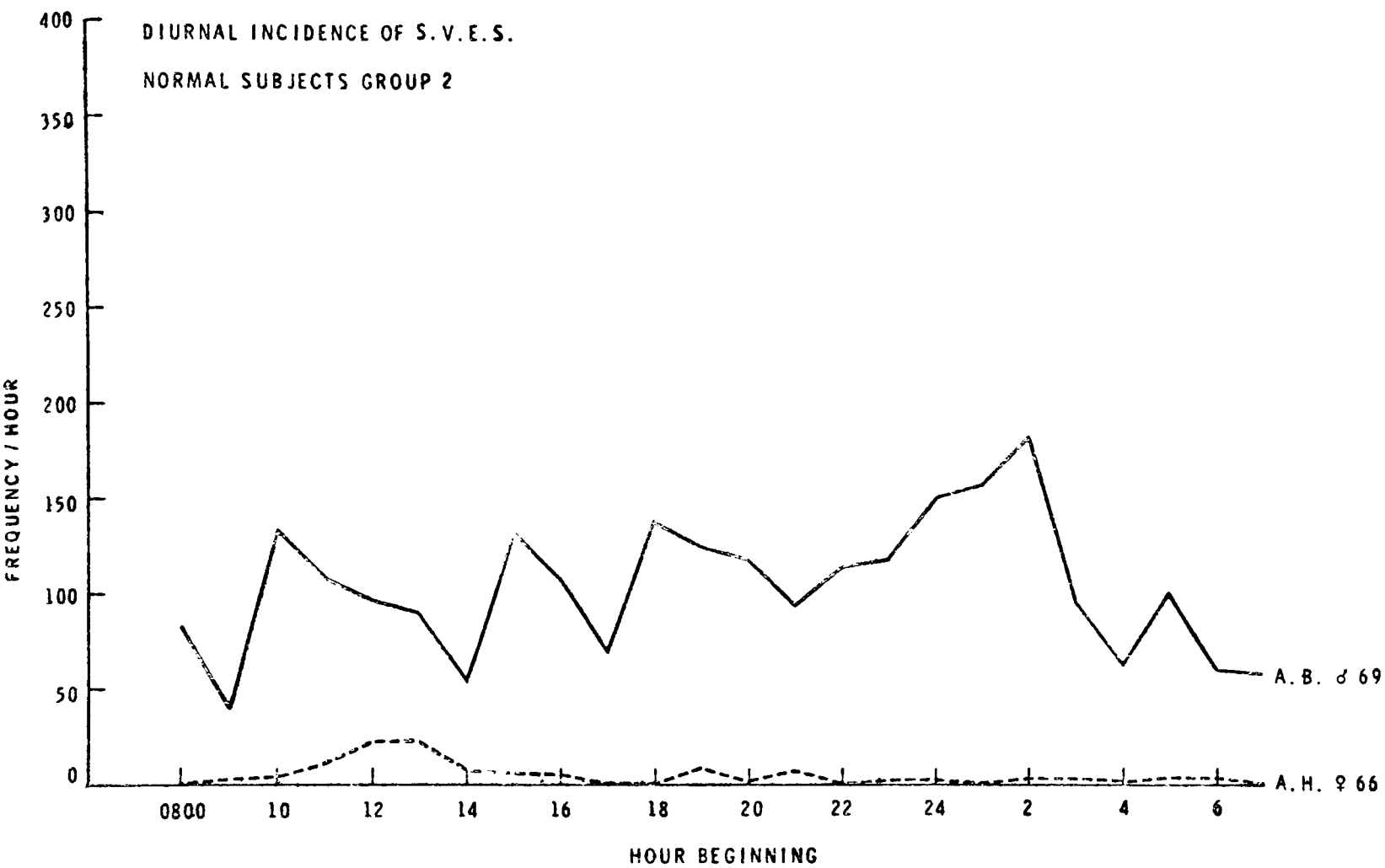


Fig. 52 Diurnal incidence of S.V.E.S.
Normal subjects Group 2 (Rural)

DIURNAL VARIATION OF HEART RATE. MEAN $\pm$ S.E.M.
50 NORMAL SUBJECTS GROUP 1

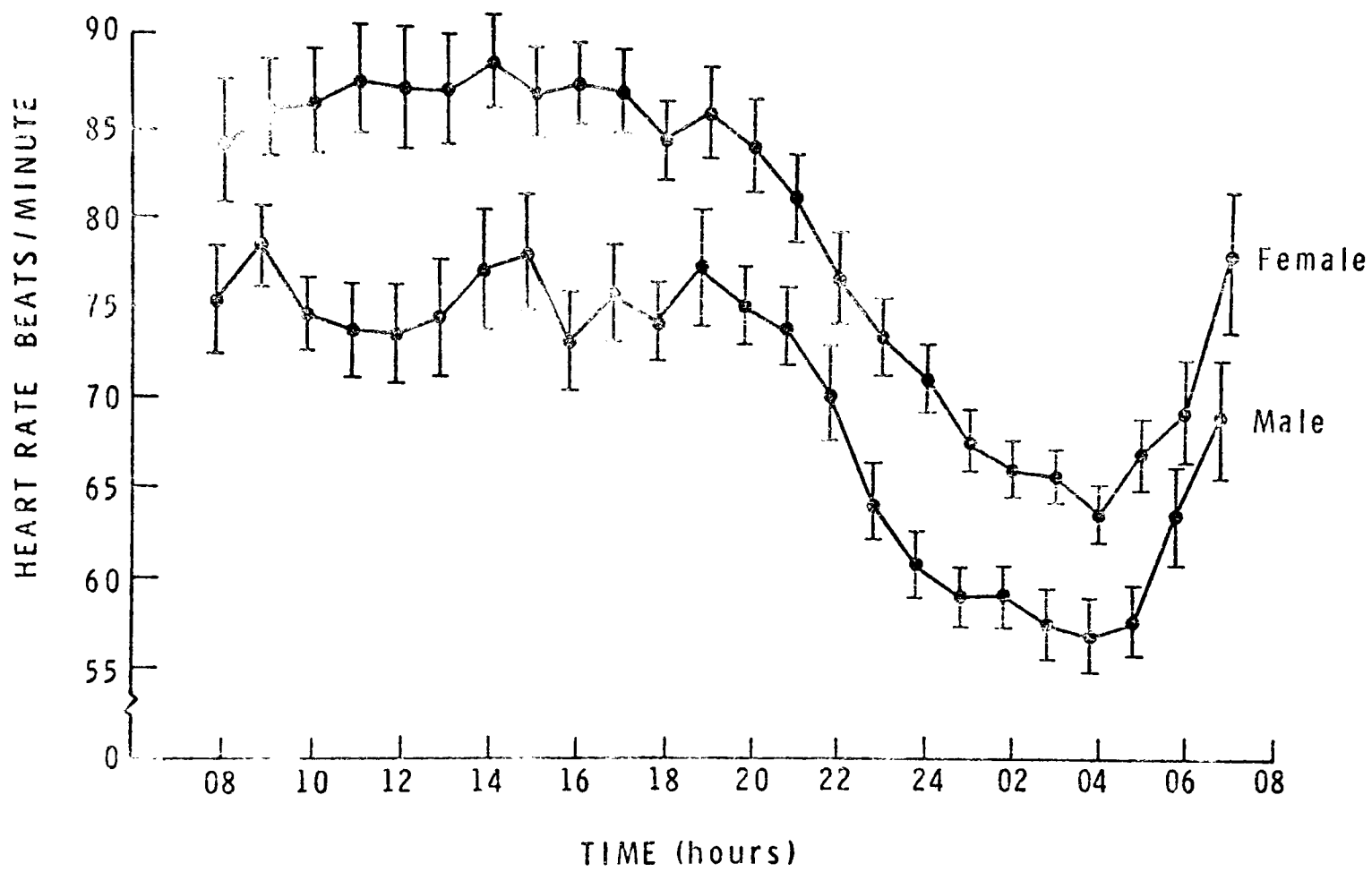


Fig. 53 Diurnal variation of heart rate
50 normal subjects Group 1 (Urban)

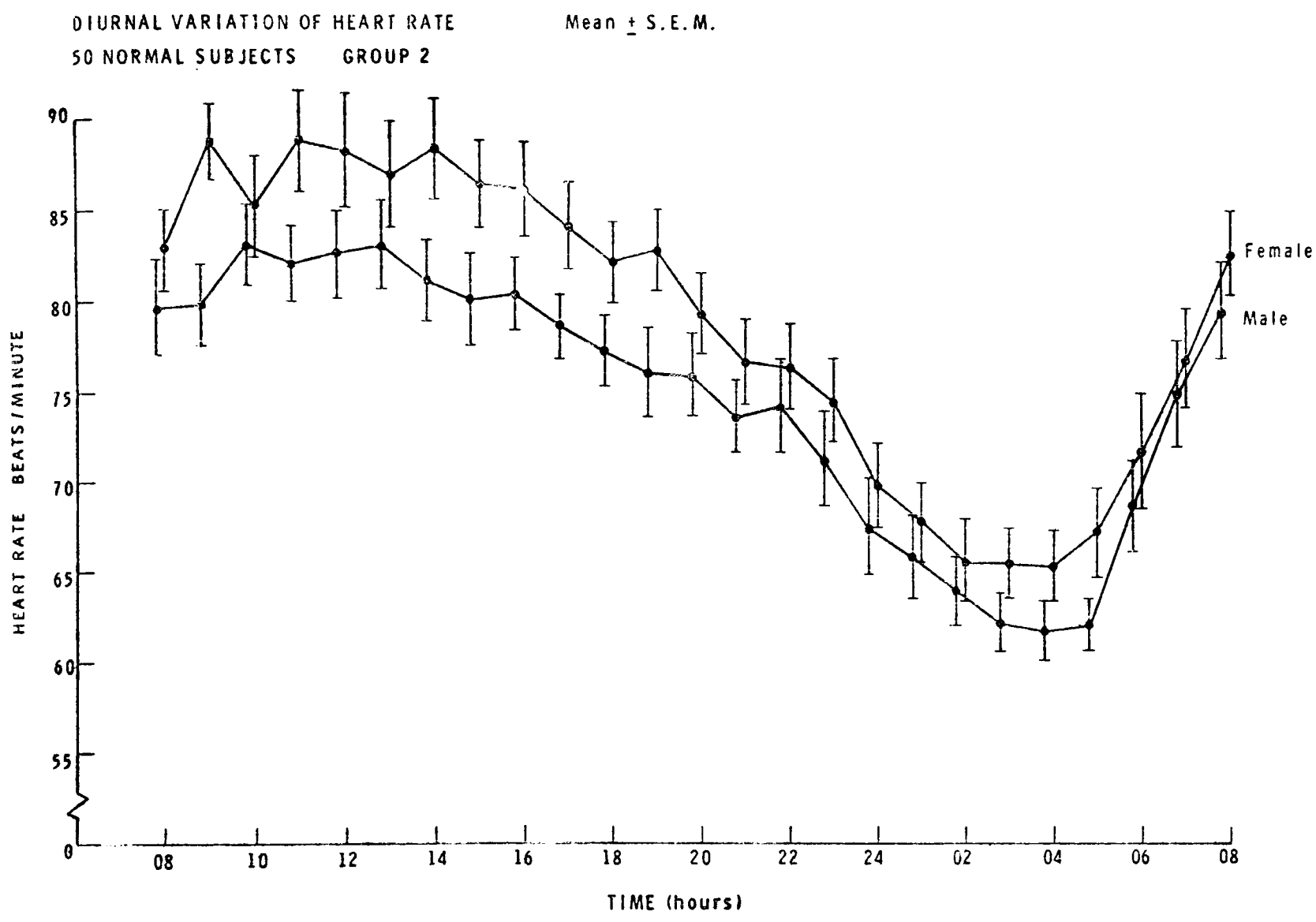


Fig. 54 Diurnal variation of heart rate
50 normal subjects Group 2 (Rural)

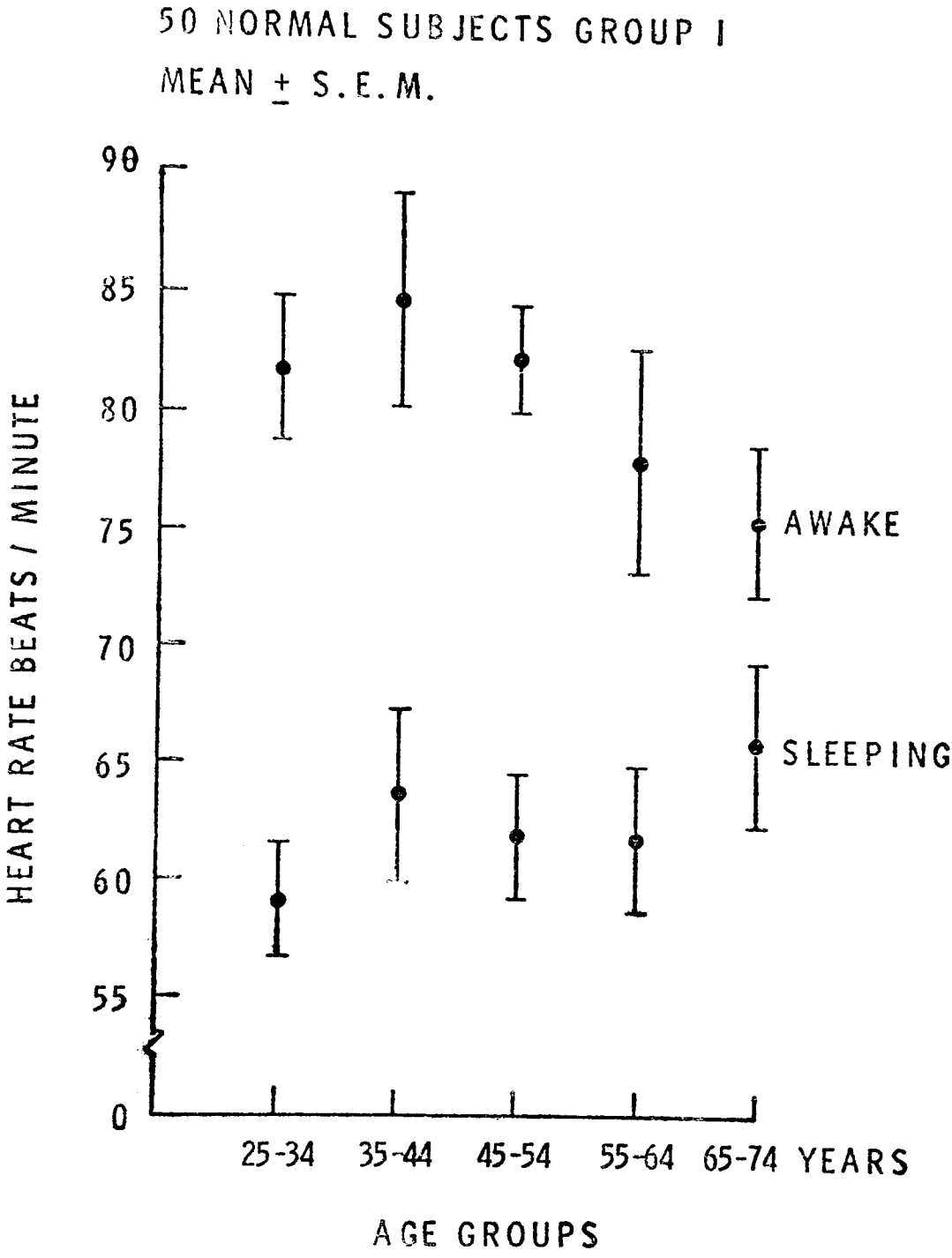


Fig. 55 50 Normal subjects Group 1 (Urban)

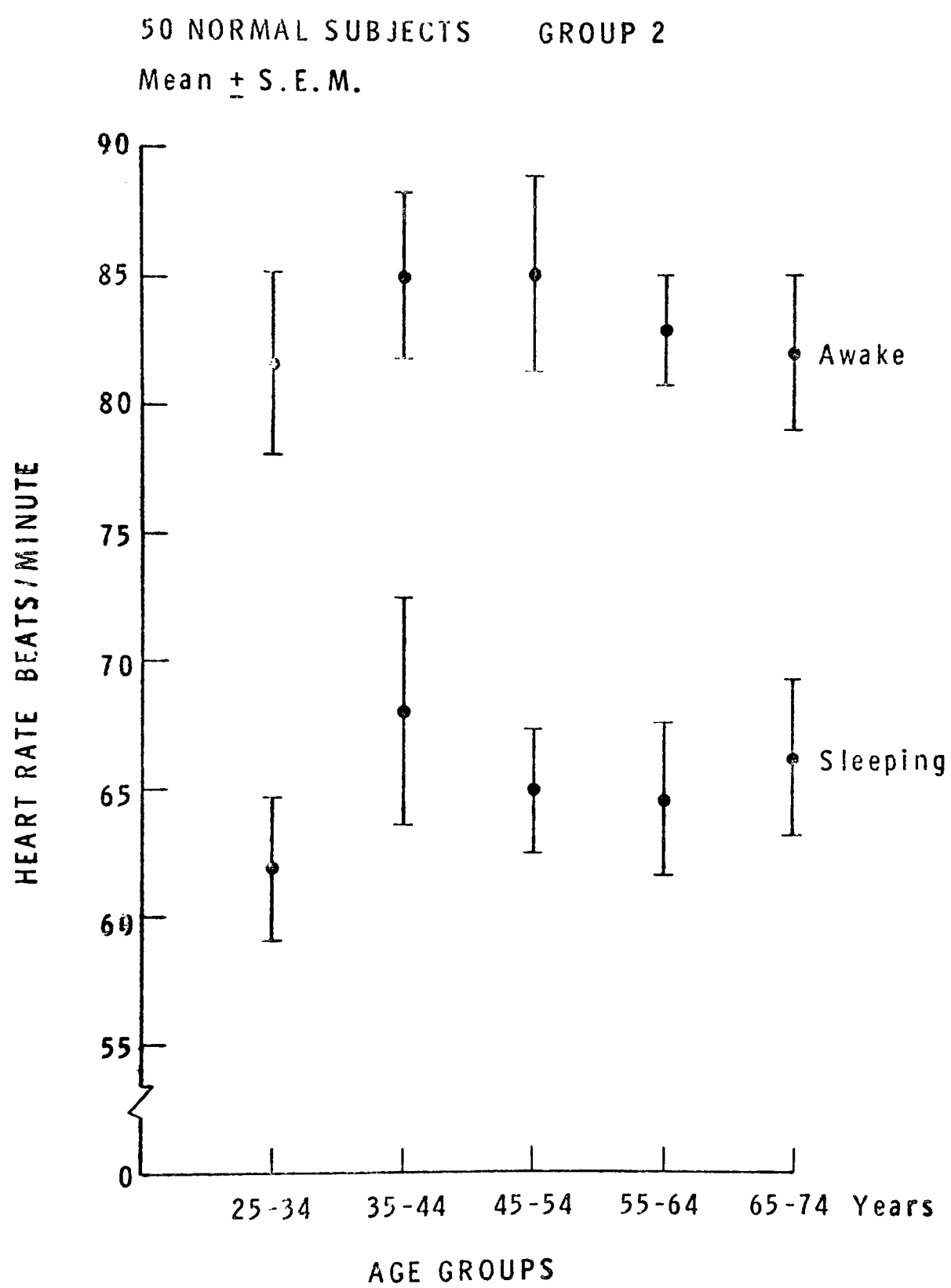


Fig. 56 50 Normal subjects Group 2 (Rural)

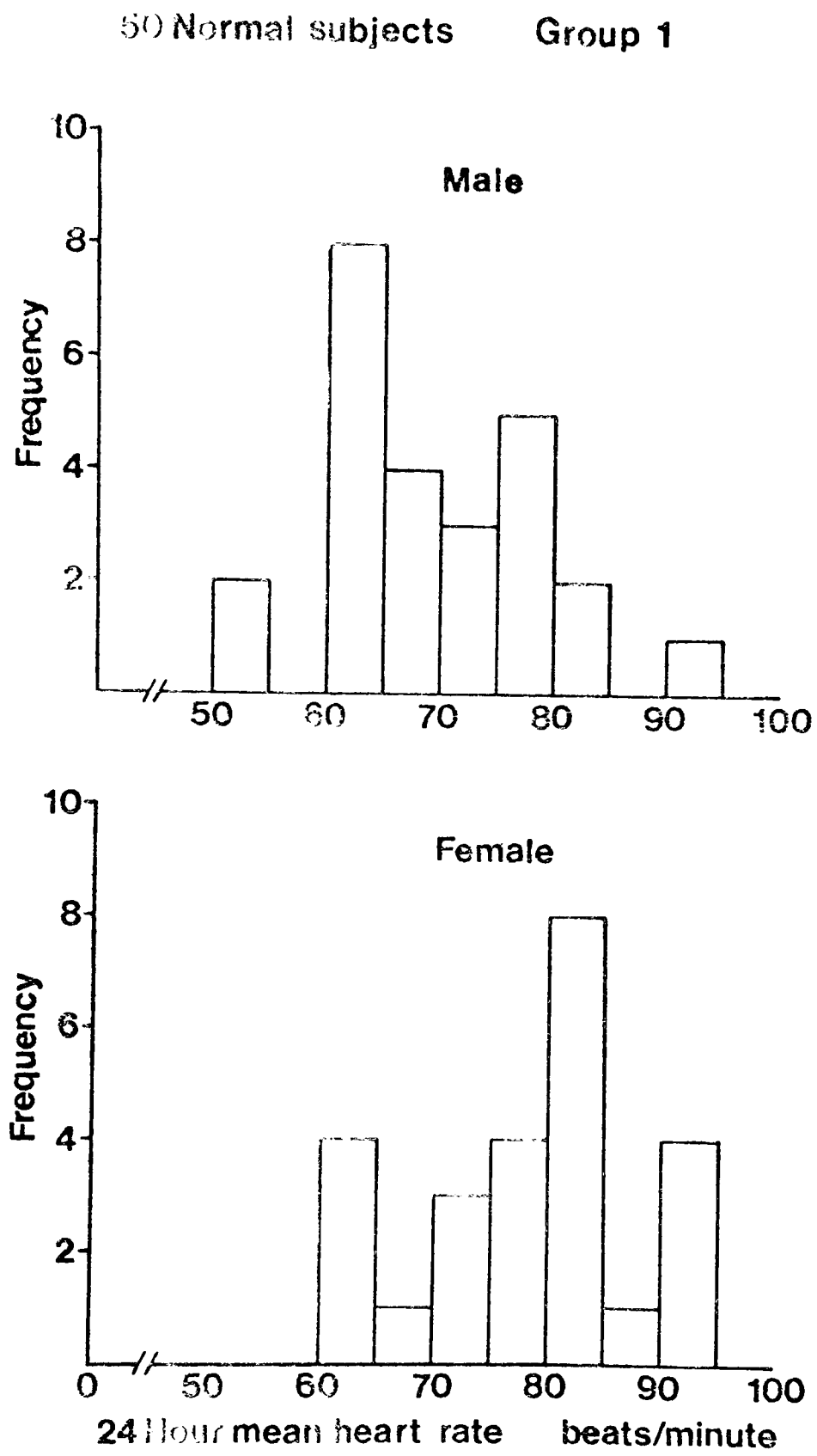


Fig. 57 50 Normal subjects Group 1 (Urban)

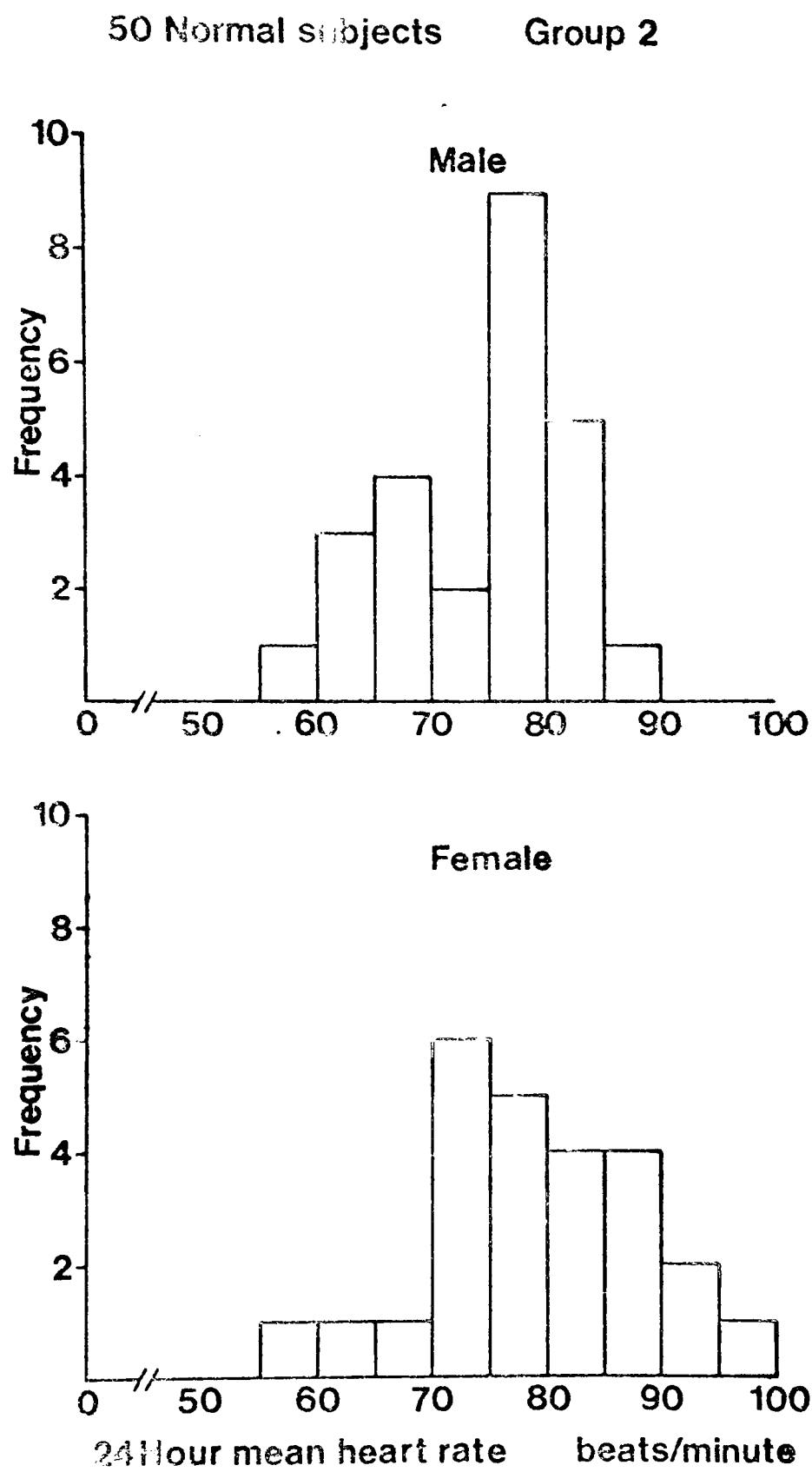


Fig. 58 50 Normal subjects Group 2 (Rural)

City subjects had a higher overall incidence of extrasystoles than country subjects. The highest incidence of V.E.S. (3.2%), however, occurred in the recording from a country subject (A.B. 1237) (Fig. 48). This was also the only case in which any extrasystoles were noted in the standard 12-lead ECG.

Diurnal variation in the incidence of V.E.S. and S.V.E.S. is shown in Figs. 48-52. From the hourly counts of normal and abnormal beats it was possible to calculate the variations in mean heart rate for males and females in both groups throughout the 24 hours, and these results are shown in Figs. 53 and 54. The mean overall heart rate and its distribution for all members of each group, both when awake and when asleep, was also determined, as shown in Figs. 55-58. The waking figures were taken from 0900 hours to 2000 hours inclusive when, from the diary forms, all the subjects reported they were awake. Similarly, the sleeping rates were from the period 0100 hours to 0400 hours inclusive, during which time all were asleep.

It will be seen that the pattern of diurnal change in mean heart rate is substantially the same for both groups and for both sexes. It is also similar to that described by Clarke et al (1976). The hourly rates from the female subjects in the urban and rural groups are virtually the same, with an average of approximately 1 beat per minute difference during the period 0900 hours to 2000 hours and 0.5 beat per minute difference between 0100 hours and 0400 hours.

The hourly mean heart rates from the males indicate a considerable difference between the groups. Those in the rural group have an almost consistently higher rate than those in the urban groups, with an average difference of 5 beats per minute during the daytime period and 5.5 beats per minute during the four hours at night. No reason for this difference could be deduced from the occupations of the members of the groups, nor from their home environments.

Fifteen of the volunteers were cigarette smokers but only nine of them exceeded ten cigarettes each day. Two were in the urban group and seven in the rural group. There was no apparent correlation between cigarette smoking and the incidence of extrasystoles. Of the twelve subjects whose 24-hour ECG showed more than one extrasystole per 100 beats, only one smoked more than 10 cigarettes each day and one less than two.

An attempt was made to correlate the presence of extrasystoles with the individual's socio-economic group as classified in 1970 by the Office of Population Census and Surveys (Appendix B). This was not entirely satisfactory for two reasons. Firstly, two members of the group containing those subjects who had more than 1:1000 extrasystoles were housewives. As is now well known, this demanding occupation was not included in the classification except possibly under the highly contentious description of "unskilled domestic worker"! Secondly, many of the older age-group had retired. If, however, these were classified by their employment immediately before retirement, then 10 of the 12 members of the group could be categorised as follows: three were managers or supervisors (S.E.G. 1.2 or 2.2), three were foremen or supervisors in S.E.G. 8z, one was a professional worker (solicitor) in S.E.G. 3, one in S.E.G. 6 as a skilled junior worker and two were ancillary workers (research assistant and physiotherapist) in S.E.G. 5.1.

4) Discussion

The findings of this survey have similarities to those of other workers but accurate comparison is difficult due to the differences in the categories of abnormality listed in each and in the ages groups

studied.

In this survey arrhythmias, including the trivial, were detected in 36 cases (36%). In the group studied by Raftery et al (1976) the figure was 28%. Brodsky et al (1977) used a group of 50 male medical students who were considered to be free of cardiovascular disease. 56% of these were found to have at least one atrial premature beat and 50% at least one premature ventricular contraction. As the age range of the medical students was 23 to 27 years the incidence of arrhythmias here appears at first sight to be considerably higher than that reported in the first two surveys. If, however, the basis for comparison is the incidence of extrasystoles more frequent than 1:1000 beats then, in the case of V.E.S., none of Brodsky's subjects reaches this level when averaged over 24 hours and, in the case of S.V.E.S., probably only one individual exceeded this level.

In the group of 86 normal subjects aged 16 to 65 years studied by Clarke et al (1976), ventricular ectopic beats were seen in 63 (73%). A total of only seven, however, had a frequency of V.E.S. exceeding five per hour which is, incidentally, similar to 1:1000 beats. Of these, only one was in the lowest age group: a female aged 25 years. Again, these findings are not dissimilar.

There still appears to be some controversy over the clinical significance which should be attached to certain patterns of arrhythmias (Bigger et al, 1977). This might be reduced if the results of surveys were to be expressed in a readily comparable manner.

CHAPTER 11

SUMMARY AND PROSPECT1) Estimated cost of analyser

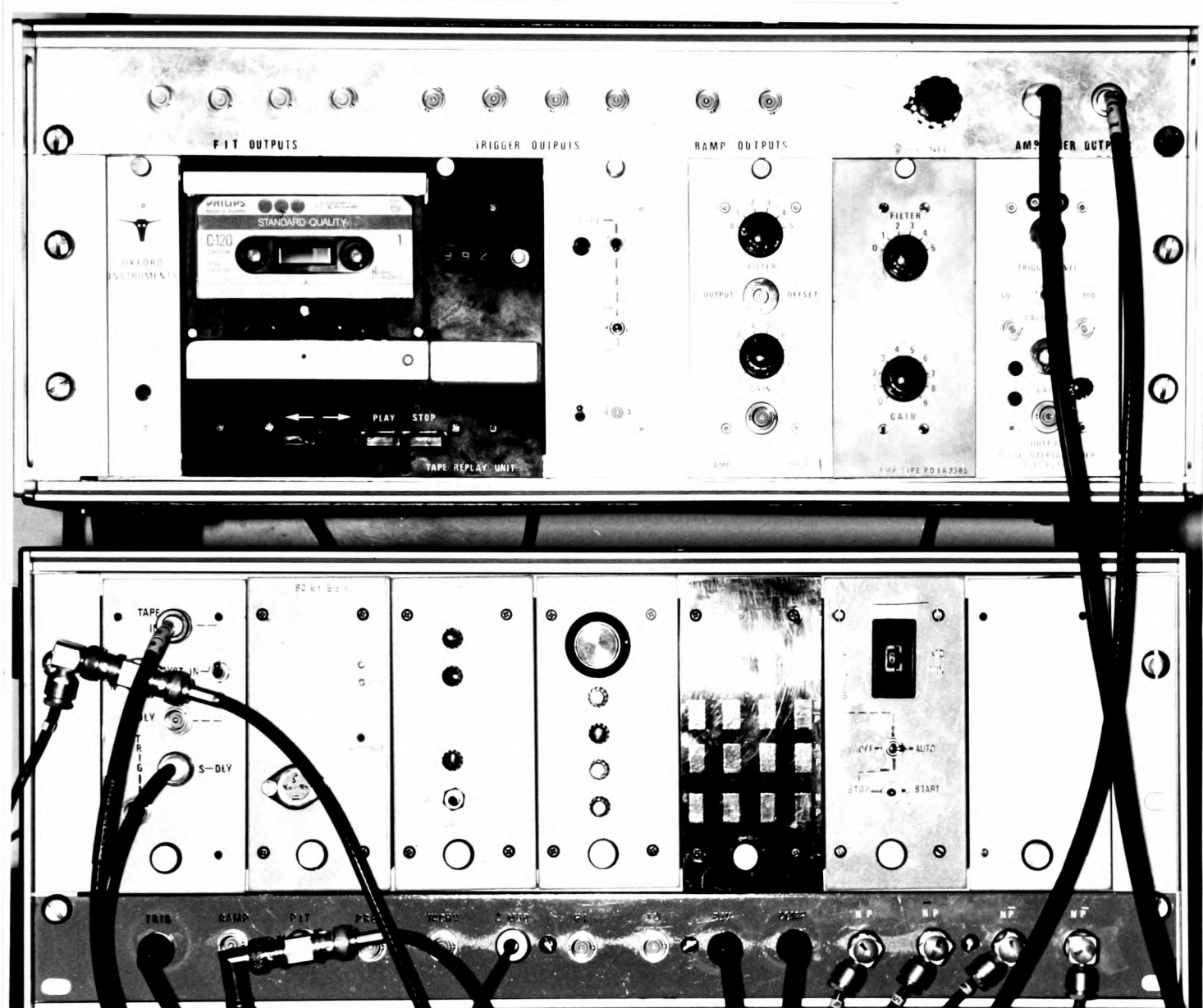
Throughout this thesis, the arrhythmia analyser has been described as "comparatively inexpensive".

When considering prototype equipment, built in a non-commercial laboratory, true cost is difficult to estimate because labour charges, in particular, tend to be ignored. Discussions with those engaged in the industrial manufacture of similar equipment suggests that materials, labour and overhead costs, together account for 20% to 25% of the price of the finished product. Therefore, it is to be expected that a "home-made" system must be considerably less expensive.

The cost of components used in the construction of the arrhythmia analyser was in the region of £250, with the analogue to digital converter being by far the most expensive single item, at £60. This amount does not include the commercial replay tape deck, the oscilloscope display-monitor or the hard copy printers, the last two being such as might be found in any physiological laboratory.

The prototype analyser evolved over a period of several years but it is estimated that an individual competent in electronics would take eight to ten weeks to build and test a duplicate.

Thus it would appear that a semi-automatic analyser of 24-hour ECGs could be constructed comparatively inexpensively in a reasonably well equipped hospital or university department of physiology, cardiology or medical physics.



1977 version of arrhythmia analyser

Fig. 59

Figure 59 shows the complete 1977 version of the analyser.

2) Other practical applications

Although the development of the arrhythmia analyser was a research project and its evolution has depended almost entirely on research and charitable funds, nevertheless it has now become a predominantly clinical tool.

During the past three years approximately 1800 tape recordings have been analysed. Some 1200^{*} of these have been made for clinical purposes but this figure does not represent the demand which has arisen since the facility became available.

Due mainly to the limited number of recorders and to delays in returning them from the more distant parts of the Oxfordshire region, the service has had to be limited to clinicians in the Departments of Cardiology and Paediatric Cardiology.

Not unnaturally, outpatients predominate and account for approximately 80% of the recordings. A single recording has been made in over 95% of cases but serial records, covering up to 15 days, have been taken in an effort to catch the more ephemeral abnormality. Most of the serial records, however, have not extended over more than three days.

The clinical problem behind the majority of requests for a 24-hour ECG has been, since the beginning of the service, the need to identify the cause of "funny turns" or "blackouts". (Pickering et al, 1976).

Initially this accounted for some 90% of requests, with the balance being directed to elucidating the focus or mechanism of some

* see Addendum, p. 158^a

transitory arrhythmias. More recently, however, the technique has been increasingly used to investigate the possible malfunction of implanted demand pacemakers and this now represents about 5% of the total clinical recordings.

This use of 24-hour ECG recording is supplementary to the usual checks of threshold and pulse wave-form which are made in the pacemaker clinics. It does, however, appear to provide a particularly reassuring check for the patient who will know that the performance of his pacemaker has been monitored for a full 24 hours and possibly also during a period in which he was doubtful about its behaviour.

There have been very few reports of this technique in the literature (Karpman et al, 1976) (Asato et al, 1976), and it is hoped that finance will be available to develop this aspect of the ambulatory monitoring service.

There are some technical problems associated with the analysis of ECG recordings from patients with prosthetic pacemakers. The voltage of stimulation pulse is high when compared with that of the QRS complex which accompanies a sinus beat and, in addition, the electrical axis is virtually always markedly different. Consequently, a recorder which has been adjusted for optimum performance when the patient is in sinus rhythm will be overloaded and introduce distortion in the presence of artificial pacemaker activity.

Fortunately, the poor high-frequency response of the tape recorder tends to attenuate the pacemaker pulse and reduces it to more manageable proportions. The analyser itself is not too incommoded by the somewhat bizarre wave-form and periods of pacing can be generally identified by the detection of "wide" beats occurring at completely regular intervals at rates in the region of 65 to 72 per minute.

Pacemaker induced arrhythmias can, of course, be detected in the same fashion as those initiated by other stimuli.

Further developments in the analyser may be necessary if in the future it should, for instance, be necessary to detect pacemaker activity in the presence of bundle branch block.

Concurrently with the clinical use of the analyser, several research projects and drug trials have been undertaken using the system and some 600 recordings have been analysed for these purposes.*

In addition to the survey of the 24-hour ECG in 100 normal subjects, described in Chapter 10 of this thesis, a study of the diurnal variation of ventricular extrasystoles (Pickering et al, 1976) and of the effects of sleep, exercise and Propanolol on the incidence of ventricular extrasystoles (Pickering et al, 1977) have been completed.

Still continuing is an evaluation of the long-term effect of the beta blocker Atenolol in a double-blind study of patients in the coronary care unit. Serial 24-hour ECGs from these patients are analysed for ventricular arrhythmias.

A study is also being undertaken of the incidence of cardiac arrhythmias in patients with neuromyopathies. Funds from the Oxfordshire Regional Health Authority, through the N.H.S. Locally Organised Research Scheme, have made it possible to start an investigation jointly with the Department of Neurology into the incidence and nature of arrhythmias associated with disturbances of consciousness.

3) Further development

Technical development of the arrhythmia analyser in the near future will be concerned mainly with interfacing it with the Data General S.200 computer which is now operating in the Department

* see Addendum, p. 158^b

of Cardiovascular Medicine. The analyser will continue in its rôle of classifying and counting premature beats, tachycardias, periods of asystole and aberrantly conducted beats, whilst the computer will at first perform mainly the "housekeeping" tasks of tabulating the data and presenting the information in a form suitable for inclusion in the patients' notes.

As mentioned earlier, in Chapter 3, the R-R interval histogram and its derivative, the R-R interval difference histogram, are effective methods of displaying the variations in heart rate, the incidence of premature beats, or the occurrence of periods of prosthetic pacemaker activity. A purpose-built histogram generator tends to be inflexible due to a limited capacity of beats per "bin" and a fixed level of resolution. These limitations do not apply if the histograms are produced by a digital computer program when the capacity of the bins can be increased to contain, for example, several hours of paced beats or, alternatively, the resolution can be increased so that a comparatively few premature beats can be demonstrated.

The writer is fortunate in having been given a further research grant from the Oxfordshire Regional Health Authority for the purchase of a Tektronix type 4006-1 terminal which will be used in association with the S.200 computer and arrhythmia analyser in a study of the effect of different collecting periods on the usefulness of this method of data presentation.

The writer believes that analogue pre-processing, followed by manipulation using digital techniques, will provide the method of choice for the analysis of the data from 24-hour ECG recordings during the next two to three years. The comparative inflexibility of analogue methods and the rapidly decreasing cost of microprocessors makes further prognostication a pointless exercise.

Ambulatory monitoring of the ECG accompanied by monitoring of the EEG and eye movements was used to see whether Propranolol could reproduce the changes in the incidence of V.E.S. which occur during sleep. The conclusions were that the suppression of V.E.S. during sleep could be largely explained by autonomically mediated changes of heart rate and that the sympathetic has a greater effect than the vagus; when V.E.S. disappear completely during sleep some other factor, unrelated to heart rate, may be involved (Pickering et al, 1977).

A study of the effects of Atenolol on arrhythmias in patients suffering from recent myocardial infarctions is still in progress. The drug has been given orally from the first day in 12 cases but no significant difference has been detected, at one week, between the incidence of arrhythmias in the treated and the control group. At one month, however, there is a significant difference. The trial is to be repeated using Atenolol administered intravenously.

An incidental discovery during analyses of the ECG recordings made during this study is that most episodes of paroxysmal ventricular tachycardia were immediately preceded by a late diastolic V.E.S. rather than an R on T phenomenon.

Information obtained from the 1200 tape recordings requested for clinical purposes helped in the solution of a variety of diagnostic problems and confirmed clinical opinion in others.

In fourteen cases an arrhythmia was shown to have occurred at the time when the patient experienced a "typical attack". In twenty cases the attack was shown not to have been accompanied by an arrhythmia.

Palpitations were shown to be due to supraventricular tachycardia in 26 cases and to ventricular tachycardia in 12 cases. Infrequent ventricular extrasystoles were shown to be the cause of the patients' problems in 58 cases and supraventricular extrasystoles in 24 cases.

The correct functioning of implanted pacemakers was confirmed in 36 cases and a malfunctioning unit detected in 2 cases.

Paroxysmal atrial flutter, Wenckebach phenomenon and paroxysmal atrial fibrillation were each detected on a single occasion, whilst short periods of asystole, 'wandering pacemaker', dropped beats and 'brady-tachy syndrome' were each seen twice.

APPENDIX A

ARRHYTHMIA ANALYSER

Circuit diagrams and method of operation

- 1 Pulse interval timer
- 2 ECG delay unit
- 3 Analyser filter (1) and (2)
- 4 Analyser filter (3)
- 5 Peak height hold and analogue divider
- 6 Logic control
- 7 Logic discriminator
- 8 Arrhythmia detector

Figures

- 1 Pulse interval timer circuit
- 2 Pulse interval timer filter frequency response
- 3 Pulse interval timer calibration
- 4 Pulse interval timer output wave-forms
- 5 ECG delay circuit
- 6 ECG delay frequency response
- 7 Analyser filter (1) circuit
- 8 Analyser filter (1) frequency response
- 9 Analyser filter (3) circuit
- 10 Analyser filter (3) frequency response
- 11 Analyser filter (3) output wave-forms
- 12 Peak height hold and analogue divider circuit
- 13 Peak height hold output levels - sinus rhythm
- 14 Peak height hold output levels - ventricular extrasystoles
- 15 Logic control circuit
- 16 Trigger pulse derivatives
- 17 Logic discriminator circuit
- 18 Comparator input levels
- 19 Arrhythmia detector circuit
- 20 Premature beat detector output levels

FUNCTION OF CIRCUIT

1) PULSE INTERVAL TIMER (P.I.T.)

This version is designed to operate from the amplified ECG replayed at 60 x recording speed. It replaces the commercial unit described in the main text and which was intended to be used at 25 x recording speed.

Method of operation

The ECG signal, amplified to approximately 2 volts peak to peak, is fed into a band pass filter composed of I.C.1, I.C.2 and their associated components. The performance of the filter is shown in Fig. and its object is to attenuate the T-wave and hence prevent double triggering should this component of the ECG wave-form be large compared with the QRS. I.C.3, R.6, R.7 and R.8 act as an inverting amplifier and pass the filtered ECG signal to an "invert and add" circuit which comprises I.C.4, D.1, D.4 and the associated resistors, R.9, 10 and 11.

This circuit enables the P.I.T. to react satisfactorily to a positive, negative or biphasic QRS complex; all will produce a negative going wave-form at the junction of diodes D.1 and D.4. The signal is applied to the non-inverting input of I.C.5 whose inverting input is connected to the -15 volt supply via the potentiometer R.V.1. This potentiometer is used as the front panel control to adjust the sensitivity of the P.I.T.

I.C.5 is used in open loop configuration and acts as a comparator. When the signal at its non-inverting input goes more negative than the reference voltage the output voltage goes negative. This is fed to the trigger input of I.C.6 via capacitor C.7.

I.C.6 is connected for monostable operation and generates an output pulse of constant amplitude and duration independent of the input wave-form. The duration of the output pulse is controlled by the time constant of R.16 and C.9 and is approximately 4 milliseconds. I.C.8 is connected for astable operation with the trigger input (pin 2) connected to the threshold input (pin 6). It therefore runs as a multivibrator generating output pulses. These output pulses are used to calibrate the P.I.T.

Values of R.23, R.24, R.25, R.V.2, R.V.3 and C.11 are chosen to provide pulse rates equivalent to heart rates of 50 per minute and 100 per minute.

I.C.9 with R.26 and C.15 acts as an integrator of the D.C. voltage supplied by R.V.4. S.1A, S.1B and S.1C are analogue switches which are operated by the outputs of monostables M.1 and M.2. When S.1A is closed and S.1B is open integration takes place. When S.1A is open and S.1B is closed the integrator is reset to zero. When S.1C is open C.16 charges to the current integrated voltage and this is fed to I.C.10 acting as an amplifier whose output is that of the P.I.T.

I.C.6 generates a pulse in response to each QRS complex. This pulse goes to the input of M.1 whose $\bar{Q}$ output then opens S.1A and whose Q output closes S.1C. The Q output also goes to the input of I.C.7 and causes it to generate a T.T.L. compatible trigger pulse. The $\bar{Q}$ output of M.1 also goes to the input of M.2 and causes it to close S.1B. As described earlier, this operation of S.1A and S.1B resets the integrator.

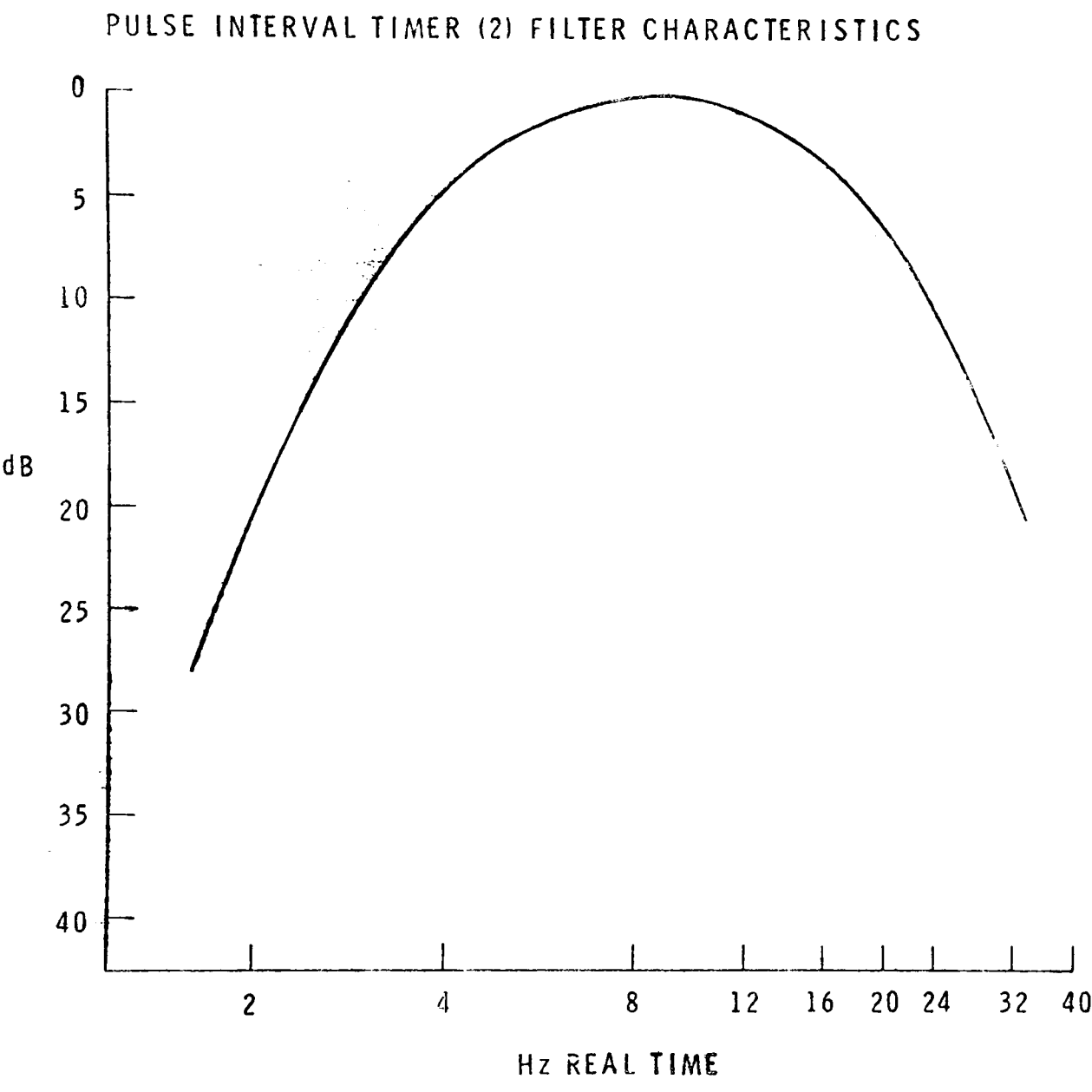
When the outputs of M.1 and M.2 return to their quiescent state after a period determined by C.12, R.17 and C.13, R.19, which in this circuit is approximately 0.2 milli-second, integration proceeds until

the next QRS complex occurs, when the cycle repeats.

Components:

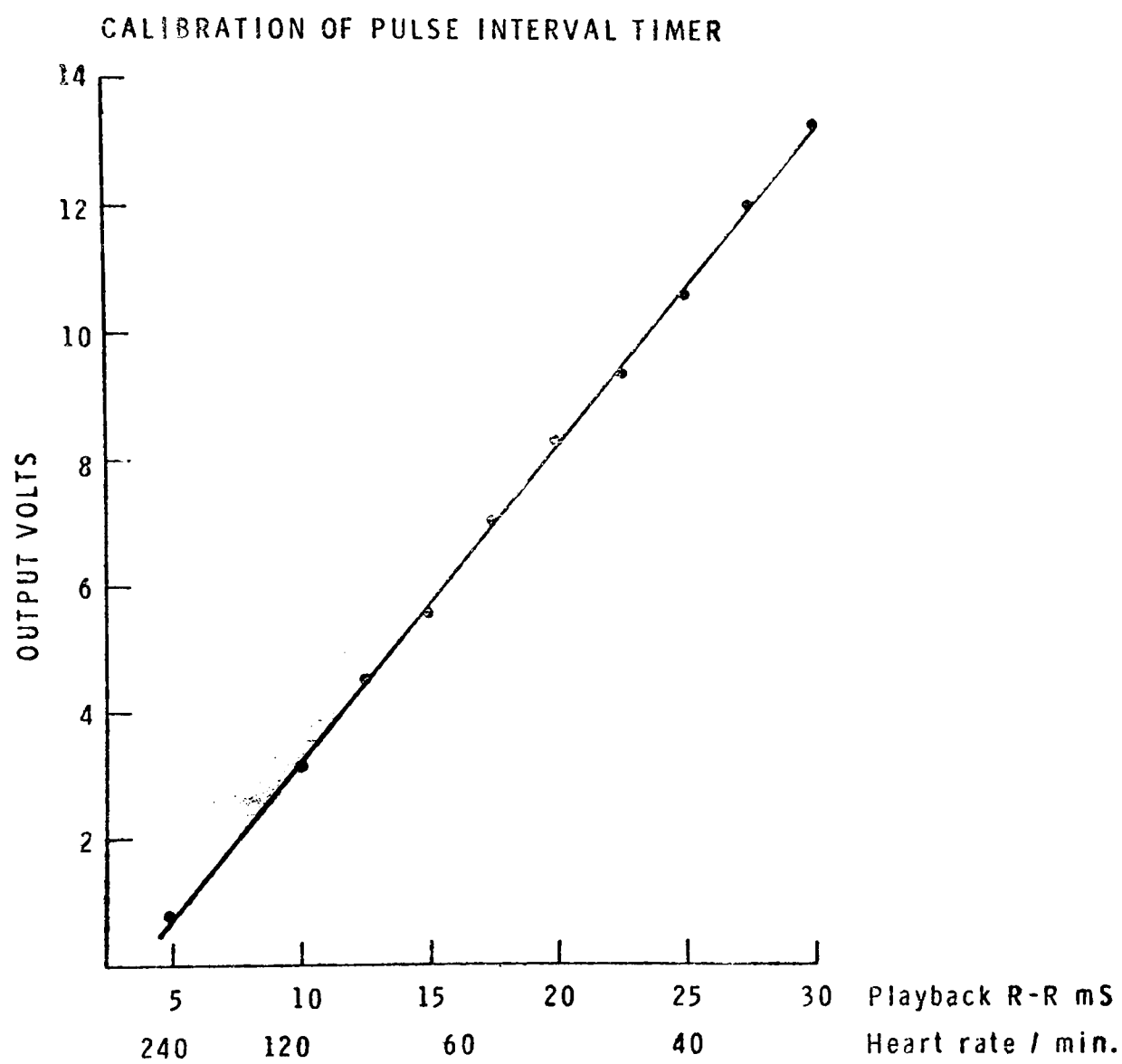
R.1	R.2					220 K Ω	
R.3	R10					12 K Ω	
R.4					5.6 K Ω		
R.5	R.7	R.9	R.11	R.27	R.32	10 K Ω	
R.6	R.20	R.28	R.29				1 K Ω
R.8	R.13	R.14					1 M Ω
R.12					100 K Ω		
R.15	R.22	R.30	R.31	22K Ω			
R.16					180 K Ω		
R.17	R.19					120 K Ω	
R.18					2.2 K Ω		
R.21					39 K Ω		
R.23					33 K Ω		
R.24					270 K Ω		
R.25					560 K Ω		
R.26					2.2 M Ω		
R.V.1	R.V.3	R.V.4	100 K Ω				
R.V.2					50 K Ω		
C.1.	C.7	C.9	C.12	C.13	C.16	0.022 mfd.	
C.2	C.5	C.6	C.8	C.10	0.01 mfd.		
C.3	C.4	C.11				0.047 mfd.	
C.14					0.033 mfd.		
C.15					0.001 mfd.		

D.1 D.4	1N.4148 Silicon diode
D.2 D.3	OA.91 Germanium diode
S.1A S.1B S.1C	MC.14016 Quad analogue switch (part)
M.1 M.2	MC.14528 Dual monostable multivibrator
I.C.1, 2, 3, 4, 5, 9, 10	Type 741 operational amplifier
I.C.6 I.C.8	Type SN.52555 precision timer
I.C.7	Type 74121 monostable



60:1 record/replay ratio

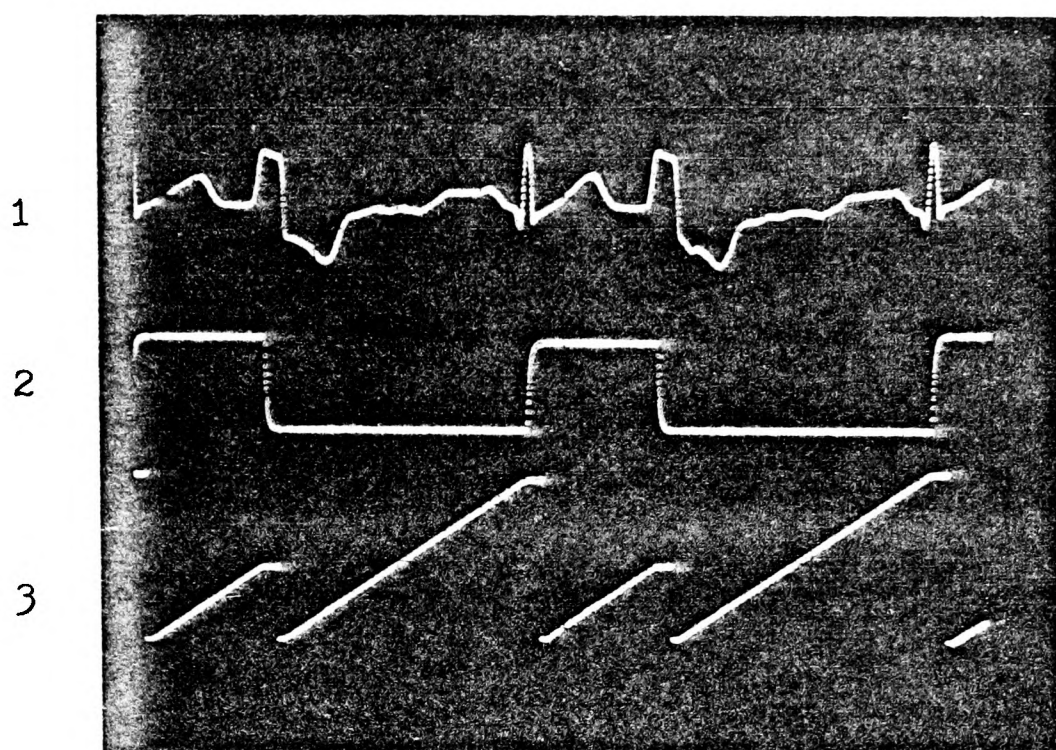
Fig. 2



60:1 record/replay ratio

Fig. 3

Pulse interval timer output wave-forms



- 1 ECG
- 2 Voltage proportional to R-R interval
- 3 Ramp amplitude proportional to R-R interval

Fig. 4

2) ECG DELAY UNIT

Method of operation

The amplified ECG wave-form is fed to the input of an analogue to digital converter (A.D.C.) I.C.3 from the output of the tape replay amplifier. This analogue signal is sampled at a rate of 200 KHz and each sampled value is compared with a reference voltage generated within the A.D.C.

If the analogue voltage input is greater than the current reference voltage, the comparator output switches the logic circuit within the A.D.C. so that the reference voltage is increased by one increment and the comparison is repeated. This process is continued until equality is reached.

A similar process is performed if the analogue input voltage is less than the current reference voltage.

The internal reference voltage is derived from a forward/backward counter built into the A.D.C. and whose output is converted from digital to analogue form by a digital to analogue converter (D.A.C.) which is also incorporated in the hybrid circuit of the A.D.C. It is the digital value of the comparator voltage at equality which appears in 8 bit parallel binary form at the output of the A.D.C.

Conversion from analogue to digital form is initiated and terminated by a square wave "strobe" pulse generated by I.C.1 whose repetition rate is governed by R.V.1.

The outputs of the A.D.C. are fed to a pair of quad input shift registers I.C.4 and I.C.5 which operate in parallel. Data enter the shift registers when the outputs of their internal clocks are at logic 1 and data are shifted when the clock outputs are at

logic 0. The operation of the clocks is controlled by the output of I.C.2 which generates pulses whose duration is governed by R.1 and C.2 and whose repetition rate is determined by negative pulses from I.C.1.

The delayed digital version of the ECG wave-form appears in 8 bit binary form at the output of the shift registers. The delay time is $(n-1)f$ where f is the clock frequency and n is the number of stages (bits) in the shift register.

In the circuit described the delay is 2.5 milli-seconds approximately, which is equivalent to 150 milli-seconds real time at a record/replay speed ratio of 60:1.

The digital representation of the ECG wave-form has to be reconverted to analogue form and to achieve this the next stage is a digital to analogue converter I.C.6. This is a ladder type converter in which an internally generated reference current is first divided into binary related components and then fed to eight digitally controlled semi-conductor switches.

The signal on each incoming line from the shift registers operates one of the switches and allows a proportion of the reference current to be supplied to an output current amplifier. The most significant bit (M.S.B.) of the binary input supplies the greatest proportion of the reference current, whilst the least significant bit supplies the smallest increment.

The output of the D.A.C. is a varying current which is proportional to the digital input. This current is transformed into a varying voltage by I.C.7 which acts as a current to voltage converter.

Components

R.1 R.2 5.6 KΩ
R.3 R.4 R.5 2.7 KΩ
R.6 10 KΩ

R.V.1 1 KΩ
R.V.2 5 KΩ

C.1 0.22 mfd.
C.2 0.0022 mfd.
C.3 47 pfd.
C.4 0.1 mfd.

I.C.1 Type 7413N dual NAND Schmitt trigger
I.C.2 Type 74121 Monostable
I.C.3 Type 540-8 A.D.C. (Hybrid Systems Inc.)
I.C.4)
I.C.5) Type 2532 Quad 80 bit static shift register
I.C.6 Type MC.1408L8 D.A.C.
I.C.7 Type 741 operational amplifier

ECG Delay

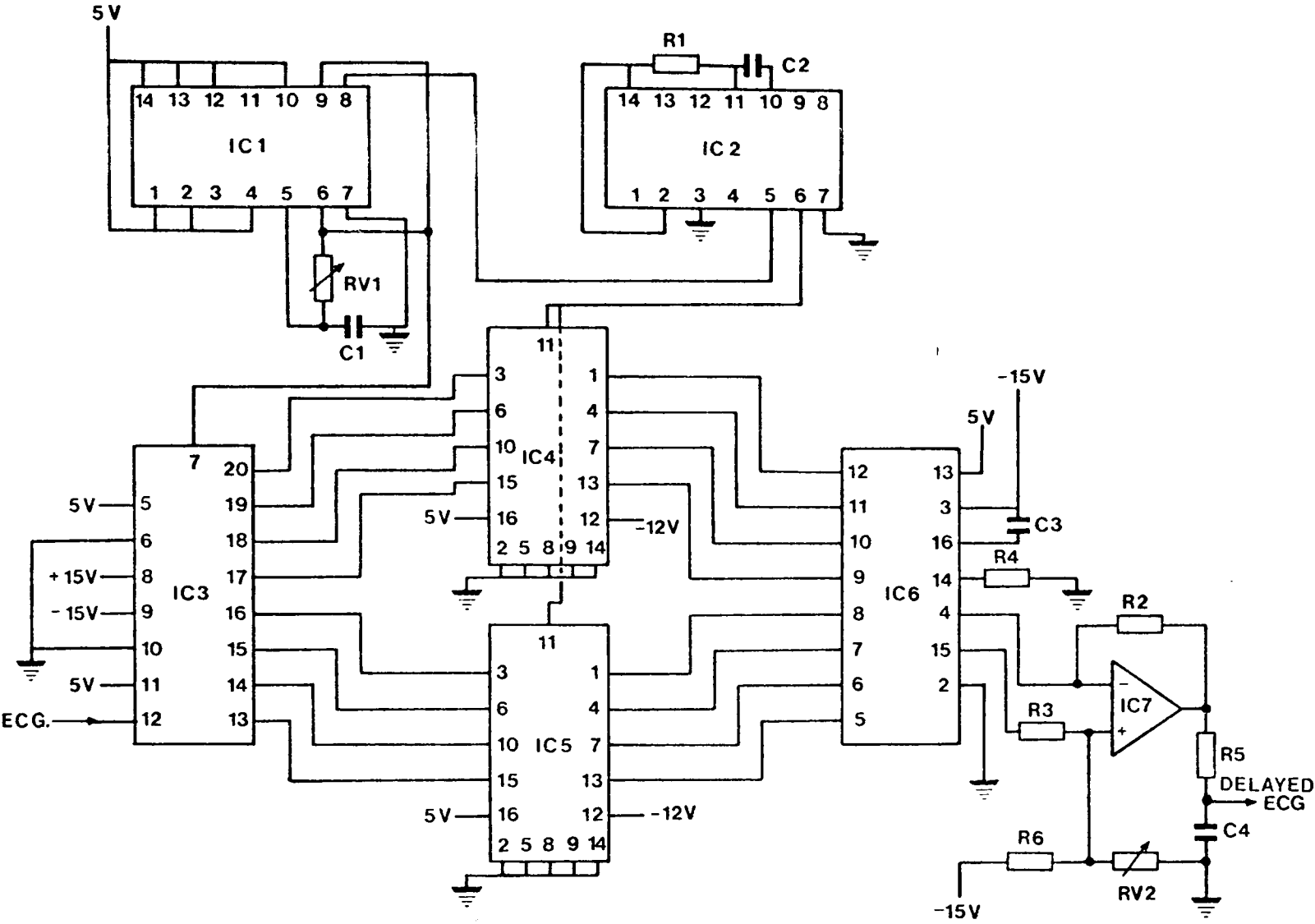


Fig. 5

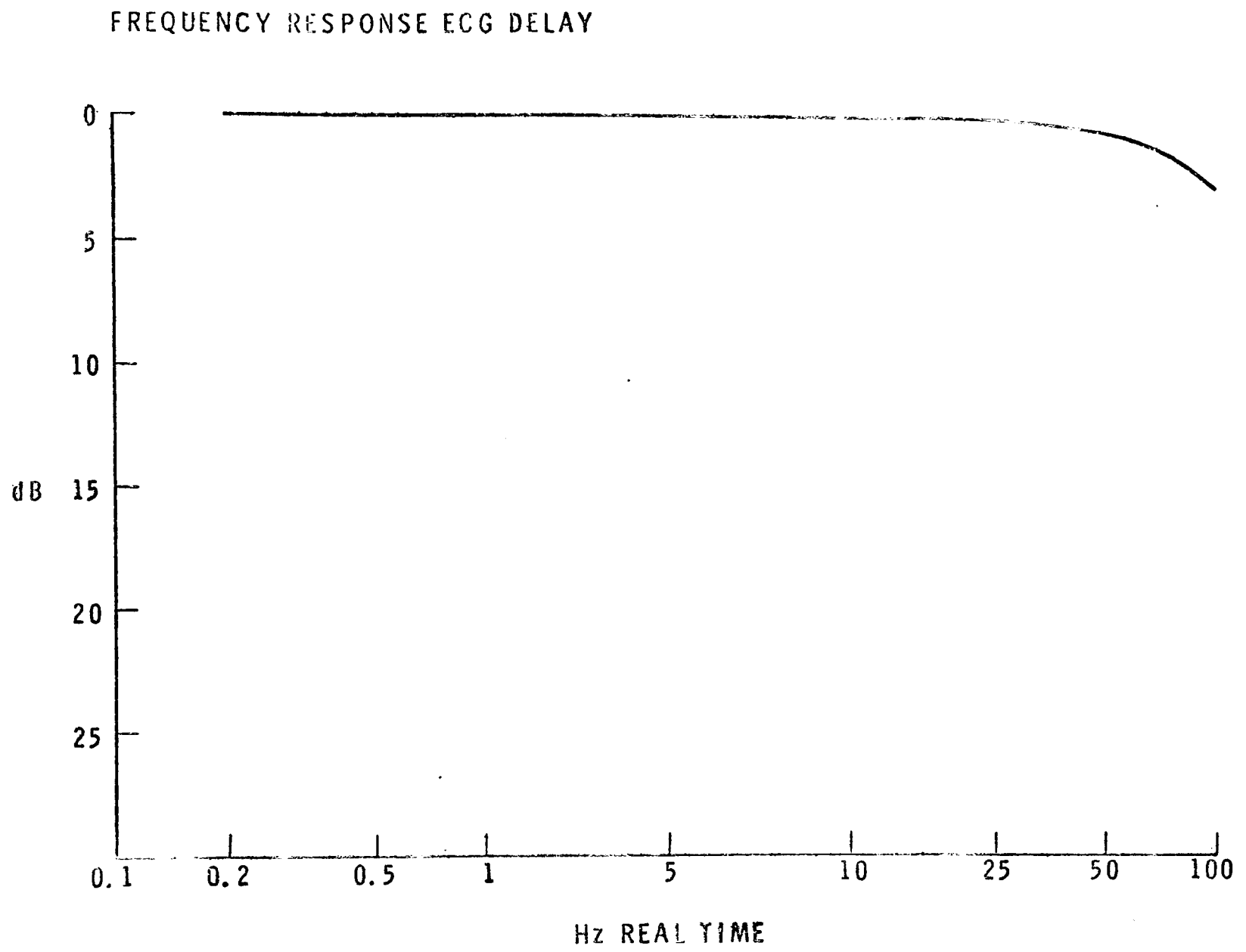


Fig. 6

3) ANALYSER FILTER (1)

This original version of the analyser filter was designed to operate at a replay speed of 25 x record speed.

In this circuit the entire ECG complex, amplified to approximately 1 volt peak to peak, is fed to the common input of two parallel band pass filters.

Each of these filters is composed of a high pass and a low pass fourth order filter in cascade. I.C.1 to I.C.4 and associated components R.1 to R.12 and C.1 to C.8 comprise a band pass filter with centre frequency 23 Hz, whilst I.C.5 to I.C.8 and associated components R.13 to R.24 comprise a band pass filter whose centre frequency is 9 Hz.

R.V.1 and R.V.2 provide variable gain control to compensate for attenuation within the filter.

The performance of the circuit is shown in Fig. .

Components

R.1	R.4	56 KΩ										
R.2	R.5	27 KΩ										
R.3	R.6	R.15	R.18	12 KΩ								
R.7	R.8	R.10	R.11	15 KΩ								
R.9	R.21	10 KΩ										
R.12	R.24	100 Ω										
R.13	R.16	150 KΩ										
R.14	R.17	82 KΩ										
R.19	R.20	R.22	R.23	39 KΩ								
R.V.1	R.V.2	10 KΩ										
C.1	C.2	C.3	C.4	C.5	C.7	C.9	C.10	C.11	C.12	C.13	C.15	0.01 mfd.

C.6 C.8 C.14 C.16 0.022 mfd.

I.C.1 to I.C.8 Type 741 operational amplifiers

QRS ANALYSER FILTER (2)

This filter was of the form of filter (1) but with
R and C component values adapted to 60 x record speed operation.

QRS Analyser Filter (I)

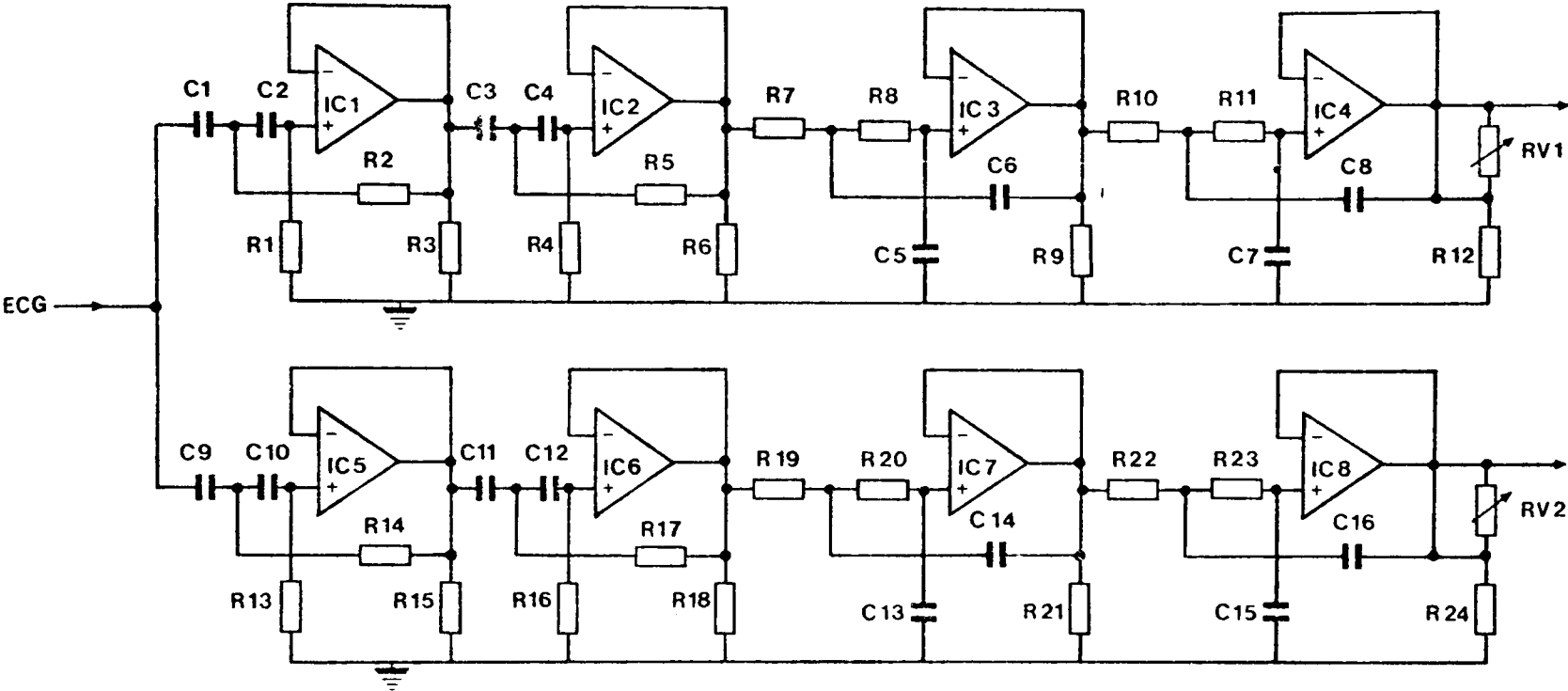


Fig. 7

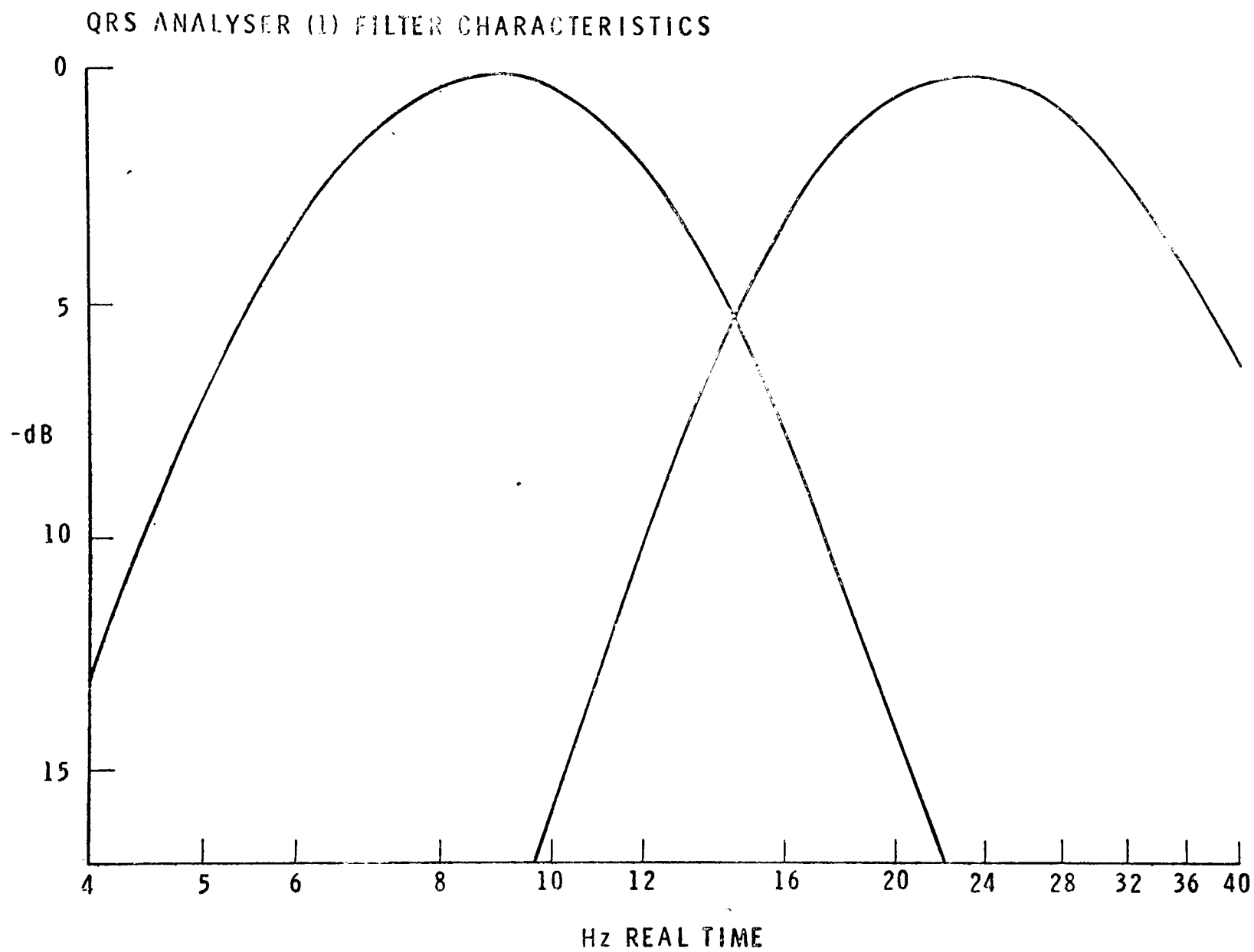


Fig. 8

4) QRS ANALYSER FILTER (3)

Method of operation

As mentioned in the main text, it was found unnecessary to continue to use a band pass filter for the lower frequency range. Consequently this version, which is currently (1977) in use, continues to use a band pass filter for the higher frequency range and a low pass filter for the lower frequency range.

As in previous versions, the band pass filter is composed of a fourth order high pass filter and a fourth order low pass filter in cascade. I.C.1 to I.C.4 with C.1 to C.8 and R.1 to R.9 form this part of the circuit.

The low pass filter for the lower frequency range is a second order version formed by I.C.5, C.9 and C.10, R.10, R.11 and R.12, and R.V.2 and R.V.3.

The two variable resistors enable the characteristics of the filter to be altered slightly, a facility which was found empirically to be useful.

R.V.1 and R.V.2 enable the attenuation within the filter to be compensated for. R.V.2 and R.V.3 form a front panel control. The input to the filter is the delay ECG wave-form amplified to approximately 2 volts peak to peak. S.1A is an analogue switch which operates the logic circuit of the analyser.

The characteristics of this filter with controls R.V.2 and R.V.3 set in the mid-position are shown in Fig.

Components

R.1	R.3	27 K Ω
R.2	R.4	12 K Ω
R.10	R.11	

R.5 R.6 R.7 R.8 5.6 K Ω

R.9 R.12 1 K Ω

R.V.1 R.V.2 R.V.3 R.V.4 10 K Ω

C.1 C.2 C.3 C.4 C.5 C.7 C.9 0.01 mfd.

C.6 C.8 0.02 mfd.

I.C.1 to I.C.5 Type 741 operational amplifiers

S.1A Type MC.14016 quad analogue switch (part)

All resistors $\pm 5\%$ tolerance

All capacitors, polyester, $\pm 20\%$ tolerance

As mentioned in the main text, component tolerances can degrade the performance of the filter so that the theoretical attenuation of 12 dB per octave per second order stage is seldom achieved.

Component tolerances can also shift the 3 dB cut-off point (f_o) by more than $\pm 20\%$ in the worst case state.

Components were selected empirically for optimum performance to minimise these effects without increase in cost.

QRS Analyser Filter (3)

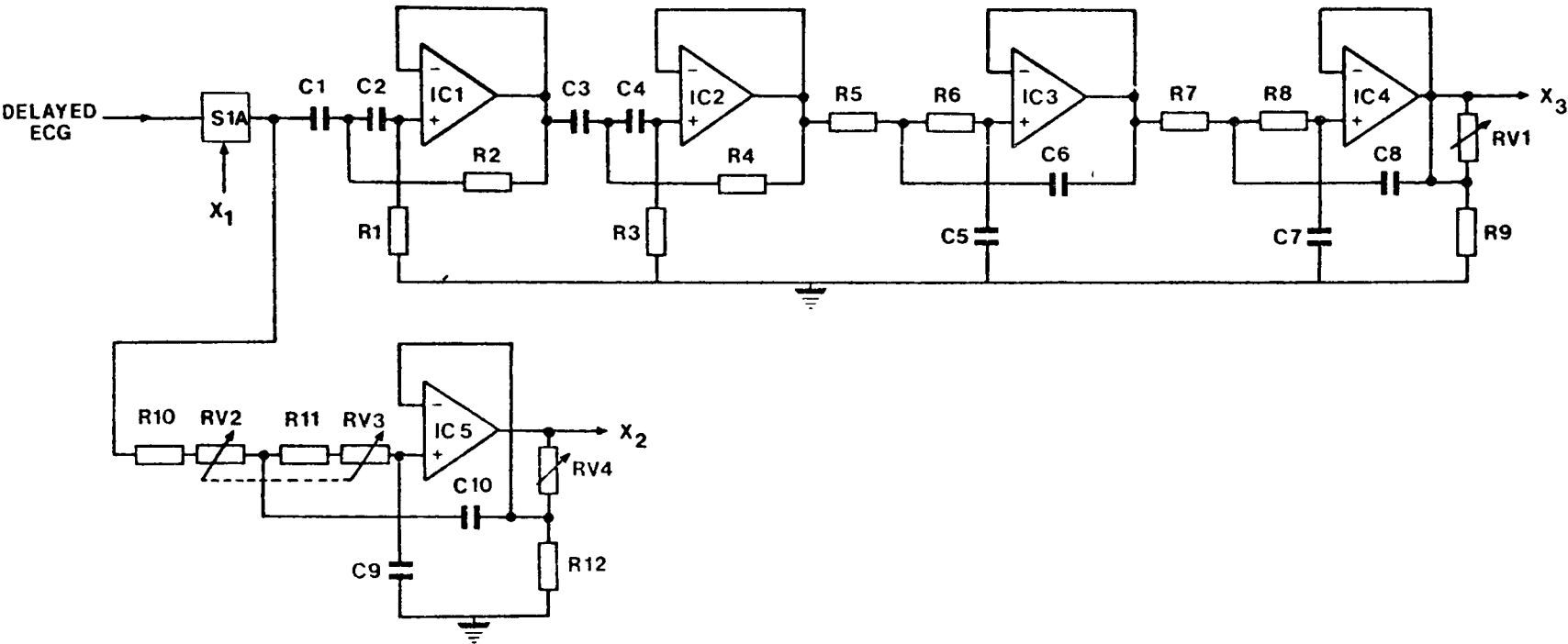


Fig. 9

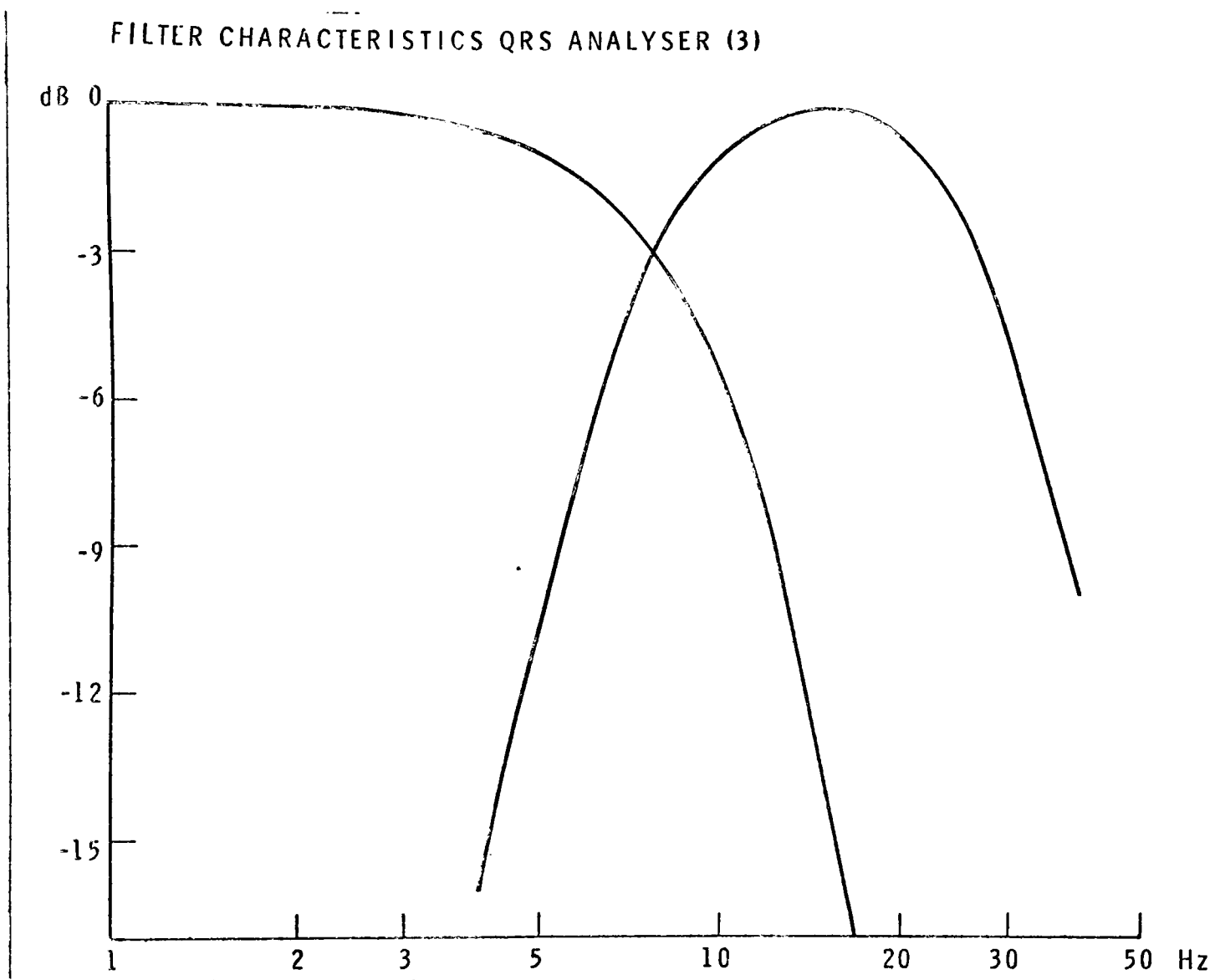
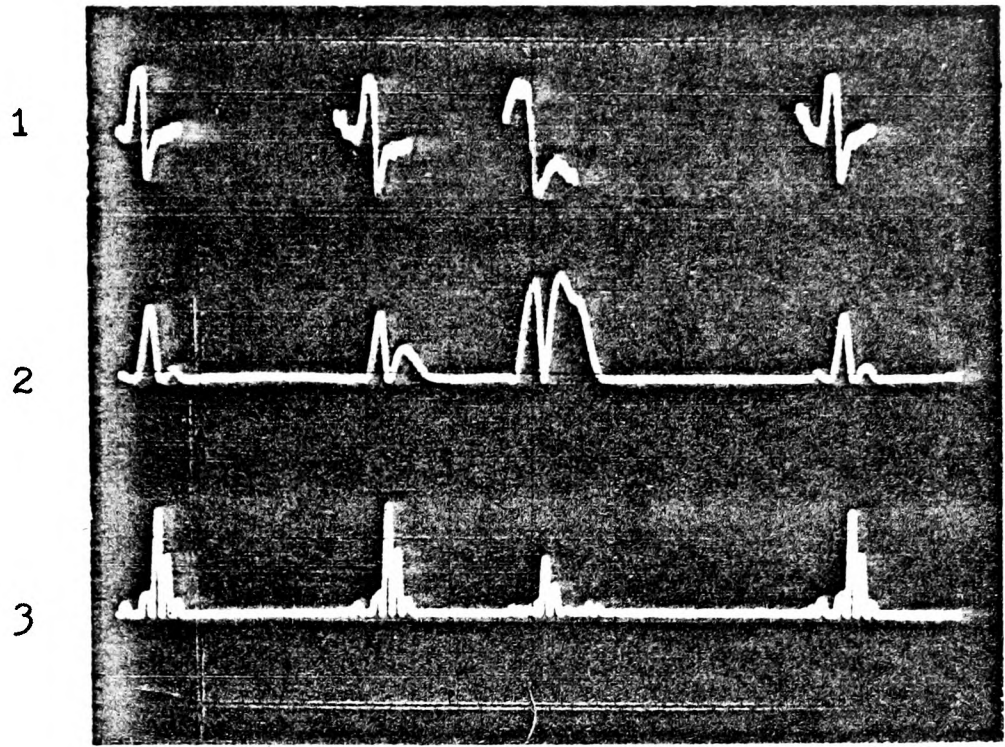


Fig. 10

Analyser filter (3) output wave-forms



- 1 Delayed ECG input to filter
- 2 Low pass filter output
- 3 High pass filter output

Fig. 11

5) PEAK HEIGHT HOLD AND ANALOGUE DIVIDER CIRCUITS

Method of operation

X.3 and X.4 are the outputs of the band pass filter and low pass filter respectively. Each is fed to an inverter/adder circuit comprising I.C.1 and I.C.5 and the associated components R.1, R.2, R.3, R.21, R.22, R.23 and D.1, D.2, D.5 and D.6.

This sub-circuit enables the analyser to operate satisfactorily from positive, negative or biphasic QRS complexes.

The output of the inverter/adder charges C.1 in the case of the band pass filter and C.2 in the case of the low pass filter.

T.1 and T.2 function as switches controlled by the trigger pulses X.0. When closed, these switches discharge the capacitors in readiness for the next charging cycle.

I.C.2 and I.C.6 are voltage followers and buffer the peak height hold circuits from the next stage. I.C.3 is basically a multiplier circuit. If, however, it is placed in the feedback path of the operational amplifier I.C.4, the two devices interact to form a divider circuit whose output is the ratio of the two inputs.

In this example the inputs are the peak voltages from the two filter circuits so the output is dependant on their relative amplitudes.

R.V.1, R.V.2 and R.25 to R.28 provide input offset voltages to compensate for spurious voltages developed within the device due to component tolerances. R.V.4 similarly provides an output offset voltage in conjunction with R.14 and R.16. R.V.3 controls the scale factor of the divider. R.11 and R.12 are chosen with values such that the device is not saturated at the maximum input signal level.

Components

R.1	R.2	R.4	R.5	R.6	R.7	)	10 KΩ
R.11	R.12	R.19	R.21	R.22	R.25	R.28	
R.3	R.23						5.6 KΩ
R.8							13 KΩ
R.10							12 KΩ
R.13							3.9 KΩ
R.14	R.15						3 KΩ
R.16							18 KΩ
R.20							1 KΩ
R.24							1 MΩ
R.26	R.27						2.2 KΩ
R.29							560 Ω
R.V.1	R.V.2						10 KΩ
R.V.3	R.V.4						5 KΩ
C.1	C.2						0.1 mfd.
D.1	D.2	D.5	D.6				0A91 Germanium diode
D.3	D.7						1N.4148 Silicon diode
D.4							7.5V Zener diode
T.1	T.2						2N.3819 Field effect transistor
I.C.1	I.C.2	I.C.4	I.C.5	I.C.6			Type 741 operational amplifiers
I.C.3							MC.1595L Linear four quadrant multiplier

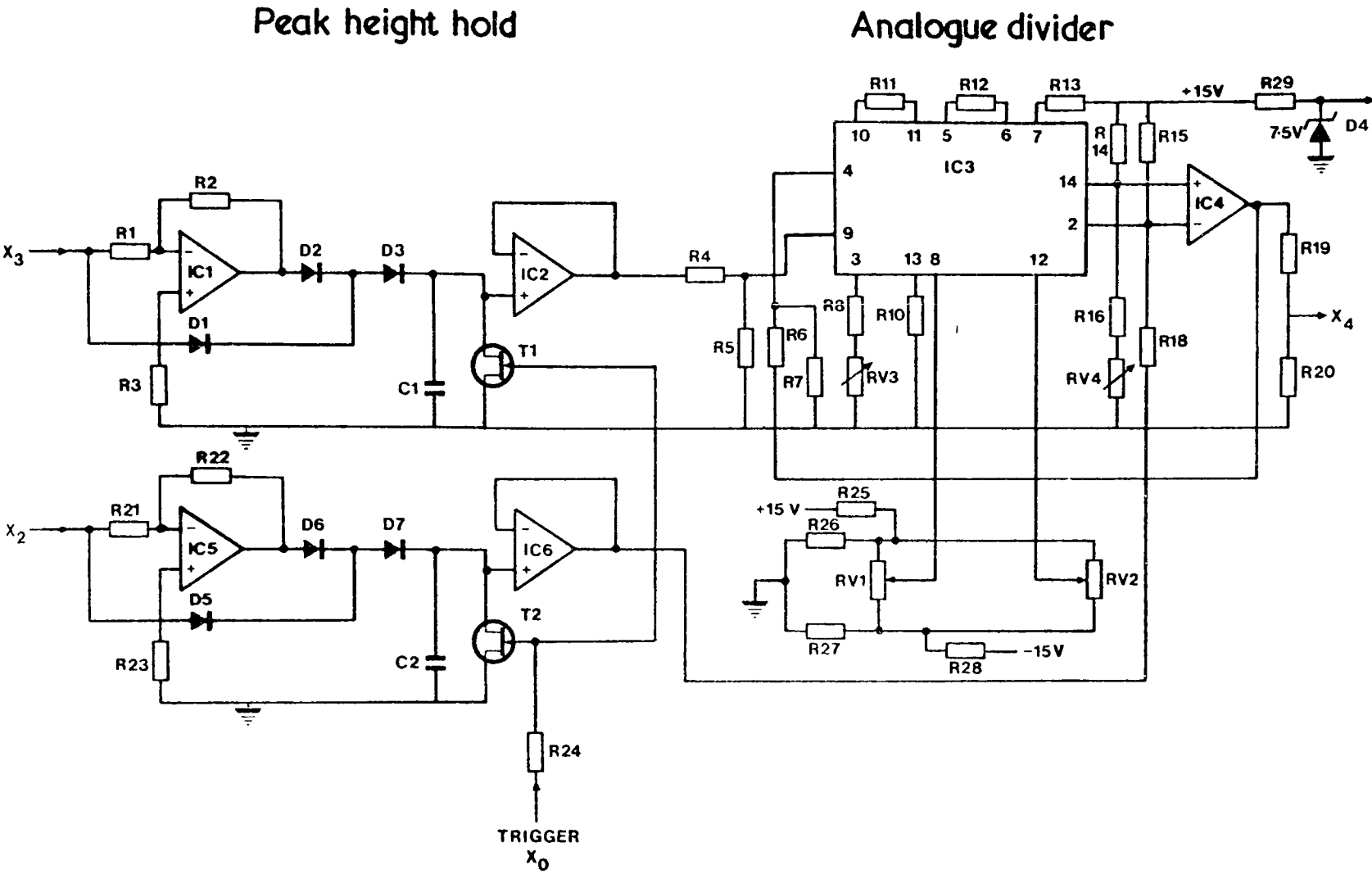
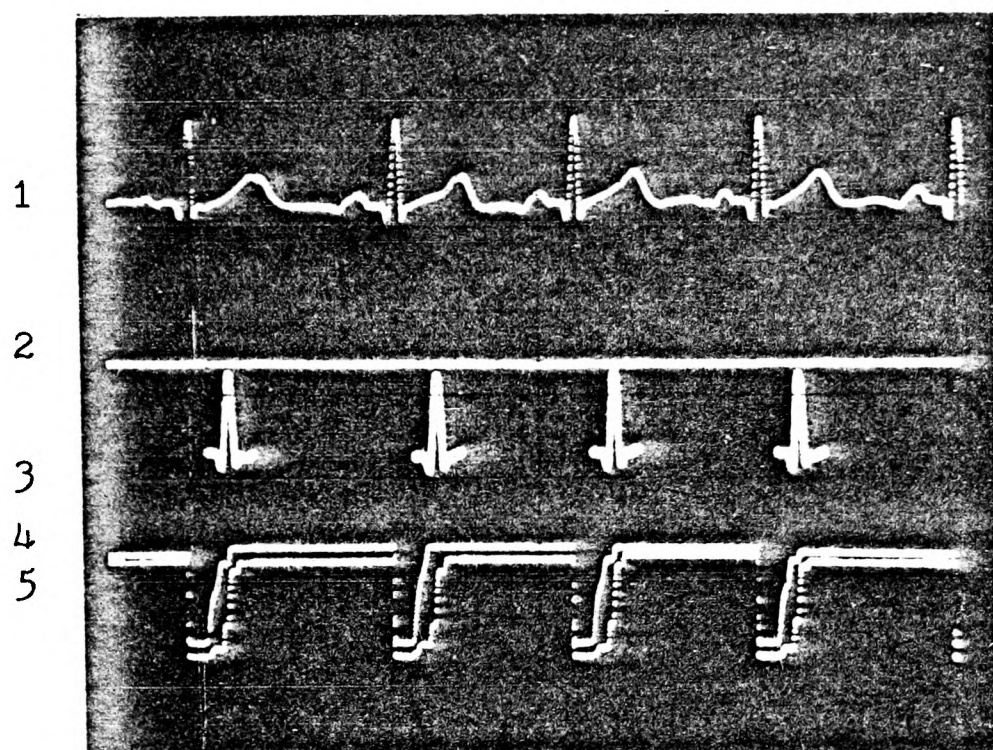


Fig. 12

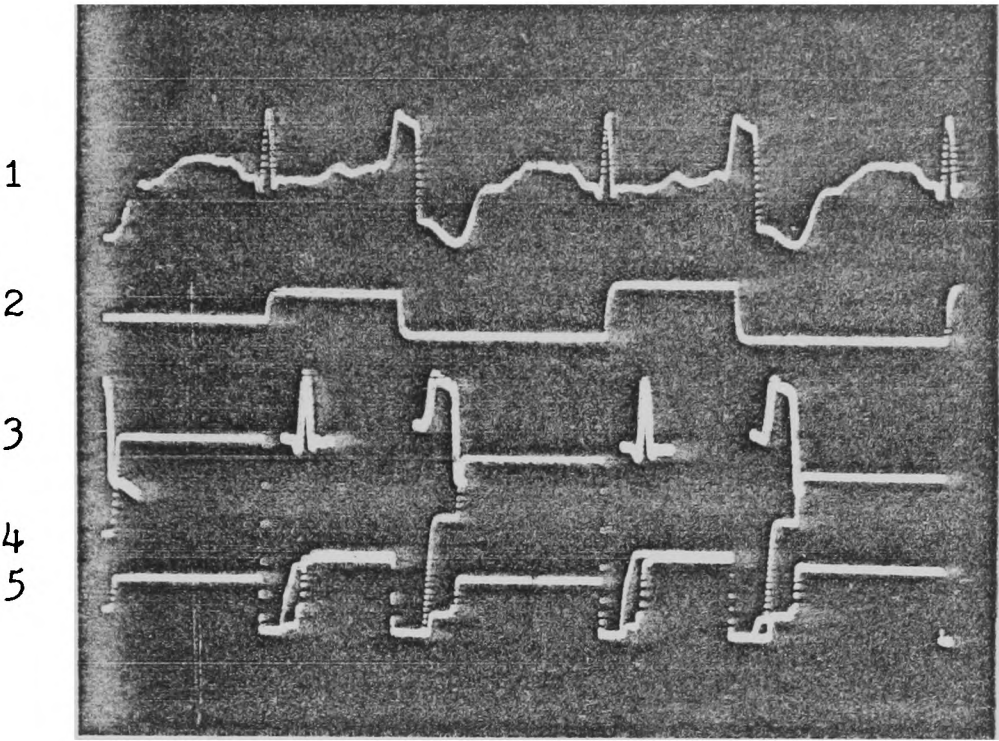
Peak height hold output levels - sinus rhythm



- 1 ECG
- 2 P.I.T.
- 3 Delayed and sampled ECG
- 4 Low pass, peak height hold output
- 5 High pass, peak height hold output

Fig. 13

Peak height hold output levels - ventricular extrasystoles



- 1 ECG
- 2 P.I.T.
- 3 Delayed and sampled ECG
- 4 Low pass peak height hold output
- 5 High pass peak height hold output

Note increase in 4 compared with 5 in presence of V.E.S.

Fig. 14

6) LOGIC CONTROL

Method of operation

The Pulse Interval Timer output trigger pulse is fed to the input of M.1 via R.1 and R.2 acting as a potential divider. Each trigger pulse causes M.1 to generate pulses of approximately 0.15 milli-second* duration at Q and $\bar{Q}$.

These pulses go to M.2 and M.3 which in turn generate pulses whose durations are determined by C.2, R.4, R.V.1 and C.3, R.5, R.V.2 respectively.

R.V.1 and R.V.2 are available as front panel controls for determining that section of the ECG complex which is fed to the filters of the analyser.

The outputs of M.2 and M.3 are combined logically by G.1 and G.2 and passed to G.3 which also receives the $\bar{Q}$ output of M.1. The output of G.3 goes to G.4 which generates the X.1 signal to operate S.1A. The output of G.4 also feeds M.4, M.5 and M.6 in series. The output of M.4 is a pulse of approximately 0.1 milli-seconds which, in effect, delays the trailing edge of the sampling pulse to allow for the phase shift in the filter networks.

The output of M.5 provides the signal X.7 which closes switch S.1B and loads the instantaneous output of the analogue divider into the comparator. The output of M.6 is buffered by transistors T.1 and T.2 and provides pulses X.5 and X.6 respectively which control I.C.4 in the case of T.1 and provides "clock" pulses to control M.1 to M.6 and the logic gates G.12 to G.15 directly in the case of T.2.

* Pulse width in micro-seconds = $0.00247 \times (RC)^{0.85}$.

(R in K Ω C in pfd.)
:

Components

R.1	R.2	R.4	R.5	10 K Ω
R.3	R.7	R.8		470 K Ω
R.6				120 K Ω
R.9	R.10			2.2 K Ω
R.11	R.12			47 K Ω
R.13				4.7 K Ω
R.V.1	R.V.2			100 K Ω
C.1	C.6			0.001 mfd.
C.2	C.3			0.1 mfd.
C.4	C.5			0.0022 mfd.
T.1	T.2			BC.109
M.1 to M.6				$\frac{1}{2}$ Type MC.14528 dual monostable
G.1 to G.4				Type MC.14011 Quad 2-input NAND

Logic Control

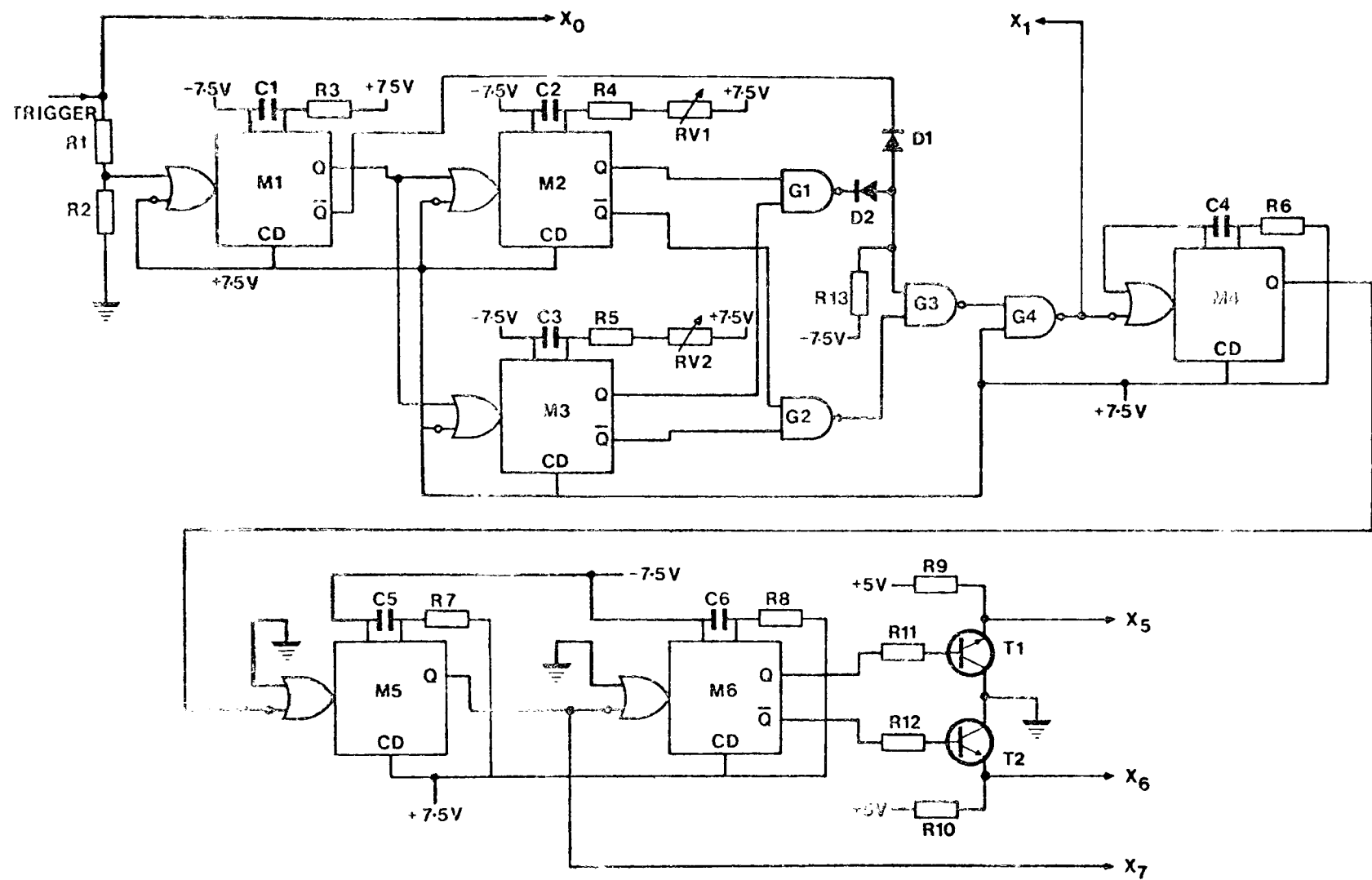


Fig. 15

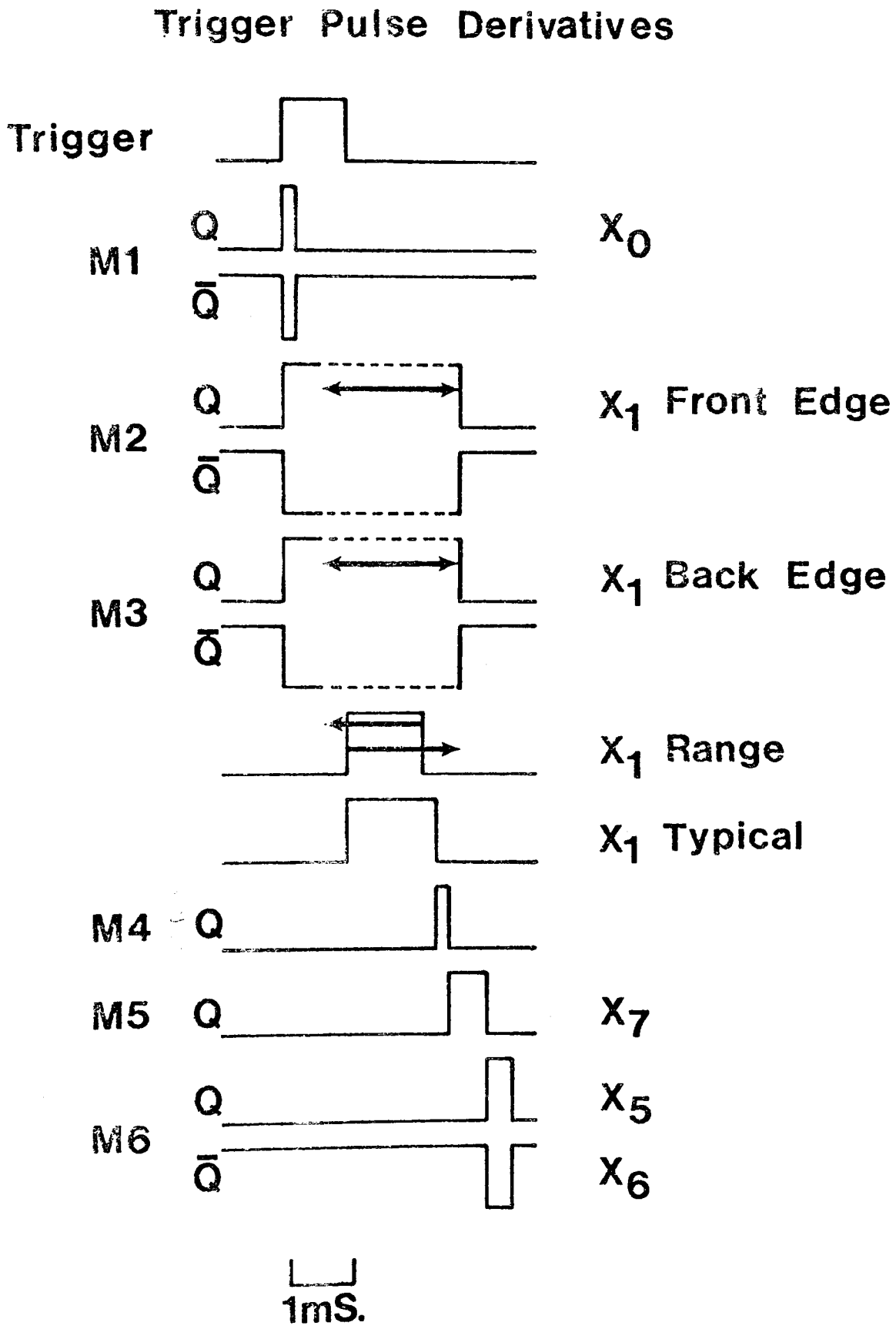


Fig. 16

7) LOGIC DISCRIMINATOR

Method of operation

The beat to beat value of the output of the analogue divider is fed via S.1B to C.1, where it is held. S.1B closes in response to each instantaneous "load" signal X.7 which is derived from the trigger pulse. The voltage on C.1 appears at the output of I.C.1 from where a proportion is supplied by R.V.1 to the inverting input of I.C.3 which acts as a comparator.

R.V.1 is a front panel control for setting "comparator" input. The beat to beat value from the analogue divider is also fed to C.2 via S.1C. The voltage on C.2 is fed via I.C.2 to the non-inverting input of I.C.3. When the voltage at this point is greater than that at the inverting input, a positive pulse is fed to the Schmitt trigger input of I.C.4, via the buffer transistor T.1.

The monostable operation of I.C.4 is controlled by the X.5 input. When this is low each output pulse from I.C.3 results in a constant width, constant amplitude pulse from I.C.4. This pulse goes to I.C.5 which generates a pulse to control S.1C. This switch only conducts when the voltage at the non-inverting input of I.C.5 is greater than that at its inverting input.

This condition only occurs when a "wide" QRS complex has resulted in a relatively high output from the low pass filter compared with that from the band-pass filter. Consequently the circuit is comparing at the inputs of I.C.3 a voltage representing wide QRS complexes with an average voltage representing only normal complexes.

The method enhances the discrimination between normal and wide QRS complexes compared with one in which the output of the analogue divider is alone compared with a reference voltage.

The remainder of the circuit provides facilities for combining the outputs of the tachycardia, premature beat and wide QRS detectors.

The output of the tachycardia detector is fed to the inputs of three bistable multivibrators, M.1, 2 and 3, operating in series. Clock pulses for these are derived from the main trigger pulse and each will generate a positive output signal for as long as tachycardia is present. These outputs are combined logically by G.1 to indicate tachycardia if three or more beats in succession at rapid rate have been detected.

The output of the premature beat detector goes to G.2 where it is combined logically with the output of G.1, to give an output at G.2, which is dependant on whether there have been 'less than 3' or '3 or more' rapid beats in succession. The output of G.2 goes to G.3, which passes a logic 0 indicating premature beats to G.12 and G.13. In the former it is combined with the output of I.C.4 and the clock pulse to indicate a wide premature beat, i.e. a ventricular extrasystole, whereas at G.13 it is combined with the clock pulse and the output of G.12 to indicate supraventricular extrasystoles.

Normal beats are defined as not wide and not premature and are determined by the inputs to G.11 and G.15.

A wide QRS, such as that associated with an intraventricular conduction defect, is indicated by G.14 whose inputs are the I.C.4 output pulse indicating a wide beat, the clock pulse and the negation of the premature beat indication pulse. The output of I.C.4 is fed to the input of M.6 and appears at its output when the device is "clocked" by the X.6 signal. If a second or third pulse is generated

by I.C.4, these are passed to M.5 and M.4 respectively. The outputs of M.4, 5 and 6 are fed to G.6 and those from M.5 and M.6 go to G.5. The output of the latter is fed to G.10, which indicates coupled beats, whilst the output of G.6 is connected to G.7 which, in turn, is linked to G.8 and G.9 to indicate ventricular tachycardia in response to three or more successive wide QRS complexes occurring at a rapid rate.

Components

R.1	1 K Ω
R.2	47 K Ω
R.3	5.6 K Ω
R.4	2.2 K Ω
R.5	3.3 K Ω
R.6	39 K Ω

R.V.1	100 K Ω
-------	----------------

C.1	C.2	0.33 mfd.
C.3		0.01 mfd.

T.1	BC.478
-----	--------

I.C.1	I.C.2	I.C.3	I.C.5	Type 741 operational amplifiers
I.C.4				Type 74121 monostable

M.1 to M.6	Type 74174 Hex.D. flip-flop
G.1 to G.15	5 x Type 7410 Triple 3 input NAND gates
S.1A, S.1B	Type 14016 quad analogue switch (part)

Truth table for 7410

Inputs			Output
1	2	3	
0	0	0	1
0	0	1	1
0	1	0	1
0	1	1	1
1	0	0	1
1	0	1	1
1	1	0	1
1	1	1	0

Logic 1 = 5 volts

Logic 0 = 0 volts

Logic Discriminator

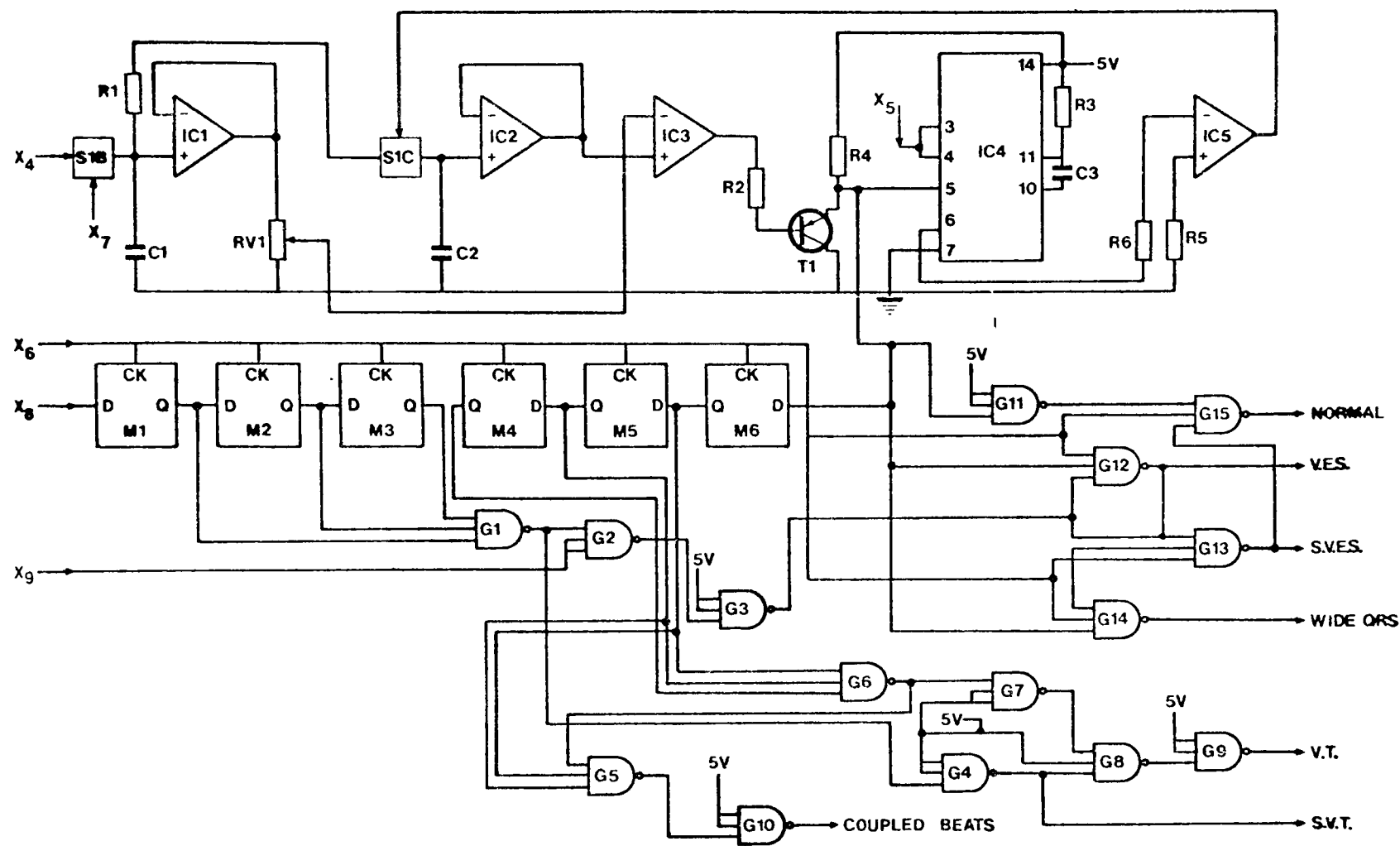
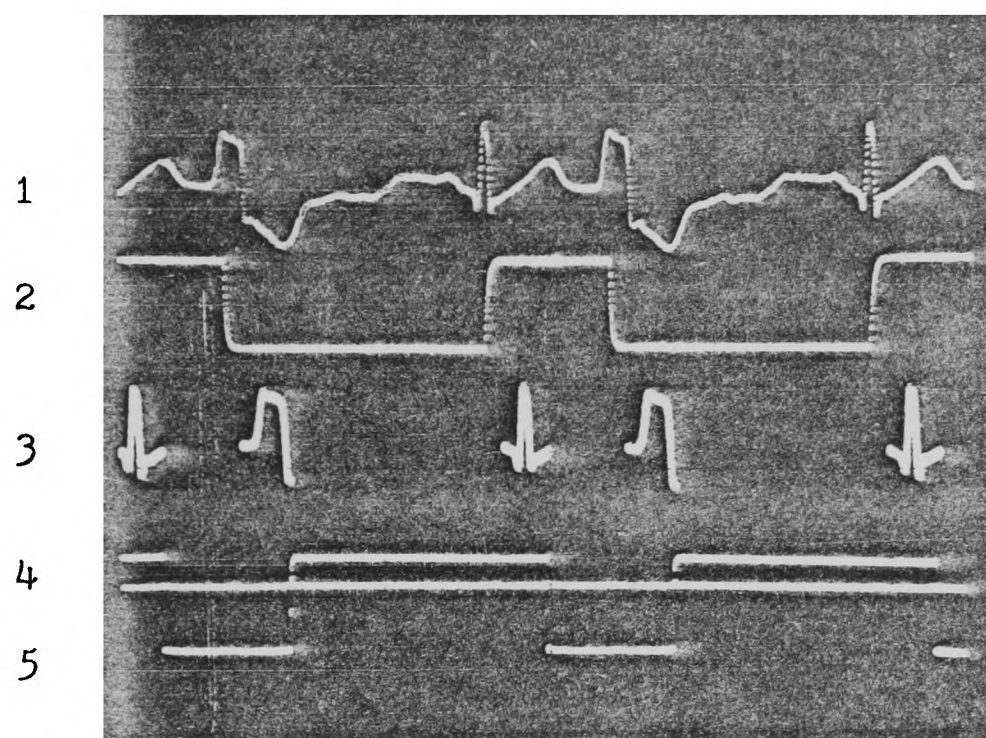


Fig. 17

Comparator input wave-form



- 1 ECG
- 2 P.I.T.
- 3 Delayed and sampled ECG
- 4 Averaged input excluding contribution from 'wide' beats
- 5 Beat to beat input from all foci

Fig. 18

8) ARRHYTHMIA DETECTOR

Initially, four circuits were employed to detect four types of arrhythmia:

premature beats (irrespective of origin),
tachycardia,
bradycardia and
gaps (short periods of asystole).

It was not found useful to detect automatically the last two phenomena and the associated circuits have been omitted from the present analyser. For completeness they are, however, included in Fig.

Method of operation

All four circuits are based on operational amplifiers acting as comparators.

The tachycardia detector consists of I.C.1 and its associated components. The output voltage, Y.1 from the pulse interval timer (P.I.T.) is fed to the inverting input of I.C.1. The magnitude of this voltage is proportional to the R-R interval and inversely proportional to heart rate.

Tachycardia, therefore, produces comparatively low voltage at the output of the P.I.T. The reference voltage at the non-inverting input of I.C.1 is obtained from the positive supply line via the potentiometer R.V.1. When the P.I.T. output voltage is less than the reference voltage, the output voltage of I.C.1 rises to saturation at +15 volts. This is attenuated by R.2 and R.4 to be compatible with the transistor-transistor logic (T.T.L.) of the analyser. R.V.1 is a front panel control calibrated in beats per minute so that the threshold of tachycardia indication can be adjusted to suit clinical needs.

The premature beat indicator comprises I.C.2 and its associated circuitry. The output voltage of the P.I.T. is 'averaged' by R.5 to R.8 and C.1, C.2 to produce a slowly changing D.C. voltage level inversely proportional to the mean heart rate during approximately the previous eight beats.

A proportion of the instantaneous P.I.T. voltage is supplied to the inverting input of I.C.2 via potentiometer R.V.3. A positive voltage swing occurs at the output of I.C.2 when the instantaneous P.I.T. voltage is less than the P.I.T. averaged value. This condition arises when a premature beat is detected.

The output of I.C.2 is made T.T.L. compatible by R.11, R.12 and D.2. R.V.3 is a front panel control calibrated in prematurity expressed as a percentage relative to the average R-R interval.

I.C.3 and its associated components form a bradycardia detector in which the averaged value of the P.I.T. output voltage summed with a variable voltage derived via R.V.2 from the supply voltage lines is compared with the voltage at the non-inverting input of the operational amplifier.

R.V.2 was available as a calibrated front panel control in earlier versions of the analyser. Bradycardia is not a phenomenon which needs to be combined logically with another output from the analyser, so the output of this circuit is not T.T.L. compatible but is available to operate a visual indicator.

The gap detector is, again, a straightforward comparator circuit based around I.C.4. The input Y.2 is a ramp voltage proportional to the R-R interval and generated by the P.I.T. The sum of this voltage and a variable proportion of the 15-volt

supply derived via R.V.4 is compared with the voltage at the non-inverting input of I.C.4. A voltage swing occurs at the output of I.C.4 if the ramp voltage plus bias voltage exceeds the voltage at the non-inverting input. Potentiometer R.V.4 determines the duration of the gap necessary to trigger an output signal from the detector and was included as a front panel control in the original version of the analyser.

Components

R.1	R.3	R.8	R.9	R.10	47 KΩ
R.2	R.11				2.2 KΩ
R.4	R.12				1 KΩ
R.6	R.7				10 KΩ
R.5					100 KΩ
R.13	R.15	R.16	R.17	R.19	470 KΩ
R.14					1.2 MΩ
R.18	R.20				10 MΩ
R.V.1					10 KΩ
R.V.2	R.V.4				100 KΩ
R.V.3					50 KΩ
C.1	C.2				0.068 mfd.
C.3					0.47 mfd.
D.1	D.2				Germanium diodes OA.91
I.C.1 to I.C.4					Type 741 operational amplifiers

Arrhythmia Detectors

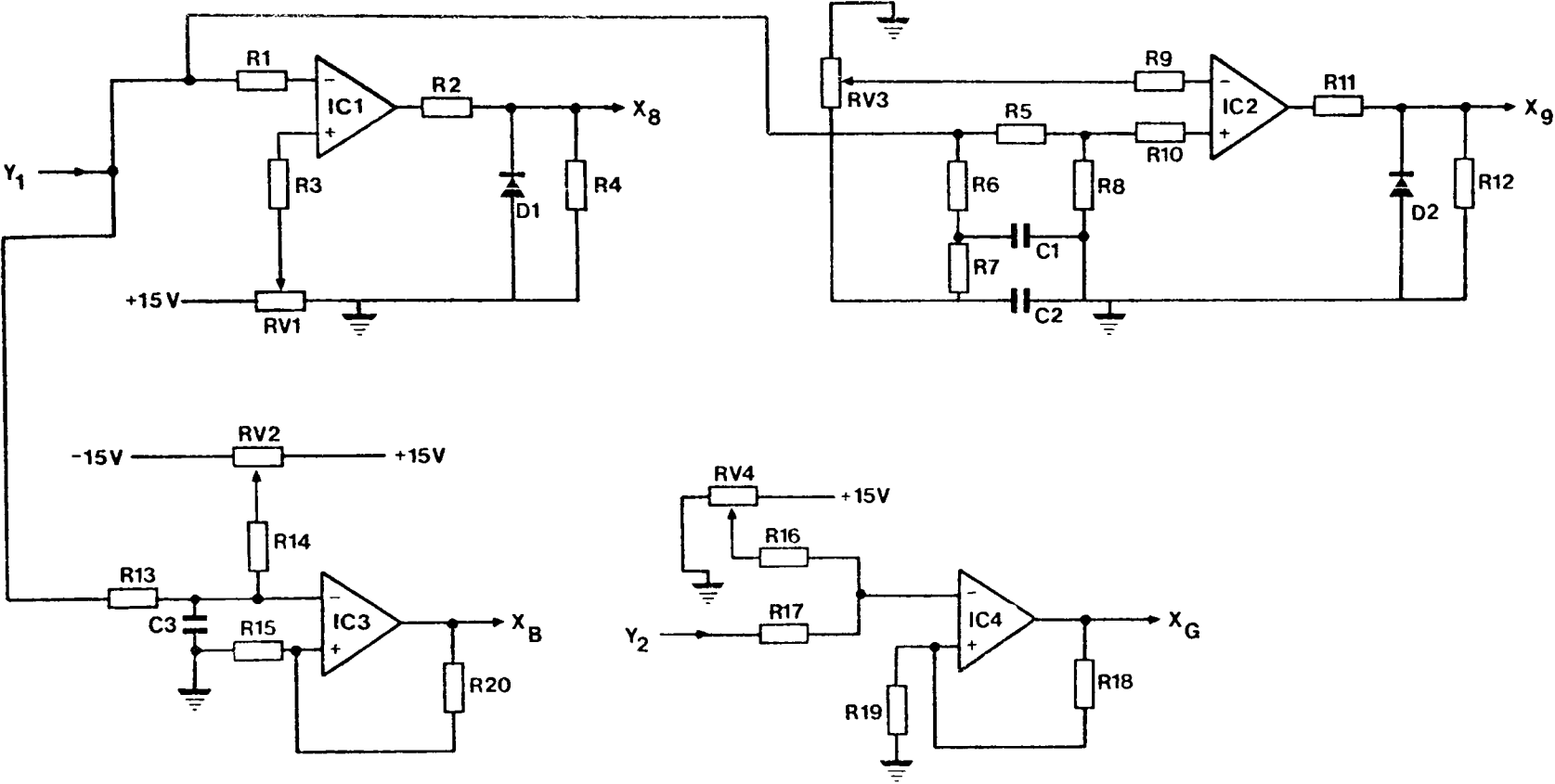
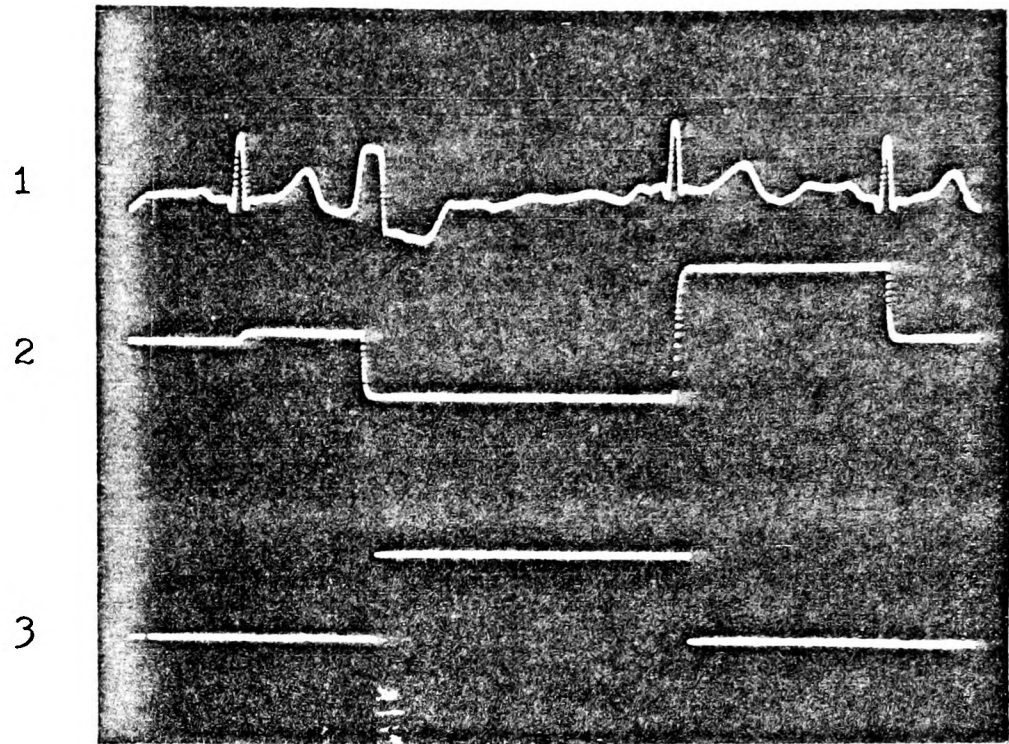


Fig. 19

Premature beat detector wave-form



- 1 ECG
- 2 P.I.T.
- 3 Premature beat detector output

Fig. 20

APPENDIX BOffice of Population Census and Surveys

CLASSIFICATION OF OCCUPATIONS 1970

(Appendix E)

SUMMARY OF SOCIO-ECONOMIC CLASSES

- S.E.G. 1.1 Employers in industry, commerce, etc. - large establishments
- (a) Social Class II Intermediate occupations
 - (b) Social Class III(N) Skilled occupations - Non-manual
 - (c) Social Class III(M) Skilled occupations - Manual*
- S.E.G. 1.2 Managers in central and local government, industry, commerce, etc. - large establishments
- (d) Social Class II Intermediate occupations
 - (e) Social Class III(N) Skilled occupations - Non-manual
 - (f) Social Class III(M) Skilled occupations - Manual
- S.E.G. 2.1 Employers in industry, commerce, etc. - small establishments
- (g) Social Class II Intermediate occupations
 - (h) Social Class III(N) Skilled occupations - Non-manual
 - (j) Social Class III(M) Skilled occupations - Manual
 - (k) Social Class IV Partly skilled occupations
 - (l) Social Class V Unskilled occupations
- S.E.G. 2.2 Managers in industry, commerce, etc. - small establishments
- (m) Social Class II Intermediate occupations
 - (n) Social Class III(N) Skilled occupations - Non-manual
 - (o) Social Class III(M) Skilled occupations - Manual
- S.E.G. 3 Professional workers - self-employed
- (p) Social Class I Professional, etc., occupations
- S.E.G. 4 Professional workers - employees
- (q) Social Class I Professional, etc., occupations
- S.E.G. 5.1 Ancillary workers and artists
- (r) Social Class II Intermediate occupations
- S.E.G. 5.2 Foremen and supervisors non-manual
- (s) Social Class III(N) Skilled occupation - Non-manual
- S.E.G. 6 Junior non-manual workers
- (t) Social Class III(N) Skilled occupations - Non-manual
 - (u) Social Class IV Partly skilled occupations

S.E.G. 7	Personal service workers	
	(v) Social Class II	Intermediate occupations
	(w) Social Class III(N)	Skilled occupations - Non-manual
	(x) Social Class III(M)	Skilled occupations - Manual
	(y) Social Class IV	Partly skilled occupations
S.E.G. 8	Foremen and Supervisors - manual	
	(z) Social Class III(M)	Skilled occupations - Manual
S.E.G. 9	Skilled manual workers	
	(aa) Social Class III(M)	Skilled occupations - Manual
S.E.G. 10	Semi-skilled manual workers	
	(ab) Social Class IV	Partly skilled occupations
S.E.G. 11	Unskilled manual workers	
	(ac) Social Class V	Unskilled occupations
S.E.G. 12	Own account workers (other than professional)	
	(ad) Social Class II	Intermediate occupations
	(ae) Social Class III(N)	Skilled occupations - Non-manual
	(af) Social Class III(M)	Skilled occupations - Manual
	(ag) Social Class IV	Partly skilled occupations
	(ah) Social Class V	Unskilled occupations
S.E.G. 13	Farmers - employers and managers	
	(aj) Social Class II	Intermediate occupations
S.E.G. 14	Farmers - own account	
	(ak) Social Class II	Intermediate occupations
S.E.G. 15	Agricultural workers	
	(al) Social Class III(M)	Skilled occupations - Manual
	(am) Social Class IV	Partly skilled occupations
S.E.G. 16	Members of armed forces	
S.E.G. 17	Inadequately described occupations	

* Including very small numbers of persons in Social Classes IV and V.

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