FROM BENCH TO BEDSIDE

This year marks the 75th anniversary of the death of Willem Einthoven (1860-1927), the pioneer of the electrocardiogram (ECG). Redmond Shouldice BE MIEI AICS from the Department of Electrical & Electronic Engineering, UCD and Gary Bass BSc(Hons), Department of Human Anatomy & Physiology, UCD outline the continuing importance of the ECG, not just in clinical cardiology, but also in a wide range of biomedical engineering applications. The origin of the ECG is described in historical and medical senses; this is followed by a description of modern analysis and implementation using digital signal processing methods.

Oxygen and the chemical nutrients required by the human body are carried in the blood, which is pumped tirelessly around its circuit by the heart muscle. This mechanical pumping action, a rhythmic contraction of muscle mass, is delicately and precisely regulated by and dependent on waves of electrical activity emanating from the sinoatrial node and propagating through a conduction network to all cells of the heart-muscle. The specialised cells, which initiate and conduct the cardiac impulse form a network consisting of three major parts. These are the sinoatrial node (the dominant natural pacemaker under normal conditions), the atrioventricular node and Bundle of His and the Bundle Branches and terminal Purkinje fibres. In some disease conditions this conduction system is perturbed; the consequent loss of contraction rhythmicity can have fatal results.

Fluctuations in the electrical potential of cardiac cells are millivolts in amplitude and milliseconds in duration and the faithful recording of these minute signals was an almost impossible task up to a century ago. The construction of an instrument capable of measuring these potential variations was a problem that Nobel prize-winning Dutch physiologist Willem Einthoven solved with his string galvanometer in 1903.

Derived from the Deprez-d'Arsonval moving-coil galvanometer, the string galvanometer consisted of a fine, silver-plated quartz wire, which was stretched in the field between the poles of a magnet and perpendicular to an optical projection system. Using this method, it was possible to achieve both a high sensitivity and short latency.

Einthoven published his first detailed description of the instrument in 1909. The limbs of his experimental subjects were immersed in several large vats of normal saline which acted as electrodes, conducting minute electrical potentials to his string galvanometer apparatus. This unwieldy setup required five operators and weighed about 300 kg.

One of the first results of this discovery was the demonstration, jointly by Einthoven and British physician-scientist Sir Thomas Lewis, that each individual has their own distinctive 'electrocardiogram' (ECG), but that the general characteristics of the ECG are similar between subjects. Einthoven named the characteristic deflections shown on the string galvanometer as P, then Q, R, S and T. Using the string galvanometer to confirm his complex mathematical derivation of the electrical activity of the heart gleaned from earlier experiments with a capillary manometer, Einthoven showed that more than just a curious epiphenomenon, the ECG precisely charts the course of electrical activity in the heart. Central to this is the electrical depolarisation causing a serial contraction and subsequent relaxation of the pump muscle. The beginning of each cardiac cycle is seen in the P wave of electrical depolarisation sweeping through the atria. There ensues a period of quiescence as the electrical propagation passes through the resistive atrioventricular node.

As the potential bursts from the nodal region and radiates through the ventricles a triplet of deflections – the QRS complex – describes this event and the sub-

tle repolarisation of the atria. Another period of electrical silence follows before the ventricles repolarise, causing the final T deflection.

The amplitude of deflection and morphology of the entire ECG is dependent upon the configuration of the recording leads. Einthoven therefore found it useful to propose standard lead placement and his standardised Leads I, II, and III were adopted. In the period that followed, Frank Wilson and colleagues studied ECG lead placement and waveform abnormalities.

A short time later, in 1938, the American Heart Association and the British Cardiac Society conjointly recommended a battery of 12 standard leads, which incorporated six precordial (or chest) locations V1, V2, V3, V4, V5 and V6 and three augmented unipolar limb leads AVF, AVL and AVR.

This new method of investigation quickly fulfilled a clear need in clinical medicine, ushering in the discipline of clinical electrocardiology. In his classic publication "Le télécardiogramme" (1906), Einthoven reported findings of great clinical significance; it was now clear that different forms of heart disease present themselves characteristically in the electrocardiogram.

He also described a system whereby hospital recordings could be transmitted over a mile of telephone wires to his laboratory – perhaps the first description of telemetric cardiac monitoring. In recognition of Einthoven's discovery of the mechanism of the electrocardiogram, he was awarded the Nobel Prize for Physiology or Medicine in 1924. Indeed, the ECG is today seen as an integral part of primary care diagnostics, and a vitally important part of the toolbox of the healthcare professional.

Current research into the ECG and its applications is as dynamic and ground-breaking today as when the first electrocardiographic signals were recorded in UCD in the laboratory of the then Head of Physiology, Prof. James Malachy O'Connor (1886-1968). A young physician Michael Moriarty, who was researching an MSc on "Experiments On The Equilibrium Of Blood and Urine in the Kidney", subsequently returned to the Department as a Demonstrator of the ECG before becoming a consultant in cardiology at the Mater Hospital in Dublin.

Traditionally, the specialised knowledge of the cardiologist has been required to interpret the multi-lead electrocardiogram, although it is increasingly becoming possible to use automated methods to elucidate useful information. For example, a signal processing methodology for measuring heart rate is implemented in many applications, one of these being wireless sports fitness devices.

Holter monitoring, or ambulatory electrocardiography, allows the recording of many hours of multi-lead ECG, generally aimed at offline processing. Arrhythmia detection and classification has become a very useful pre-screening approach to aid the cardiologist in diagnosis. Standard 12 Lead ECG may be used for stress (exercise) testing; this may detect cardiac problems that are not apparent when resting.

High resolution ECG acquisition has made possible the accurate quantification of the onset of characteristic peaks of cardiac electrical depolarisation and repolarisation; this can provide an insight into the nodal conduction times. The variability observed in ECG signals associated with respiration can give an insight into cardiopulmonary health. Also, sleep apnoea screening may be achieved by analysis of electrocardiographic signals, without reference to electroencephalographic (brain activity) or electromyographic (muscle activity) recordings. Improvements in computer processing power and storage capacity make body surface potential mapping – akin to a regular mesh of electrodes placed on the chest wall – more realisable for research and diagnostic work. This configuration can provide a more complete view of the cardiac electrical vector than individual electrodes.

From a signal analysis viewpoint, detection of the dominant R wave peak – as seen in Lead II – provides a straightforward method of inferring heart rate from the cardiac cycle length. Suitable filtering may be applied to remove any baseline shift in the recording, simplifying peak extraction. It is possible to reduce detection errors by including peaks occurring only at suitable intervals, using prior knowledge of the likely range of cardiac cycle conduction time variability.

For instance, a typical RR interval lasts about 800 ms; thus, an interval of 300 ms or 1600 ms is unlikely to give a true reflection of cycle time. The reciprocal of these RR intervals is a measure of heart rate; such acquisition and processing can be implemented in many devices, for example in sports fitness equipment. Such equipment can be used by athletes to evaluate their fitness level; some models allow wireless communication with a PC to maintain an exercise schedule and keep a record of cardiac output.

Many arrhythmias are detectable with specialised classification software, particularly useful for incorporation into implantable pacemakers or defibrillators. A template matching approach – morphological detection – may be carried out to check for certain predefined waveforms and a decision then made as to whether to deliver an appropriate remedial shock.

Further developments in implantable cardiac devices include the detection and storage of P, QRS and T characteristics and the potential to deliver these wirelessly to the Internet for remote analysis by a cardiologist. In this fashion, device settings could be updated from the remote location without further user intervention; patients would no longer have to contemplate a journey to their doctor to discover if a recent shock had been efficacious or not.

Medtronic, a large US pacemaker and defibrillator manufacturer, is planning such a secure network, whereby doctors could monitor their patients remotely and suggest that the overall cardiac control device market could be thirteen billion dollars by 2005. Where possible, most telemetric processing
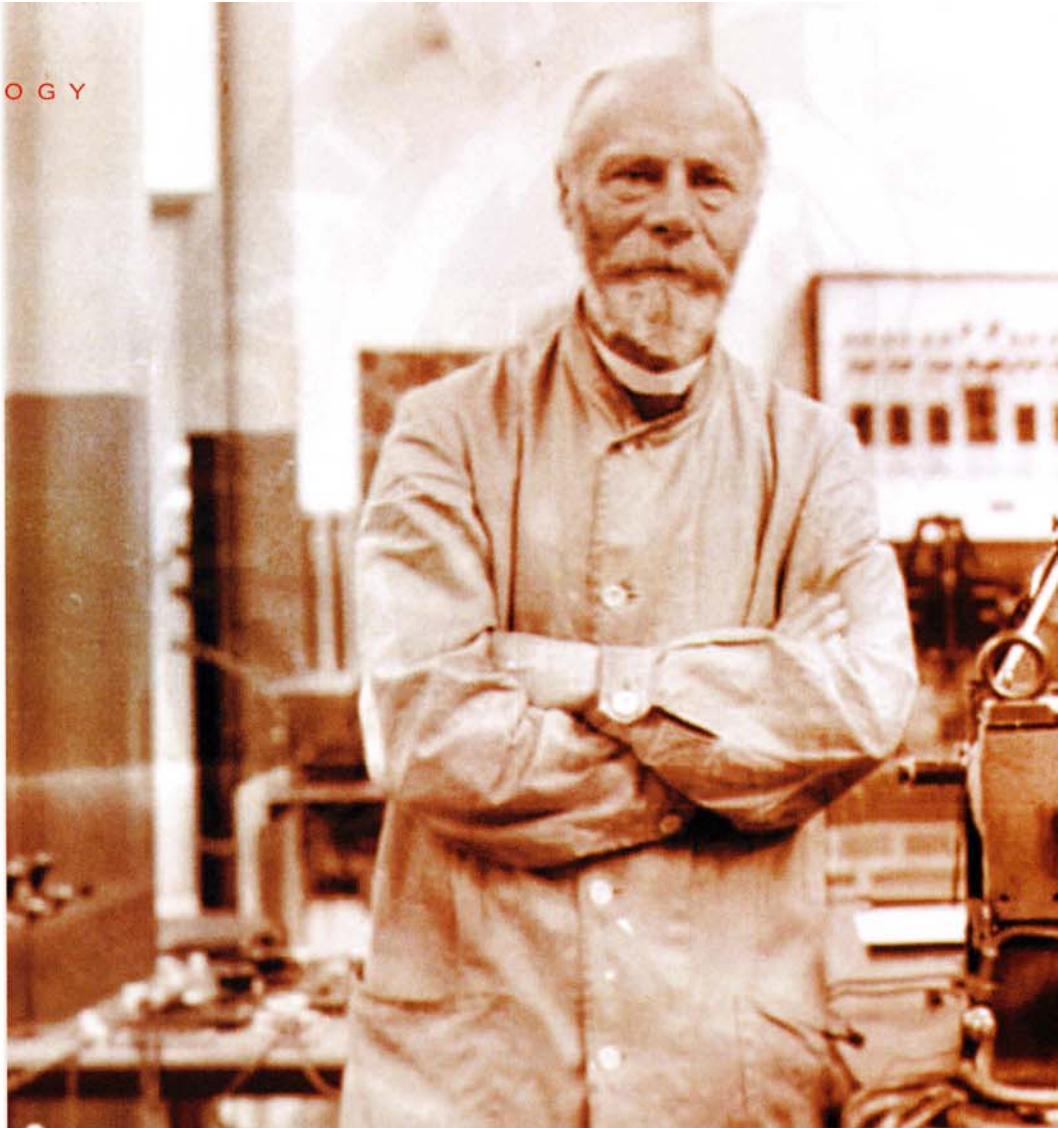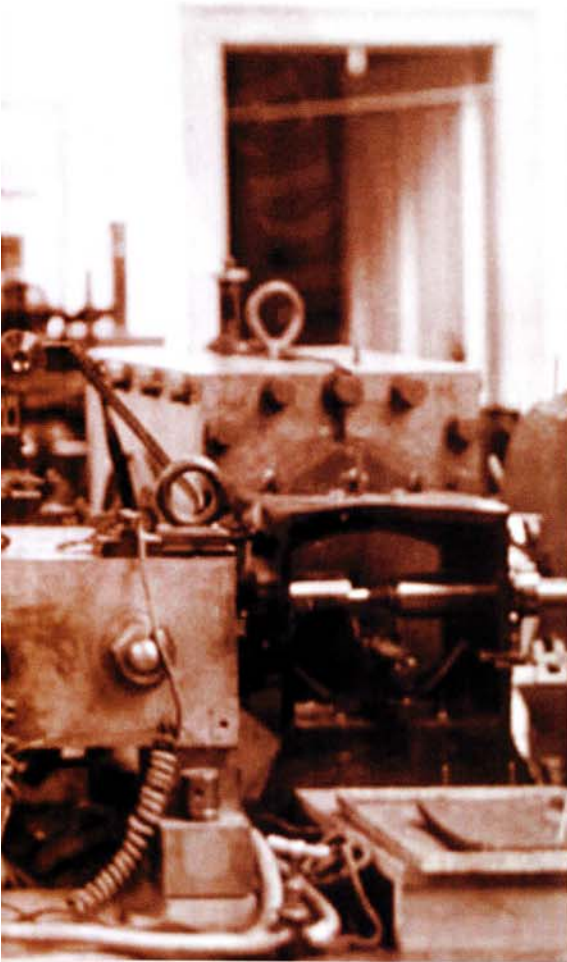
would be done by a tabletop device connected to a phone line/Internet connection, using a simple radio frequency analogue link to the implantable device. The power consumption of the cardiac device must be kept as low as feasible, to prolong battery life and thus delay the surgery required for replacement.

The continuous electrocardiogram recordings provided by Holter monitors, often over a 24 to 48 hour period, allow transient cardiac episodes such as intermittent arrhythmias or silent ischæmia to be captured using post-hoc analytic techniques. Typically a Holter system comprises two or more chest electrodes, a monitor and a recording device. Some newer, low power models can acquire digital signals directly from the electrodes and record to flash memory cards for later processing. These tend to be less bulky than traditional cassette based analogue recording ambulatory monitors – and certainly more portable than Einthoven's original 300 kg design! It is important that the chest electrodes are attached securely; a memo function may also be available on the device should a patient wish to mark a period of strenuous exercise.

As an alternative to continuous recording, some monitors are designed to be triggered by the patient when they are experiencing a cardiac episode. In this case, their ECG is recorded for some minutes, for the cardiologist to review. Some hospital units incorporate arrhythmia detection and can communicate potentially serious conditions to a remote monitoring point.

Advances in digital signal processing techniques have simplified the classification of ECG characteristic points other than the R peak. Of particular interest to the authors is the PR interval as it denotes the conduction time from the dominant sinoatrial node to and then across, the atrioventricular node. To aid extraction of the P wave, the modified Lead II may be useful as it serves to highlight atrial activity.

This lead configuration is also know as the Lewis lead, named after the pioneering Sir Thomas Lewis of University College Hospital, London. A high resolution ECG signal is essential to facilitate accurate offline automated marking; this may be achieved by using specialised biomedical amplifiers, analogue bandpass filtering and sampling at 1000 Hz.

Typically a digital notch filter is then applied to remove any 50 Hz power line noise present. The characteristic points of the ECG may then be extracted using techniques such as template matching or wavelet tracking. The resulting intervals can provide a fascinating insight into propagation times between various points in the heart in a non-invasive, patient-friendly manner.

Such clinical research grade ECG data is available to the UCD Digital Signal Processing Lab of the Department of Electronic and Electrical Engineering as part of ongoing collaborative work with the Department of Human Anatomy and Physiology, UCD and the Respiratory Sleep Laboratory at St Vincent's University Hospital, Dublin.

A valuable application of the RR ECG characteristic interval is to quantify the extent of respiratory modulation, an indicator of cardiorespiratory health. This respiratory sinus arrhythmia, i.e. the modulation of the sinus node, is increasingly being used by anæsthesiologists to estimate the efficacy of drug administration.

This variability may be quantified using certain bands of the RR interval spectrum to provide an indication of parasympathetic nerve activity, a branch of the autonomic nervous system – the system that maintains the heart beat without conscious user intervention. Healthy subjects exhibit a greater level of heart rate variability than those suffering from pathologies; the variability is seen to diminish while under anaesthetic, due to respiratory depression.

Heart rate and its variability may also be used to augment psychophysiological measures of stress, whereby increased rate coupled with loss of variability is seen as an indicator of overall stress.

Sleep apnoea, a condition wherein a person ceases to breathe during sleep, affects an estimated five per cent of the adult population of Ireland. Diagnosis can often be costly, requiring overnight recordings of the encephalogram, pulse oximetry and ECG recordings. Members of the UCD Digital Signal Processing Research Group have developed a method to diagnose apnoea based on the ECG data alone. The team's work (1) showed that low-frequency fluctuations in the characteristics of the recorded heart signal were different during normal breathing and apnoea; this change may be attributable to an alteration of autonomic nervous input to the heart from the brain and perhaps also due to the effect of chest movement on the recorded signal.

A more generalised approach to electrocardiography involves body surface potential mapping; this can provide a view of the cardiac electrical activity as part of the overall body surface potential distribution. Due to the large number of lead points required on the chest harness – often more than 128 – digital signal processing methods such as multichannel digital sampling, multiplexing, storage and online/offline analysis on a PC workstation are particularly appropriate. For ambulatory applications, it may be feasible to carry out offsite analysis, across a suitable communications link.

Now, almost a century after Einthoven's groundbreaking development of the electrocardiogram, a prediction by Sir Thomas Lewis in 1912 that "The time is at hand, if not already come, when an examination of the heart is incomplete if this new method is neglected" has particular resonance in this exciting synthesis of the sciences of clinical physiology and biomedical engineering signal processing.

Reference:
(1) de Chazal P., Heneghan C., Sheridan E., Reilly R., Nolan P., and O'Malley M. "Automatic Classification of Sleep Apnea Epochs using the Electrocardiogram", Computers in Cardiology, 2000.

Bibliography:
Fisch C., "Centennial of the string galvanometer and the electrocardiogram", J Am Coll Cardiol. 2000 Nov 15;36(6):1737-45.
Nelson C., Geselowitz D., 1976, The theoretical basis of electrocardiology. Clarendon Press, Oxford.
Nobel Lectures, Physiology or Medicine, 1922-1941. The Nobel e-museum, http://www.nobel.se

Gary Bass and Redmond Shouldice have worked on collaborative medical engineering research since 1996, when they received a special award from the National Rehabilitation Board for their Young Scientists submission 'Oscillating Chemical Clock 'B-Z' Reaction and Nonlinear Electronic Circuitry as Analogues for Cardiac Instabilities'. They formed Deterministic Chaos (an Internet consultancy) in 1999 and are currently pursuing doctoral studies in UCD.