The Evolution of Pacemakers

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An Electronics Perspective, from the Hand Crank to Advanced Wavelet Analysis

Around 40% of all human deaths are attributed to cardiovascular diseases. Cardiac pacing has become a therapeutic tool used worldwide with more than 250,000 pacemaker implants every year. The purpose of this article is to detail the significant advances in cardiac pacing systems. Our focus is on the evolution of circuit designs applied in pacemakers. Future pacemaker features and further improvements are also pointed out.

Since the first artificial pacemaker was introduced in 1932, much has changed and will continue to change in the future [1]–[3]. The complexity and reliability in modern pacemakers has increased significantly, mainly due to developments in integrated circuit (IC) design. Early pacemakers merely paced the ventricles asynchronously, not having the capability of electrogram sensing. Later devices, called *demand mode pacemakers*, included a sense amplifier that measured cardiac activity by avoiding competition between paced and intrinsic rhythms. By the introduction of demand pacemakers, the longevity increased since pacing stimuli were only delivered when needed. In 1963, pacemakers were introduced having the capability to synchronize ventricular stimuli to atrial activation. Since that time, clinical, surgical, and technological developments have proceeded at a remarkable rate, providing the highly reliable, extensive therapeutic and diagnostic devices that we know today. Modern pacemaker topologies are extremely sophisticated and include an analog part (comprising the sense amplifier and a pacing output stage) as well as a digital part (consisting of a microcontroller and some memory), implementing diagnostic analysis of sensed electrograms, adaptive rate response, and device programmability.

Pacemakers have become smaller and lighter over the years. Early devices weighed more than 180 g, whereas today, devices are available weighing no more than 25 g [4]. This weight reduction has occurred partly due to the development of high-energy-density batteries. Finally, there have been remarkable advances in cardiac lead technology. Novel electrode tip materials and configurations have provided extremely low stimulation thresholds and low polarization properties [5].

In this article, we will concentrate on the evolution of analog circuit designs applied in cardiac pacemakers. First, the electrical operation of the heart is described. The following section treats the history and development of cardiac pacing systems as well as their circuit descriptions. Then, some new features in modern pacemakers are discussed. Finally, the conclusions are presented.

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Cardiac pacing has become a therapeutic tool used worldwide.

The Heart

Excitation and Conduction System

The heart is composed of atrial and ventricle muscle that make up the myocardium and specialized fibers that can be subdivided into excitation and conduction fibers. Once electrical activation is initiated, contraction of the muscle follows. An orderly sequence of activation of the cardiac muscle in a regularly timed manner is critical for the optimal functioning of the heart.

The excitation and conduction system, responsible for the control of the regular pumping of the heart is presented in Figure 1. It consists of the sinoatrial (SA) node, internodal tracks, Bachmann's bundle, the atrioventricular (AV) node, the bundle of His, bundle branches, and Purkinje fibers. Cardiac cells are able to depolarize at a rate specific for the cell type. The intrinsic rate of AV-nodal cells is about 50 beats per minute (bpm), whereas Purkinje fibers depolarize at a rate of no more then 40 bpm. During normal sinus rhythm, the heart is controlled by the SA node having the highest intrinsic rate of 60–100 bpm, depending on the hemodynamic demand. The right atrial internodal tracks and Bachmann's bundle conduct the SA-nodal activation throughout the atria, initiating a coordinated contraction of the atrial walls. Meanwhile, the impulse reaches the AV node, which is the only electrical connection between atria and ventricles. The AV node introduces an effective delay, allowing the contraction of the atria to complete before ventricular contraction is initiated. Due to this delay, an optimal ventricular filling is achieved. Subsequently, the electrical impulse is conducted at a high velocity by the His-Purkinje system comprising the bundle of His, bundle branches, and Purkinje fibers. Once the bundle of His is activated, the impulse splits into the right bundle branch, which leads to the right ventricle and the left bundle branch serving the left ventricle. Both bundle branches terminate in Purkinje fibers. The Purkinje fibers are responsible for spreading the excitation throughout the two ventricles, enabling a coordinated and massive contraction [6].

Cardiac Signals

Surface Electrocardiogram

The electrocardiogram (ECG) is a recording from the body surface of the electrical activity generated by the heart. The ECG was originally observed by Waller in 1899 [7]. In 1903, Einthoven introduced electrophysiological concepts still in use today, including the labeling of the waves characterizing the ECG. He assigned the letters P through U to the waves avoiding conflicts with other physiologic waves studied at that time [7]. Figure 2 depicts a typical ECG signal.

ECG signals are typically in the range of ± 2 mV and occupy a bandwidth of 0.05–150 Hz. The morphology of the ECG waves depends on the amount of tissue activated per unit of time as well as the relative speed and direction of cardiac activation. Therefore, the physiological pacemaker potentials, i.e. the SA-nodal potentials, generated by a relative small myocardial mass are not observed on the ECG. The first ECG wave within the cardiac cycle is the P-wave, reflecting atrial depolarization. Conduction of the cardiac impulse proceeds from the atria through a series of specialized cardiac structures (the AV node and the His-Purkinje system) to the ventricles. There is a short relatively isoelectric segment following the P-wave. This is the PQ interval, which is related to the propagation delay (0.2 s) induced by the AV node (Figure 1). Once the large muscle mass of the ventricles is excited, a rapid and large deflection is observed on the surface ECG. Depolarization of the ventricles is represented by the QRS complex or R-wave (Figure 2). Following the QRS complex,

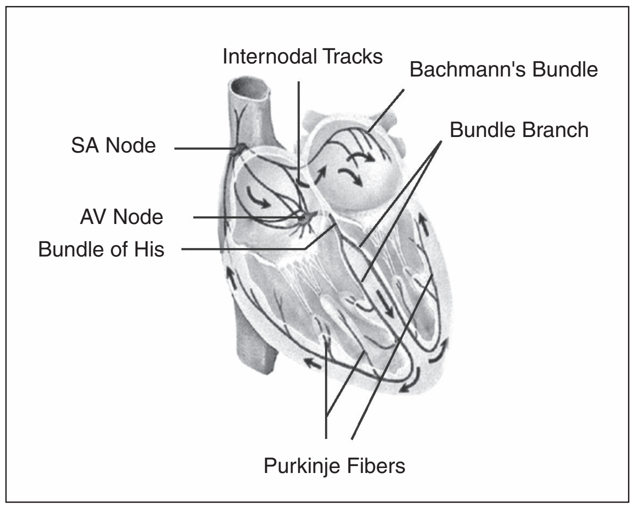

Fig. 1. The cardiac conduction system.

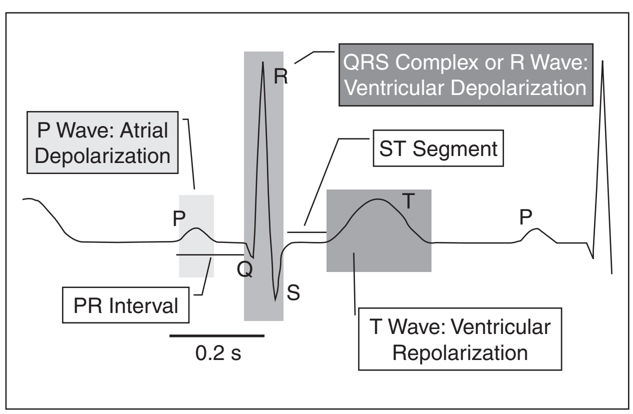

Fig. 2. Typical electrocardiogram.

another isoelectric segment, the ST interval, is observed. The ST interval represents the duration of depolarization after all ventricular cells have been activated, normally between 0.25 s and 0.35 s. After completion of the ST segment, the ventricular cells return to their electrical and mechanical resting state, completing the repolarization phase observed as a low-frequency signal known as the T-wave. In some individuals, a small peak occurs at the end or after the T-wave and is called the U-wave. Its origin has never been fully established, but it is believed to be a repolarization potential [8].

Intracardiac ECG

An intracardiac ECG (IECG) is a recording of changes in electric potentials of specific cardiac locations measured by electrodes placed within or onto the heart by using cardiac catheters. The IECG can be recorded between one electrode and an indifferent electrode, usually more then 10 cm apart (unipolar electrogram) or between two more proximate electrodes (<15 mm) in contact with the heart (bipolar electrogram). Sensing the intrinsic activity of the heart depends on many factors related to the cardiac source and the electrode-tissue interface where complex electrochemical reactions take place. In most situations, it is desirable that the IECG does not contain signals from other, more distant cardiac chambers. Bipolar lead systems are much less sensitive to far-field potentials and electromagnetic interference (EMI) sources obscuring the cardiac signal.

Cardiac Diseases—Arrhythmias

Arrhythmias (or dysrhythmias) are due to cardiac problems producing abnormal heart rhythms. In general, arrhythmias reduce hemodynamic performance including situations where the heart's natural pacemaker develops an abnormal rate or rhythm or when normal conduction pathways are interrupted and a different part of the heart takes over control of the rhythm. An arrhythmia can involve an abnormal rhythm increase (tachycardia: >100 bpm) or decrease (bradycardia: <60 bpm) or may be characterized by an irregular cardiac rhythm, e.g., due to asynchrony of the cardiac chambers. An artificial pacemaker can restore synchrony between the atria and ventricles.

The History and Development of Cardiac Pacing

Artificial Pacemakers

An artificial pacemaker is a device that delivers a controlled, rhythmic electric stimulus to the heart muscle in order to maintain an effective cardiac rhythm for long periods of time, ensuring effective hemodynamic performance. The indication for implanting a permanent pacemaker and selection of the appropriate mode of operation are mainly based on the type of cardiac disease involved such as failure of impulse formation (sick-sinus syndrome) and/or impulse conduction (AV-block).

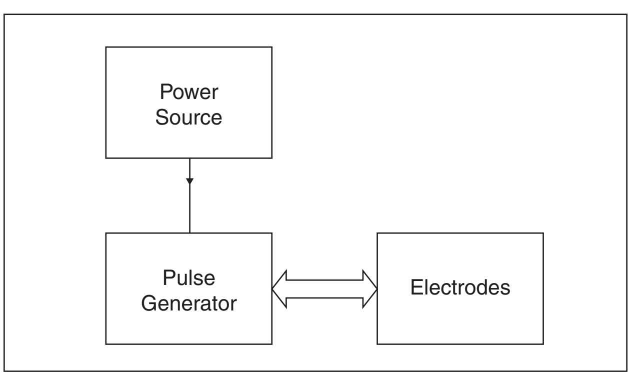

Fig. 3. Basic pacemaker functional block diagram.

Functionally, a pacemaker comprises at least three parts: an electrical pulse generator, a power source (battery), and an electrode (lead) system (Figure 3) [9].

Different types of output pulses (e.g., monophasic and biphasic) can be used to stimulate the heart. The output stimulus provided by the pulse generator is the amount of electrical charge transferred during the stimulus (current). For effective pacing, the output pulse should have an appropriate width and sufficient energy to depolarize the myocardial cells close to the electrode. Generally, a pacemaker can provide a stimulus in both chambers of the heart. During AV block, ventricular pacing is required because the seat of disease is in the AV node or His-Purkinje system. However, in case of a sick sinus syndrome, the choice of pacemaker will be one that will stimulate the right atrium.

A pacemaker utilizes the energy stored in batteries to stimulate the heart. Pacing is the most significant drain on the pulse generator power source. The battery capacity is commonly measured in units of charge (amperehours). Many factors will affect the longevity of the battery, including primary device settings like pulse amplitude and duration and pacing rate. An ideal pulse generator battery should have a high energy density, low self-discharge rate, and sufficient energy reserve between early signs of depletion and full depletion to allow for safe replacement of the device.

The electrical connection between the heart and the implanted pulse generator is provided by an implantable electrode catheter called *lead*. In an implantable pulse generator system, commonly, two types of lead systems are used. A unipolar lead system has a single isolated conductor with an electrode located at the tip. A bipolar lead has two separate and isolated conductors connecting the two electrodes, i.e., the anode and cathode, usually not more than 12 mm apart. The cathode refers to the electrode serving as the negative pole for delivering the stimulation pulse and the anode to the positive pole. For unipolar pacing-sensing systems, the distance between anode and cathode easily exceeds 10 cm. Its cathode is typically located at the lead tip, whereas the pulse generator housing, usually located in the pectoral region, is used as anode. Several types of bipolar leads exist, including the coaxial lead allowing a diameter in the range of 4–5 F (French = 0.33 mm), which is comparable to state-of-the-art unipolar leads. The sensing behavior of bipolar lead systems outperforms their unipolar counterparts by providing a better signal-to-interference ratio. Especially for sensing atrial activation, bipolar electrodes are less sensitive to far-field potentials generated by the ventricles. Moreover, bipolar leads are less sensitive to EMI sources and skeletal muscle potentials. However, owing to their construction, bipolar leads are stiffer and more complex from a mechanical construction point of view.

Hyman's Pacemaker

In the early 20th century, many experiments such as drug therapy and electrical cardiac pacing had been conducted for recovery from cardiac arrest. Initial methods employed in electrically stimulating the heart were performed by applying a current that would cause contraction of the muscle tissue of the heart. Albert S. Hyman stated that

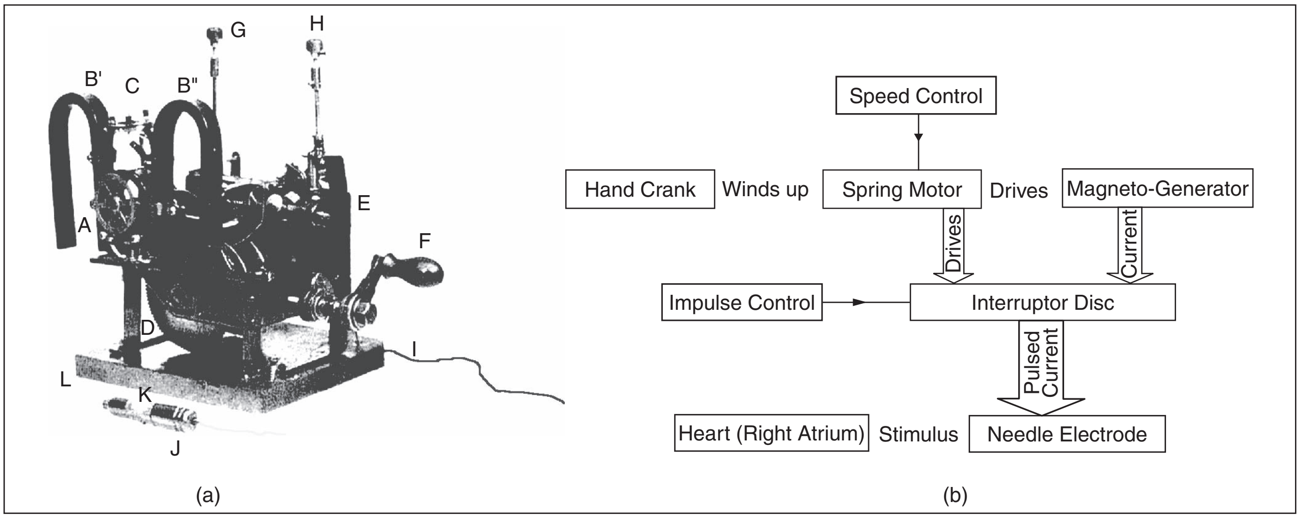

Fig. 4. (a) The first artificial pacemaker by Hyman. (b) Block diagram of Hyman's pacemaker.

> the introduced electric impulse serves no other purpose than to provide a controllable irritable point from which a wave of excitation may arise normally and sweep over the heart along its accustomed pathways.

Hyman designed the first experimental heart pacemaker in 1932 [10] [Figure 4(a)].

Hyman's pacemaker was powered by a hand-wound, spring-driven generator that provided 6 min of pacemaking without rewinding. Its operation is as follows: The hand crank (F) winds the spring motor (D), which drives the magneto-generator (A) at a controlled speed (E and H) and causes the interrupter disc (not shown) to rotate. The magnetogenerator supplies current to a surface contact on the interrupter disc. The companion magnet pieces (B′ and B″) provide the magnetic flux necessary to generate current in the magneto-generator. Subsequently, the interrupter disc produces a pulsed current at 30, 60, or 120 bpm, regulated by the impulse controller (G), which represents the periodic pacing waveform delivered to the electrode needle (L). The neon lamp (C) is illuminated when a stimulus is interrupted. In Figure 4(b), a block diagram of Hyman's pacemaker is given [11].

Dawn of the Modern Era—Implantable Pacemakers

The origin of modern cardiac pacing started when the first pacemaker, developed by Dr. Rune Elmqvist, was used in a patient in 1958 by Dr. Ake Senning [12]. In 1959, the engineer Wilson Greatbatch and the cardiologist W.M. Chardack developed the first fully implantable pacemaker [13]. This device was essentially used to treat patients with complete AV block caused by Stokes-Adams diseases, delivering a single-chamber ventricular pacing. It measured 6 cm in diameter and 1.5-cm thick, and the total weight of the pacemaker was approximately 180 g. The pacemaker circuit delivered 1-ms wide pulses to the electrode, a pulse amplitude of 10 mA and a repetition rate of 60 bpm. The average current drain of the circuit under these conditions was about 12 μA, which, energized by ten mercury-zinc cells, gave a continuous operation life estimated at five years. The schematic of the implanted pacemaker is shown in Figure 5 and consists of a pulse forming (square-pulse) oscillator and an amplifier.

Basically, the cardiac pacemaker includes a blocking oscillator [14], which is a special type of wave generator used to produce a narrow pulse. The blocking oscillator is closely related to the more common two-transistor a-stable circuit, except that it uses only one amplifying device—a transistor. The other is replaced by a pulse transformer, which provides inductive regenerative positive feedback. The transistor of the blocking oscillator is normally cut off between pulses and is only conducting during the time that a pulse is being generated. The operation of a blocking oscillator during a single cycle may be divided into three parts: the turn-on period, the pulse period, and the time interval between adjacent pulses (relaxation period). The turn-on period occurs when the supply voltage Vcc is applied to the circuit, R1 and R2 provide a forward bias current, and transistor Q1 conducts. The current flow through Q1 and the primary (L1) of T1 induces a voltage in the secondary (L2). The positive voltage of L2 is coupled to the base of the transistor through C1. This yields more

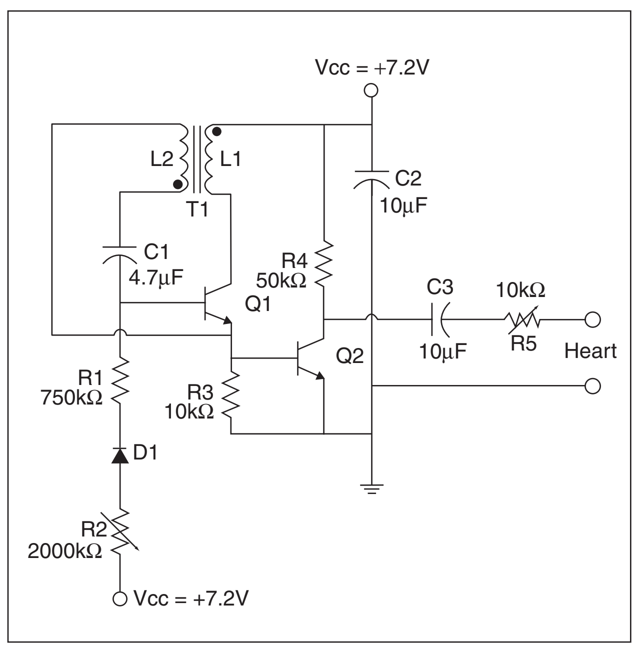

Fig. 5. A schematic of the first implanted pacemaker.

collector current and, consequently, more current through L1. Sufficient voltage is applied very rapidly to saturate the base of Q1. Once Q1 becomes saturated, the circuit can be defined as a series RL (resistance-inductance) circuit, and the current increase in L1 is determined by the time constant of L1 and the total series resistance. During the pulse period, the voltage across L1 will be approximately constant as long as the current increase through L1 is linear. The pulse width depends mainly on the time constant $\tau_C = L/R$, where R is the equivalent series resistance. After this time, L1 saturates. C1, which has been charged during the pulse period, will now discharge through R1 and cut off Q1. This causes the collector current to stop, and the voltage across L1 returns to 0, shaping the relaxation period. Transistor Q2 implements the amplifier.

Demand Pacemaker

As was shown in the previous section, the early pacing devices simply delivered a fixed-rate pulse to the ventricle at a preset frequency, regardless of any spontaneous activity of the heart. These pacemakers, called *asynchronous* or *fixed-rate pacemakers*, compete with the natural heart activity and can sometimes even induce arrhythmias or ventricular fibrillation (VF). By adding a sensing amplifier to the asynchronous pacemaker in order to detect intrinsic heart activity and thus avoid this competition, one obtains a demand pacemaker, which provides electrical heart-stimulating impulses only in the absence of natural heartbeats. The other advantage of the demand pacemaker compared to the fixed rate system is that now the battery life of the system is prolonged because it is only activated when pacing stimuli are needed.

Berkovits introduced the demand concept, which is the basis of all modern pacemakers, in June 1964. In Figure 6, a suitable block diagram of a demand pacemaker is given. Intracardiac electrodes of conventional demand pacemakers serve two major functions, namely pacing and sensing. Pacing is achieved by the delivery of a short, intense electrical pulse to the myocardial wall where the distal end of the electrode is attached, similar to the early pacing devices. However, the same electrode is used to detect the intrinsic activity of the heart (e.g., R-waves in the ventricle). The electrical pulse generator consists of the following components: a sense amplifier circuit, a timing control circuit, and an output driver circuit (electrical impulse former).

The schematic of the pulse generator designed by Berkovits is given in Figure 7 [15]. The general function of this circuit is to make the timing circuit responsive to cardiac activity. This allows inhibition of the pacing pulse from the pulse generator whenever the heart beats on its own. To achieve such function, the sense amplifier plays a fundamental role. It is designed to amplify and normalize the cardiac signal. Also, the sense amplifier is configured to filter out undesired signals such as P- and T-waves and 50-Hz or 60-Hz interference. The electrical signals picked up by the electrodes are coupled through capacitor Cc1 to the input of the amplifier, comprising transistors Q1 and Q2. The maximum gain of this amplifier stage is above 50. Alternating current (AC) signals at the collector of Q2 are coupled through capacitor C_{c2} to the bases of both transistors Q3 and Q4. This implements an absolute value function, since signals of positive polarity turn on Q3 and Q5, and signals of negative polarity turn on Q4.

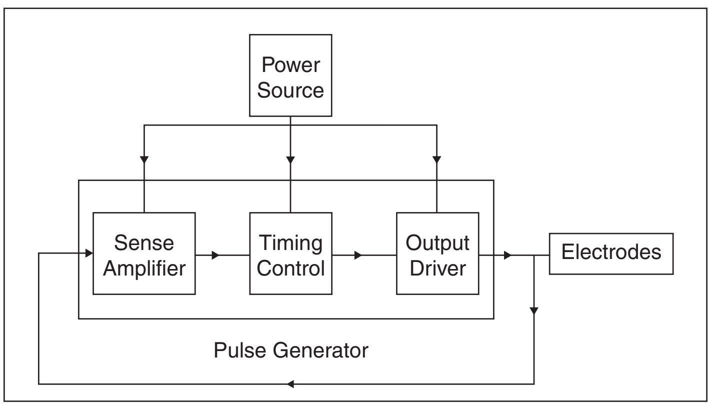

Fig. 6. Basic demand pacemaker functional block diagram.

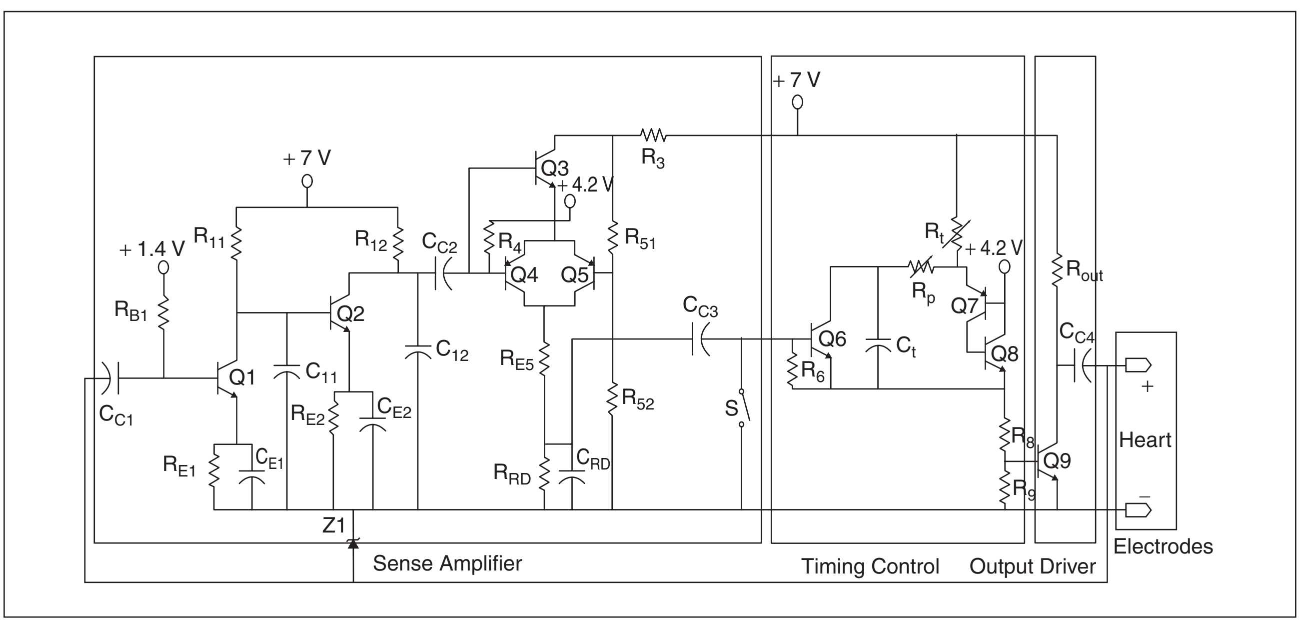

Fig. 7. A schematic of the pulse generator of the first demand pacemaker.

A bandpass filter with a bandwidth of 20–30 Hz is incorporated in the sense amplifier. Three differentiators (R_{B1} and C_{c1}, R_{E1} and C_{E1}, and R_{E2} and C_{E2}) limit the low-frequency response of the detecting circuit to discriminate against the P- and T-waves and any other frequencies well below 20 Hz. Two integrators (R_{I1} and C_{I1}; R_{I2} and C_{I2}) are designed to reduce high-frequency noise components well above 30 Hz. However, these filters are not fully effective in preventing the triggering of Q6 by 50 Hz or 60 Hz signals. For this reason, a rate discrimination circuit (including resistors R_{E5} and R_{RD} and capacitor C_{RD}) is provided.

The switch S is used only to define the operation mode of the system, being either free-running mode (switch closed) or demand mode (switch opened). In free-running mode, the switch is closed and, therefore, transistor Q6 remains cut off. When the switch is opened, i.e., in the case of a pacemaker required to operate in the demand mode, each pulse transmitted through capacitor C_{c3} to the base of transistor Q6 causes the transistor to conduct. Capacitor C_t discharges through the collector-emitter circuit of the transistor. In such a case, the timing cycle is interrupted, and the junction of capacitor C_t and resistor R_p does not increase in potential to the point where transistors Q7 and Q8 are triggered to conduction. After capacitor C_t has discharged through transistor Q6, the transistors turn off. The capacitor then starts charging once again, and the new cycle begins immediately after the occurrence of the last heartbeat.

When no signal is fed to the base of transistor Q6, Q6 remains nonconducting and will not affect the charging of capacitor C_t. The timing control circuit, which determines the pulse duration (1 ms) and the repetition rate (72 pulses per minute) of the pulse generator, is made up of transistors Q7 and Q8; capacitor Ct; and resistances R_p, R_t, R_8, and R_9. The pulse duration is determined by the time constant $\tau_p = C_t R_p$ and the rate, mainly by $\tau_r = C_t R_t$. During the charging period, both transistors are off. As C_t charges, this creates a regenerative turn on of both Q7 and Q8, which is sustained as long as C_t can supply current, a time determined primarily by resistor R_p. During this time, the output transistor Q9 is turned on, causing current to flow in the electrode circuit. The output driver comprises transistor Q9, resistor R_{out}, and capacitor C_{c4}. After 1ms, C_t is discharged; transistors Q7, Q8, and Q9 turn off; and the pulse is terminated.

Finally, to avoid damage to the circuit due to high-voltage signals from the electrodes, a zener diode (Z1) was placed between the terminals of the electrode.

A variation of this concept is the demand-triggered pacemaker, which stimulates every time it senses intrinsic heart activity, i.e., the stimulus falls directly on the natural QRS.

Dual-Chamber Pacemaker

A dual-chamber pacemaker typically requires two pacing leads: one placed in the right atrium and the other placed in

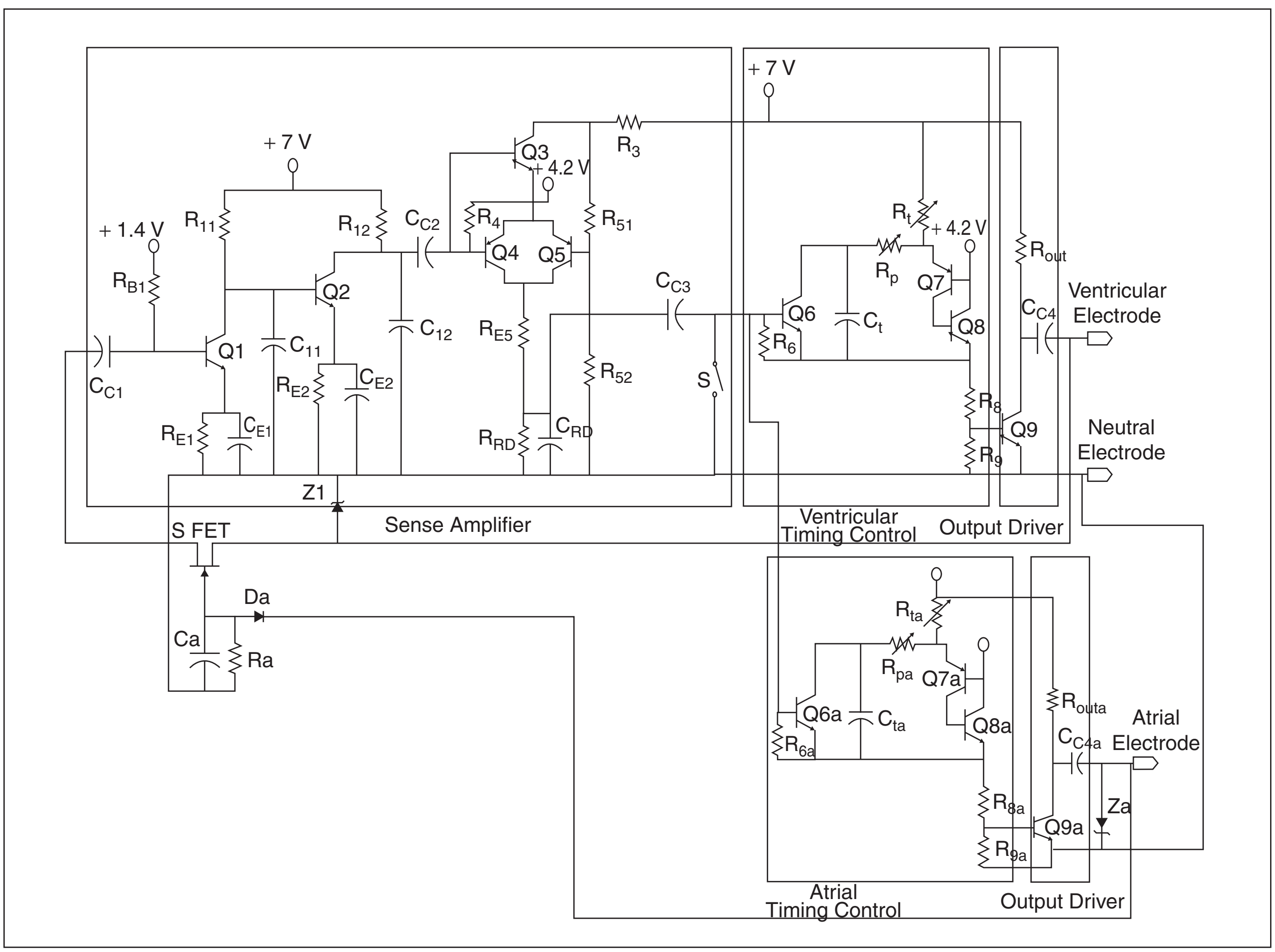

Fig. 8. Schematic of the dual-chamber demand pacemaker.

Since the first artificial pacemaker was introduced in 1932, much has changed and will continue to change.

the right ventricle. A dual-chamber pacemaker monitors (senses) electrical activity in the atrium and/or the ventricle to see if pacing is needed. When pacing is needed, the pacing pulses of the atrium and/or ventricle are timed so that they mimic the heart's natural way of pumping.

Dual-chamber pacemakers were introduced in the 1970s. One of the first descriptions of a dual-chamber pacemaker was given by Berkovits in 1971. Berkovits announced a bifocal (AV sequential) pacer that sensed only in the ventricle but paced both chambers. In the presence of atrial standstill or a sinus-node syndrome plus AV block, the bifocal pacemaker could deliver a stimulus to the atrium and then, after an appropriate interval, to the ventricle. Berkovits improved on his original design given in Figure 8 with a dual-chamber demand pacemaker. A schematic of this design is given in Figure 8 [16]. In accordance with the principles of the demand pacemaker design, a sense amplifier is provided to detect intrinsic ventricular activity. The timing control circuits determine both atrial and ventricular time-out stimulating period. However the atrial-stimulating impulse is generated first, and, after a predetermined time interval (200 ms), the ventricular-stimulating impulse is generated. Three electrodes are provided: a neutral electrode, an electrode for atrial stimulation, and an electrode for ventricular pacing and sensing. The field-effect transistor (FET) switch (S FET) is inserted in the feedback path of the ventricular electrode in order to avoid erroneous detection because of the atrial contraction. The S FET is normally conducting. The negative pulse generated at the atrial electrode is transmitted through the diode D_a, charging the capacitor C_a, and turning off the switch. When the atrial-stimulating terminates, C_a discharges through resistor R_a and turns on the switch again. In this manner, the sense amplifier is disabled during each atrial stimulation and for a short interval thereafter.

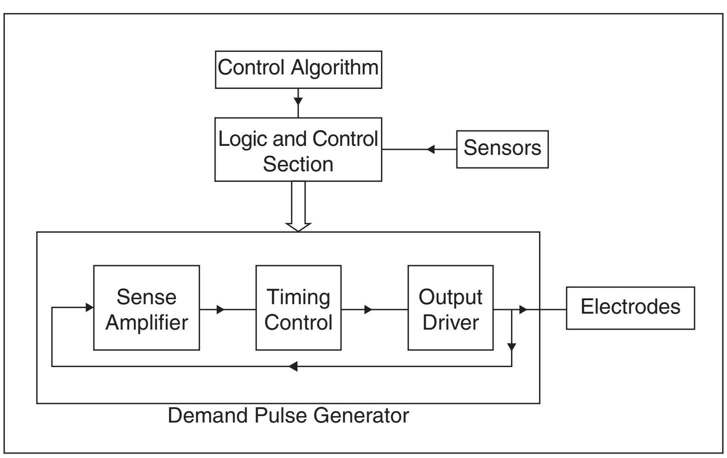

Fig. 9. A block diagram of a rate-responsive pacemaker.

More sophisticated dual-chamber pacemakers that sense intrinsic activity and pace in both chambers were developed, with their first use in late 1977.

Rate-Responsive Pacemaker

The latest innovations include the development of rate-responsive pacemakers in the early 1980s, which could regulate their pacing rate based on the output of a sensor system incorporated in the pacemaker and/or lead. A sensor system consists of a device to measure some relevant parameter from the body (e.g., body motion, respiration rate, pH, and blood pressure) and an algorithm in the pacemaker, which is able to adjust the pacemaker response in accordance with the measured quantity. Modern rate-responsive (also called frequency-response) pacemakers are capable of adapting to a wide range of sensor information relating to the physiological needs and/or the physical activity of the patient.

A block diagram of a rate-responsive pacemaker is given in Figure 9. The system is based on a pacemaker having a demand pulse generator, which is sensitive to the measured parameter. Many rate-responsive pacemakers currently implanted are used to alter the ventricular response in single-chamber ventricular systems. However, rate-responsive pacing can also be done with a dual-chamber pacing system.

New Features in Modern Pacemakers

Detection and Sensing Circuitry

A modern pacemaker consists of a telemetry system, an analog sense amplifier, analog output circuitry, and a microprocessor acting as a controller. Nevertheless, the sense amplifier plays a fundamental role in providing information about the current state of the heart. State-of-the-art implantable pulse generators or cardiac pacemakers include real-time sensing capabilities that are designed to detect and monitor intracardiac signal events (e.g., R-waves in the ventricle). A sense amplifier and its subsequent detection circuitry, together called the *front-end*, derive only a single event (characterized by a binary pulse) and feed this to a microcontroller that decides on the appropriate pacing therapy to be delivered by the stimulator. Over the years, huge effort has been put into the improvement of sense amplifier and detection circuitry.

The dynamic range of the atrial and ventricular electrograms sensed by an endocardial lead typically lies between 0.5–7 mV and 3–20 mV, respectively. Slew-rates of the signals range 0.1–4 V/s. For the QRS complex, spectral power concentrates in the band 10–30 Hz. The T-wave is a slower signal component with a reduced amount of power in a band not exceeding 10 Hz. Amplification of intrinsic cardiac signals requires circuitry that is robust against artifacts generated from noncardiac electromagnetic sources located outside or inside the patient. Introduction of electronic article surveillance (EAS) systems has raised concerns with regard to the possible interaction between emitting field sources and the sense amplifiers of medical implantable devices like pacemakers [17], implantable cardioverter defibrillators, and insertable loop recorders (ILRs) [18]. Other sources of EMI include cellular phones, airport metal detector gates, high-voltage power lines [19], electro-cautery devices, and magnetic resonance imaging (MRI) equipment [20]. The more sensitive atrial-sensing channel of a brady-arrhythmia device is more prone to detection of EMI. Any type of EMI having sufficient amplitude could cause the pacemaker to react in a clinically undesirable way, either inhibiting or triggering stimuli. Fortunately, noise reversion algorithms and circuits mostly provide reliable discrimination between EMI and intrinsic cardiac activity.

In Figure 10, a suitable block diagram of a sense amplifier for cardiac signal detection is given [21]. The IC or chip consists of a voltage-to-current (V-I) converter, a bandpass filter, an absolute value circuit, an adaptive threshold circuit, and a comparator circuit. Additionally, an EMI filter is implemented outside the chip for EMI cancellation. This usually is a second-order bandpass filter to suppress dc and signals beyond 1 kHz. The V-I converter is required as the input and output quantities of the EMI filter are voltages, and the applied circuit technique for the remainder of the sense amplifier is inherently current-mode. The bandpass filter is used to specifically select intracardiac signals, in our case being the QRS complex or R-wave, and to minimize the effect of the overlapping myocardial interference signals and low-frequency breathing artifacts. The center frequency of the bandpass filter is located at 25 Hz. The reason to use an absolute value circuit is to be independent from the electrode position in the heart. Accommodation to changes in the average input signal level is realized using the adaptive threshold circuit. At the end of the block schematic, the detection signal (a binary value) is generated depending on a threshold level.

A test signal is applied to the system to verify the performance and efficiency of the complete sense amplifier according to Figure 10. A typical intracardiac signal measured in the ventricle, shown in Figure 11(a), is applied to the input of the system. The transient response of the circuit is shown in Figure 11(b). The system is clearly able to detect the R-wave, which represents the cardiac event that the circuit was supposed to detect.

Morphological Analysis

In pacemakers, one of the challenges is the reduction of unnecessary therapies delivered to the patient when the heart rate dynamics becomes comparable to that of lethal tachyarrhythmias like ventricular tachycardia (VT) or VF. This situation includes supra-VT (SVT) that may occur as a result of atrial fibrillation. As heart rate does not discriminate between lethal tachyarrhythmias like VT/VF and SVT or atrial tachyarrhythmias, the morphology of the QRS complex, or more specifically, the R-wave morphology, can be used for a more accurate discrimination between SVT and VT.

In addition, to ensure efficient use of the memory available in an implantable device, the incidence of false positives, erroneously triggering automatic storage, should be minimized. For ILRs, promoting factors include the low-amplitude electrogram signal as a result of the limited vector available for pseudo-ECG measurement and the presence of muscle electromyography (EMG) and mechanical disturbance of the electrode tissue interface. Therefore, signal analysis methods improving discrimination of signals from noise are of great importance. Since, usually, signal and noise components share the same spectral bands, the scope of linear signal processing methods is rather limited.

Since the information retrieved by the above front-end circuit is reduced to a single event, morphological attributes of the electrogram are completely suppressed. Recent research and clinical studies report details on how morphological aspects of the electrogram relate to various pathological states of the heart and on how the wavelet transform (WT) can contribute efficiently to analysis.

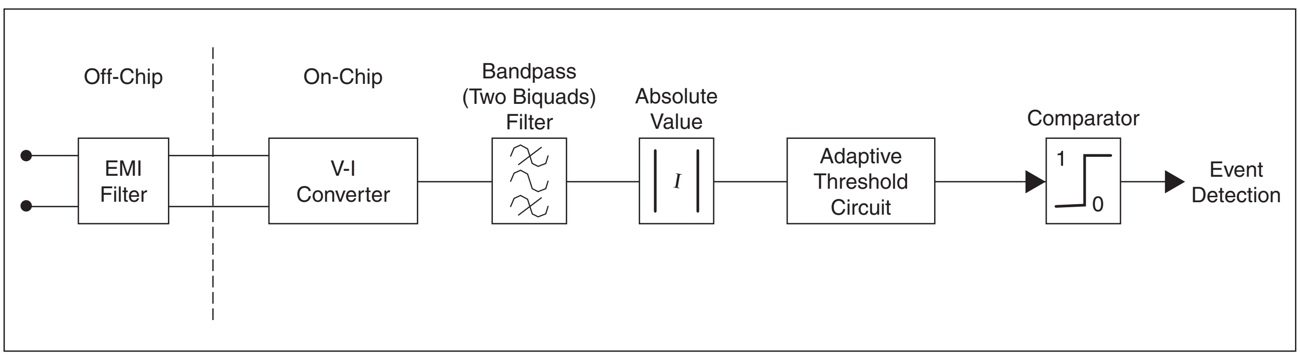

Fig. 10. A block diagram of a sense amplifier.

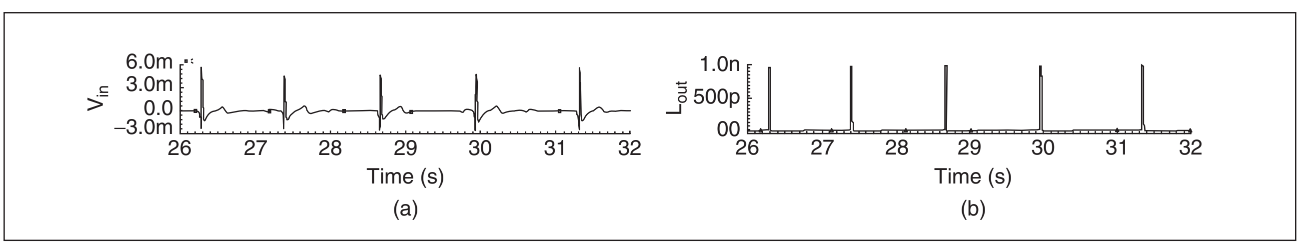

Fig. 11. Transient response of the complete sense amplifier circuit: (a) input voltage and (b) output current.

The WT is a merited technique for the analysis of nonstationary signals, like cardiac signals. Signal analysis methods derived from wavelet analysis [22] carry large potential to support a wide range of biomedical signal processing applications, including noise reduction [23], [24], feature recognition [25], and signal compression. Wavelets allow the analysis of the electrogram by focusing on the signal at various levels of detail in analogy with inspection of a sample with a microscope at various levels of magnification. As one can see in Figure 12, at very fine scales (smaller values of Scale a), details of the electrogram, i.e., the QRS complex, are revealed while unimpaired by the overall structure of the signal. At coarse scale (larger values of the Scale a), the overall structure of the electrogram can be studied while overlooking the details. Note that by this global view, both the QRS complex and T-wave can be detected. Analyzing the structure of the electrogram over multiple scales allows discrimination of electrogram features over all scales from those only seen at fine or coarse scales. Based on such observation, the presence or absence of electrogram features related to proximal or distal electrophysiological phenomena can be discriminated. Then, being a multiscale analysis technique, the WT offers the possibility of selective noise filtering and reliable parameter estimation. An algorithm based on wavelet analysis that compares morphologies of baseline and tachycardia electrograms based on differences between corresponding coefficients of their WTs has been found highly sensitive for VT detection [26]. Whereas smoothing attenuates spectral components in the stop band of the linear filter used, wavelet denoising attempts to remove noise and retain whatever signal is present in the electrogram.

Off-line ECG analysis, like Holter analysis, employs the discrete WT implemented in the digital domain using multi-rate filter banks [27]. In these applications, the WT provides a means to reliably detect QRS complexes. However, in patient-worn external applications (e.g., intelligent Holter devices), it

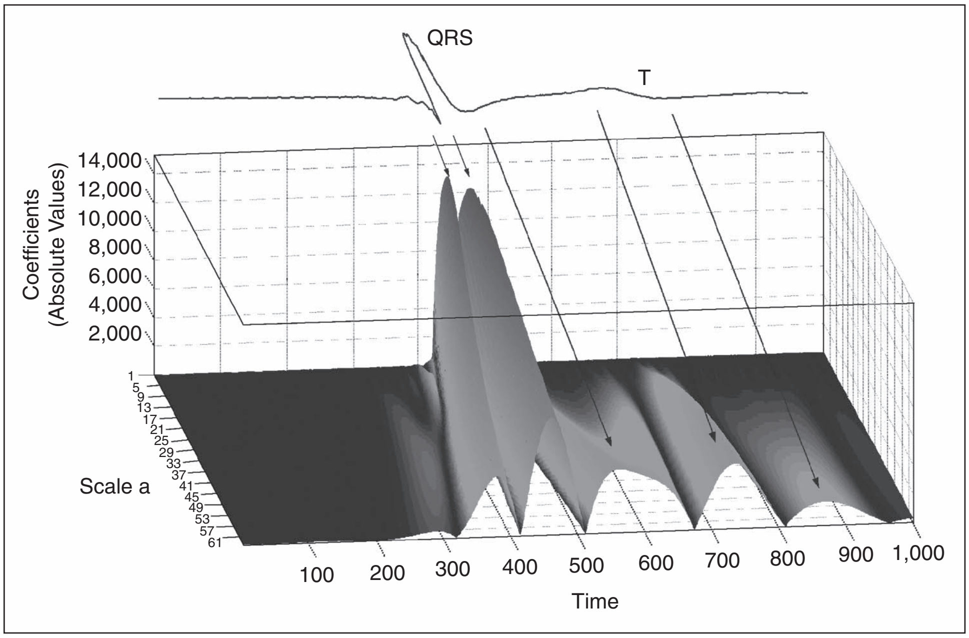

Fig. 12. Wavelet analysis of an intracardiac signal.

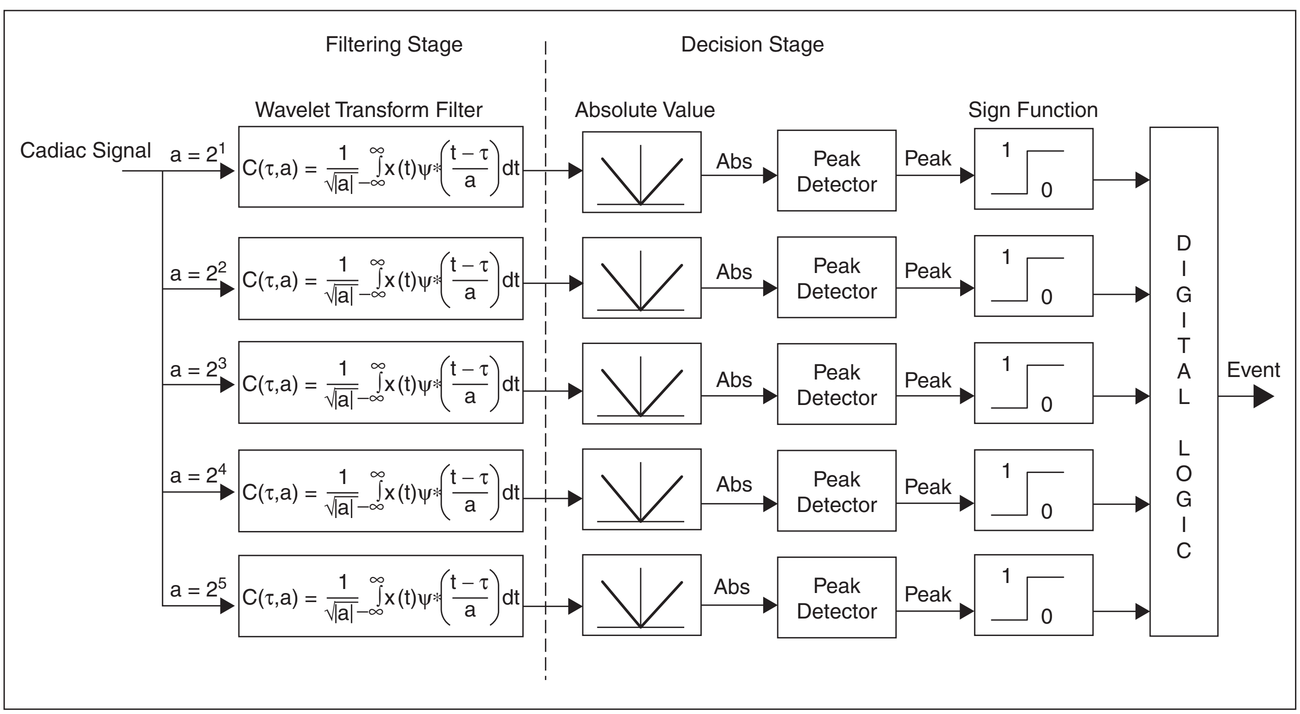

Fig. 13. Block diagram of the wavelet system.

is not favorable to implement the WT by means of digital signal processing due to the high power consumption associated with analog-to-digital conversion and computation.

Therefore, a method for implementing the WT in an ultralow-power analog way by means of dynamic translinear (DTL) circuits has been developed [28], [29]. The main advantage of DTL circuits with respect to other low-power techniques is the ability to handle a large dynamic range in a low-voltage environment. It allows for the implementation of a large variety of transfer functions described by (possibly nonlinear) polynomial differential equations. Moreover, only transistors and capacitors are required to realize these functions. Since, in conventional ultralow-power designs, resistors would become too large for on-chip integration, their superfluity is a very important advantage. Other advantages are that DTL circuits present a high functional density and are theoretically process and temperature independent.

In Figure 13, a first prototype wavelet-based system has been defined [28]. At the input, a wavelet filter is situated that implements an approximation to the first derivative Gaussian WT, a function most widely used for frequency analysis among wavelet functions. The complete filter comprises multiple scales in parallel in order to compute the WT in real time. As mentioned previously, the main idea of the WT is to look at a signal at various windows and analyze it with various resolutions.

Subsequently, the signal is fed through an absolute value circuit, followed by a peak detector, to generate an adjustable threshold level. It has been shown in [30] that the two maximas with opposite signs of the WT correspond to the QRS complex. The final signal-processing block is a comparator in order to detect the modulus maxima position. The time localization of the modulus maxima and the classification of characteristic points of the cardiac signal are processed by digital logic circuitry.

The wavelet system allows for easy decomposition of the IECG signal into components appearing at different scales (or resolutions) using short windows at high frequencies and long windows at low frequencies. This feature can be used to distinguish cardiac signal points from severe noise and interferences, as one can see in Figure 14. Figure 14(b) shows a typical ventricular signal with 50-Hz interference (input signal), and Figure 14(c) gives the WT at various scales. We can see in Figure 14(d) that both modulus maxima of the QRS complex for a specific scale ($a = 2^4$) of the WT indeed have been detected.

The obtained results for a typical cardiac signal demonstrate a good performance in generating the desired WT and achieving correct QRS complex detection.

The Electronics Research Laboratory of Delft University of Technology, together with the University of Maastricht and Medtronic Bakken Research Center, is currently investigating a fully integrated implementation of the analog WT circuit to be used in pacemakers. In addition, further analysis techniques

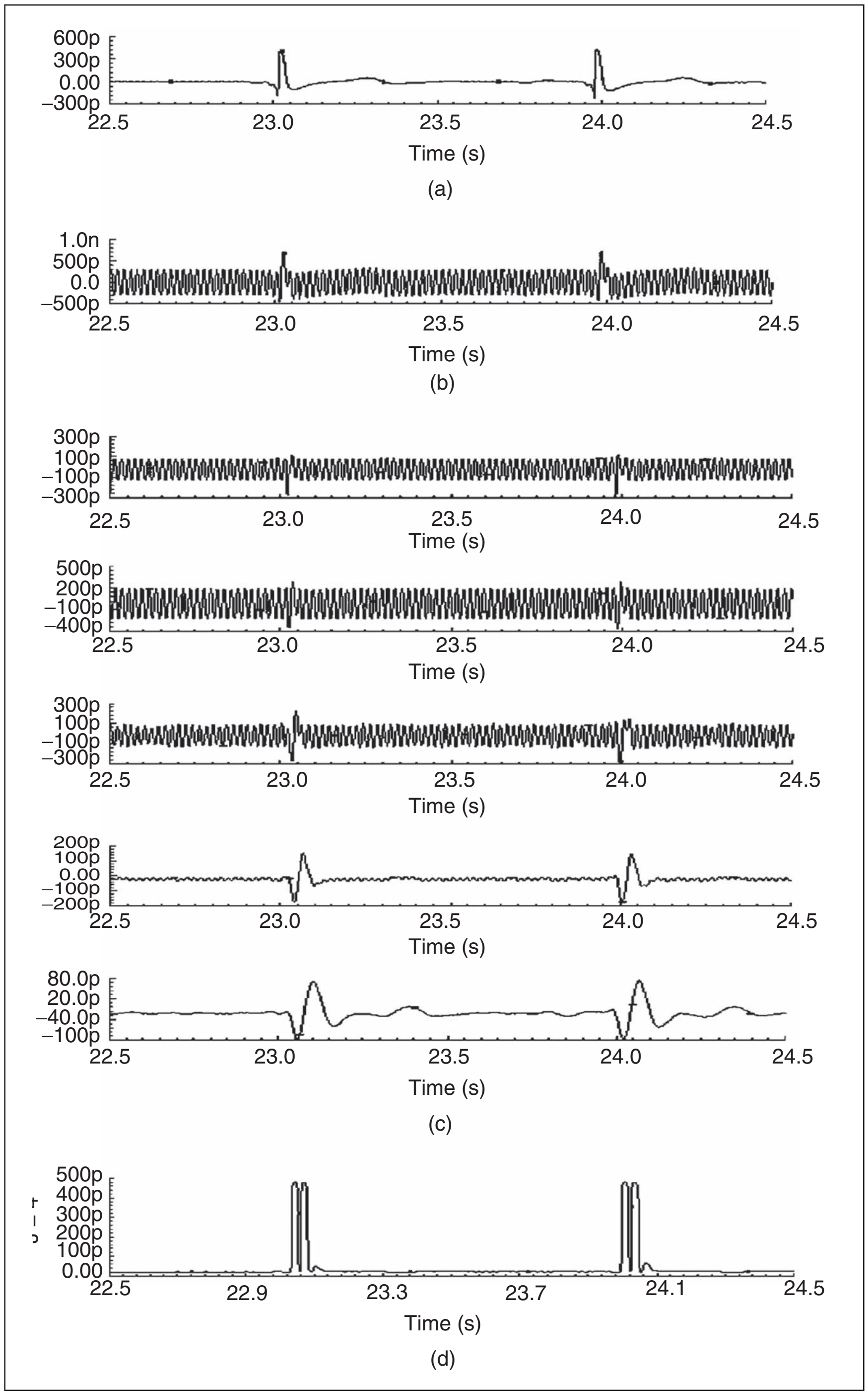

Fig. 14. (a) Ventricular signal. (b) Ventricular signal with 50 Hz interference. (c) The wavelet transform at five subsequent scales. (d) QRS complex modulus maxima detection for j=4.

of cardiac signals using wavelets are being developed. Research on concepts such as the mathematical modeling of cardiac signals and pathologies and the design of WT-based algorithms for intelligent sensing and feature extraction are in progress. It remains to be demonstrated in clinical practice that these novel signal analysis methods will contribute to the further development and application of dynamical electrocardiography. It is clear, however, that implantable devices can document arrhythmias that typically escape from more conventional means of diagnosis. If they should be a method of last resort or if they should be applied early in the diagnostic chain deserves further clinical research including cost-effectiveness considerations.

Conclusions

A brief overview of the history and development of circuit designs applied in pacemakers has been presented. The advances in IC designs have resulted in increasingly sophisticated pacing circuitry, providing, for instance, diagnostic analysis, adaptive rate response, and programmability. Also, based on future trends for pacemakers, some features and improvements for modern cardiac sensing systems have been described.

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