Retrospectroscope

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Contributions of the Vacuum Tube to Early Electrophysiological Research

Modern-day bioelectric recorders such as the ECG and EEG are common, providing useful clinical information. However, their present-day perfection had to await the generation of knowledge about fundamental bioelectric events, which required the creation of sensitive and rapidly responding potential recorders. Despite the initial lack of such devices, a considerable amount of electrophysiological knowledge was acquired with quite primitive instruments. However, addition of the vacuum tube amplifier to these early instruments and to the Braun (cathode-ray) tube provided the first clinical electrographic instruments. This article recounts some of this early background and traces the evolution of the amplifier from the Edison lamp to the Fleming valve (diode) to the DeForest Audion (triode) and to the first amplifiers used for electrocardiography and electroencephalography.

Overview

By the late 1830s, when sensitive slowly responding galvanometers (multipliers of the Oersted effect) were becoming available, it was known that certain living tissues (e.g., nerve and muscle) produced short-duration transient electrical signals. However, there was no instrument that could determine their time course. Alternating current generators (alternators) appeared at the same time, and there was no way of determining their current waveform. The problem was solved by Lenz in 1854 [25] when he devised the method of time sampling, which employed a small point contact on the alternator shaft and a fixed contact that it engaged with every revolution of the shaft. The attenuated output of the alternator was connected to a slowly responding galvanometer via these contacts. With any position of the fixed contact, the galvanometer was presented with a train of short-duration pulses and, with the passage of time, produced a steady reading. Then, a different angular position was chosen for the fixed contact, and the procedure repeated. A plot of galvanometer deflections versus angular positions of the fixed contact produced the waveform of the generator. Lenz called his apparatus a rheotome; i.e., current slicer [22]. Many years ago in Canada, as an undergraduate engineer, the author used the same device, which was known as the Joubert point contact.

The Lenz time-sampling method was used by Bernstein in 1868 [4] to chart the fractional millisecond waveform of the action potential of frog nerve. The adaptation involved a rotating shaft carrying two pairs of contacts, one for delivering a stimulus, the other for connecting the galvanometer to electrodes on the excitable tissue that was stimulated with each rotation of the shaft. By measuring the terminal galvanometer readings obtained for different angular positions of the sampling contacts that connected the galvanometer to the electrodes on the excitable tissue, it was possible to plot a graph of the amplitude and duration of the evoked nerve action potential, which lasted only about 0.5 msec.

The First Bioelectric Recorders

Elegant and ingenious as was this time-sampling technique, it did not permit the recording of a spontaneously arising bioelectric event. Therefore, it was not known if the time-sampled reproduction had the same waveform as a spontaneously arising bioelectric event. Obviously, a sensitive rapidly responding potential recorder was needed; such a device, called the capillary electrometer, was devised by Marey and Lippmann in 1876 [27], who recorded the electrical activity of the spontaneously beating amphibian heart [18]. The capillary electrometer consisted of a tiny meniscus of mercury (Hg) in contact with sulfuric acid (H_2SO_4) in a capillary tube. When current traversed the Hg/H_2SO_4 interface, the half-cell charge distribution changed, thereby changing the surface-tension contour of the meniscus. A high-intensity arc lamp beam traversed the meniscus and a cylindrical lens allowed continuous photography of the height of the meniscus. The capillary electrometer was also used by Waller in 1889 [30] to record the first human electrocardiograms. He also devised the body-surface leads that were optimal; these were later used by Einthoven, and they are still in use today (called leads 1, 2, and 3).

There is an interesting sidelight to the capillary electrometer, namely that it was used by DeForest in the late 1800s to measure the potential of a Clark electrochemical cell and its dependence on temperature. This fact was reported by DeForest in his 1950 autobiography [9].

The need for a sensitive, rapidly responding galvanometer was being felt by telegraphers, who desired to signal rapidly over long lines. To meet this need, Kelvin created his reflecting galvanometer and patented it in 1858 [24]. Interestingly, it was the first device to display the electrical activity of the brain. In 1875, Caton [8] in the UK used the Thomson (Kelvin) reflecting telegraphic galvanometer to display the electrical activity of exposed rabbit brain. His report, which appeared in the *British Medical Association Journal,* occupied only 21 lines of a half-page column. In part, the report stated:

In every brain hitherto examined, the galvanometer has indicated the existence of electric currents. The external surface of the grey matter is usually positive in relation to the surface of a section through it. Feeble currents of varying direction pass through the multiplier [galvanometer] when the electrodes are placed on two points of the external surface, or one electrode on the grey matter, and one on the surface of the skull. The electric currents of the grey matter appear to have a relation to its function. When any part of the grey matter is in a state of functional activity, its electric current usually exhibits negative variation. For example, on the areas shown by Dr. Ferrier to be related to rotation of the head and to mastication, negative variation of the current was observed to occur whenever those two
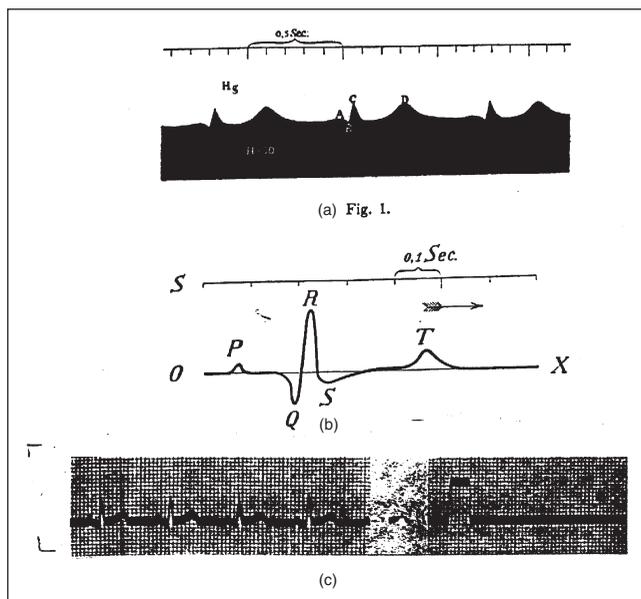
1. Capillary electrometer record of the human electrocardiogram (a), its corrected value (b) and a string-galvanometer record of the human electrocardiogram (c).

acts respectively were performed. Impressions through the senses were found to influence the currents of certain areas; e.g., the currents of that part of the rabbit's brain which Dr. Ferrier has shown to be related to movements of the eyelids, were found to be markedly influenced by stimulation of the opposite retina by light.

No recordings of the movement of the spot of light on the scale of the Kelvin galvanometer have been found [19] perhaps because, at that time, telegraphic operators used to read the dots and dashes of the Morse code by watching the movements of the spot of light on the galvanometer scale. Nonetheless, Caton's description clearly shows that he witnessed the fluctuating potentials that we now know exists as the electroencephalogram. Also important is the fact that Caton was the first to report visual-evoked potentials.

The First Electrocardiograph

By the 1870s, submarine telegraphic cables were being laid, and the need for a rapidly responding galvanometer with a very high sensitivity was pressing. To meet this need, in 1897 Ader [1] in France, created the first slender-wire (string) galvanometer. Ader's telegraphic recorder consisted of a slender taut wire (20 μm diam.) suspended in a narrow gap between the poles of a permanent magnet. A hole was drilled through the poles of the magnet and a bright light was shone through the holes. The wire (string) was placed so that it intercepted the light passing through the holes. When telegraphic current was applied, the string moved sideways, casting a moving shadow on the screen that consisted of moving photographic paper.

Sensitive as the capillary electrometer was, its response time was quite long. To obtain a true voltage-time record, the graphic records had to be corrected. It was the agonizingly slow response and the need for correction of the recordings that so frustrated Einthoven such that he sought a better instrument. He was aware of Ader's string galvanometer used for receiving telegraphic signals over long submarine cables and used its principle. In 1901, Einthoven [13] substituted a silvered-quartz filament (string) for

Ader's slender wire. Einthoven's string galvanometer employed a quartz filament suspended between the pole faces of a strong electromagnet. Electrocardiographic current flowing in the string caused a sidewise motion, which was photographed continuously via holes in the pole faces, to record the human electrocardiogram—thereby introducing clinical electrocardiography (ECG). The thick baseline in these records was the shadow of the undeflected string. Figure 1 shows a capillary electrometer record of the human ECG, its correction, and a string-galvanometer ECG. An estimate of the sinusoidal frequency response of the capillary electrometer is 0 to a few Hz; that for the typical string galvanometer is 0-30 Hz. However, the response time differed from subject to subject because of differing electrode-subject resistance. The method of adjusting the sensitivity to achieve 1 mV/cm sensitivity relied on adjusting the tension in the string. For his clinical work with the string galvanometer, Einthoven was awarded the 1924 Nobel Prize for Physiology and Medicine; the citation read "for his discovery of the mechanism of the electrocardiogram."

The First Electroencephalograph

By reducing the tension in the string of the Einthoven galvanometer to increase the sensitivity, in 1929 Berger [3] was able to record the first human electroencephalogram using scalp electrodes.

Sensitivity Versus Response Time

Just after the turn of the 20th century, the string galvanometer was the only sensitive and moderately rapidly responding device available to electrophysiologists. If the tension in the string was increased, it provided the speed of response needed for many rapidly changing bioelectric events; but then it lacked sensitivity. The capillary electrometer had reasonable sensitivity, but it could not meet the requirement of rapidity of response.

Meanwhile, in other fields, the same requirements for high sensitivity and rapidity of response were becoming of major concern; one field was wire and wireless telegraphy, where the need was to signal over longer distances and more rapidly, both of which were revenue producers.

To meet the needs of those in power engineering, a variety of low-sensitivity, rapidly responding mirror galvanometers were developed, such as the Blondel (1893) [5] and Duddell (1897) [12] instruments. These, however, were too insensitive for reproducing telegraphic and bioelectric signals. Thus, there were rapidly responding low-sensitivity recorders; the missing element was an amplifier, which was provided by the triode vacuum tube, patented by DeForest in 1907 and 1908 [10, 11], the evolution of which will now be described.

Development of the Triode Vacuum Tube and the First Amplifier

Two events led directly to DeForest's development of the triode vacuum tube, originally called the Audion. It was later called the thermionic tube, because in the early days, it was believed that ionized gas was needed for its operation. The first step in the appearance of the Audion derived from Edison's quest for a means to prevent darkening of the glass envelope surrounding the carbon filament in his electric lamp, invented in 1879. He tried many things, among which was the inclusion of a metal plate inside the lamp. In 1884, he wrote as follows:

I have discovered that if a conducting substance is interposed anywhere in the vacuous space within the globe of

an incandescent electric lamp, and said conducting substance is connected outside the lamp with one terminal, preferably the positive one of the incandescent conductor, a portion of the current will, when the lamp is in operation, pass through the shunt-circuit thus formed, which shunt includes a portion of the vacuous space within the lamp.

Figure 2 is an illustration of Edison's lamp containing the metal plate. Edison did not know what to do with this phenomenon, so he patented it in 1884. This phenomenon became known as the "Edison Effect" and was the first step along the road to the vacuum diode, followed by the triode, and then the triode amplifier.

It should be noted that wireless telegraphy had been practiced for sometime since the discovery of Hertz in 1883, that electromagnetic waves traveled through space, and the need for a reliable detector (rectifier) was pressing. Hertz had no detector; he used a miniature spark gap to provide the evidence of detection of electromagnetic waves. The first practical and reliable detector was the coherer, described in 1897 in detail by Branly [6], which was originally reported in 1891. In his 1897 paper, Branly reported that his coherer (the term originated by Lodge in the UK) was used by Marconi in his first wireless experiments. Branly's coherer consisted of a capsule of metal filings and insulating powder between two electrodes, thereby creating one of the first solid-state diodes. However, the first practical and reliable detector was the Fleming valve (patented in 1906) [14], an Edison lamp with a wire electrode circumscribing the filament, as shown in Fig. 3. Also shown in Fig. 3 is Fleming's wireless radio receiver, consisting of a galvanometer (ℓ) connected in series with his valve and the secondary coil (k), the primary (m) of which was connected to an antenna (n) and ground (o). When the Hertzian spark-gap transmitter wireless signals were received, the Fleming valve rectified them, and the galvanometer (ℓ) was deflected. This was the radio receiver that Fleming described to Marconi by letter. According to Shiers [29], Fleming wrote: "I have been receiving signals on an aerial with nothing but a mirror galvanometer and my device."

It is useful to observe that Fleming was an engineer at the Edison-Swan Lighting Co. in the UK and had access to electric lamps and their construction. He named his detector a "valve" because it conducted in one direction. In the UK, all vacuum tubes are called valves to this day.

Meanwhile, DeForest in the US had been seeking a better detector for wireless telegraphic signals, and he apparently used the same method as Fleming, which resulted in a bitter controversy. After DeForest's difficulties with his use of the Fleming valve and his unsuccessful lawsuit over use of the Fessenden electrolytic rectifier, DeForest pressed on with the search for a better detector for wireless telegraphic signals. In the meantime, he used carborundum (silicon carbide) as his detector, thereby avoiding litigation, because this device had been described previously and was not patentable.

From DeForest's autobiography, we learn of the experiments that he performed using the Edison effect with the metal-plate electrode in the lamp [9]:

I wrapped a piece of tin foil around the outside of the cylindrical-shaped glass tube and connected this third electrode to the antenna or to one terminal of the high-frequency tuner. I then realized that the efficiency could be still further enhanced if this third electrode were introduced within the tube. I therefore had McCandless construct another "Audion" — as I now for the first time began to call it. This new device contained two plates with

a filament located midway between them. This detector showed distinct improvement over its predecessors.

It now occurred to me that the third, or control, electrode could be located more efficiently between the plate and the filament. Obviously, this third electrode so located should not be a solid plate. Consequently, I supplied McCandless with a small plate of platinum, perforated by a great number of small holes. This arrangement performed much better than anything preceding it, but in order to simplify and cheapen the construction I decided that the interposed third electrode would be better in the form of a grid, a simple piece of wire bent back and forth, located as close to the filament as possible.

Figure 4 shows DeForest's wireless telegraphy receiver using the Audion as the detector and a galvanometer (I) that displayed the Morse code signals. Also shown is a picture of one of the first Audions. Parenthetically, both spherical and cylindrical glass envelopes were used for the first Audions.
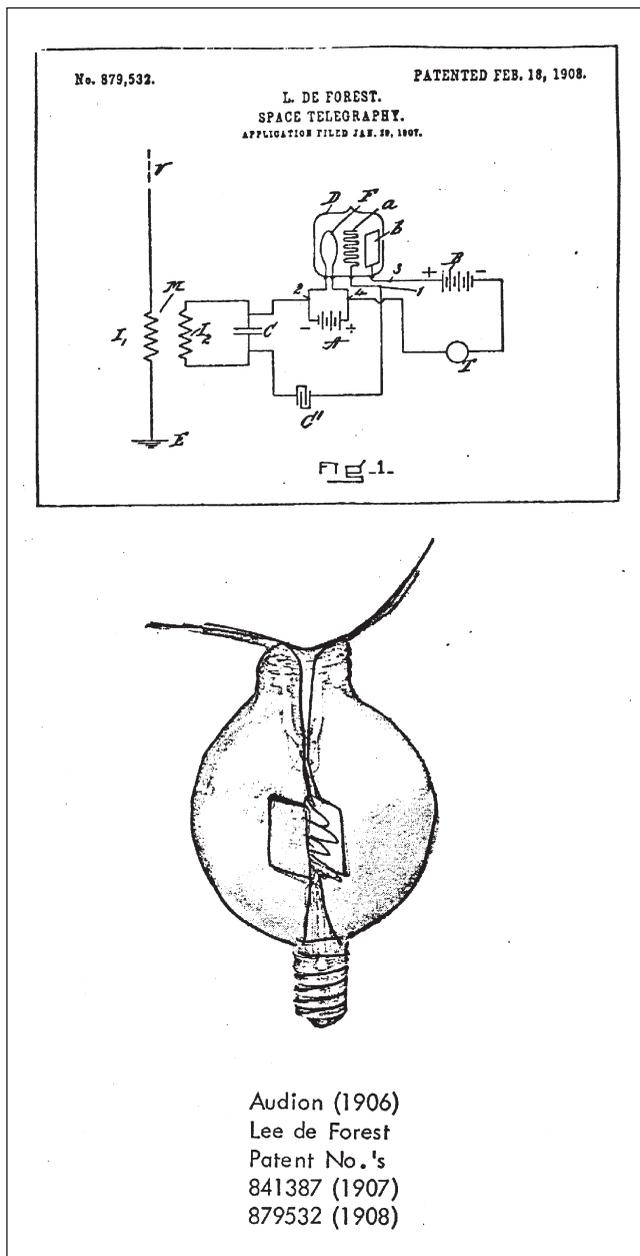
DeForest's Audion functioned extremely well as a detector for radiotelegraphic signals. It not only provided the rectifier action of Fleming's valve, it also provided amplification and thereby allowed detection of very weak signals.

Patent No. 307,031,
October 21, 1884
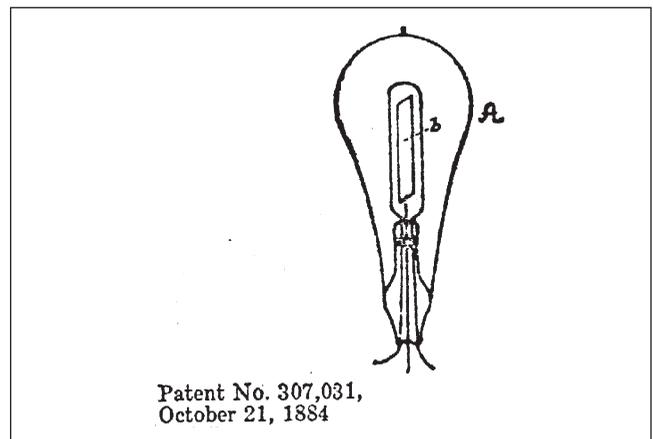
2. Illustration of Edison's lamp containing the metal plate that gave rise to the "Edison Effect." From UK Patent 307,031, issued 1884 [14].
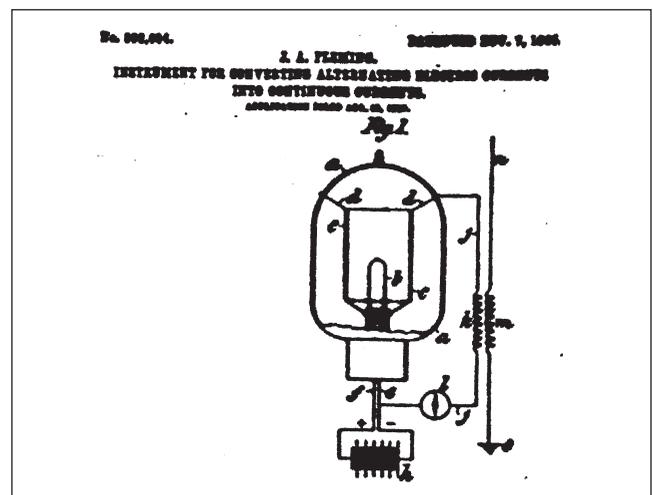
3. Fleming's wireless telegraphic receiver using his "valve," an Edison lamp with a rectangular wire electrode surrounding the carbon filament (from Fleming's UK patent [14]).

No. 879,532.   PATENTED FEB. 18, 1908.
L. DE FOREST.
SPACE TELEGRAPHY.
APPLICATION FILED JAN. 29, 1907.

FIG. 1.

Audion (1906)
Lee de Forest
Patent No.'s
841387 (1907)
879532 (1908)

4. DeForest's Audion and its use for the detection of wireless telegraphic signals (US Patent 879,532 issued Feb. 19, 1908 [10]). F = filament, a = grid and b = plate.

Use of the Audion (triode) as an amplifier did not occur immediately, but its use in this role was propelled by the need to amplify weak long-line telephone signals. Therefore, there was a need for DeForest to show that the Audion could provide amplification. In his autobiography he described his amplifier experiments as follows:

For with the Audion bulbs we were then using, more or less gassy, designed entirely as radio detectors, and with coarse grid structure, it was by no means a simple thing to obtain any observable degree of amplification of telephone signals. For three tedious weeks Van would merely shake his head. Finally Charlie and I secured a degree of amplification which could not be questioned or denied."

"Waal," finally drawled Van Etten, "the thing do boost!"

At last we had triumphed. Thereupon I set about cascading two Audion tubes, the 'wing,' or plate, circuit of the first Audion feeding the grid circuit of the other Audion by induction through a properly designed telephone repeater coil, or transformer (I had the shop wind dozens of these during the experiments).

To obtain more amplification from a single Audion, DeForest raised the plate voltage and ran into a new problem; the gas in the Audion ionized. DeForest then evacuated his Audion to a hard vacuum, thereby solving this problem. But he still needed to demonstrate amplification conclusively. He designed the following demonstration, which is described in his autobiography.

I had obtained a small loud-speaker, which was nothing more than a large telephone receiver with a short elbow-shaped, double-mouthed horn attached thereto. My method of measuring the relative amplitude levels obtained under varying conditions was truly simple, ready-made, but effective. Instead of the "transmission units" of the telephone engineer, I measured my gains in 'blocks' and "half blocks!" I placed the loud-speaker in the laboratory window and walked down the street until the threshold of clear audibility was reached. After I had obtained a "two-block" gain, I felt reasonably satisfied with the Audion amplifier.

In DeForest's development of the amplifier, the filament was energized by a series of 1.5 V cells, called the A batteries. The plate was energized by the B battery. Later, bias was provided by a C battery. To this day, the A battery carries the same designation, and plate voltage is designated E_B.

The First Electrophysiologic Applications of the Vacuum Tube Amplifier

Desirous of recording small-amplitude nerve and muscle action potentials, Forbes and Thacher in [15] constructed a single-stage amplifier using DeForest's Audion. In their paper, they cited his patents (841,387 and 879,532 issued in 1907 and 1908, respectively) and credited Horatio B. Williams of Columbia University for suggesting the combination of the string galvanometer and the vacuum-tube amplifier.

Forbes and Thacher developed three circuits for coupling the Audion to the string galvanometer. Because the maximum signal that the string galvanometer displays is rarely over a few millivolts, and because it has a frequency response extending to dc, precautions had to be taken to protect the string from the high plate voltage of the Audion. The strategies that they used are shown in Fig. 5. In (a), the string galvanometer (G) was placed in the detector position of a Wheatstone bridge, with the Audion forming one arm and resistors (R_1, R_2, R_3) forming the other arms. The electrodes on the nerve (N) were connected between the grid (g) and the filament (f); the plate (p) was connected to the bridge. Photographic recording of the motion of the string reproduced the nerve action potentials.

Figure 5(b) shows the second circuit developed by Forbes and Thacher, which employed a large capacitor (C) to couple the string galvanometer (G) to the plate circuit of the Audion. Parenthetically, they were concerned about the small leakage current of the capacitor, which produced a small steady deflection of the string.

Transformer coupling, as shown in Fig. 5(c), was used to join the string galvanometer (G) to the plate circuit of the Audion.

Each of the circuits shown in Fig. 5 has its unique characteristics. The bridge circuit of Fig. 5(a) provided a frequency response from 0 Hz to the limit of the string galvanometer (about 30 Hz), but the bridge had to be balanced before connecting the string, otherwise it would be damaged. With the circuit shown in Fig. 5(b), the low-frequency response was limited by the size of the capacitor (C); but the circuit was easy to use and protected the string galvanometer, which while connections were being made, could be short circuited. When all was ready, the short circuit could be removed for recording. The circuit shown in Fig. 5(c) limited the low-frequency response because of the transformer (T). However, the string galvanometer was well protected from the high plate voltage and leakage current was not a problem.

It should be observed that coupling the string galvanometer to the Audion only provided added sensitivity. Forbes and Thacher reported that a maximum amplification of 40 was possible, thereby providing a recording sensitivity of about 25 μV/cm. However, addition of the Audion did nothing to improve the high-frequency response of the string galvanometer, which could have been improved (with a sensitivity loss) by increasing the tension in the string.

Pointing out the long response times of the capillary electrometer and the string galvanometer for recording nerve action potentials, Gasser and Erlanger [17] turned their attention to the Braun [7] cathode-ray tube. However, they found it to be too insensitive because of the high voltage used to accelerate the electron stream. Ultimately, they discovered the Johnson hot-filament cathode-ray tube, which contained a little gas and operated with an an-

ode of about 300 V. Johnson and Croft of the Western Electric Co. provided them with a unit that had a long-persistence green phosphor. Immediately, Gasser and Erlanger set themselves the task of building a cathode-ray oscilloscope using a multistage amplifier and a stimulator that triggered the oscilloscope sweep, thereby enabling display of the time between stimulus and response (nerve action potential).

The oscilloscope-synchronized stimulator built by Gasser and Erlanger was a triumph of electromechanical technology. Figure 6 is a reproduction of their apparatus. Gasser had previous experience with a vacuum tube amplifier connected to the
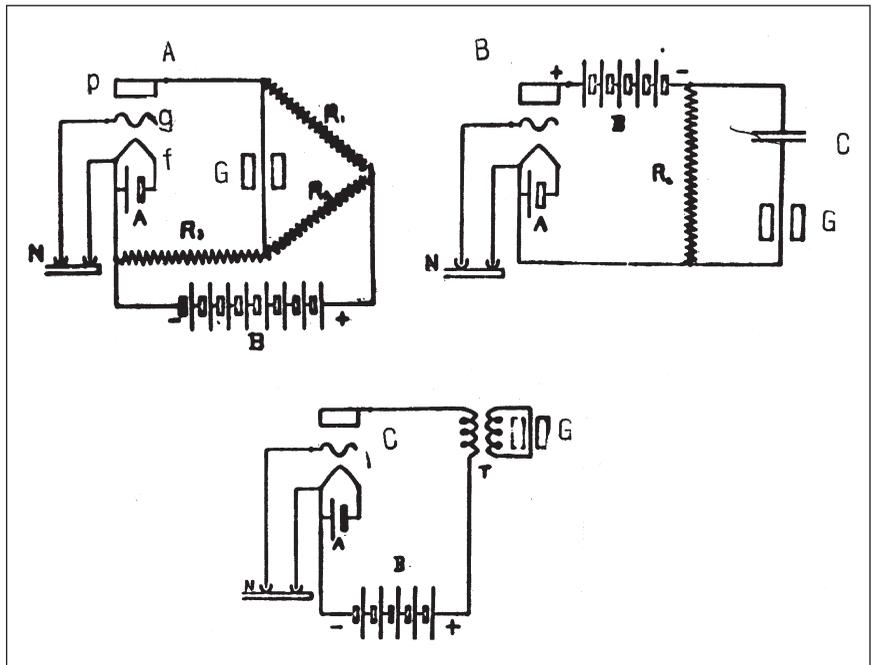
5. The three circuits used by Forbes and Thacher in which DeForest's Audion (triode) was used to drive the string galvanometer (G). (Redrawn from [15].)
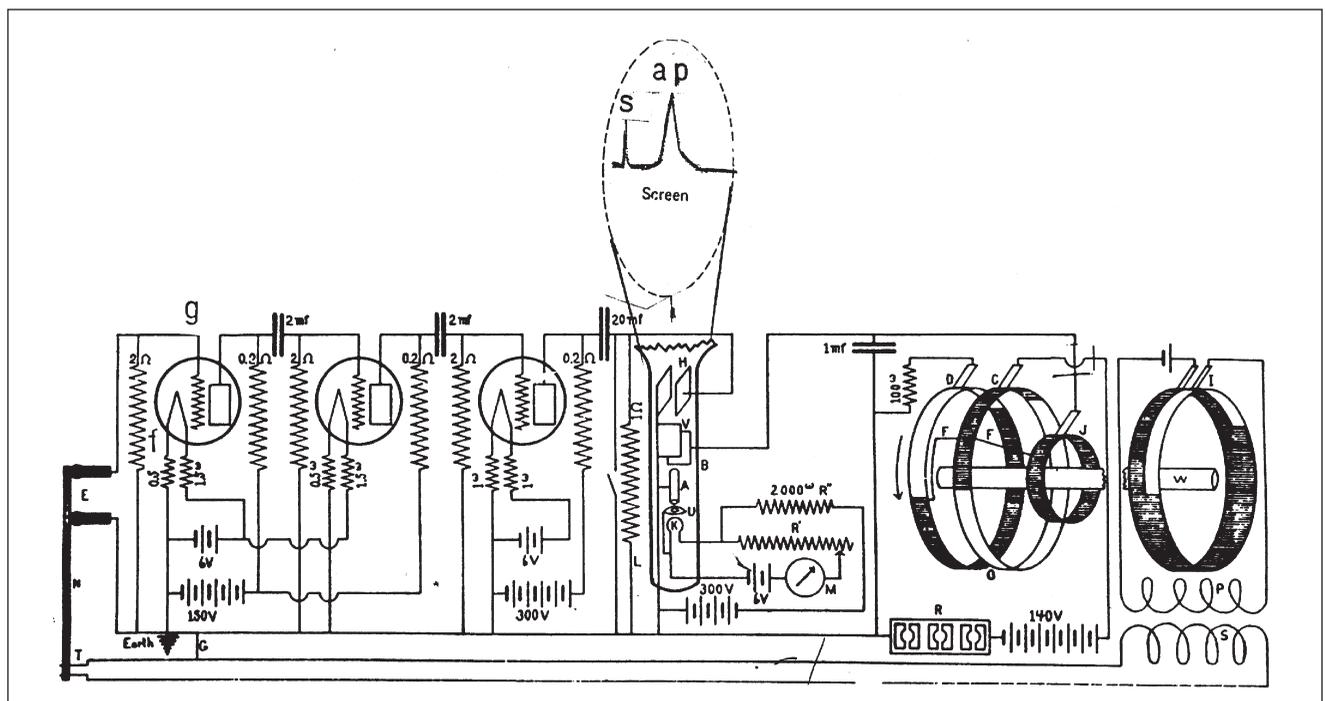
6. The circuit used by Gasser and Erlanger to display nerve action potentials on the cathode-ray tube. (Redrawn from [17].)

string galvanometer, so securing amplification with a resistance-capacity coupled amplifier was familiar. The challenge was to couple the amplifier to the deflecting plates of the cathode-ray tube to provide a time (sweep) axis, and to synchronize the stimulator with onset of each sweep. The latter two functions were provided by a rotating commutator (rheotome), shown on the right of Fig. 6.

The nerve (N) was connected to two electrodes via $Zn/ZnSO_4NaCl$ electrodes, which were connected to the input grid (g) and the filament (f), which was grounded. The nerve under the upper (g) electrode was crushed so that only the electrical activity under the other electrode was recorded. Each stage of the amplifier provided a gain of 20.

The stimulus derived from an induction coil (PS) was delivered to the nerve by electrodes T. With each rotation of the commutator shaft, a pulse was delivered to the induction coil and the time-axis generating capacitor (l mf) started to charge and the spot on the oscilloscope screen moved to the right with a velocity determined by the 1 μf (mf) capacitor and the resistance in the resistance box, R. The commutator ran at 20/sec; therefore there were 20 stimuli (s) and sweeps of the time base per sec. Consequently, the evoked action potential (ap) appeared as a standing wave on the cathode-ray tube screen. Because they had no camera, photographic paper was placed on the face of the cathode-ray tube. An exposure time of 10 sec was adequate to obtain contact prints.

With the apparatus of Fig. 6, Gasser and Erlanger were able to show that the propagation velocities of action potentials in nerve fibers depended on their diameters. They received the Nobel prize in 1944 for Physiology and Medicine for their discoveries of the highly differentiated function of single nerve fibers.

One of the great laws of signaling in the nervous system was discovered with very simple equipment, which relied on the vacuum-tube amplifier. In 1928, Adrian and Bronk [2] developed the recording system shown in Fig. 7, which consisted of a single-stage, single-sided vacuum-tube amplifier connected to a capillary electrometer (C) via a 1 μf blocking capacitor. Headphones could be connected to the amplifier output. Alternatively, a loudspeaker (LS) could be connected to the amplifier via a two-stage amplifier in the box B. The amplifying system was not designed for high-fidelity reproduction, it was created to identify the frequency of the nerve impulses in single nerve fibers of the rabbit phrenic nerve, which innervates the diaphragm. Electrodes on single nerve fibers were connected to the grid (g) and

filament (f) of the triode, and the action potentials were displayed and photographed with the capillary electrometer, and heard as clicks in the headphones or reproduced by the loudspeaker. With quiet breathing, the action potentials were heard to increase in frequency during inspiration, and to cease during expiration when the elastic recoil of the chest occurred. They stated that the availability of sound reproduction greatly facilitated photographic recording of the capillary electrometer excursions. By a series of ingenious experiments with this and better apparatus later, they discovered that intensity of action is signaled in the nervous system by the frequency of the action potentials in a single nerve fiber as well as that the action potentials were all the same. Adrian clearly showed that the action potential is the currency of the nervous system. In fact, not known to him, he had discovered frequency modulation. In 1932, Adrian shared the Nobel Prize for Physiology and Medicine with Sherrington for their discoveries of the function of the neurone.

The First Vacuum-Tube Electrocardiograph

The fragility of the string and its need for replacement was a great inconvenience. The large size of the Einthoven ECG and the trouble with the electromagnet overheating contributed to the need for a better instrument. Prior to 1930, Marvin [28] proposed and constructed a portable, battery-operated ECG (US patent 1,837,913 issued December 22, 1931). Figure 8 is a schematic of his instrument, which is a three-stage, single-sided, resistance-capacity coupled vacuum-tube (6,7,8) amplifier connected to a rapidly responding mirror galvanometer. A switch (S) allowed connection of the amplifier to electrodes on the left arm (LA), right arm (RA), and left leg (LL), thereby enabling recording leads 1, 2, and 3. The photographic recording was on 35 mm (movie) film and Fig. 8 (bottom) shows an artifact-free ECG. A means was provided for inscribing a 1 mV calibration signal on the record.

This elegant first portable ECG was shown at conventions and was used routinely at the General Electric Hospital. It was described in a publication by Mann in 1930 [6]. There was little interest shown in this very useful and practical ECG, perhaps one reason being that the records did not look like those made with the string galvanometer. Maybe the time constant was too short, causing distortion to the P and T waves. What is more likely is that the Marvin ECG tracing did not have a thick baseline, as did the string galvanometer records. The thick baseline was the shadow of the string and characterized ECG records until the late 1940s.

The string galvanometer was used in clinical medicine until well after the end of World War II (1945). However, the event that made the vacuum-tube ECG acceptable was invention of the heated stylus recorder by Haynes in 1936 [21]. Thermosensitive paper, which was blackened by heat, was drawn over a rounded edge, and the heated stylus, about 1.5 mm wide, inscribed the ECG in rectangular co-ordinates with a thick baseline.

Development of the Modern EEG

The first to publish an English-language verification of Berger's observations were Jasper and Carmichael in 1935 [23], then at Brown University in the US. On the scalp they placed silver electrodes (1-2 cm diam.), covered with flannel and soaked in saline.
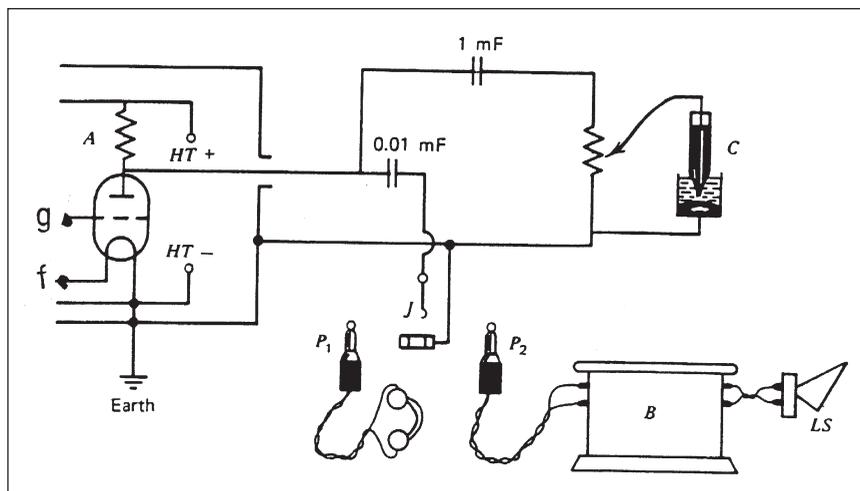
7. The single stage (Audion) triode amplifier used by Adrian and Bronk to display nerve action potentials with the capillary electrometer (C) and to listen to them using headphones or via a second amplifier (B) used to drive a loudspeaker (SL).

These electrodes were connected to an amplifier/mirror-oscillograph system. No details of the equipment were given. Jasper and Carmichael [23] were able to confirm Berger's findings and extend them, showing that with a two-channel system used to record the EEG of a girl with a convulsive disorder, the alpha wave frequency was 10/sec on the left side of the head and 6-8/sec on the right side, one of the early indications that the EEG was altered by brain pathology.
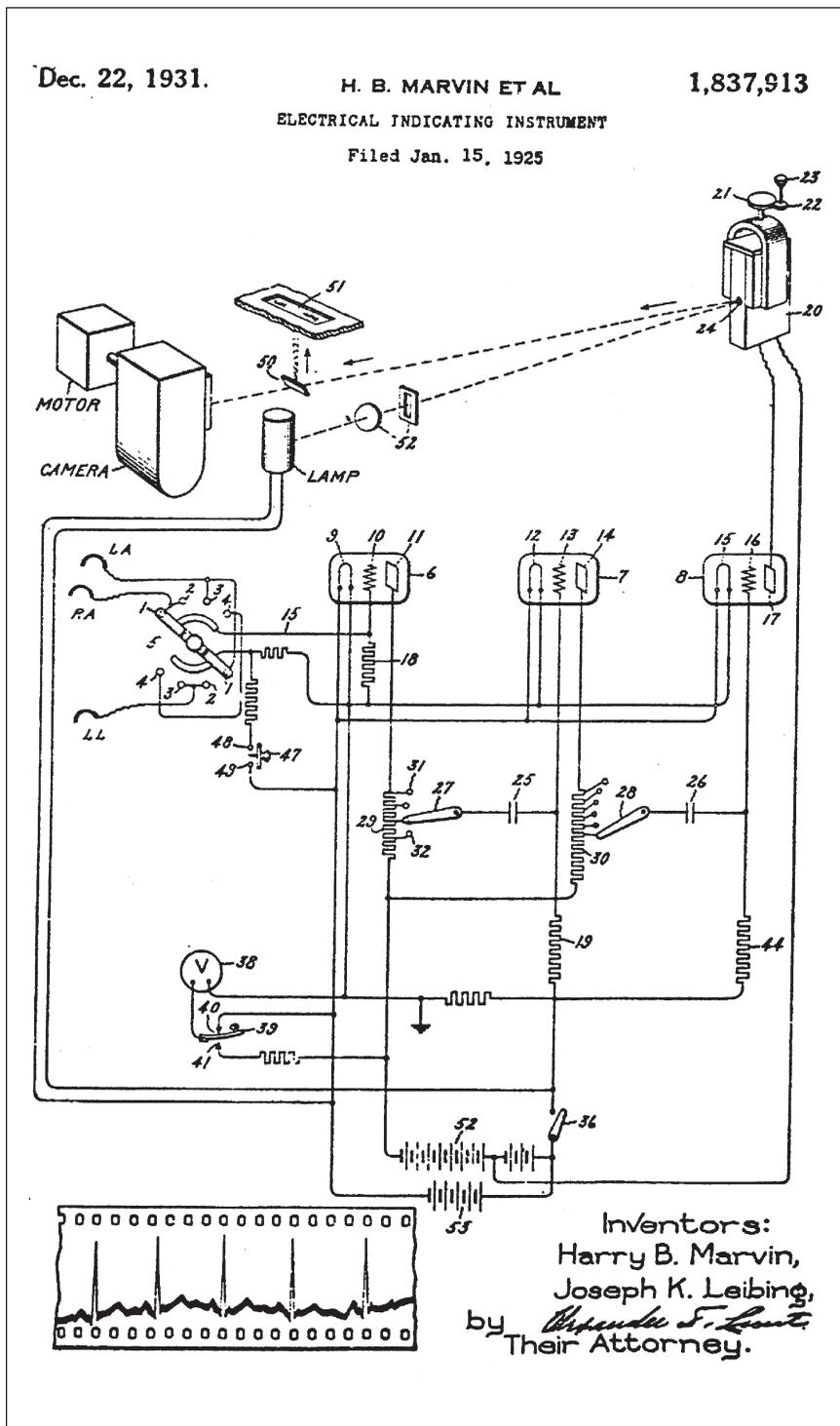
Meanwhile, at Harvard University (Boston, MA), Gibbs, et al. [20], were pursuing their interest in epilepsy. Recognizing the potential of the EEG for the diagnosis of epilepsy, they initiated a series of studies that occupied many decades. Their EEG consisted of an ink-writing telegraphic recorder, called the Undulator. In December 1935, they published their first paper on EEG, which carried a footnote that read: "This paper is no. XVII in a series entitled Studies in Epilepsy." Citing the Berger papers and that of Jasper and Carmichael, Gibbs, et al., stressed the importance of direct-inking pens for immediate viewing of the EEG, so that the effect of environmental factors could be identified immediately. They reported:

> The method is exceedingly simple. Electrical contact is made to two points on the subject's head. Except for the study of grand mal epileptic seizures we regularly employ as electrodes two hypodermic needles inserted one into the scalp at the vertex of the skull and the other into the lobe of the left ear. Enough procaine hydrochloride is injected previously to insure the continued comfort of the subject.

The ink-writing EEG used by Gibbs, et al., was built by Garceau in 1935 [16], who obtained a model 2A Boehme Undulator (Fig. 9), from J.W. Milnor of the Western Union Telegraph Co. To it, he connected a five-stage amplifier, preceded by a two-stage, single-sided preamplifier (Fig. 9). Garceau stated that by tightening the springs on the Undulator, a frequency response up to 40 Hz was obtained. This then was the first direct-inking EEG in the USA.

8. The first portable vacuum-tube (Audion) amplifier used for recording the human electrocardiogram. From patent 1,837,913, Dec. 22, 1931, (filed Jan. 15, 1925) [28].

Lee DeForest, Creator of the Triode Vacuum Tube

Lee DeForest, inventor of the triode vacuum tube, was born in Council Bluffs, Iowa, on 26 August 1873, the son of Henry Swift DeForest and Margaret Robbins DeForest. His father was a congregational minister of Hugenot origin; his mother was the daughter of a congregational minister. Lee grew up in Talledego, Alabama, where his father was president of the Talledego Negro College from 1879 to 1896, when he died, not living to share his son's victories.

In 1893, Lee entered the Sheffield Scientific School of Yale University, pursuing the mechanical engineering degree, during which time he took courses in electricity. He received the B.S. degree in 1896 and continued at Yale to pursue the Ph.D. degree, which he received in 1899. The title of his thesis was the "Reflection of Hertzian Waves From the Ends of Parallel Conductors," clearly establishing his interest in wireless transmission. DeForest's first job was with the Western Electric Company in Chicago where, with the collaboration of Edward Smythe, he invented a
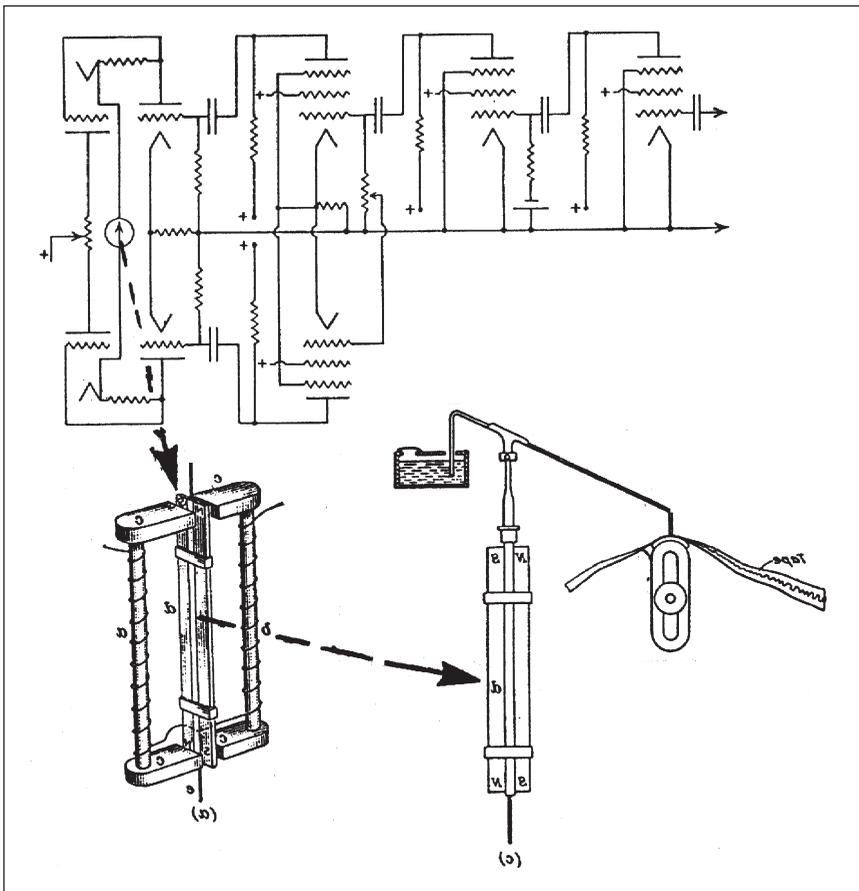
9. The first ink-writing EEG in the US, built by Garceau (1935) consisting of multiple cascaded stages of resistance (4 μF)-capacitance (10^6 ohms) coupling screen grid vacuum tubes. The recorder, an Undulator, was a telegraphic recorder consisting of a pair of magnets, the deflection of which was produced by current from the cathode-follower push-pull output stage of the amplifier feeding coils a,b of the Undulator. (Circuit redrawn from [16], and the Undulator drawing courtesy of G. Elliott, Picton, Ontario, Canada).

radio receiver using an electrolytic detector that made possible the use of headphones for listening to wireless messages. Whether DeForest knew it or not, Fessenden had already used and patented such an electrolytic detector, and DeForest was sued and lost the lawsuit. However, he persisted in his search for a more efficient detector of radio waves. At that time the only other detector was the Branly coherer, which consisted of a capsule of metal filings and a powder between two electrodes. It functioned only for a short time and had to be tapped (decohered) to restore its operation. As stated above, in the UK, Fleming had developed and patented the vacuum tube diode (valve) and demonstrated its use for receiving wireless signals. DeForest's development of the triode (Audion) as a detector for radio signals was described above in the main text of this article.

Meanwhile, DeForest did not have an easy time creating wireless telegraphic communication facilities. In addition to litigation with Marconi, Fleming, and Fessenden, his own company came under the management of unscrupulous stock manipulators. DeForest became aware of this situation in March 1910, when he was in Honolulu supervising the construction of one of his wireless telegraph stations. In his autobiography he stated:

I was visited by two men who quietly informed me that as United States marshals they had an order from the federal

judge in San Francisco for my arrest ... stunned I inquired the cause ... use of the mails to defraud read their papers.

Fortunately, DeForest had two friends on the board of directors who promptly put up $10,000 bail; DeForest did not have to go to jail. However, the stock manipulators were subsequently prosecuted.

By inventing and developing electric circuits for the Audion, DeForest laid the cornerstone for all future wireless broadcasting. However, a review of his some 300 issued patents reveals his wide-ranging interests and contributions. For example, one patent, issued in 1907, describes the cold-cautery radio knife, now known as electrosurgical cutting. This appears to be the first electrosurgical unit in the US. The patent was licensed to George K. Woodworth of Brookline, MA. Other patents describe sound recording and reproduction, including the electric phonograph. His contributions to the technology of talking motion pictures are found in many of his patents. He created novel microphones and loudspeakers, and he describes making musical tones electrically. His patents also describe a color television system, as well as a way of synchronizing television pictures. More than these, however, he patented methods for determining aircraft height, speed, and direction. Very important to vacuum-tube and lamp technology was his patented method of creating a durable glass-to-metal seal. His last patent was issued on 28 November 1949, which describes a high-voltage generator. He was 76 at that time.

DeForest received many honors and awards for his numerous contributions. He was president of the IRE in 1930 and a Fellow in 1918. Long after his death, the US postal service issued an 11-cent stamp honoring him in 1973 on the occasion of the 100th anniversary of his birth.

The demands of DeForest's work took their toll on his personal life. His first marriage ended in divorce in a little more than a year; during this time he was developing the Audion. His second marriage, to Nora Blatch in 1908, produced a daughter, Harriet in 1909, but ended in divorce in 1911. On 23 December 1912, he married Mary Mayo, who gave him a daughter, Eleanor, in 1919. A second daughter, Marilyn, was born in 1924. A first son, Lee Jr., was born in 1926, but died two days after birth. This event devastated the DeForests, and a divorce followed in 1929. In the following year, Lee married Marie Moquini, an actress. They lived in Hollywood until his death on 30 June 1961. His widow accumulated a treasure of Lee's possessions and gave them to the Perham Foundation in Los Altos, CA, where they are now being cataloged.

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Cellular/Tissue Engineering

Artificial Thymus
Media contact: Michael Baum, NIST

Researchers at Cytomatrix and Massachusetts General Hospital have generated an "artificial thymus" that can efficiently generate large quantities of a wide range of human T-lymphocyte cells, a key element of the body's immune system. The work was supported in part by the NIST Advanced Technology Program (ATP).

The current methods of culturing T-cells are inefficient because they only "expand" certain subpopulations of T-cells. The Cytomatrix technique not only is more efficient in producing more cells but it also produces many different types of T-cells with a wide range of functions. The key insight was that geometry plays a critical role in the maturation of T-cells. Organs are three-dimensional; conventional cell culturing techniques are two dimensional. The Cytomatrix techniques used a porous metal and carbon materials as a three-dimensional matrix to support thymus cells from mice and T-cell progenitor cells from human bone marrow. A similar matrix design has been used for bone repair. For more technical information you can contact Cytomatrix President Mark J. Pykett.

Although such tissue engineering solutions are promising, significant technical challenges remain before the aforementioned technologies can be commercialized and mankind can reap the benefits. To address these challenges ATP supports basic technologies and promotes alliances that industry will need to make possible the tissue engineering therapies of the future. For more information about the program, you can visit its website at http://www.atp.nist.gov.