

# **INTRODUCTION TO BIOMEDICAL ENGINEERING**

## **PART III: Biomedical Signal Processing: An Introduction.**

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**Textbook: Eugene N. Bruce, “*Biomedical Signal Processing  
and Signal Modeling*”,**

**John Wiley & Sons, Inc., New York, 2001.**

**Reference: Robert B. Northrop, “*Signals and Systems  
Analysis in Biomedical  
Engineering*”,**

**CRC Press LLC, 2003.**

## COURSE OUTLINE

### **(I) Introduction to Biomedical Signals:**

- **Signals from Physiological Systems —  
ECG, EEG, EGG, EMG, ERG, etc.**
- **Signals from Man-Made Instruments —  
CW Doppler Ultrasound signals, MRI signals,  
Positron Emission Tomography (PET) signals, etc.**
- **Continuous-Time (CT) and Discrete-Time (DT)  
Signals.**
- **Purposes of Processing Biomedical Signals.**

### **(II) Introduction to Linear System Theory:**

- **Properties of Operators and Transformations.**
- **The Impulse Response of a Linear System.**
- **Convolution Form of a linear shift-invariant (LSI)  
System.**
- **Relation to Signal Processing.**
- **Frequency Response of Discrete-Time Systems.**

### (III) Modeling CT Signals as Sum of Sine Waves.

- **Orthogonal Functions and Sinusoidal Basis Functions.**
- **Relationship of CT Fourier Transform (CTFT) to Frequency Response.**

### (IV) Modeling DT Signals as Sum of DT Sine Waves.

- **The DT Fourier Series.**
- **Fourier Transform of DT signals.**
- **Sampling Process and Sampling Theorem.**

### (V) Noise Removal and Signal Compensation.

- **Linear Digital Filters.**
- **Digital Filtering of Biomedical Signals.**

#### Information for Further Reference:

(1)

10/27	陳津渡		芝加哥大學 教授	星期一下午 4:30—5:20 R143	cchen3@uchi cago.edu	生命的造影：正電子斷層影像 -Imaging of Life: <b>Positron Emission Tomography (PET)</b>
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**A Biomedical Signal is generally acquired by a sensor, a transducer, or an electrode, and is converted to a proportional voltage or current for processing or storage.**

**Electrocardiogram (ECG)** – The electrical potential at the electrode or the potential difference between two electrodes induced by the presence of time-varying electrical activity in cardiac muscle. ECG is useful for a physician to obtain considerable insight about whether the contractions of the heart are occurring normally.

**Electroencephalogram (EEG)** – The recording of brain electrical activity from electrodes on the scalp. EEG is used to determine if a person is asleep and to identify the sleep state.

**Electrogastrogram (EGG)** – An electrogastrogram is similar to an electrocardiogram (EKG) of the heart. It is a recording of the electrical signals that travel through the muscles of the stomach and control the muscles' contraction.

**Electromyogram (EMG)** – The signal recorded by placing electrodes in, on, or near a muscle and amplifying the electrical potential or the potential difference between two electrodes induced by the generation and propagation of action potentials along muscle fibers.

**Electroretinogram (ERG)** – The electroretinogram (ERG) is a retinal signal that is evoked by visual stimuli, but which is not necessarily a part of the visual cascade. But, similar to the visual cascade it is evoked by light absorption in the photoreceptors and therefore is an epi-phenomenon of the visual cascade. We measure the ERG non-invasively in human subjects by positioning a small thread (DTL electrode) on the cornea of the subject. The DTL electrode is not disturbing and is conducts electrical currents, so that the ERG can be measured. The visual stimulator is a computer controlled color monitor.

## Continuous-Time (CT) and Discrete-Time (DT) Signals

The signals resulting from these measurements are generally *continuous-time (CT) signals* denoted by  $x(t)$ . (Figure 1)

The signals taken from the sampling the values of a continuous-time signal at integer multiples of some fundamental time increment represent the *discrete-time (DT) signals* denoted by  $x(n)$ . (Figure 2)

Mathematically, we write

$$x(n) = \sum_{n=0}^{\infty} x(t)\delta(t - nT), \text{ where } T \text{ is the sampling period.}$$

**Example 1.2 of Text:**

## PURPOSES OF PROCESSING BIOMEDICAL SIGNALS

Why biomedical signals are “Processed” ?

- (1) To remove unwanted signal components that are corrupting the signal of interest.
- (2) To extract information by rendering it in a more obvious or more useful form.
- (3) To predict future values of the signal in order to anticipate the behavior of its source.

*Signal Processing* can be viewed as the manipulation of a signal (input) for the purpose of either extracting information from the input signal or producing an alternative representation of the input signal. (Figures 1.8, 1.9 of Text)

**Example:** *Example 1.6 of Text.*

## INTRODUCTION TO LINEAR SYSTEM THEORY

A linear system can be viewed as any physical device or set of rules which transforms one variable (i.e., signal)  $x(t)$  into another variable (or signal)  $y(t)$  linearly. (Figure 1.5 of Text) In equation form:

$$y(t) = T[ x(t) ]$$

- (1) **Linearity:**  $T[ \bullet ]$  is a *linear* transformation if it is both *additive* and *homogeneous*. That is,  $T[ ax_1(t) + bx_2(t) ] = aT[ x_1(t) ] + bT[ x_2(t) ]$ .
- (2) **Causality:**  $T[ \bullet ]$  is a *causal* transformation if its output at any time depends on the input at that time or at earlier times but not on the input at future times. That is,  $y(t) = T[ x(t) ]$  for any time instant  $t_0$ ,  $y(t_0)$  depends on  $x(t)$ , for  $t \leq t_0$  only.
- (3) **Time-Invariant Property:**  $T[ \bullet ]$  is a *time-invariant* transformation if shifting of the input in time by an amount  $t_0$  only has the effect of shifting the output in time by the same amount. That is,  $y(t) = T[ x(t) ]$ , then  $y(t - t_0) = T[ x(t - t_0) ]$ . So, we can say that  $T[ \bullet ]$  is independent of the chosen time origin.

### The Impulse Response of A Linear Time-Invariant System

Consider a unit impulse  $\delta(n)$  called a delta function with

$$\delta(n) = 1, \quad n = 0 \quad \text{and} \quad \delta(n) = 0, \quad \text{otherwise.}$$

A linear time-invariant (LTI) system  $T[ \bullet ]$  with input  $\delta(n)$  produces the output  $y(n)$  as follows:

$$y(n) = T[ \delta(n) ] = h(n)$$

which is defined as the impulse response of the LTI system.

A Discrete-Time (DT) system is called a *finite impulse response* (FIR)

system if its  $h(n) = 0$ , for all  $n > K$ , where  $K < \infty$ . Otherwise, the LTI system is called *infinite impulse response (IIR)* system.

### Convolution Form of a linear shift-invariant (LSI) System

For a given discrete input signal  $x(n)$ , we can express it as follows:

$$\begin{aligned} x(n) &= \dots + x(-2)\delta(n+2) + x(-1)\delta(n+1) + x(0)\delta(n) + x(1)\delta(n-1) + x(2)\delta(n-2) + \dots + \\ &= \sum_{i=-\infty}^{\infty} x(i)\delta(n-i). \end{aligned}$$

$$\text{Then, } y(n) = T[x(n)] = \sum_{i=-\infty}^{\infty} x(i)T[\delta(n-i)] = \sum_{i=-\infty}^{\infty} x(i)h(n-i).$$

This represents a fundamental expression of the input-output relationship of an LTI DT system known as the *convolution* sum. In general, it is symbolized as

$$y(n) = x(n) * h(n).$$

By a change of variables, the convolution sum also can be written as

$$y(n) = \sum_{i=-\infty}^{\infty} x(n-i)h(i).$$

Figures 3.6 ~ 3.7.

### Relation to Signal Processing

Applying a signal to the input of an LTI system produces an output that is a modified form of the input signal as shown by the convolution sum equation.

*Low-Pass Filters* attenuate rapid changes in the input more than slow ones.

*High-Pass Filters* relatively unattenuate the rapid changes but its output for a slowly varying input will be close to zero.

(Figure 3.10 of Text)



The process of convolving the impulse response of an LTI system with an input signal is the time-domain representation of *filtering*. Hence, convolution is a key concept for understanding the modification of signals by filters.

*(Example 3.10 of Text)*

### Frequency Response of Discrete-Time Systems

In many applications, we may be interested in knowing the response of an LTI system to an input signal in terms of quantitative description of the transformation properties of the LTI system.

Moreover, in many physical systems, frequency-dependent behavior is a universal phenomenon which is another indication of the filtering properties of a system.

*(Example of Figure 4.1 of Text)*

#### *Generalized Frequency Response:*

Consider the LTI system with impulse response  $h(n)$ , input  $x(n)$ , and output  $y(n)$ . Let  $x(n) = a \exp(j\omega n)$ ,  $\forall n$ . The output is found by convolution to be

$$\begin{aligned} y(n) &= \sum_{k=-\infty}^{\infty} h(k)x(n-k) = \sum_{k=-\infty}^{\infty} h(k)a \exp[j\omega(n-k)] \\ &= a \exp(j\omega n) \sum_{k=-\infty}^{\infty} h(k) \exp[-j\omega k] \\ &= x(n)H(e^{j\omega}), \end{aligned}$$

where  $H(e^{j\omega}) = \sum_{k=-\infty}^{\infty} h(k) \exp[-j\omega k]$  is called the generalized frequency response of the LTI system.  $y(n)$  is a scaled version of the input. Any input signal for which the output of an LTI system is simply a scaled version of the input is known as an *eigenfunction* of an LTI system. So,  $\exp(j\omega n)$  is an eigenfunction of an LTI system.

Magnitude (or Gain) Response:  $|H(e^{j\omega})|$

Phase Shift Response:  $\arg(H(e^{j\omega}))$

(*Example 4.4 of Text* The Frequency response of a DT lowpass filter)

*Biomedical Example: The Frequency Response of an Auditory System in Figure 4.15 of Text.*

### Modeling CT Signals as Sum of Sine Waves

*Example: Figure 5.1 of Text*

In this case, we use sinusoidal waves with different periods to model the measured signal data. First, we use the sine wave with period equal to 24 hours for approximation (*Figure 5.2(a)*). The corresponding error curve can be approximated by a sinusoidal wave with period equal to 8 hours (*Figure 5.2(b)*). Finally, these two sinusoidal waves are added to model the original data. A better approximation of the original data can be obtained. Hence, in this way, it would be possible to model the noisy periodic signal as a sum of sine waves.

### Orthogonal Functions and Sinusoidal Basis Functions

Define an operator  $Q[\bullet]$  and a set of functions  $P = \{p_i(t), i = 1, 2, \dots, K\}$ . The functions in  $P$  are said to be orthogonal under the

operator  $Q[\bullet]$  if 
$$Q[p_i(t)p_j(t)] = \begin{cases} 0 & i \neq j \\ \alpha & i = j \end{cases},$$

where  $\alpha$  is a constant. This indicates that we can express a function  $x(t)$  as a weighted sum of  $p_i(t)$ ,  $i = 1, 2, \dots, K$ . For example, let  $x(t) = a p_1(t)$ . Then, we have

$$\frac{1}{\alpha} Q[x(t)p_j(t)] = a$$

if  $j = 1$  and the result is zero if  $j \neq 1$ . That is, the operation of  $x(t)$  with each function  $p_j(t)$  in the set  $P$  is a scalar that expresses “*how much*” of each function  $p_j(t)$  is present in  $x(t)$ . The set of orthogonal functions is termed a *basis set*. Any function  $x(t)$  can be expressed as

$$x(t) = \sum_{i=0}^K a_i p_i(t).$$

### Sinusoidal Basis Functions:

Consider the basis functions given by a set of orthogonal trigonometric functions:  $\sin(n\omega t)$ ,  $\cos(m\omega t)$ , for  $\forall m, n$ .

Let the operator  $Q[\bullet] = \int_0^T [\bullet] dt$ , where  $T = 2\pi/\omega$ .

Then, a periodic function  $x(t)$  with period =  $T$  can be expressed as the **Fourier series**:

$$x(t) = \sum_{n=0}^{\infty} [a_n \cos(n\omega t) + b_n \sin(n\omega t)],$$

where the coefficients  $a_n$  and  $b_n$  can be obtained as follows:\

$$a_n = \frac{2}{T} \int_0^T x(t) \cos(n\omega t) dt, n > 0$$

$$a_0 = \frac{1}{T} \int_0^T x(t) \cos(0) dt = \frac{1}{T} \int_0^T x(t) dt,$$

$$b_n = \frac{2}{T} \int_0^T x(t) \sin(n\omega t) dt, n \geq 0.$$

Hence,

$$x(t) = a_0 + \sum_{n=1}^{\infty} [ a_n \cos(n\omega t) + b_n \sin(n\omega t) ]$$

we can see that  $x(t)$  is represented as the sum of its mean value over a cycle plus deviations from that mean value.

### Complex Exponential Form of the Fourier Series:

We can rewrite  $x(t)$  as follows:

$$\begin{aligned} x(t) &= a_0 + \sum_{n=1}^{\infty} [ a_n \cos(n\omega t) + b_n \sin(n\omega t) ] \\ &= a_0 + \sum_{n=1}^{\infty} \left[ a_n \left( \frac{\exp(jn\omega t) + \exp(-jn\omega t)}{2} \right) + b_n \left( \frac{\exp(jn\omega t) - \exp(-jn\omega t)}{2j} \right) \right] \\ &= a_0 + \sum_{n=1}^{\infty} \left[ \left( \frac{a_n - jb_n}{2} \right) \exp(jn\omega t) + \left( \frac{a_n + jb_n}{2} \right) \exp(-jn\omega t) \right] \\ &= \sum_{n=-\infty}^{\infty} c_n \exp(jn\omega t) . \end{aligned}$$

$$\text{where } c_n = \frac{a_n - jb_n}{2}, c_{-n} = \frac{a_n + jb_n}{2}, c_0 = a_0,$$

### Relationship of Continuous-Time Fourier Transform (CTFT) To Frequency Response

From  $x(t) = \sum_{n=-\infty}^{\infty} c_n \exp(jn\omega t)$ , we can write

$$c_n = \frac{1}{T} \int_{-\infty}^{\infty} x(t) \exp(-jn\omega t) dt.$$

Let  $X(\omega) = \int_{-\infty}^{\infty} x(t) \exp(-j\omega t) dt$ , then  $c_n = \frac{1}{T} X(n\omega)$

$$\begin{aligned} \text{Hence, } x(t) &= \sum_{n=-\infty}^{\infty} c_n \exp(jn\omega t) = \frac{1}{T} \sum_{n=-\infty}^{\infty} X(n\omega) \exp(jn\omega t) \\ &= \frac{1}{2\pi} \sum_{n=-\infty}^{\infty} X(n\omega) \exp(jn\omega t) \omega. \end{aligned}$$

Consider  $T \rightarrow \infty$ , then  $\omega \rightarrow d\Omega$ , and  $n\omega \rightarrow \Omega$ .

We get 
$$x(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} X(\Omega) \exp(j\Omega t) d\Omega.$$

This describes the reconstruction of  $x(t)$  from a function of frequency  $X(\Omega)$ . As a result,  $X(\Omega)$  is termed the *Fourier transform* (FT) of  $x(t)$  while  $x(t)$  is termed the *inverse Fourier transform* (IFT) of  $X(\Omega)$ .

Utilizing the FT of any signal, we are able to investigate the frequency contents of the signal. So,  $X(\Omega)$  can also be called the frequency response of  $x(t)$ .

*(Example 5.10 of Text)*

The frequency response of a general LTI system is given by

$$H(\omega) = \int_{-\infty}^{\infty} h(t) \exp(-j\omega t) dt$$

which is the FT of the impulse response of the LTI system.

### Fourier Transform of DT signals

Based on the FT relationship, we can write the FT of a DT signal  $x(n)$  as follows:

$$X(e^{j\omega}) = \sum_{n=-\infty}^{\infty} x(n) \exp(-jn\omega)$$

And the IFT of  $X(e^{j\omega})$  is given by

$$x(n) = \frac{1}{2\pi} \int_{-\infty}^{\infty} X(e^{j\omega}) \exp(jn\omega) d\omega.$$

This leads to the following important relationship describing the input/output of an LTI system:

Consider the case: Let  $x(n) = \exp(jn\omega)$  = an eigenfunction of any LTI system. So,  $y(n) = H(e^{j\omega}) \exp(jn\omega)$ .

Next, let  $x(n) = \frac{1}{2\pi} \int_{-\infty}^{\infty} X(e^{j\omega}) \exp(jn\omega) d\omega$ .

$$\begin{aligned} \text{Then, } y(n) &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \mathbf{H}(e^{j\omega}) \mathbf{X}(e^{j\omega}) \exp(jn\omega) d\omega. \\ &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \mathbf{Y}(e^{j\omega}) \exp(jn\omega) d\omega. \end{aligned}$$

Hence,  $\mathbf{Y}(e^{j\omega}) = \mathbf{H}(e^{j\omega})\mathbf{X}(e^{j\omega}) = \text{Fourier transform of } y(n) = h(n) * x(n)$ .

→ Fourier transform of  $h(n) * x(n) = \mathbf{H}(e^{j\omega})\mathbf{X}(e^{j\omega})$ .

### Sampling Process and Sampling Theorem

To sample a continuous-time signal  $x(t)$  is to represent  $x(t)$  at a discrete number of points,  $t = nT$ , where  $T$  is the sampling period, which is the time between samples, and  $n$  is an integer that establishes the time position of each sample. This process is illustrated in the following figure. For the sampling process to be useful, we must be able to show that it is possible to sample in such a way that the signal  $x(t)$  can be reconstructed from the samples. The easiest way is to discuss in the frequency domain.

(I) First, the sampled  $x(t)$ , denoted  $x_s(t)$ , is written as

$$x_s(t) = x(t) p(t),$$

where  $p(t)$ , called the sampling function, models the action of the sampling switch in the figure. In general, the sampling function  $p(t)$  is assumed to be the periodic pulse train of period  $T$  illustrated in the figure.

(II) Next, we derive the spectrum or the Fourier transform of  $x_s(t)$ , and from this spectrum we are able to choose appropriate values  $T$ .

Since  $p(t)$  is a periodic, it can be represented by a Fourier series as follows:

$$p(t) = \sum_{n=-\infty}^{\infty} C_n \exp(jn2\pi f_s t),$$

where  $\omega_s = 2\pi f_s = 2\pi/T$  and  $C_n$  is the  $n$ th Fourier coefficient of  $p(t)$ , given by

$$C_n = \frac{1}{T} \int_{-T/2}^{T/2} p(t) \exp(-j2\pi n f_s t) dt$$

$$\rightarrow x_s(t) = \sum_{n=-\infty}^{\infty} C_n x(t) \exp(jn2\pi f_s t)$$

Now the Fourier transform of  $x_s(t)$  is defined by

$$X_s(f) = \int_{-\infty}^{\infty} x_s(t) \exp(-j2\pi f t) dt$$

$$\rightarrow X_s(f) = \int_{-\infty}^{\infty} \sum_{n=-\infty}^{\infty} C_n x(t) \exp(jn2\pi f_s t) \exp(-j2\pi f t) dt$$

$$\rightarrow X_s(f) = \sum_{n=-\infty}^{\infty} C_n \int_{-\infty}^{\infty} x(t) \exp(jn2\pi f_s t) \exp(-j2\pi f t) dt$$

$$\rightarrow X_s(f) = \sum_{n=-\infty}^{\infty} C_n \int_{-\infty}^{\infty} x(t) \exp\{-j2\pi[f - nf_s]t\} dt$$

Since the Fourier transform

$$X(f - nf_s) = \int_{-\infty}^{\infty} x(t) \exp\{-j2\pi[f - nf_s]t\} dt$$

Thus the Fourier transform of the sampled signal can be written

$$X_s(f) = \sum_{n=-\infty}^{\infty} C_n X(f - nf_s)$$

which shows the spectrum of the sampled continuous-time signal,  $x(t)$ , is composed of the spectrum of  $x(t)$  plus the spectrum of  $x(t)$  translated to each harmonic of the sampling frequency. Each of the translated spectra is multiplied by a constant, given by the corresponding term in the Fourier series expansion of  $p(t)$ .

In theory, we shall assume  $p(t)$  to be composed of an infinite train of impulse functions of period  $T$ . Thus,

$$p(t) = \sum_{n=-\infty}^{\infty} \delta(t-nT)$$

$$\rightarrow C_n = \frac{1}{T} \int_{-T/2}^{T/2} \delta(t) \exp(-jn2\pi f_s t) dt$$

$$\rightarrow C_n = \frac{1}{T} = f_s \quad \text{for all } n.$$

$$\rightarrow \boxed{X_s(f) = f_s \sum_{n=-\infty}^{\infty} X(f - nf_s)}$$

(III) Finally, we can reconstruct the original CT signal  $x(t)$  from  $x_s(t)$  perfectly as follows: Using a low-pass filter (called a **reconstruction filter**) to pick up the frequency content  $C_0 X(f)$ .

(IV) Sampling Theorem:

We can see that the original CT signal  $x(t)$  from  $x_s(t)$  perfectly if  $x(t)$  is bandlimited, i.e.,  $X(f)$  is zero for  $|f| \geq f_h$  and

$$f_s - f_h \geq f_h$$

i. e., 
$$f_s \geq 2f_h \quad (\text{Hertz})$$

Hence, the minimum sampling frequency is  $2f_h$ , where  $f_h$  is the highest frequency in  $x(t)$ . In general,  $2f_h$  is known as the **Nyquist Rate**.

(V) The effect of sampling at too low a rate:

If  $x(t)$  is sampled below the **Nyquist Rate**, i. e.,

$$f_s - f_h \leq f_h$$

then the adjacent spectra overlap making it impossible to recover  $x(t)$  by filtering as shown by the following figure. This effect is known as **aliasing**.

### (V) Noise Removal and Signal Compensation

Removing noise from a signal probably is the most frequent



application for processing biomedical signals.

**Example 1: Reducing the ECG artifact in an EMG recording. (*Figure 8.1 of Text*)**

To record an EMG from muscles on the torso, the ECG is commonly superimposed on the EMG signal because of the physical proximity of the heart and the large electrical amplitude of the ECG compared to many EMG signals. From the figure, we observe that the frequency contents of the EMG and ECG signals seem to overlap below about 30 Hertz. So, removal of the ECG signal by filtering the EMG recording with a high-pass filter will necessarily remove some EMG signal component also. However, the ECG can be reduced in some degree through the high-pass filtering.

**Example 2: Removing noise from an Ultrasound signal. (*Figure 8.22 of Text*)**

To obtain the velocity of movement of red blood cells in a vessel may be measured by passing an ultrasound beam through the vessel wall and determining the Doppler shift of frequency of the reflected beam. Now using a 2-MHz ultrasound wave passes through the temporal region of the skull without excessive attenuation, we are able to measure blood flow velocity in arteries of the brain of humans. Usually, blood flow velocity in the middle cerebral artery ( $V_{MCA}$ ) is measured in Figure 8.22(c).

The signal was sampled at  $f_s = 100$  and it is desired to remove the high-frequency noise using a digital filter. We use a low-pass digital filter with cutoff frequency = 10 Hz to achieve this purpose. Two

types of digital filters, i. e., Hamming window filter and Equiripple filter, are employed.

Figure 8.22 (a) plots the impulse response for each of these two filters.

Figure 8.22(b) plots the frequency response for each of these two filters.

- The Hamming window filter has a smaller stopband gain but its transition band is about twice the width of that of the Equiripple filter.

**Example 3:** The biomedical signal to be processed is the pressure in the left ventricle of the heart ( $P_{LV}$ ). The maximum derivative of this signal (during a given heart beat) is often considered as index of myocardial contractility. We use a **digital differentiator** to achieve this goal.

Figure 8.23(a) shows a sample of  $P_{LV}$ .

Figure 8.23(b) and (c) plot the impulse response and the frequency response of the digital differentiator.

Figure 8.23(d) depicts a portion of the original signal and its derivative signal which appears to reflect the maximum derivative occurs during the upstroke of the ventricular pressure.

## **ECG Signals**

### The Electrocardiogram

[How the Electrocardiograph Works](#)

[Correlation of the ECG with Heart Sounds](#)

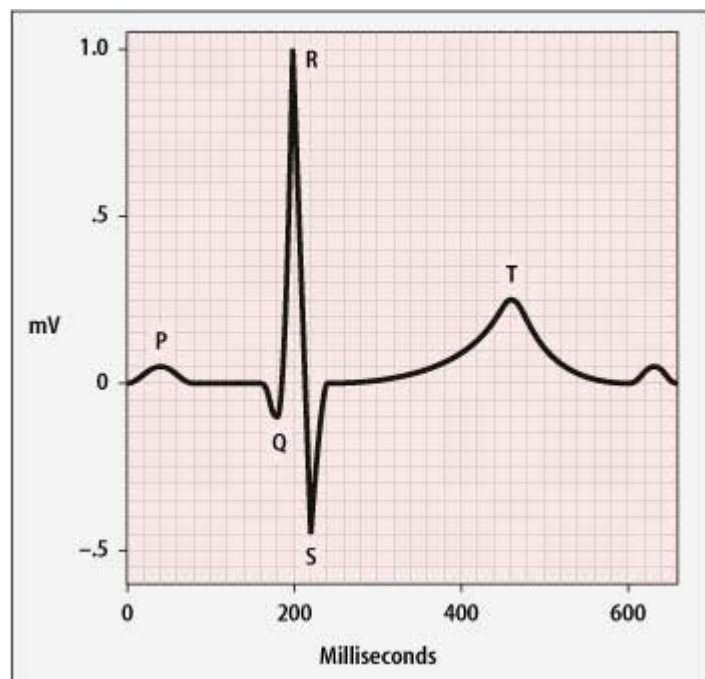
[Glossary Terms](#)

A pair of surface electrodes placed directly on the heart will record a repeating pattern of changes in electrical “action potential.” As action potentials spread from the atria to the ventricles, the voltage measured between these two electrodes will vary in a way that provides a “picture” of the electrical activity of the heart. The nature of this picture can be varied by changing the position of the recording electrodes; different positions provide different perspectives, enabling an observer to gain a more complete picture of the electrical events.

### **Summary**

The body is a good conductor of electricity because tissue fluids contain a high concentration of ions that move (creating a current) in response to

potential differences. Potential differences generated by the heart are thus conducted to the body surface where they can be recorded by surface electrodes placed on the skin. The recording thus obtained is called an electrocardiogram (ECG or EKG).



The electrocardiogram indicates the conduction of electrical impulses through the heart, measures and records both the

intensity of this electrical activity (in millivolts), and the time intervals involved.

**How**                    **the** There are two types of ECG recording  
**Electrocardiograph** electrodes, or "leads." The bipolar limb  
**Works** leads record the voltage between electrodes placed on the wrists and legs. These bipolar leads include lead I (right arm to left arm), lead II (right arm to left leg), and lead III (left arm to left leg). In the unipolar leads, voltage is recorded between a single "exploratory electrode" placed on the body and an electrode that is built into the electrocardiograph and maintained at zero potential (ground).

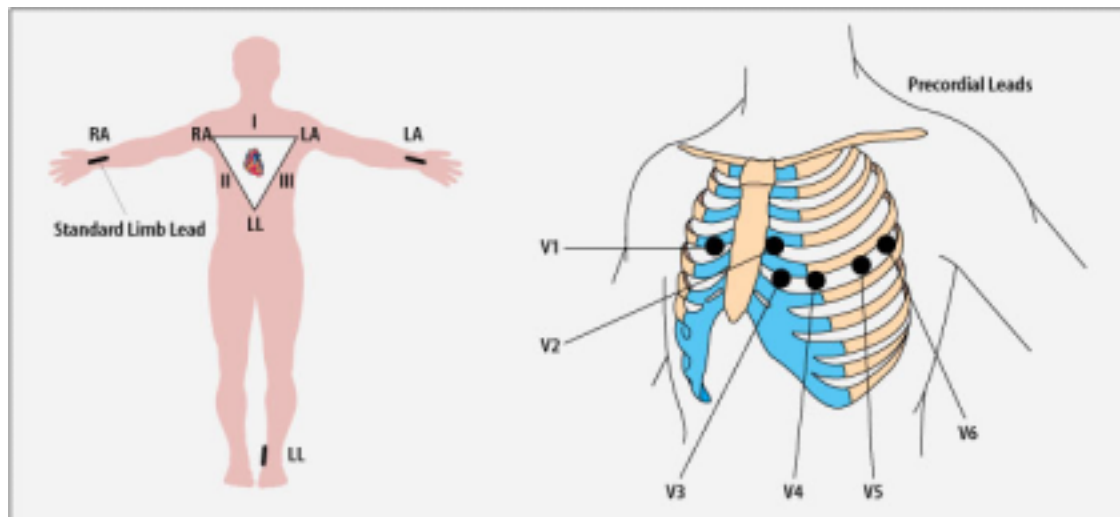
The unipolar limb leads are placed on the right arm, left arm, and left leg;

these are abbreviated AVR, AVL, and AVF, respectively. The unipolar chest leads are labeled one through six, starting from the midline position (see below). There are thus a total of twelve standard ECG leads that “view” the changing pattern of the heart’s electrical activity from different perspectives. This is important because certain abnormalities are best seen with particular leads and may not be visible at all with other leads.

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The placement of the bipolar leads and the exploratory electrode for the unipolar chest leads in an electrocardiogram (ECG); (RA = right arm, LA = Left arm, LL = left leg.)

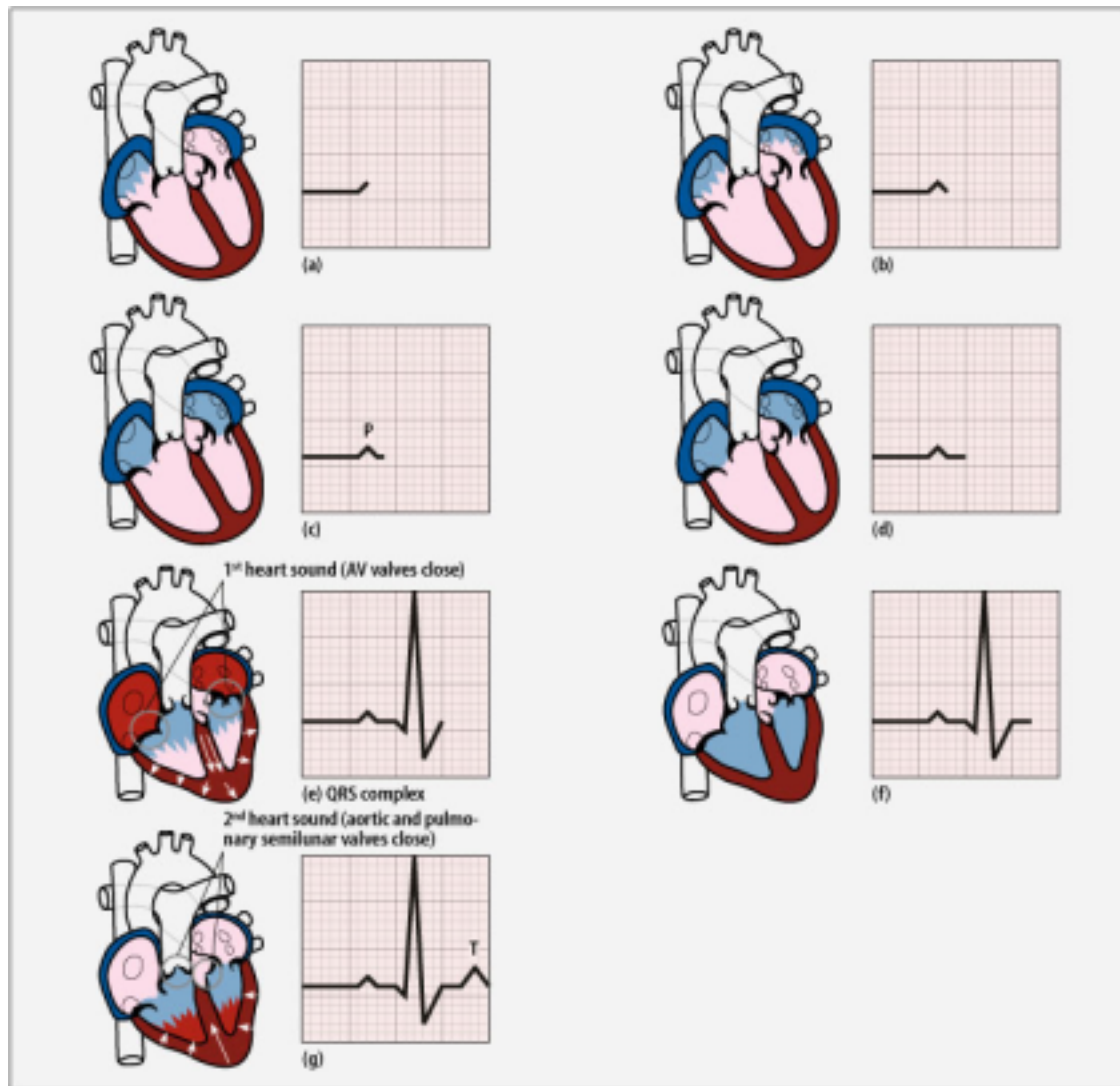
Each cardiac cycle produces three distinct ECG waves, designated P, QRS, and T. It



should be noted that these waves are not action potentials; they represent changes in potential between two regions on the surface of the heart which are produced by the composite effects of action potentials in many myocardial cells. For example, the spread of depolarization through the atria causes a potential difference that is indicated by an upward deflection of the ECG line. When about half the mass of the atria is depolarized, this upward deflection reaches a maximum value, because the potential difference between the depolarized and unstimulated portions of the atria is at a maximum. When the entire mass of the atria is depolarized, the ECG returns to baseline because all regions of the atria have the same polarity. The spread of atrial depolarization thus creates

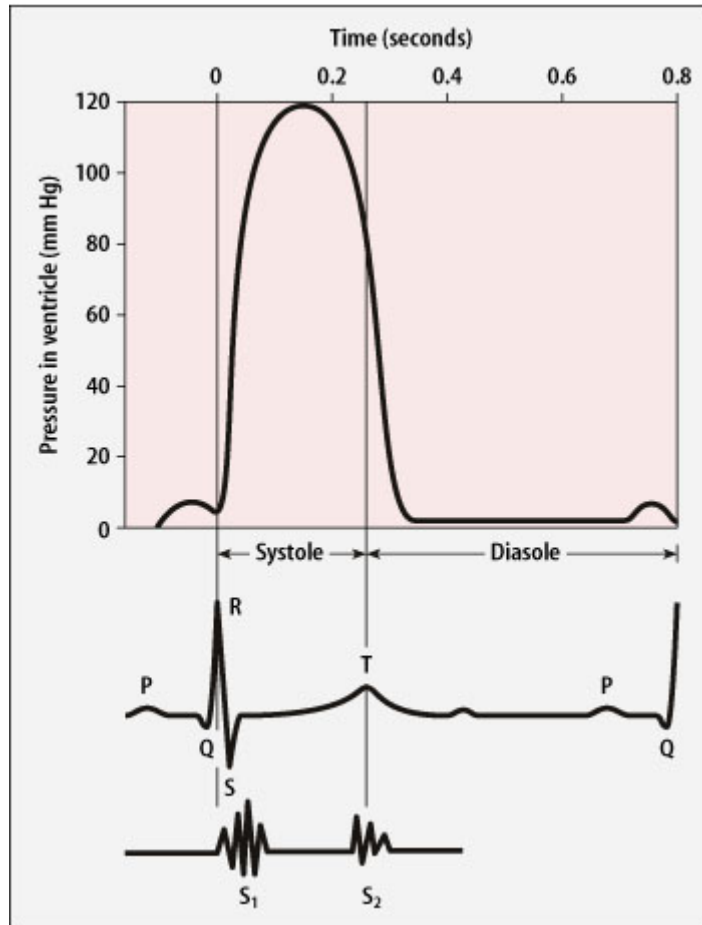
the P wave.

Conduction of the impulse into the ventricles similarly creates a potential difference that results in a sharp upward deflection of the ECG line, which then returns to the baseline as the entire mass of the ventricles becomes depolarized. The spread of the depolarization into the ventricles is thus represented by the QRS wave. During this time the atria repolarize, but this event is hidden by the greater depolarization occurring in the ventricles. Finally, repolarization of the ventricles produces the T wave (see illustration below).



The conduction of electrical impulses in the heart, as indicated by the electrocardiogram (ECG). The direction of the arrows in (e) indicates that depolarization of the ventricles occurs from the inside (endocardium) out (to the epicardium), whereas the arrows in (g) indicate that repolarization of the ventricles occurs in the opposite direction.

**Correlation of the Depolarization of the ventricles, as ECG with Heart indicated by the QRS wave, stimulates Sounds** contraction by promoting the uptake of  $Ca^{++}$  into the regions of the sarcomeres. The QRS wave is thus seen to occur at the beginning systole. The rise in intraventricular pressure that results causes the AV valves to close so that the first heart sound (S1, or lub) is produced immediately after the QRS wave (see following illustration).



The relationship between changes in intraventricular pressure and the electrocardiogram during the cardiac cycle. The QRS wave (representing depolarization of the ventricles) occurs at the beginning of systole, whereas the T wave (representing repolarization of the ventricles)

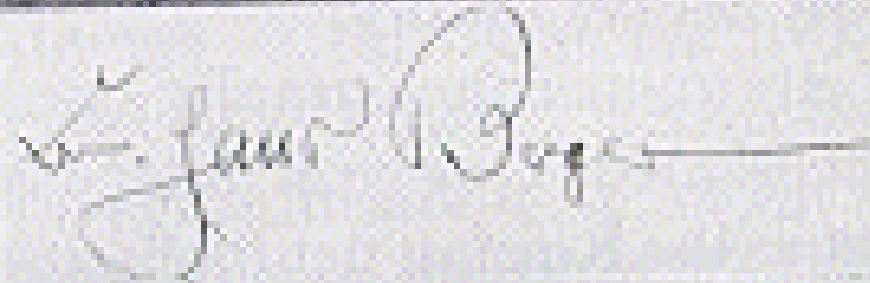
**occurs at the beginning of diastole.**

Repolarization of the ventricles, as indicated by the T wave, occurs at the same time that the ventricles relax at the beginning of diastole. The resulting fall in intraventricular pressure causes the aortic and pulmonary semilunar valves to close so that the second heart sound (S<sub>2</sub>, or dub) is produced shortly after the T wave in an electrocardiogram begins.



## EEG Signals

# The History of the Electroencephalogram



In 1929, a German psychiatrist named **Hans Berger**, who worked in the city of Jena, announced to the

world that:

- it was possible to record the feeble electric currents generated on the brain, without opening the skull, and to depict them graphically onto a strip of paper.



Berger named this new form of recording as the [electroencephalogram](#) (EEG, for short);

- that this activity changed according to the functional status of the brain, such as in sleep, anesthesia, hypoxia (lack of oxygen) and in certain nervous diseases, such as in epilepsy.

**First EEG recorded by Hans Berger, circa 1928.**

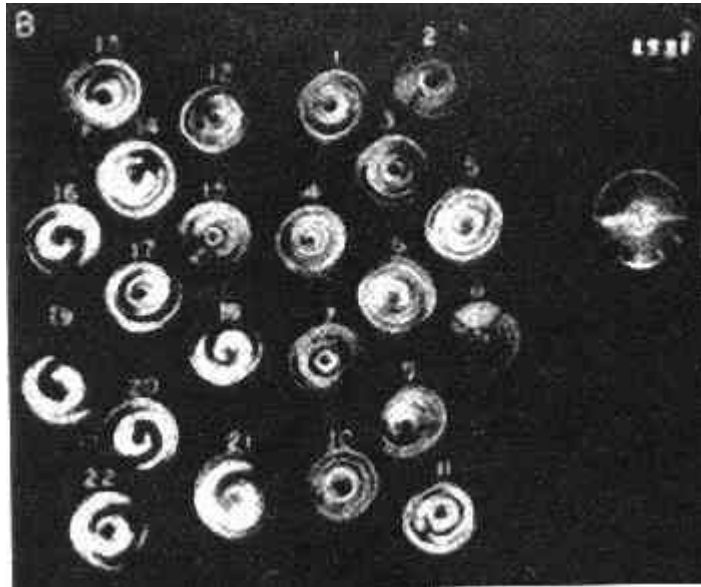


These were revolutionary discoveries, and, in fact, Berger founded an entirely new and very important branch of medical science, named **clinical neurophysiology**.

Berger electrodes were too large to made detailed topographical studies of the EEG (in other words, to use electrical activity recorded from the brain to pinpoint areas of sensory projection, the localization of tumors or of epileptic foci, etc.).



This was left to W. Gray Walter, a remarkable British scientist, who, in 1936, proved that, by using a larger number of



electrodes pasted to the scalp, each one having a small size, it was possible to identify abnormal electrical activity in the brain areas around a tumor, and diminished activity inside it.

Impressed with the possibilities of building bidimensional maps of the EEG activity over the brain surface, W. Gray Walter invented the **toposcope** in 1957.

This was a remarkably complex device and showed Grey Walter's inventiveness (besides being a physician, he was also an engineer). It had 22 cathode ray tubes (similar to a TV tube), each of them connected to a pair of electrodes

attached to the skull. The electrodes (and their corresponding tubes) were arranged in a bidimensional geometrical array, such as that each tube was able to depict the intensity of the several rhythms which compose the EEG in a particular area of the brain (the frontal , parietal and occipital lobes, etc.). This array of CRT tubes, were photographed face up, so that a kind of phosphorescent spiral display showed simultaneously which kind of rhythm was present in a particular part of the brain.

Gray Walter asked his subjects to perform several mental tasks, with the result that the EEG rhythms were altered in different ways, times and parts of the brain. He was the first to prove, for instance, that the so-called alpha rhythm (present during a resting state) disappears from almost all the brain during a mental task which demands awareness, being substituted by a faster rhythm, the beta waves.

It was immediately apparent to neurologists that the toposcope could be a great help to locate epileptic foci (the points where a convulsion originates in the brain, due to a local lesion, tumor or functional alteration). However, it was very complex and expensive and it did not achieve commercial success or widespread use.

The topographic study of brain electrical activity was born again only when fast desktop computers became available in the 80s. Thus, [EEG brain topography](#) was developed and is widely in use today. It is also called Color Brain Mapping.

## **The Brain is Electric...**

Technical developments in the field of electrical measurement and recording in the last quarter of the 19th century made possible one of the greatest triumphs of modern neuroscience: the discovery, made by a German

psychiatrist named Hans Berger, that the human brain has a continuous electrical activity, and that it can be recorded (see the [History of the Electroencephalogram](#)).



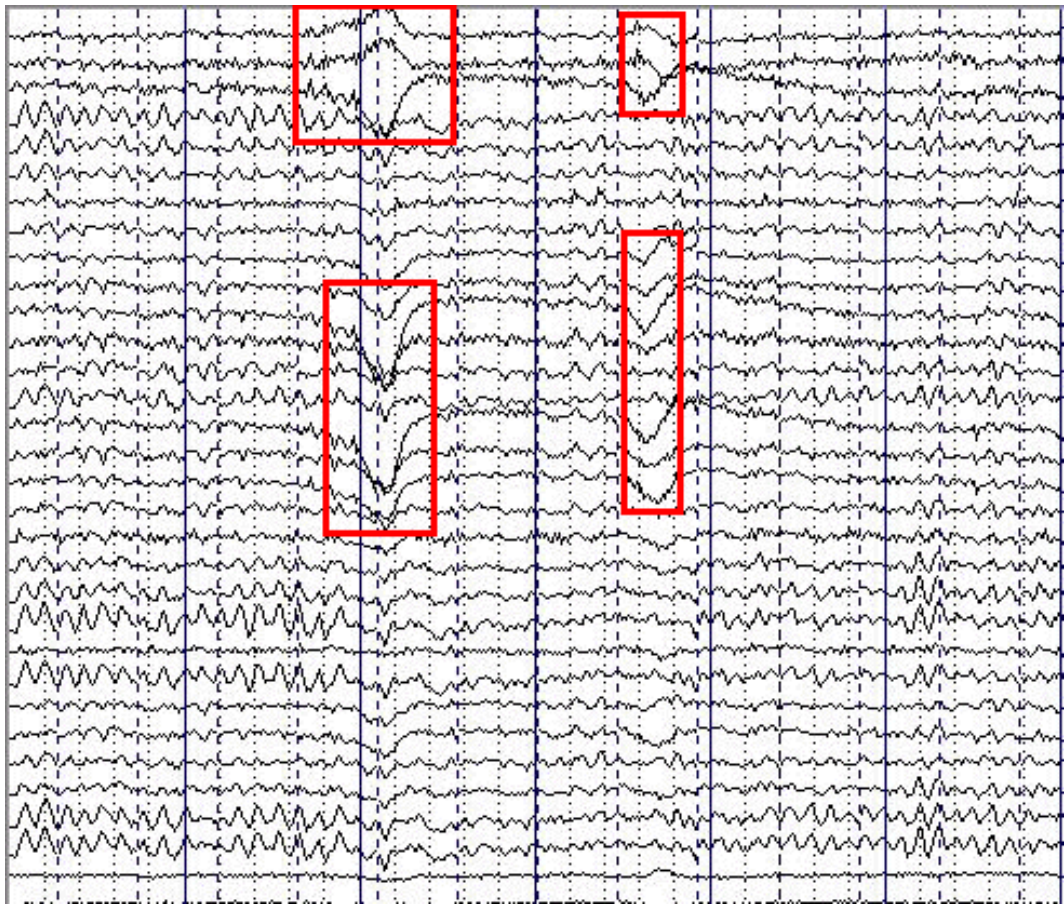
The [electroencephalographic recording](#) is usually taken by electrodes (small metallic discs) pasted by an electricity conducting gel to the surface of the skull's skin (scalp). A powerful electronic amplifier increases several hundreds or thousands of times the amplitude of the weak signal (less than a few microvolts) which is generated in this place. A device called **galvanometer**, which has a inkpen attached to its pointer, writes on the surface of a paper strip, which moves continuously at a fixed speed past it. The result is a wiggly "wave" like the picture above. One pair of electrodes usually make up a **channel**. EEG recordings, depending on its use, can have from 8 to 40 channels

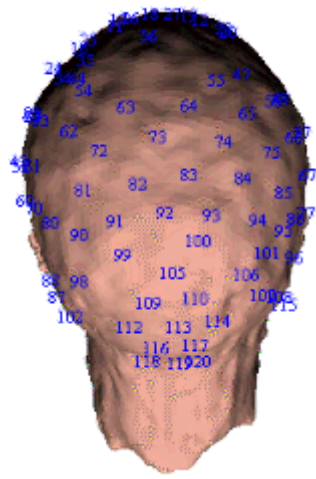
recorded in parallel. This is called **multichannel EEG recording**.

Since the times of Berger, it is known that the characteristics of EEG activity change in many different situations, particularly with the [level of vigilance](#): alertness, rest, sleep and dreaming. The frequency and the amplitudes of waves change, and they have been labelled with names such as alpha, beta, theta and delta. Particular mental tasks also alter the pattern of the waves in different parts of the brain (See the article on the [physiological basis of dreaming](#), in the last issue of **Brain & Mind**). Electroencephalograms are also used in neurology and psychiatry, mainly to help diagnose diseases of the brain, such as epilepsy (convulsions caused by a chaotic activity of neurons), sleep disorders and brain tumors.

## Building Maps of the Mind

An important application of multichannel EEG is to try to find the location of a epileptic focus (a small spot in the brain where the abnormal activity originates and then spreads to other parts of the brain) or of a tumor, even when they are not visible in a x-ray or CT scan of the head.





*A 32-channel EEG using a modern recorder.*

Each horizontal tracing corresponds to an electrode pair placed on a particular area of the patient's scalp, forming a regular grid-like pattern.

By noting the set of channels where abnormal waves occur (such as those marked in red), the neurologist is able to infer the parts of the brain where the abnormality is located. This is very difficult to scan and to interpret, and subject to many errors, however, when the number of abnormal channels is large, or the nature of changes is complex. A precise bidimensional location of a focus or tumor is impossible to achieve.

So, what is the solution ? The computer, of course.



## **Computers and Brain Waves**

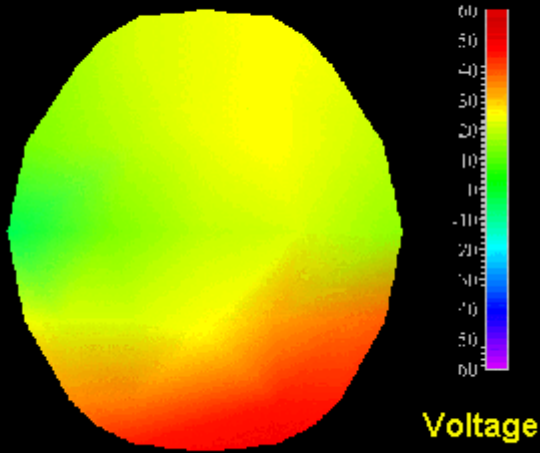


In order to use the superior power and flexibility of the computer to store and to analyze the EEG and other biosignals, an invention was of fundamental importance: the so-called **analog-digital converter** (or DAC). Essentially, it is an electronic device that takes a continuously variable wave and transform it to a list of numbers (each number being a measurement of the wave's amplitude at regular time intervals. These measurements are called samples, so the whole process is also named **sampling**). Sampling is performed at a high speed (100 to 200 times per second), and the resulting numbers are stored onto the computer's disk. Each channel of EEG has its own separate DAC process, in parallel with the others, and this proceeds in real time.

Once all the numbers which were recorded along a period of time are inside the computer, special software programs are used to display the waves in the video screen, print it



## EEG Topographic Map



out, etc. Mathematical techniques working with these large arrays of numbers are used to do filtering, frequency and amplitude analysis and color

mapping. This approach is called **quantitative EEG**, because it's different from the traditional approach, which doesn't make any measurements on the tracings; instead, it relies on qualitative assessment or overall appearance of the patterns of waves.

## EEG Brain Topography

With the possibility of recording simultaneously a great number of digitized channels of EEG, a new technique was born: **EEG brain topography**, at the end of the 80s. In this

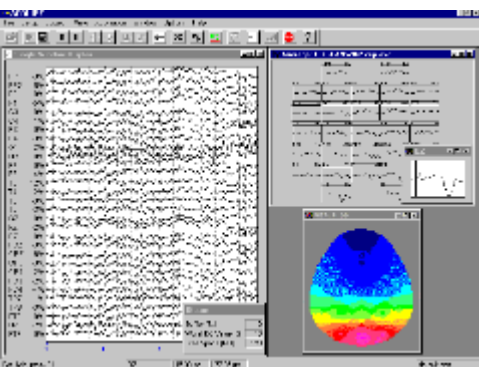
technique a large number of electrodes is placed onto the head, following a [geometrical array](#) of even-spaced points. A special software inside the apparatus' computer, plots the activity on a color screen or printer, by coding the amount of activity in several tones of color (for example, black and blue might depict low EEG amplitude, while yellow and red might depict larger amplitudes). The spatial points lying between electrodes are calculated by mathematical techniques of interpolation (calculating intermediary values on the basis on the value of its neighbors), and thus a smooth gradation of colors is achieved.

This approach gives a much more accurate and representative view of the location of alterations of rhythm, amplitude, etc., in relation to the surface of the skull. Neurologists working with the EEG brain topographic system were soon able to differentiate several kinds of diagnoses (including some mental diseases whose biological origin, or ethiology, was previously unknown).

Pinpointing the exact location of EEG alterations was also made much more easier. In addition, the use of the [cinè mode](#) (animations using several sequential pictures taken from the brain maps) made possible the dynamic study of brain function in action.

### **What For ?**

EEG brain topography is not performed in all cases requiring a recording of the brain activity. Its main indication is to determine the presence of tumors and focal disease of the brain (including epilepsy, arteriovenous mal-formations and stroke). It is also appropriate when disturbances in consciousness and vigilance are present, such as narcolepsy (the abrupt onset of sleep), coma, etc.. In addition, EEG brain topography is being increasingly used to monitor the effects of withdrawal of psychoactive drugs, and in infectious diseases of the brain, such as



meningites, as well as to follow up patients who were subjected to brain operations. In psychiatry, EEG brain topography has been of value in identifying disorders of biological origin, such as schizophrenia, dementias, hyperactivity and depression, brain atrophy and attention deficit disorders in children.



Today, there are many commercial EEG brain topography systems in use. They are generally installed in PC- or Macintosh-based microcomputer platforms, and can be easily operated by technicians or physicians, due to the Windows-based software which comes with the package. This software is highly flexible, permitting the programming of many recording configurations and parameters, as well as to

build a reference database of images, composed of typical patient cases in several pathologies. Usually, the multichannel records can be shown side by side with the reconstructed topographical brain map. In addition, several maps taken in different epochs can be **displayed side by side**.

## EGG Signals

### **Electrogastrogram (EGG)**

#### **What is an electrogastrogram?**

An electrogastrogram is similar to an electrocardiogram (EKG) of the heart. It is a recording of the electrical signals that travel through the muscles of the stomach and control the muscles' contraction.

#### **When is an electrogastrogram used?**

An electrogastrogram is used when there is a suspicion that the muscles of the stomach or the nerves controlling the muscles are not working normally. Usually this suspicion arises when there is a problem with recurrent nausea and vomiting, signs that the stomach is not emptying food normally. If the electrogastrogram is abnormal, it confirms that the problem probably is with the

stomach's muscles or the nerves that control the muscles. The electrogastrogram can be considered an experimental procedure since its exact role in the diagnosis of diseases of the stomach has not been defined yet.

### **How is an electrogastrogram done?**

For an electrogastrogram, several electrodes are taped onto the abdomen over the stomach in the same manner as electrodes on the chest for an electrocardiogram. The electrodes sense the electrical signals coming from the stomach's muscles, and the signals are recorded on a computer for analysis. Recordings are made both fasting and after a meal with the patient lying quietly. The study takes two or three hours.

### **How are the results of the electrogastrogram evaluated?**

In normal individuals there is a regular electrical rhythm

generated by the muscles of the stomach--just as in the heart--and the power (voltage) of the electrical current increases after the meal. In patients with abnormalities of the muscles or nerves of the stomach, the rhythm often is irregular or there is no post-meal increase in electrical power.

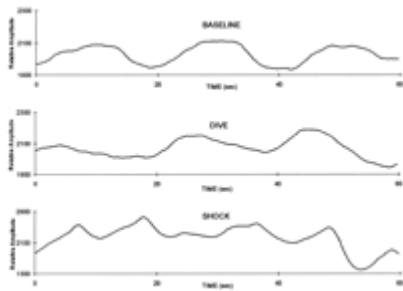
### **Are there any side effects of an electrogastrogram?**

There are no side effects. The study is painless.

### **Are there alternatives to the electrogastrogram?**

No, there are no alternatives; however, other studies, for example, antro-duodenal motility studies or gastric emptying studies may give additional information since abnormal electrical activity of the stomach often results in abnormal muscular activity and reduced emptying of food from the stomach.





**View larger version**

Fig. 1. EGG tracings during the baseline period and during the shock and dive stimuli. The segments shown are 1 minute in duration and are from the same subject. Notice the change in frequency during the shock stimulus compared with the baseline period and the relative lack of change in frequency during the dive stimulus compared with the baseline period.

## Effects of Shock and Dive Stimuli on Emotions

## EMG Signals



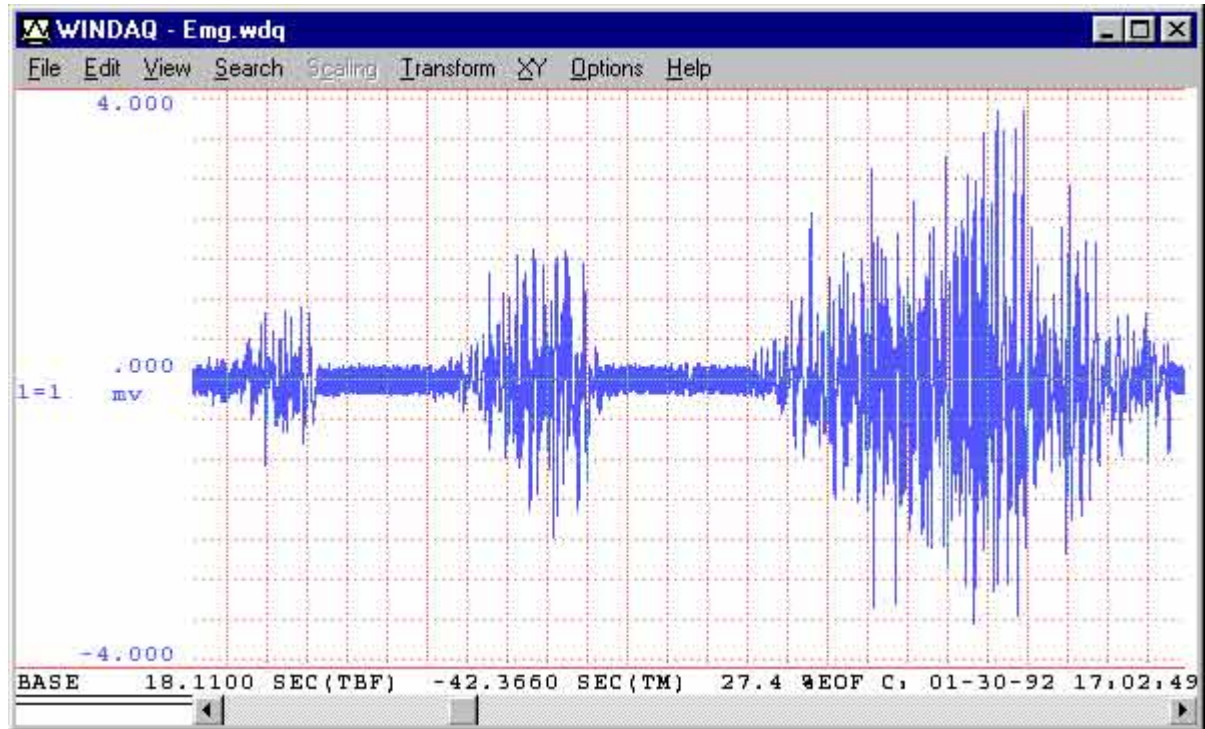
**The Electromyogram (EMG) records the electrical activity in muscles. It can diagnose diseases of the nerves and muscles. This test can help determine the cause of muscle weakness, spasms, paralysis, pain in the arms, hands, legs or face. It can detect conditions such as pinched nerves, inflamed muscles and carpal tunnel syndrome. The electrode, a tiny needle, is inserted into a muscle to record its electrical activity. It records activity during the insertion, while the**

muscle is at rest, and while the muscle contracts. An amplifier increases the strength of the electrical signal from the muscle. An oscilloscope, which resembles a television or computer screen, displays the image. Speakers are used so the sounds produced by the electrical signals can be analyzed. After the first muscle is tested, the electrode may be inserted into another muscle. The total testing time may range from just a few minutes to more than an hour, depending upon how many muscles are tested. After the exam, you may feel tenderness in the tested muscles. There is a slight risk of minor, localized inflammation in muscles during the test. This usually lasts only a few hours.

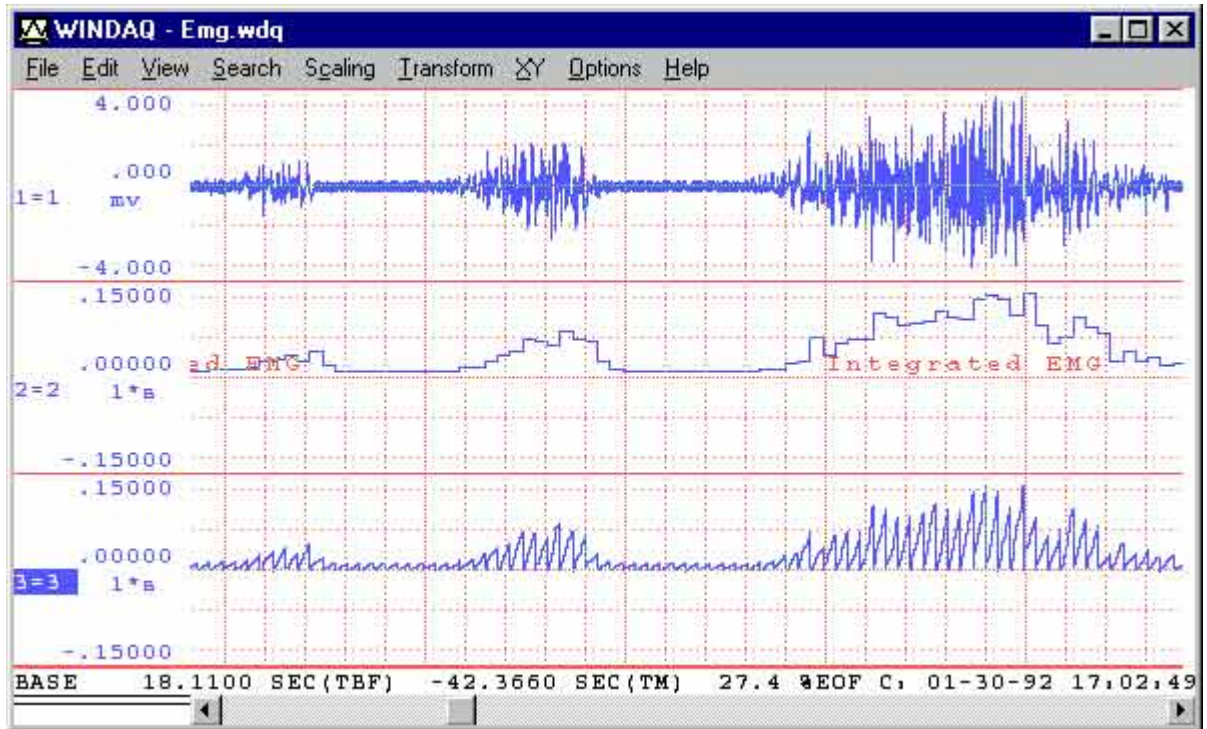
### **An EMG Application**

Deriving an activity index from an EMG waveform is a specific application of the integral. The following example illustrates how the rectification and integration functions of Advanced CODAS are applied to an EMG channel to

derive an activity index. The EMG signal shown in **Figure 2** was obtained from a bioelectric amplifier connected to a pair of surface electrodes placed several centimeters apart over the biceps muscle. The signal was acquired with a WINDAQ data acquisition system installed in a Toshiba Portable personal computer. The output of the bioelectric amplifier was connected to the input of the WINDAQ board through an option 01 module and a total gain of 1000 was applied using the live, interactive program capabilities of WinDac acquisition software. A sample rate of 1000 samples per second provided better than 100Hz response. This is similar to the best response that could be achieved with a pen-type oscillographic chart recorder. **Figure 2** shows the acquired EMG signal with a compression factor of 16 applied, equivalent to slowing down a chart recorder's paper speed by a factor of 16.



**Figure 2** — *The original EMG signal acquired by skin surface electrodes placed several centimeters apart over the biceps muscle. Other than the duration and intensity of the muscular contraction, the waveform conveys little meaningful information in this state.*



**Figure 3 — Channels 2 and 3 illustrate the activity index waveform. The Channel 2 shows the activity index with sample/hold enabled, while Channel 3 shows the activity index with sample/hold disabled.**

## **ERG Signals**

**As early as 1865 Holmgren found that a light stimulus could cause a change in the electrical potential of the amphibian eye. Shortly afterwards, similar findings were reported by Dewar from Scotland. He showed that light illumination through the pupil, which had previously been covered, caused a slight movement of a galvanometer, suggestive of a positive electrical change in the cornea relative to the back of the eye (Armington, 1974). This light-induced electrical activity of the eye was called the electroretinogram. Nowadays the electroretinogram response is commonly abbreviated to the ERG.**

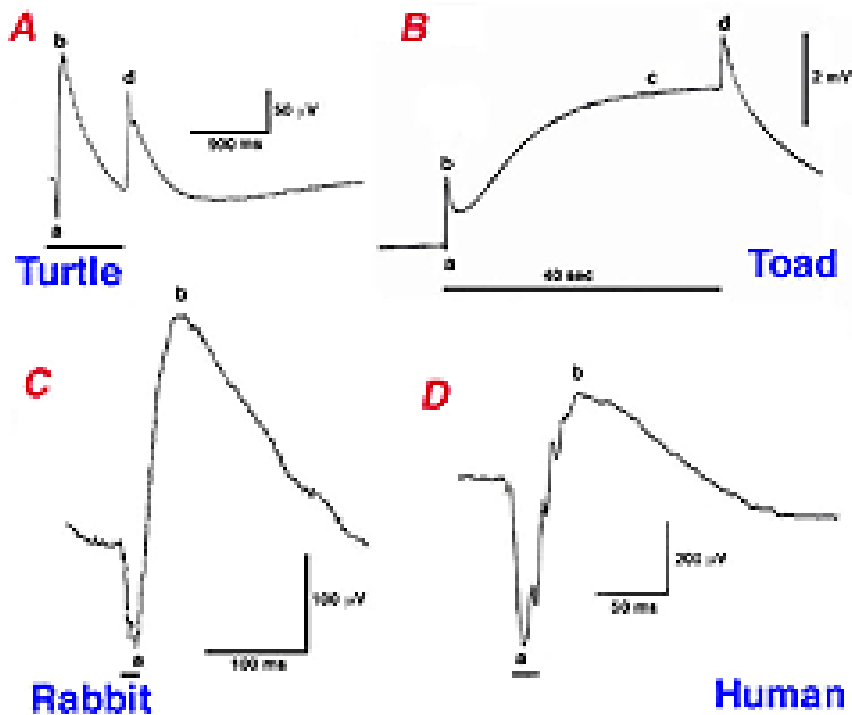
**Gotch (1903) was the first to report that the response of the eye to a light flash consisted of two waves; first the cornea became negative and then a positive wave of larger amplitude appeared. Later Einthoven and Jolly (1908) separated the ERG response into three waves. The first wave to appear immediately after turning on a light stimulus was**

**negative on the cornea. It was followed by a positive wave and a final slower wave that was also positive. Einthoven and Jolly (1908) suggested that the light stimulus triggered a chain of reactions leading to the formation of products A, B and C, and that every electrical wave indicated a change in a 'relevant' product. These authors' work was the foundation for the form of analysis of the ERG used to the present day. The waves are called a-, b- and c-waves. An additional corneal-positive wave, that is more rarely recorded at the termination of the light flash, is called the d-wave.**

**Figure 1 shows ERG responses from different species. These responses are to bright light stimuli applied in the dark-adapted state. The ERG of the turtle eye (Fig. 1A) as elicited by a long (900ms) step of light, shows an a-wave and b-wave complex separated from the d-wave which is generated at stimulus offset. A bright light stimulus of 40sec duration is used to record the ERG of the bullfrog in figure 1B (Oakley, 1977). The a-wave and b-wave are followed by the slow corneal-positive c-wave. After termination of the**



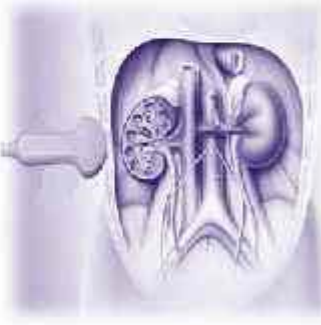
**stimulus, a d-wave develops. The ERG responses of the rabbit (Fig. 1C) and the human (Fig. 1D) are elicited by fast bright flashes (50 or 100ms in duration) and therefore, only the a-wave and b-wave are seen. In the human response (Fig. 1D), fast oscillations can also be seen on the ascending limb of the b-wave. These ERGs in the different species clearly differ in amplitude and pattern. Some of this variability is due to species differences, particularly, the relative densities of rods and cones, while technical factors such as duration and intensity of photostimulation and method of recording also affect the waveform. Nevertheless, ERG responses of turtle, bullfrog, rabbit and human (Fig. 1), in addition to those recorded from other vertebrate species, are characterized by the basic features of a negative a-wave followed by a positive b-wave.**



**Fig. 1. (A) ERG response of turtle *Pseudemys scripta elegans* elicited by a 900ms light stimulus in order to separate the a-wave and b-wave from the d-wave. (B) The ERG of the bullfrog elicited by a long (40sec) light stimulus in order to show the c-wave in addition to the a-, b- and d-waves (Oakley, 1977). (C) The ERG response of a rabbit to a flash (20\_s) flash of white light. (D) The ERG response from a human as typically recorded in the clinic. Note the fast oscillations on the ascending limb of the b-wave. Calibration bars are denoted separately for each ERG response. (59 K jpeg image)**

## CW Doppler Ultrasound Signals

Diagnostic Ultrasound is an important tool in today's sophisticated medical diagnostics. Nearly every medical discipline benefits from this relatively inexpensive method providing an accurate view of the inner organs of the human body without exposing any radiation to the patient.



Continuous improvements in technology are leading to higher resolution images and thus to new applications, which is also an important contribution to cost reduction by replacing more expensive and harmful diagnostics.

Diagnostic ultrasound is the most innovative sector of the diagnostic imaging market today and constitutes the largest imaging

modality worldwide.

As an independent supplier, *sonoTECH* provides research and development services to the worldwide ultrasound community.

*sonoTECH* is uniquely positioned to serve as an extension to the customer's research and development operations by providing state of the art ultrasound know-how.



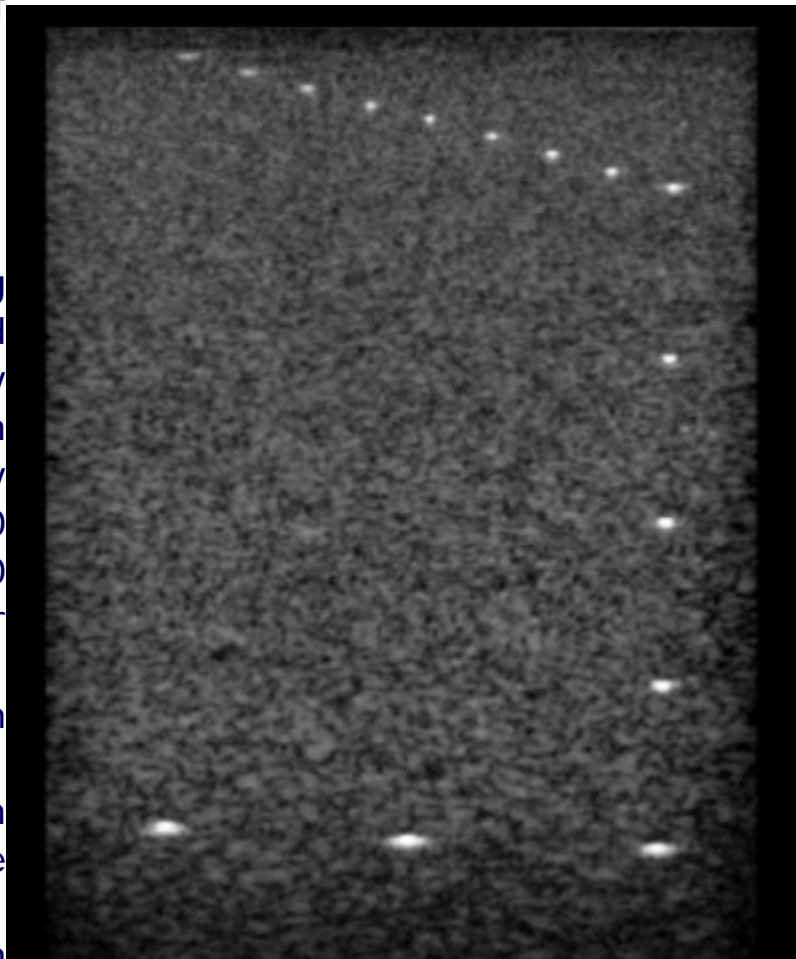
*sonoTECH's* technical expertise covers every item throughout ultrasound imaging and Doppler technology from low noise front ends, high performance analog or digital beam formers, spectral and color Doppler processing modules to digital scan converters and cine loop subsystems.

## Ultrasound

### Know-how

*sonoTECH's* engineering department has developed a number of successful technologies including:

**Analogue Beam Forming** for linear and curved array transducers in the frequency range from 1.0 MHz to 10.0 MHz. Our sophisticated analogue beam forming technology with 32 or more channels achieves an outstanding image quality at a very competitive cost level. The high dynamic range in combination with the low noise levels results in

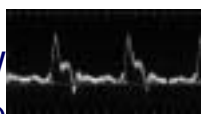


sharp, clear and  
crisp 2D,  
Spectral Doppler  
and Color Flow  
images.

The Imaging  
System for  
**Mechanical**  
**Probes** (2 MHz  
to 15 MHz),  
including  
digitally  
controlled servo  
module for  
mechanical  
probes, which  
supports  
transducer  
geometries up to  
360 degrees.

**Digital Beam**  
**Forming** allows  
finer delay  
quantization,  
higher phase  
accuracy and  
more versatility  
for linear-curved  
and phased  
array high end  
ultrasound  
systems.

Our CW and  
interleave  
(duplex) PW  
highly sensitive  
**Spectral**



## Doppler

Modules with FFT  
Spectrum  
Analyzer and  
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Processing.

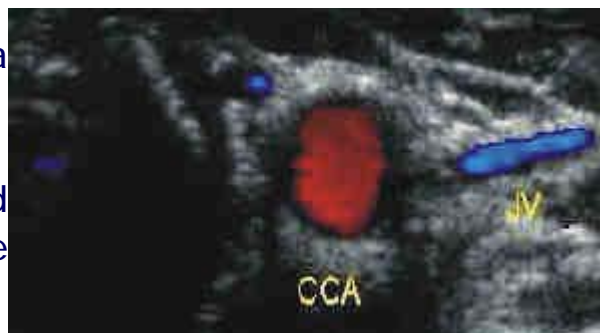
The **Digital  
Scan Converter**  
performs  
continuous  
zooming of living  
and even frozen  
images, with  
cine loop  
capabilities of up  
to 256 images  
for linear and  
sector  
geometries with  
scan angles up to  
360 degrees.

## The Physiological Channels

Module including  
ECG.

## The Color Flow Processing

Module uses a  
second  
generation,  
highly advanced  
multi gate  
autocorrelation  
technique in  
combination with



an improved  
(lossless)  
stationary echo  
canceller for  
higher flow  
sensitivity and  
resolution even  
at lowest blood  
velocities.

This is achieved  
by using the  
paralleled  
processing  
power of ten  
high speed signal  
processors.

All **Color  
Doppler modes**  
like velocity  
mode,  
velocity-variance  
mode, intensity  
mode,  
directional  
intensity mode,  
tissue doppler  
mode and  
B-Flow are  
supported at  
fundamental and  
harmonic  
frequencies.



## **MRI Signals**

### **Medical Applications**

#### **Multiple Sclerosis**

**MRI is providing scientists with a clear view of the circuitry of the brain, and it is showing them how the brain works, as well as how disease causes it to malfunction. For example, multiple sclerosis (MS) is a chronic, progressive disease that afflicts roughly a quarter-million Americans. Typical symptoms include loss of balance, paralysis, numbness, visual disturbances, incontinence, and even dementia. These symptoms, resulting when components of the immune system misguidedly attack specialized sheaths that insulate connections between nerve cells, vary greatly, making diagnosis difficult. But MRI can overcome such diagnostic uncertainties because it readily shows those damaged sheaths as small, whitish spots.**

**MRI also can help doctors determine whether or when a patient with early-stage MS needs treatment. Even when a patient appears clinically stable, the disease can be stealthily ravaging the brain, and such early-stage MS patients usually should be treated, whereas those whose MRIs show few active lesions may safely delay treatment.**

**Researchers are developing other, potentially more accurate ways to monitor MS with MRI. Dr. Richard Rudick and Dr. Elizabeth Fisher of the Cleveland Clinic Foundation use MRI to measure brain volumes with precision. Among healthy men and women 20-50 years old, 87 percent of the brain volume is tissue and the remaining 13 percent is water, with less than one percent variability. However, among individuals with MS, the tissue fraction declines by about 0.7 percent**

**annually. Measuring these declining tissue volumes may enable physicians to determine how long individual patients have had MS and to more accurately predict the course of the disease. "It looks as if the atrophy severity and the**

**change in atrophy score predict the patient's status 6-8 years down the line," says Dr. Rudick. This use of MRI also might help determine whether a patient's treatment is working, as well as the effectiveness of new drugs being tested in clinical trials.**

## **Stroke**

**Another devastating brain disease, stroke, is the third leading cause of death in the U.S. About 550,000 strokes occur annually, killing roughly 100,000 people and leaving many others severely disabled. One such patient, a retired college professor who was writing a book when stricken, was left paralyzed and with so little short-term memory that she was usually unable to recall which close friend had visited her as recently as an hour earlier.**

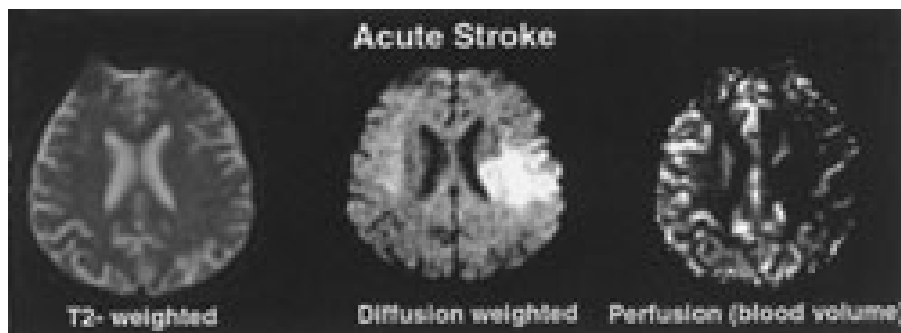
**Most strokes occur when a brain artery is blocked, either by a clot growing on the vessel wall, or, as in the case of this college professor, by one that the blood swept into the brain from elsewhere in the body. Less often, in about 20-25**

**percent of cases, a stroke may result from a ruptured blood vessel. In both cases, brain tissue that becomes deprived of oxygen quickly dies. However, knowing the cause of stroke is critical for determining how stroke patients are treated. Strokes caused by clots are treated with clot-busting thrombolytic drugs, provided the patient reaches the hospital within three to six hours of onset. However, if the stroke arises from a hemorrhage such drugs need to be resolutely avoided because they can make matters worse.**

**Most patients with an acute stroke receive a CT scan before MRI, because CT is particularly sensitive to bleeding in the brain and also because such instruments are cheaper and thus more widely available than MRI. While CT shows bleeding, MRI can reveal the size and location of the stroke far more accurately and precisely than CT. This more detailed information can be vital when making treatment decisions.**

**A recently developed MRI technique, called diffusion imaging (Fig.2), can diagnose strokes within minutes, revealing the location and size of damage. Diffusion imaging highlights the random movement, or diffusion, of water, which decreases when a stroke kills nerve cells. Thus, where neurons are dying, there is a net flow of water from the extracellular spaces into the cells. Since water diffuses relatively freely outside cells, while its movement is constrained inside cells by all the cellular machinery, there is less than ordinary diffusion in the vicinity of the stroke, and this difference shows up clearly on diffusion MRI. That movement of water from the extracellular spaces into the dying neurons takes place because normal, healthy cells, including neurons have a lower concentration of salt than the surrounding extracellular fluids. Therefore salt leaks into the neurons, like water seeping into a boat through tiny holes in the gunwales, and so the neurons have to bail it. They have special pumps just for this task. But as a clot chokes off the blood, the bailing pumps lose their energy**

**supply and stop working, and the cell dies. Salt flows inward and water follows.**



**Figure 2. Three different MRI imaging protocols of a patient 20 min after a stroke event. The T2 weighted image in the first panel shows some structural information about the patient's brain but no evidence of the site of the stroke. The diffusion weighted image, which monitors the random movement of water, shows a distinct lesion on the right side of the patient (right side of middle panel). This is representative of decreased water diffusion in the area of the stroke, where there are dead neurons. The third panel shows a perfusion image, which demonstrates regions of the brain where there is reduced blood flow. The region of reduced blood flow in this patient (dark areas) is**

**identifiable by the lower contrast and structural detail. This is larger than the area highlighted in the diffusion-weighted image, which may indicate that there may be additional neuronal cell loss. Courtesy of Drs. Steven Warach and Lawrence Lator, National Institutes of Neurological Disorders and Stroke, National Institutes of Health, MD.**

**One challenge in treating strokes is that most victims do not reach the hospital quickly enough to be candidates for thrombolytic drugs, which ordinarily are effective only when used within about three hours of onset. But Dr. Chelsea S. Kidwell of the University of California, Los Angeles and her colleagues are developing a means for using MRI imaging information to predict whether particular patients might benefit from such thrombolytic treatments at times following that usual three-hour window. "We believe that the information we are obtaining from the MRI will indicate if there is still salvageable tissue beyond these absolute time**

**windows, and that this information could then be used to make treatment decisions," says Dr. Kidwell.**

**The central area of the stroke, where the blood supply is choked off, may be surrounded by an area where the blood flow is merely restricted, stressing the still-undamaged nerve cells. A recently developed technique called perfusion-weighted MRI can measure this blood flow (Fig. 2). Combined with diffusion-weighted images, it can provide valuable information about how the stroke may progress. If an area of low blood flow surrounds the central area of the stroke, the stroke is likely to spread, unless normal blood flow is quickly restored. But if not, doctors can be pretty sure that the stroke has run its course and that further treatment with thrombolytic drugs offers no benefit.**

**Within hours following a stroke, the brain begins adapting to its new limitations, marshalling regions that normally have nothing to do with the tasks that the damaged region had been performing. Sometimes, however, the damage**



**overwhelms this limited ability of other brain segments to adapt to performing new activities. Using functional MRI (see box previous page), Dr. Marcel Just of Carnegie Mellon University is developing therapies that aim at improving the damaged brain's capacity to deal with its changed circumstances. For instance, patients whose language networks are damaged by stroke often can no longer understand complex sentences. Based on functional MRI studies, Dr. Just learned that the undamaged brain sometimes enlists the prefrontal cortex to reason through unfamiliar tasks. To engage the prefrontal cortex to help language-impaired stroke patients overcome some of their speech-associated difficulties, Dr. Just has presented them with sentences, asking them to find the verb, and to explain the action. He finds that, over a month, some patients improve so much that they could again analyze complex sentences as quickly as subjects with normal brains. Functional MRI studies indicate that the patients' prefrontal cortices again are active when the patients converse.**

## **Brain Surgery**

**It is no accident that brain surgeons use many, if not all, the MRI tools that are available. Operating on the brain is delicate and complex for many reasons. The skull is difficult to penetrate, nerve cells are easily damaged and slow or impossible to repair, and anatomic landmarks are difficult to discern. Even with MRI to help in visualizing the functional anatomy of the brain, brain surgeons are afforded a view that is more like that from a tiny porthole rather than a picture window.**

**Thus, despite their value, conventional MRI maps of the brain have shortcomings. When tumors or otherwise diseased tissues are extracted, the brain undergoes seismic-like shifts, rendering the original map inaccurate. "When the tumor comes out, it leaves this hole," says Dr. Jolesz of Brigham and Women's Hospital. "The remaining cortex is falling in, and so there are deformations.**

**You can't use the original image to guide the surgery."**

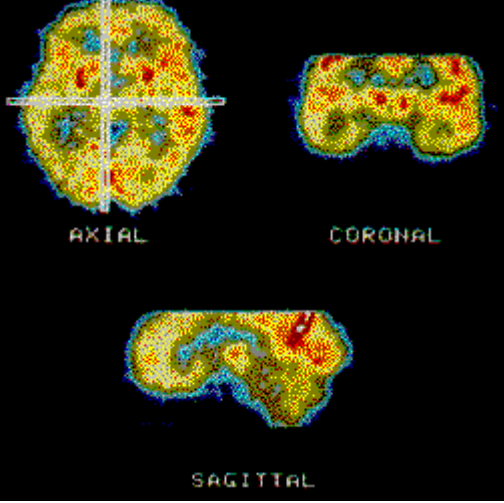
**Edema, or swelling that occurs during surgery may also shift the terrain. At Brigham and Women's, however, recent improvements being made to conventional MRI mapping procedures are changing all that.**

**Before surgeons ever scrub for surgery, they review three-dimensional composites of various MRI images of their patients' respective brains to plan the best path to a particular damaged area and to avoid causing incidental damage, such as "big bleeds." First, conventional MRI provides a structural map, pinpointing the tumor and major arteries in its vicinity. Additionally, functional MRI maps help to locate centers of speech, movement, and other critical functions.**

**Typically during MRI-guided brain surgery, a patient lies upon a platform that spans two magnets shaped like huge tires that are spaced far enough apart for members of the surgical team to stand between them. Initially, a monitor**

**above the surgical field displays the same image that the surgeon studied, but aligned precisely with the patient's brain, providing the surgeon with the virtual equivalent of X-ray vision. Throughout the operation, the MRI system provides a series of fresh images, each new one overlaying its predecessor on the screen, thereby updating any shifts within the anatomic terrain. Moreover, a special probe enables the surgeon to monitor specific sites along the incision within the brain, providing fresh images that appear immediately upon the screen above.**

**Not only does this MRI-based technology reduce the danger of damaging the brain, it also enables surgeons to remove more of each tumor that they encounter. Before this image-guided surgery became available, up to 80 percent of operations ultimately failed because they left bits of low-grade tumor behind.**



**PET Signals**



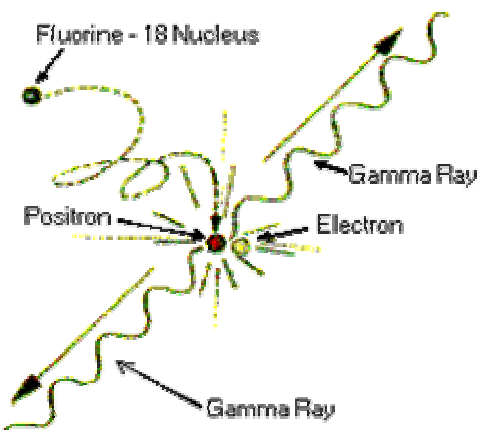
## *Positron Emission Tomography*

[Welcome Page](#)

### **What is PET?**

**The name "PET" comes from Positron Emission Tomography. It is a new scanning technique in medical research. PET allows us, for the first time, to measure in detail the functioning of distinct areas of the human brain while the patient is comfortable, conscious and alert. We can now study the chemical process involved in the working of healthy or diseased human brains in a way previously impossible. Before the advent of the PET scanner, we could only infer what went on within the brain from post-mortems (dissections after death) or animal studies.**

## **Positron Emission Tomography**



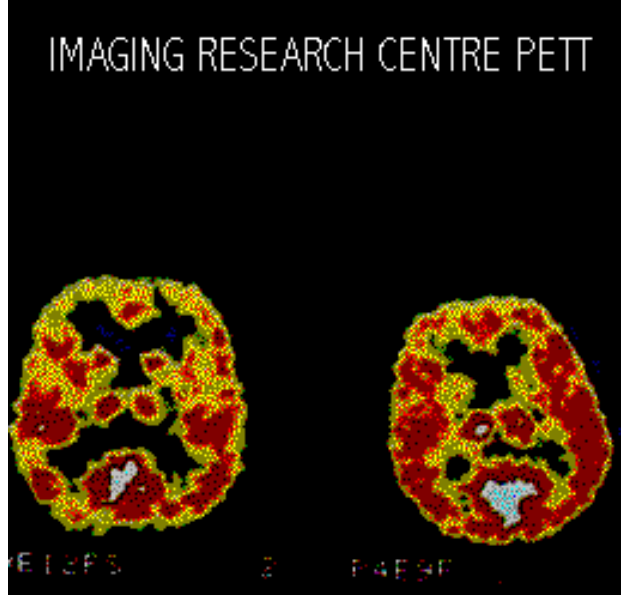
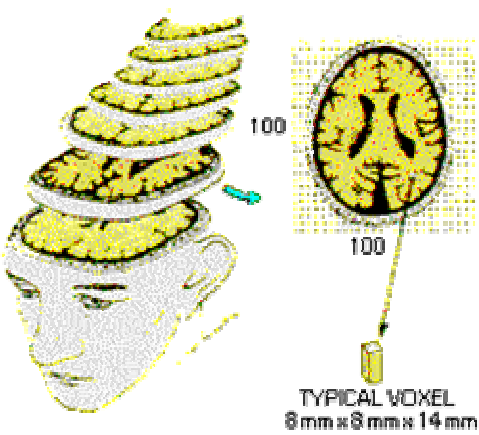
**PET represents a new step forward in the way scientists and doctors look at the brain and how it functions. An X-ray or a CT scan shows only structural details within the brain.**

**The PET scanner gives us a picture of the brain at work.**

**Positron: Antimatter equivalent of the electron**

**A positron is an anti-electron. Positrons are given off during the decay of the nuclei of specific radioisotopes. A type of radioactive fluorine produced at TRIUMF for the PET programme is a positron emitter. When matter collides with its corresponding antimatter, both are annihilated. When a positron meets an electron, the collision produces two gamma rays having the same energy, but going in opposite directions. The gamma rays leave the patient body and are detected by the PET scanner. The information is then fed into a computer to be converted into a complex picture of the patient working brain.**

## Typical "Slice"



### How does it work?

A conventional "X-ray" is taken by firing X-rays through a person and onto a film. This "shadow" image shows some structures in the body, such as cartilage and bone. A CT scanner uses fine streams of X-rays. By firing them through the body from several directions, the CT scanner is able to build up a composite picture of anatomical details within a "slice" through the person. Magnetic Resonance Imaging (MRI) does much the same thing, but using magnetic and radiowave fields. In contrast, the PET scanner utilizes radiation emitted from the patient to develop images. Each patient is given a minute amount of a radioactive pharmaceutical that closely resembles a natural substance used by the body. One example of such a pharmaceutical produced at TRIUMF is 2-fluoro-2-deoxy-D-glucose (FDG),

**which is similar to a naturally occurring sugar, glucose, with the addition of a radioactive fluorine atom. Gamma radiation produced from the positron-emitting fluorine is detected by the PET scanner and shows in fine detail the metabolism of glucose in the brain.**



**How does it feel to have a PET scan?**

**During a scan the patient reclines on a comfortable couch with his or her head inside the large,**

**doughnut-shaped Positron Emission Tomograph. While the patient head must be kept very still, the only real discomfort involved may be the pinprick of a hypodermic needle as a minute amount of radiopharmaceutical is injected. The radiopharmaceutical could be administered as an intravenous injection or inhaled as a gas. How it is administered depends on the radiopharmaceutical. Which**

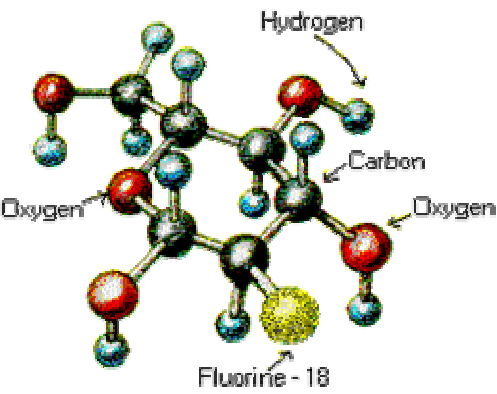


**one is chosen depends on what function the scientist wants to study.**

**What does a PET scan show?**

**The brain function being studied during a PET scan determines which radiopharmaceutical is used. Oxygen-15 can be used to label oxygen gas for the study of oxygen metabolism, carbon monoxide for the study of blood volume, or water for the study of blood flow in the brain. Similarly, fluorine-18 is attached to a glucose molecule to produce FDG for use in the observation of the brain sugar metabolism. Many more PET radiopharmaceuticals exist, and research is under way to develop still more to assist in the exploration of the working human brain. For example, dopa, a chemical active in brain cells, is labelled with positron-emitting fluorine or carbon and applied in research on the communication between certain brain cells which are diseased, as in dystonia, Parkinson disease, or schizophrenia.**

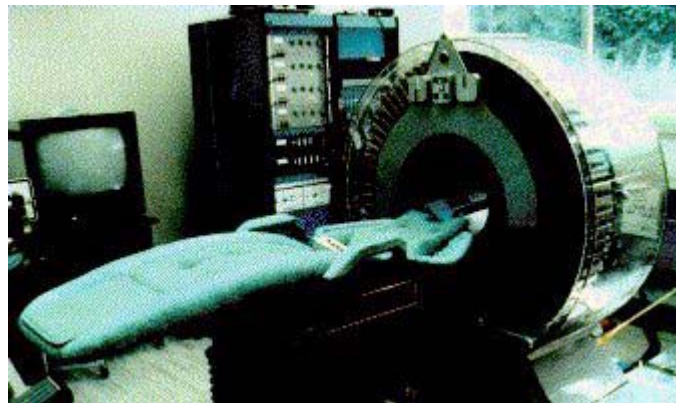
**2-fluoro-  
2-deoxy-D-glucose  
"FDG"**



**How much radiation does a patient get?**

**PET scans using radioactive fluorine in FDG would result in patients receiving exposures comparable to (or less than) those from other medical procedures, such as the taking of X-rays. Other scanning agents - for instance, 6-F-dopa or radioactive water - normally cause even less exposure.**

**cyclotrons and radiochemistry laboratories at the TRIUMF project that are the source**



**of the PET scanning agents. The laboratories are linked to the UBC Health Sciences Centre Hospital by the world longest "pea shooter", a 2.4 km pneumatic pipeline used for**

## **the PET: Research tool of the future**

**The PET programme at TRIUMF and UBC is in a unique position among world medical research centres in having many of the expensive major facilities required to mount a powerful PET programme. These include the delivery of PET scanning agents in the shortest possible time. These facilities have a capacity that has not been equaled by any other university/health sciences centre in the world.**