The Origin of Biopotentials
(Review of physiological concepts)

- Bioelectric phenomenon is of immense importance to biomedical engineers because these potentials are routinely recorded in modern clinical practice.

- ECG (Electrocardiogram), EMG (Electromyogram), EEG (Electroencephalogram), ENG (Electroneurogram), EOG (Electro-oculogram), ERG (Electroretinogram), etc. are some examples of biopotentials. **We will briefly look at origin of ENG, EMG and ECG in this talk.**

- As engineers, we should have a good physical insight into the nature of electromagnetic fields generated by bioelectric sources. Therefore we could contribute to quantitative solution of biological problems.

To understand the origin of biopotentials we need to focus on:

- **Bioelectric phenomena at the cellular level**

- **Volume conductor fields of simple bioelectric sources**

- **Volume conductor fields of complex bioelectric sources**

- **Volume conductor fields as a necessary link between cellular activity and gross externally recorded biological signals**
**Electrical Activity of Excitable Cells**

Biopotentials are produced as a result of electrochemical activity of excitable cells: i.e., nervous, muscular (cardiac and smooth) and glandular cells

**Factors influencing the flow of ions across the cell membrane**

1. Diffusion gradients

2. Inwardly directed electric field (inside negative, outside positive)

3. Membrane structure (availability of pores; $K^+$, $Na^+$ and permeability of membrane to different ions)

4. Active transport of ions across membrane against established electrochemical gradients

- Electrically these cells exhibit a **resting membrane potential** [Nernst (1) and Goldman/Hogkin and Katz equation (2)]

\[
V_m = \frac{RT}{nF} \ln \frac{[K^+]_e}{[K^+]_i} \tag{1}
\]

\[
V_m = \frac{RT}{nF} \ln \frac{\{pK [K+]_e + pNa [Na+]_e + pCl [Cl-]_e\}}{\{pK [K+]_i + pNa [Na+]_i + pCl [Cl-]_i\}} \tag{2}
\]

- When appropriately stimulated, they generate an action potential (flow of ions across the cell membrane and generation of a propagating wave of depolarization along the membrane)
Bioelectric phenomena at the cellular level

Recording of action potential of an invertebrate nerve axon
A very important topic in electrophysiology is the relationship between intracellular and extracellular potentials, especially in nerve or muscle fibres.

The relation between extracellular potentials (A-E), transmembrane potential \( V_m \) (part F) and the second derivative of \( V_m \) (part G).

**Note:**

The relationship between transmembrane (action potential) \( V_m \) (monophasic) and volume conductor (extracellular field) potential \( \frac{d^2 V_m}{dt^2} \) (triphasic). Students interested in the biophysics of this topic should refer to: Bioelectric Phenomena by Robert Plonsey.
Volume conductor fields of simple bioelectric sources

Transmembrane \( (E_t = V_m) \) and extracellular action potentials \( (E_x) \) obtained from different excitable tissues. *Note the monophasic and triphasic shapes.*

a. Frog semitendinous muscle

b. Toad sartorius muscle

c. Rabbit atrium

d. Squid giant axon
Volume conductor fields of complex bioelectric sources

Electrogenesis of Electro-neurogram (ENG)

Consider the bioelectric source as an active nerve trunk (thousands of nerve fibres bundled together in a nerve trunk).

When activated, the extracellular field in a volume conductor appears quite similar to that of a single fibre. See the figure below:

Note:
- The extracellular field potential is a signal formed from the contribution of the superimposed electric fields of the component sources within the trunk.
- The general form of the response is *triphasic* as expected!

Clinical Application
Measurement of Neural Conduction Velocity

Why is it important?
• Conduction velocity in a regenerating nerve fibre is slowed following nerve injury.

How do we measure it?
• Stimulate a motor nerve at 2 points a known distance part along its course.
• Subtract the shorter latency from the longer latency
• Find the conduction time between stimulating electrodes

\[ \text{Velocity} = \frac{\text{known distance}}{\text{conduction time}} \]

For more on this subject and the variety of methods used in measuring the neural conduction velocity refer to Webster and physiology texts.
The electromyogram (EMG)

Skeletal muscle is organized functionally on the basis of the motor unit. This is shown in the figure below:
Diagram of a single motor unit (SMU)

- The motor unit is the smallest unit that can be activated by a volitional effort (all constituent muscle fibres are activated synchronously)

- Single motor unit (SMU) consists of a single motor neuron and the group of skeletal muscles that it innervates

- SMU is a distributed unit bioelectric source in a volume conductor consisting of all other muscle fibres, both active and inactive

- The evoked extracellular field potential from the active fibres of an SMU has a triphasic form of 3-15 ms duration and 20-2000 µV amplitude depending on the size of SMU
The figure below shows motor unit potentials from a normal muscle under graded levels of contraction. At high levels of activity, many sophisticated motor unit responses give rise to a complicated response (interference pattern).
A variety of electrodes have been developed for EMG recording

The figure below shows the needle and wire electrodes used in recording the EMG signal

The EMG is also of considerable clinical value

The shape of SMU potentials is modified by disease

The figure below shows the EMG response for a normal subject and one with neuropathy

EMG response of a normal and an abnormal subject. Note the changes due to pathology.

Note:
In presence of disease, both excitability of neurons and the velocity of propagation along them may decrease or disappear ➔ desynchronization!
**Electrocardiogram (ECG)**

**The conduction system of the heart**

- It consists of the sinoatrial (SA) node, the internodal tracts, the atrioventricular (AV) node, the **bundle of His**, the right bundle branch (RBB), the left bundle branch (LBB), and the **Purkinje** network.

- The conduction system of the heart and representative electrical activity from various regions is shown in the figure below.

The conduction system of the heart and representative electrical activity

![Heart Diagram](image)

**Note:** The contribution of electrical activity of various tissues of the heart in genesis of the ECG signal (the lowest trace)
• The rhythmic electrical activity of the heart (cardiac impulse) originates in the SA node.

• The impulse then propagates through internodal and interatrial (Buchman’s bundle) tracts.

• As a consequence, the pacemaker activity reaches the AV node by cell-to-cell atrial conduction and activates the right and left atrium in a very organised manner.

• Because atria and ventricles are separated by fibrous tissue, direct conduction of cardiac impulse from the atria to the ventricles can not occur and activation must follow a path that starts in the atrium at the AV node.

• The cardiac impulse is delayed in the AV node for about 100 msec. It then proceeds through the bundle of His, the RBB, the LBB and finally to the terminal Purkinje fibres which arborize and invaginate the endocardial ventricular tissue.

• The delay in the AV node allows enough time for completion of atrial contraction and pumping of blood into the ventricles.

• Once the cardiac impulse reaches the bundle of His, conduction is very rapid, resulting in the initiation of ventricular activation over a wide range.

• The subsequent cell-to-cell propagation of electrical activity is highly sequenced and coordinated resulting in a highly synchronous and efficient pumping action by the ventricles.

• Essentially, an overall understanding of the genesis of the ECG waveform (cardiac field potentials recorded on the body surface) can be based on a cardiac current dipole placed in an infinite (extensive) volume conductor.

• In the early 1900, Einthoven (the father of electrocardiography) postulated that the cardiac excitation could be viewed as a vector.
• He drew an equilateral triangle with two vertices at two shoulders and one at the navel.

• With the cardiac vector representing the spread of cardiac excitation inside the triangle, the potential difference measured between two vertices of the triangle (known as the limb leads), is proportional to the projection of the vector on each side of the triangle (see the figure below.)

![Einthoven equilateral triangle diagram](image)

Einthoven equilateral triangle. The vertices are: LA (left arm), RA (right arm) and LL (left leg). RL is the right leg used as a reference for potential difference measurements and is not shown. I, II and III represent electrocardiographic frontal limb leads. The + and - represent connection to the terminals of a biopotential amplifier. Lead I is the potential difference between LA and RA. Lead II is the potential difference between LL and RA. Lead III is the potential difference between LL and LA.

• Based on the aforementioned concepts, electrocardiographers have developed an oversimplified model to explain the electrical activity of the heart.

• In this model, the heart is considered as an electric dipole (points of equal positive and negative charges separated from one another by a distance), denoted by a dipole moment vector \( \mathbf{M} \), that can change its magnitude and direction.
• This dipole moment (amount of charge x distance between positive and negative charges) is called the *cardiac vector*.

• As the wave of depolarisation spreads throughout the cardiac cycle, the magnitude and orientation of the cardiac vector changes and the resulting bioelectric potentials appear throughout the body and on its surface.

• The potential differences (ECG signals) are measured by placing electrodes on the body surface and connected to biopotential amplifier (described in detail later).

• In making these potential measurements, the amplifier has a very high input impedance to minimally disturb the cardiac electric field that produces the ECG signal.

• As it was discussed before, when the depolarisation wavefront points towards the recording positive electrode (connected to the + input terminal of the bioamplifier), the output ECG signal will be positive-going, and when it points towards the negative electrode, the ECG signal will be negative-going.

• The time varying cardiac vector produces the surface ECG signal with its characteristic P wave, QRS complex and T wave during the cardiac cycle.

• The QRS complex is the most prominent part of an ECG signal and it has a range of 0.5 to 4 mV. The ECG signal has a frequency range of 0.01 to 250 Hz. The standard clinical bandwidth used for the ECG signal is 0.05-100 Hz. For monitoring applications, such as for intensive care patients and ambulatory patients, the bandwidth is restricted to 0.05-50 Hz. More on this in Chapter 6.
The Electroencephalogram (EEG)
EEG is the recorded representation of bioelectric potentials generated by the neuronal activity of the brain.

Basically, the brain is a gelatinous mass suspended in the meninges, the cerebrospinal fluid, skull and scalp.

The brain is composed of three major subdivisions: cerebellum, brainstem (medulla, pons, midbrain, diencephalon) and cerebrum.

The cerebellum is mainly involved with skeletal muscle functions and maintenance of balance. It coordinates smooth and directed movements.

The brain stem is the stalk of the brain and serves as a relay station for all afferent (sensory) and efferent (motor) nerve fibres between the spinal cord and higher brain centres. It also gives rise to ten of the twelve cranial nerves, which supply the muscles and glands of the head and major organs in the thoracic and abdominal cavities.

Throughout the entire brainstem runs a core of tissue called the reticular formation, which serves as a highly complex cluster of neurones involved in integration of information from many afferent pathways as well as from numerous other parts of the brain.

The cerebrum consists of the right and left hemispheres. The outer part of the cerebral hemispheres, the cerebral cortex, is a cellular shell 1.5 – 4 mm thick of grey matter.

The cerebral cortex is highly convoluted and is the most complex integrating center of the nervous system. It brings together basic sensory information into meaningful perceptual images and formulates ultimate decisions for control over the motor systems of the body.

The cerebral cortex is comprised of two layers: the paleocortex and the neocortex.

The paleocortex is located on the median surface and the base of the brain and the neocortex is present on the superior and lateral aspects of the cerebral hemispheres.

The neocortex is composed of six layers and its cells can be categorized
as pyramidal and non-pyramidal cells. There are approximately $10^{10}$ neurones in the human cerebral cortex, about 75% of, which is pyramidal.

- Pyramidal cells, named originally after their shape, have several characteristics. Their cell bodies are commonly triangular in shape, with the base down and the apex directed toward the cortical (superficial) surface.

- The cell bodies vary in size, from axial dimensions of $15 \times 10 \mu m$ up to $120 \times 90 \mu m$. A typical pyramidal cell consists of a long apical dendrite, about 2 mm long, that ascends from the apex of the cell body and enters the overlaying layers and terminally branches within the outermost layer of the neocortex.

- There is a dominant apical dendritic tree, looking like a forest of similarly oriented, densely packed units in the superficial layers of the neocortex, where extensive branching occurs.

- There is also a basilar dendritic system that extends out spherically from the cell body.

- Pyramidal cells also have an axon that emerges from the cell body and enters the subcortical white matter.
- The axons of all pyramidal cells terminate in excitatory synapses. The
initial segment of pyramidal cells is unmyelinated, as their recurrent branches.

- Axons of some pyramidal cells turn back toward the cortical surface to end via their many dendritic branches on the dendrites of other cells.

- It has been shown by electrophysiological studies that under normal circumstances, propagating action potentials in axons do not contribute significantly to surface cortical recordings.

- There reason being that action potentials travel in a large number of axons (running in many different directions relative to the surface) in a temporally asynchronized way. Therefore, their net contribution to the surface EEG is minimal and negligible.

- It has been shown that the vertically oriented pyramidal cells with their long apical dendrites running parallel to one another are the major contributors to the electrogenesis of the cortical field potentials (EEG signal).

A highly schematic representation of a pyramidal cell and its role in the generation of surface EEG signal

Let’s consider a single pyramidal cell, and explain how potential changes in
one part of the cell relative to other parts could generate the EEG signal.

- Excitatory synaptic inputs to the branches in the apical dendritic tree of the pyramidal cells cause depolarization of the dendritic membrane.

- This leads into generation of an excitatory postsynaptic potential (EPSP)

- As a result, a radially oriented dipole is set up and subthreshold current flows in a closed path through the cytoplasmic core of the dendrites and cell body of the cell, returning to the synaptic sites via the conducting extracellular medium.

- The lines of current flow make the extracellular medium close to the cell body act as a source with + polarity and the upper part of the apical dendritic tree to act as a sink with – polarity.

- This leads into recording a negative potential at the cortical surface.

- In case of inhibitory synaptic inputs to the branches in the apical dendritic tree, an inhibitory postsynaptic potential (IPSP) is generated with a reversal in the polarity of the current dipole, which leads into a generation of a positive cortical recording.

- Therefore, the influence of a particular dendritic postsynaptic potential on the cortical recording depends on its net excitatory or inhibitory effect and on its location relative to the measurement site.

In summary, the EEG (electroencephalogram) signal is a recording of the electrical activity of the brain. The EEG signal recorded at the cortex or the scalp is generated by the polled activity of billions of cortical and subcortical regions. The origin of the EEG signal is based on the electrical activity of the pyramidal cells. The EEG potentials primarily reflect the summated fluctuations of excitatory and inhibitory postsynaptic potentials in the pyramidal cells of the upper layers of the cerebral cortex. For reasons of geometry as well as because of extreme extracellular attenuation, action potentials from firings of pyramidal cells contribute only minimally or not all to the generation of the EEG signal.
• All we need to contend ourselves with at this stage is that the EEG or brain waves are summation of neural depolarizations in the brain due to the stimuli from the five senses as well as from thought processes (indeed a very complex source). More on this in physiology in the Nervous System topic

• EEG potentials have random-appearing waveforms with peak-to-peak amplitudes ranging from less than 10 mV to over 100 mV. Required bandwidth is from below 1 Hz to over 100 Hz.

• EEG is recorded with 3 types of electrodes:
  1. Scalp
  2. Cortical ➔ Electrocorticogram (recording from surface of cortex)
  3. Depth Electrodes ➔ recording from depth of brain (thin insulated needles of various designs)

• No matter where the recording is obtained from (scalp, cortex or depth of the brain), the fluctuating potentials represent a superposition of the volume conductor fields produced by a huge variety of active neuronal current-generators.

• On the surface of the brain (i.e. Electrocorticogram), we can record voltages on the order of 10 mV! but, typical EEG electrodes measure the electrical activity propagated through skull bone and is attenuated from 1 to 100 µV.

• EEG potentials vary as a function of position over the surface of the skull, making it necessary to select sets of electrodes grouped around Frontal, Parietal, Temporal and Occipital lobes.
The EEG Signal

- The character of the EEG signal is highly dependent on the degree of the activity of the cerebral cortex, i.e. waves change markedly between states of wakefulness and sleep.
- Much of the time, EEGs are irregular and no general pattern can be observed. Other times, distinct patterns emerge.

- The EEG waveform is divided into four wave groups:
  1. The Alpha Waves (α) → 8-13 Hz
  2. The Beta Waves (β) → 14-30 Hz
     (The Gamma Waves (γ) → 22-30 Hz or higher)
  3. The Theta Waves (θ) → 4-7 Hz
  4. The Delta Waves (δ) → <3.5 Hz

Note: During periods of mental activity, the waves usually become asynchronous rather than synchronous, so the magnitude of summed potentials decrease in spite of cortical activity.

- In general there is a relationship between cerebral activity and the frequency of the EEG rhythm.
- Frequency increases progressively with higher degrees of activity.

Examples:
- δ-Waves (<3.5 Hz) occur in surgical anesthesia and sleep.
- θ-Waves (4-7 Hz) occur in emotional stress and frustration.
- α-Waves (8-13 Hz) occur during relaxed states.
- β-Waves (14-30 Hz) occur during intense mental activity.
Sleep Patterns

The EEG changes that occur as a human subject goes to sleep
EEGs in Diagnosis

The purpose of the clinical EEG is to help neurologists diagnose disease. The pathological states most commonly diagnosed using EEG are:

- Brain death (legal death)
- Brain tumors
- Epilepsy
- Multiple Sclerosis
- Sleep Disorder
- Evoked responses (diseases of the audio, visual and tactile senses)

- Modern life sustaining equipment like respirators, kidney dialyzers, ventilators, artificial heart pumps have changes the definition of death

- A sustained absence of EEG signal is a clinical measure of brain death and can be used in deciding whether to transplant a heart, liver, or lung or whether to shut down the life sustaining equipment

Some Representative Abnormal EEGs

Petit mal epilepsy – Minor form of seizure, clouding of consciousness and loss of contact with the environment

Grand mal epilepsy – Sudden loss of consciousness, falling down, tonic contractions (stiffening of muscles) followed by twitching and jerking movements of the limbs

Psychomotor seizures are parietal seizures characterized by: semi-purposeful movements, changes in consciousness, hallucinations and illusions
EEG Electrode Positions

- In electroencephalography, the electrodes are placed in an arrangement referred to as the 10-20 system

- This is a placement scheme devised by the International Federation of Societies of Electroencephalography

- The electrodes are placed along a line drawn on the skull from the root of the nose, the nasion, to the inion ossification (bump on the occipital lobe)

- The first mark is placed 10% of the distance along this line and others are arranged at 20% intervals

Diagrammatic representation of the International 10-20 system for EEG electrode placement on the scalp
The EEG signal path is comprised of:
Scalp (biosignal source) ➔ EEG electrodes ➔ Junction box ➔ channel selector ➔ differential amplifier bank ➔ filters ➔ display

A junction box is shown below: