The Origin of Biopotentials

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INTRODUCTION

- Bioelectric potentials are produced as a result of electrochemical activity of a certain class of cells, known as excitable cells that are components of nervous, muscular, or glandular tissue (*bez doku*).
 - Nerve, skeletal, cardiac and smooth muscle
- Electrical activity of excitable cells:
 - By default, excitable cells are at the **RESTING POTENTIAL**
 - When they are excited, they produce an ACTION POTENTIAL

RESTING POTENTIAL

Imagine taking two electrodes and placing one on the outside and the other on the inside of the plasma membrane of a living cell. If you did this, you would measure an electrical potential difference, or voltage, between the electrodes. This electrical potential difference is called the **membrane potential**.



Ion Concentration in a Cell

- In neurons and their surrounding fluid, the most abundant ions are:
- Positively charged (cations): Sodium (Na⁺) and potassium (K⁺)
- Negatively charged (anions): Chloride (Cl⁻) and organic anions.
- In most neurons, K⁺ and organic anions (such as those found in proteins and amino acids) are present at higher concentrations inside the cell than outside.
- In contrast, Na⁺ and Cl⁻ are usually present at higher concentrations outside the cell. This means there are stable concentration gradients across the membrane for all of the most abundant ion types.



BIG letters = high concentration tiny letters = low concentration

How Ions Cross the Membrane?

- Very thin lipoprotein complex
 - 7 to 15 nm
 - essentially impermeable to intracellular protein and other organic anions (A-).
- Some channels, known as leak channels, are open in resting neurons letting ions flow.



- Ion channels that mainly allow K⁺ to pass are called **potassium channels**, and ion channels that mainly allow Na⁺ to pass are called **sodium channels**.
- The membrane in the resting state is only slightly permeable to Na⁺ and rather freely permeable to K⁺ and Cl⁻.
 - Permeability of the resting membrane to potassium ion (P_K) is approximately 50 to 100 times larger than its permeability to sodium ion (P_{Na}).

Other ions are also present, including anions that counterbalance the positive charge on K⁺, but they will not be able to cross the membrane in our example.



Every time a K⁺ ion leaves the cell, the inside of the cell becomes negative relative to the outside, setting up a difference in electrical potential across the membrane.



If K+ can cross via channels, it will begin to move down its concentration gradient and out of the cell.

The movement of Kt ions down their concentration gradient creates a charge imbalance across the membrane.

The charge imbalance opposes the flow of kt down the concentration gradient. Eventually, the electrical force driving K⁺ back into the cell is equal to the chemical force driving K⁺ out of the cell. When the potential difference across the cell membrane reaches this point, there is no net movement of K⁺ in either direction, and the system is considered to be in equilibrium.



Equilibrium Potential

- The electrical potential difference across the cell membrane that exactly balances the concentration gradient for an ion is known as the equilibrium potential.
- The steeper the concentration gradient is, the larger the electrical potential that balances it has to be.



Both K⁺ and Na⁺ contribute to resting potential in neurons

- □ Na⁺ will try to drag the membrane potential toward its (positive) equilibrium potential.
- K⁺ will try to drag the membrane potential toward its (negative) equilibrium potential.
- However, it will be *closer* to the equilibrium potential of the ion type with higher permeability



- The Na⁺ and K⁺ concentration gradients across the membrane of the cell (and thus, the resting membrane potential) are maintained by sodium-potassium pump. If the Na⁺ K⁺ pump is shut down, the Na⁺ and K⁺ concentration gradients will dissipate, and so will the membrane potential.
- It actively transports Na⁺ and K⁺ against their electrochemical gradients.
- The energy for this "uphill" movement comes from ATP hydrolysis.
- For every molecule of ATP that's broke down, 3 Na⁺ are moved from the inside to the outside of the cell, and 2 K⁺ are moved from the outside to the inside.
- Pump makes membrane slightly more negative than it would otherwise be. It maintains steady Na⁺ and K⁺ gradients.

RESTING POTENTIAL

- Transmembrane potential of a cell arises due to diffrences in ionic concentrations as well as diffusion across a membrane.
- At rest, the net transport of ions accross the membrane is zero. This gives rise to a resting potential difference (voltage) accross the membrane.
- Electrically the membrane can be described as a leaky capacitor, since structurally it is comprised of a thin dielectric material (the lipoprotein complex) that acts as a charge separator



- Concentration of K+ determines the potential difference accross the membrane.
- K+ tens to diffuse from inside to outside.
- However, there is electrical field from external to internal medium inhibiting outward flow of K+ ions.
- The external medium of the cell is 40-90mV more positive than internal medium.
- At rest electrical field and diffusion cancels each other out resulting **no ion flow**.



This resting potential difference is given by the Nerst Equation (or Nerst Potential)
R : Universal gas constant

$$E_{\rm K} = \frac{RT}{nF} \ln \frac{[{\rm K}]_{\rm o}}{[{\rm K}]_{\rm i}} = 0.0615 \log_{10} \frac{[{\rm K}]_{\rm o}}{[{\rm K}]_{\rm i}}$$

T : Absolute temperature N : Valence of K (=1) F : Faraday constant [K]i : Intracellular concentration [K]o : Extracellular concentration

Resting membrane is approximated to a potassium membrane. Effect other ionic species is included in Goldman–Hodgkin–Katz (GHK) equation.

$$E = \frac{RT}{F} \ln \left\{ \frac{P_{\mathrm{K}}[\mathrm{K}]_{\mathrm{o}} + P_{\mathrm{Na}}[\mathrm{Na}]_{\mathrm{o}} + P_{\mathrm{Cl}}[\mathrm{Cl}]_{\mathrm{i}}}{P_{\mathrm{K}}[\mathrm{K}]_{\mathrm{i}} + P_{\mathrm{Na}}[\mathrm{Na}]_{\mathrm{i}} + P_{\mathrm{Cl}}[\mathrm{Cl}]_{\mathrm{o}}} \right\}$$

P is the permeabitity coefficient

If the permeability of ions except potassium is zero then equation becomes Nerst equation.

Example

Example: Concentration of potassium at the outside of membrane is [K⁺]_o=1 millimoles per liter (mmol/L), and concentration of potassium at the inside of membrane is [K⁺]_i=100 (mmol/L) then what is potential accross the membrane?

Answer:

$$E_{\rm K} = \frac{RT}{nF} \ln \frac{[{\rm K}]_{\rm o}}{[{\rm K}]_{\rm i}} = 0.0615 \log_{10} \frac{[{\rm K}]_{\rm o}}{[{\rm K}]_{\rm i}} \quad ({\rm V}) = -123 {\rm mV}$$

Example

For frog skeletal muscle, typical values for the intracellular and extracellular concentrations of the major ion species (in millimoles per liter) are as follows.

Species	Intracellular	Extracellular
Na ⁺	12	145
K^+	155	4
$C1^-$	4	120

Assuming room temperature (20°C) and typical values of permeability coefficient for frog skeletal muscle (P_{Na}=- 2 x 10⁻⁸ cm/s, P_K=2 x 10⁻⁶ cm/s, and P_{CI}=4 x 10⁻⁶ cm/s), calculate the equilibrium resting potential for this membrane, using the Goldman equation.

Answer

$$E = \frac{RT}{F} \ln \left\{ \frac{P_{\rm K}[{\rm K}]_{\rm o} + P_{\rm Na}[{\rm Na}]_{\rm o} + P_{\rm Cl}[{\rm Cl}]_{\rm i}}{P_{\rm K}[{\rm K}]_{\rm i} + P_{\rm Na}[{\rm Na}]_{\rm i} + P_{\rm Cl}[{\rm Cl}]_{\rm o}} \right\}$$

$$E = 0.0581 \log_{10} \left[\frac{P_{\rm K}(4) + P_{\rm Na}(145) + P_{\rm Cl}(4)}{P_{\rm K}(155) + P_{\rm Na}(12) + P_{\rm Cl}(120)} \right]$$
$$= 0.0581 \log_{10} \left(\frac{26.9 \times 10^{-6}}{790.24 \times 10^{-6}} \right) = -85.3 \,\mathrm{mV}$$



Example

□ The giant axon of the squid is frequently used in electrophysiological investigations because of its size. Typically it has a diameter of 1000 µm, a membrane thickness of 7.5 nm, a specific membrane capacity of 1pF/cm², and a resting transmembrane potential v_m of 70mV. Assume a uniform field within the membrane and calculate the magnitude and direction of the electric field intensity E within the membrane.

Answer

The membrane is quite thin, serves as a charge separator, and can be represented by a parallel-plate capacitor with E directed inward.

$$\mathbf{E} = \frac{v_{\rm m}}{d} = \frac{70 \times 10^{-3}}{7.5 \times 10^{-9}} = 9.33 \times 10^6 \,{\rm V/m}$$

Recording Of Action Potential Of An Invertebrate Nerve Axon



Recording Of Action Potential Of An Invertebrate Nerve Axon

Indifferent electrode An electronic stimulator supplies a brief pulse of current to the axon, Amp Recording strong enough to excite the axon. A micropipet recording of this activity is made at Axon a downstream site via a penetrating External bathing medium micropipette. Electronic stmulator The movement artifact is recorded (a) as the tip of the micropipette drives through the membrane to record Potential overshoot $(v_m > 0)$ Membrane potential (wm), mV resting potential. A short time later, Movement artifact Action potential an electrical stimulus is delivered to the axon; its field effect is recorded instantaneously at downstream -80 measurement site as the stimulus artifact. The action potential Stimulus artifact however, proceeds along the axon Resting potential with a constant conduction velocity. (b) The time period L is the latent period ot transmission time from stimulus to recording site.

THE ACTIVE STATE

- Another property of an excitable cell is its ability to conduct an action potential when adequately stimulated.
- The principal way of communication by neurons are by generating and propagating action potentials (APs).
- Action potential is a brief reversal of the membrane potential with a stimulation total amplitude of 100mV (-70mV to +30mV).
- An adequate stimulus is one that brings about the depolarization of a cell membrane that is sufficient to exceed its threshold potential and thereby elicit an all-or-none action potential (brief transient disturbance of the membrane potential), which travels in an unattenuated fashion and at a constant conduction velocity along the membrane.
- □ For a nerve fiber, stimulation of $\Delta V \approx 120 \text{mV}$ and the duration approximately 1ms is required.
- Further increases in intensity or duration of stimulus beyond that required for exceeding the threshold level produce only the same result.

Depolarization Phase

- Property of an excitable cell is its ability to conduct an action potential
- As a depolarizing stimulus arrives at the cell membrane, a few Na+ channels open, permitting Na+ ions to enter the cell.
- The increase in positive ions inside the cell depolarizes the membrane potential (making it less negative),
- Brings it closer to the threshold at which action potential is generated.





- If the depolarization reached the threshold potential (resting potential +10mV) additional voltage-gated Na channels open. Action potential is generated
- Positive Na+ ions rush into the cell, the voltage across the membrane rapidly reverses and reached its most positive value.

Rising Phase



- At the peak of the action potential, two processes occur simultaneously.
 - First, many of the voltage-gated Na channels begin to close.
 - Second, many of the K channels open, allowing positive charges to leave the cell.
- This causes the membrane potential to begin to shift back towards the resting membrane potential.

Falling Phase



 As the membrane potential approaches the resting potential, voltage-gated K channels are maximally activated and open.

Hyperpolarization



- The membrane actually repolarizes beyond the resting membrane voltage.
- This undershoot occurs because more K channels are open at this point than during the membrane's resting state.
- Allows more K+ ions to leave the cell.

Recovery Phase



- The return to steady state continues as the additional K channels that opened during the action potential now close.
- The membrane potential is now determined by the subset of K channels that are normally open during the membrane's resting state.



Propagation of an Action Potential along a Nerve Cell



Charge Distribution In The Vicinity Of The Active Region Of An Unmyelinated Fiber Conducting An Impulse

- Region of the fiber undergoing a transition into the active state (the active region) at an instant of time is usually small relative to the length of the fiber.
- A reversal of polarity is shown within the active region because of depolarization of the membrane to positive values of potential.
- The membrane lying behind the active zone is repolarized membrane.
- From charge distribution at the left of active region, *solenoidal* (closed-path) current flows in the pattern
- Self-excitatory process: each new increment of membrane being brought to the threshold level by lines of current from the active source region.
- The membrane stays in the active state for only a brief period of time and ultimately repolarizes completely.



Local Circuit Current Flow In The Myelinated Nerve Fiber

- The myelinated nerve fiber is activated, conduction proceeds through a process of local circuit current flow, much as in the case of the unmyelinated nerve fiber
- There are differences, however, in that the sources for action current flow are localized at the nodes of Ranvier and are therefore not uniformly distributed along the axonal membrane, as in the case of the unmyelinated fiber.
- Thus myelinated nerve fiber conduction proceeds via
 - rapid, sequential activation of the nodes of Ranvier, and
 - local circuit current provides the underlying mechanism for bringing the nodal membrane voltage to threshold.





Volume Conductor Electrical Field

- Most biomedical recordings occur on the surface of the body
- How does microscopic cellular electrical activity conduct to the body's surface for gross, external measurement such as ENG, EMG and ECG?
- Volume conductor electric field (VCEF) is a model for link (mapping) between
 - microscopic electrical activity generated within the bioelectric source
 - macroscopic potential distribution produced at the surface of the body
- VCEF describes flow of action current through the conducting medium
 - conducting medium = infinite (relative to source) volume conductor
- two components of the model
 - bioelectric source modeled as a constant current source.
 - conducting medium modeled as an electrical load.
- lends to insight into the interpretation of recorded waveforms



Volume Conductor Fields

The problem consists of two parts: (1) the bioelectric source and (2) its bathing medium or electrical load. The bioelectric source is the active cell, which behaves electrically as a constant-current source, delivering its solenoidal activation current to the resistive bathing medium over a large range of loading conditions.



Volume Conduction

Ohm's law for a volume conductor

J=σE

- up where J is current density (mA/m²), σ (1/Ωm)is conductivity and E (V/m) is electrical field.
- Where σ range in the body from 0.006 (Ωm)⁻¹ (Bone) to 1.5 (Ωm)⁻¹ (Cerebrospinal fluid)
- Volume conduction of the body is important to bioinstrumentation for two main reasons:
- It allows to measure heart, brain muscle etc. Activity on the surface of the body.
- It quantifies safety limits on the operation of electrical bioinstrumentation with human subjects.
Example

- Assume an electric shock of 120Vdc is applied to a man from his hand as shown in the figure. Arm parameters are given as L=1m, A=25cm², σ=0.5 (Ωm)⁻¹. What will be the current passing through subject's arm?
- □ Answer:

 $J = \sigma E \rightarrow I/A = \sigma V/L \rightarrow V = I\sigma^{-1}L/A = RI$ then

 $R = \sigma^{-1}L/A -> R = 800\Omega$

I=V/R=120/800=150mA (lethal)



Biopotential

- Biopotentials (EEG, ECG, EMG, ...) result from volume conduction of currents sourced and sunk by collections of electrically active cells (neurons, myocytes) into the extracellular medium.
- Source can be modeled as a current monopole
 Current emanates radially from the source. Conservation of current for any R

$$I = 4\pi R^2$$
. $J(R)$, $J = \frac{I}{4\pi R^2}$

Electric field due to volume conduction

$$E(R) = \frac{1}{\sigma}J(R) = \frac{I}{4\pi\sigma R^2}$$

Potential due to volüme conduction of point source +I.

$$V(R) = -\int E(R)dR = \frac{I}{4\pi\sigma R}$$



Example

A single cell generates a 100mV action potential in 1ms. The cell diameter is 20µm and its membrane capacitance is 1µF/cm². What is the amplitude of the extracellular potential at 10cm distance? Assume σ =0.1 (Ω m)⁻¹.

Answer:

V

$$-I = C \frac{dV_m}{dt}$$

$$C = 1\mu F/cm^2 \cdot \pi \cdot (20\mu m)^2 \approx 12.6 pF$$

$$\frac{dV_m}{dt} = \frac{\Delta V_m}{\Delta t} = \frac{100mV}{1ms} = \frac{100V}{s}$$

$$I = -1.26mA$$

$$V(10cm) = \frac{I}{4\pi\sigma R} = \frac{-1.26mA}{4\pi 0.1(\Omega m)^{-1}0.1m} = -10mV$$

- For every source of current in the body, there must be another and matching sink of current, balancing to zero net current for net change conservation.
- The simplest model for this is a dipole.
- \Box V=+ ∞ at the source
- \Box V=- ∞ at the sink
- □ V=0 at the midplane between source and skin or at ∞ distance from source and sink





Current Dipoles In the Body

- Current dipoles are everwhere in the body
- Action potentials trvaleling along axons



Systolic waves in cardiac myocytes tissue



Origins of Biopotential



Extracellular field potentials (average of 128 responses) recorded at the surface of an active (1 mm-diameter) frog sciatic nerve in an extensive volume conductor. The potential was recorded with

(a) both motor and sensory components excited (Sm + Ss),

(b) only motor nerve components excited (*Sm*), and

(c) only sensory nerve components excited (*Ss*).



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Organization of Peripheral Nervous System

- □ A sense organ, consisting of many individual sense receptors that respond preferentially to an environmental stimulus of a particular kind, such as pressure, temperature, touch, or pain.
- A sensory nerve, containing many individual nerve fibers that perform the task of transmitting information (encoded in the form of action potential frequency) from a peripheral sense receptor to other cells lying within the central system (brain and spinal cord).



Organization of Peripheral Nervous System

- **The central nervous system (CNS)** central integrating station.
 - Information is evaluated, and, if warranted, a "motor" decision is implemented.
 - Action potentials are initiated in motor-nerve fibers associated with the motor-nerve trunk.
- A motor nerve, serving as a communication link between the CNS and peripheral muscle.
- The effector organ, ex skeletal muscle fibers -- contract (shorten) in response to the driving stimuli (action potentials) conducted by motornerve fibers.



Knee Jerk Reflex



http://faculty.pasadena.edu/dkwon/PNS%20and%20propioception/peripheral%20nervous%20system%20and%20propioception_file s/textmostly/slide49.html

Block diagram of control system



- This simple reflex arc has many of the features of a negativefeedback loop, in which the control variable is muscle length.
- CNS acts as the controller,
- the muscle spindle as a feedback length sensor, and
- the muscle-limb system as the process to be controlled.

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Neuromuscular Junction: Communicating link between neurons and muscle fibers

- a neurotransmitter substance acetylcholine (ACh) diffuses across a very small fluid-filled gap region approximately 20nm in thickness.
- Once ACh reaches the postjunctional membrane, it combines with a membrane receptor complex that activates an ion channel, which leads to a relatively brief transient depolarization of the postjunctional membrane and subsequently to the initiation of an action potential that propagates away from the junctional region.
- a time delay on the order of 0.5 to 1.0 ms occurs.



Contractile elements within muscle fiber



Electroneurogram (ENG)

- ENG can measure conduction velocity in a peripheral nerve. Conduction velocity can show nerve regenerating following nerve injury.
- In general, the study of evoked field potentials from sensory nerves has been shown to be of considerable value in diagnosing peripheral nerve disorders.



- Conduction velocity in a peripheral nerve is measured by stimulating a motor nerve at two points a known distance apart along its course.
- Subtraction of the shorter latency from the longer latency gives the conduction time along the segment of nerve between the stimulating electrodes.

Example ENG Measurement

□ Stimulus from wrist and elbow with square pulse of approximately 100 V amplitude with a duration of 100 to 300 µs





Motor-nerve conduction velocity

• *In vivo* measurement of the conduction velocity of a motor nerve may be obtained as:



- For example, the peroneal nerve of the left leg may be stimulated first behind the knee and second behind the ankle.
- A muscular response is obtained from the side of the foot, using surface or needle electrodes.

 Peroneal nerve injury can cause decreased sensation, muscle atrophy and loss of movement in the leg or foot. This can occur for a variety of reasons, most commonly in people who already have diseases of the nerve such as neuropathy, those who are very thin, or have had something directly compressing on the nerve. This can occur from crossing the legs, a knee injury, tight casts or placement of the leg during a surgery.



Peroneal Nerve



No.	Site	Lat.(ms)	Lat.ND	Amp.	Amp.ND	Dur.(ms)	Stim.
1	Ankle	3.60	<5.5	4.190mV	>2.5	8.60	100mA
2	Below Knee	12.75	<12.9	5.430mV	>2.5	7.90	99mA
3	Above Knee	14.60	<14.9	5.450mV	>2.5	8.00	99mA







 https://www.youtube.com/watch?v=VXiGw oNr-Hk

Reflexly evoked field potential

- When a peripheral nerve is stimulated and an evoked field potential is recorded in the muscle it supplies,
- Sometimes possible to record a second potential that occurs later than the initial response.
- Example: Stimulation of the medial popliteal nerve with pulses of increasing magnitude



J. A. R. Lenman and A. E. Ritchie, *Clinical Electromyography*, 2nd ed., Philadelphia: Lippincott, 1977; reproduced by permission of the authors.



- Mixed peripheral nerve such as the posterior tibial nerve is stimulated by a stimulus of low intensity,
 - only fibers of large diameter are stimulated because they have the lowest threshold.
- These large fibers are sensory fibers from muscle spindles that conduct toward the CNS and ultimately connect with motor fibers in the spinal cord via a single synapse.
- The motoneurons discharge and produce a response in the gastrocnemius muscle of the leg (the H wave).





- Stimulus of medium intensity,
 - Smaller motor fibers in the mixed nerve are stimulated in addition to the sensory fibers, producing a direct, short-latency muscle response, the M wave
- With still stronger stimuli,
 - Impulses conducted centrally along the motor fibers may interfere with the production of the H wave (these excited motor fibers are in their refractory period)
 - Only an M wave is produced



Electromyogram (EMG)

- EMG detects the electrical potential generated by muscle cells activated electrically or neurologically
 - composed of superimposed motor unit action potentials (MUAPs) from several motor units

Motor unit

- a single motor nerve fiber and the bundle of muscle fibers
- is the smallest unit that can be activated by a volitional effort, in which case all constituent muscle fibers are activated synchronously.
- Single motor unit (SMU) is a bioelectric source located in a volume conductor consisting of all other muscle fibers.
- The evoked field potential from the active fibers of an SMU
 - has a triphasic form of brief duration (3 to 15 ms)
 - amplitude of 20 to 2000 mV
 - frequency of discharge varies from 6 to 30 per second



Electromyogram (EMG)

- One of the disadvantages of recording the EMG by using the convenient surface electrodes is that they can be used only with superficial muscles and are sensitive to electrical activity over too wide an area.
- Various types of monopolar, bipolar, and multipolar insertion-type electrodes are commonly used in electromyography for recording from deep muscles and from SMUs.
- These types of electrodes generally record local activity from small regions within the muscle in which they are inserted.
- Often a simple flne-tipped monopolar needle electrode can be used to record SMU fleld potentials even during powerful voluntary contractions. Bipolar recordings are also employed.
- Various types of electrodes are discussed in the following courses.

- Figure shows motor unit potentials from the normal dorsal interosseus muscle under graded levels of contraction.
- At high levels of effort, many superimposed motor unit responses give rise to a complicated response (the interference pattern) in which individual units can no longer be distinguished.
- Note that when a muscle contracts progressively under volition, active motor units increase their rate of firing and new (previously inactive) motor units are also recruited.
- Shape of SMU potential can indicate peripheral neuropathy, can be modified by disease or regenerating nerve fibers cause scatter or desynchronization in the EMG pattern.



The Electrocardiogram (ECG)

- Electrocardiogram: measures potentials on body surface due to neuromuscular activity of the heart
 - ideally, but often see interference from other neuromuscular activities
- Source of ECG signal is electrical activation sequence of the heart's ventricle leads to production of closed-line action currents that flow in the thoracic volume conductor leading to potentials that can be measured on the outer surface of the medium.



Anatomy of the Heart

Chambers

- Right & Left Atria
 - blood storage chambers
- Right & Left Ventricles
 - function as a blood pump

- Conducting System
 - Sinoatrial (SA) node
 - Atrioventricular (AV) node
 - Bundle of His
 - Right/Left bundle branches
 - Purkinje fibers



Right?? --- Left??

- Anatomical Connectivity
 - Right: to Lungs
 - re-oxygenate blood
 - Left: to Circulatory system
 - deliver oxygen to the body
- Activity Phases
 - Resting phase
 - diastole
 - Pumping phase
 - systole



Anatomy and Function of Heart

- Four-chambered pump for the circulatory system.
- Main pumping function is supplied by the ventricles.
- Atria are merely antechambers to store blood during the time the ventricles are pumping.
- Resting or filling phase of the heart cycle is referred to as *diastole*
- Contractile or pumping phase is called systole.



Electrophysiology of the Heart

- The heart comprises several different types of tissues (SA and AV nodal tissue; atrial, Purkinje, and ventricular tissue).
- Representative cells of each type of tissue differ anatomically to a considerable degree.
- They are all electrically excitable
- Each type of cell exhibits its own characteristic action potential



Cardiac muscle cell

- Millions of individual cardiac cells (15 x 15 x 150 µm long), relatively long and thin,
- There is considerable branching and interconnecting (anastomosing).
- The cells are surrounded by a plasma membrane that makes end-to-end contact with adjacent cells at a dense structure known as the intercalated disk.



• Each fiber contains many contractile *myofibrils* that follow the axis of the cell from one end (intercalated disk) to the other.

http://www.buzzle.com/articles/cardiac-muscle-structure.html



- Electrical activation of the ventricle leads to the production of closed-line action currents that flow in thoracic volume conductor (considered a purely passive medium containing no electric sources or sinks)
- Potentials measured at the outer surface of this medium—that is, on the body surface—are referred to as *electrocardiograms*, or ECGs.

http://www.apsubiology.org/anatomy/2020/2020_Exam_Reviews/Exam_1/CH18_Electrocardiogram.htm

ECG

- P wave is produced by atrial depolarization,
- QRS complex primarily by ventricular depolarization,
- T wave by ventricular repolarization.
- The manifestations of atrial repolarization are normally masked by the QRS complex.



- The P-R and S-T intervals are normally at zero potential, the P-R interval being caused mainly by conduction delay in the AV node.
- The S-T segment is related to the average duration of the plateau regions of individual ventricular cells.
- A small additional wave, called the U wave, is sometimes recorded temporally after the T wave.


Atrioventricular block – Complete heart block



Complete heart block

- Cells in the AV node are dead and activity cannot pass from atria to ventricles.
- Atria and ventricles beat independently, ventricles being driven by an ectopic (other-than-normal) pacemaker.

First-degree Heart Block



- AV block wherein the node is diseased (examples include rheumatic heart disease and viral infections of the heart).
- Although each wave from the atria reaches the ventricles, the AV nodal delay is greatly increased.
- This is first-degree *heart block*

Premature Ventricular Contraction - Normal ECG followed by an ectopic beat



Ectopic beat

- An irritable focus, or *ectopic pacemaker*, within the ventricle or specialized conduction system may discharge, producing an extra beat, or *extrasystole*, that interrupts the normal rhythm.
- This extrasystole is also referred to as a premature ventricular contraction (PVC).

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Paroxysmal Tachycardia



Paroxysmal tachycardia

• An ectopic focus may repetitively discharge at a rapid regular rate for minutes, hours, or even days.

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Atrial Flutter



• The atria begin a very rapid, perfectly regular "flapping" movement, beating at rates of 200 to 300 beats/min.

Atrial Fibrillation



- The atria stop their regular beat and begin a feeble, uncoordinated twitching. Concomitantly, low-amplitude, irregular waves appear in the ECG, as shown.
- This type of recording can be clearly distinguished from the very regular ECG waveform containing atrial flutter.

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Ventricular Fibrillation



mmm Ventricular fibrillation

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- Mechanically the ventricles twitch in a feeble, uncoordinated fashion with no blood being pumped from the heart.
- The ECG is likewise very uncoordinated, as shown.

Eye Anatomy



- Normal eye is an approximately spherical organ about 24 mm in diameter
- Retina, located at the back of the eye, is the sensory portion of the eye.
- The light-transmitting parts of the eye are the cornea, anterior chamber, lens, and vitreous chamber, in the order in which these structures are traversed by light.

http://www.intechopen.com/books/topics-in-adaptive-optics/the-need-for-adaptive-optics-in-the-human-eye

Eye Anatomy

 A transparent fluid, the aqueous humor, is found in the anterior chamber. It is normally maintained at a pressure (20 to 25 mm Hg) that is adequate to inflate the eye against its resistive outer coats (the sclera and choroid).



- This makes possible the precise geometrical configuration of the retina and the optical pathway that is necessary to ensure formation of a clear visual image.
- Aqueous humor is the essential link between the circulatory system and the lens and cornea, which themselves lack blood vessels.

Eye Anatomy

- Light comes in through the pupil, focused by cornea and lens onto the retina, passes through the aqueous and vitrious humors and several layers of neural tissue (ganglion cells, bipolar cells) before it reaches the photoreceptors.
- Two types of photoreceptors occur in the human retina:
- rods (the agents of vision in dim light) and
- cones (the mediators of color vision in brighter light).
- Both rods and cones are differentiated into outer and inner segments.



 The first stage in the transduction of light to neural messages is the absorption of photons by photopigments (*rhodopsin*) localized in the outer segments of the retina's photoreceptors.

- In the living eye, the neurons in the retina are all quite transparent so as not to interfere with the light on its way to the photoreceptors.
- None of the peripheral cells in the retina the receptors, horizontal cells, bipolars, or amacrine cells - generate action poentials.
- It is only when you get to the level of the ganglion cells with axons that reach a rather long distance into the brain that you get action potentials.





- When the retina is stimulated with a brief flash of light, a characteristic temporal sequence of changes in potential can be recorded between an exploring electrode—placed either on the inner surface of the retina or on the cornea—and an indifferent electrode placed elsewhere on the body (usually the temple, forehead, or earlobe).
- These potential changes are collectively known as the electroretinogram (ERG),

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- Clinically recorded with the aid of an Ag/AgCl electrode embedded in a special contact lens used as the exploring electrode.
- The saline-filled contact lens is in good contact with the cornea, which is very thin and in intimate contact with the aqueous humor and passive fluid medium of the inner eye.
- The contact lens is usually well-tolerated by the subject and permits long examinations without discomfort.



- First part of the response to a brief light flash is the *early-receptor* potential (ERP) generated by the initial light-induced changes in the photopigment molecules.
- Appears almost instantaneously with the onset of the light stimulus.
- The second component, with a latency of 1 to 5 ms, is the *late-receptor potential* (LRP), found to be maximal near the synaptic endings of the photoreceptors and reflects the outputs of the receptors.
- ERP and LRP sum to form the leading edge of the a wave.

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- The b wave is generated by activity of the bipolar and ganglion cells of the inner layers of the retina.
- Best seen in laboratory experiments under conditions where the retinal artery supplying the inner layers of the retina is occluded, and the b wave is abolished.



- The c-wave is not generated by the retina itself, but rather by the pigment epithelial layer in which the tips of the external segments are embedded.
- This is shown experimentally by chemically ablating the pigment epithelium or using an isolated retina preparation.
- The d wave is the off-response of the retina to the light stimulus.

Electro-oculogram (EOG)

- In addition to the transient potential recorded as the ERG, there is a steady corneal-retinal potential.
- This steady dipole may be used to measure eye position by placing surface electrodes to the left and right of the eye (e.g., on the nose and the temple).
- When the gaze is straight ahead, the steady dipole is symmetrically placed between the two electrodes, and the EOG output is zero.
- When the gaze is shifted to the left, the positive cornea becomes closer to the left electrode, which becomes more positive.
- There is an almost linear relationship between horizontal angle of gaze and EOG output up to approximately 30° of arc.
- Electrodes may also be placed above and below the eye to record vertical eye movements.



Eyes at 15° to Right

Electro-oculogram

- EOG, unlike other bipotentials, requires a dc amplifier.
- EOG is in the microvolt range, so recessed Ag/AgCl electrodes are required to prevent drift.
- Necessary to abrade the skin to short out changes in the potential that exists between the inside and the outside of the skin.
- A noise is present that is compounded of effects from EEG, EMG, and the recording equipment; Equivalent to approximately 1° of eye movement.
- EOG data suffer from a lack of accuracy at the extremes.
- Specifically eye movements of less than 1° or 2° are difficult to record, whereas large eye movements (for example, greater than 30° of arc) do not produce bioelectric amplitudes that are strictly proportional to eye position.
- Frequently the method of choice for recording eye movements in sleep and dream research,
- Recording eye movements from infants and children,
- Evaluating reading ability and visual fatigue.

Brain

- Central nervous system (CNS) consists of the spinal cord lying within the bony vertebral column and its continuation, the brain, lying within the skull
- The brain is the greatly modified and enlarged portion of the CNS, surrounded by three protective membranes (the meninges (beyin ve omurilik zarı)) and enclosed within the cranial cavity of the skull.



- Spinal cord is surrounded by downward continuations of the meninges, and it is encased within the protective bony vertebral column.
- Brain and spinal cord are bathed in a special extracellular fluid called *cerebral spinal fluid* (CSF).

http://pharmacal.co.uk/pages/nervoussystemcns.html

- Division of the brain into three main parts—cerebrum (beyin), brainstem (beyinsapı), and cerebellum (beyincik) provides a useful basis for the study of brain localization and function.
- The brainstem (*medulla, pons, midbrain, diencephalon*) is the oldest part of the brain.



- As being short extension of the spinal cord and it serves three major functions as:
 - a connecting link between the cerebral cortex (*beyinzari*), spinal cord, and cerebellum;
 - an integrative center for several visceral (*içorgansal*) functions (e.g., control of blood pressure and ventilation).
 - an integration center for various motor reflexes.

http://www.nytimes.com/health/guides/disease/epilepsy/background.html

- Diencephalon is the most superior portion of the brainstem; its chief component and largest structure is the *thalamus*.
- The thalamus serves as a major relay station and integration center for all of the general and special sensory systems, sending information to their respective cortical reception areas.



- It serves as the gateway to the cerebrum.
- Another major component of the diencephalon is the *hypothalamus*, which integrates functions of the autonomic nervous system and along with the pituitary gland (*hipofiz bezi*), regulates functions of the thyroid, adrenal, and reproductive glands (*salgı bezi*).

http://www.nytimes.com/health/guides/disease/epilepsy/background.html



 The larger cerebrum occupies a special dominant position in the central nervous system and conscious functions of the nervous system are localized within this structure.

Brain lobes and functions



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Fig. 9-15

Communication within nervous system



Electrical Activity

- Two-way communication links exist between the brain and spinal cord. Information is transmitted to the brain by means of a frequency-modulated train of nerve impulses upon reaching specific areas of the brain, stimulates the activity of resident neurons.
- Similarly, the decision to implement a motor action in response to the initial stimulus is manifested in the electrical activity of cortical neurons in specific areas of the brain.
- The pattern of activity is specific to the type of motor action to be taken.

- Electrical activity in either ascending or descending nerve fiber tracts may be represented to a first approximation by an action current dipole oriented in the direction of propagation (bioelectric source model).
- One should be aware that the properties (e.g., size, bulk conductivity) of the volume-conductor medium can change along the length of a particular fiber tract between the spinal cord and the cortex.
- The median nerve was stimulated and compound action potentials were recorded from the subject's forearm. Although not shown in this figure, sensory fibers in the median nerve thus activated, initiate activity in the general sense pathways to the brain.
- Averaged field potential recordings can be taken at a variety of points along the ascending pathways [e.g., from spinal cord and brain stem tracts taking note of the crossed nature of the pathway, and finally at the cortex itself (postcentral gyrus)].



- Averaged sensory evoked potentials in response to brief auditory "clicks" or flashes of light are also routinely recorded as the auditory evoked response (AER) and the visual evoked response (VER), respectively.
- Brainstem auditory evoked response (BAER) is a test to measure the brain wave activity that occurs in response to clicks or certain tones.
- You lie on a reclining chair or bed and remain still. Electrodes are placed on your scalp and on each earlobe. A brief click or tone will be transmitted through earphones you are wearing during the test. The electrodes pick up the brain's responses to these sounds and record them. You do not need to be awake for this test.

Bioelectrical Potential from Brain

- Unipolar recordings of the cortical surface potential relative to that of a remote reference potential,
 - May be viewed as a measurement of the integrated field potential at a boundary of a large volume conductor which contains an array of action current sources.
- Under normal conditions, action potentials conducted by axons in the cortical medium contribute very little to the integrated surface potential,
 - since there are many axons in the cortex which run in many directions relative to the surface and which fire asynchronously.
- Consequently, their net spatial and temporal influence on the field potential at the surface is negligible.
- Cortical surface potential is largely due to the net effect of local postsynaptic potentials of cortical cells

 Activation of the input zone creates a postsynaptic potential. The integrative zone, which consists of the axon hillock domain, summates the postsynaptic potentials and initiates an action potential. The conductive zone, which consists of the axon domain, propagates the action potential.



Bioelectrical Potential from Brain

•Exception-- in the case of a response evoked by the simultaneous (synchronous) stimulation of a cortical input

 (e.g., direct electrical stimulation of thalamic nuclei or their afferent (getiren) pathways, which project directly to the cortex via thalamocortical axons—the cortical input).

•These synchronous responses are called *evoked potentials* and they are of relatively large amplitude

- A potential change recorded at the surface is a measure of the net potential (current resistance IR) drop between the surface site and the distant reference electrode.
- If all the cell bodies and dendrites of cortical cells were randomly arranged in the cortical medium, the net influence of synaptic currents would be zero as resulting net potential of axons.
- Any electrical change recorded at the surface must be due to the orderly and symmetric arrangement of some class of cells within the cortex.



- Pyramidal cells of the cerebral cortex are oriented vertically, with their long apical dendrites running parallel to one another.
- Potential changes in one part of the cell relative to another part create "open" potential fields in which current may flow and potential differences can be measured at the cortical surface.

- The bodies of this type of cell are commonly triangular in shape, with the base down and the apex directed toward the cortical surface. They consist of
 - (1) a long apical dendrite (up to 2 mm in length) that ascends from the apex of the cell body through the overlaying cellular layers, and which frequently reaches and branches terminally within the outermost layer of the cortex;
 - (2) dense dendritic arborization occurring at the base of the pyramidshaped cell (largely horizontally-basilar dendrites);
 - (3) a single pyramidal cell axon which can emerge from the inner surface of the cortex as projection fibers to other areas of the cortex, or to other structures (e.g., the thalamus, cerebellum, or spinal cord).





- Synaptic inputs to the apical dendritic tree
 cause
 depolarization of the dendritic
 membrane.
- Current flows through cell body returning to the surface synaptic sites via the extracellular bathing medium.



 The extracellular medium about the soma behaves as a source (+), while the upper part of the apical dendritic tree behaves as a sink (-).

- Apical dendrites of pyramidal cells constitute a meshwork of similarly oriented, densely packed units in the outer layers of the cortex.
- As multiple synaptic endings on the dendritic tree of each cell become active, current can flow in either direction between the dendritic process depending on whether the synapses are excitatory or inhibitory.
- The source-sink relationship between dendrite and cell is that of a constantly shifting current dipole, where variations in dipole orientation and strength produce wavelike fluctuations in the surface field potential.


Electroencephalogram (EEG)

- Electric recordings from the exposed surface of the brain or from the outer surface of the head demonstrate continuous oscillating electric activity within the brain. Both the intensity and the patterns of this electric activity are determined to a great extent by the overall excitation of the brain resulting from functions in the brainstem reticular activating system (RAS).
- The undulations in the recorded electric potentials (Figure 4.27) are called brain waves, and the entire record is called an electroencephalogram (EEG).

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month

Mar Mar and Ma

nn**Δ**] 50 μV

Electroencephalogram (EEG) -

- Conventionally, the electrical activity of the brain is recorded with three types of electrodes—scalp, cortical, and depth electrodes.
- When electrodes are placed on the exposed surface (cortex) of the brain, the recording is called an *electrocorticogram* (ECoG).
- Thin insulated needle electrodes of various designs may also be advanced into the neural tissue of the brain, in which case the recording is referred to as a *depth recording*.
- Whether obtained from the scalp, cortex, or depths of the brain, the recorded fluctuating potentials represent a superposition of the field potentials produced by a variety of active neuronal current generators within the volume conductor medium.

Resting rhythm of brain

- The intensities of the brain waves on the surface of the brain (recorded relative to an indifferent electrode such as the earlobe) may be as large as 10 mV, whereas those recorded from the scalp have a smaller amplitude of approximately 100 μ V.
- The frequencies of these brain waves range from 0.5 to 100 Hz
- Characteristics is highly dependent on the degree of activity of the cerebral cortex.
 - Example, the waves change markedly between states of wakefulness and sleep.
- Usually the brain waves are irregular, and no general pattern can be observed. However, distinct patterns resulting from specific abnormalities of the brain, such as epilepsy do occur.
- Brain waves occur in normal persons belongs to one of four wave groups (*alpha, beta, theta,* and *delta*).

Alpha Wave

Alpha

mmmmmmm

- Alpha waves are rhythmic waves occurring at a frequency between 8 and 13 Hz.
- They are found in EEGs of almost all normal persons when they are awake in a quiet, resting state of cerebration.
- These waves occur most intensely in the occipital region but can also be recorded, at times, from the parietal and frontal regions of the scalp.
- Their voltage is approximately 20 to 200 $\mu\text{V}.$
- When the subject is asleep, the alpha waves disappear completely.



Alpha Wave

- When the awake subject's attention is directed to some specific type of mental activity, the alpha waves are replaced by asynchronous waves of higher frequency but lower amplitude.
- Figure demonstrates the effect on the alpha waves of simply opening the eyes in bright light and then closing them again.
- Note that the visual sensations cause immediate cessation of the alpha waves; these are replaced by low-voltage, asynchronous waves.



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EXAMPLE 4.5 Design a system that would provide nonvisual feedback to a subject who wished to maximize the amplitude of his EEG alpha waves. Explain its operation.

ANSWER

- Three electrodes over the occipital lobe detect the 100 μV EEG
- and feed a differential amplifier with a gain of 10,000.
- A band-pass filter centered at 10 Hz selects the alpha waves, which are demodulated and filtered to yield a dc voltage proportional to amplitude.
- A voltage-to-frequency converter increases the frequency of an acoustic tone, and the subject attempts to maximize the frequency.

Beta

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- Beta waves normally occur in the frequency range of 14 to 30 Hz, and sometimes—particularly during intense mental activity—as high as 50 Hz.
- These are most frequently recorded from the parietal and frontal regions of the scalp.



- They can be divided into two major types: beta I and beta II.
- The beta I waves have a frequency about twice that of the alpha waves.
- They are affected by mental activity in much the same way as the alpha waves (they disappear and in their place appears an asynchronous, low-voltage wave).
- The beta II waves, on the other hand, appear during intense activation of the central nervous system and during tension.

Theta

mmmm

- Theta waves have frequencies between 4 and 7 Hz.
- These occur mainly in the parietal and temporal regions in children, but they also occur during emotional stress in some adults, particularly during periods of disappointment and frustration.



- For example, they can often be brought about in the EEG of a frustrated person by allowing the person to enjoy some pleasant experience and then suddenly removing the element of pleasure.
- This causes approximately 20 s of theta waves.

Delta

- Delta waves include all the waves in the EEG below 3.5 Hz.
- Sometimes these waves occur only once every 2 or 3 s.
- They occur in deep sleep, in infancy, and in serious organic brain disease.
- They can also be recorded from the brains of experimental animals that have had subcortical transections (*enlemesine kesme*) producing a functional separation of the cerebral cortex from the reticular activating system.
- Delta waves can thus occur solely within the cortex, independent of activities in lower regions of the brain.

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Subject is awake.

Rapid-eye-movement sleep.

Subject is sleeping.

Subject is sleeping well.

- a) Different types of normal EEG waves,
- b) Replacement of alpha rhythm by an asynchronous discharge when patient opens eyes.



3 Hz spike-and-doom 50 µV pattern and may cause interruption in consciousness

Spreads throughout brain and causes convulsions]^{100 μν} (*kasılma, çırpınma*), diagnosed as large amplitude from different parts of the scalp

> 2 to 4 Hz waves with superimposed 14 Hz waves and causes amnesia and unwanted motor action

(c) Representative abnormal EEG waveforms in different types of epilepsy.



Three types of electrode connections:

(1)Between each member of a pair (bipolar),

(2)Between one monopolar lead and a distant reference electrode

(usually attached to one or both ear-lobes), and

(3) between one monopolar lead and the average of all.

The 10–20 electrode system This system is recommended by the International Federation of EEG Societies.



Figure 4.29 The electroencephalographic changes that occur as a human subject goes to sleep The calibration marks on the right represent 50 mV. (From H. H. Jasper, "Electrocephalography," *in Epilepsy and Cerebral Localization*, edited by W. G. Penfield and T. C. Erickson. Springfield, 111.: Charles C. Thomas, 1941.)

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