EE416 Cheat Sheet

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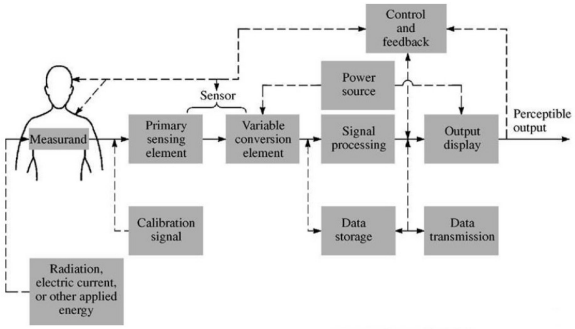
Contents

1 Introduction

Components of a Generalized Medical Instrumentation System:



Medical Measurement Constraints:

- Small magnitude and low frequency signals
- Many crucial variables in living systems are inaccessible due to the lack of proper sensor-measurand interface
- Not possible to turn off a biological system or remove a part of it during measurements
- Inherent variability of the measurand across time and subjects
- Many feedback loops among physiological systems
- Unknown safety level of the externally applied energy

Accuracy: Measure of total error without regard to the type or the source of error.

$$ACC = \frac{TrueValue - MeasuredValue}{TrueValue}$$

Precision: Expresses the number of distinguishable alternatives from which a given result is selected.

Resolution: The smallest incremental quantity that can be measured with certainty.

Reproducibility / Repeatability: The ability of an instrument to give the same output to equal inputs applied over some period of time.

Range: The range of an instrument is generally considered to include all the levels of input amplitude and frequency over which the device is expected to operate.

Sensitivity: Determines how small a variation of a variable or a parameter can be reliably measured.
Static sensitivity of an instrument or a system: Slope $\frac{\Delta y}{\Delta x}$

Drift: Occurs when all output values increase or decrease.

Zero Drift / Offset Error: When all the output values increase or decrease by the same fixed amount.

Sensitivity Drift: Slope of the calibration curve changes as a result of the interfering and/or modifying input. This causes a drift in the output proportional to the magnitude of the input.

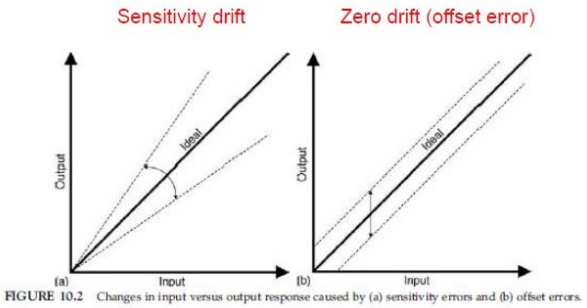


FIGURE 10.2 Changes in input versus output response caused by (a) sensitivity errors and (b) offset errors.

System Linearity: Homogenity & Additivity (o kadar sinyal aldın yeter gayrı)

Design Criteria for Medical Systems:

Signal: Sensitivity, range, differential or absolute input, input impedance, transient and frequency response, accuracy, linearity, reliability

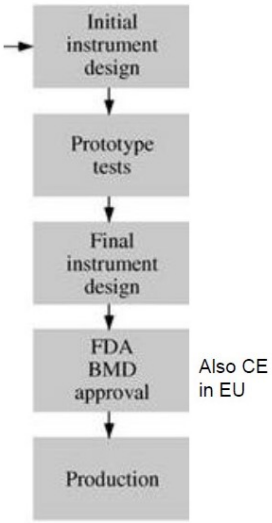
Environmental: Specificity, signal-to-noise ratio, stability (temperature, humidity, pressure, acceleration, shock, vibration, radiation), power requirements, mounting size & shape

Medical: Invasive vs. non-invasive, tissue-sensor interface requirements, material toxicity, electric safety, radiation and heat dissipation, patient discomfort

Economic: Cost, availability, warranty, consumable requirements, compatibility with existing equipment

Ethical!

Design Process for Medical Systems:



2 Sensors

Transducer: A device that converts one form of energy to another.

Sensor: Converts a physical measurand to electric output.

Actuator: Converts an electric signal to a physical output.

3 Excitable Cells

Excitable Cell: An excitable cell is one that actively conducts an input voltage/current change from one location on its membrane to the other.

Cells can passively contribute to the conduction of an electrical signal as well: When an ionic current is injected to through the cell membrane, the membrane voltage changes in response, which can be considered as a electrical signal. The injected ions will naturally disperse within the cytoplasm, hence creating conduction and making the electrical signal propagate across the cell. Even though this signal decays over time and space, still the cell can be considered to contribute to signal propagation. For example, the signal propagation in the dendrites of nerve cells occurs in this fashion.

However, this is not what we mean by an excitable cell. For a cell to be described as 'excitable', it has to contribute to this conduction phenomenon actively, by which we mean that it has to have a maintained imbalance in ionic concentrations across its membrane. When the input current is injected or the membrane voltage exceeds a certain threshold, these ionic concentrations change spontaneously, making the membrane voltage peak (action potential) and further contributing to the propagation of the signal by exciting the neighboring patch of the membrane. Energy expenditure is due to the establishment and maintenance of the ionic concentration imbalance. **Properties of Excitable Membranes:**

Accomodation/habituation denotes the adaptation of the cell to a continued or repetitive stimulus. This is characterized by a rise in the excitation threshold.

Facilitation denotes an increase in excitability (decrease in threshold voltage) after the application of a hyperpolarizing (one that further lowers the membrane potential, negative input current) input.

Latency denotes the delay between the application of the stimulus and the triggered action potential.

Refractory Period denotes the impossibility or difficulty in triggering a second action potential after another first one. There are two kinds of refractory periods:

Absolute Refractory Period refers to the segment immediately following the peak of the action potential, until approximately halfway to the resting voltage. In this period, no matter how large the input current amplitude, it will not trigger an action potential. Absurdly large current inputs may affect the membrane voltage waveform, but still they will not trigger an action potential.

Relative Refractory Period refers to the period approximately around and after the sodium conductance reaches half its resting value. During the relative refractory period, a current pulse that normally trigger an action potential is denied of an action potential, but still a reasonably larger current input may trigger an action potential.

Temporal Mapping/Summation refers to the fact that two consecutive pulses that are individually incapable of triggering an action potential, may trigger an action potential. These two insufficient pulses are considered to be 'summed' in time, hence the name temporal summation.

Pulse Frequency Modulation refers to the fact that an input step current of sufficient amplitude triggers an action potential train, whose frequency is modulated by the amplitude of the step current.

Anode-Breakdown Excitation occurs after a hyperpolarizing current pulse ends. At the termination of the hyperpolarizing pulse, one or more action potentials may be observed.

Myelinated Axon: The nerve cells have three main parts: Dendrites, soma (or the cell body) and the axon. The electrical signal comes in (passively) through the dendrites and in conveyed to the next nerve cell through the axon. The axon can be considered like a long electrical cable.

On certain axons (especially those that need fast conduction), there can be certain cells of mostly lipid content that are wrapped around the axon. These wrapped cells are called as Myelin sheaths. A myelinated axon can produce action potentials only in between the empty section where the axon is bare, sections called nodes of Ranvier. The propagation from one end of a Myelin sheath to the other is extremely fast compared to regular action potential propagation, and so these sheaths speed immensely.

However, an axon cannot be fully covered with a Myelin sheath either. Because during regular action potential propagation current loops form locally in and out of the cell membrane in close proximity. For propagation to occur, these loops are necessary. No current loop can form over a section covered with Myelin sheath, and so the loop must start and close at consecutive nodes of Ranvier, which is what makes signal propagation much faster from an electrical point of view. If the whole axon were covered, it would be very difficult/impossible for the current loops to form, and so conduction would not occur.

Transmembrane Potential: The potential of the inside of the cell measured with respect to the outside. (Remember, it is easier to locate the ground of the voltmeter outside the cell than locating it on the inside.) This voltage is due to the imbalance of ionic concentrations on the inside and the outside of the cell. Its main constituent ions are Sodium, Potassium and Chloride (All the other ions are represented under the name Chloride, however among those Chloride is the dominant one.)

For a single ion species p, the transmembrane potential is given by the Nernst Equation:

$$V_p = -\frac{RT}{z_p F} \ln\left(\frac{[p]^{in}}{[p]^{out}}\right)$$

For multiple ions, it is given by the Goldman Equation. The constituents are Sodium, Potassium and Chloride.

$$V_m = -\frac{RT}{F} \ln\left(\frac{P_K[K]^i + P_{Na}[Na]^i + P_{Cl}[Cl]^o}{P_K[K]^o + P_{Na}[Na]^o + P_{Cl}[Cl]^i}\right)$$

The coefficients P's signify the contribution of each ion to the membrane voltage, and in a sense represent their mobility across the membrane (their conductivity).

Action Potential: Action potential is a behavior very specific to excitable cells. It is of (mostly) fixed amplitude and has a very specific shape. It propagates unattenuated along the axon. Thanks to the refractory period property, it propagates in only one direction. Naturally, it starts at the connection of the axon to the soma, at the axon hilock, and propagates onwards until it reaches the synapse. However, if an action potential is triggered artificially along the axon, it propagates in both directions.

Excitatory Stimulation: Excitatory/Depolarizing stimulation increases the membrane potential. If the increased membrane potential crosses a certain threshold value, an action potential is triggered.

Inhibitory Stimulation: Inhibitory/Hyperpolarizing stimulation decreases the membrane potential, taking it further away from the threshold. A sudden release of a hyperpolarizing input may trigger one or more action potentials.

Generation of an Action Potential: After the membrane voltage surpasses the voltage threshold, the first ionic component to react is Sodium. Sodium conductance rises rapidly, creating the high peak of the action potential curve. Following that, the Potassium conductance

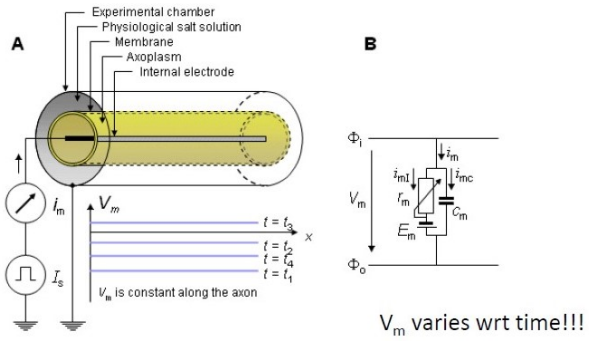
rises more slowly, thus attenuating the action potential. The effect of the Potassium conduction lasts longer, which in part creates the lower-than-resting potential for the duration of the refractory period.

Sodium-Potassium Pumps: When the equilibrium condition is checked, if there exists no active mechanism over the membrane, eventually the concentrations would have to be equalized due to entropy because to keep the membrane voltage steady, a passive but steady efflux of Potassium is balanced out with a constant influx of Sodium. To keep the concentrations as needed, active ionic pumps exist across the membrane to work against this fluxes to keep the concentrations fixed.

Strength-Duration Curve for a Stimulation Pulse: For a stimulation pulse to generate an action potential response, it needs to be both of sufficient amplitude and of sufficient duration. The border between triggering and non-triggering impulses on the impulse strength versus impulse duration plane is called the Strength-Duration Curve. Any pulse above this line triggers an action potential, and those below cannot trigger an action potential. The current amplitude that triggers an action potential with an infinite duration pulse is called the rheobase current. The minimum duration of the impulse that triggers an action potential with an amplitude double the rheobase current is called chronaxy.

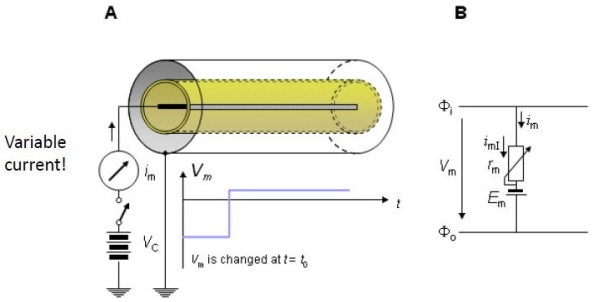
Donnan Equilibrium: Donnan Equilibrium is a concept that describes a selective membrane experiment with multiple ionic species. Its central assumption is that the ionic flows for different species are governed independently. This assumption disregards any interaction between the ionic species. It is as if the ions are in separated parallel containers, the membrane potential being their only common interaction point.

Space Clamp: The fixation of the parameter is in terms of space. This means that different parameters do not vary along the axon of interest. This is provided by the thin conductor inside the axon and the long cylindrical conductor encapsulating the axon. These two conductors fix the membrane voltage all along the axon, making it only a variable of time. The stimulation is made via the internal thin conductor, which varies the membrane voltage throughout the axon uniformly. This makes the entire axon behave as a single patch.



The important remark to make here is that the membrane current in the space clamp procedure includes the capacitive current as well, since the membrane voltage is variable across time.

Voltage Clamp: This fixation of the parameter is in terms of the membrane voltage. Fixing the membrane voltage ensures that the capacitive current component is eliminated from the total membrane current, and so the behavior of ionic components can be analyzed.



Synaptic Transmission:

General Description: (From Malmuvio & Plonsey)

1. The neurotransmitter is manufactured by the neuron and stored in vesicles at the axon terminal.
2. When the action potential reaches the axon terminal, it causes the vesicles to release the neurotransmitter molecules into the synaptic cleft via exocytosis.
3. The neurotransmitter diffuses across the cleft and binds to the post-synaptic neuron.
4. The activated receptors cause changes in the activity of the post-synaptic neuron.
5. The neurotransmitter molecules are released from the receptors and diffuse back into the synaptic cleft.
6. The neurotransmitter is re-absorbed by the pre-synaptic neuron. This process is known as reuptake.

Neuromuscular Junction:

1. Action potential on the motorneuron reaches its distal ending at the pre-synaptic terminal (interface with its target muscle).
2. Membrane depolarization causes the voltage gated Calcium channels to open, causing the influx of Calcium at the pre-synaptic motorneuron.
3. Calcium molecules cause the synaptic vesicles to fuse with the membrane.
4. ACh from synaptic vesicles is released into the synaptic cleft via exocytosis.
5. ACh diffuses across the synaptic cleft towards the post-synaptic ACh channels in the muscle membrane. A pair of ACh molecules bind to a single channel to open it.
6. The now-open ACh channels cause influx/efflux of Sodium anf Potassium, depolarizing the muscle membrane and starting an action potential.
7. Within ∼2 msec after ACh binding, ACh is released back into the synaptic cleft from the sole feet and diffuses back into the synaptic cleft. It no longer acts on the post-synaptic muscle membrane.
8. The enzymes (chlorinesterase) accumulated around the borders of the gutters destroys the ACh.

End-Plate Potential (EPP): The end-plate refers to the muscle membrane at the neuromuscular junction, and EPP refers to the electric potential arising as a result of ACh binding. Miniature EPP (MEPP) is the increase in potential due to a single vesicle of ACh. MEPPs are observed due to the occasional random release of ACh into the synaptic cleft. A normal EPP is the result of many MEPPs occurring simultaneously, which serves to prove the quantal release of ACh. Each vesicle of ACh holds about the same amount of ACh.

When considered as a discrete event (quantal release), the statistics can be considered to be governed by the Poisson distribution:

$$P(x) = \frac{n!}{x!(n-x)!}p^x(1-p)^{(n-x)}$$

gives the probability that x number of vesicles being released out of n possible sites, with a probability of release per site of $p \in [0,1]$. As n is increased and dominates over x and $p << 1$, the distribution becomes an exponential distribution, which is continuous this time:

$$P(x) = \frac{m^x e^{-m}}{x!}$$

where $m = np$ is the average number of quantal release per trial or the average number of vesicles secreted for an action potential. m can be estimated experimentally as

$$m \approx \frac{\text{mean amplitude of EPP}}{\text{mean amplitude of MEPP}}$$

(recall the quantal nature of ACh release).
If the post-synaptic region is voltage-clamped, the value that reduces the membrane current to zero during transmitter release is called as the reversal potential, found by setting the membrane current to zero:

$$V_m^{rev} = \frac{g_K E_K + g_{Na} E_{Na} + g_{Cl} E_{Cl}}{g_K + g_{Na} + g_{Cl}}$$

4 Extracellular Potentials

Extracellular Potentials: We usually do not have the means to measure the membrane potential of a single cell, so we measure the potentials over the body, and so our measurements are the result of many many cells superposed. These potentials we measure are called as extracellular potentials. The body is treated as a distributed resistive and capacitive material with local batteries.

Quasi-static Assumptions for Biological Tissues: The time-varying bioelectric currents and voltages in the human body can be examined in the conventional quasi-static limit.

- All currents and fields behave, at any instant, as if they are stationary.
- The description of the fields resulting from the applied current sources is based on the understanding that the medium is resistive only.
- The phase of the time variation can be ignored (i.e. all fields vary synchronously).
- The capacitive components of tissue impedance is negligible in the frequency band of internal bioelectricity events. The volume conductor currents are essentially conduction currents and only tissue resistivity must be specified.
- The electromagnetic propagation effects cen be neglected.
- The inductive effects can be neglected.

Lead Vector: The potential ϕ at due to any dipole $\bar{p}$ can be written as

$$\phi = c_x p_x + c_y p_y + c_z p_z = \bar{c} \cdot \bar{p}$$

This vector $\bar{c}$ is the lead vector associated with the field point (lead). The lead vector is a property of the lead and volume conductor and does not depend on the dipole vector $\bar{p}$. The bipolar lead measurements can also be defined in this manner:

$$\phi_{ij} = \phi_i - \phi_j = \bar{c}_i \cdot \bar{p} - \bar{c}_j \cdot \bar{p} = (\bar{c}_i - \bar{c}_j) \cdot \bar{p} = \bar{c}_{ij} \cdot \bar{p}$$

5 Anatomic Systems

5.1 Muscles

Types of muscular tissue:

Striated/Skeletal Muscles are connected to bones via tendons, responsible for voluntary contraction, form an essential part of the organ of support and motion.

Smooth muscles are responsible for involuntary contraction and are found in the digestive tract, wall of the trachea, uterus and bladder. Their contraction is controlled by the brain via the autonomic nervous system.

Cardiac muscle is also a striated muscle in structure, but differs from it in important aspects. Its contraction is involuntary, and it generates a much longer electric pulse than skeletal muscles do when excited (∼300 ms). Correspondingly, mechanical contraction lasts longer as well. The electrical activity of one cardiac muscle cell spreads to all the other surrounding muscle cells, owing to an elaborate system of intracellular junctions.

Motor Unit: A motor unit consists of a single motorneuron and all the muscle fibers it synapses with via end plates.

Motor Unit Recruitment: When an increase in the strength of a muscle's contraction is necessary to perform a task, the brain increases the number of simultaneously active motor units within the muscle. This process is known as motor unit recruitment.

Motor Unit Action Potentials (MUAP): A MUAP is the extracellular potential generated by a single motor unit. Considering that the measurements are dominantly due to the fibers (which outnumber the single neuronal action potential), it consists of the superposition of the action potentials on the muscle membranes, occurring over the measurement location. MUAP

Amplitude depends on the radius of the muscle fiber and the distance between the active muscle fiber and the recording site.

Shape depends on the tissue between the fiber and the recording site, the size of the recording electrodes and the chemical properties of the metal-electrolyte interface. The shape of a MUAP from the same electrode and the same motor unit tend to remain the same, and MUAPs from different motor units tend to have different characteristic shapes.

Tonus is the constant state of slight tension in the muscles that serves to maintain the muscle in a state of readiness.

5.2 Cardiovascular System

Cardivascular System = Heart + Circulatory System

Two Circulations:

Systemic Circulation is responsible for the delivery of the blood to the body. The blood is sent out from the heart as oxygenated and returns to it deoxygenated.

Pulmonary Circulation is responsible for the delivery of the blood to the lungs. The blood is sent out to be cleaned as deoxygenated, and returns to the heart oxygenated.

Blood delivers oxygen and nutrients to every cell and removes the waste products and carbon dioxide from them. The network carrying 'clean' blood from the heart to the cells is made of arteries, arterioles and capillaries. The 'dirty' blood returns to the hears through venules and veins.

Functions of the Heart:

- Generating blood pressure
- Routing blood: Separating pulmonary and systemic Circulations
- Ensuring one-way blood flow through heart valves
- Regulating blood supply by changing in contraction rate and force to match the blood delivery to changing metabolic needs

Heart Wall is composed of three layers:

Epicardium is the serous membrane of smoother outer surface of the heart.

Myocardium is the middle layer composed of the cardiac muscle cells and is responsible for contraction.

Endocardium is the smooth inner surface of the heart chambers.

Pericardium is an outer layer that protects the heart.

Heart Skeleton consists of a plate of fibrous connective tissue between the atria and the ventricles. It has fibrous rings around the valves to support them, serves as electrical insulation between atria and ventricles and provides a site for muscle attachment.

Heart Valves regulate the blood flow.

Tricuspid valve regulates blood flow from the right atrium to the right ventricle.

Pulmonary valve controls blood flow from the right ventricle into the pulmonary arteries.

Mitral valve lets the oxygen-rich blood from the lungs into the heart pass from the left atrium into the left ventricle.

Aortic valve lets the oxygen-rich blood pass from the left ventricle into the aorta, and then to the whole body.

Cardiac Cycle:

1. Systole: Period of isovolumic contraction. AV and semilunar valves are closed.
2. Systole: Period of ejection. Semilunar valves are opened, AV valves are still closed.
3. Diastole: Period of isovolumic relaxation. Semilunar and AV valves are closed.
4. Diastole: Passive ventricular filling. Semilunar valves are closed, AV valves are open.
5. Diastole: Active ventricular filling. AV valves are opened, semilunar valves are closed.

Conduction System:

1. Electrical signal begins in the sinoatrial (AS) node, which is a natural pacemaker. It propagates through the atria and causes the atria to contract.
2. The signal then passes to the atrioventricular (AV) node, where it is delayed to have proper filling in the ventricles.
3. The AV node sends the signal to the ventricles via the bundle of His.
4. The signal is then propagates further into the ventricular myocardium by the Purkinje fibers.

SA Node Action Potential: Aside from the depolarization and repolarization phases, the action potential waveform also has a prepotential section in the beginning, where the membrane potential rises linearly. After this rising potential crosses the voltage threshold, the action potential is triggered. This mechanism that makes the membrane potential rise continuously is what makes the SA node a natural pacemaker.

5.3 Central Nervous System

Central Nervous System = Brain + Spinal Cord

Matters of the Brain:

White Matter is the bundles of axons, each coated with a Myelin sheath.

Gray Matter is the masses of cell bodies and dendrites covered with synapses.

In the spinal chord, the white matter is at the surface and gray matter is on the inside. In the mammal brain, it is reversed.

Mapping of the Cortex: The area of the motor cortex controlling a body part is not proportional to the size of that body part. Instead, it is proportional to the number of motor neurons running to it.

Cerebellum consists of two deeply convoluted hemispheres. Although it represents almost 10% of the weight of the brain, it contains as many neurons as all the rest of the brain combined. It is responsible for the coordination of the body movements.

Spinal Cord is made of 31 pairs of spinal nerves. It connects a large part of the peripheral nervous system to the brain. It also acts as a minor coordinating center responsible for some simple reflexes like the withdrawal reflex.

Sympathetic and Parasympathetic Systems refer to the two kinds of stimulations that can be applied to certain organs.

Sympathetic system stimulation, in a broad sense, makes the body ready to fight or flee. Pupils are dilated, heart rate and force is increased, digestive activities are suppressed overall, glycogen is converted to glucose in the liver, urine secretion is decreased and the bronchial muscle is relaxed. The body is getting getting tense and ready to act.

Parasympathetic system stimulation makes the body more relaxed. Pupils are constricted, heart rate and force is decreased, digestive activity increases overall, urine secretion increases and the bronchial muscle is contracted. The body is taking care of itself, now that it is in a safer place to do so.

6 Electro...

6.1 ...neurogram

Electroneurogram (ENG) is a method used to visualize the directly recorded electrical activity of the neurons in the central nervous system or the peripheral neural system. It can be used to determine if the neural path is damaged/broken, and to measure the neural conduction velocity.

Voluntary vs. Involuntary Contraction:

Voluntary Contraction may spread over about 100 ms because all the motor units do not fire at the same time. Each motor unit may produce several action potentials depending on the signals sent from the central nervous system.

Contraction due to Electrical Stimulation is more useful in testing. Stimulation time is well defined and all muscle fibers fire at nearly the same time. A typical stimulating pulse may have an amplitude of 100 V lasting around 0.1-0.5 s.

Neural Conduction Velocity can be measured by applying stimulation from one place, and obtaining the time delay between two measuring locations (one of which can be located at or near the stimulation site). It is very difficult if not possible to do this via voluntary contraction.

6.2 ...myogram

Electromyogram (EMG) is a diagnostic procedure to test the health of muscles and the nerve cells that control them. EMG signals are composed of superimposed MUAPs from several motor units.

6.3 ...oculogram

6.4 ...encephalogram

Typical EEG Waveforms:

Spontaneous activity is measured on the scalp or on the brain and is called the electroencephalogram. The amplitude of EEG is about 100 μV when measured on the scalp, and about 1-2 mV when measured on the brain. As the phrase 'spontaneous activity' implies, this activity goes on continuously in the living individual.

Evoked potentials are those components of the EEG that arise in response to a stimulus (which may be electric, auditory, visual, etc.) Such signals are usually below the noise level and thus not readily distinguished, and one must use a train of stimuli and signal averaging to improve te signal-to-noise ratio.

Single-neuron behvaior can be examined through the use of microelectrodes which impale the cells of interest. Through studies of the single cell, one hopes to build models of the cell networks that will reflect actual tissue properties.

Methods of functional brain mapping:

Functional MRI: Blood Oxygen Level Dependent (BOLD) imaging, depending on the oxyhemoglobin and deoxyhemoglobin levels in the blood.

Positron Emission Tomography: To conduct the scan, a short-lived radioactive tracer isotope is injected into the living subject.

6.5 ...cardiogram

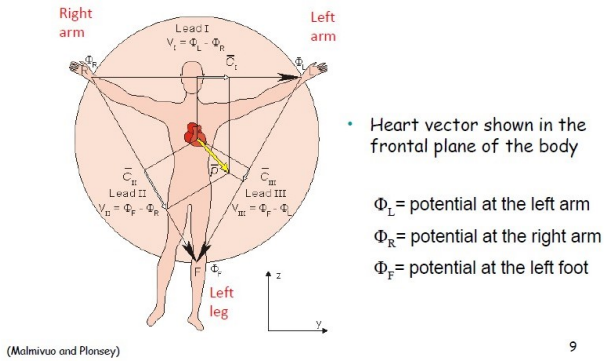
12 Lead System is the most commonly used clinical ECG system. There are 10 electrodes and 12 leads.

Electrodes: Right Arm, Left Arm, Left Leg, Right Leg (reference) + 6 chest electrodes.

Leads: These are the waveforms derived from the electrode measurements.

I, II, III: Einthoven's lead system, 2 of them are independent. | These 6 leads
aV$_R$, aV$_L$, aV$_F$: augmented leads derived from V$_R$, V$_L$, V$_F$. | are limb leads.
V$_1$-V$_6$: precordial leads

Einthoven's Triangle: The extensions of the torso, i.e. the legs and arms act as conductors that replicate the electrical activity occurring in the places where they connect to the torso. The measurements taken from the ends of the arms and the left leg hence can be thought to form an equilateral triangle, with the heart located at the center. The bipolar limb leads, hence can be though to form vector along the sides of the triangle. This triangle is called as the Einthoven's Triangle, and it is used together with the lead measurements to obtain a vector diagram of the electrical activity of the heart, both with magnitude and directionality.



Important remarks:

- The bipolar lead measurements are the projections of the heart dipole vector on to the lead vectors.
- Only two of the main (non augmented) limb leads are independent:

$$\begin{aligned} \text{Lead I: } V_I &= \Phi_L - \Phi_R \\ \text{Lead II: } V_{II} &= \Phi_F - \Phi_R \\ \text{Lead III: } V_{III} &= \Phi_F - \Phi_L \end{aligned}$$

One can use the Kirchhoff's Law to show that

$$V_I + V_{III} = V_{II}$$

Wilson Central Terminal is used in the definition of the leads, and has the potential equal to the average of the three main limb leads.