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Medizinische Fakultät Mannheim
der Universität Heidelberg
Universitätsklinikum Mannheim

Biomedical Engineering
Biosensors & Physiological Signals I – Gaining Access to Physiological Signals

Christian Licht

Schedule

Day	Date	Time	Lecturer	Topic
Tuesday	03.11.2020	13:00-14:30	Licht	Biosensors & Physiological Signals I
Tuesday	10.11.2020	13:00-14:30	Licht	Biosensors & Physiological Signals II
Thursday	12.11.2020	13:00-14:30	Tönnes	Bioelectrical Signals: EEG & ECG
Tuesday	17.11.2020	13:00-14:30	Reichert	Medical Imaging: MRI
Thursday	19.11.2020	13:00-14:30	Tönnes	Medical Imaging: CT, Xray & US
Tuesday	24.11.2020	13:00-14:30	Schnurr	Medical Imaging: Other
Thursday	26.11.2020	13:00-14:30	Andoh	Blood Flow & Pressure I
Tuesday	01.12.2020	13:00-14:30	Andoh	Blood Flow & Pressure II
Thursday	03.12.2020	13:00-14:30	Schnurr	Machine Learning I
Tuesday	08.12.2020	13:00-14:30	Schnurr	Machine Learning II
Thursday	10.12.2020	13:00-14:30	Schnurr	3D Printing
Tuesday	22.12.2020	13:00-14:30	All	Recap - Exam Preparations
Tuesday	26.01.2021	10:00-12:00	Schnurr, Tönnes	Exam
Wednesday	03.02.2021	08:30-10:00	Schnurr, Tönnes	Repeat Exam

Materials

Slides are available from our website:
https://www.umm.uni-heidelberg.de/inst/cbtm/ckm/lehre/

Further reading :

Medical Physics and Biomedical Engineering
BH Brown, RH Smallwood, DC Barber, PV Lawford and DR Hose, 1999, ISBN 0 7503 0367 0.

Medical Instrumentation Application and Design, John G. Webster, 4th edition, 2009, ISBN-13 978-0471-67600-3.

Lecturer: Christian Licht

Bachelor of Science:	Medical Engineering – HS Furtwangen
Master of Science:	Biomedical Engineering – University of Twente
PhD:	Multinuclear NMR – Heidelberg University

Computer Assisted Clinical Medicine
Medical Faculty Mannheim
Heidelberg University

Christian.Licht@medma.uni-heidelberg.de
Phone:+49 (0) 621 383 5119

Biosensors & Physiological Signals I

Objectives

- Function and types of electrodes
- Limiting factors - Noise
- Bioelectric Amplifiers

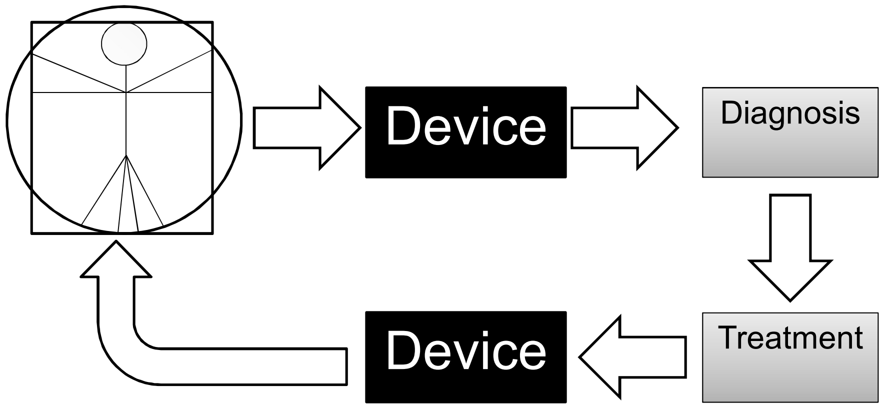
Biomedical Engineering - Definition

BE is the application of engineering principles and techniques to the medical field

It combines the skills of engineering with medical and biological sciences to improve healthcare diagnosis and treatment

system, apparatus, instruments, programs
for
detection, therapy, supervision, prevention of diseases
and
compensation and facilitate disabilities.

Physiological Signals



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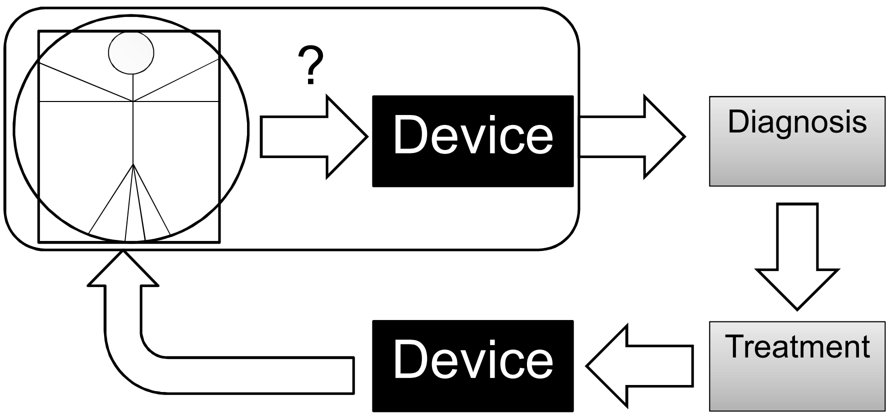
Physiological Signals



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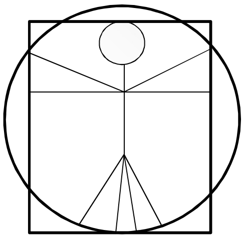
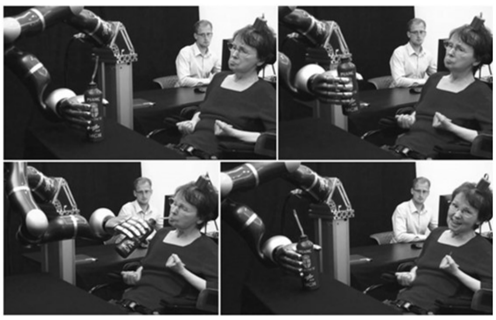
Types of Physiological signals

1. Electrical signals
2. Magnetic signals
3. Fluid movement
4. Pressure
5. Temperature
6. Frequencies
7. Volumes



Electrical Signals in Action

Example



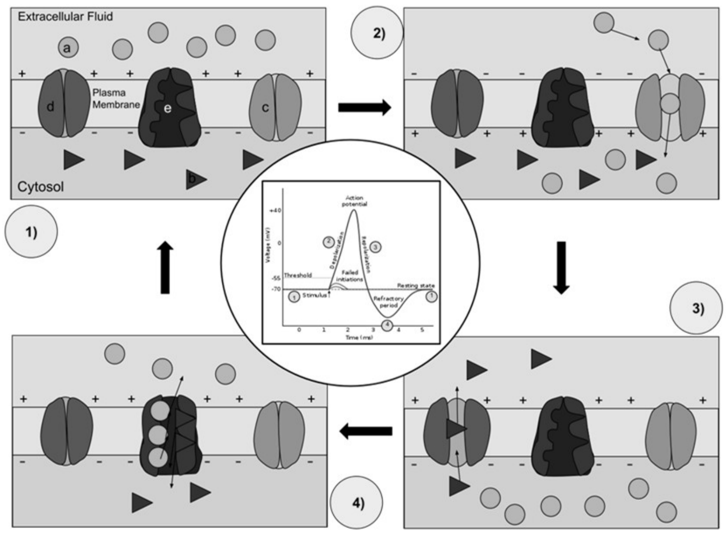
LR Hochberg *et al.* Reprinted by permission from Macmillan Publishers Ltd: Nature (**485**, 372-375), copyright (2012)

Requirements

Body → Device

Electrodes
Transducers
Amplifiers

Electrical Signal – Action Potential



https://en.wikipedia.org/wiki/Action_potential#/media/File:Membrane_Permeability_of_a_Neuron_During_an_Action_Potential.svg

Electrical Signal – Action Potential

Hodkin Huxley model:
https://www.mathworks.com/matlabcentral/fileexchange/46740-hhrun-hodgkin-huxley-model-simulation-for-user-defined-input-current

Electrodes and their function

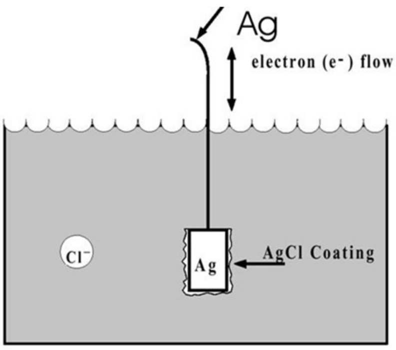
Function:

- Conductor to establish electrical contact with a nonmetallic part
  - Can be regarded as a transducer
  - Necessary to establish electrical contact with the body

- Function based on electrochemical reactions, for example silver/ silver-chloride electrode

$$Ag^{+} + e^{-} \rightleftharpoons Ag$$
$$AgCl + e^{-} \rightleftharpoons Ag + Cl^{-}$$

Silver/ Silver Chloride Electrode

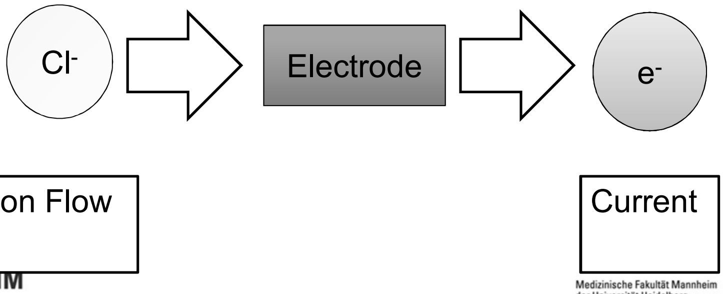


$$Ag^{+} + e^{-} \rightleftharpoons Ag$$
$$Ag^{+} + Cl^{-} \rightleftharpoons AgCl$$

Md A Abrar, https://www.researchgate.net/post/How_can_I_fabricate_a_Ag_AgCl_reference_electrode

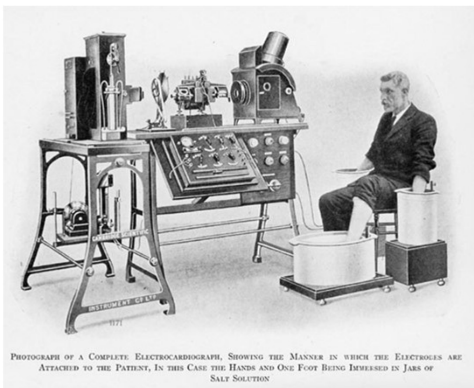
Electrodes and their function

- Chloride or Chloride ions (Cl^-) are electrolyte in the body and body fluids
- Cl^- is involved in physiological processes e.g. acid/base balance, transmission of impulses



Electrolytes are useful for the transport of ions

- What happens if we establish contact between a metal electrode and human skin?
  - Not much…
- What happens if we establish contact between a metal electrode, an electrolyte and human skin?
  - Ions will diffuse in/out of the electrode
  - Generation of electrode potentials



https://commons.wikimedia.org/wiki/File:Willem_Einthoven_ECG.jpg

A reference is needed to measure an electrode potential

- Second electrode needs to be used as reference
  - Electrode potentials of different elements are characterized in comparison to the standard hydrogen electrode (SHE)
- In an ideal case, the difference in potential would then be only due to signals produced by the body

$$E^0 = E^0_{cathode} - E^0_{anode}$$

Material	Electrode potential
$Zn \rightleftharpoons Zn^{2+} + 2e^-$	$-763\ mV$
$H_2 \rightleftharpoons 2H^+ + 2e^-$	$0\ mV$

John G. Webster, "Medical Instrumentation Application and Design", 4th edition, 2009.

A reference is needed to measure an electrode potential - Exercise

A galvanic cell that consists of a SHE (reference electrode) in one beaker and a Cu strip (working electrode) in another beaker containing a solution of Cu^{2+} ions. When the cricuit is closed, the voltmeter indicates a potential of 0.34V. The SHE begins to dissolve to form H^+ ions, and Cu^{2+} ions are reduced to Cu in the other compatment.

a. Indicate the half reactions occuring at each electrode.

b. Calculate the standard electrode potential of the Cu electrode.

A reference is needed to measure an electrode potential – Exercise - Answers

a. Half reactions:

$$Cu^{2+} + 2e^{-} \rightarrow Cu$$
$$H_2 \rightarrow 2H^{+} + 2e^{-}$$

b.

$$E^0 = E^0_{cathode} - E^0_{anode}$$
$$(=) 0.34\text{V} = E^0_{Cu^{2+}/Cu} - E^0_H = E^0_{Cu^{2+}/Cu} - 0V$$
$$(=) E^0_{Cu^{2+}/Cu} = 0.34V$$

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Types of electrodes

What types of electrodes are used for biomedical applications?

1) Micro electrodes
2) Needle electrodes
3) Surface electrodes

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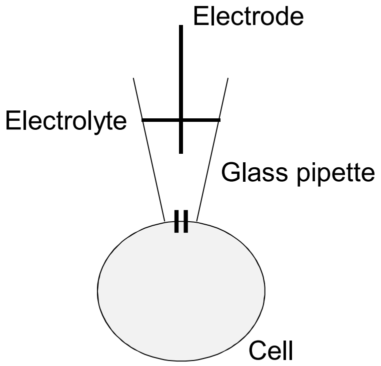
Micro electrodes



- Very small
- Can penetrate a single cell
- Tip size can be ~ 5 μm
- Used for Patch Clamp techniques
- Arranged in arrays

Needle electrodes

- Tip size ~ 200 μm
- Used for electromyography → potentials from a small group of motor units is recorded
- Must be sterlilized before use!
- Also used to carry high frequency electrical currents

Surface electrodes – Metal plate electrodes

- Metallic conductor
  - In contact with skin
- Contact to skin established by gel
- Fixed by surgical tape
  - Prone to measurement errors due to displacement
  - Sensitive to movement artifacts
- Very simple to use
- Type of skin preparation plays an important role

Surface electrodes - Floating electrodes

- Adhesive layer fixes the electrode
- Electrolyte pool is insensitive to motion
- electrochemical equilibrium is conserved during motion

Silver/silver chloride reference electrode

https://commons.wikimedia.org/wiki/File:Ag-AgCl_Reference_Electrode_wide.jpg

- Needed to record stable potentials
- Plug is in contact with the potential source
- Gives a stable potential to about 1 mV over a period of several hours
- Reusability

Refreshing key electrical concepts

- Ohm‘s law:
  - V = I R
    - where V is the voltage, I is the current and R is the resistance
  - **J** = σ **E** (approximation, assumption current is proportional to electric field)
    - where **J** is current density vector, σ is the conductivity of the medium and **E** is the electric field
  - **V** = **I Z** (time variant)
    - where **Z** is the impedance
- Impedance
  - **Z** = **R** + j**X**
    - where **R** is resistance and **X** is reactance (vectors in a complex plane)
- Reactance
  - $X = X_L + X_c = \omega L - 1/\omega C$
    - where X_L is the inductive reactance, X_c is the capacitive reactance ω is the angular frequency, L is the inductivity and C is the capacitance
- Power:
  - $P = V I = I^2 R = V^2 / R$

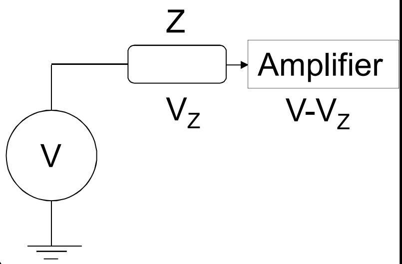
Electrodes and currents

- Assume two electrodes
- Inject a current in one electrode
- Current will spread out radially
- Current density: $I_v = \frac{I}{2\,\pi r^2}$

Hint: current density is the current per unit area of cross section

Electrode impedance

- Modeled as a voltage source and a resistor
- Impedance is a contact quality measure
  - Bad contact => high impedance
- Due to impedance, voltage will be lost
  - Reduce electrode impedance to maximize power transfer & to reduce noise
  - Electrode/ skin interface impedance will always be present!
- From Ohm’s law one can derive an equation for the electrode impedance
  - $electrode\ impedance\ = \frac{\rho}{\sqrt{2\,\pi A}}$



ρ: Resistivity of the medium
A: Finite area of electrode

Physiological Signals

Objectives

- Function and types of electrodes
- Limiting factors - Noise
- Bioelectric Amplifiers

Amplitude of Biomedical Signals

Type of bioelectrical signal	Typical amplitude
ECG/EKG	1 mV
EEG	100 µV
Electromyogram (EMG)	300 µV
Nerve action potential NAP	20 µV
Transmembrane potential	100 mV
Electro-oculogram EOC	500 µV

B.H. Brown et al., *Medical Physics and Biomedical Engineering*, 1999, table 9.2. The typical amplitude of some bioelectric signals.

- Need to minimize noise!

Johnson noise

- Some sources of noise can be eliminated:
  - Purification of skin, electrode movement
  - Interference of other devices
- Noise caused by thermal movement of charge carriers can not be eliminated
- Estimation of noise amplitude is of crucial importance
  - Noise might be bigger than signal of interest

Current	# of electrons per second
1 A	$\approx 6 \times 10^{18}$
1 μA	$\approx 6 \times 10^{12}$
1 pA	$\approx 6 \times 10^{6}$

B.H. Brown et al., *Medical Physics and Biomedical Engineering*, 1999, chapter 9.3.2.

Johnson noise: The root mean square noise voltage is proportional to temperature and resistance of the conductor.

$$V^2 = 4kTR\ df$$

Calculation of thermal noise between two electrodes

The total resistance measured between two electrodes is 1 kΩ and the recording system has a bandwidth of 5 kHz in order to record nerve action potentials at a temperature of 23°C (≈ 300K). Calculate the expected thermal noise between two electrodes applied to the body. ($k = 1.37 \times 10^{-23} W\ s\ \deg^{-1}$)

$$\frac{V^2}{2R} = 2kT\ df$$

Calculation of thermal noise between two electrodes

The total resistance measured between two electrodes is 1 kΩ and the recording system has a bandwidth of 5 kHz in order to record nerve action potentials at a temperature of 23°C (≈ 300K). Calculate the expected thermal noise between two electrodes applied to the body. ($k = 1.37 \times 10^{-23} W\ s\ \deg^{-1}$)

$$\frac{V^2}{2R} = 2kT\ df$$

Solution:

$V = (4 \times 1.37 \times 10^{-23} W\ s\ \deg^{-1} \times 300K \times 10^3 \Omega \times 5 \times 10^3 Hz)^{1/2} = \mathbf{0.2867}\ \mu V$

Physiological Signals

Objectives

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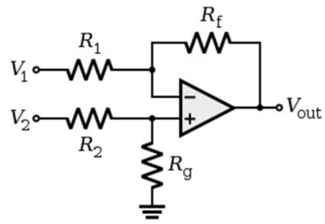
Differential amplifier



https://commons.wikimedia.org/wiki/File:Op-Amp_Differential_Amplifier.svg

$$CMRR = 20\log\left(\frac{signal\ gain}{common\ mode\ gain}\right)$$

$$signal\ gain = \frac{V_{out}}{V_{in}} = \frac{V_{out}}{(V_a - V_b)}$$

$$common\ mode\ gain = \frac{V_{out}}{V_{cm}} = \frac{V_{out}}{(V_a + V_b)/2}$$

- Signal of interest is connected between (+) and (-)
- External electric field influence input signals (+) and (-)
  - V_{out} is never 0
- Imperfection of the amplifier is given by the common mode rejection ratio (CMRR)

Differential amplifier

Realistic differential amplifier:

$$V_{out} = G(V_a - V_b) + 0.5(V_a + V_b)G_{cm}$$

Example

- $V_{cm} = 100\ mV$
- Signal of interest (EEG): $V_{in} = 100\ \mu V$
- Goal: Reduce the interfering signal (V_{cm}) to 1% of V_{out}
- Calculate CMRR in order to achieve that

$$CMRR = 20\log\left(\frac{signal\ gain}{common\ mode\ gain}\right)$$

$$signal\ gain = \frac{V_{out}}{V_{in}} = \frac{V_{out}}{(V_a - V_b)}$$

$$common\ mode\ gain = \frac{V_{out}}{V_{cm}} = \frac{V_{out}}{(V_a + V_b)/2}$$

Differential amplifier

Example

- $V_{cm} = 100\ mV$
- Signal of interest: $V_{in} = 100\ \mu\text{V}$
- Goal: Reduce the interfering signal (V_{cm}) to 1% of V_{out}
- Calculate CMRR in order to achieve that

$$required\ signal\ gain = \frac{V_{out}}{100\ \mu V}$$

$$required\ CM\ gain = \frac{\frac{V_{out}}{100}}{100\ mV}$$

$$CMRR = 20 \times \log\left(\frac{V_{out} \times 10^{2} \times 10^{-1}}{V_{out} \times 10^{-4}}\right) = 100\ dB$$

Summary

- Electrodes convert ion flow into electrical current
- Type of electrode must be chosen for the specific purpose
- Minimum noise is produced by the thermal motion of ions and electrons
- Noise appears in every measurement and it is dependent on temperature, resistance and bandwidth
- CMRR is important to increase accuracy of amplifiers