SUMMARY OF THE COURSE
in master's programme Biomedical Engineering
Course 362.177 Biophysics

Old exam questions

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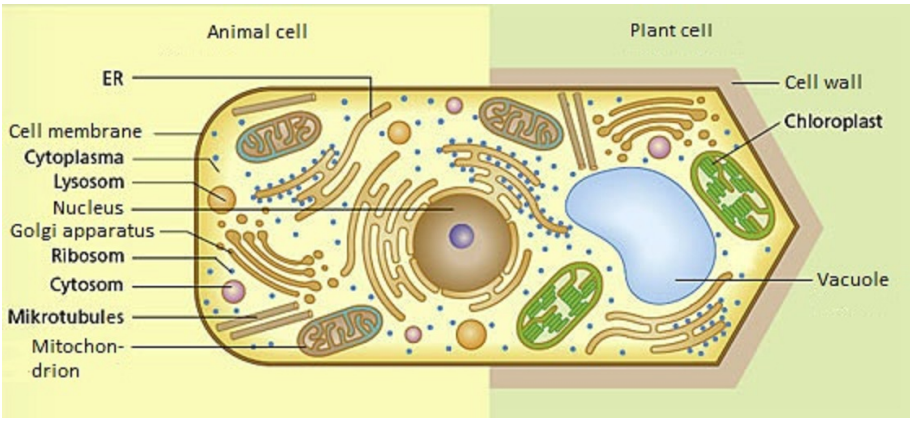
Contents

1 Biophysics of the cell

1. **Name 6 cell organelles and a keyword for their function.**



Nucleus Contains DNS, Brain of the cell

Lysosom corrode (zersetzen) of polymers

Mitochondria ATP building

endoplasmatic Reticulum Translation and Transport

Golgi-Apparat modification of Proteins

Zentriol Transport and Stabilisation

2. **What are the different types of tissue? Brief description of the properties.**

Tightly packed tissue Cell under consideration is mechanically coupled with its surrounding neighboring cells (connecting proteins in the cell membrane). Guarantees stability against shear and tensile forces. Examples: epithelial tissue (skin), striated muscle, Adipose tissue, Nerves

Tissue of low cell packing density Mechanical cohesion of the disorderly distributed cells is provided by an extracellular fibrous matrix. Example: Connective tissue, Cartilage tissue

3. Binding types, secondary and tertiary structures.

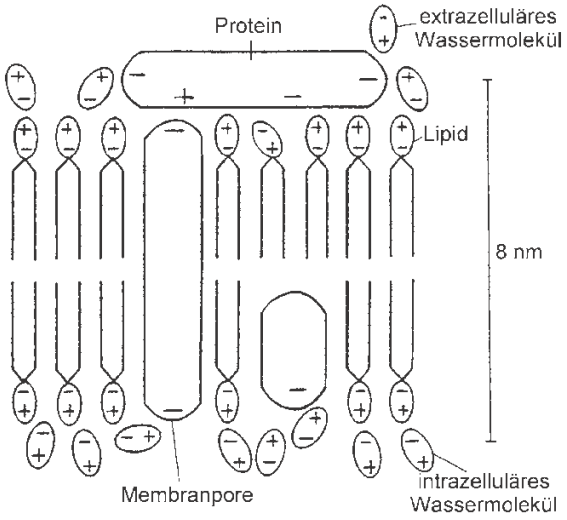
Bonding types:

- Covalent bond
- Ional bond
- Polar bond
- Hydrophobic bond
- a combination of several bonds leads to a higher overall stability

Secondary structure Spatial arrangement of close neighboring amino acids. e.g. double helix

Tertiary structure Three-dimensional structure of the chain consists of several secondary structures. e.g. proteins

4. Schematic structure of a cell membrane (biomembrane). What function do they fulfil?



Separation of the cells and thus maintenance of the internal milieu. Insertion and attachment of proteins. Transport of ions through spatial channels.

5. Enzymes/Liptides?

Enzymes are proteins that control the probability of molecular reactions. Example: Conformational change of a biomolecule.

Lipids are fat-like substances that are insoluble in water. Essential for building cellular structures. consist of 2 distinctly different parts:

6. **Structural formula for any peptide.**

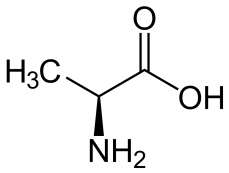


Figure 1: Alanin $C_3H_7NO_2$

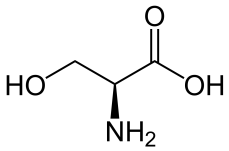
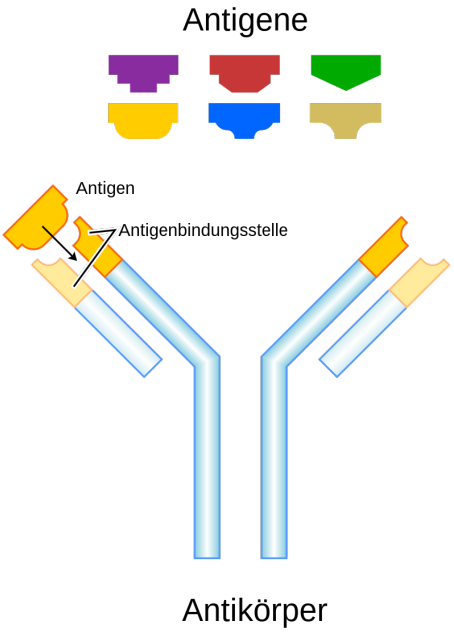


Figure 2: Serin $C_3H_7NO_3$

7. **Antigen/antibody?**



Antigens are molecules or foreign body structures to which antibodies can bind. Antigens are usually proteins, lipids, carbohydrates or other complex molecules. Any substance that specifically binds with an antibody is called an antigen.

Antibodies is a protein that can bind specifically to a certain antigen according to the lock-and-key principle. Its main task is to fight foreign bodies that harm the organism.

8. **Draw an amino acid with any residue?**

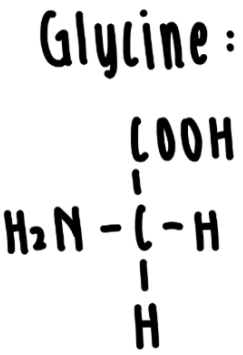


Figure 3: Glycine

9. **Which 3 types of residues can be distinguished in the amino acid?**

   a) Electrically inactive residues - Hydrophobic
   b) Polar residues - Hydrophilic
   c) Charged (ionic) residues - electrostatic alternation

10. **Conformational/charge complementarity (KLK)?**

    All variants of biological information processing are based on the KLK principle! Consists of two types of complementarities:

    Conformation Geometric fit $\rightarrow$ lock-and-key principle

    Charge Electrically charged end positions $\rightarrow$ electrostatic force coupling

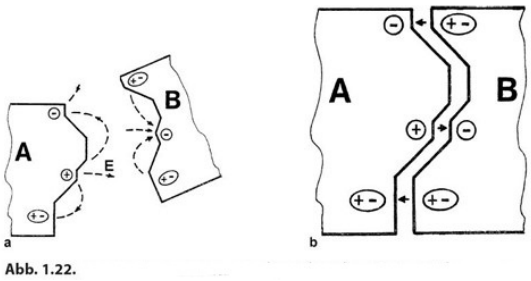


Figure 4: Figure description: Schematic representation of the coupling of two molecular ends A and B by KLK (a) Non-saturated scattering fields of free ends. (b) Coupled state of reduced energy content.

11. Sketch a Ribonucleic acid (RNA) molecule. Where is it used?

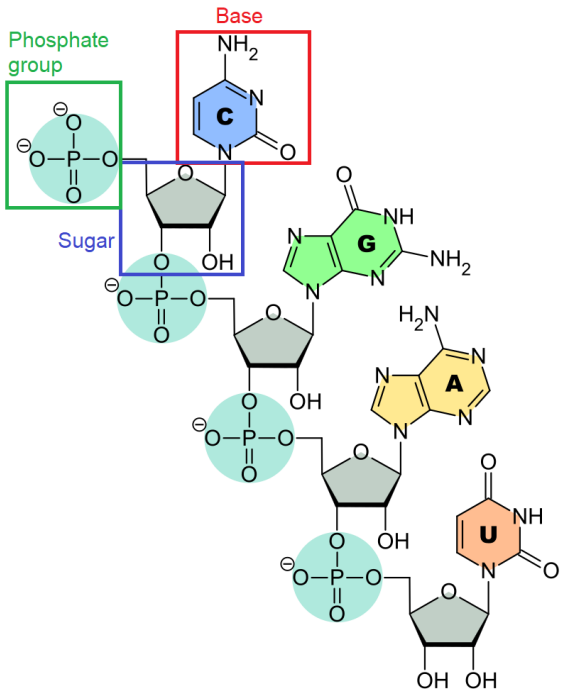


Figure 5: Top to bottom: Cytosine, Adenine, Guanyin and Uracil.

RNA is used in protein synthesis. As mRNA, it is transported to a ribosome where it serves as a blueprint for the formation of a protein. The tRNA docks onto the mRNA and forms the individual amino acids which together form a protein (3 bases code for 1 amino acid).

12. Deoxyribonucleic acid (DNA)-molecule

Here, a different sugar is present and it consists of the bases Adenine(A), Cytosine(C), Guanine(G) and Thymine(T). Another difference to RNA is that it consists of 2 primary chains, which form a compound ladder that is also wound into a double helix. There is a KLK complementarity between A and T and G and C.

13. How does the DNA duplication (replication) take place? Draw a sketch

Topoisomerase End spining of the DNA

Helicase Splitting of the DNA

Primase Attach of short RNA segments, so-called primers, which are used to initiate the actual strand synthesis.

DNA-Polymerase Continuously link matching deoxyribonucleotides to form the new complementary strand.

Only in lagging strand:

Okazaki-Fragment Short sections of the subsequent strand of DNA

DNA-Ligase Linking the fragments to form an entire strand

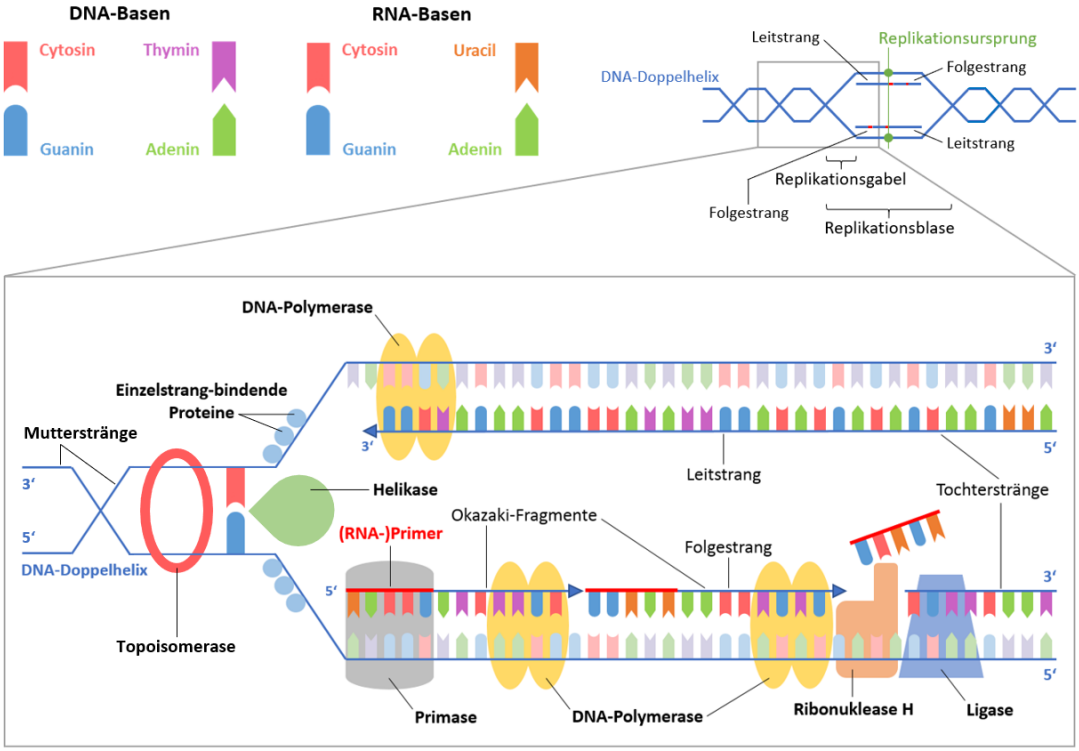


Figure 6: Top: lagging strand; Bottom: leading strand)

14. Principle of protein synthesis (DNA $\longrightarrow$ protein)?

Trankritption

a) The DNA segment contained in the gene is exposed.

b) The matrix strand relevant for reading is unfolded by local inhibition of the electronic base binding.

c) In analogy to DNA duplication, nucleotides are added to the unfolded matrix strand via KLK.

d) The nucleotides are chemically (covalently) linked, resulting in an mRNA.

e) After uncoupling of the mRNA, the DNA closes. The mRNA moves from the nucleus to the cytoplasm.

Translation

a) The mRNA binds to a ribosome.

b) The tRNA attaches the mRNA to each triplet by electrostatic attraction. It is important that the identification region of the tRNA matches the base triples on the mRNA.

c) Depending on the Base triple a specific amino acid is released by the tRNA.

d) The amino acids is covalent linkage to the other ones and forms a protein.

e) The tRNA is uncoupling and the next one can attach.

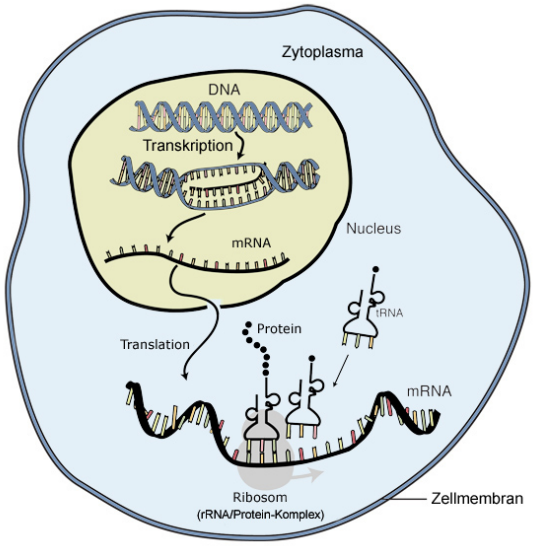


Figure 7: Transcription takes place in the nucleus. Translation in the ribosome.

15. Genetic code protein coding.

The nucleotides (Adenine, Guanine, Cytosine, Uracil) of an RNA encode the 20 amino acids of the corresponding type. Thus, 3 positions (4^3 = 64) are sufficient for clear coding.

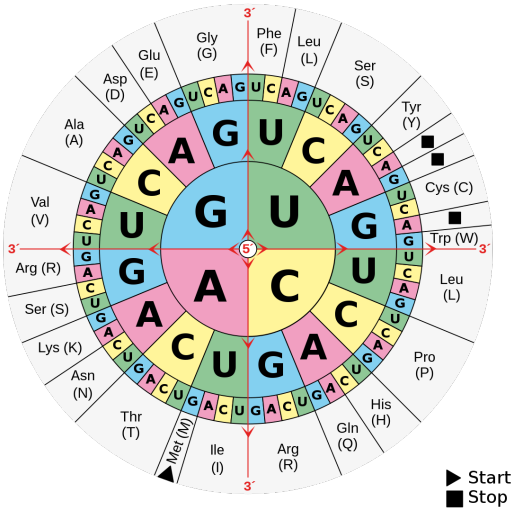


Figure 8: Base-Triple.

16. Introduction of a foreign gene?

The specific introduction of a foreign gene into a cell can be carried out using recombinant DNA technology.

a) The DNA containing the gene to be inserted (= fragment G) is divided into fragments by a cutting enzyme. $\longrightarrow$ fragments F, G, H, ...

b) Plasmids (= DNA carrier molecules) are separated using the same cutting technique. $\longrightarrow$ Fragment P

c) The two solutions are mixed with each other, resulting in recombination of the fragments. The aim is to create a combination, in the form of a ring, between the gene to be inserted and the plasmid. $\longrightarrow$ Fragment G+P

d) The G+P ring is introduced into the cell via the cell membrane.

e) The cell is stimulated to divide.

f) Through selective procedures only those cells are cultivated that contain the G+P ring. The protein that these cells produce is further used.

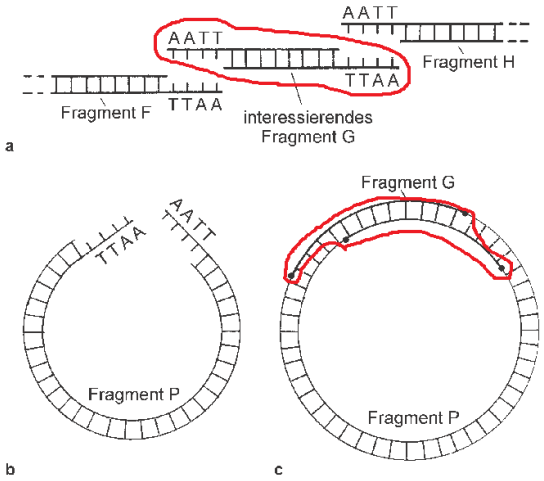


Figure 9: Possible process steps for introducing a foreign gene into a cell. (a) Specifically cut foreign DNA with the foreign gene of interest in fragment G. (b) Specifically cut vector plasmid as fragment P. (c) P and G make up the plasmid chimera.

17. Specify genetic engineering techniques.

Cloning the targeted introduction of a foreign gene into a cell (= recombinant DNA technology).

Cell fusion combination of the genetic material of two cells in a hybrid cell.

18. Explain the process of cell fusion?

Cell fusion = fusion of cells A and B. Electrical variantion

a) an watery medium contains both A and B cells. Prerequisite: The electrical conductivity is lower than that of the intercellular fluid.

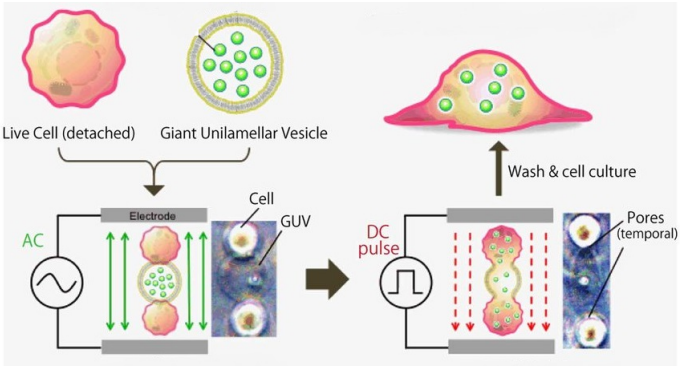
b) 2 electrodes are now used to apply a high-frequency alternating electric field at the frequency of the intercellular flux. The frequency must be high enough to enable the high-resistance cell membranes to be bridged by displacement currents (greater than 100 kHz). This leads to polarisation and thus to an attracting force between the cells. This results in cell chains which are energetically favourable and form current paths of minimal impedance.

c) The membrane contact points form a bottleneck of the current conduction and thus the molecular order of the cells (lipid heads, protein positions. . .) is disturbed by the effect of force. Now a DC pulse is impressed which leads to a complete destruction of the local order. This causes a channel between the cells in contact.

d) The membrane edges now fuse and thus fusion takes place.

e) Now hybrid cells A+B are formed, which however have the total volume of both cells and the sum of the genetic material. A fusion is now achieved by cell division, whereby a stability of the resulting cells is not guaranteed.

f) A repetition of the steps yields multiple fusions with increasing probability.



2 Analytical methods in biophysics

1. **Resolution of Transmission electron microscope (TEM), Scanning electron microscope (SEM), light microscope? One viewing example each.**

Method	Δx_{opt} [nm]	Example
TEM	0.3	DNS-structure, membrane-structure
SEM	3	Shape of blood-cells, organells of Freeze-fracture preparations
Light microscope	200	cells, blood-cells, bacteria, mitochondria

2. **Tick the appropriate characteristics for each microscopy method.**

	SEM	TEM	STM
Resolution below 1 nm achievable		✓	✓
Requires samples thinner than 1 μm		✓	
Operation requires high voltage (kV range)	✓	✓	✓
Image formation througe scanning mechanism	✓		✓
Maps the surface topography	✓		✓
Only works with conductive samples		✓	

3. **Light microscope? Formula? What is aperture?**

   Optical or light microscopy involves passing visible light transmitted through or reflected from the sample through a single lens or multiple lenses to allow a magnified view of the sample. The resulting image can be detected directly by the eye, imagine on a photographic plate, or captured digitally.

   Numerical aperture is the ability to gather light and to resolve fine sample details at a fixed object distance. The higher the NA value, the more details you can get from your sample. To calculate the numerical aperture, the following formula can be used:

$$NA = n \cdot \sin(\sigma)$$

NA	Numerical aperture	[ ]
n	refractive index	[ ]
σ	half angular aperture	[°]

4. Light microscope: contrast?

Contrast is given when different points x, y have different values for intensity I. Contrast refers to the difference between light and dark areas of an image.

$$I(x,y) = I_0 \cdot e^{-(C \cdot [M] \cdot \varepsilon \cdot d)}$$

$I(x,y)$	contrast	[W/m^2]
I_0	intensity	[W/m^2]
C	concentration	[mol/m^3]
$[M]$	location-dependent concentration	[ ]
ε	extinction	[m^2/mol]
d	thickness	[m]

5. How is the ph value defined? What does it indicate? Colouring?

The pH value results from:

$$pH = -\log[H]$$

The pH value is used to specify the acidity or basicity of an aqueous solution. Acidic solutions are measured to have lower pH values than basic/alkaline solutions.

Colouring is used to increase the contrast. The most effective corresponding procedure is based on the mechanism of electro adsorption. By this, we understand the attachment of particles to a substrate via electrical attraction forces, supported by diffusion forces as a result of strong concentration differences. If the medium has a high pH value, all structures are marked.

6. UV light with light microscope?

$\lambda = 10 - 350\,nm$

UV-Microscopie specific molecules absorb long-wave UV-light.

Flurescence microscopy specific substances absorb UV-light and emit normal light. The microscope us a mercury or xenon lamp to produce UV-light. It is useful for measuring physiological and biochemical events in living cells.

7. SEM/TEM/Scanning tunneling microscope (STM)?

TEM The microscope consists of a Gluh cathode. At the anode, the electrons are accelerated, this is done in a vacuum. After the condenser lens the beam passes through the sample, where the electrons get transmitted though/absorbed by the sample. Then through the objective lens and is then expanded by the projective lens. The beam now hits a fluorescent screen, whereby the sample can be made visible immediately.

SEM The difference to TEM is that the lowest magnetic lens receives deflection coils. Sawtooth-shaped coil currents cause a deflection in the x and y direction. With this method, the high-energy electrons are backscattered and secondary electrons are released. These are directed to a detector and converted into photons. An electrical signal is generated at the output of the PM amplifier. According to its scanning point, it is displayed brighter or darker on an image tube. This method is used to scan the surface of samples.

STM The probe is attached to a piezocritall tripod via an electron-conducting sample. The crystals are changed in length with the voltages Ux;Uy;Uz. If a voltage U is now applied between the probe and the sample, a tunnel current of strength I is generated that depends on the distance. Now, at a constant z, the current I(x; y) can be used for imaging. In this way, 3D structures can be reconstructed.

8. How do magnetic lenses work?

The lens consists of a coil with a magnetic core ring, which generates an inhomogeneous magnetic field inside. An entering electron hits this magnetic field and is deflected by the Lorentz force. The result is a helical path that leads to a focal point.

9. X-ray microscopy

$\lambda = 100 - 0.01\,nm$
In general, x-ray is transmitted through the material, atoms absorb the X-ray radiation and the resulting image is from reflection, absorption/transmission. Practically no sample preparation is necessary, and the lateral resolution is in the μm range. Low interaction with the sample.

Methods:

Grid principle The X-ray beam hits a thin copper foil which focuses the beam to a point source. Under the foil lies the sample which is detected by the absorption in a detector location.

Projection Merthod Sample is placed at some distance from the target foil. The beam is widened.

High-resolution X-ray microscopy The beam is focused by zone plates. Proteins and the water in the cells have a very different absorption coefficient (ε) $\rightarrow$ water window; this gives you a high contrast.

10. Properties and principle of X-ray structure analysis? Explanation of the Laue conditions. Definitions of quantities.

It is not a microscopic procedure, because the image is only produced after mathematical processing. It allows the measurement of biological molecules. The sample must be crystalline.

The Rontgen source consists of a Gluh cathode and these are accelerated onto a copper target, whereby the electrons are shot out of the innermost K-shell, which are

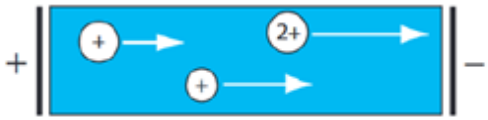
replaced by the L-electrons that follow! A K-radiation quantum is created, whereby this represents a Rontgen radiation. The sample is now transilluminated with the X-ray beam and reflections appear on a detector screen, which allow conclusions to be reached about the sample.

Laue condition = Description of diffraction effects on crystals. If the condition is fulfilled, maximum interferences occur.

$$d \cdot \sin(\theta) = n \cdot \lambda$$

d	Distance	[m]
θ	Scattering angle	[°]
n	Refractive index	[ ]
λ	Wavelength	[m]

11. Describe the principle of electrophoresis with the help of a sketch. What voltages are necessary? Which carrier materials are there?



Electrophoresis is a laboratory technique to separate the mixtures of substances or particles in an electric field. It refers to the electromotive force (EMF) that is used to move the analytes (molecules, proteins, etc.) through an electrolyte chamber (a gel matrix, usually). The seperation is based on the differences in:

- size of the molecule
- electric charge of the molecule

Current:
Depends on which carrier material is used and what Ions should be analyse. For Agarose-gel analysis by separation of Na^+ Ions 1 kv is needed.

Carrier materials:

- Agarose- and polyacrylamide gel
- Cellulose acetate film

12. How does DNA mapping work?

This is a characterisation of larger molecular sections based on the distribution of enzymatic cutting sites.

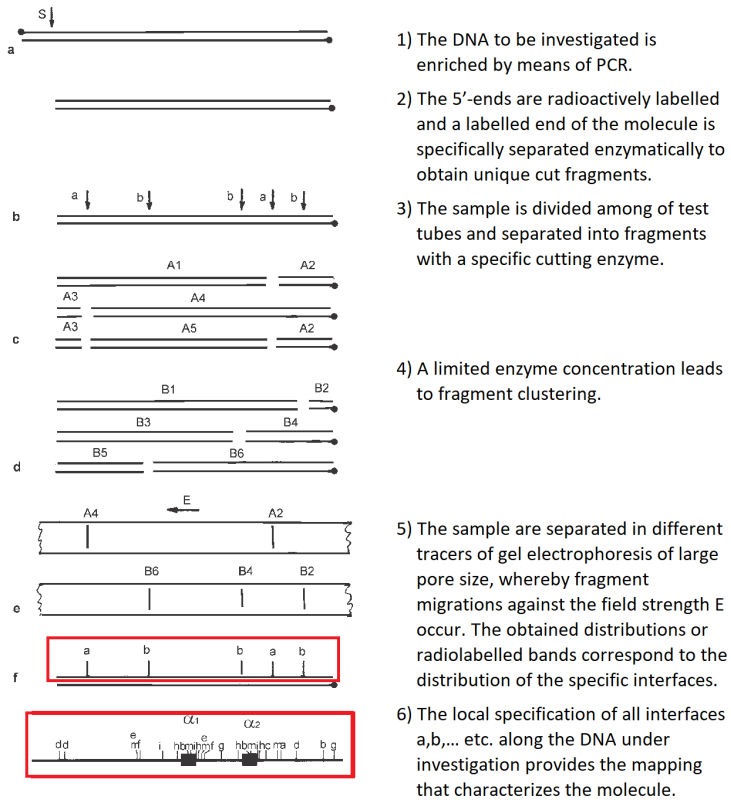
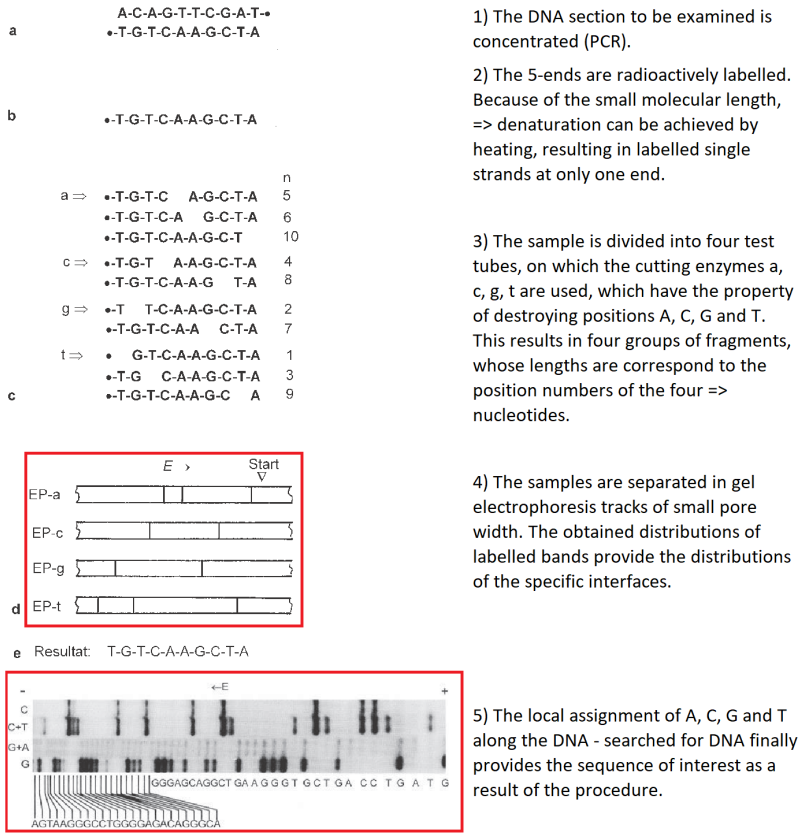


Figure 10: Functional steps of DNA mapping.
(a) DNA section under consideration with radioactively labelled 5'-ends, before and after separation of a 5'-end by a cutting enzyme s.
(b) Potential cutting sites of two cutting enzyme types a and b.
(c) After application of a, sample A with molecule fragments A1...A5 (A2 and A4 labelled).
(d) After application of b, sample B with fragments B1...B6 (B2, B4 and B6 marked; other unlabelled fragments not sketched).
(e) Results of electrophoresis (with start on the left) of A and B showing only labelled bands.
(f) Mapping as a result of the procedure

13. How does DNA sequencing work? Principle by means of electrophoresis, in individual process steps.



1) The DNA section to be examined is concentrated (PCR).

2) The 5-ends are radioactively labelled. Because of the small molecular length, => denaturation can be achieved by heating, resulting in labelled single strands at only one end.

3) The sample is divided into four test tubes, on which the cutting enzymes a, c, g, t are used, which have the property of destroying positions A, C, G and T. This results in four groups of fragments, whose lengths are correspond to the position numbers of the four => nucleotides.

4) The samples are separated in gel electrophoresis tracks of small pore width. The obtained distributions of labelled bands provide the distributions of the specific interfaces.

5) The local assignment of A, C, G and T along the DNA - searched for DNA finally provides the sequence of interest as a result of the procedure.

Figure 11: Functional steps of DNA sequencing for a DNA section with N = 10 positions.
(a) DNA section under consideration with radioactively labelled 5' ends.
(b) Single strand obtained by thermal denaturation.
(c) After application of specific cutting enzymes a, c, g and t, whereby double cuts are not taken into account. The length of labelled fragments corresponds to the position number n.
(d) Results of the four electrophoresis approaches. EP-a to EP-t when only labelled bands are shown.
(e) Sequence as a result of the procedure.

14. What is 2D Electrophoresis, Sodium dodecyl sulphate (SDS) electrophoresis, electrofocusing?

2D Electrophoresis Has two dimensions. First dimension is isoelectric focusing where seperation occurs by charge (PI). The second dimension has seperated occuring by mass.

SDS electrophoresis Proteins are so strongly labelled by negatively charged SDS

(sodium dodecyl sulphate) so strongly that the amount of the total charge is proportional to the number of amino acid positions.

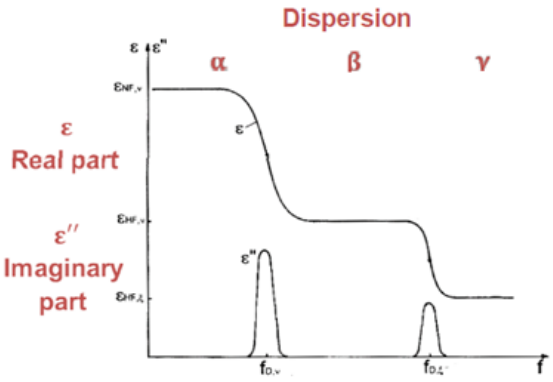
Electrofocusing The strong scattering of the isolectric point (PI) is used. A gradient of pH is built up in the carrier by opposing an acidic anode with a strongly alkaline cathode. The applied proteins now move until they have reached a location characterised by pH = PI.

15. Principle of the mass spectrometer (Matrix-assisted Laser Desorption/Ionization (MALDI))? How can large molecules be ionised?

Mass spectroscopy is a method for measuring the mass-to-charge ratio of particles. For a known charge, q, the mass, m, can be determined. The molecules are ionised by e.g. a laser beam. These ionised molecules are evaluated in the analysis chamber on the basis of their flow time.

Ionization:
The large molecules are placed in a UV-absorbing matrix and bombarded with a laser.

16. Diagram of ε of different materials. Draw $\alpha,\ \beta,\ \gamma$ dispersion.



α-Dispersion low frequency range (typically, 0 – 10 kHz)

β-Dispersion high frequency range (typically, 0.1 – 10 MHz)

γ-Dispersion microwave range (typically, 0.1-30 GHz).

17. Give complex permittivity, definition and Local curve.

The complex permittivity (= relative permittivity, substance-dependent permittivity number) is a measure of the field-weakening effects of the dielectric polarisation of the medium. It depends on the type of material, frequency, temperature and externally acting fields.

$$\varepsilon = \varepsilon_0 \cdot \varepsilon_r$$
$$\underline{\varepsilon} \equiv \varepsilon_r = \varepsilon' - i\varepsilon''$$

ε	permittivity	[As V^{-1} m^{-1}]
ε_0	vacuum permittivity	[As V^{-1} m^{-1}]
ε_r	relative permittivity	[ ]
$\underline{\varepsilon}$	complex permittivity	[ ]
ε'	real part of the realtive permittivity	[ ]
ε''	imaginary part of the relative permittivity = dielektric loses	[ ]

Alternating fields of high frequency convert electromagnetic field energy into thermal energy. This is because the materials will repolarise quickly and frequently. This occurring thermal loss is called dielectric loss and is described by the imaginary part ε''. Clearly above the dispersion frequency f_D, $\underline{\varepsilon}$ is real and losses do not occur. Maximum losses occur for the frequency f_δ.

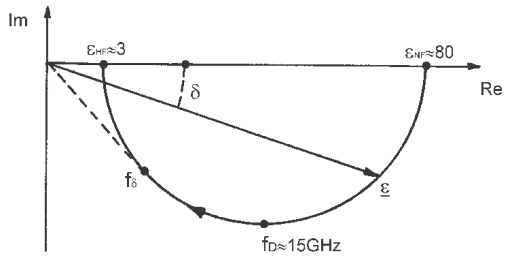


Figure 12: The spatial curve of the complex permittivity is drawn by means of the Cole-Cole curve. Example shows the values for water. δ = loss angle; ε_{LF} = permittivity at lower frequencies; ε_{HF} = permittivity at higher frequencies

18. (diagram of permittivity given) Explain dispersion using the sketch. What types of dispersion are there in biological media? What causes the dispersion types?

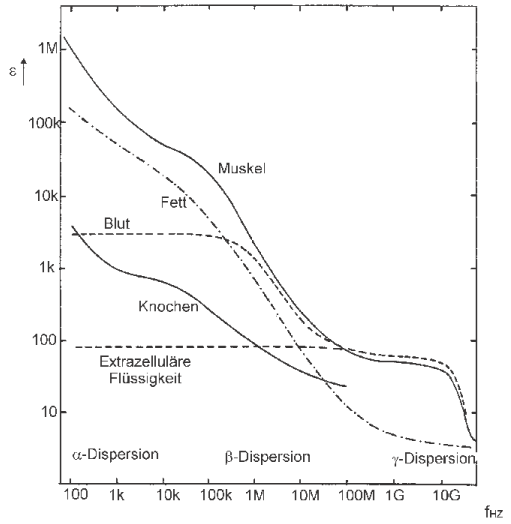


Figure 13: Typical permittivity curve versus frequency f for various biological media. The curves given for transversely striated muscle tissue apply to field directions normal to the fibre axis.

Dispersion Is the relationship of a physical quantity, in this case permittivity, to the frequency of a wave.

α **-dispersion** By redistribution of the ion cloud in the cell. But this is controversial because the electrical impedance superimposes the signal.

β**-dispersion** LF: Orientation polarisation HF: Displacement polarisation

γ**-dispersion** LF: The capacitance of the cell is determined by the low membrane conductivity. Since the membranes are connected in series. HF: The capacitance of the cell is determined only by the intracellular fluid. Since the membrane is bypassed by displacement currents.

19. Displacement/orientation polarisation, phase boundaries metal/electrolyte in relation to dispersion.

Displacement polarisation Occurs with γ dispersion in the High frequency range (HF). A field intensity E acting on the matter causes a shift of the centre of gravity of the electrons with respect to that of the protons.

Orientation polarisation Occurs with γ dispersion in the Low frequency range (LF). This is an orientation of such molecules at the field E, which also show a polar moment for E = 0.

Metal/electrolyte phase boundaries Occurs in α dispersion. When a negative voltage is applied, ions and water molecules attach themselves. These form a layer that has an insulating effect.

20. Sketch and describe the function of a magnetic field coil. Draw magnetic field lines and the movement of the electron. Give the formula for the force on the electron.

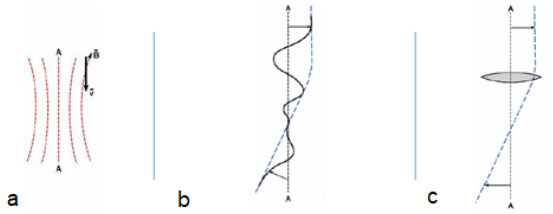


Figure 14: (a) shows the magnetic field and the initial velocity of an electron. (b) shows that the magnetic forces cause the electron to spiral around the lens axis, in increasingly small twists, focusing it. The beam diverges past the focus point. This result is similar to (c), the optical lens.

In a magnetic field, the moving electron is subject to the Lorentz force. It is perpendicular to the magnetic field lines, and to the direction of the movement of charge.

Lorentz force equation:

$$F = e(B \cdot V)$$

F	Force	[N]
e	Charge	[As]
B	Magnetic field	[kg/A s^2]
V	Velocity	[m/s]

21. Match the letters in the sketch to the given terms: Ion source, vacuum pump, ion chamber, analysis chamber, detector system, mass spectrum. Explain the functional principle of mass spectroscopy.

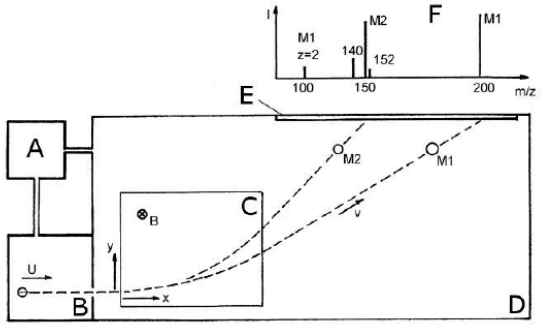


Figure 15: A = vacuum pump, B = Ion source, C = ion chamber, D = analysis chamber, E = detector system, F = mass spectrum

22. a) Please name three essential differences between light microscopy and electron microscopy. b) Please name three structures within the cell that are only visible under the electron microscope and three other intracellular structures that are already visible under the light microscope

Table 1: a)Three essential differences between light microscopy and electron microscopy.

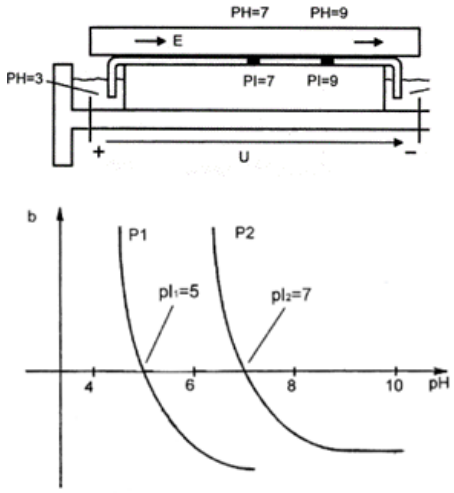
Differences	Light microscopy	Electron microscopy
Thickness object	$\geq 5\,\mu m$	$\leq 0.1\,\mu m$
Illumination source	Light	electron beam
Vacuum	Not required	essential

b) Visible structures:

Light microscopy Nucleus, Lysosomes, large Mitochondria

Electron microscopy Cell membrane, Ribosomes, Filaments

23. Explain the principle of electro-focusing with the help of a sketch (e.g. carrier medium). What is the isoelectronic point?



Electrofocusing is a sub type of electrophoresis featuring a pH-gradient in the carrier material. The varying pH is relevant to stop proteins at their IP (isoelectric point). Different types of proteins form bands corresponding to their pH = pH(isoelectric).

The isoelectric point of a protein is the specific pH-value, where the entire protein molecule has an electrical net charge of zero. At the isoelectric point, the protein behaves electrically neutral.

24. Electrophoresis of nucleic acid.

See question 12.

25. What is the resolution of an X-ray microscope, properties?

$\Delta x_{opt} = 50\,nm$
Properties see question 9.

26. Explain the phenomenon of β dispersion using muscle cells.

Explanation see question 18.

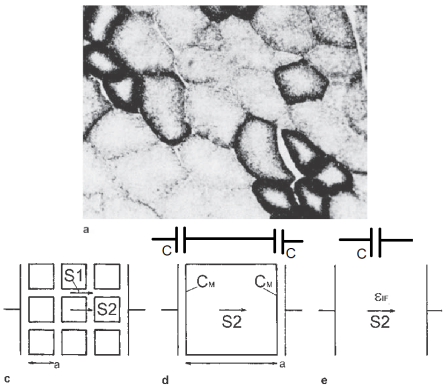


Figure 16: Model for estimating the β dispersion of biological tissues. (a) Transversely striated muscle tissue in cross-section (microscopic image). (c) Approach of cubic cells with current path S1 through the extracellular cleft and current path S2 through the membranes. (d) Membran enveloped single cell as smallest element. (e) Membrane-loose cell as a result of membrane bridging by displacement currents occurring at high frequency.

3 Neurobiophysics

1. **Passive membrane properties? Cable model? Conductance of the membrane versus frequency?**

   Passive properties Lipid-basic-structure is molecularly dense, preventing the passage of ions. Current flow happens mainly through pores. Corresponding structures carry predominantly negative fixed charges $\longrightarrow$ electrostatic affinity for positive ions. Therefore, small cations such as K^+ , Na^+ are involved in the current flow.

   Cabel modell Fiber is represented by four poles connected in series (quiescent/inductive voltage is neglected). allows estimation of passive propagation (remote effect) of a voltage u(x) predetermined at a location x and superimposed on quiescent voltage U. G'M and C'M are now related to the length. (following two figures)

   Conductivity

   - order of magnitude 1 mS/cm^2
   - strongly fluctuating due to fluctuating density of the membrane pores $\longrightarrow$ strongly insulating function!

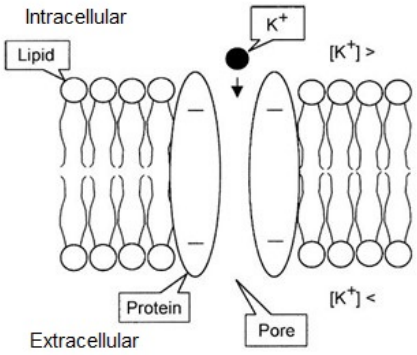


Figure 17: Schematic figure to show the simplest passively working type of pores in a membrane. The transport is possible for small ions, which are under the influence of a diffusion force and an electrostatic force.

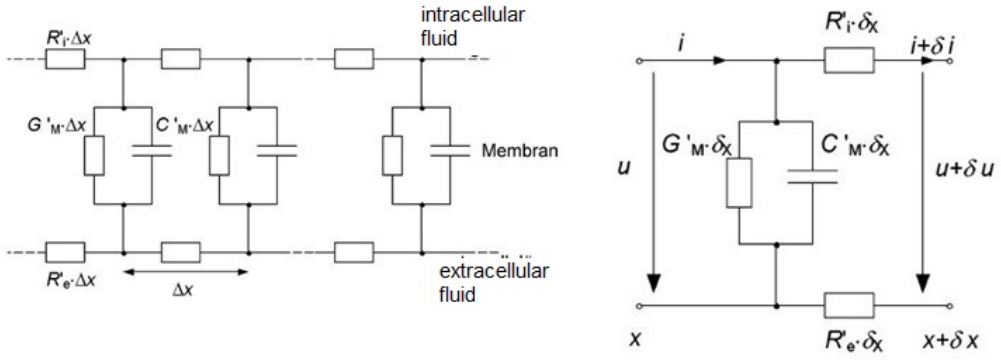


Figure 18: Left: Cable model of a cylindrical cell section (without taking into account the of the so-called quiescent stress U) Right: Modeling of an infinitesimally small length section $\Delta x \longrightarrow \delta x$

2. How is the resting membrane voltage generated in a cell? Measurement

Generation Observation of a pore, which is opened at time 0. Since a stronger concentration of K-ions is present in the intracellular space than in the extracellular space, K-ions will diffuse outward as a result of the diffusion force F_d. At the same time, because of the lack of positive charge in the interior, a voltage $U \neq 0$ builds up. The corresponding average field strength $E = \frac{U}{d_M}$ (d_M = thickness of membrane) leads to an electrostatic restraining force Fe, which brings the ion migration to a standstill as it increases to F_d. The migrated K-ions give a layer of positive space charge density ρ on the outside of the membrane; a corresponding counter-layer with negative ρ is to be expected on the inside, above all by migration of dissociated macromolecules. The overall result is an electrical double layer (analog to the charge of capacitor plates) with the molecular lipid double layer as the center.

Mearurement A microelectrode is inserted into the cell and a second “indifferent” electrode, which has a larger contact area, is applied extracellularly. With the help of a voltmeter, a voltage of -70 mV can be measured.

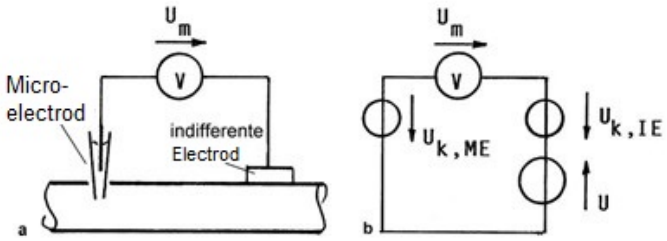


Figure 19: Measurement of the membrane resting tension U on a cylindrical cell surrounded by extracellular fluid. (a) Possible experimental arrangement of a pierced microelectrode (pointed glass capillary filled with electrolyte in which an electrolyte, in which a chlorinated metal filament is immersed) and an externally applied electrode (metal + salt bridge). (b) Equivalent circuit diagram (see Eq.: Um = Uk,ME + U – Uk,IE)

3. **Ion pump**
   = How does the Sodium–potassium pump (Na/K-ATPase) (= ion pump) work? What happens when it is blocked, e.g. by opiates?

   Ensures that excess ions, that have changed location are transported back in other ways. For this purpose, special membrane pores are used which contain an asymmetrically constructed protein with ion-specific active groups (in the sense of an enzyme). The active group is initially in the cell interior affine for Na-ions (KLK-Passung = Conformation/charge complementarity) and releases them again in the extracellular space after translocation. Affinity for K-ions and their translocation into the cell interior is now formed. Ion pumps work under ATP consumption.

   Opiates:
   G-Strophantin (Oubain), partially inhibits the Na/K-ATPase, thus increasing the intracellular sodium concentration. This causes a lower driving force of the Na/Ca transporter which pumps Ca out of the cell. The increased Ca level in the heart muscle cells causes an increased contraction performance.

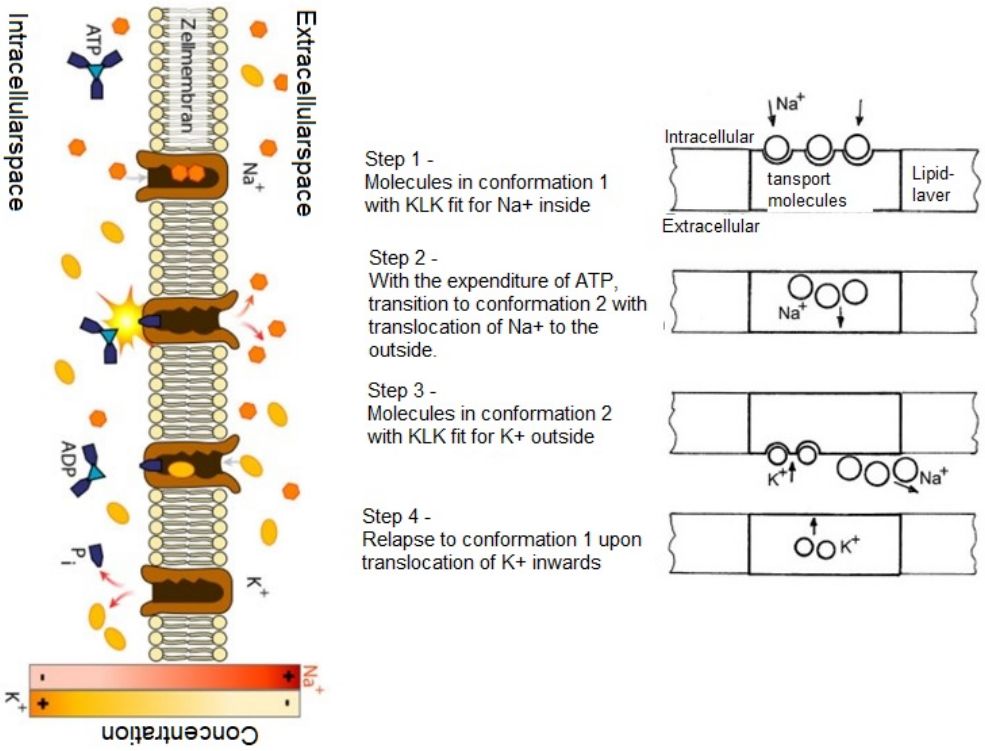


Figure 20: Figure description: (Page 163) Active transport through the Na/K ion pump to maintain the of the flow equilibrium (four functional steps). (1) A molecule in Conformation 1 with KLK-Passung for Na+ inside. (2) After usage of ATP transformation in 2nd Conformation issued by translocation of Na+ to the outside space (3) The molecule in 2nd Conformation with KLK-Passung for K+ outside (4) Return in 1st Conformation issued by translocation of K+ to the inside space

4. Calculate membrane potential in general and with Chlorine (Cl)

Nernst-equation $\longrightarrow$ general:

$$U = \frac{R \cdot T}{F} \cdot \ln\left(\frac{[K^+]_e}{[K^+]_i}\right) = 58\,mV \cdot \ln\left(\frac{[K^+]_e}{[K^+]_i}\right) = -83\,mV$$

Goldman-equation $\longrightarrow$ Cl:

$$U = \frac{R \cdot T}{F} \cdot \ln\left(\frac{p_K \cdot [K^+]_e + p_{Na} \cdot [Na^+]_e + p_{Cl} \cdot [Cl^-]_i}{p_K \cdot [K^+]_i + p_{Na} \cdot [Na^+]_i + p_{Cl} \cdot [Cl^-]_e}\right) = -70\,mV$$

U	Current	[V]
R	Gas constant; 8.314	[J/mol K]
T	Temperature	[K]
F	Faraday-Constant; 9.648	[C/mol]
p	Permeability	[m/s]
c	Molar concentration	[mol/m^3]

5. How does an action potential develop? How does it spread? Sketch

Action potentials occur through the opening of sodium channels . Due to the high concentration difference of sodium ions, positive particles flow into the cell, the potential changes from about -70 mV to +30 mV (depolarisation). The sodium channels are subsequently inactivated. In the further course, repolarisation occurs. In this process, positively charged potassium ions flow out of the cell by means of potassium channels that open with a time delay. In some cell types, repolarisation is followed by a small hyperpolarisation before the resting potential of about -70 to -80 mV is reached again.

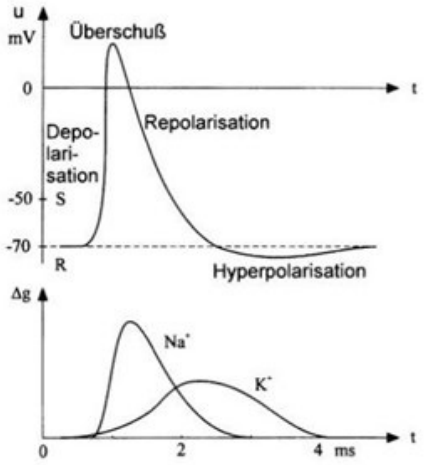


Abb. 3.15.

Figure 21: For a fast neuron typical Time course of the action impulse (R=level of resting voltage, S=level of threshold). The time course becomes clearer with a time-limited increase of the permeabilities g_{Na} and g_K.

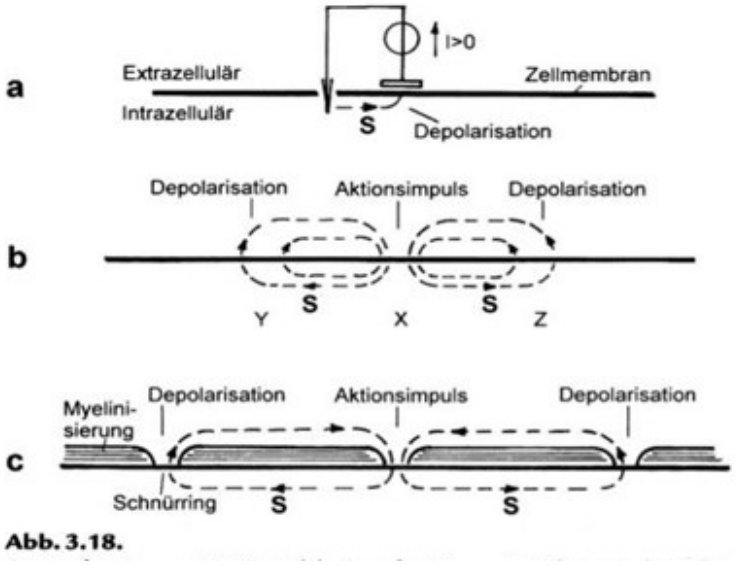
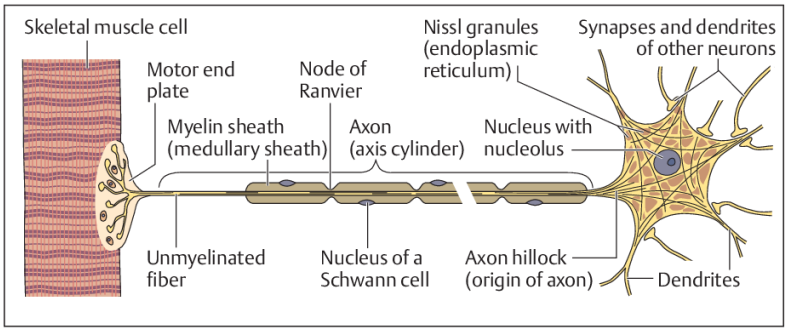


Figure 22: Mechanism of propagation of an action impulse along an axon. (a) Stimulus electrodes generate an outward current in the region X of the outlined section of the cell membrane, which leads to local depolarization. (b) After reaching the threshold, an AI builds up at X. The diffusion current, which is now directed inward, is supplemented by compensating currents distributed compensating currents on both sides to form self-contained circuits. The currents have a depolarizing effect on the left and right side of the stimulus site, whereby AIs occur in regions Y and Z. (c) In the case of myelination, the current flow is concentrated the current flow is concentrated at the lacing ring, thus extending beyond the length of an insulating section and the AI conduction velocity v increases accordingly.

6. What are mylinised fibres (sketch)? Why are they faster?



The nerve fibres are insulated by the glial cells. The compensatory current can only close at the short non-insulated sections - the so-called node of Ranvier. As a result, millimetre-long sections are bridged abruptly (= saltatory). This enables faster signal transmission.

7. Describe in key words the mechanism of contraction of a muscle fibre after electrical stimulation.

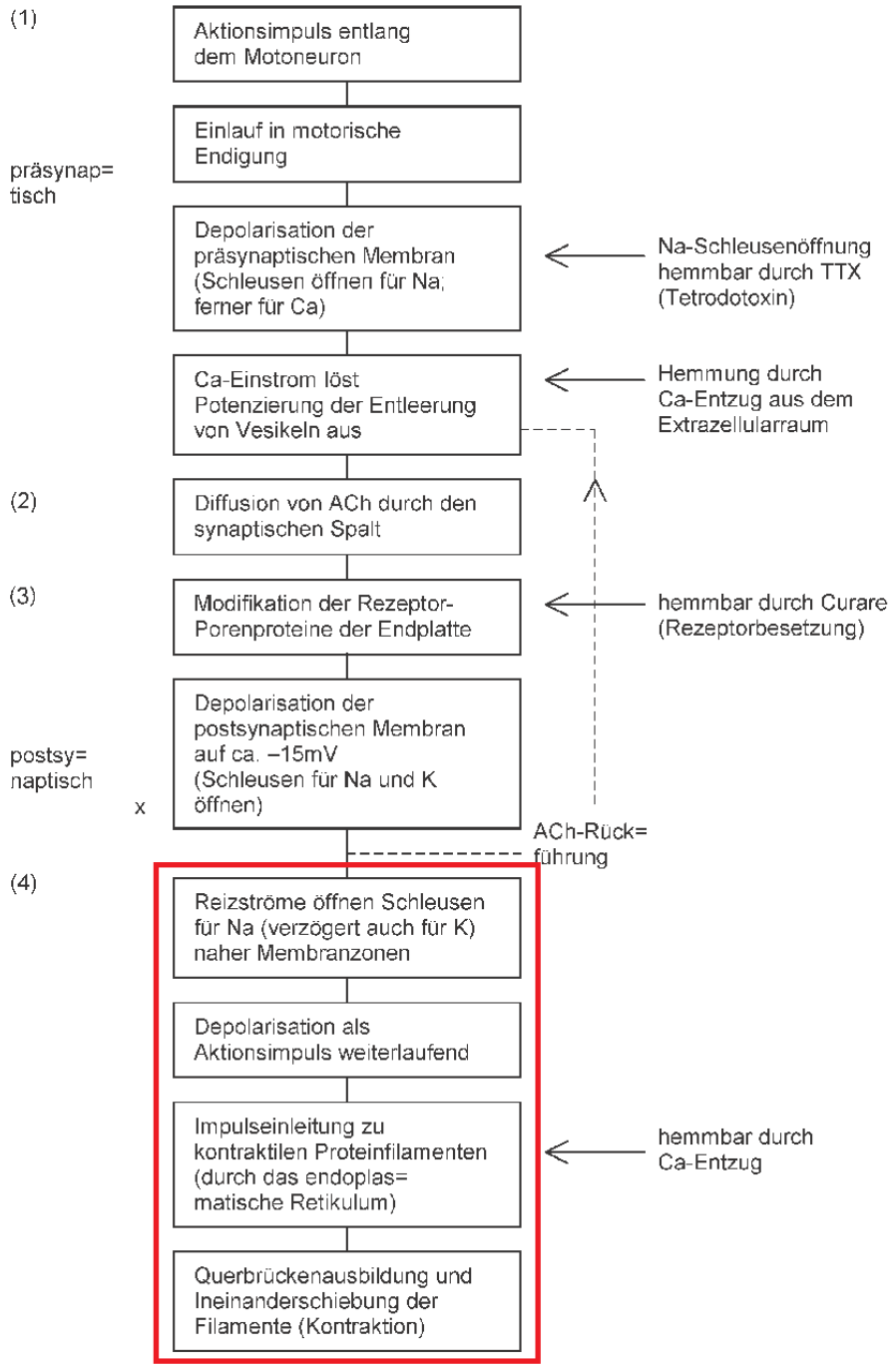


Figure 23: Functional sequence of neuromuscular impulse transmission (functional steps 1-3) and the mechanism of muscle contraction (step 4). Up to the step marked "x", the flow chart also applies to central synapses.

8. **Name three differences between Excitatory postsynaptic potential (EPSP) an AI.**

   - Pores released at EPSP open for K^+ and Na^+ simultaneously.
   - AI needs ATP
   - in AI voltage-gated channels open, in EPSP transmitters open
   - EPSP can vary in intensity, AI is “all-or-nothing”

9. **Description & control muscle contraction mechanism and how can you regulate/control it?**

   Contraction mechanism The AI generated by the synapses propagate along the muscle membrane at 1m/s and regions caught by the depolarization come to contraction at the end of the AI. With a high frequency of the impulses (from 50 Hz) a static maintenance of the state of contraction can be seen.

   Regulatie/control

   - Activation of different parts of the fiber belonging to the muscle
   - Activation of different numbers of synapses on one fiber (at cm-large distances)
   - Variation of the AI impulse-train-frequency and the impulse-train-duration and thus the speed and extent of the I-band retraction.

10. **Explain excitatory synapse.**

    Excitatory synapses form in the postsynaptic cell an EPSP which causes a depolarisation.

11. **Explain inhibitory synapse**

    Inhibitory synapses lead in the postsynaptic cell to an Inhibitory postsynaptic potential (IPSP), which inhibits (unterdrücken) depolarisation.

12. **The toxin Tetrodotoxin (TTX) from the puffer fish blocks selective voltage-gated sodium channels. Does this change the membrane resting potential?**

    No. Tetrodotoxin is strongly hydrophilic and selectively blocks the voltage-gated sodium channels of the nerve cells. This means that no action potentials and the transmission of nerve impulses is blocked. The membrane resting potential is not effected.

13. **What does the black widow’s poison do when uncontrolled Ca^{2+} leaks out?**

    The toxin continuously releases action potentials that leads to cramps and pain. When the transmitter supply is exhausted (erschöpft), no more real stimulus information can be transmitted. The result is paralysis. Death occurs when the respiratory centre is affected by this paralysis.

14. **How does the refractory phase occur after an action impulse?**

    K pores are open for a long period of time during the AI. Due to the corresponding

outflow of the K^+, the actual AI is followed by so-called post potentials during which the membrane is refractory after the AI, i.e., can only be re-excited to a very limited extent.

15. Explain superposition law? (Fire rule).

The superposition principle means that waves can overlap without influencing each other.

Fire rule:

$$u_{AH} = U_{A,AH} + \Delta u_{AH} > U_{S,AH}$$

u_{AH}	Axon hill Voltage	[V]
$U_{A,AH}$	Current of synapse A at the axon hill	[V]
Δu_{AH}	Intensity on the Axon hill	[V]
$U_{S,AH}$	Threshold voltage at the Axon hill	[V]

A large number of EPSPs, with a small counteraction of IPSPs, must interact to reach the threshold $U_{S,AH}$ and lead to Temporal and spatial integration across all N PSPs occurs. As a firing rule it follows that an AI is triggered at that time t, at which the AH-voltage is valid. Furthermore, a delay of the pulses at the AH of 1 ms applies.

16. Sketch a possible interconnection of 3 neurons that results in temporal contrast.

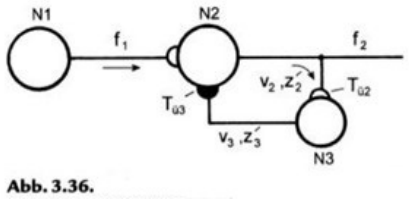


Figure 24: Series connection of two excitatory neurons N1 and N2 (with strongly schematized representation). Involvement of an intermediate neuron N3 excited via a collateral, counter coupling intermediate neuron N3 provides temporal contrast.

17. Sketch a possible interconnection of 3 neurons that results in spatial contrast.

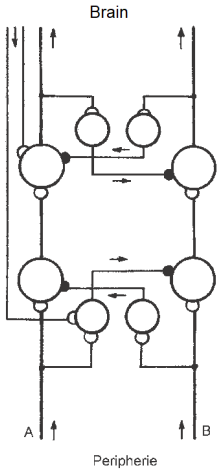


Figure 25: Spatial contrasting using the example of two parallel pathways of receptors A and inhibitory intermediate neurons of receptors A and B in the direction of the brain. In addition, the pathways from the brain are indicated as excitatory for A and inhibitory for B.

18. Reflex loop (knee reflex), what happens at the neuronal level?

The temporal strain pattern corresponding to the hammer blow releases a sequence of AIs of falling pulse repetition frequency in path A in the course of an analogue/digital conversion. The AIs travel in the direction of the spinal cord, where a switchover takes place. They generate a sequence of EPSPs on motor neurons (pathway B), which supply the stretched plug muscle. Together with EPSPs from other synapses, a temporal depolarisation pattern of an analogous nature is generated at the respective axon sphere. As a result, the motor neuron generates a sequence of AIs with a falling pulse repetition rate. The AIs run via B to the extensor muscle and cause it to contract in the sense of an analogue/digital conversion, whereby the leg protrudes.

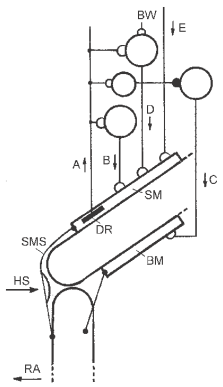


Figure 26: Reflex loops using the knee tendon reflex.

19. What are alpha waves in Electroencephalography (EEG)?

Is a largely sinusoidal course in the EEG signal. They occur when the eyes are closed and relaxed.

20. Give a simple circuit that describes (approximately) the electrical properties of the cell membrane of a nerve cell. Why is this circuit only approximately valid?

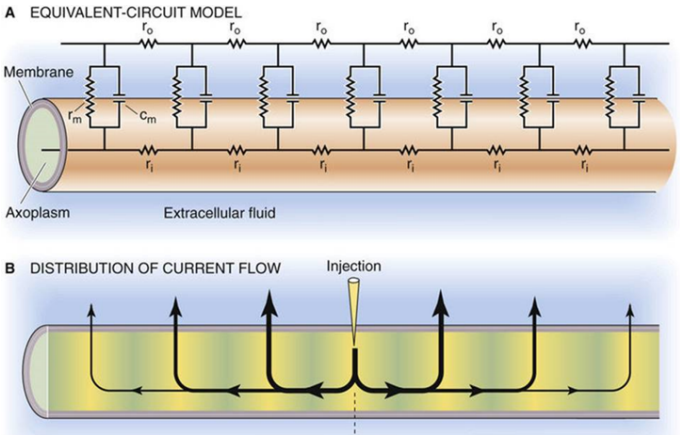


Figure 27: Reaction of an axon to an external current.

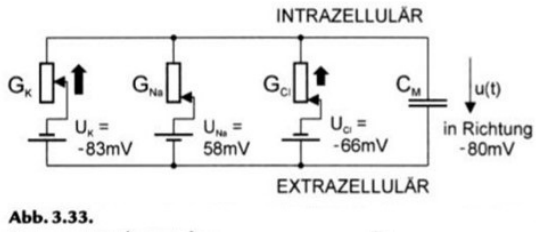


Figure 28: Generation of the membrane potential in the axon.

Since the conductivity does not correspond to the permeability, this model is only approximately correct.

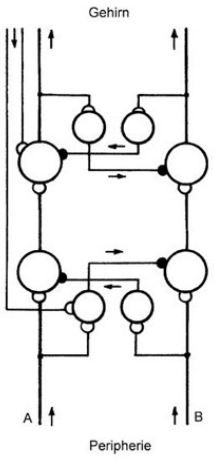
21. Give three mechanisms that allow the dosage of contraction and force unfolding of muscles.

- Activation of an increasing number of synapses of a fiber (produces increased contraction.)
- Increasing AI pulse train frequency(increases the magnitude of I-band intake and thus contraction, up to saturation.)
- Increasing impulse sequence duration (increases contraction and prolongs its effectiveness.)

22. Describe gene expression

Gene expression refers in a broad sense to how a gene (a specific genetic information) is manifested and expressed. In a narrower sense, gene expression is the biosynthesis of proteins based on specific genetic information.

23. Spatial contrast, sketch and description.



Two parallel paths are sketched, which carry information from two peripheral receptors A and B to the brain via two switching points each. At both points, inhibitory neurons act into the other pathway, resulting in a behavior of mutual rivalry.

4 Electromagnetic Biological Interactions

1. **Explain the concept of overtemperature and its progression over time when there is a step change in energy in a biological medium.**

   If a human body (body temperature 37 °C) is abruptly supplied with heat, thermoregulatory reactions start in the body (e.g. sweating, increased breathing rate). How well a tissue can regulate the temperature in the body depends on its specific heat capacity and blood flow. Tissues with a high specific heat capacity can absorb more heat energy. Those with good and fast blood flow (α and A) can release more heat energy. If there are no regulatory reactions, this would mean a linear increase in body temperature.

   Muscle $c\uparrow\ (\alpha \cdot A)\uparrow \longrightarrow$ Slow exponential increase in body temperature.

   Fat $c\downarrow\ (\alpha \cdot A)\downarrow \longrightarrow$ Fast exponential increase in body temperature.

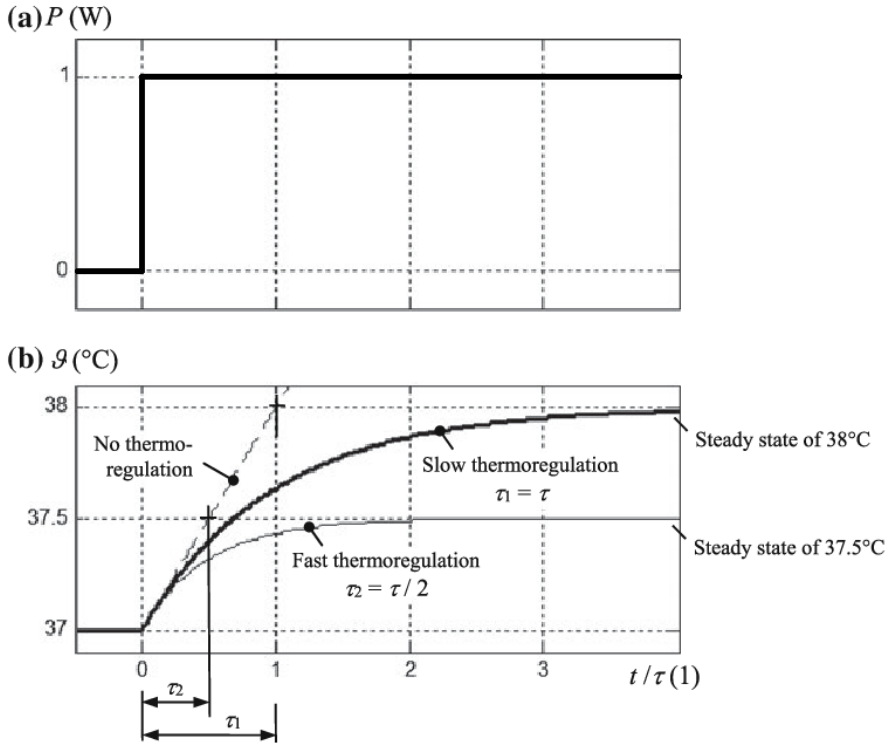


Figure 29: Thermoregulatory response of biological tissue. (a) A step-wise supply of the electromagnetic power P into tissue as a thermal stimulus. (b) The resulting increase in the tissue temperature ϑ is shown in response to this stimulus.

No thermo-regulation:

$$\vartheta(t) = \vartheta(0) + \left(\frac{P}{c} \cdot \Delta t\right)$$

With thermo-regulation:

$$\vartheta(t) = \frac{P}{\alpha \cdot A} \cdot \left(1 - e^{-t/\tau}\right) \cdot \varepsilon(t)$$

$$\tau = \frac{m \cdot c}{\alpha \cdot A}$$

$$P \cdot \varepsilon(t) \longrightarrow heat - inducing\ power\ in\ tissue$$

$\vartheta(t)$	tissue temperature	[K]
P	power	[W]
α	blood flow velocity in (regulatory) dilated vessels	[m/s]
A	vessels contact area in tissue	[m^2]
t	time	[s]
τ	time constant	[W/K m^3]
$\varepsilon(t)$	Heaviside step function	[ ]
m	mass of the exposed tissue	[kg]
c	specific heat capacity	[W s/K kg]

2. Current flow through the body.

A flow through the organism is characterised by the fact that a sequence of tissue layers must be flowed through, which are characterised by a different conductivity (γ). Therefore, in the case of layers lying in series, e.g. skin/muscle tissue/fatty tissue, constant changes in Current density (S) lead to abrupt changes in Electric field (E) and thus also power density (p). After a longer exposure time to the current, the total voltage (U) decreases. This means that destructive mechanisms are at work, which increasingly degrade the cell membranes. Causes are e.g. local overheating, coagulation of the tissue, ...

$$p = E \cdot S = \gamma \cdot E^2$$

p	Power density	[W/m^3]
E	Electric field	[V/m]
S	Current density	[J]
γ	Conductivity	[S/m]

3. **Describe neuronal effects of external electric fields.**
   = Describe neuronal effects in the E-field.

   Neural effects are interactions of the field with excitable cells, i.e. with neurons, muscle fibres and the fibres of the heart muscle tissue.

   The applied surface charges (E_{ext}) generate their own electric field (E_I) within the cell membrane, that disturbs the electric field of the resting membrane (E_R) on the left side of the cell. Here, the membrane voltage (u) decreases from its resting value U_R (-70 mV < 0) and thus becomes even more negative = hyperpolarised. In contrast, on the right side of the cell, the induced field E_I opposes E_R, so that the resulting voltage u increases towards more positive values = depolarised. If the depolarisation reaches a certain value, an impulse for action (AIs) can be expected to be triggered.

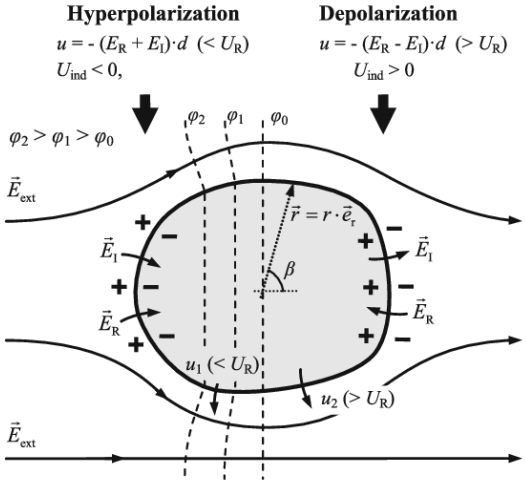


Figure 30: An excitable elongated cell exposed to a transverse external electric field (E_{ext}).

4. **Discuss frequency dependence of the threshold.**

   In the case of a sinusoidal current waveform, 4 frequency ranges can be distinguished:

   a) Low frequencies = high Threshold value (S_S) $\longrightarrow$ Accommodation
   b) Minimum S_S at 30-100 Hz $\longrightarrow$ technically used range
   c) Increasing S_S with increasing frequency
   d) Displacement currents from 30 kHz $\longrightarrow$ no neural effects

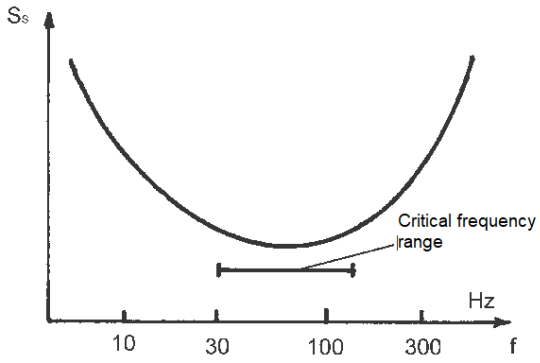


Figure 31: Threshold value S_S of the current density for triggering an action pulse for the case of sinusoidal current progression of the frequency f . The resulting "critical frequency range" falls - in a very disadvantageous way with regard to the electrical accident - in the area of the mains frequency.

5. **What is ventricular fibrillation and its causes? Add a diagrammatic representation and explain a possible termination of ventricular fibrillation.**

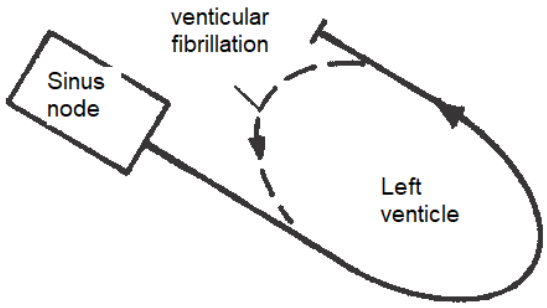


Figure 32: Schematic representation for the interpretation of ventricular fibrillation as a feedback of the excitation.

In ventricular fibrillation, the ventricular frequency is greatly increased and the mechanical pumping function of the heart comes to a stop. Ventricular fibrillation at 1000 mA.

Normal state Normally, the action impulse comes from the sinus node. It gradually and increasingly covers the entire pathway and only after global repolarisation does the sinus node generate the next impulse.

Triggering Here there is a disturbance of the spatial/temporal depolarisation pattern. They are characterised by the fact that the impulse is transferred to the initial area of the pathway analogue to an oscillating circuit feedback. Thus, an autonomous upright circular movement is created, which is characterised by strongly increased frequency. In this way, the coordinated pumping power is lost.

Remedy Defibrillation - This involves injecting a high current impulse into the thorax, resulting in global excitation of the heart. This excitation leads to a globally repolarised state and the excitation sequence is again determined by the sinus node.

6. Effect of non-ionising radiation.

Thermal effect The radiation decreases in intensity as it passes through the biological matter, while the matter absorbs energy.

Photochemical effect A molecular order state (Z1) is transformed into another order state (Z2) in a defined way. A generally known effect is the conversion of the so-called pro-vitamin D2 (Z1) present in the organism into vitamin D2 (Z2). UV light breaks a C-C bond, which leads to the conversion.

7. Relationship of ionising energy to its effect?

Ionisation energy W_i is the minimum energy required to remove an electron from a water molecule and thus ionise it.

The limit condition for ionising effect is:

$$W > W_i = e \cdot U_i$$

W	Quantum energy	[eV]
W_i	Ionisation energy	[eV]
e	Elementary charge	[ ]
U_i	Acceleration voltage	[V]

8. Differences between thermal and photochemical effects? (Microwave).

See also question 6.

Thermal effect:

- Infrared radiation
- Visible light
- Ultraviolet radiation

Photochemical effect:

- Photosynthesis $\longrightarrow$ Visible light 650 nm
- Vitamin D production $\longrightarrow$ Limit between UV-B and UV-C at about 280 nm
- Skin cancer $\longrightarrow$ UV-Light

9. Ionised radiation? Genetic and non-genetic effects. Hit theory?

Ionising radiation is a term for any particle or electromagnetic radiation that is capable of removing electrons from atoms or molecules.

Hit theory Hit = Appearance of a certain biological effect.
The probability of the actual appearance of a certain type of hit is described by the so-called hit theory. As the radiation dose (D) increases, more hits occur.

Depending on the number of hits, these represent certain effects (e.g. DNA double-strand breakage at high dose = many hits). Important! Increasing the intensity of the radiation does not mean a change in the effect, but an increased probability of hits that occurs.

Genetic effects Radiation-induced Changes in nucleic acids. Event types of DNA changes:

- Separation of bases
- Molecular attachments
- Strand breaks

Non-genetic effects Changes in proteins (but also in other biomolecules) in an immediate way. Lose functionality due to the following event types:

- Ionisation of uncharged positions
- Neutralisation of charged positions
- Generation of positions with radical character
- Separation of molecular fragments
- Attachment of molecular fragments

10. What criterion distinguishes non-ionising radiation from ionising radiation? Give explanations of photochemical effects.

The differentiation is made on the basis of the radiation. The ionisation energy of the radiation must be high enough to remove an electron from a water molecule. This ionises the molecule. Ionisation energy W_i for water 12.56 eV. If the energy below this threshold than we talk about non-ionising radiation.

Photosyntehsis Conversion of carbon dioxide and water into glucose and oxygen.

Vitamin D production Conversion of pro-vitamin D2 in vitamin D2.

Skin cancer Loss of complementary base bonds.

11. Threshold value for square pulse.
= What is the effect of the current density curve for rectangular current pulses?
= Discuss the course of the threshold current for a rectangular pulse.

$$\frac{S_L \cdot d}{\gamma} \approx 30\,mV$$

S_L	Density line current	[A/m^2]
d	Membrane thickness	[m]
γ	Membrane conductivity	[S/m]

Short pulses are characterised by a very high threshold. The reason for this is that the current flowing through the membrane is composed of an exponentially increasing conduction current of density S_L (Density line current) and an exponentially decreasing displacement current of density S_V (Density displacement current). The AI is only triggered when the 30 mV membrane voltage threshold is reached. From a certain switch-on time T onwards, there is no further reduction of S_S (Threshold value). Since the displacement current S_S drops to 0. The minimum value of S_S is then called Rheobase (S_R).

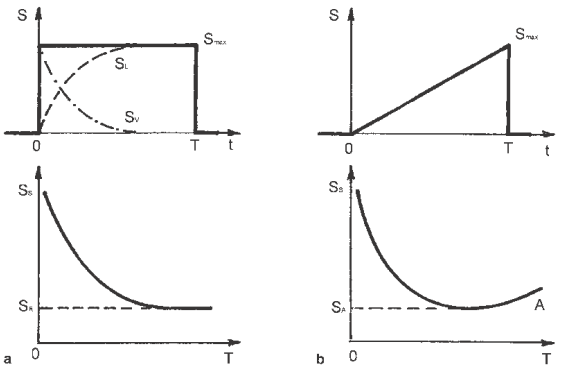


Figure 33: Threshold value S_S of the current density for triggering an action pulse for the case of current pulses of amplitude S_{max} and duration T. (a) Rectangular pulse (with splitting of S into its components). S_R Rheobase. (b) Ramp-like pulse. S_A Minimum of the threshold above which the phenomenon of accommodation (A) occurs.

12. Describe the threshold value curve when creating a current ramp.

See question 11.

List of Abbreviations

AI Action impulses

Cl Chlorine

DNA Deoxyribonucleic acid

EEG Electroencephalography

EPSP Excitatory postsynaptic potential

HF High frequency range

IPSP Inhibitory postsynaptic potential

KLK Conformational/charge complementarity

LF Low frequency range

MALDI Matrix-assisted Laser Desorption/Ionization

Na/K-ATPase Sodium–potassium pump

RNA Ribonucleic acid

SDS Sodium dodecyl sulphate

SEM Scanning electron microscope

STM Scanning tunneling microscope

TEM Transmission electron microscope

TTX Tetrodotoxin