Biophysics-I&II

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Summary Biophysics-1

CHAPTER 1 - Properties of gasses and liquids

Gas: A fluid form of matter that fills the container it occupies and can easily be compressed into a much smaller volume (gas is a substance at higher temperature than its critical temperature, vapor is a gaseous form of matter at a temperature below its critical temperature). 1[mol] ($6.022 \cdot 10^{23}$ molecules) of an ideal gas at 0[°C] and 1[bar] occupies **22.414** [L] (= mole-volume).

- **Ideal** G.: A hypothetical gas whose pressure-volume-temperature behavior can be completely accounted for by the ideal gas equation:

  $p \cdot V = n \cdot R \cdot T$ [N·m]

  p, pressure [N/m^2]
  V, volume [L] [m^3]
  n, molar amount [mol]
  R, gas constant. 8,314 [J/(K·mol)]
  T, Temperature [K]

Brownian Motion: The haphazard movement of tiny particles suspended in a gas or liquid resulting from bombardment by the fast-moving molecules of the gas or liquid; it ceases at absolute zero (solid, i.e. 0 [K]) and gradually increases with temperature (liquid state) and if temperature increase persists, to exceed the vapor pressure (gaseous phase). As temperature rises, so does diffusion due to increased Brownian motion.

- **Average quadratic deviation**: The positive average distance covered by a particle small enough to experience Brownian motion; it increases with the time interval and decreases with the size of the particle:

  $$\bar{x}^2 = \frac{R \cdot T \cdot \Delta t}{3 \cdot n \cdot \pi \cdot \eta \cdot r} \quad [m^2]$$

  R, gas constant 8.3144 [J/mole·K]
  T, temperature [K]
  t, time (time interval) [s]
  n, number of particles [1/mol]
  η, viscosity of medium [Pa·s]
  r, radius of particle [m]

Diffusion: (L. diffundere, to pour out) Random thermal motion of suspended or dissolved molecules causes their dispersion from regions of higher concentration to regions of lower concentration. The net movement of suspended or dissolved particles from a more concentrated region to a less concentrated region by virtue of their kinetic energy of individual molecules (a result of random, i.e. Brownian motion); the process tends to distribute such particles uniformly throughout the medium.

- **Fick's 1st Law of Diffusion**: An equation defining the rate of solute diffusion through a solvent. Diffusion through a medium, in which the resulting motion of diffusion follows the least significant concentration of the dissolved substance within the medium; rate of diffusion in water 1/10 of that in air; the current of diffusion is expressed as:

  $$I_i = \frac{dm}{dt} = D \cdot A \cdot \frac{dc}{dx} \quad [kg/s]$$

  dm/dt, mass over time [g/s]
  D, coeff. of diffusion [m^2/s]
  A, surface ⊥ diff.-gradient [m^2]
  c, concentration [g/m^3]
  x, distance of diff. grad. [m]

Liquid: A fluid form of matter that takes the shape of a container it occupies and is almost incompressible.

Drag: The resistance to movement of an object through a medium, increasing with viscosity, density of the medium, the surface area, and shape of the object.

Flow: Motion of fluids in pipes show two distinct flow regimes (see also viscosity and Reynolds principle):

- **Laminar** F.: Turbulence-free flow of fluid in a vessel or past a moving object; a parabolic gradient of relative velocity exists in which the fluid layers closest to the wall or body have the lowest relative velocity while those near or at the center have maximum velocity). Resistance is the drop in pressure of laminar flow and rises linearly with speed.
- **Turbulent** F.: As the flow speed of real fluids increases; its ability to follow the contours of a solid obstacle decreases; it tears off the surface and forms a wave of turbulence, carrying away energy (flow profile is no longer parabolic). Resistance of turbulent flow rises nonlinear with speed.

Hagen-Poiseuill's Law: The law stating that flow rate is determined by the pressure difference, viscosity of liquid, and the diameter of the tube. In laminar flow, the flow is directly proportional to the driving pressure with resistance being independent of flow. It is the pressure difference required to maintain the flow, and it is directly proportional to the average speed of the flow rate ($V/t \approx r^4$); a doubled radius result in a 16-fold increase of the rate of flow.

$$\frac{V}{\Delta t} = Q = \frac{\pi \cdot (p_2 - p_1) \cdot r^4}{8 \cdot \eta \cdot l} \quad [m^3/s]$$

V, volume	[m^3]
π, 3.14159	[-]
p, pressure (p-difference)	[N/m^2]
r, radius	[m]
η, coefficient of viscosity	[Pa·s]
l, length of tube	[m]
t, time (time interval)	[s]

F_F - **Friction**: The resistive forces that arise to oppose motion of an object past another with which it is in contact;

- **Stoke's** F.: Terminal sinking speed; i.e. friction of a falling ball in a liquid or gas:

$$F_S = 6 \cdot \pi \cdot \eta \cdot r \cdot v \quad [N]$$

6·π (sphere), 6·3.14159	[-]
η, coeff. of viscosity	[N·s/m^2]
r, radius	[m]
v, terminal sinking velocity	[m/s]

Osmosis (Gk. osmos, impulse, thrust): The passive diffusion of water, or any solvent, across a differentially permeable membrane in the absence of other forces, the movement of water during osmosis will always be from a region of greater water potential to one of lesser water potential - it is therefore a thermodynamic process.

- Π - O. **Pressure**: It is the pressure potential that can be developed by a solution (mixture) separated from pure solvent by a differentially or semipermeable membrane; it is an index of the solute concentration of the solution; (i = 1 for entire molecules; i = 2 for dissociated molecules): and often referred to as **Van't Hoff's** equation:

$$\Pi = i_i \cdot c_i \cdot R \cdot T \quad [J/mol]$$

i, dissociation factor	[-]
c, molar concentration	[mol/L]
R, gas constant 8.3144	[J/(mol·K)]
T, temperature	[K]

R_e - **Reynold's Number**: The tendency of a flowing gas or liquid to become turbulent is proportional to its flow velocity and density; it is inversely proportional to its viscosity; R_e indicates the change from laminar to turbulent flow. By increasing the flow speed, a laminar flow sooner or later will change into a turbulent one:

$$R_e = \rho \cdot v_{AV} \cdot d/\eta \quad [-]$$

v_{AV}, average velocity of medium	[m/s]
η, viscosity index of medium	[Pa·s]
d, diameter of tube	[m]

R_e of 1000 is considered to be the threshold number by which laminar flow switches over to become a turbulent flow; $R_{e\ of\ blood}$ = 20-50; $R_{e\ of\ air}$ = 1000; $R_{e\ in\ lungs}$ <1000

η **Viscosity**: The internal resistance, or friction, offered to an object moving through a fluid (it is a constant that is specific to gases or liquids). Cohesion and viscosity increase with falling temperature. The pulling force **F** by which each flow stratum is pulled forward, is found to be directly proportional to **v** and **A** and inversely proportional to the distance between each laminar flow stratum.

$$F = \eta \cdot A \cdot \frac{dv}{dx} = \frac{\eta \cdot v \cdot A}{x} \quad [N]$$

F, pulling force per stratum	[N]
η, coefficient of viscosity	[N·s/m^2] = [Pa·s]
v, velocity of a single stratum	[m/s]
A, area of an flow stratum	[m^2]
x, thickness of 1 flow stratum	[m]

CHAPTER 2 - The law of thermodynamics

Thermodynamics (TD; Gk. therme, heat; dynamics, power) It is the study of kinetic energy in the form of heat and its transformation to other forms of energy.

1st Law of T.: States that in all processes, the total energy of the universe remains constant (energy conservation; i.e. energy cannot be lost or gained, just transformed).
simplified as: $dU = dQ - dW = \Delta H - p \cdot \Delta V$
A change in **enthalpy** (H) is equal to the heat supplied at constant pressure, while it ignores the change of work.
Extended equation including electrical and chemical energy:
$dU = dQ - -dW = dQ - [p \cdot dV + \Psi \cdot dq + \sum(\mu_i \cdot dn_i)]$

2nd Law of T. (restriction of the 1st law): States that the degree of randomness, or **entropy**, tends to increase.
Heat will never spontaneously flow from a cold object to a hot object (inexistence of perpetual mobile).

3rd Law of T.: It states that is not possible to reach absolute zero (0[K] or -273.2[°C]). The entropy of a perfect (idealized) crystalline substance at 0[K] is zero - quantum mechanic is required to explain deviations from this rule. As temperature rises, the freedom of motion increases too and so does entropy (S). Generally, one can say that entropy of a substance increases when it melts, when it vaporizes, and as its temperature is raised; it also increases by allowing its particles greater freedom of movement, i.e. any increase in volume.

U, internal energy	[J]
Q, heat	[J]
W, work	[J]
S, entropy	[J/mol]
T, temperature	[K]
p, pressure	[N/m^2]
V, volume	[m^3]
q, charge	[A·s]
Ψ, electrical potential	[V] = [J/(A·s)]
μ_i, electrochem. potential	[J/mol]
n, molar amount	[mol]

H - **Enthalpy**: A thermodynamic quantity used to describe heat change taking place at constant pressure.

G - **Free Enthalpy** (also known as **free energy**): The energy of a system that is free to do work. It is a thermodynamic quantity used to describe heat changes taking place at constant pressure (isobar) and temperature (isotherm); it is therefore, the total entropy (S) of a system and its surroundings; i.e. reservoir of energy that can be obtained as heat;
dG defines the available (reversible) energy content of a substance; if negative, the system can supply energy (exergonic), whereas if positive, the system requires energy (endergonic) to achieve a change: $G = U + p \cdot V - T \cdot S$
change of free enthalpy: $dG = (dU + p \cdot dV + V \cdot dp) - dT \cdot S - T \cdot dS$
simplified: $dG = \mathbf{dH} - T \cdot dS$

U, internal energy	[J]
p, pressure	[N/m^2]
V, volume	[m^3]
T, temperature	[K]
S, entropy	[J/mol]
H, enthalpy	[J/mol]
G, free energy of change	[J/mol]
Ψ, electrical potential	[V] = [J/(A·s)]
μ_i, electrochem. potential	[J/mol]
n, molar amount	[mol]
Q, heat	[J]

- **Gibb's Equation**: The thermodynamic equation that summarizes the 1st and the 2nd law of TD.
  $dU = \{T \cdot dS\} - \{p \cdot dV + \Psi \cdot dq + \sum(\mu_i \cdot dn_i)\}$
  (for reversible processes only; it represents the sum of an extensive with its intensive variable (see also variable of state).

S - **Entropy**: A direct measure of the randomness or disorder of a system.
$dS = k \cdot \ln(w) = dQ/T$; is the change in entropy (S) of reversible processes (e.g. in an ideal gas); whereas, in nature, any change in heat is irreversible; i.e. $dS > dQ/T$.

k, Boltzman const.	$1.381 \cdot E^{-23}$[J/K]
w, thermodynamic probability = $2^{\#\text{ of molecules involved}}$	[-]

Biophysical Reflection of the **Laws of Thermodynamics**: According to the three laws of thermodynamics, each law can be explained more precisely by assigning the Boltzmann Speed distribution to the 1st law of TD, while assigning the Arrhenius EQ to the 2nd law of TD.

Maxwell-Boltzmann Speed Distribution (MBSD): Out of the 1st law of TD it is obvious that an increase in internal temperature evidently will boost the internal energetic content. This results in a net increase of the average speed of the enclosed particles (molecules, atoms, etc.). The MBSD displays the most probable spectrum of molecular speeds available of a system at a particular temperature; e.g. molecular oxygen has an average speed of 200[m/s] at 73[K], whereas it increases to about 400[m/s] at 273[K] (compare w/ Brownian motion).

$$f_{(v)} = \frac{4}{\sqrt{\pi}} \left(\frac{m}{2 \cdot k \cdot T} \right)^{3/2} \cdot v^2 \cdot e^{-m \cdot v \cdot v/(2 \cdot k \cdot T)} \quad [kg/s]$$

m, mass	[g]
k, Boltzman con.	$1{,}381 \cdot E^{-23}$[J/K]
T, temperature	[K]
v, speed	[m/s]

The most probable speed v_{max} is that speed for which $f_{(v)}$ is maximum:

$$v_{(rms)} = \sqrt{\frac{3 \cdot k \cdot T}{m}} \quad v_{max} = \sqrt{\frac{2 \cdot k \cdot T \cdot N_A}{M_M \cdot n}} \quad [m/s]$$

N_A, Avogadro's numb.	$6{,}022 \cdot E^{23}$ [1/mol]
M_M, molecular mass	[g/mol]

Arrhenius Equation (AE): Based on the 2nd law of TD, the AE yields the information about the distribution of the particles (atoms, molecules, etc.) within the system. The empirical equation for commonly observed temperature dependence of reaction rates is: $\ln(k) = \ln(A)-(E_a/(R\cdot T))$.

The Arrhenius parameters are the factor A and the activation energy E_a. An Arrhenius plot is a graph of ln(k) against 1/T; if the plot is a straight line, then the reaction is said to show Arrhenius behavior:

e.g.: $k = A\cdot e^{-Ea/(R\cdot T)}$; $\ln(k) = -(E_a/R \cdot 1/T) + \ln(A)$

rearranged as a linear equation: $y = k \cdot x + d$

for a reaction at 2 different T's: $\ln(k_2/k_1) = E_A\cdot(T_2-T_1)/(R\cdot T_1\cdot T_2)$

E_a, activation energy [J/mol]
k, rate constants [1/s]
A, collision frequency [-]
e, eulers number 2.7183 [-]
R, gas constant 8.314[J/mol]
T, temperature [K]

Variable of State (VoS): Within a closed system such as in an ideally sealed chamber (an imaginary perfectly insulated entity) with no losses or gains whatsoever from or to the outside, every sub-entity (e.g. dV as a fractionated value of the whole) characterizes the entire entity.

Conjugated VoS: Extensive and intensive VoS are inter-connected physical relationships; any change of an intensive variable results in a change of its conjugated (extensive) variable; e.g. T(int) with S (ext) etc. - see table below. Another conjugated example is the interconnected relationship of electrical current, voltage, and resistance: I = U/R (expressed as a linear eq.) = U·(1/R); with I being an extensive and U the intensive variable.

Intensive variable (relative entity)	Extensive variable (absolute entity)
Temperature (T)	Entropy (S)
Pressure (p)	Volume (V)
Electrical potential (Ψ)	Charge (q)
Chemical potential (μ)	Molar amount (n)
Electrical voltage (V)	electrical current (I)

- **Extensive** VoS: Pertaining to the environment; it is thought to be additive in that the sum of one parameter represents the hole; e.g. entropy S, volume V, charge q, mole n, etc.
- **Intensive** VoS: Relative variables that refer to a reference value; thus, are implicitly connected to the system as a constant (the same throughout the entity); e.g. temperature T, pressure p, electrical potential Ψ, chemical potential μ, etc. Reference values in a closed system can be freezing temperature 0[°C] or 273.2[K], atmospheric pressure 1[atm], electrical ground potential 0[V], etc.

Thermodynamic Forces: As a main consequence of the laws of TD, several chemo-physical applications result; these implications are implemented in the diffusion process, electrochemical potentials, Donnan and Nernst equations.

Potential: Any electric potential (energy pressure) per amount of charge, measured in volts [V], and often called voltage; i.e. the voltage above zero;

$V = PE/q$ $[J/(A\cdot s)] = [J/C] = [V]$

PE, potential energy [J]
q, charge [A·s] [C]

Balanced systems are in equilibrium; thus do not require external energy to reach it; whereas, unbalanced systems do require energy from outside to maintain the unbalanced state; e.g. Na-K-pump.

- **Electrochemical Potential** (Nernst Diffusion): Mass transport coupled with transport of charge in electrolytes and ions. It describes the balance of solutes separated by a semipermeable membrane; if the solute is the same on both sides of the membrane and the ion concentration is very low (liquids) or for gaseous solutions, (at standard pressure and temperature conditions) then:

  $\Delta\bar{\mu}_i = \mu_i^a - \mu_i^i = \mu_i + z_i\cdot F\cdot\Psi$ [J/mol]

  $= z_i\cdot F\cdot(\Psi^a-\Psi^i) + R\cdot T\cdot\ln(c_i^a/c_i^i)$ [J/mol]

  $\Delta\bar{\mu}_i$ = electrochemical potential + concentration difference

  for more concentrated solutions, the activity (rather than concentration) has to be used: $a_i = \gamma_i\cdot c_i$

  z_i, ionic charge (integer) [-]
  F, Faraday const. $9.649\cdot E^4$ [A·s/mol]
  Ψ, electrical potential [J/(A·s)] = [V]
  c, concentration [mol/L]
  R, gas constant 8.314 [J/(mol·K)]
  γ_i, coefficient of activity [-]

- **Electrode Potential**: An electrochemical process that generates electricity by means of a spontaneous redox reaction; e.g. metal dipped into an aqueous solution: $Me \leftrightarrow Me^+ + e^-$.

  ECS-**Electrochemical Series**: The voltage measured as a redox reaction occurs at the electrode when all solutes are 1[mol/L] and all gases are at ambient pressure of 101[kPa].

  Standard P.: Contribution of an electrode to the standard cell potential (half cell reaction of 1st order electrodes).

- **Electrode**: An electrical circuit element used to make contact with a solution, a tissue, or a cell interior; used either to measure potential or to carry current.

  1st order E.: Metal in salt (measurement of cations); e.g. galvanic or voltaic cell.

$$\Delta\Psi = \Psi^S + \frac{R\cdot T}{z_i\cdot F}\cdot\ln(c_{Me^+}) \quad [V]$$

Ψ^S, reference std. potential [V]
c_{Me^+}, cation concentration [mol/L]

2nd order E.: Metal in heavily soluble salt-solution (measurement of anions); e.g. batteries.

$$\Delta\Psi = \Psi^S + \frac{R\cdot T}{z_i\cdot F}\cdot\ln(K_{SP}) - \frac{R\cdot T}{z_i\cdot F}\cdot\ln(c_{A^-}) \quad [V]$$

K_{SP}, solubility constant [var]
c_{A^-}, anion concentration [mol/L]

Anode: (Gk; an, up) The positive electrode at which oxidation occurs and to which negatively charged ions (anions) are attracted; e.g.: Cl^-.

Cathode: (Gk; cat, down) The negative electrode at which reduction occurs and to which positively charged ions (cations) are attracted; e.g.: Na^+.

Balanced Potential: The state in which the system automatically falls back whenever opposite charges have the chance to neutralize each other; under such circumstances the net flux across the membrane is zero. Balanced systems are in equilibrium; thus do not require external energy to reach it; whereas, unbalanced systems do require energy from outside to maintain the unbalanced state; e.g. Na-K-pump.

- **Diffusion** Potential: The potential arising out of the passive dispersion of ions (anions and cations with different mobility) as a result of random thermal motion.
- **Fick's 1st Law of Diffusion**: An equation defining the rate of solute diffusion through a solvent. Diffusion through a medium, in which the resulting motion of diffusion follows the least significant concentration of the dissolved substance within the medium;
  The rate of diffusion in water 1/10 of that in air;
  the current of diffusion is expressed as:

$$I = D\cdot A\cdot\frac{dc}{dx} \quad [kg/s]$$

D, diffusion coefficient [m^2/s]
A, surface ⊥ diff.-gradient [m^2]
c, concentration [kg/m^3]
x, distance of gradient [m]

- **Nernst Diffusion** Potential: The potential resulting out of passive diffusion across a semipermeable membrane.

$$I_i = \frac{dq_i}{dt} = D_i\cdot A\cdot\frac{d\mu_i}{dx} \quad [V]$$

μ_i, electrochem. potential [J/mol]
Ψ, electrical potential [V]
R, gas constant 8.314 [J/(mol·K)]
γ_i, coefficient of activity [-]

- **Nernst Equation**: Equation for calculating the electrical potential difference across a membrane that will just balance the concentration gradient of single species of ions.

$$\Delta\Psi = \frac{R\cdot T}{z_i\cdot F}\cdot\ln\frac{c_i^a}{c_i^i} = 0.058\cdot\log\frac{c_i^a}{c_i^i} \quad [V]$$

z_i, ionic charge [-]
F, Faraday constant $96.485\cdot E^3$[A·s/mol]
$\Delta\Psi$, potential difference [V]
c_i^a, c_i^i, int./ext. ion conctrtn. [mol/L]

- **Goldman Equation**: The equation describing the equilibrium potential for a system in which more than one species of diffusible ions are separated by a semi- permeable membrane; if only one species can diffuse across the membrane the equation reduces itself to the Nernst equation:

$$\Delta\Psi_{MRP} = \frac{R\cdot T}{F}\cdot\ln\frac{P_{Cl^-}\cdot c_{Cl^-}^{\,i} + P_{Na^+}\cdot c_{Na^+}^{\,i} + P_{K^+}\cdot c_{K^+}^{\,i}}{P_{Cl^-}\cdot c_{Cl^-}^{\,o} + P_{Na^+}\cdot c_{Na^+}^{\,o} + P_{K^+}\cdot c_{k^+}^{\,o}} \quad [V]$$

E_X, potential difference [V]
c_x^i, int. ion concentration [mol]
c_x^o, ext. ion concentration [mol]
P_X, permeability constant [-]

Limitations for the application of the GE:
Constant electrical field; homogenous membrane; ion transport within the membrane is not coupled to an active process (which is not met by the actively working Na-K-pump that requires ATP to work properly).

- **Donnan** Potential: The potential resulting out of the electro-chemical equilibrium that develops when two solutions are separated by a membrane permeable to only some of the ions in the solution.

$$\Delta\Psi = \frac{R\cdot T}{F}\cdot\ln(r) \quad [V]$$

r, Donnan quotient [-]
$r = c_{K^+}^{\,I}\, c_{K^+}^{\,II} = c_{A^-}^{\,II}\, c_{A^-}^{\,I}$

Unbalanced Potential: It is the energy requiring translocation of a substance across a membrane, usually against its concentration or electrochemical gradient; also called active transport; e.g. Na-K-pump.

$$\Delta\Psi_{diff} = \frac{R\cdot T}{F} \cdot \frac{z_K\cdot P_K\cdot n_K + z_A\cdot P_A\cdot n_A}{z_K^{\,z}\cdot P_K\cdot n_K + z_A^{\,z}\cdot P_A\cdot n_A} \cdot \ln\frac{c_{II}}{c_I} \quad [V]$$

$P_{A,K}$, permeability coeff. of anions and cations;
n, molar amount [mol]

- **Fick's 2nd Law of Diffusion**: is the connection of the flux j of diffusion particles to the driving force based on the description of the local change in particle density, $\rho(x,y,z,t)$.
  $\partial c/\partial t = D\cdot\Delta c$
- **Goldman-Hodgkin-Kotz Equation** (2nd Fick's law): The ionic flux across the membrane is determined by the charge of the ionic species, the electrical potential, the concentration gradient and the migration velocity across the membrane;

$$I_i = \frac{p_i\cdot z_i\cdot F\cdot\Delta\Psi}{R\cdot T} \cdot \frac{c_i^{\,a} - c_i^{\,a}\cdot e^{z_i\cdot F\cdot\Delta\Psi/(R\cdot T)}}{1 - e^{z_i\cdot F\cdot\Delta\Psi/(R\cdot T)}} \quad [V]$$

R, gas constant 8.314 [J/(mol·K)]
T, temperature [K]
c, concentration [mol/L]
p, migration velocity [m/h]
z, ionic property [-]
F, Faraday const. $9.649\cdot E^4$ [A·s/mol]

Plasma Membrane (zoology) or **Plasmalemma** (botany) or simply **Cell Cortex**: The biological envelope (bilayer) that surrounds all cells, plastid, mitochondrion etc.; consists of a single phospholipid bilayer (generally 40% lipid and 60% shared proteins). All membrane phospholipids are very flexible with quite dynamic characteristics (fluid-mosaic model); besides that PMs are also amphipathic, i.e. having both a hydrophobic tail (fatty acid-CH_2-end) and a hydrophilic head (organic-phosphate-glycerol group). The PM separates electric charges and actively transports ions via membrane- or ion pumps, regulating the constant flow of materials into / out of the cell, allowing water, ions, and certain organic molecules to pass through, while allowing toxic or useless by-products of cellular metabolism to exit the cell.

Cell **Potential**s:

- **Action** P. (AP): Transient all-or-none reversal of a membrane potential in nerve cells produced by a regenerative inward current in excitable membranes originating from a nerve's hillock as a nerve impulse, or spike. A typical AP starts with depolarization, followed by an overshoot, and a final phase of repolarization (depends greatly upon Na^+/K^+ availability and the proper function of Na^+- / K^+-channels) and does not require ATP; instead it uses the PE generated by the membrane pumps. Depolarization is predominantly characterized by the conductance of Na^+; whereas, repolarization predominantly by K^+.
  All-Or-None Response of AP: Pertaining to the independence of response magnitude from the strength of the stimulus; response is "all" if the stimulus achieves threshold and "none" if the stimulus fails to achieve it.
- **Threshold** P.: The potential just large enough to produce the response e.g., action potential, muscle twitch, etc., by opening the sodium (Na^+) channels.
- **Membrane** P. (MP): The electric potential measured from within the cell relative to the potential of the extracellular fluid (by convention is 0); i.e.: potential difference between opposite sides of the membrane; it is a dynamic equilibrium of in- and out-flowing ions under the precondition that mobility of both anions and cations are the same:

$$\Delta\Psi = \frac{R\cdot T}{z_i\cdot F}\cdot\ln\frac{c_{II}}{c_I} \quad [V]$$

c_I, internal ion concentration [mol/L]
c_{II}, external ion concentration [mol/L]

- **Membrane Resting** P. (MRP): The active pumping activity of the Na-K-pump (unstimulated membrane potential of a cell at rest) lowers the MRP from +30mV to an average of -60 to -80mV (can be up to -100mV).
  Na-K Pump: Membrane proteins responsible for active extrusion of Na^+ out of the cell at the expense of metabolic energy ($ATP + H_2O \leftrightarrow ADP + P_i + H_2O$). In some Na-pumps, there is a 3:2 exchange of intracellular Na^+-ions for extracellular K^+-ions; i.e. for each $2K^+$-ions taken in, $3Na^+$-ions are transported out.

Measuring devices for cell potentials:

- **Glass-Capillary Pipette Micro**-E.: The lumen of a hollow glass electrode is filled with an electrolyte solution connected by a Ag-wire to the input of an amplifier.
- **Patch-Clamp Method**: A method of investigation ion current transfer on a single sodium channel, with a 2µm tip- microelectrode held onto by gentle suction.

CHAPTER 3 - Biomechanics of Hearing:

Detector: (L. detegere, to uncover) A device used to monitor a distinctive physical or chemical parameter.

Motion D.: Detective device to monitor motion of a fluid, gas or object; the hair cells of the inner ear typically represent motion detectors in that the fastness of the movement is registered.

Pressure D.: Device used to monitor a pressure gradient of a gas, liquid, solid; the tympani at the outer-middle ear interface represents such a detecting device in that it registers the pressure of a sound wave.

Diffraction: The deviation of sound from rectilinear propagation. The bending of sound around an obstacle or through a narrow slit occurs in such a way that low frequencies experience a larger degree of diffraction than higher frequencies; a process thought to take place in the cochlea - essential for discriminating individual frequencies. Low frequencies are decoded at the far end of the coiled cochlea (helicotrema), while high frequencies are decoded near the oval window, at the straight section of the cochlea.

Fourier Analysis: A real wave-function can be decomposed into a sum of harmonic terms using the technique of Fourier analysis (a mathematical method that will resolve any periodic waveform into a series of simple sine waves[1]):

$$v(x,t) = \sum_{n=1}^{N/2} a_n(t) \cdot \sin(2 \cdot n \cdot \pi \cdot x / L) + b_n(t) \cdot \cos(2 \cdot n \cdot \pi \cdot x / L) = \sum_{n=1}^{N/2} a_n(t) \cdot \sin(2 \cdot n \cdot \pi \cdot x / L + \delta_n)$$

Loudness (Intensity): The physiological sensation directly related to sound intensity or volume. Sound is an amplitude modulated wave (information contained within the amplitude of the signal); relative loudness or sound level:

Absolute intensity (synonymous of P = I·U in electronics): v_{eff}, fastness [m/s]

$I_{SL} = v_{eff} \cdot p_{eff}$ $[N \cdot m/(s \cdot m^2)] = [J/(s \cdot m^2)] = [W/m^2]$ p_{eff}, pressure $[N/m^2]$

Relative sound intensity level: I_S, sound intensity $[J/(s \cdot m^2)]$ = $[W/m^2]$

$I_{SL} = 10 \cdot \log(I_S/I_0)$ [decibel, dB] I_0, threshold intensity $[W/m^2]$

Reflection: The fraction of sound energy that is reflected from a surface is large of the surface is rigid and smooth and less if the surface is sift and irregular; reflection of sound is often referred to as echo.

Reflection Index: Similarly as in electronics, reflection can be summarized in a simple formula:

$$R = \frac{Z_T - Z_A}{Z_T + Z_A}$$ [-]

Z_T, Resistance of terminator [Ω]

Z_A, Resistance of sound to air [Ω]

R can fluctuate between the extremes of 0 and 1. A tube with a fixed end ($Z_A = \infty$) and one with both ends open ($Z_A = 0$) result in a reflection index of 1; consequently, the perfect impedance is found once $Z_A = Z_T$ with R approaching zero (is achieved in the middle ear where pressure conversion takes place). The outer ear represents a resonance body with the tympani at the rear representing the fixed end; the node at the tympani shows maximum pressure at minimum fastness of the pressure wave (tympani as a pressure detector). The inner ear with the oval window on one side and the round window on the other side can be seen as a resonance body with both ends open; open ends result in maximization of fastness, whereas, pressure of sound wave is almost zero; important for the hair cells of the cochlea acting here as motion detectors.

Sound: Sound is an adiabatic pressure wave; i.e. the pressure differences between compression and rarefaction (constituting the wavelength) of a sound wave cannot equalize each other; also referred to as a longitudinal wave.

Speed of S.: In a medium such as air, the speed of sound is highly dependent upon temperature: 330 [m/s] at 0°C; 340[m/s] at 20°C, since hotter air has more KE, therefore molecules vibrate more vigorously, which results in better sound conduction; sound channeling occurs in layers of hot and cold air.

f - **Frequency**: A body undergoing simple harmonic motion (SHM), the number of vibrations it makes per second:

$f = 1/T$ [1/s] = hertz, [Hz] T, period [s]

v - **Fastness**: The speed at which a vibrating particle passes on a propagating stimulus; equivalent to the frequency of sound: $v_{eff} = s/t$ [m/s]

p - **Soundpressure**: The force exerted when alternating pressure patterns of compression and rarefaction strike a solid object, which can cause the object to swing according to the stimulating frequency (resonance):

$p_{eff} = F/A$ $[N/m^2]$

λ- **Wavelength**: The distance between successive crests, throughs, or identical parts of a wave [m].

$T = \lambda/c = 1/f$ [1/s] c, speed of sound [m/s]

[1] http://webphysics.davidson.edu/Faculty/wc/WaveHTML/node31.html

Spectrum: A longitudinal wave phenomenon that consists of successive compression and refraction of an elastic medium through which the wave travels (requires a compressible and expandable medium - can be solid, liquid, or gaseous.

Infrasonic S.: A sound of a frequency too low to be heard by the normal human ear - below 20 [Hz].

Sound S.: The audible frequency range between 20 and $20 \cdot E^3$[Hz].

Ultrasonic S.: A sound of a frequency too high to be heard by the normal human ear - above 20[kHz].

Ear: Frequency analyzing mechano-receptor, converting acoustical stimuli into electrical stimuli (see SSD-manual p.35[2]).

Inner E.: Is a tapered tube wound into a spiral like the shell of a snail, housing the sound detecting organ of Corti. Sound enters the oval window and leaves via the round window (migrating wave). There, the vibratory movement of the basilar membrane, with respect to the tectorial membrane produces shear forces on the stereocilia of the cochlea hair cells (motion detector) with high pitches near the oval window and lower ones at the helicotrema. Thus, hearing is a process of detecting locations rather than frequencies. Furthermore, every hair cell possesses a distinct mechanical resonance frequency that is in accordance with its frequency detecting location to increase stimulus response and to facilitate masking. Distinctive frequencies are discriminated in conjunction with the basilar sound localization and the brains analytical capacities (Fourier transformation performed in the brain).

Middle E.: Mechanical amplifier (35dB, equivalent to a 3162-fold amplification) and pressure converter 20:1. The auditory ossicles of the middle ear (malleus, incus, and stapes), connecting the tympanic membrane and the oval window. To avoid impedance mismatch and to enable the convection of maximal power from the outer to the inner ear, the reflection index at a center frequency of 3kHz is almost zero.

Outer E.: Sound-capturing device that resembles a resonance tube with a fixed end (tympani as the main pressure detector). This structure results in an overall pressure amplification of 5dB. The average length of the auditory tube (meatus) is about 27mm. According to standing wave theory, the wave pattern for such a vibration at a fixed end results in a $\lambda/4$ wave. Using the frequency-wavelength relationship ($f = c/\lambda$), such a standing wave must have a center frequency of 3kHz. This frequency perfectly matches with the threshold pattern of hearing - which is lowest around that particular frequency.

Masking of frequencies: Neuronal control of hair cilia to maximize stimuli (peaks) and to suppress background noise and other interferences within the basilar membrane to achieve an additional narrowing of a particular spectral bandwidth.

Sound Localization (determination of origin of sound): Horizontal time (binaural) differences between signal perception of the ears and further signal processing in a parallel array of neurons allow the exact allocation of the sound source in space. Discrimination of emanating frequencies above or below ones head (vertical plane) is mainly achieved by the pinnae of the two ears. It changes the quality of the sound entering the ear. Localization is mainly achieved by two mechanisms (see SSD-manual p.25[2]):

Intensity Differences: Spreading sound follows a pattern characterized as the inverse square law. Sound intensity varies inversely with the square of the distance separating them (Intensity $\cong 1/\text{distance}^2$); observable only with frequencies >2kHz (as low frequencies can are diffracted by the head)

Time Lag mechanism: The ability to discriminate minute differences between the left and the right ear of the incoming pressure wave. The time difference is proportional

to the angle of incident sound. Δl, width of head [m]

$\Delta t = \Delta l/c = \sin(\theta)$ c, speed of sound 340 [m/s]

Tuning curves: Neuro-physiological signal processing by masking certain frequencies. Individual neurons in the auditory cortex respond to a range of stimuli. There are neurons that are broadly tuned, while others are very narrowly tuned. Narrowly tuned neurons act as filters, permitting only signals with particular properties to pass to the next level. Each neuron is most sensitive to a particular frequency (threshold energy that stimulates the neuron), but it can be stimulated by other frequencies within some range. Sounds outside the tuning curve of a neuron fail to activate it at normal energy levels.

Webner Fechner Law: Sensation increases arithmetically as a stimulus increases geometrically; the least perceptible change in stimulus intensity above any background bears a constant proportion to the intensity of the background.

$dE \propto \log(I)$.....the smaller the difference, the larger the intensity.

The logarithmic relation between the intensity of the stimulus and the intensity of the response thus "compresses" the high-intensity end of the scale, which greatly extends the range of discrimination.

[2] http://www.sbg.ac.at/ipk/avstudio/pierofun/qld/SSD.pdf

CHAPTER 4 - Biophysics of Vision:

Eye: Organ of visual (photo-) reception that includes optical processing of light; e.g.: vertebrate eye:

Blind spot: The optic disc as it is also known, is a small area of the retina with no light receptor cells; it represents the openings through which the fibers of the ganglion neurons emerge as the optic nerve.

Fovea (area centralis): In the mammalian retina, the area with the highest visual resolution due to small divergence and convergence in the pathway linking photoreceptors to ganglia cells;

Iris: The pigmented circular diaphragm located behind the cornea of the vertebrate eye.

Lens System: The series of optical devices that focuses incoming light rays onto the fovea. It consist of the cornea, the anterior chamber, the lens and the vitreous humor.

- **Lens**: The lens of an eye is a converging lens (biconvex, a lens that is thicker in the middle than at the edges) and refracts parallel rays passing through it to a focus.
- L. **Accommodation**: Increase in curvature of the lens in order to bend the light-rays toward the central fovea (adjustment of focal length). The fibers of the zonula (ciliary processes) exert outwardly directed tension around the perimeter of the lens; radially arranged ciliary muscle (suspensory ligaments) adjust the amount of tension exerted on the lens. When the ciliary muscles relax, the lens flattens by elastic tension exerted by the muscle of the ciliary processes, which pull the perimeter of the lens outward - objects far from the eye appear sharp. Objects close to the eye are brought into focus when the ciliary muscles contract. The parasympatic nerves directly control accommodation.

  $\frac{1}{f} = \frac{n_2 - n_1}{n_1} \cdot \left(\frac{1}{r_1} - \frac{1}{r_2} \right)$ [1/m]

  f, focal length [m]
  $n_{1,2}$, refraction index [-]
  $r_{1,2}$, radius of curvature [m]
- L. **Distortions**: Abnormalities in the refractive power and homogenous properties of the lens tissue.
  Astigmatism: A defect caused when the radius of curvature is not uniformly the same throughout the lens; i.e.: the inability to focus simultaneously light-rays arriving in different planes.
  Chromatic Aberration: Chromatic distortion of an image produced by a lens or lens-system (red refracts more than blue light).
  Spherical Aberration: Parallel incoming rays at the edge of a lens do not meet at the focal point as do rays which are closer to the axis of lens.
- L. **Equation**: The lens of the eye is an optical instrument which focus or disperses incoming light waves and has converging properties; i.e. a convex lens, which is thicker in the middle than at the edges, causing parallel rays passing through it to converge them to the focal point:

  $1/d + 1/d' = 1/f$ [m]

  L. **Magnification**: $M = -d/d'$ [-]

  d, distance of object [m]
  d', distance of image [m]
  f, distance of focus [m]

  People with short sightedness have a higher curvature of the main lens, thus, experience a higher magnification (subjective) of the lens system than do people with normal eyesight.
- L. **Rays**: Three principle rays characterize the lens' behavior:
  The 1st, incoming ray is parallel to the lens' axis and will be deflected to pass the focal point past the lens.
  The 2nd, center-seeking ray passes straight through the center without a deflection.
  The 3rd, incoming ray that strikes the focal point will be deflected to a parallel beam past the lens.
- **Power** of a L. (diopters): The focal length, f [m] of a convex lens is given as 1/f or D [1/m]; the shorter the focal length the greater the power. A healthy human lens can cover a range of approx. +14 D (close range vision). The refractive power of the entire visual apparatus is about +59D (relaxed eye, viewing at infinity).

Angle of vision: The coarse angle of vision is determined by the overlapping but slightly shifted visual fields of both eyes that are superimposed at the visual cortex of the brain to obtain a 3-D image. Each monocular angle is outlined at the peripheral retina (housing predominantly rods, responsible for luminance detection) while the resolution is mainly determined by the fovea (housing cones, responsible for color vision).

Rayleigh's Criterion: (also known as resolution) determines whether two remote sources can be clearly distinguished with the eye; it is primarily limited by the distance between receptors on the retina (in humans fluctuates around 100μm):

$\theta_R = 1.22 \cdot \lambda / (2 \cdot r)$ [rad]

λ, wavelength [m]
r, radius of object [m]

$360° = 2 \cdot \pi$ [rad]
$1' = 2.909 \cdot 10^{-4}$ [rad]
$1'' = 4.848 \cdot 10^{-6}$ [rad]

Photo Receptors: Cones and rods are the light detecting elements of the retina. Both detectors house staples of membranous disks in which rhodopsin molecules are embedded into the bilayer. The outer segment of both receptor types are wrapped by a membranous sheath that not only holds the membranous discs in place, but also acts like a fiber optic cable that conveys the light all the way back to the last disc.

Cone: The color (C) receptor cell that has a tapered outer segment in which the lamellar photosynthetic membranes remain continuos with the surface membrane; responds to one out of three particular colors (Red, Green, Blue); hue is calculated by differences of the RGB-values. Cones are only found in and near the fovea.

Rod: The illuminance (Y) receptor cells very sensitive to light, based on cellular physiology and on high degree of convergence onto second order cells; not sensitive to a particular frequency, rather to the full visible spectrum, hence cannot convey information about color.

Rhodopsin: A purplish red, light-sensitive chromoprotein with 11-*cis* retinal as its prosthetic group; found in the rods and cones of the retina.

The area covered by such a molecule is about $1 \cdot E^{-16} cm^2$; according to Lambert-Beer, the staple has to have a certain thickness to maximize visual sensitivity; i.e. 30-40µm thick to absorb 99% of incoming photons.

Lambert Beer: Characterizes absorption properties of liquids or gasses containing moderate quantities of a solute. If the solute does not represent the solvent itself, this law as a semi-quantitative measurement can be used to determine its concentration:

$I_{(x)} = I_0 \cdot e^{-A \cdot c \cdot d}$

I_0, initial photon intensity	$[W/m^2]$
A, area of the molecule	$[m^2]$
d, depth of penetration	[m]
c, concentration	$[part./m^3]$

Absorption is maximized further, if the penetrating electrical field vector of the incoming photon is parallelly aligned with the dipole moment of the rhodopsin molecule. Any deviation of that angle will result in weakened absorption (according to the deviating angle of the dipole moment relative to the electrical component of the light), and therefore in a less intense signal.

R. **Isomerization**: Rhodopsin changes its steric conformation into the straight, all-*trans* configuration when it absorbs one photon. The *trans* form decomposes quickly to retinal and opsin. The later, via an enzymatic amplification cascade, changes the electrical resistance of the membrane, causing hyperpolarization (1 photon causes a net transport of $1 \cdot E^5$ ions capable of generating a spike in the form of an action potential).

R. **Regeneration**: Rhodopsin is reconstituted out of retinal and opsin via an isomerase-activity, by returning the retinal to the bent 11-*cis* configuration; this can take several minutes and is one reason for prolonged visionary images, when switching off light suddenly.

CHAPTER 5 - Biomechanics of Blood Circulation

Blood: The fluid (composed of 45% solid compounds and 55% liquid - hematocrit) circulated by the heart in a vertebrate, carrying oxygen, nutrients, hormones, defensive proteins (albumins and globulins, fibronigen etc.), throughout the body and waste materials to excretory organs; it is functionally similar in invertebrates.

- **Hematocrit**: The percentage of blood volume occupied by red blood cells; 40-50% in humans, i.e. 55% plasma (liquid phase) and 45% cells and cell fragments (solid phase).

Erythrocyte: (Gk. eruthros, red + cutos, hollow vessel) A red blood cell whose main function is transporting oxygen to the tissues. Hemoglobin is the O_2 carrying pigment of the erythrocytes, formed by the developing erythrocate in bone marrow. A complex protein composed of four heme groups and four globin polypeptide chains plus several hundreds amino acids

Leukocyte: (Gk. leukos, white or colorless + cutos, hollow vessel) White blood cells; functions in the body's defense against invading microorganisms or other foreign matters; are divided in four classes: phagocytes (neutrophils and monocytes), eosinophiles, basophiles, and lymphocytes.

Plasma: The liquid portion of blood or lymph.

Thrombocyte: (Platelete) A disc-shaped cell fragment important in blood clotting.

Blood Flow: The circulatory system itself is a hydrodynamic system, using laminar flow for the steady transport of blood, avoiding turbulent conditions that would favor deposits in the vessels - which would sharply disrupt efficiency; the velocity of flow is related to the total cross-sectional area of a certain part of circulation. In laminar flow, the flow is directly proportional to the driving pressure, and resistance is independent of flow; according to the **Hagen-Poiseuill's Law**, the rate of flow can be simplified to $Q \approx r^4$; i.e. doubling the radius results in a 16-fold increase in the flow rate.

Because the allover cross sectional area of capillaries equals or is greater than that of the main artery, the average speed of flow within capillaries must be very low ($\varnothing_{\text{main vessel}} \leq \sum$ of $\varnothing_{\text{ of all branching vessels}}$), allowing diffusion processes to take place with the surrounding tissues. The flow profile of blood in vessels is not ideally parabolic, but rather flattened at the maximal flow speed vector ($\bar{v} = v_{max}/2$). This retarding effects is mainly caused by the viscous nature of blood, in that the faster it flows, the larger viscosity becomes - the more erythrocytes within the liquid (hematocrit), the less blood behaves according to Newton's model of liquids.

The amount of blood passing a certain stretch in an artery (speed of flow) can be measured in several ways.

- **Electromagnetic measurements**: A cathedra inserted in an artery detects minute changes of an externally applied magnetic field.
- **Indicator Method**: Injection of an inert dye into the blood path and its subsequent dilution within an arterial section provides information about the flow pattern of that particular section; basically, one measures the concentration of dye per time unit.
- **Doppler Effect**: The relative motion of wave source and receiver (to each other) causes a shift in the emitted frequency. A motion towards each other causes an increase of the emitted frequency; whereas motion away from each other lowers the emitted frequency.

$$f' = \frac{c \pm v_R}{c \pm v_S} \cdot f_0 \qquad [1/s]$$

c, speed of sound 330[m/s]

v_R, v_S, speed of receiver, sender [m/s]

f_0, source frequency [1/s] = [Hz]

This effect can be used to monitor the change in blood flow (speed) if the vessel under investigation is subject to wall depositions; i.e. arterial sclerosis.

The use of ultrasound is an non-invasive method to record the flow speed within any artery (wave resistance of human tissue to this sound spectrum is less than in the auditory frequency range). The frequency shift, caused by the flowing blood stream within the artery can be registered with the detector - the faster the flow of blood the more intense the shift towards higher frequencies (usually both emitter and detector are integrated in one ultrasound head).

Blood Pressure (BP): Force exerted by blood against the walls of blood vessels, due to contraction of the heart and influenced by the elasticity of the vessel walls; clinically, a measure of the pressure in arteries during ventricular systole and ventricular diastole (see SSD-manual p.33[3]).

Measuring BP (according to Riva-Rocci): Wrapping an inflatable cuff around a patient's upper arm and pumping in air until the pressure in the cuff prevents blood from flowing into the main artery in the arm whether the heart's ventricles are pumping or not, provokes an artificial reflection node. No sound is heard from a stethoscope placed on the artery as it remains closed. Once the nurse releases air from the cuff until its pressure is less than the pressure exerted on the blood by the beating ventricle. The artery opens when the ventricle contracts, but then slaps shut from the force of the cuff when the ventricle relaxes. The sound of the artery opening and closing can be heard through the stethoscope (**systole**, the phase of contraction of the heart muscle, especially of the ventricles). As more air is released from the cuff, the pressure in the cuff eventually becomes less than the pressure exerted on the blood even when the ventricles are at rest, i.e., the pressure exerted by the artery muscles. Once again, there is no sound because the artery is permanently open (**diastole**, the phase of relaxation or dilation of the heart muscle; especially of the ventricles).

Heart: The heart pumps a certain amount of blood-volume into the arteries. The elasticity of the arterial walls converts this pressure wave into a pulsatile wave that propagates along the arterial walls all the way along to the tinniest capillaries (propagation of the pressure wave occurs almost at the speed of sound). The flow of blood instead, is a lot slower and propelled by the repeated pulsatile travelling along the arterial walls.

Cardiac Cycle: The two most important components of the left ventricle diagram are the ***diastolic*** and ***systolic*** pressure. These two curves are volume-pressure curves. The heart can be considered a pressure pump, in that blood is transported in a cyclic manner.

- **Diastole**: The diastolic pressure curve is determined by filling the heart with progressively greater quantities of blood and then measuring the diastolic pressure immediately before ventricular contraction occurs, which is the end-diastolic pressure of the ventricle (relaxed myocardium);
- **Systole**: The systolic pressure curve is determined by preventing any outflow of blood from the heart and measuring the maximum systolic pressure that is achieved during ventricular contraction at each volume of filling.

Elasticity (Young's) **Module**: It predicts the speed of propagation of pulsatile waves, as caused by the heart:

$$v = \sqrt{\frac{E \cdot h}{\rho \cdot d}} \quad [m/s]$$

E, elasticity module	$[g/(m \cdot s^2)]$
d, diameter of vessel	[m]
ρ, density of blood	$[g/m^3]$
h, vessel wall thickness	[m]

The propagating pulsatile wave should not be subject to dampening effects, which would otherwise bring blood transportation to a halt. For this purpose, artery, arteriole, and capillary have to narrow progressively to keep the elasticity module as low as possible - ratio of h:d is constant!

Propagation of pulsatile wave is homogenous in tube-like vessels. Branching, with subsequent narrowing of the cross surface area can cause distortions of the propagation as a result of an improperly matched cross surface area between the main and the branching section ($\varnothing_{\text{main vessel}} = \sum$ of $\varnothing_{\text{of all branching vessels}}$).

- **Aneurysm**: A saclike enlargement of a blood vessel caused by a weakening of its wall.

Womersly's Number: The extent of deviation of the relationship between pressure and flow as predicted by Poiseuille's law is indicated by the value of the constant α:

$$\alpha = r \cdot \sqrt{\frac{2 \cdot \pi \cdot f \cdot n \cdot \rho}{\eta}} \quad [-]$$

r, radius of vessel	[m]
f, frequency of heartbeat	[1/s]
n, order of harmonics	[-]
ρ, density of blood	$[kg/m^3]$
η, viscosity of blood	[Pa·s]

Once $\alpha \geq 3$, then the speed of blood flow equals the speed of the pressure wave travelling along the arterial walls.

[3] http://www.sbg.ac.at/ipk/avstudio/pierofun/qld/SSD.pdf

CHAPTER 6 - Biomechanics of Respiration

Skin: The external covering of the body that consists of a superficial, thinner epidermis (epithelial tissue) and a deeper, thicker dermis (connective tissue) that is anchored to the subcutaneous layer. Respiration via the skin contributes to about 28% of the total body respiratory exchange of oxygen and 54% of carbon dioxide. Total surface area of the skin is roughly $2m^2$ in comparison to about $100m^2$ of alveolar surface in the lungs.

Lung: The principal air-breathing organ of most land vertebrates are soft, elastic, and inverted sacs that are suspended in the thoracic cavity, and enclosed by the fluid filled pleural sac. Ventilation of the lungs is passive because of the activity of the diaphragm and the expandable rib cage, which draws fresh air in and allows stale air to rush back out.

Lung **Capacity**: The preset averaged but fixed volumetric parameters that the lungs can perform; in contrast to lung volumes. In mammalians, split into the following sectors (see SSD-manual p.31[4]):

- **Inspiratory Capacity** = the tidal volume + inspiratory reserve volume; the amount of air (3.5L) that a person can breath beginning at the normal expiratory level and distending the lungs to the maximum.
- **Functional Residual Capacity** = expiratory reserve volume + residual volume; the amount of air remaining in the lungs at the end of normal expiration (approximately 2.3L).
- **Vital Capacity** = inspiratory reserve volume + tidal volume + expiratory reserve volume. It is the maximum amount of air that a person can expel from the lungs after first filling the lungs to the maximum extent and then expiring to the maximum extent (roughly 4.6L).
- **Total lung Capacity** = vital capacity + residual volume. Maximum volume to which the lungs can be expanded with the greatest possible inspiratory effort (approx. 5.L)

Lung **Volume**: The pulsate, thus dynamic average volume describing the inhalative parameter (in contrast to lung capacity):

- **Dead space Volume**: The total volume of air that is not directly involved in gas transfer during each cycle of inspiration; it is basically the volume of the naso-bucal area, trachea, bronchi, and bronchioli.
- **Residual Volume**: The volume of air left in the lungs after maximal expiratory effort.
- **Tidal Volume**: The volume of air moved in or out of the lungs with each breath.

Respiratory tract: The branched and aired compartment of the mammalian body that is used in the transfer of gasses. It consists of the trachea that subdivides the lungs in bronchi; the later branch repeatedly in an unsymmetrical manner, leading to terminal bronchioli and the terminally attached alveolar sacs. The cross sectional area increases with the decreasing diameter of the airway generation. The average flow of gas slows down the closer the air molecules get to the alveolar sac. Thus, enabling diffusion across the membrane bound air-blood interface.

Alveoli: (L. small cavity) A thin-walled, saclike, microscopic structure, surrounded by blood capillaries, in the vertebrate lung where gas exchange takes place. Each lung contains millions of alveoli and together both lobes represent a total surface area of about $100m^2$ - analogous to the intestinal infoldings to achieve a net increase in surface area.

- **Surfactant**: A surface-active substance that tends to reduce surface tension. When water forms a surface with air, the water molecules from the surface of the water tend to attract each other (surface tension of water); as a result, the water surface tends to contract along with the alveoli keeping away gases from penetrating. The energy required to expand an alveolar sac is:

$E_{Pot} \propto \alpha \cdot A$	$[kg \cdot m^2/s^2] = [N \cdot m] = [J]$	α, surface tension coeff.	[-]
		A, surface area	$[m^2]$
$\Delta p = 4 \cdot \alpha / r$	$[N/m^2] = [Pa]$	r, alveolar radius	[m]

Exhalation is thus facilitated, once the alveolar sacs reach a certain diameter that results in further contraction due to the surface tension of water; the residual air volume makes sure that alveolar sacs do not collapse. This also implies that the surface tension coefficient is not static but rather a dynamic variable.

Bronchi: Branches of the respiratory passageway including primary bronchi (the 2 divisions of the trachea), secondary or lobar bronchi (divisions of the primary that are distributed to the lobes of the lung), and tertiary or segmental bronchi (divisions of the secondary that are distributed to bronchio-pulmonary segments of the lung).

Bronchioles: Branch of a tertiary bronchus further dividing into terminal bronchioles (distributed to lobules of the lung), which divide into the respiratory bronchioles (distributed to alveolar sacs).

Tracheae: The *unsymmetrically* branched networks of hollow air passages, that end in air capillaries. Flow pattern in the trachea is generally laminar until it reaches the alveolar sacs. Similarly as in blood flow, the increasing cross-sectional area causes a net decrease in the flow of air to and from the alveolar sacs, allowing the diffusion processes (gas exchange) to take place.

[4] http://www.sbg.ac.at/ipk/avstudio/pierofun/qld/SSD.pdf

Transport Mechanism: Several physical transport mechanisms prevail in each human lung.

Convection: The mass transfer is due to a passively driven pumping motion of the thoracic muscles; it depends upon alveolar ventilation, partial diffusion pressure, and perfusion (the passage of blood over or through an organ, a tissue, or a cell; i.e. capillary blood volume within the alveolar sacs).

Diffusion: The dispersion of O_2 / CO_2 molecules as a result of random thermal motion is the main mean of transportation at the air-blood interface of alveolar sacs.

- **Reynolds Number**: Flow of air in the human respiratory tract (trachea and bronchi) is predominantly laminar; bifurcation results in turbulent hot spots, thus increasing breathing resistance, the increased flow is a compromise to ensure sufficient supply of oxygen and efficient removal of carbon dioxide to and from the alveolar sacs.

Oxygen Un/Loading of Erythrocytes: Hemoglobin consists of 4 polypeptide chains, each with a heme group. Hemoglobin A, the predominant hemoglobin in adults, has a subunit structure of $\alpha_2\beta_2$ (see biochemistry) and exhibits 3 different kinds of allosteric effects (see SSD-manual p.31[5]):

- **Sequential Model**: The Oxygen binding curve is sigmoidal, which means that the binding of oxygen is cooperative. The binding ligand to a subunit changes the conformation of that particular subunit which increases the affinity of the other subunits for the ligand.
- **Bohr Effect**: The allostoric linkages between the binding of H^+, CO_2, and O_2. H^+ and CO_2 promote the release of O_2 from hemoglobin.
- **BPG** (2,3-biphosphate-glycerate): The affinity of hemoglobin for O_2 is further regulated by BPG, a small molecule with a very high density of negative charge. BPG binds tightly to deoxy-hemoglobin but not to oxy-hemoglobin. Hence, BPG lowers the oxygen affinity of hemoglobin (occurs in close proximity of the target tissue).

Particle Deposition in the Lungs: According to a particle's physical characteristics, several means of deposing an airborne particle in the lung can occur. Alveolar deposition is most common in tiny particles (approaching molecular dimensions - few nm; e.g. $PM_{2.5}$, $PM_{1.0}$), while bronchial deposition is predominant in the upper respiratory tract (particles >10nm that get trapped in the nose or the mucus of the trachea and bronchi).

According to these extremes, particle deposition is grouped in (see Aerosol Physics p.9[6]):

- **Diffusion**: The dispersion of atoms, molecules, or ions as a result of random thermal motion is the main mean of transportation at the air-blood interface of alveolar sacs.
- **Impaction**: Particles being inhaled posses a certain speed, that, according to both its mass and diameter are not able to follow the (anatomically) preset trajectory, which result in deposition mostly at branching bronchi due to inertia.
- **Sedimentation**: Particles of organic or inorganic origin that accumulate in a loose, unconsolidated manner due to the gravitational pull of the earth.

Clearance: Stimulation of irritant receptors in the lung (trachea, bronchi, and bronchioles) by mucus and dust (aerosols) or other irritant particles causes reflex *bronchio-constriction* (a rapid contraction of smooth muscle tissue after a deep breath) and coughing. It is a major countermeasure to get rid of airborne particles and excess mucus that have accumulated on to the bronchial and tracheal walls.

[5] http://www.sbg.ac.at/ipk/avstudio/pierofun/qld/SSD.pdf

[6] http://www.sbg.ac.at/ipk/avstudio/pierofun/transcript/aerosol1.pdf

Summary Biophysics-2

CHAPTER 7 - System Theory[7]

System: An assembly of dynamically interacting units that can be mathematically described by the application of linear differential equations. Each unit can be assigned a system variable that describes its properties, while system parameters describe the interaction between those units. The sum of all system variables describes the system. The state of a system at a certain instant of time is characterized by the (time dependent) state variable.

Modeling: The transfer of observed variations within a system into diagrams of single, double, triple, or more variables resulting in a multi-dimensional orientation. Processes taking place within such a system can be described mathematically by using differential equations (y = dx/dt).

Parameters: A variable unit required to describe a system;

- **System Variable**: The measurable and quantifiable variables of a single unit, itself part of the entire assemblage of many units making up the system. The sum of all system variables comprises the system; e.g. the population density of a predator-prey relationship in a biotope; nerve cells that display a time-dependent firing frequency; or kinetics in chemistry in which the rate reaction, at a given temperature results in a dynamic equilibrium (homeostasis):

  $A + B \leftrightarrow AB$

  $dy_A/dt = c_A \cdot k_{1+} - k_{1-} \cdot y_B + k_{AB} \cdot y_B - k_{BA} \cdot y_A$

  $dy_B/dt = c_B \cdot k_{2+} - k_{2-} \cdot y_B + k_{AB} \cdot y_A - k_{BA} \cdot y_B$

  c_A, c_B, initial concentrations of reagents A, and B

  k_{1+}, k_{1-}, supply rate of raw material "A" fro/to outside

  k_{2+}, k_{2-}, supply rate of raw material "B" fro/to outside

  k_{AB}, k_{BA}, rate of formation/dissociation of product AB
- **System Parameter**: The constant that describes the way of interaction of units within the system; sometimes also described as the coupling factor that connects one unit with the next; e.g. in a prey-predator relationship it is the factor that describes the way the predator interacts with the prey population (prey density).
- **System State**: The present condition - the state at a particular instant that changes with time.

  Stable State: A response as a result of changed input conditions; any change in the surrounding environment will trigger a series of sequences until the system is again in dynamic equilibrium; e.g. greenhouse effect;

  Stationary State: The time-independent state; $y \neq f(t)$; e.g. a stemcell in its actual state can differentiate into a specific cell type (irreversible process); by doing so it reaches a stable and final state.

  Variable of State (Zustandsvariable): The variables that can be assigned a measurable quantity at a given time.

  Vector of State: The directed trend of a variable that follows along a distinct trajectory (in a 2D-system within the plane, for 3D-systems within space). Once the system is in the process of finding a dynamic equilibrium, every dynamic process can be assigned a direction; therefore, each system can also be described by knowing the trajectory of the system response.

System Responses: Important biological systems rely on periodic events (cardiac cycle, menstrual cycle, cell cycles, etc.).

Equifinality: Various different initial conditions eventually will lead to the same stationary final state, as long as the regulatory bandwidths are not exceeded. It is a common property of open systems that display an aperiodic response pattern (mathematically described by using linear differential-equations of 1st order), that are subject to altering external parameters. Thus, mathematical models (linear differential equation) help to describe the reaction pattern of a system, even without knowing the exact reaction pathways.

Oscillation: A dissipative and periodic response of open systems (is an extension of equifinality). The periodic motion is referred to as harmonic motion caused by the interaction of two or more state variables; other cyclic patterns include the hormone cycles, diurnal cycles, enzymatic cycles, operon activities, etc.

- **Attractor**: The stationary oscillating response (i.e. equipotential state) of the system, which approaches (but never reaches) the oscillating trajectory (equipotential line). It is the most stable state that requires the least amount of energy to maintain it (similar to a valley surrounded by mountains). It is usually outlined in a state diagram by two variables and follows a more or less circular pathway (analogous to Lissajou figures). The attractor has the tendency to approach the equipotential line as close as possible.

  Strange Attractor: A cyclic system in which the trajectory is not a closed loop. Even tough it reveals a certain regularity, successive cycles never follow the previous trajectory. Such deviations are the result of external disturbances that act upon the response pattern, causing the system to behave unpredictable. Although it does not follow a preset trajectory, the cycles of a strange attractor do have certain regularities - similar to periodic events that look strictly periodical, but at a closer look, they reveal minor irregularities, that give each new cycle a unique aspect.
- **Dissipative Property**: (Gk. energy consuming): In the absence of dampening effects, vibrating or oscillating systems require energy (supplied from the outside) to maintain oscillation.

[7] http://www.apmaths.uwo.ca/~bfraser/version1/nonlinearlab.html

- **Equipotential Line** (Ergodic Process, or Grenzzyklus): The idealized periodic oscillation that does not fall back to a stable resting point. Regardless of the initial conditions, the system always assumes cyclic behavior by approaching the oscillating pathway preset by the equipotential line.

System Types: According to the relationship with the surrounding environment, systems are grouped in:

Closed System: A (hologenic) system that does not interact with the surrounding environment; i.e. no flux into o out of the system does occur; e.g.: in thermodynamics (an idealized heat engine can be described entirely with the ideal gas equation, $p \cdot V = n \cdot R \cdot T$), with p, V, T representing the system variables. In terms of a chemical reaction, this implies that there is no input or outflow of reactants or products to or from the surrounding environment:

$y_{A(t)} + y_{B(t)} = y_A + y_B = \text{constant};$ $(k_{1+} = k_{1-} = k_{2+} = k_{2-} = 0)$

The sum of all variables has to be constant; furthermore, the result does not depend on the reaction rate, but by the initial conditions in which they take place.

Open System: A (merogenic) system that does interact with the surrounding environment; e.g. biological processes; i.e. homeostasis of a single cell of the human body or a damped simple harmonic oscillation.

$dy/dt = A_y + k_0$

$y_{i(t)} = y_i + \sum\{a_i \cdot e^{-\beta \cdot t} \cdot \cos(\omega \cdot t + \varphi)\}$

The stationary state in an open system does not depend upon the initial conditions.

The stationary state in biological systems is characterized by a steady state (dynamic equilibrium) of the change in parameters acting from the outside; e.g. greenhouse effect.

k_0, exchange rate with the surrounding environment

y_i, stationary state [var]

a_i, maximal amplitude [var]

β, damping constant [1/s]

t, time [s]

$\cos(\omega \cdot t + \varphi)$, damping term of fading oscillation

Non-Linear Systems: Any system whose system variable is coupled with another one; i.e. they display cyclic behavior (reveal oscillating patterns); such systems cannot be described by linear differential equations but require a non-linear differential approach. An integral constituent of such system is a feedback loop that is able to respond accordingly.

- **Feedback Loop** (FL): The regulatory pathway of any system that feeds the outgoing signal via a secondary pathway back to modulate the input signals in a positive or negative manner.

  Negative FL.: An increasing output signal has a suppressing effect on the triggering signal. Instantaneous negative feedback usually suppresses any oscillation while a delayed response facilitates cyclic patterns; e.g. in an enzymatic reaction, the catalytic processes (buildup of products) gradually suppresses the substrate required to generate products; e.g. operon in cells, which is a regulatory protein and a group of genes whose transcription is self-regulated. The excessive buildup of products will trigger a genetic reaction that inhibits substrate formation by the operon. Mathematically, it is described by a non-linear differential equation:

  $dy_{product}/dt = (y_{substrate} \cdot y_{gene}) - (k_{product} \cdot y_{product})$ k, reaction rate [1/s]

  Positive FL.: An increasing output signal causes a further increase in the input signal until the system "collapses". The implementation of countermeasures avoids collapse. Such systems are known to have autocatalytic response pattern. Voltera-Lotka (predator-prey) model do have these properties. The Hare-Lynx cycle (prey-predator) is a classical regulative cycle based on supply and demand. Hare (prey) population periodically rise when vegetation is abundant and fall when food becomes scare. When hare population rise, lynx (predator) also increase and devour more of their prey, ultimately causing a crash in the hare population. Reversely, a crash in lynx will soon trigger a boom in hare population. Both crash and boom cycles of prey and predator are closely linked to each other. Mathematically, both populations can be described by non-linear differential equations:

  $dy_A/dt = y_A - y_{AB}$ $dy_B/dt = y_{AB} - y_B$

- **Van der Pol Equation**: The van der Pol equation is a model of an electronic circuit that appeared in very early radios. This circuit arose back in the days of vacuum tubes. The tube acts like a normal resistor when current is high, but acts like a negative resistor if the current is low. So this circuit pumps up small oscillations, but drags down large oscillations. This behavior is known as a relaxation oscillation. The equation describes this non-linear system-oscillation as it follows along the path outlined by the attractor: [8]

  $$\frac{d^2x}{dt^2} + x + \varepsilon \cdot (x^2 - 1) \cdot \frac{dx}{dt} = 0$$

[8] http://www.apmaths.uwo.ca/~bfraser/version1/vanderpol.html, http://www.cmp.caltech.edu/~mcc/Chaos_Course/Lesson3/Demo1.html

Coupled Non-Linear Systems: Is a multi-dimensional system that generates two distinct states; it involves the interaction of two Voltera-Lotka (prey-predator) systems. Interaction of this sort creates a response that will have irreversible effects.

- **Discriminative System**: A change of state in the system caused by a switching event, which inhibits the system to change into its original initial state; e.g. stemcells can differentiate into specific cells, but also can differentiate into another stemcell. A differentiated cell instead cannot become a stemcell anymore.
  Another practical example is the temperature regulation of a heater; the preset value will be approached by the current value via an exponential pattern according to the control parameter. If for whatever reasons the system response cannot approach a stable state, bifurcation conducts the system to an alternative and stable state.
  $dy/dt = k \cdot y + k_0$ (solutions of such a differential equation will result in an exponential function).
  Bifurcation: The attempt of a biological system (via control parameters) to approach a preset stationary state; if such a state cannot be reached, the system responds with a bifurcation - whichever stationary state is closer, the respond will guide the system to that alternative stable state.
  Hysteresis: The response of a system that moves along certain response paths. Such backward and forward system responses do not occur on identical pathways (trajectory), but rather enclose an area, i.e. envelope.
- **Dissipative Structure**: A process that requires energy to take place. Several different states can be reached within the same system (requires that both initial conditions and the sequences in which changes occur are known). Practical example of a dissipative structure is the aerobic anabolism of glucose (Fru-6-P) into lactate (pyruvate) - see below, fractals - glycolysis (p.19).
  Brusselator: A model used to simulate the response patterns of biological systems depending upon the initial state. The oscillation approaches a stable state by moving along a cyclical trajectory in which the amplitude gradually decreases until a final stable state is reached. The pertaining mathematical relations are[9]:

  $$dy_A/dt = 1 - y_A + y_A^2 \cdot y_B - y_A \cdot y_C$$
  $$dy_B/dt = \quad - y_A^2 \cdot y_B - y_A \cdot y_C$$

  A Brusselator is thus able to mimic biological response patterns even without knowing the precise interactions that control it:
  i) it is an open system
  i) uses non-linear equations
  i) is based on a positive feedback loop
  i) approaches one or more attractor(s) or (un)stable states
  i) mimics bifurcation, and
  i) allows modeling of dissipative systems
  Reaction Diffusion Mechanism (Belousov-Zhabotinsky Reaction[10]): A practical approach to confirm the theoretical reflections of the Brusselator. It is a chemical and dissipative reaction showing oscillating patterns; e.g. two opposing chemical agents alternatively dominate in the reaction by creating an ever-changing wave pattern. This spatial wave pattern result out of the periodic association and subsequent dissociation of the Redox-system bromat (BrO_3) and Cerium (Ce^{4+}). After an initial lag time, the cyclic reaction starts to swing between the alternating maxima of Br^- and Ce^{4+}/Ce^{3+}; selected reaction steps are as follows:

$BrO_3^- + Br^-$	$\rightarrow$	$HBrO_2 + HOBr$	Rate = $k_1[BrO_3^-]\cdot[Br\text{-}]$
$HBrO_2 + Br^-$	$\rightarrow$	$2HOBr$	Rate = $k_2[HBrO_2]\cdot[Br\text{-}]$
$BrO_3^- + HBrO_2$	$\rightarrow$	$2HBrO_2 + 2Ce^{4+}$	Rate = $k_3[BrO_3^-]\cdot[HBrO_2]$
$2HBrO_2$	$\rightarrow$	$BrO_3^- + HOBr$	Rate = $k_4[HBrO_2]_2$
oxid. species + Ce^{4+}	$\rightarrow$	0.5 stoichiometric factor of Br^-	Rate = $k_c[Z]\cdot[Ce^{4+}]$

  Both amplitude and period are not dependent upon the initial concentrations of the reactants and can be mathematically simulated. Practical applications are found in the simulation of Leopard skin pigmentation, Zebra pattern, water molds creeping pattern, etc. The use of such a mathematical model yields results even without knowing the exact biochemical mechanisms behind it.

[9] http://www.cmp.caltech.edu/~mcc/STChaos/Brusselator.html
[10] http://www.cmp.caltech.edu/~mcc/STChaos/Barkley.html
http://online.redwoods.cc.ca.us/instruct/darnold/DEProj/Sp98/Gabe/bzreact.htm,
http://www.cs.bham.ac.uk/~jfm/qmcomp/2001/lecture10/sld004.htm

Chaotic Systems: It is a system that cannot be described precisely. Initially the system behaves like any other linear or non-linear system; the shift to chaotic behavior occurs only once the control parameter exceeds a certain level; as the control parameters fall again below the threshold levels, response patterns switch back to non- or linear system behavior. Mathematically, such a system can be described by using "the 1st derivative" of differential equations where discrimination occurs at certain points[11].

$dx_t/dt = k' \cdot x_t$

A classical example of a chaotic system can be found in a stopcock-dripping pattern. The flow rate of water determines the control parameter.

i) Initially, with a low aperture, the drop frequency is fairly regular.

i) Increasing the flow rate, the drop pattern changes from a regular single event to a double dripping pattern, involving two asynchronous drops per period (bifurcation).

i) A further increase in the flowrate causes the system to change from a periodic pattern to a multitude of irregular falling droplets or even a continuous thread of water - the system becomes chaotic.

Chaotic states:

- Deterministic S.: A causal connection between action and reaction; i.e. a value on the abscissa (x-axis) corresponds to a distinct result on the ordinate (y-axis).
- Stochastic S.: There is no relation whatsoever between action and reaction; the response is purely accidental, thus unpredictable.
- Chaotic S.: A mixture of deterministic and stochastic response patterns - as seen in the Zhabotinsky reaction.

Graphic tools to display chaotic response patterns:

- **Bifurcation Diagram**: A simple x-t diagram that switches from a single deterministic response to either one or another deterministic response. The decision which of the two deterministic states will occur is solely dependent upon the control parameter. In certain cases bifurcation can lead to 2, 4, 8, etc. separate states.
- **Next Amplitude Plot** (**Next-Period** Plot or **Stroboscopic** Plot): A 2-dimensional plot with a diagonal originating from 0 at a 45° angle (line of identity). Each mark in the plot is a function of the previous mark $f(x_i) = x_i+1$. The identity line originating from 0 and crossing the diagram at a 45° angle splits the diagram into two triangular halves. The crossing angle of the system graph with the identity line displays the stability of the system. The system is stable if the slope of the tangent at the crossing graph with the identity line is <1; the system is unstable if the slope of the tangent is >1.

  Iteration (L. iterare, to repeat): Incrementation of the previous value by 1; i.e.: $x_{i+1} = f(x_i)$. Thus, the Next-Amplitude plot is a graph of the form of x_{i+1} vs. x_i.

  Line of Identity: An auxiliary line originating at 0 that crosses the 2-dimensional plane at a 45° angle. It is used as a reference line to which unstable states bounce back and forth as they approach stability (stationary state) or an attractor (oscillating pattern). A stable state is indicated as the x_i^{th} value approaches 0, while an oscillating patterns is indicated by the values of $x_i^{th} > 0$ (attractor).
- **State Diagram**: A 2-dimensional plot in which each of the interacting variables are assigned an axis (e.g. y_A the abscissa, y_B the ordinate). In multi-dimensional relationships, these diagram can assume multi-dimensionality; i.e. spatial diagram for 3 interacting variables, 4D-diagram for 4 interacting diagrams, etc. Linear relationships in closed systems occur along a more or less linear path, while non-linear relationships in open systems can result in circular patterns (oscillations).
- **Time-Variable Graph**: The simplest type of diagram in which a single variable is plotted on the vertical axis (ordinate) and the time along the horizontal (abscissa) axis.

Practical Applications of Chaotic Systems: Besides the dropping stopcock example, several other biological system display chaotic behavior. Under certain circumstances even the dynamic population relationship (predator-prey system) does reveal a chaotic response. Ideally, such a system oscillates periodically, but as one control parameter (e.g. increasing the predator population) exceeds a stable state (or threshold), readjustment due to self-regulation ultimately will cause the system to behave chaotically. Mathematically such a relationship can be described with logistic equations.

- **Logistic equation**: It describes interaction among system variables; e.g. prey predator systems. According to the formula stated below, a k-factor of 2.7 ($x_i = 0.9$) produces an aperiodical dampened response; a k-factor of 3.4 yields a regular iteration (bifurcation), while k = 3.9 generates a chaotic response (multitude of bifurcations).

  $x_{i+1} = k \cdot x_i \cdot (1 - x_i)$ k, control parameter

[11] http://www.apmaths.uwo.ca/~bfraser/version1/iterated.html

Fractals (L. fractus, to break): A method used to quantify a chaotic system by creating to create irregular fragments.[12] The extending and folding of chaotic systems give strange attractors, such as the Lorenz Attractor, the distinguishing characteristic of a nonintegral dimension. This nonintegral dimension is most commonly referred to as a fractal dimension. The classical Euclidean geometry is a description of lines, ellipses, circles, etc. However, fractal geometry is a description of algorithms. There are two basic properties that constitute a fractal.

i), is self-similarity, which is to say that most magnified images of fractals are essentially indistinguishable from the unmagnified version. A fractal shape will look almost, or even exactly, the same no matter what size it is viewed at. This repetitive pattern gives fractals their aesthetic nature.

i) fractals have non-integer dimensions. This means that they are entirely different from the graphs of lines and conic sections found in fundamental Euclidean geometry.

- **Roessler System** (RS): A model that uses coupled non-linear differential equations to simulate chaotic behavior. It is characterized by a strange attractor; i.e. RS oscillates along a "strange" attractor without ever reaching it. Being chaotic, fluctuations cannot be predicted with statistical probabilities. By the use of the bifurcation diagram, a Roessler system reveals a sequential series of deterministic and chaotic states. Chaotic responses usually follow bifurcation by suddenly changing from the deterministic state into a chaotic state[13].
  The next amplitude plot of a RS [$x_{i+1} = f(x_i)$], typically reveals a graphical pattern in the form of an upside down "U-turn". Thus, it is a:
  i) coupled system with a negative feedback loop;
  i) can be mathematically described at least with one non-linear differential equation;
  i) approaches a strange attractor (unstable);
  i) any disturbances of the system merely relies upon the attractor and not from the extent of the disturbance;
  samples of a RS are the Heisenberg's *Uncertainty Principle*, which states that it is impossible to know simultaneously both momentum and the position of a particle with certainty. Another example involve the theory that a single flap of a butterfly's wings can trigger a major meteorological event somewhere else on the planet.
  Examples of RS equations:
  $dx/dt = -y - z;$
  $dy/dt = x + a \cdot y$
  $dz/dt = b + z \cdot (x-k)$

Fractal Geometry: A method used to find out if a system under investigation does have chaotic properties. Fractal parameters will trigger a chaotic or distinct response. Several methods are available to describe it; although, according to the methods applied, they yield slightly different results.

Practical Application of Fractals:

- **Action Potential** (AP): Transient all-or-none reversal of a membrane potential produced by a regenerative inward current in excitable membranes originating from the hillock area; i.e.: nerve impulse, or spike. APs have chaotic properties that enables the cell to respond in manifold ways according to the stimulus applied. Dysrhythmia (sometimes called arrhythmia) is a general term that refers to an abnormality or irregularity in the heart rhythm as a result of chaotic response patterns in that one or several control parameters are preset at a level that induces chaotic behavior - even normal cardiac activity reveals slight arrhytmia.
  The Hodgkin and Huxley Equation mathematically describe the time and voltage dependence of membrane conductivity along nerve axons for Na^+ and K^+. It displays chaotic behavior as well.
- **Glycolysis**: (Gk. glyk, sweet; lysis, dissolution) Embden-Mayerhof Pathway - a series of reactions that converts glucose to pyruvate with the concomitant production of a small amount of ATP (highly exergonic). Pyruvate is then shuttled into the cells. The series of reactions does not require the presence of oxygen to occur.
  Application of Fructose-6-Phosphate (F6P) causes a shift from a periodic oscillation within the ATP/ADP-loop to a chaotic response; i.e. the response pattern increases from distinct states to infinite states (response possibilities - not to be confused with noise!). Here F6P acts as a control parameter, in that, once F6P-application is halted, the ATP/ADP-loop returns back to its oscillating pattern.
- **Zhabotinsky Reaction**: The formation of a spatial wave pattern due to an oscillating association and dissociation of the Redox-system bromat (BrO_3) and Cerium (Ce^{4+}) described above.

[12] http://math.bu.edu/DYSYS/applets/

[13] http://www.apmaths.uwo.ca/~bfraser/version1/rosslerintro.html

Cybernetic Systems and Control Loops (CS): A system that actively attempts to resist any change caused by external influences. System reaction is brought about by a negative feedback loop. Feedback is widely employed by both biological and engineering control systems to maintain a preselected value; e.g. protein synthesis, cell division (lesions of the skin trigger cell production and ultimately result in the formation of a scar = overshoot in cell production), hormone homeostasis, body temperature, light-sound reaction patterns, muscle contraction, etc.

$y_{(t)} = \int_{-\infty}^{+\infty} z_{(\tau)} \cdot h_S \cdot (t-\tau) d\tau$

$Y_{(\omega)} = \frac{H_S \cdot (W + H_R \cdot X_\omega)}{1 + H_R \cdot H_S}$

Mathematically, CS are obtained by faltungsintegral (linear and time invatiant systems) or Fourier transformation: $z_{(\tau)}$, control parameter (steuer/stellgrösse)
τ, time constant
H_S, h_S, H_R, h_R, response function of regler (R) and strecke (S)
Fourier transformation: $\omega = 2 \cdot \pi \cdot f$, angular frequency

The most common types of control systems involve the:

Solid state CS: the aim of such a CS is to hold a prefixed output value even though input heavily fluctuates.

Mobile state (folgeregler) CS: The output signal changes according to the dynamics of the disturbances of the input; the CS adjusts itself until a new dynamic equilibrium is reached (long-term response pattern).

- **Proportional** CS (P): The response (output value) of such a regulator is directly proportional to the input level.
  $y_{(t)} = V_P \cdot x_{(t)}$ V_P, amplification factor of system
- **Delayed Proportionality** CS (PT): The response (output value) of such a regulator is directly proportional but somewhat delayed to the input signal. Such regulators display low-pass properties; i.e. slow changes will be passed on to the output while fast changes are unrecognized. V_P, amplification factor of system
  $T_1 \cdot (dx/dt) \cdot y_{(t)} + y_{(t)} = V_P \cdot x_{(t)}$ T_1, time constant of the system
- **Proportional-Differential** CS (PD): The response (output value) of such a regulator is composed of one component that is directly proportional to the input signal $V_P \cdot x_{(t)}$ and another one that constitutes the differential component; the differential unit is responsible for the high-pass property of the entire unit, as it generates a positive spike upon an increase in signal input V_P, amplification factor of system
  $y_{(t)} = V_P \cdot T_D \cdot dx_{(t)}/dt$ T_D, time constant of the system
- **Proportional-Integral** CS (PI): The extended time constant and amplification generate a linear increase at the output as long as the input signal is fed into the system. The slope of the output is determined by the signal strength at the input. V_P, amplification factor of system;
  $T_1 \cdot y_{(t)} = (V_P/T_1) \int x_{(\tau)} dt$ T_1, time constant of the system

Practical Application: Muscle Contraction can be considered a good example of control loop system. The bones of the upper and lower arm serve as levers, and the joints act as fulcrums for the levers. The resistance may be the weight or a part of the body that is to be held. In this particular case the effector muscle *Biceps brachii* acts as the control loop under the control of a α-motor neuron. The muscle spindle as the receptor is integrated within the *B.brachii* and detects any stretching stimulus (e.g. a mass held in the palm of the hand); it passes the information on to the α-motor neuron in order to stimulate the muscle to maintain the mass in position. The CNS is capable of control the contraction of the *B.brachii* via the α-motor neuron (preset value). Furthermore, the CNS is also capable to controlling a γ-motor neuron that suppresses or increases the receptor's sensitivity.

Stability of Control Loops: Control systems with delayed responses (delay line) tend to become unstable when quick changes at the input require fast replies. Once the input stimulus reaches a frequency that results in a phase shift of the output (Bode criteria), the system tends to become unstable if the amplification at this stage is >1. The upper frequency limit is reached (grenzfrequenz).

- **Nyquist Criterion**: A system is unstable when the denominator approaches 0 (response function $(H_R \cdot H_S) = -1$).
  $Y_{(\omega)} = \frac{H_S \cdot (W + H_R \cdot X_\omega)}{1 + H_R \cdot H_S}$
  H_S, h_S, H_R, h_R, response function of regler (R) and strecke (S)
  Fourier transformation: $\omega = 2 \cdot \pi \cdot f$, angular frequency
- **Bode Criterion**: A system is unstable when the frequency shift between input and output approaches -180° ($-\pi$) with an amplification still >1.
  W, external disturbing input

Practical Application: The pupillary reflex system has an extended recovery time. Contraction of radially oriented muscle fibers enlarges the pupil. The contraction of these muscles is controlled by a neuronal reflex that originates in the retina. Changes in pupillary diameter are transient. After a response to a sudden change in illumination, the pupil gradually returns after several minutes to its average size. The feedback loop can be interrupted by focusing through the pupil at a tiny spot onto the retina, which causes the iris to remain widely open.

Weber-Fechner Law: In acoustics, the sensation increases arithmetically as a stimulus increases geometrically; the least perceptible change in stimulus intensity above any background bears a constant proportion to the intensity of the background.

CHAPTER 8 - Radiation Physics

Atomic States: The most balanced atomic state is one that requires the least energy to maintain it. Electromagnetic or thermal radiation is able to provide enough energy to lift electrons from their ground state to an elevated level. If the energetic input is high enough, the loss of one or more electrons (ionization) can be brought about.

Ground State: An atom as a whole is in its ground state, when the orbiting electrons are in their lowest possible energy state. At low temperatures, atoms (and molecules) tend to be in their ground states. Atoms in the ground state do not radiate (see transcript Riepe *Indoor Air Analysis* p.56).

Excited State: Any mechanism that can pump energy into an atom. A collision with another atom, with a proton, or an electron can boost the energetic content of the atom. Furthermore, outer electrons orbiting around the atomic nuclei tend to become excited through collisions (mechanically induced due to elevated temperatures). Even discrete amounts of incoming radiation ($E = h \cdot \nu$) can raise the electron to the next upper orbiting level. The atom has been converted into the excited state. Relaxation is brought about when the lifted electron falls back into its ground state by emitting the energetic amount that was required to boost it to that particular level (quantum jump - i.e. the energy difference between the excited state and the ground state or between different exited states).

Ionization: It is the conversion of neutral atoms to cations by the removal of electrons; e.g.: $H(g) \rightarrow H^+(g) + e^-(g)$. The energy required to split the electron from the atom (to raise it up and out of the nuclear attractor potential) varies in each element. For the hydrogen atom (H) it is $13.6[eV] = 2.176 \cdot E^{-18}$ [J]; in terms of distance =121.6[nm].

Ionization in biological systems occurs in several steps (for further details, see also p.24):

- **Physical** I.: Absorption of in/direct acting ionizing radiation by living tissue; takes $\approx 1 \cdot E^{-13}$ sec.
- **Physical-Chemical** I.: Intermolecular exchange of radiation energy (genotypic damages); takes $\approx 1 \cdot E^{-10}$ sec.
- **Chemical** I.: Generation of abnormal biomolecules (radicals) triggering a chain reaction; requires $\approx 1 \cdot E^{-6}$ sec.
- **Biogenic** I.: Phenotypic expression of damaged source codes (mutations, biochemical changes); takes years.

Direct Ionizing Radiation: The sort of radiation that deprives the target atoms of its electrons causing protonization; e.g. $H \rightarrow H^+ + e^-$. In biological systems it can be the fracture of a DNA molecule.

Indirect Ionizing Radiation: Radiation that hits an atom, which results in secondary emissions. And they generate fragments that ionize the target atoms. In biological systems such effects can be observed when the penetrating radiation generates radicals (OH-radicals) by striking a water molecule that interacts with the DNA molecule causing mutations due to strand-breakage.

Radiation: A spontaneous process in which an atomic nucleus chips apart. When a nucleus suffers alpha or beta decay, it is often left in an excited state. In such an unstable state, it emits the excess energy in the form of gamma quantum. The emission of a gamma ray during the transition of a nucleon is similar to the emission of photons or an X-ray originating from an atomic electron in transition ($E = h \cdot c/(\lambda \cdot 1.60E^{-19})$ given in [eV]).

α - **Alpha** D.: Regarded as the fission of the nucleus into two smaller nuclei; fission occurs spontaneously because of an instability in the original nucleus. α-radiation is thus a stream of He- nuclei (2p+2n - positively charged). Under the influence of an electric field, the positively charged particle beam is deflected towards the negative pole. Even though alpha rays do not penetrate deeply, they can be very harmful if inhaled ($E_\alpha \approx 5$MeV).

β - **Beta** D.: A beta particle is set free once a neutron is liberated from a decaying nucleus. A free neutron is unstable and further decays into a proton, an electron and an antineutrino. β-radiation is thus a stream of beta particles ejected by certain radioactive nuclei. As they have *negative* electric charge (electrons), they are deflected towards the positive pole upon exposure to an electric field. Beta rays pass through almost everything; they are only stopped when encountering metal ($E_\beta \approx 0.5$-2MeV).

γ - **Gamma** R.: A high-frequency electromagnetic radiation (photons) that is emitted by decomposing nuclei of radioactive atoms. They have *no charge* at all, hence are not deflected by an electric or magnetic field. These are the farthest-reaching particles, and can only be shielded with materials of high density, such as lead ($E_\gamma \geq 50$keV).

n-**Neutron** R.: The particle beam consisting of neutrons (no charge) resulting out of decomposing nuclei.

p-**Proton** R.: The beam of ionized H-atoms (deprived of their electron) that possess one positive charge.

d-**Deuterium** R.: The charged beam of a heavy ^{2}H-atom (twice the charge of ^{1}H) generated in particle accelerators.

X-ray: a very short electromagnetic radiation ($\lambda_X > \lambda_\gamma$). They are emitted after relaxation of excited electron of the innermost shells (contrary to the outermost excitement of electrons in a florescence lamp). Such electromagnetic radiation does not possess any charge, therefore, they won't be deflected by an electromagnetic field at all.

Particle-Wave Dualism: (Also called De-Broglie wavelength) Any particle moving with a constant momentum is associated with a monochromatic wave [$\lambda = h/(m \cdot v)$] and is determined by its total energy ($f = E/h$). As with all waves, it moves with a phase speed given by $v = f \cdot \lambda$, which is usually different but related to the speed of the particle. Every particle (e, p, atoms, mice, you, planets, sun) has a wavelength that is related to its momentum.

Biophysics and Radiation: Exposure of ionizing radiation to organic matter or living tissue to radiation will deposit in them discrete amounts of energy. Absorbence can occur directly by the target tissues (DNA) or indirectly via the

formation of radicals (potential mutagens). Quantification of radiation is essential to determine the dose and effect relationship.

Flow Rate (Flux =fluenz): The flow rate of ionizing radionuclides is characterized by the ratio of penetrating particles per time and area.

$$\text{Flux} = \frac{\text{particles}}{t \cdot A} \qquad [1/(s \cdot m^2)]$$

t, time [s]
A, surface area [m^2]

Activity: The number of nuclear decays occurring in a given quantity of material in a time interval, divided by that time interval; usually given as decays per second or Bequerel [Bq].

- **Specific** A.: The activity of a material (specified radionuclide) divided by the mass or volume of that material.

Dose: A specified quantity of a therapeutic or harmful agent to be administered or taken at one time or at stated intervals. In the case of ionizing radiation, it can be easily quantified. Highly energetic radiation causes ionization when penetrating matter; non-ionizing radiation though, does not enable simple quantification due to the diffuse absorption of energy without a direct measurable entity (modified intermolecular energy transfer). Thus, dose does not represent a common reference point, because electromagnetic radiation (UV, VIS, IR, α-particles, etc.) results in different cause and effect patterns.

- **Absorbed** D.: Dosimetric unit of the average energy per exposed mass unit

$$D = \frac{dE}{dm} \qquad [Gy] = 100[rad]$$

E, average energy [eV]
m, mass [kg]

- **Exposure** D.: The ionic dose emitted by an X-ray or röntgen tube that is absorbed by a mass unit. Being density dependent, X usually refers to NTP standards (normal temperature and pressure conditions). The conversion from charged to absorbed energy requires a conversion factor in the form of a mass absorption coefficient, that is given by μ/ρ. This relationship characterizes the energy that is required to generate ion pairs like H^+, e^-.
  X used to be given in Roentgen [R], which is the equivalent of $2.58 \cdot E^{-4}$ [C/kg].

$$X = \frac{dQ}{dm} \qquad [C/kg]$$

Q, charge [A·s]
m, mass [kg]

- **Equivalent** D.: It characterizes the **L**inear **E**nergy **T**ransfer and highlights the total amount of charged particles per distance. As low energy particles like photons (E = h·ν) do not cause ionization, the power of ionization gradually rises when particles exceed the threshold energy level of 3.4eV {$E = h \cdot c/(\lambda \cdot 1.6 \cdot E^{-19})$ [eV]}. Particles around 1[MeV] posses the greatest interactive potentials with living tissues, while it declines sharply with particles possessing more than 10[MeV]. The latter posses so much kinetic energy that the particles simply pass through matter at such high speeds that they do not interact with tissue anymore.

$$\text{LET} = \frac{dE}{dx} \qquad [Gy] = 100[rad]$$

E, average energy [eV]
x, radiation depth [m]

Relative Biological Efficiency: Relative dosimetric determination of a reference radiation (e.g. γ source) over a test radiation (e.g. α source). Per definition, the test is established in a way that compatibility is reached upon a death rate of 50% in an exposed cell culture.

$$\text{RBE} = \frac{\text{dose (X)}}{\text{dose (test)}} \cdot 100 \qquad [\%]$$

X, dose of X-ray [C/kg]
dose of test radiation [C/kg]

Relative biological efficiencies for α-rays can reach values of 20; i.e. only $1/20^{th}$ of the dose equivalent is required to reach the same effect as obtained by using X-rays only.

Entity	SI-Unit	Definition	Old unit	Symbol	Conversion
Activity (A)	Becquerel [Bq] = [1/s]	Number of radioactive decays per time unit	Curie	[Ci]	$1[Ci] = 37 \cdot E^9$ [Bq]
Energetic dose (D_E)	Gray [Gy] = 1[J/kg]	Total absorbed radiation energy per mass unit	Rad	[rd]	$1[rd] = 10 \cdot E^{-3}$ [Gy]
Equivalent dose (D_{EQ})	Sievert [Sv] = =1[J/kg]	Energetic dose multiplied by radiation factor (unit-less quantity based on α,β,γ)	Rem (röntgen equivalent man)	[rem]	$1[rem] = 10 \cdot E^{-3}$ [Sv]
Ionic dose (D_{ion})	[C/kg]	Electric charge generated in air-filled ionization chamber divided by the mass of air contained	Röntgen	[R]	$1[R] = 258 \cdot E^{-6}$ [Bq]
Power of D_E	[Gy/s] or [Gy/h]	Energetic dose per time unit	Rad/s or Rad/h	[rd/s] or [rd/h]	$1[rd/s] = 10 \cdot E^{-3}$ [Gy/s]
Power of D_{EQ}	[Sv/s] or [Sv/h]	Equivalent dose per time unit	Rem/s or Rem/h	[rem/s] [rem/h]	$1[rem/s] = 10 \cdot E^{-3}$ [Sv/s]
Power of D_{Ion}	[A/kg]	Ionic dose per time unit	Röntgen /s or Röntgen /h	[R/s] or [R/h]	1[R/s] = 0.93 [A/kg]

Radionuclides: An unstable nuclear species that decomposes by emitting radioactivity. For medical diagnosis, such substances are administered intravenously. Under these circumstances, the injected agent should not accumulate in a target organ but should be excreted rapidly. In certain cases however, involuntary take up of radionuclides can occur by several major pathways, while clearance (excretion) is achieved predominantly by the kidneys[14].

Incorporation: Take up of radionuclides can occur as follows:

- **Ingestion**: Via contaminated food and water, as well as exposed bronchial mucus that is shedded due to ciliar motion and ultimately swallowed. The target organ is the gastrointestinal tract (GI). The average dwelling time in the stomach lasts about an hour, while it steadily increases as it proceeds into the following sections of the GI-tract. As the radionuclides are gradually released, the duodenum experiences already a more prolonged exposure. Dwelling time along with exposure increase further in the ileum, to reach maximum concentration in the colon. All together, dwelling time within the GI-tract is about 42 hours.
- **Inhalation**: Intake of airborne radionuclides is followed by the diffusion across the alveolar air-blood barrier.
  Gas: Usually, radioactive gasses are exhaled as rapidly as they have been taken up during inhalation.
  Aerosol: Aerosols, instead do not leave the thoracic airways, and can remain there for a very long time. Deposition of radioactive aerosol particles can be extracted quite rapidly by the ciliar beat of the epithelium (transfer rate, $K_r \approx 24h$), while alveolar deposition takes longer to be removed, since these particles have to cross the air-blood barrier for elimination by the circulatory system (transfer rate, $K_b \approx$days). Their hydrophobic and hydrophilic properties are of essential importance since they can be readily absorbed or not. According to these properties, transfer rates of aerosols are grouped in 3 classes (class D (<10d), W (>10, <100d), and Y (>100d).
- **Percutane**: Certain gasses are able to diffuse through the dermal layer into tissues and capillaries.

Clearance: Excretion of radioactive substances does take place. Certain substances do readily deposit within the bones, thus, lowering the clearance ability considerably.

- **Defecation**: Most hydrophobic long-living radioactive substances can be expelled from the body via this way. Due to the prolonged retention times, it is not recommended to analyze feces for their radioactive contents.
- **Sweating**: Water-soluble, radioactive substances can leave the body via the sweat glands of the skin.
- **Urination**: Most hydrophilic radioactive substances though, leave the body via the enriching tasks of the liver and kidneys. As the majority of radionuclides are expelled from the body via the liquid fraction, it is suitable to measure the activity after the incorporation of radioactive substances.

Target Tissue of radionuclides: Once in the body, radionuclides become diffused via the circulatory and the lymphatic systems. According to their affinity and their metabolic involvement of that substance, certain elements do readily accumulate in distinct target organs; i.e. Iodine in the thyroid glands, Strontium in the bones, etc.

As body tissue may absorb α-, and β- rays quite easily, detection of accumulated radionuclides is possible only by indirect determination of γ-rays via γ-counters. The emanating activity is merely a physical phenomenon, thus it can be expressed mathematically as: $A = K \cdot N$

$A_{(t)} = A_0 \cdot e^{-KA \cdot t}$ [Bq] = [1/s]

K, radioactive decay probability	[1/s]
K_A, K_B -"- of component A and B	[1/s]
N, number of radioactive atoms	[-]
A_0, initial activity	[1/s]
t, time	[s]

- **Transportation** from one target organ to the next involves complex biological pathways. With the help of compartment models, the pathway of radionuclides within the body can be emulated. To denote the amount of substance relocated per time unit, the transfer rate (K_b, as a simplified approximations) is used:
  $A_{(t)} = A_0 \cdot e^{-KB \cdot t}$ [Bq] = [1/s]
  As both radioactive decay and biological kinetics follow more or less the same exponential pattern, which make it possible to add them up: $K_{eff} = K_A + K_B$
- **Half-life**: The time required for half the atoms of a radioactive element to decay. In general, if no additional input is administered, radio-nuclides are completely expelled after $6 \cdot T_A$; it is expressed as:
  $T_r = \ln(2) / k_A$

$$T_{eff} = \frac{T_A \cdot T_B}{T_A + T_B} \quad [s]$$

k_A, decay rate constant	[1/s]
T_A, radioactive half life in compart. A	[s]
T_B, radioactive half life in compart. B	[s]

- **Bone Seekers**: Certain radioactive elements (Sr, Pu, Ra) as well as Pb (non radioactive) are readily incorporated into bony tissue and can cause severe harm. Bone marrow as the blood generating site encapsulated by compact bone, can suffer severe damage by the surrounding radioactive emitters. As these substances are integrated into the bony tissue, they are rarely released in larger quantities. In certain cases, bone seeking elements have increased their fortifying effects on the bone tissue as they represent a source of irritation because they stimulate extra osteoblast production and deposition.

[14] http://www.ldeo.columbia.edu/dees/ees/lithosphere/lab12/radionuclides/index.html

Ionization: It is the conversion to cations by the removal of electrons; e.g.: $H(g) \rightarrow H^+(g) + e^-(g)$.

Spectra of Ionizing Radiation: For technical reasons, the spectrum of ionizing radiation is split into the following categories: $1 \cdot E^{15}$[Hz] = 1[PetaHz]; $1 \cdot E^{18}$[Hz] = 1[ExaHz]

Spectrum		wavelength	equivalent frequency	equivalent energy
UltraViolet:	UV-a	400[nm] - 315[nm]	79.95[PHz] - 95.17[PHz]	310.3[eV] - 394.1[eV]
	UV-b	315[nm] - 280[nm]	95.17[PHz] - 107.1[PHz]	394.1[eV] - 443.3[eV]
	UV-c	280[nm] - 70[nm]	107.1[PHz] - 428.3[PHz]	443.3[eV] - 1.773[keV]
Roentgen:	X-Ray	100[nm] - 1[pm]	299.8 [PHz] - 29979[EHz]	1.241[keV] - 124.1[MeV]
Gamma:	γ-Rays	300[pm] - <1[fm]	99.93[EHz] - >29.98·E^{24}[Hz]	413.8[keV] - >124.1[GeV]

For the hydrogen atom (H) it is 13.6[eV] = $2.176 \cdot E^{-18}$ [J]; in terms of distances 121.6[nm].

Ionization in biological systems occurs in several steps:

Physical effects of Ionization: Penetration and absorption by living tissue of in/direct ionizing radiation; takes $\approx 1 \cdot E^{-13}$ sec.

- **Direct Ionizing Radiation**: Radiation that results in immediate ionization of the target tissue; such effects can be caused by α, β, and p-rays. As they emit charged particles (e^-), they can interact with the atoms of the target tissue by being either deflected away from the atom or attracted towards the nucleus.
  Deflection away from the atom results in a loss of energy of the charged particle, which is used to ionize the atom. Deflection toward the nuclues is possible when the charged particle possesses enough kinetic energy to pass through the electron shells. Thus by being attracted rather than deflected, the energy loss results in the emission of photonic energy in the form of X-rays (bremsstrahlung).
  Photoelectric effect: The absorption of a photon ionizes the atom by causing the emission of an electron with no secondary emission of radiation.
  Compton scattering: If the energy of the incident photon is much greater than the ionization energy, both an electron and a photon (secondary radiation) will be given off.
  Electron-positron pair creation (pair-building effect): Photonic gamma radiation striking an atom creates an electron-positron pair (e^- and e^+); any excess radiation is still powerful enough to knock out further electrons. A positron and any electron that come together totally obliterate each other.
- **Indirect Ionizing Radiation**: Atoms that absorb a gamma photon, or are brought into the excited state by a collision with a massive particle (X-ray tube) they emit gamma photons of appropriate frequency. Similarly, this effect is used during the nuclear chain reaction of ^{238}U. The collision by which the neutron hits the large U-atom follows according to the principles of elastic collision postulated by Newton:
  $^1_0n + {}^{238}U \rightarrow {}^{239}U^* \rightarrow {}^{239}U + \gamma$
  The Poisson distribution predicts the highest speed of the neutron by which this reaction can take place; in that the less energetic the neutrons are the more efficient, they are trigger the reaction (e.g. water used to slow the speed of neutrons in nuclear reactors).

Physical-Chemical effects of Ionization: Intermolecular exchange of radiation energy by the genome (genotypic damages) occur within $\approx 1 \cdot E^{-10}$ seconds. A photon or a charged particle (Compton effect) that hits a water molecule generates a charged H_2O^+-molecule that interacts with neighboring H_2O-molecules to form OH-radicals:

$H_2O + h \cdot \nu \rightarrow H_2O^+ + e^-$ with the resulting H_2O^+-cation triggering the formation of radical: $H_2O^+ \rightarrow H^+ + OH\bullet$

If the fragmented products do not drift apart, they can merge to reform $H_2O^+ \cdot e^-(aq) = H_2O(l)$

- **Radical**: Any neutral fragment of a molecule (atom, molecule, ion) containing at least an unpaired electron; e.g. •NO; •O•; $\bullet CH_3$; in biological tissues, it is mostly OH•. They are formed as a result of <u>indirect ionizing radiation</u>. Radicals are atoms or molecules with strong oxidative powers. The Potential to generate radicals is determined by the G_{value}. It states how many radicals can be generated with an energy packet of 100eV:

  $$G_{value} = \frac{\text{number of water radicals}}{100\text{eV}} \quad [1/\text{eV}]$$

  $G_{OH\bullet} = G_{H\bullet}$ 2.3 [1/eV]
  $G_{e\text{-}(aq)}$ 0.6 [1/eV]

  The damaging effect caused by radicals becomes evident once they diffuse through the tissue into the nucleus of a cell causing strand breakage of the DNA molecule which is beyond the internal repair capabilities. Usually triggering death. A tiny fraction of damaged cells are able to survive in their mutated form, triggering the growth of cancerous tissue or the release of malfunctioning proteins.
- **Antioxidants**: Molecules that are able to inactivate free radicals; e.g. biomolecules such as vitamin C, E, and beta-carotene. Other molecules able to act as antioxidants usually contain a thio (SH-) group. Oxygen itself acts both as an antioxidant and a as radical forming agent.

Chemical effects of Ionization: Generation of abnormal biomolecules that may alter the function of certain anabolic processes or simply trigger abnormal reactions (buildup of radicals and formation of preneoplastic lesions); takes $\approx 1 \cdot E^{-6}$ sec.

Biogenic effects of Ionization: Phenotypic expression from a damaged source code (mutations, biochemical changes) may result in tumors or other malfunctions; it usually requires years to be detected.

- **Target Theory**: It states that at least two sectors of a cell or two distinct radiation events have to hit that cell to trigger the cells suicide mechanism. The sort of radiation required to trigger this mechanism is typically related to heavy mass radiation as with α-rays; in order to damage the cells genome. α-radiation is the most effective. Furthermore, several aspects have to be considered upon which this theory is based on:
  i) Radiation is emitted in discrete units (quantized) never as a continuos spectrum.
  i) Any radiation targeting a cell (hits) takes place according to the Poisson distribution - a pool of many molecules exposed to a rather limited "spray" of radiation particles (photons).
  i) Biological effects are only visible once a certain number of hits have penetrated the cells nucleus (according to statistics, at least 2, to 3 hits).
- **Single Hit Curves**: Cell death is brought about by a single hit.
- **Multiple Hit Curves**: Certain tissues tolerate quite higher doses of radiation. These cells can withstand cell death after e.g. 49 hits while the 50^{th} triggers programmed cell death due to improper functioning repair mechanisms.

Non-Ionizing Radiation: Electromagnetic radiation that includes all those wavelengths that are below the ionization threshold. As long as the threshold energy-level of ≈330[eV] or $53 \cdot E^{-18}$[J] or the equivalent frequency of 80[PHz] is not exceeded, ionization usually won't occur:

$E = h \cdot \nu$	[J]	h, Planck's constant	$662.5 \cdot E^{-36}$ [J·s]
$\nu = c/\lambda$	[1/s]	ν, frequency	[1/s]
		λ, wavelength	[m]
		c, speed of light	$29.9792458 \cdot E^{9}$ [m/s]

According to the CIE (commission of illumination), the ionization threshold in human tissue is located within the UV-b spectrum.

Spectra of Non-Ionizing Radiation: Due to technical reasons the spectrum of non-ionizing radiation is split into the following categories: $1 \cdot E^{12}$[Hz] = 1[TeraHz]; $1 \cdot E^{15}$[Hz] = 1[PetaHz]

Spectrum	wavelength	equivalent frequency	equivalent energy
Longwave: LW	<199.9[km] - 56.56[km]	<150[kHz]- 530[kHz]	<621.1[peV]- 2.195[neV]
Mediumwave: AM	56.56[km] - 18.74[km]	530[kHz] - 1.6[MHz]	2.195[neV] - 6.625[neV]
RF's: SW/FM/HF	700[m] - 100[μm]	42.83[MHz] - 299.8[GHz]	0.1773[neV] - 1.241[eV]
Microwaves: μ-ray	500[mm] - 1[mm]	14.99[GHz] - 29.98[THz]	62.07[μeV] - 124.1[meV]
InfraRed: IR-c	1[mm] - 3[μm]	29.98[THz] - 9.99[PHz]	0.1241[eV] - 41.37[eV]
IR-b	3[μm] - 1.4[μm]	9.99[PHz] - 21.41[PHz]	41.37[eV] - 88.67[eV]
IR-a	1.4[μm] - 780[nm]	21.41[PHz] - 38.44[PHz]	88.67[eV] - 159.1[eV]
Visible VIS	780[nm] - 400[nm]	38.44[PHz] - 79.95[PHz]	159.1[eV] - 310.3[eV]
UltraViolet: UV-a	400[nm] - 315[nm]	79.95[PHz] - 95.17[PHz]	310.3[eV] - 394.1[eV]
UV-b	315[nm] - 280[nm]	95.17[PHz] - 107.1[PHz]	394.1[eV] - 443.3[eV]
UV-c	280[nm] - 100[nm]	107.1[PHz] - 299.8[PHz]	443.3[eV] - 1241[eV]

Physical Parameters to quantify Non-Ionizing Radiation:

B - **Irradiance**: The intensity of incoming solar radiation is dependent upon the incident angle and the transmission factors of the atmosphere:

$B_{(\lambda,\theta)} = H_{(\lambda)} \cdot T_{(\lambda,\theta)} = H_{(\lambda)} \cdot e^{-(\tau 1 + \tau 2 + \tau 3/\cos\theta)}$

τ_1, ozone, τ_2, Rayleigh scattering, τ_3, Mie scattering

H, solar irradiance in space [???]
T, transmission factor [-]
τ, absorption within atmosphere [-]

I- **Light Intensity**: The intensity of the radiation flux per spatial angle that follows the inverse square law; the flux ϕ [lumen, lm], is the amount of radiation emitted by a light source.

$I = d\phi/d\Omega$ Candela = [cd]

Ω, spatial angle [rad]

B - **Illuminance**: The amount of radiation per surface area;

$B = d\phi/dA$ [lx]

ϕ, light flux (lumen) [Lm]
A, surface area [m^2]

Dose: While ionizing radiation is determined by the energy absorbed per mass unit, due to the difficulties of quantifying the absorbed energy, absorption of non-ionizing radiation is defined as the energy per unit of area, or even more simpler, the photons (quanta) penetrating a unit area.

$\varepsilon = E/A$ [J/m^2]

$\varnothing = \phi/A$ Einstein = [$1/m^2$]

E, Energy [J]
A, surface area [m^2]
ϕ, photon flux [Lm]

Energy Level (Jablonski) **Diagram**: The scheme revealing the electronic transition levels of a chromophoric molecule (molecules that are able to absorb non-ionizing electromagnetic radiation).

Quantum Number: It describe the distribution of electrons, labels the state of the electron and specifies the value of a property in an atom or molecule (see also chemistry - atom)

1. *n* - **Principal** QN (shell number): The average distance of the electron from the nucleus in a particular orbital.
2. *l* - **Angular Momentum** QN (subshell of one shell): Its value reflects the orbital shape: **s**, **p**, **d**, **f**, **g**, **h**.
3. m_l - **Magnetic** QN: Describes the orientation of the orbitals in space; e.g. $m_l = 5$ gives -2/-1/0/1/2 etc.
4. m_s - **Electron Spin** QN: According to the electromagnetic theory, spinning electrons posses a magnetic orientation; ($m_s = n$) m_s can either be $-^1/_2$ (↓)or $+^1/_2$(↑); with m_s =3 giving 3 magnetic spins: $-^1/_2$ / $+^1/_2$ / $-^1/_2$.

   Paired Electrons: Two electrons with opposite spins (↑↓).

   Parallel Electrons: Electrons with spins in the same direction (↑↑).

   Singlett State: Is considered to be the orientation of molecular (chromophoric) electron spin in paired or parallel electrons that *do not result* in a change of the electron spin upon excitation; i.e. one of the two spinning electrons is raised into a higher energetic state without change of its spinning orientation.

   Triplett State: Is considered to be the orientation of molecular (chromophoric) electron spin in paired or parallel electrons that *result* in a change of the electron spin upon excitation; i.e. one of the two spinning electrons is raised into a higher energetic state while experiencing a change of its spinning orientation.

Energized molecules, with electrons raised to excited states return to their ground states via several different pathways:

Internal Conversion (IC): A type of relaxation in excited electron that involves the transfer of excess energy of a species in the lowest vibrational level to a lower electronic state. A very fast but non-irradiating transition ($1 \cdot E^{-15}$s) from the excited singlett state to a lower singlett or ground state (or excited triplett state to a lower triplett state or ground state).

- **Fluorescence**: After an initial absorption of a photon, it is the brief (w/n $1 \cdot E^{-8}$s) emission of electromagnetic radiation (particularly in the visible region) from singlett state electrons as they fall back to their ground states. Fluorescence bands consist of a host of closely spaced lines.

Intersystem Crossing (ISC): A very fast but non-irradiating transition ($1 \cdot E^{-12}$s) from the excited singlett state to a lower triplett state.

- **Phosphorescence**: After an initial absorption of a photon, it is the extended (w/n $1 \cdot E^{-3}$s to minutes) emission of electromagnetic radiation (particularly in the visible region) from triplett state electrons as they fall back to their ground states.

Application of Ionizing- and **Non-Ionizing Radiation**:

Spectroscopy: A spectroscope is an optical instrument that separates light into its constituent frequencies in the form of spectral lines. Spectroscopic means are based on the fact that circling electrons do posses potential energy that is usually zero if these electrons are found to be in their ground state. Upon excitation by light or heat energy, these electrons are raised into energetically more active states (comparable to an increase in their potential energy).

- **Molecular Absorption S**. (MAS): A highly selective method based on the absorption of UV/VIS/IR-radiation emitted by a primary radiation source and absorbed by the atom in the ground state (generates an extinction spectrum). The absorption of EMR occurs in bands that consist of large numbers of closely spaced vibrational and rotational lines.

  A flame atomizer (for elements with low ionization energy, i.e. alkali and alkaline earth metals), or a graphite furnace (for elements that require higher ionization energies, i.e. transition metals, lanthanides, actinides, metalloids, nonmetals, etc.) generates the atomic vapor; i.e. nebulization converts the sample into a mist of finely divided droplets. A jet of a compressed gas carries the sample into a heated region where atomization takes place.

  $I = I_0 \cdot e^{-\varepsilon(\lambda) \cdot c \cdot d}$

  $\varepsilon = \frac{1}{c \cdot d} \cdot \log \frac{I_0}{I}$

  I_0, initial light intensity [cd]
  ε, extinction coefficient (here) [1/(mol·m)]
  c, concentration [mol/L]
  d, thickness of sampling path [m]

- **Fluorescence S**. (FS): A method that utilizes the fluorescence characteristics of the analyte.

  Molecules that absorb electromagnetic radiation are raised into an excited state. The excited species then relax to the ground state, by emitting their excess energy as photons, producing an emission spectrum. Fluorescence emission is very short ($1 \cdot E^{-5}$ seconds or less - in contrast, phosphorescence may go on for several minutes or even hours). Vibrational relaxation involves transfer of the excess energy of a vibrationally excited species to molecules of the solvent. This process takes place in less than $1 \cdot E^{-15}$ seconds and leaves the molecules in the lowest vibrational level of an electronic state. Fluorescence methods are 10 to 1000 times more sensitive than absorption methods. The use of chromophores (1.4-DiHydrohy-PhthaloNitril - DHPN) enables the examination of the surrounding environment by detecting slightest changes in emission spectra according to the properties of the surrounding medium (mostly shielding or quenching effects).

  Molecular Fluorescence S. (MFS): A classical example of MFS is the fluorimetric determination of intercellular pH. For this purpose DHPN with its pH-dependent emission characteristics is introduced into the cytosol. As the DHPN molecule is introduced into a cell, it interacts with the cytosol by either attaching 2 protons (H^+) in acidic medium or releasing them under basic conditions. By releasing each proton separately, DHPN passes through several ionic transitions states: DHPN, $DHPN^-$, $DHPN^=$. According to the ionic state, the emission spectra after excitation shift from 453nm under acidic conditions to 483nm in basic conditions (difference between excitation and emission wavelength is always around 82nm). Along with the wavelength shift, a decrease in fluorescence intensity occurs. A pH of 6 generates the strongest emission signal, while pH-levels above and below generate less intense fluorescence peaks.

  The intensity of the emission peaks is determined by the yield of quanta. It can be either measured or determined according to kinetic rate reactions:

  $\phi = \frac{\text{number of emitted photons}}{\text{number of absorbed photons}} \qquad 0 < \phi < 1$

  $\phi = k_F \cdot \tau = k_F \cdot \frac{k_F}{k_F + k_{ISC} + k_{IC} + k_Q[Q]}$

  τ, average duration of emission [s]
  k_F, reaction speed (rate) of fluorescence [1/s]
  k_{ISC}, rate of intersystem crossing [1/s]
  k_{IC}, rate of internal conversion [1/s]
  k_Q, rate of quenching [1/s]

  Quenching: It involves attenuation of fluorescence by some other species (often an anion) in a solution. This effect can go as far as the surrounding solution shields off the emitted photons by entirely absorbing it. Quenching requires direct contact, since it is based on inelastic collision amongst the molecules to ground the chromophores excited energy state (2^{nd} order collision effects). Certain additives (I_2, acrylamide, O_2, etc) do have such properties. Fluorescence can be detected as soon as the chromophore is separated from these species, while fluorescence fades out once the chromophore is in direct contact with these species.

  By applying pulsed laser light to excite chromophores, fluorescence takes place according to the following relationship:

  $F_{(t)} = F_0 \cdot e^{-t/\tau E}$

  F_0, fluorescence intensity at time = 0 [rel.F-power]
  t, time [s]
  τ_E, average duration of emission [s]

  The decrease in fluorescence versus time can occur according to a mono-exponential pattern (based on a single exponential decrease pattern) or by a bi-exponential pattern (two different exponential patterns superimposed upon each other).

  Molecular Fluorescence-Depolarization S. (MFDS): This technique enables the investigation of molecular, thermal motion. MFDS utilizes the depolarizing effect of a molecular sample upon excitation with polarized light. Absorption of polarized light requires that the dipole moment of the chromophore is parallel aligned to the

electric field vector of the incident light source. As the chromophore is under the influence of Brownian motion (thermal motion - more in liquid than in solid phase) and as the emission of fluorescence radiation lags behind excitation, the emitted light is found to be in any of the polarization planes (anisotropy due to rotational and vibrational shifts in the plane-polarizational angle). Anisotropy can be mathematically expressed as:

$$r = \frac{I_{II(t)} - I_{\perp(t)}}{I_{II(t)} - 3I_{\perp(t)}} \qquad 0 < r < 1/3$$

$I_{II(t)}$, fluorescence intensity parallel to DM
$I_{\perp(t)}$, fluorescence intensity perpendicular to DM

Anisotropy versus time:

$$r_{(t)} = \sum_{I=1}^{n}(\beta_i \cdot e^{-t/\phi i})$$

β_i, constant [-]
t, time [s]
ϕ_i, rotational relaxation time [s]

Dipole Moment (DM): The electrostatic force required to align a dipolar molecule parallel to the electrostatic field. It increases as the separation of the molecular charge decreases and is the product of charge and distance in a molecule. The overall DM is obtained by adding the individual vector-amounts of the involved atoms.

- **Nuclear Magnetic Resonance S**. (NMRS): Both the electrons circling around the nucleus, as well as the nucleus itself posses a magnetic orientation in space. Such a nuclear momentum arises only if the nuclear species (either neutrons or electrons or both) are present in odd numbers. An even number of nuclear species does not posses a nuclear spin momentum ($\mu = 0$). As the nucleus is always surrounded by the same number of electrons and protons, the magnetic spin quantum number (m_s) can be used to determine if a nuclear spin is formed. Thus, only species with a magnetic field vector of $^1/_2$ or 1 can be used in NMR.
  Soft organic tissue is primarily made of the following atomic species (hydrogen H, Oxygen O, Carbon C, Phosphorous P, and Nitrogen N). Each of these atoms possess a certain electromagnetic property:

Element of soft organic tissues	^{1}**H**	^{31}**P**	^{14}**N**	^{12}**C**	^{16}**O**
Nuclear species	1p	15p; 16n	7p; 7n	6p; 6n	8p; 8n
Electron spin orientation of outermost shell	↑	↑↓ ↑↓ ↑	↑↓ ↑↓ ↑ ↑ ↑	↑↓ ↑↓ ↑ ↑	↑↓ ↑↓ ↑↓ ↑ ↑
Magnetic spin quantum number (m_s)	$^1/_2$	$^1/_2$	1	0	0

  μ - **Magnetic** (**Dipole**) **Moment**: The electrostatic force required to align a nucleus parallel to the magnetic field. As Brownian motion is responsible for atomic vibrations, any movement of a charge in space possesses magnetic properties.
  B_0 - **Externally applied magnetic field**: By applying an external magnetic field of 1-6[T]esla = [V·s/m^2], those nuclear species with magnetic spin properties will aligned themselves parallel to the external field. The forced orientation according to the magnetic field causes the Brownian motion to turn into a gyrating pattern with an angular frequency ω_0. Alignment of the nuclear species in the magnetic field -- based on thermal random motion -- can be parallel or anti-parallel. The stronger the applied magnetic field the more pronounced the gyration will be, and the greater the energy difference between anti-parallel and parallel orientation ($\Delta E = E_{antiparallel} - E_{parallel}$).
  $\Delta E = 2 \cdot \mu \cdot B_0 = h \cdot f$ .... with $\omega = 2 \cdot \pi \cdot f \rightarrow f = \omega\ 1/(2 \cdot \pi)$ .... $\Delta E = \hbar \cdot \omega$
  Brownian motion at room temperature cannot be neglected. It accounts for spontaneous shifts from the $E_{antiparallel}$ to $E_{parallel}$ orientation and vice versa. The number of nuclei in the higher energetic state ($E_{antiparallel}$) is distributed according to Boltzmann's law:

$$\frac{n_{antiparallel}}{n_{parallel}} = e^{-\Delta E/(k \cdot T)} = e^{-2 \cdot \mu \cdot Bo/(k \cdot T)} =$$

n, molar amount [mol]
k, Boltzman const. $1{,}381 \cdot E^{-23}$ [J/K]
T, temperature [K]

  As very low numbers of nuclei are in the more energetic state (slightly less than half of $2 \cdot E^6$; e.g. 999995/1000005), thus NMR utilizes an effect that is expressed only very weakly.
  Chemical Shift: The frequency shift as a result of the shielding chemical environment. Interaction of the nuclei with their molecular environment weakens the externally applied magnetic field.

$$B_{eff} = B_0 - B_{CS} = B_0 - B_0 \cdot \sigma = B_0 \cdot (1 - \sigma)$$

B_0, external magn. field [T]
σ, shielding constant [-]

  The total range of chemical shifts in ^{1}H NMR spectroscopy that uses an induction frequency of 100MHz is roughly 100-500Hz (approx. 3-10ppm). Being so weak and because $B_0 \propto f_{res}$, it is a lot more practical to measure the frequency difference Δf between the resonance signals of the sample and that of a reference compound (in ^{1}H NMRS, Tetra-methyl-silane - TMS). For this purpose the dimensionless quantity δ is defined:

$$\delta = \frac{(\omega_{induced} - \omega_{relaxed}) \cdot 1 \cdot E^6}{\omega_{induced}} = \frac{(f_{induced} - f_{relaxed}) \cdot 1 \cdot E^6}{f_{induced}} \quad [ppm]$$

ω, angular frequency [Hz]
f, frequency [Hz]

Larmour Frequency: The transmitter radio frequency (RF) that is equal to $\Delta E = h \cdot f$. It is applied perpendicularly to the static magnetic field and is used to raise more nuclear species into the more energetic (anti-parallel) state. Once the RF is switched off, relaxation of the energized nuclear species takes place within $t = 1 \cdot E^{-6}$secs. Relaxation of those few species that underwent such transitions emit a RF equal to the gyromagnetic frequency. Relaxation (free induction decay) takes place according to an exponential time pattern that is detected by a receiver. Subsequential Fourier transformation results in a spectrum of several frequencies. According to the shielding effect by the surrounding electrons or molecules, it yields the chemical shift from the induced frequency.

Relaxation Patterns: Two major relaxation patterns are known:

i) T_1-Relaxation or **Spin-Lattice coupling**: The coupling mechanism of neighboring molecular nuclei. The RF-induction signal lifts the spinning H^+-nuclei (protons) into the anti-parallel (energetically higher state). Upon cessation of the RF, relaxation takes place with a delayed pattern than the molecular surroundings as the relaxation energy is repetitively swapped back and forth between nuclei of neighboring molecules to excite and relax each other.

i) T_2-Relaxation or **Spin-Spin coupling**: The coupling mechanism of neighboring H^+-nuclei. A RF-signal lifts the spinning electrons into the energetically higher state. As neighboring protons interact with each other by altering each others relaxation frequency, it result in characteristic multiplet pattern. According to Pascal's triangle, an isolated nuclei of ^1H NMR yields just one peak ($-X\mathbf{H_x}$ n=0 $\rightarrow$ 1), in a 2-spin system there is a doublet ($-X\mathbf{H_x}$ coupled to -H; n=1 $\rightarrow$ 1:1), in a 3-spin system there is a triplet ($-X\mathbf{H_x}$ coupled to $-XH_2$; n=2 $\rightarrow$ 1:2:1), in a 4-spin system there is a quadruplet ($-\mathbf{H_2}$ coupled to XH_3; n=3 $\rightarrow$ 1:3:3:1), and so forth.

NMR Tomography: The method by which soft tissue can be scanned in-vivo. Nuclei exposed to a homogenous external magnetic field will emit the same frequency upon cessation of the perpendicularly oriented RF-signal. In order to obtain spatial information, the magnetic field has to be converted to some sort of in-homogeneity. This is achieved by altering the magnetic field in a way that a field gradient is formed; i.e. magnetic field is not of the same strength along the poles of the electromagnet. By doing so, every proton emits a different frequency that is related to the magnetic field intensity in its particular position in space. As the relation between relaxation frequency and magnetic field intensity is known, a 2-dimensional image (slice) of the object can be made. Superimposing several 2-dimensional images, a 3-dimensional image is obtained