2 Molecules to metabolism

Introduction
- living organisms control their composition by complex web of chemical reactions that occur within water
- compounds of carbon, hydrogen and oxygen are used to supply and store energy
- proteins act as enzymes, genetic information is stored in DNA

2.1 Molecules to metabolism

Molecular biology
- explaining of living processes in terms of chemical substances involved
- discovery of DNA structure (1953) started revolution in biology
- possibility of explaining biological processes from structure of molecules and how they interact
- many molecules are important: some as simple as water, most varied and complex are nucleic acids and proteins
- nucleic acids comprise DNA and RNA: used to make genes
- proteins are varied in structure and carry out huge range of tasks
- relationship between genes and proteins is at the heart of molecular biology
- approach to molecular biology is reductionist

Carbon compounds
- carbon can be used to make huge range of different molecules; organisms have limitless possibilities for chemical composition
- carbon atoms can form four covalent bonds (strongest bond between atoms), more than most other atoms: molecules can have complex structures
- bonds between carbon atoms, also other elements (hydrogen, oxygen, nitrogen, phosphorus)
- four bonds can be single covalent bonds or two single and one double

Classifying carbon compounds
- four main classes of carbon compounds, have different properties: different purposes
- carbohydrates: characterized by composition: carbon, hydrogen, oxygen (hydrogen to oxygen ratio is 2:1)
- lipids: insoluble in water, include steroids, waxes, fatty acids, triglycerides
- proteins: composed of one or more chains of amino acids, all contain carbon, hydrogen, oxygen, nitrogen; two of the 22 contain additionally sulphur
- nucleic acids: chains of subunits called nucleotides, contain carbon, hydrogen, oxygen, nitrogen, phosphorus; two types: ribonucleic acid (RNA), deoxyribonucleic acid (DNA)

Metabolism
- organism carry out many different chemical reactions which are catalyzed by enzymes
- most reactions happen in cytoplasm, some are extracellular
- metabolism is the sum of all reactions that occur in an organism
- consists of pathways, happens in small steps; mostly chains of reactions, can be cycles

Anabolism
- build up larger molecules from smaller parts
- anabolic reactions require energy, usually in form of ATP
- includes: protein & DNA synthesis, photosynthesis, synthesis complex of carbohydrates

Catabolism
- larger molecules are broken down into smaller ones
- catabolic actions release energy
- includes: digestion of food, cell respiration, digestion of complex carbon compounds

2.2 Water

Hydrogen bonding in water

- water molecule: covalent bonds between oxygen and two hydrogen atoms
- bond involves unequal sharing of electron: polar covalent bond: hydrogen atoms have a partial positive charge, oxygen has a partial negative charge
- attraction between water molecules is a hydrogen bond (intermolecular force)
- Hydrogen bond is weak, collectively they give water unique properties

Properties of water

- <u>cohesive properties</u>: binding of molecules of the same type
- water molecules stick to each other due to hydrogen bonding: useful for water transport in plants: water sucked trough xylem vessels at low pressure: only works when water isn't separated by suction forces
- <u>adhesive properties</u>: hydrogen bonds can form between water and other polar molecules: water sticks to them
- useful in leaves: water adheres to cellulose in cell walls, water evaporates, water drawn from nearest xylem vessel, keeps cell wall moist: absorb carbon dioxide for photosynthesis
- <u>thermal properties</u>: high specific heat capacity, latent heat of vaporization and boiling point
- high specific heat capacity: hydrogen bonds restrict motion of molecules and increase temperature required to break them; energy needed to raise temperature of water is large, to cool down water must lose large amounts of energy: thermally stable habitat
- high latent heat of vaporization: when molecule evaporates it separates from molecules in liquid (heat needed for process is latent heat): evaporation has a cooling effect: sweating as example
- high boiling point: highest temperature it can reach in liquid state; water is liquid over broad range of of temperatures
- <u>solvent properties</u>: polar nature of water forms shells around charged molecules preventing them to clump (keeping them in solution); partially negative oxygen pole attracted to positively charged ions, partially pos. hydrogen pole attracted to negatively charged ions: both dissolve

Hydrophilic and hydrophobic

- hydrophilic: substances that are chemically attracted to water
- all substances that dissolve in water are hydrophilic, as do substances that water adheres to
- some substances are insoluble, molecules are hydrophobic if they don't have a negative or positive charges (nonpolar); all lipids are hydrophobic
- two nonpolar molecules surrounded by water brought together by random movement will behave as if they were attracted to each other
- water molecules are more attracted to each other than to the nonpolar molecules: nonpolar molecules join together in water: hydrophobic interactions

2.3 Carbohydrates and lipids

Carbohydrates

- glucose, fructose, ribose are monosaccharides (single sugar units)
- monosaccharides can be linked to make larger molecules: disaccharides (two monosaccharides, e.g. maltose (2x glucose), sucrose (glucose, fructose); polysaccharides (many monosaccharides), e.g. starch, glycogen, cellulose (linked glucose molecules)
- condensation reaction (anabolic process, uses ATP): when linking monosaccharides, one loses -OH and the other -H which forms water, reaction yields water

Lipids

- all lipids are insoluble in water
- triglycerides (three fatty acids with one glycerol) as one of principal groups
- fats are liquid at body temperature but solid at room temperature, oils are liquid at both
- triglyceride is made by condensation reaction, three water molecules produced, ester bond created (-OH group on glycerol reacts with -COOH of fatty acid)
- triglycerides act as energy stores, can be released by anaerobic respiration, also conduct heat badly and are used as insulators

Fatty acids
- basic structure: chain of carbon atoms, hydrogen linked by single covalent bonds: hydrocarbon chain: one end is the acid part (carboxyl group: -COOH)
- most living organisms have length of hydrocarbon chain between 14 and 20 carbon atoms
- some fatty acids have carbon atoms linked by single covalent bonds, other have one ore more double covalent bonds (can bond only with one hydrogen)
- fatty acid with single bonds contains as much hydrogen as possible: saturated fatty acid
- with one double bond it is a monounsaturated and more than one it's polyunsaturated fatty acid

Unsaturated fatty acids
- in living organisms hydrogen atoms nearly always on the same side of double bonded carbon atoms: these are cis-fatty acids; hydrogens on opposite sides are trans-fatty acids
- cis-fatty acids: hydrocarbon chain has a bend, bad for packing in regular arrays, lower melting point, liquid at room temperature: oils
- trans-fatty acids: no bend, higher melting point, solid at room temperature, produced artificially

2.4 Proteins
Amino acids and polypeptides
- polypeptides are chains of amino acids linked by condensation reactions: happens on ribosomes during translation
- polypeptides are the main component of proteins
- condensation reaction involves amine group ($-NH_2$) and carboxyl group (-COOH), water is eliminated, new bond is called peptide bond
- dipeptide consists of two molecules; oligopeptides have less than 20; over 20 is polypeptide

The diversity of amino acids
- amino acids linked by ribosomes share some identical features: carbon atom in the centre of molecule is bonded to amine group, carboxyl group and hydrogen atom and R group (this is different in each amino acid)
- twenty different amino acids are used by ribosomes
- amine and carboxyl groups are used for forming peptide bond, R group gives its character
- the twenty amino acids are chemically very diverse due to differences in R groups
- some proteins contain amino acids not in the basic 20; in most cases it is one of these 20 being modified after a polypeptide has been synthesized (e.g. collagen: polypeptides contain proline which is changed to hydroxoproline to stabilize)

Polypeptide diversity
- ribosomes link amino acids one at a time until polypeptide is fully formed
- peptide bonds can be made between any amino acid so any sequence is possible
- huge range of possible polypeptides

Genes and polypeptides
- living organisms produce small fraction of possible amino acid sequences, still an organism produces polypeptides with thousands of different sequences: information has to be stored
- amino acid sequence of each polypeptide is stored in coded form in base sequence of a gene
- most genes in a cell store amino acid sequence of a polypeptide: genetic code used for it: three bases code for each amino acid (polypeptide with 400 amino acids = 1200 bases, but in reality always longer: extra base sequences at both ends and sometimes at certain points in middle)
- base sequence coding for polypeptide is known as “open reading frame”: open reading frames only occupy small proportion of total DNA of species (puzzle to molecular biologists)

Proteins and polypeptides
- integrin: membrane protein with two polypeptides, like folding knife: can be adjacent or unfold when working
- collagen: three long polypeptides, wound together into rope-like molecule giving greater tensile strength, winding also allows small amount of stretch
- hemoglobin: four polypeptides, associated non-polypeptide structures: transport oxygen better

Protein conformations
- conformation of protein is the three-dimensional structure, determined by amino acid sequence
- fibrous proteins (collagen) are elongated (often repeating structure), many proteins are globular
- amino acids added one by one to form polypeptide; always added in same sequence for particular polypeptide
- in globular proteins polypeptides fold up to develop final conformation, stabilized by R groups
- globular proteins soluble in water have hydrophilic R groups on outside and hydrophobic inside
- membrane proteins have hydrophobic regions on outside which attract to centre of membrane
- in fibrous proteins amino acid sequence prevents folding and ensures that it is elongated

Protein functions
- no other carbon compound can compare with versatility of proteins
- functions: catalysis, muscle contraction, cytoskeleton, tensile strengthening, blood clotting, transport of nutrients and gases, cell adhesion, membrane transport, hormones, receptors, packing of DNA, immunity
- proteins have many biotechnological uses; expensive, still not easy to synthesize artificially

Proteomes
- proteome: all of the proteins produced by a cell, tissue or organism
- genome: all of the genes in a cell, tissue or organism
- genome of organism is fixed, proteome is variable (different cells make different proteins, also may vary in one cell over time)
- proteome reveals what is actually happening in an organism
- each person has a unique proteome due to differences of activity and small differences in amino acid sequence of proteins

2.5 Enzymes
Active sites and enzymes
- catalysts: speed up chemical reactions without being altered themselves
- found in all living cells and can be secreted to work outside of cell
- enzyme-substrate specificity: one enzyme can only catalyze one biochemical reaction
- active site: special region where substrates bind to (shape and chem. properties must match)
- substrates are converted into products while bound to active site, then released, freeing the active site for the next reaction

Enzyme activity
- substrate molecule can only bind if it moves very close to active site: collision
- with most reactions the substrates are dissolved into water: all molecules are in contact with each other and in continual motion
- most substrate molecules are smaller than enzyme: move faster
- random movement of substrate and enzyme cause collisions: orientation is important too

Factors affecting enzyme activity
- temperature increase: particles are given more kinetic energy: higher chance of colliding: enzyme activity increases
- temperature increase: bonds in enzyme vibrate more: bonds can break: structure including active site changes: enzyme is denatured: enzyme activity decreases
- pH scale for acidity (logarithmic): acidity due to hydrogen ions
- pH: enzymes have optimum at highest activity: if pH is increased or decreased activity decreases, eventually stops
- pH: hydrogen ions change structure of enzyme: beyond certain concentration structure is irreversibly altered: denaturation
- not all enzymes have same pH optimum
- enzyme cannot catalyze until substrate binds to active site
- substrate concentration: decrease of concentration decreases number of collisions: enzyme activity decreases and vice versa

- substrate concentration: increase of concentration: increasing occupation of enzymes: rate of reaction decreases: with increasing concentration enzyme activity rises less but never reaches maximum

Denaturation
- structure of enzyme (protein) can be irreversibly altered: high temperature, high or low pH
- substrate either cannot bind or when it binds the reaction isn't catalyzed
- in many cases enzymes get insoluble in water

Immobilized enzymes
- Buchner brothers (1897): show that enzymes can catalyze reactions outside of living cells
- over 500 enzymes have commercial uses: enzymes are usually immobilized
- immobilization: attachment of enzyme to another material or into aggregation which restricts enzyme movement
- advantages: enzyme can be separated from products, after take-out of reaction mixture they can be recycled, increases stability of enzyme to changes in temperature and pH, enzyme can be exposed to higher substrate concentrations

2.6 Structure of DNA and RNA
Nucleic acids and nucleotides
- materials extracted from nuclei of cells
- two types: DNA and RNA: large molecules that are constructed by linking nucleotides to form a polymer
- consist of three parts: sugar (five C-atoms: pentose), phosphate (acidic, negatively charged), base (contains nitrogen, one or two rings in structure)
- base and phosphate are linked by covalent bonds to pentose sugar
- phosphate of one nucleotide and sugar of another are linked by covalent bonds and form a strong backbone
- four different bases which can be linked in any sequence
- base sequence stores information and backbone ensures stability and security

Differences between DNA and RNA
- sugar in DNA is deoxyribose, sugar in RNA is ribose: DNA has one oxygen atom less
- two polymers of nucleotides in DNA, only one in RNA; polymers are referred to as strands: DNA is double stranded and RNA is single stranded
- bases in DNA are adenine, cytosine, guanine and thymine; in RNA thymine is replaced by uracil

Structure of DNA
- strand consists of chain of nucleotides linked by covalent bonds
- strands are parallel but in other directions: antiparallel: one in 5' to 3', the other 3' to 5'
- strands are held together by hydrogen bonds between nitrogenous bases
- adenine always paired with thymine and cytosine with guanine: complimentary base pairing

2.7 DNA replication, transcription and translation
Semi-conservative replication of DNA
- before cell division: strands of double helix separate: each serves as a template for the new strand: result is two DNA molecules, both of one original and one newly synthesized: semi-conservative replication
- complimentary base pairing: base sequence on the template strand determines the base sequence on the new strand

Helicase
- DNA strands must separate in order to be replicated
- helicases, a group of enzymes, separate and unwind the strands using ATP
- ATP is used to be able to break hydrogen bonds

DNA polymerase
- carries out the assembly of the new strands
- moves along the strand, adding one nucleotide at a time
- brings nucleotides into region where hydrogen bonds could form but unless it is the correct base the nucleotide breaks away again and no hydrogen bond is formed
- links the new nucleotide to the strand once a hydrogen bond has formed
- nucleotide is added by covalent bonds: phosphate group is 5' terminal, pentose sugar 3': adds 5' of free nucleotide to 3' end of existing strand
- very high degree of fidelity

Transcription
- two processes are needed to produce a specific polypeptide using the base sequence of a gene: transcription is the first process
- synthesis of RNA, using DNA as a template
- RNA is single stranded, hence transcription only occurs along one DNA strand
- outline: RNA polymerase binds on DNA at the beginning of a gene, RNA polymerase separates DNA and adds RNA nucleotides with complimentary bases (uracil instead to thymine), RNA polymerase forms covalent bonds between RNA nucleotides, RNA separates from DNA and double helix reforms, transcription stops at the end of a gene
- product is RNA molecule with base sequence complimentary to DNA: base sequence is identical to the other DNA strand (exception uracil)
- to make a RNA copy of one DNA strand, the other strand is transcribed
- DNA strand with same base sequence as RNA strand is the sense strand, the template strand is the antisense strand

Translation
- second process to produce specific polypeptide is translation
- synthesis of polypeptide with amino acid sequence determined by the base sequence of a RNA molecule
- takes place on ribosomes
- ribosomes are complex structures consisting of a large and small subunit with binding sites for each molecule that takes part in translation
- each subunit is composed of RNA molecules and proteins
- part of the large subunit makes the peptide bonds between amino acids to link them into polypeptides

Messenger RNA and the genetic code
- RNA carrying the information for synthesizing a polypeptide is called messenger RNA (mRNA)
- average mRNA length is 2'000 nucleotides
- only certain genes will be transcribed when they are used so only certain mRNA will be available in the cytoplasm
- if a cell needs a lot of a particular polypeptide it will make many mRNA copies
- other types of RNA are transfer RNA (tRNA, involved in decoding base sequence of mRNA into amino acid sequence during translation) and ribosomal RNA (rRNA, part of the structure of the ribosome)

Codons
- genetic code: enables to convert base sequence on mRNA into an amino acid sequence
- living organisms use triplet code: three bases code for an amino acid
- different codons can code for the same amino acid: code is degenerate
- three codons are „stop“ codons that code for the end of translation
- amino acids are carried on tRNA: each amino acid is carried by a specific tRNA which has a three base anticodon complimentary to the mRNA codon for that particular amino acid

Codons and anticodons
- three components work together to synthesize polypeptides by translation: mRNA (sequence of codons for the amino acid sequence), tRNA (anticodon of three bases binding to a

complimentary codon on mRNA and carry the amino acid corresponding to that codon), ribosomes (binding site for mRNA and tRNA and catalyst the assembly of the polypeptide)
- main events of translation: mRNA to small subunit of ribosome, tRNA with anticodon binds to ribosome, another tRNA binds to ribosome (two are maximum), ribosome binds first amino acid to second amino acid with a new peptide bond, ribosome moves along and first tRNA is released, another tRNA binds, ribosome makes a new peptide bond between the amino acids
- the process of adding further amino acids is repeated until a stop codon is reached
- accuracy depends on complementary base pairing: mistakes are very rare

2.8 Cell respiration

Release of energy by cell respiration

- all living cells perform cell respiration: organic compounds are broken down to release energy
- example: energy is released in muscle fibers by breaking down glucose into CO_2 and water
- carbohydrates and lipids are often used, but amino acids and proteins may also be used
- plants use carbohydrates or lipids previously made by photosynthesis
- cell respiration is carried out using enzymes to retain as much as possible of energy in usable form: adenosine triphosphate (ATP); to make it a phosphate group is linked to adenosine diphosphate (ADP); the energy required comes from the breakdown of organic compounds
- ATP is not transferred from cell to cell, all cells need continuous supply: cell respiration is an essential function of life in all cells

ATP is a source of energy

- ATP is used for synthesizing large molecules (DNA, RNA, proteins), active transport, moving things in cell (chromosomes, vesicles, protein fibers in muscles)
- energy from ATP is immediately available: it is split to ADP and phosphate
- ultimately all energy is converted to heat; heat cannot be reused
- cells require a continual source of ATP for cell activities

Anaerobic respiration

- glucose is broken down in anaerobic respiration without using oxygen; yield of ATP is small but quick: useful in short but rapid burst of ATP, oxygen supplies running out, oxygen-deficient environments (waterlogged soils)
- products of anaerobic respiration are not same in all organisms
- in animals glucose is converted to lactic acid which dissolves to lactate
- in yeast and plants glucose is converted to ethanol and carbon dioxide
- lactate and ethanol are toxic in excess and must be removed or produced in small quantities

Aerobic respiration

- with oxygen, glucose can be fully broken down to release more energy than in anaerobic cell respiration: anaerobic respiration yields 2 ATP per glucose while aerobic yields over 30
- aerobic cell respiration involves series of chemical reactions, water and CO_2 are produced
- water is useful while carbon dioxide is a waste product
- in eukaryotic cells most reactions happen in the mitochondrion

2.9 Photosynthesis

What is photosynthesis?

- living organisms require complex carbon compounds: some can make them only using light energy and simple inorganic substances: photosynthesis
- photosynthesis is an example of energy conversion

Wavelengths of light

- sunlight is made up of all wavelengths of electromagnetic radiation our eyes can detect
- other wavelengths are invisible to us
- shorter wavelengths (X-rays, ultraviolet radiation) have high energy; longer wavelengths (infrared radiation, radio waves) have low energy
- visible light (400-700nm) has wavelengths longer than ultraviolet but shorter than infrared
- violet and blue are the shortest wavelengths, red is the longest

- wavelengths detected by our eyes are those used for photosynthesis: penetrate Earth's atmosphere in larger quantities than others, so are particularly abundant

Light absorption by chlorophyll

- first stage in photosynthesis is light absorption which involves chemical substances (pigments)
- pigments absorb light and appear colored to us; pigments absorbing all colors appear black
- main photosynthetic pigment is chlorophyll, all appear green to us because they absorb red and blue light very effectively

Oxygen production in photosynthesis

- in photosynthesis water molecules are split (photolysis) to release electrons for other stage
- all oxygen generated in photosynthesis comes from photolysis of water
- oxygen is a waste product and diffuses away

Effects of photosynthesis on the Earth

- prokaryotes were first organisms to perform photosynthesis
- one consequence of photosynthesis is rise in oxygen concentration of atmosphere
- Great Oxidation Event (2'400 - 2'200 million years ago) oxygen concentration to 2%
- first glaciation happened at same time: probably due to reduction of greenhouse effect, rise in oxygenation decreased methane levels and photosynthesis decreased carbon dioxide
- increase in oxygen caused oxidation of dissolved iron in water: precipitates in water: distinctive rock formation is produced (banded iron formation)
- 750-635 million years ago there is a significant rise from 2% to 20% of oxygen: period when many groups of multicellular organisms were evolving

Production of carbohydrates

- plants convert carbon dioxide and water into carbohydrates by photosynthesis: require energy
- endothermic: chemical reaction that involves putting in energy
- reactions combining smaller molecules to make larger ones are also often endothermic
- energy for conversion of carbon dioxide into carbohydrates is obtained from light
- energy from light is converted to chemical energy in carbohydrates

Limiting factors

- rate of photosynthesis is affected by temperature, light intensity, carbon dioxide concentration
- each of the factors can limit the rate if they are below the optimum: limiting factor
- only one of the factors is actually limiting the rate: factor the furthest from optimum