Physical biology

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08-01-2024

1.1 Life

Common description uses 5 characteristics:

- made of cells
- they replicate
- they evolve
- store information (genes)
- use energy

1.2 Cellular theory

- 1665 Hook -> first microscope -> **dead cells**
- 1660-1680 Van Leeuwenhoek -> more potent microscopes -> **live cells and microorganisms**
- 1831 Brown -> **defines the nucleus**
- 1838 Schleiden (for plants), 1839 Schwann (for animals) and 1857 Virchow define the cellular theory:
  - The cell is the unit of structure for life
  - Cells retain a dual existence as individuals and building blocks
  - (Virchow 1857) All cells come from other cells

1.3 Theory of evolution

Darwin and Wallace create the theory of evolution, two main principles:

- All species are related by common ancestors.
- Characteristics of species change from generation to generation.

The key insight was their description of the process that pushes for that change: **natural selection**.
This means that you can draw a **tree of life** from the common ancestor to the current extant species.

1.4 Chromosomic theory of inheritance and central dogma

Chromosomes are made of a single DNA molecule, and some of it's segments that codify the products in the cell are called genes.
The central dogma of microbiology states that the flow of information is unidirectional:

- DNA
- -transcription-> mRNA
- -traduction-> protein
- -> specific trait

1.5 Taxonomy

Naming organisms, started by Carl Linnaeus, binomial system, ex:

<gender> <species>: quercus robur (oak)

Added a hierarchy of taxonomical groups:

species < gender < family < order < class < phylum < kingdom

Can be drawn for all species in a phylogenetic tree, where the closest the branch, the more closely related the species.
Recent genetic studies have shown that this is obsolete, and currently life is classified in three domains:

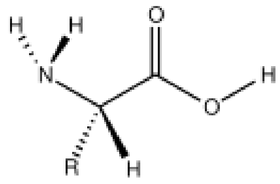
- Bacteria
- Archaea
- Eukarya (cells with well defined nucleus, plants, fungi, animals, ...)

2.0 Biomolecules

There's organic and inorganic molecules that are part of a living being, we will focus on the organic ones:

2.1 Proteins

Polymers of aminoacids joined by peptide bonds, structure of an aminoacid:



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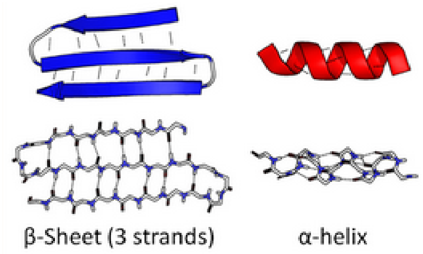
Note the amino group NH_2, the carboxyl acid group $COOH$, and the lateral chain with the root R, characteristic of every aminoacid.
They are joined by condensation, when the $COOH$ group creates a peptidic bind with the $NH2$ of the next.

2.2 Protein structure

There's 4 structure levels:

- Primary: peptidic bonds between single aminoacids in the protein
- Secondary: hydrogen bonds between the O of a $COOH$ group in one aminoacid and the NH_2 of another, can create two different shapes:
  - α-helix - R groups facing outwards
  - β-sheet



- Tertiary: **when R groups are involved**, there's many kind of folds, but only a few bonds that can happen:
  - **Hydrogen bonds** between $COOH$ carbonyl group and the lateral chain
  - **Hydrogen bonds** between two lateral chains or R groups
  - **Covalent bonds**, commonly di-sulfur bridge between cysteine R groups
  - **Ionic bonds** between R groups
  - **Hydrophobe interactions and van der Waals forces**, when in water, the hydrophile lateral chains push the hydrophobe R groups together, and then van der Waal forces keep them stable
- Quaternary: Combination of polypeptide, bound by similar bonds than the tertiary structures.

Folding is often facilitated by a specific type of proteins called **chaperones**. These molecules are generated in big quantities when there's a high rise in temperature. They attach themselves to the hydrophobe sections of unfolded proteins to prevent other molecules from attaching and allow the protein to re-fold itself before any unfolded aggregates get created.

2.3 Protein function

The functionality of a protein is strongly related to it's folding, two proteins with the same aminoacid sequence cat behave really differently, for example prions are proteins that when folded in a specific way, become infectious.
When a protein loses it's folding it's said it gets **denaturated**, this can happen for many reasons (heat, pH, ...).
They are the more versatile of the molecule groups, having many functions:

- **Catalytic/enzymes**: they speed up many chemical reactions.
- **Defensive**: Antibodies and other proteins attack and destroy viruses and bacteria
- **Movement**: Motor protein and contractile proteins move substances within the cell, the cells themselves and the whole body (muscles).
- **Signaling**: They are involved in the transport and reception of signals, sometimes bound to the cell membrane to interact with neighboring cells.
- **Structural**: collagen of the skin and tendons, membrane proteins.
- **Transport**: They allow that some molecules enter and leave the cell, or transport them throughout the body (hemoglobin).

2.4 Nucleic acids

Formed by **nucleotides**: a pentose sugar (ribose with OH on 2'/deoxyribose with H on 2'), a nitrogenous base (bound to the carbon 1'), and a phosphate (bound to the carbon 5').
Note that **nucleoside** is just the pentose sugar and the base.
Bases can be one of:

- Cytosine - Pyrimidine
- Uracil (RNA)/Thymine (DNA) - Pyrimidine
- Guanine - Purine
- Adenine - Purine

The nucleotides are bound with phosphodiester bonds (covalent bonds) on 5' and 3', and form a directed chain, always written from the nucleotid with the phosphate (5') free, to the one with the OH (3') free.
That is also the direction they are synthesized.
They form two main structures:

- **RNA**:
  - Sugar: ribose
  - Bases: A-U, G-C
  - Structure: simple strand
  - Function: transport, structural, etc.
- **DNA**:
  - Sugar: deoxyribose
  - Bases: A-T, G-C
  - Structure: double helix strand bound by hydrogen bonds of the bases
  - Function: carries the genetic information

In order to polymerize the nucleotides, the potential energy of the nucleotides is increased by adding phosphates, creating triphosphate nucleosides or **activated nucleotides**, then when they get polymerized they need water and generate inorganic pyrophosphate. Ex. ATP (adenine + 2 phosphates -> adenosin triphosphate)

2.5 DNA structure

The **primary structure** of the nucleic acids is just the sequence of basis it's made of.

The **secondary structure** is built by hydrogen bonds between the R groups, and for DNA is an **antiprallel double helix**, where the bases are matched only between complementary purines and pyrimidines (G-C has 3 hydrogen bonds, A-T has two hydrogen bonds).
The helix (2 nm wide) does a turn (3.4 nm) every 10 base pairs (0.34 nm), where the two strands phase is not symmetric, creating one small and one big gap between them.

The **tertiary structure** DNA is usually packed with proteins, in eucaryotes these are histones, the bundle is called **chromatin**, and it comes in two flavors, a more packed one that is not ready for transcription **heterochromatin** and a lightly packed one ready for transcription, **euchromatin**.

2.6 RNA structure

The **primary structure**: same as DNA, it's the sequence of basis.

The **secondary structure**: the most common is the stem loops (horquilla), where a single strand bends over itself to create a loop and a double helix section with itself.

The **tertiary structure**: secondary structures fold to generate a great variety of forms for RNA.

2.7 RNA types

There's three main types of RNA:

- **mRNA (messenger RNA)**:
  - Transports information from the nucleus to the cytoplasm
  - Gets translated in the ribosomes to generate proteins
  - Single strand

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- **rRNA (ribosomal RNA)**:
  - It's a structural part of the ribosomes
  - There's several types that form the small and big subunits of the ribosome along with proteins
  - Single strand with secondary structure
- **tRNA (transfer RNA)**:
  - Transports aminoacids to the ribosome
  - Simple strand with clover-like secondary structure

2.8 Carbohydrates

Made out of **monosaccharides**, they are composed by carbon, hydrogen and oxygen and are mainly used either as energy storage, or as structural molecules.
They have one carbonyl group ($C = O$), several hydroxyl ($-OH$) and a variable number of carbon-hydrogen bonds ($C - H$).

- **monosaccharides**: simplest of sugars, made of a single strand of carbons, with a carbonyl group and one or more hydroxyl (ex. glucose, fructose, galactose).

- **disaccharides**: formed by two monosaccharides when the hydroxyl groups bond (by condensation) to form **O-glycosidic bonds** (ex. 2 x glucose -> maltose + $H2O$, glucose + galactose -> lactose + $H2O$)
- **oligosaccharides and polysaccharides**: for groups of 2-10 monosaccharides bonded by glycosidic bonds, we call them oligosaccharides, and when they have more monosaccharides, we call them polysaccharides. (ex. starch, cellulose, chitin, glycogen).

2.9 Carbohydrates: polysaccharides

They have mainly two functions, **structural** and **energy reserve**. They also have a role in cell identification (ex. sperm attaching to the ovule). The main polysaccharides of life are:

- **Starch**
  - reserve molecule used by plants
  - amylose and amylopectin (both made of α-glucose)
  - amylose has a lineal helix structure
  - amylopectin has a ramified helix structure
- **Glycogen**
  - reserve molecule used by animals, fungi and some bacteria
  - made of α-glucose, very similar to amylopectin but it's even more ramified
- **Cellulose**
  - Structural support for plants and many algae
  - parallel chains of β-glucose joined with hydrogen bonds
- **Chitin**
  - Structural support for insects and fungi
  - parallel chains of NAG (N-acetylglucosamine) joined with alternating hydrogen bonds
- **Peptidoglycan**
  - Structural for bacteria
  - parallel chains joined with peptide bonds (using a chain of 4 aminoacids from NAM)
  - alternating NAG and NAM, N-acetylmuramaic acid, like NAG but with 4 aminoacids on C-3

2.10 Lipids

Main characteristics (classified by their physical attributes, not chemical structure like polysaccharides):

- Insoluble in water
- Soluble in organic solutions (ethanol, chloroform, ether, ...)
- Three main elements, **carbon, hydrogen and oxigen**, smaller amount of others **nitrogen, phosphorous, sulfur**.
- can be found bonding to other molecules with **covalent bonds (glucolipids)** or **non-covalent (lipoproteins)**.

Common ones (among others):

- Phospholipids
- Triglycerides
- Steroids

2.11 Steroids

Composed of 4 fused rings (steroid rings) and an isoprene.
Amphiphile molecules.

Main functions:

- Signaling - hormones (ex. testosterone)
- Structural - changing membrane fluidity (ex. cholesterol)

2.12 Triglycerides

Composed of a glycerol molecule with 3 fatty acids attached with ester bonds (if 2 fatty acids -> diglyceride, if 1 monoglyceride)

They are neutral molecules.

Can be split into:

- Oils: when they have non-saturated fatty acids (liquid at room temperature), common in plants.
- Fats: when they only have saturated fatty acids (solid at room temperature), common in animals.

Main functions is energy reserve.

2.13 Phospholipids

Components of **cell walls**, formed by a **glycerol** attached to **two fatty acids or isoprenoids** and a **phosphate**, and a **variable polar molecule** attached to the phosphate.

They are **anphypathics**, with the fatty acids being non-polar, and the head polar.

They make structures like **liposomes** (doubled-layered sphere), **micelles** (single layered sphere) and bilayer sheets.

Archaea use isoprenoids and **eukarya and bacteria** use fatty acids.

3 Cell structure

3.1 Procaryote cells

Procaryote cells reproduce by binary fission (no mitosis/meiosis). Are usually smaller than eukaryotes (1/10).

- **Nucleoid**: contains the super-coiled chromosome (usually circular DNA + non-histone proteins), with many genes (chunks that contain RNA building information)
- **Plasmids**: small circular strands of supercoiled DNA independent from the nucleoid, also contain genes.
- **Ribosomes**: Generate proteins from RNA strands, made up of a small and a large subunit.
- **Cytoskeleton**: Structures the cell interior and it's shape, and take a main role in cell division.
- **Membrane complexes**: Some photosynthetic species commonly have infoldings of the cellular membrane that contain enzymes and pigment molecules.
- **Cell wall**: To resist the osmosis pressure, most bacteria and archaea have a stiff cell wall. In most bacteria the cell wall main component is the modified polysaccharide peptiodglycan. While archaea use many other substances.
- **Specialized organelles**: Some species have "organelles" that contain enzymes, or other structures.
- **Flagellum**: Made to move through water, the common building block between archaea and bacteria is the rotating motor at the base of the flagellum where it joins the membrane.

- **Fimbriae**: smaller than the flagellum and without motor, usually more numerous allows bacteria to glue themselves to other cells or surfaces.

3.2 Eukaryote cells

Defined as having a well differentiated nucleus.

3.2.1 Common organelles

- **Nucleus**: Double membrane formed by the **nuclear envelope** and the **lamina** lattice that gives it shape. It contains the densely packed chromatin (chromosomes with histamines, **heterochromatin**) in the exterior and the less densely packed ones in the interior (**euchromatin**), with one central tightly packed region called **nucleolus**. The nucleus synthesizes RNA, and also proteins from RNA, for example the **nucleolus** produces the large and small ribosomal units. It has many **nuclear pores** that allow the traffic of proteins and other molecules from inside and outside the nucleus.

- **Rough Endoplasmic Reticulum (endomembrane system)**: It's the part of the ER closest to the nucleus, that has many ribosomes attached to it, forming a network of sacs and flattened tubules. The ribosomes on it's surface produce proteins that get into the lumen and get folded and processed and will either stay in the ER to be used or packaged in vesicles and sent to other destinations (other organelles, membrane, even to other cells).

- **Smooth Endoplasmic Reticulum (endomembrane system)**: This is the part of the ER that has no ribosomes attached. It contains enzymes that can synthesize lipids, or modify them and other toxic molecules. It also serves as reservoire of Ca^+.

- **Golgi apparatus (endomembrane system)**: Most of the proteins generated by the RER pass through the **cis** side of the Golgi apparatus, where they are merged with the **cisterna**, and pass from cisterna to cisterna where they react with the different enzymes on each, towards the **trans** side where they get packaged in vesicles and sent to their destinations.

- **Peroxisomes**: Generated when empty vesicles from the ER get filled with peroxisome-specific enzymes from teh cytosol. They are centers for redox reactions, that usually generate hydrogen peroxide as a side-product, so the peroxisome has specific enzymes to catalyze the reaction to transform it into water and oxygen.

- **Mitochondria**: In charge of the creation of ATP from carbohydrates, lipids and proteins. With a double bilayer membrane (this is 4x layers). The inner membrane forms **cristae** sacs, and contains the **mitochondrial matricx** (fluid inside). They are highly dynamic in shape. Each has many copies of a usually circular chromosome called **mitochondrial DNA (mtDNA)**, that contains the genes for **mitochondrial ribosomes** among others. These ribosomes are smaller than the ones in the cytosol and produce some of the mitochondria proteins.

- **Cytoskeleton**: Extensive system of protein fibers, split in three main subsystems:
  - **Actin filaments**: Made of actin, they:
    - maintain cell shape by resisting tension (pull)
    - move cells via muscle contraction or cell crawling
    - divide animal cells in two
    - move organelles and cytoplasm in plants, fungi and animals
  - **Intermediate filaments**: Made of several different proteins, they:
    - maintain cell shape by resisting tension (pull)
    - anchor nucleus and some other organelles (ex. nuclear lamina)
  - **Microtubules**: Made of $\alpha-$ and $\beta - tubulin$ dimers forming an empty tubule. They originate from the **microtubule organizing centre (MTOC)**. Plants usually have many, animals and fungi usually have only one, called **centrosome**, in animals is composed by two elements called **centrioles**. They have several functions:
    - maintain cell shape by resisting compression (push)
    - move cells via flagella or cilia
    - move chromosomes during cell division
    - assist formation of cell plate during plant cell division
    - provide tracks for intracellular transport (through kinesin)

- **Plasma membrane**: Bi-layer membrane made mainly of Phospholipids, with proteins embedded on one side or through the membrane, they control the traffic of substances from inside and outside the cell. There's three types of transport:
  - Osmosis (no extra energy required): Movement of water through the membrane from the side with less solute to the side with more (diffusion of water).
  - Passive transport (no extra energy required)
    - Simple diffusion: Movement of non-polar substances through the membrane (like osmosis for non-water molecules, ex. O_2, CO_2).
    - Facilitated diffusion: Movement of water soluble substances through specialized canal proteins embedded in the membrane. Might also happen with proteins that join the substance to pass the membrane.
  - Active transport (requires energy, ATP): It goes against the concentration gradient, or with substances that can't pass the membrane through diffusion. It uses transport proteins, and might involve the co-transport of substances, either the same direction (**synporter**) or the opposite (**antiporter**).

3.2.2 Animal only

- **Lysosomes (endomembrane system)**: Generated from the Golgi apparatus, contain enzymes specialized on the hydrolyzation of different molecules (proteins, nucleic acids, lipids and carbohydrates). They maintain an acid interior by using ion pumps on their membrane so the hydrolases keep being effective.

- **Centrioles**: Part of the centrosome of the animal cells, formed by two elements and a diffuse matrix of proteins where all the microtubules get formed, they are an important part of cell division and get themselves duplicated in it's early stages.

- **Extra cellular matrix**: Similar to the cell wall of plants, but more diffuse mixture of secreted proteins and polysaccharides that often support the animal cell.

3.2.3 Plant only

- **Vacuoles**:
- **Chloroplasts**: They have a double membrane like mitochondria, and their own DNA and ribosomes. Unlike mitochondria though, the inner membrane does not wrap to form crests, but instead a third membrane forms sac-like **thylakoids** that are stacked into connected **grana**. They have pigments like chlorophyll and carotene in their **stroma** (fluid filled space inside the inner membrane) that convert light energy into chemical energy that then the enzymes use to produce sugars.
- **Cell wall**: Made out of cellulose, it wraps the plant cell and gives it mechanical strength. It also limits the volume.