1 Carl (Chapter 1-2 + handout))

Draw the DNA molecule and explain its structure and function

DNA is made up of the four nucleidic acids *adenin, thymin, cytosin*, and *guanine*. The structure of DNA (deoxyribonucleidic acid) is a so called *polymer* – long strings of similar units. These units, the nucelotides, stack neatly in an α-helical structure. Our bodies contain about a meter of DNA, wound up in protein "spools", themselves forming complexes called *nucleosomes*.

The genetic message in DNA encodes only the polypeptides primary structure (i.e. not how it folds), and is central in order for organisms to produce the necessary proteins, components and RNA molecules.

The helix of DNA is made up by two strings of polymers built by the different nucleotides, that by themselves might repel each other, but are by hydrogen bonds bound together. The four different nucleotides are on the other hand attached to the backbone of the polymer, constructed by sugar molecules and phosphate groups. Roughly every sugar molecule is connected to a nucleotide.

Explain the flow of genetic information in the cell.

The flow of genetic information can be summarized in five steps:

1. DNA holds the blueprint for information. During cell division, DNA is copied by a machine called DNA polymerase. For other uses however, DNA contains genes that in turn contain *regulatory* and *coding* regions which specify the sequence of amino acids (making up proteins etc.) that are to be produced.

2. *RNA polymerase* reads DNA in a process called *transcription*. It does so by attaching to the DNA, and thereafter traversing it, drawing the DNA string through a slot, adding successive monomers. This resulting chain is so-called **mRNA**. In eucaryotic cells, mRNA leaves the cell through pores in the membrane and enters the *cytosole*. The energy needed to

drive RNA polymerase comes from the nucleotides themselves, which come in high-energy NTP-form. The polymerase cuts of two out of three phostphate groups from each NTP as the nucelotide is added to the chain of transcript.

3. In the cytosole, ribosomes bind the transcript and and walks along it, building up a polypeptide. This is a process called *translation*, and builds up so-called **tRNA** molecules. These in turn bind to triplets of monomers and carry corresponding amino acid monomers to be added to the growing polypeptide chain.

4. The polypeptide either spontaneously folds into a new state, or does so by **chaperones** – auxiliary proteins.

5. The folded protein forms a part of the cells architeture.

The overall process might be descrived by the schematic

$$Cell \to DNA \xrightarrow{transcription} mRNA \to ribosome \xrightarrow{translation} (tRNA \to)\ protein.$$

How does the genetic code work?

DNA is made up by three different parts – a phosphate group, a pentose sugar and a nitrogenous acid (e.g. adenin). The acid bases are four, and therefore gives rise to 4^3 different combinations, resulting in the possibility of the creation of 20 different amino acids (some are the same even though they are built differently).

RNA is then involved in the transcription of patterns from the DNA, constructing **mRNA** molecules. The pattern for protein synthesis is then read and translated in the ribosome, where **tRNA**thereafter adds amino acids to the intended sequemce. The protein is then formed, and can continue on to fold.

How big is a human cell? A bacterium? DNA?

DNA Width: 2 nm, Length: As long as you want it. In humans, about 2 m in total. Each base pair is about .5 nm, where we have ca 3 billion base pairs.

Cell Volume: Sperm cell – 30 μm^3, red blood cell – 100 μm^3, to maximally a fat cell – 600000 μm^3, and oocytes – 4000000 μm^3.

Bacterium Length: .2–.3 μm^3, to maximally about 250μm^3 long, and .75 wide.

How much DNA do we have in a cell?

Meterwise.

What is a gene, and how many do we have?

A gene is the region that is responsible for the actual coding of RNA and proteins. It is the part of the chromosome that is actually effectively transcribed. We have about 20000–25000.

How can different cells do different things with the same genetic program?

What defines the function of a protein?

Essentially the way it folds. The primary structure is pretty much the definition of the protein; the secondary structure describes the folding of the protein, resulting in the overall shape of the protein. More complex proteins consists of multiple polypeptide subunits that form the quaternary structure, e.g. hemoglobin, which has four subunits. All in all, the structure of the protein define the function, since it determines the transport and the activation.

What functions may proteins have?

Enzymes (catalysing reactions), antibodies (binding to viri etc.), messenger (e.g. hormones), structural parts (e.g. microtubuli, filaments), transport/storage (binds to atoms and molecules).

What is the plasma membrane, and what things do we find there?

The plasma membrane is what protects the cells interiors from the exteriors. It also allows the cell to move, by being able to change its shape. All cells do this through the **bilayer membrane**. These shapes form spontaneously and are very simple in nature. It consists of two layers of molecules

– primarily phospholipids. It is only about 4 nm thick, but can cover billions of square nanometers.

The bilayer membrane is constructed by molecules with hydrophobic tails and hydrophillic heads, making it so that these layers form with heads pointing outward from the center of the membrane wall.

What structural elements help define the shape of a cell?

Macromolecular assemblies (e.g. microtubuli, actins) that form the so called **cytoskeleton** of the cell, in effect building up the different organelles for eukaryotes. Actin filaments lies under the surface of the cell and form a thin meshwork – the actin cortex. Microvilli, filopodia and lamellipodia are full of actin-fibers which cross-link the one another to form stiff bundles that help to push these structures out of the cell. Furthermore, actin filaments form the "highways" along which single-molecule motors walk to generate muscle contractions and other phenomena.

How can things be transported in cells?

Through binding to proteins, diffusion and drift through microtubuli. Also osmosis. Larger transpors are performed through **cytosis**, where proteins form vesicles form the intended cargo to travel in.

What is metabolism?

Metabolism is the process of maintaining the living state of an organism. It is made up of two things:

- Anabolism – synthesis of things needed by the cells
- Catabolism – breakdown of scrap to form things that the cell can use

How is energy stored and converted in plants and animals?

Energy is stored in fats, carbohydrates and proteins in animals. In plants, they mainly take up sunlight and water in order to rearrange atoms into sugars and fats. Plants consume order – not energy.

What is the function of ATP and ADP?

ATP and ADP are energy carriers. They are built up by the nitrogenous acid adenin and a duo- or tri-phosphate group. The mitochondria produces them in order to send them out as energy packages throughout the body. ATP contains a lot of energy due to the energy stored in the bond between the second and thrid phosphate group. Both ATP and ADP are essential for the body to be able to perform even the most basal functions, such as the pumping of ions through the cell membrane, or muscle contraction.

How can complexity arise from simple building blocks?
Complexity arises from simple building blocks, or processes, due to the linkage of many things.

2 Bosse (Chapter 3-6)

2.1 Chpt. 3 - The Molecular Dance (Problems 3.1, 3.2)

What does the ideal gas law say about the mean kinetic energy? It is equal (on average) to $E_k = \frac{3}{2}kT$.

What does the Boltzmann distribution say in the limits of high/low T? High: All states equally possible.
Low: All particles in ground state.

Explain the Arrhenius rate law. The rate of a chemical reaction mainly depend on temperature through the factor $e^{-E_{barrier}}/kT$, where $E_{barrier}$ is some temperature independent constant inherent to the reaction.

Problems Problem 1: a) Mean? b) Standard deviation?
Problem 2: Use that $mgh \approx \frac{mv^2}{2}$?

2.2 Chpt. 4 – Random Walks, Friction, and Diffusion (Problems 4.1, 4.8)

How does the diffusion law arise in random walk models of Brownian motion? The mean is zero, but not the expected distance walked from the origin. Remember that in 2D $\langle \mathbf{r}^2 \rangle = 4Dt$, and in 3D $\langle \mathbf{r}^2 \rangle = 6Dt$. Drift? Include variance in step length (i.e. make it variable).

How can one use Stokes' law to determine the viscosity of a fluid? Constant force: terminal velocity proportional to force.

$$D_{model} = \frac{l^2}{2\Delta t}$$
$$\zeta_{model} = \frac{2m}{\Delta t}$$

will imply

$$D \cdot \zeta = m(l/\Delta t)^2 = \langle mv^2 \rangle \overset{IGL}{=} kT$$

Stoke's law:

$$\zeta = 6\pi\eta R$$

Einstein derived a relation between the friction coefficient ζ and the diffusion constant D, for a body in a viscous fluid. What is so remarkable about it? It gives an easy measure of kT from macroscopic measurements. The relation is *universal(!)*: we always get kT, independent on the type of molecule and solvent. We have no dependence on mass and such. Smaller molecules will experience less drag (i.e. less friction ζ), but larger molecules will diffuse easier. (Not as easily halted by other particles.)

What is flux and what does the continuity eq. mean? The flux is the amount of solute/substance/substrate that pushes through an area in a given time. The continuity equation essentially states that all matter going ut of a cell must go into a cell. There is no spontaneous loss or gain of matter.

Explain Fick's law and how it leads to the Diffusion eq. Fick's law states that the flow through a cell wall is given by the equation

$$j = -D\frac{dc}{dx}$$

by some constant D. By investigating how the concentration changes due to this, we get

$$\frac{dc}{dt} = -\frac{dj}{dx}.$$

Combined we get

$$\frac{dc}{dt} = D\frac{d^2c}{dx^2}$$

which is what we call the *diffusion equation.*

Show how the Gaussian sol. for the diffusive growth of a point-like drop (of e.g. ink) reflects the diffusion law. TBD

2.3 Chpt. 5 – Life in the Slow Lane: The Low Reynolds-Number World (Problems 5.2, 5.4)

1. Why should one expect the atmosphere to be of the order of 104 m high? The concentration is proportional to the Boltzmann probability of a particle being there. $E \sim mg/kT$ with values gives a typical height $1/z^* = (mg/kT)^{-1} \approx 10^4$.

2. How does a centrifuge work? We have a gravitational pull on the water (or liquid) equal to $F = V\rho g$, as well as a gravitational pull on the actual particle in question, so that $\Delta U = mg\Delta z - V\rho g\Delta z$. This all applies to a solute of some sort. The sedimentation force is determined by the derivative of this w.r.t. position.

   In a centrifuge the inward force is given as $f = -mr\omega^2$. The drift velocity must thereby be $v_{drift} = -mr\omega^2/\zeta$. In equilibrium, we have $j = 0$, and so

   $$0 = D(-\frac{\partial c}{\partial r}) + r\omega^2 m/kT \cdot c$$

   with solutions $c \sim const e^{r^2\omega^2 m\beta/2}$.

3. What is required for a situation to yield a low Reynolds number R? Give a biological example of the peculiarity of a low R?

2.4 Chpt. 6 – Entropy, Temperature, and Free Energy (Problems 6.2, 6.5)

1. What does the Statistical Postulate say?

2. What is the thermodynamical definition of temperature?

3. State the Second Law of thermodynamics. A subsystem strives to minimize its (Helmholtz) Free Energy. Why is this said to involve a competition between entropy and energy?

4. What is pressure, thermodynamically?

5. A macroscopic system consists of a large number N of identical, non-interacting molecules, each of which can be in either of two states, labelled + and −, with resp. energies $E_\pm = E_0 \pm \Delta E$. Show that at temperature T, the mean energy per molecule, E/N, will be very close to $E_0 - \Delta E \tanh(\Delta E/kT)$. (tanh is the hyperbolic tangent function; it is increasing and satisfies $|tanhx| < 1$.)

3 Anders (Chapter 7,8,9)

Suggested exercises: 7.4, 7.5, 9.4, 9.5

3.1 Practice questions

Figure 7.14 shows solubilities of small nonpolar molecules in water. Discuss the fact that the measured solubilities decrease with increasing temperature.

It is widely believed that the native state of many proteins represents a global free-energy minimum. Why?

Exercise 8

Let $r_{ee} = r(L) - r(0) = \int_0^L ds\hat{t}(s)$ denote the end-to-end vector of a worm-like chain. Show that

$$\langle \mathbf{r_{ee}^2} \rangle \approx 2\epsilon L \tag{1}$$

where ϵ is the persistence length. What is the corresponding result for a freely jointed chain (random walk) with step length a?

Exercise 10

Hemoglobin binds four oxygen molecules cooperatively. Discuss the mechanism and functional importance of this cooperativity.