Light vs. Retina
How light invades the human body

The fact that our body, especially our eyes, get in touch with light is inevitable and ordinary. Life without light is as is known almost not possible. No machines, no modern technologies, no research, no development without light. Maybe there would neither be computers nor internet. Maybe, this contest would not even exist without light because nobody has the ability to write and nobody is able to read the essays.

Which chemical or other processes are behind our ability to see? What happens to light before being converted to an electric signal? To which degree are these processes useful for possible development in the future? In the following, answers to these questions will be proposed.

To begin first, what is light encountering first on its journey to our eyes? Photons debouch through the cornea to the lens and end up on the retina. Here two types of cells react to light. First, the *cones* (ca. 100 mio. cells) are responsible for seeing bright light and for the perception of colours. Secondly, the *rods* (ca. 3 mio. cells) detect dim light, but no colours. This is the reason, why identifying colours at night time is nearly impossible. Cones and rod cells are called photoreceptor cells. Exposition to light is bringing them to action, resulting in a molecular movement and, finally, eliciting a nerve impuls.

To understand how light is absorbed and transmitted it is helpful to examine the structure of cone and rod cells. Human rod cells are longer, but not as wide and tapered as cone cells. Different parts of the cells have different functions: The *outer segment* consisting of about 1000 *disks* serves as photoreceptive area. The disks enlarge the surface of cell membranes thus offering more area for light to be absorbed. In contrast to cones, where disks are attached to the outer plasma membrane, the disks in rods form intracellular organelles. The outer segment is connected to the *inner segment* by a non-motile *cilium* (thin „stem“ consisting of microtubules). The inner segment including many organelles such as mitochondria and ribosomes generates *adenosine triphosphate (ATP)* and has a high rate of protein synthesis. Other parts of the inner segment are the nucleus and the synaptic terminal forming a synapse with a bipolar cell.

How is light absorbed? In order to be able to absorb light photoreceptor cells carry a light absorbing group. In the disks of rods and cones *rhodopsin* a compound of the protein *opsin* and the so-called prosthetic group *1-cis-retinal* is located. 11-cis-retinal is essential for the function of opsin, because no light will be absorbed without it. Opsin and 11-cis-retinal are linked as a Schiff-base (general structure: $R_2C{=}NR'$).

The aldehyde group from 11-cis-retinal is connected with the amino group of an amino acid residue of opsin. During the process of seeing light causes a change in geometry of the C11-C12 double bond of 11-cis-retinal of rhodopsin to *all-trans-retinal* (Fig. 1). So, one photon has induced isomerisation. This isomersation causes a photodissociation (chemical

compound breaks down through influence of a photon) with some intermediate stages.

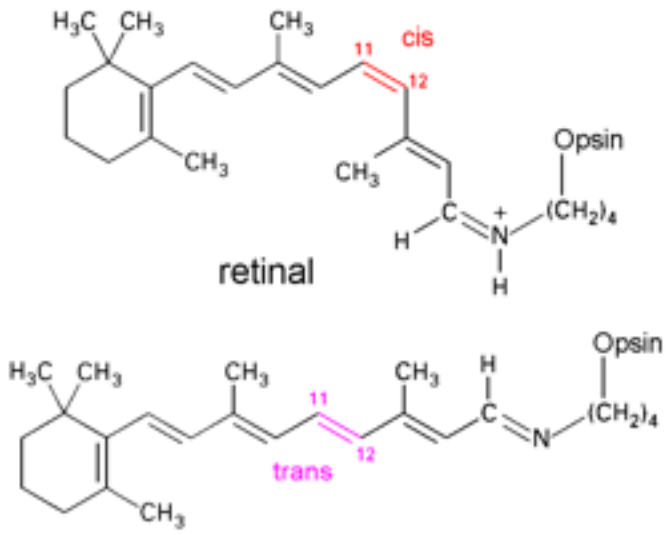

Figure 1. 11-cis-retinal-and all-trans-retinal

After three stages the Schiffbase compound in metarhodopsin I is deprotonated. Metarhodopsin II is produced. Through a hydrolysis, opsin and the all-trans-retinal are formed. The all-trans-retinal diffuses away from opsin because it does not match to the binding site for 11-cis-retinal. Subsequently, it is deoxidised to *all-trans-retinol (Vitamin A)*. Vitamin A is oxidised to the aldehyde all-trans-retinal and then again isomerised by a change in geometry to produce 11-cis-retinal for a new reaction chain of isomerisation.

2.) What causes the change in molecular geometry? A decisive role is played by the nucleotide *cyclic guanosine monophosphate (cGMP)*. The cGMP is a ligand of sodium ion channels and regulates ion channel conductance. The intra- and extracellular fluids of a photoreceptor cell contain sodium and potassium ions. Inside the cell the concentration of the potassium ions is high, the concentration of sodium ions is low. Outside the cells it is the reverse. The Na+/K+ pump keeps this difference in balance. In dark light the concentration of cGMP is very high, so sodium ion channels are open and sodium ions can easily get into the outer segment to reduce the negative charge density. For balance, a ion current of potassium ions arises in the direction to the inner segment. When light is absorbed, the ligand-gated sodium channels of the outer segment are blocked. The blockade of the Na+ influx is related to the isomerisation of metarhodopsin II, which causes an enzyme cascade: Metarhodopsin II activates the protein *transducin* by exchanging g*uanosine diphosphate (GDP)* for g*uanosine triphosphate (GTP)*. Activated transducin brings *phosphodiesterase (PDE)* to action, that hydrolyses cGMP. The light-induced decrease of cGMP concentration leads to inhibition of sodium ion channels in the plasma membrane (Fig. 2).

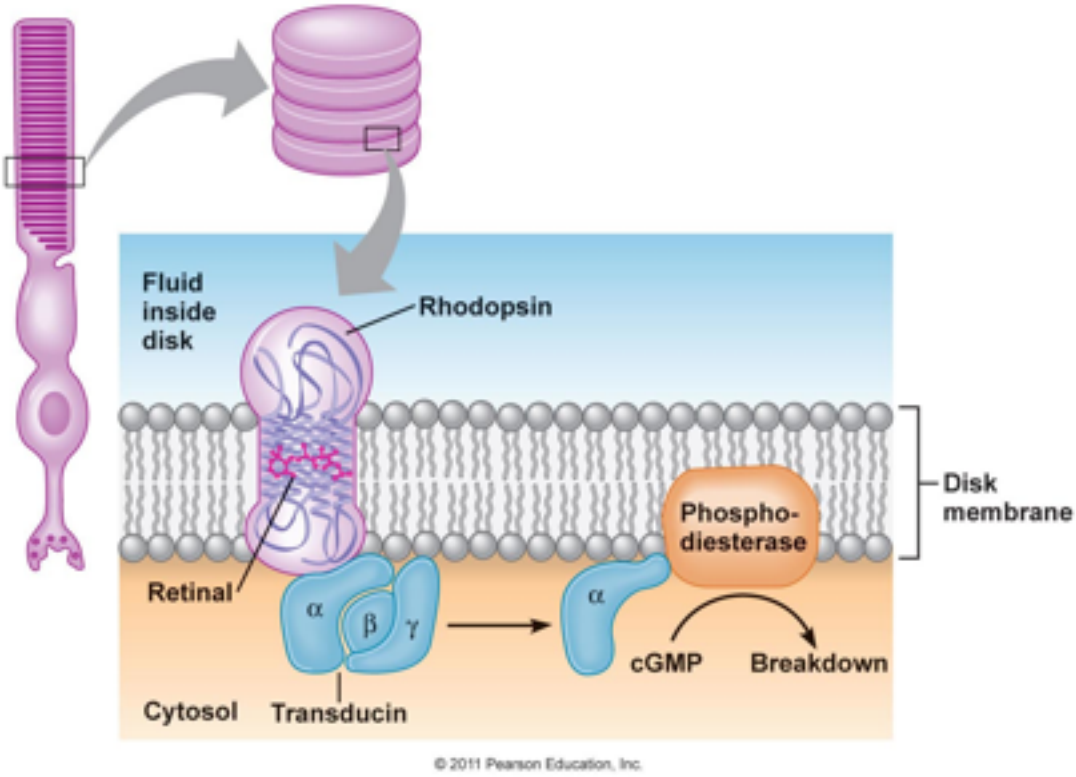

Figure 2. Light-induced enzyme cascade.

3.) The outer segment is hyperpolarised by reduced Na+ influx. This light-induced hyperpolarisation is then passively transmitted through plasma membrane to the synaptic terminal. This signal includes information about the perceived luminous energy and is then passed down by way of synapses to further cerebral processes. This process is inactivated, when metarhodopsin II and transducin are inactivated. The latter carries *GTPase*, which is a enzyme for the hydrolysis of the bound GTP to GDP. So PDE is no more activated. In addition, enzyme *opsin kinase* phosphorylates and bounds to *arrestin* (protein for regulating signal transduction). Hence bounding with transducin is inhibited.
One single photon effects the activation of about 500 transducin molecules, leading to closure of hundreds of sodium ion channels.

During constant illumination functional characteristics of photoreceptor cells are changed. We know this adaptation to light when proceeding from dark to bright light: It glares. On bright light all cGMP-conducted ion channels close and plasma membrane are hyperpolarised. If illumination remains constant, the membrane potential drops. So a new increase of intensity of light can be detected. Bright light does not glare any longer.
To sum up, vitamin A (all-trans-retinol) is isomerised to produce the light-sensitive chromophore 11-cis-retinal. Light activates rhodopsin and reverses isomerisation. This leads to the activation of transducin and thus phosphodiesterase. So, sodium ion channels are inhibited because of the absense of cGMP. People are able to see even in glare light due to the hyperpolarisation of their photoreceptor cells.

What is the practical dimension of these research results? One example could be the

development of extremely energy efficient photosensors. They should incorporate an artificial cell in which the protein rhodopsin is included. When light induces the above mentioned reactions, a light switch is turned on and off through electric impulses. In addition, light may be adjusted, so a light system varies light intensity on its own.

Another application, could ameliorate retina problems (e.g. a loss of rods). New rod cells could be synthesised containing rhodopsin. These cells are then implanted or rather transplanted into the eyes. Patients come out with improved vision.

Apart from this, an electronic circuit linked to reactions (isomerisation, cGMP deactivation) could be integrated into a camera. Therefore, the camera is able to take photos with a very high resolution and adapts to glare light.

To conclude, light per se advances human life not only by being present everyday. Future discoveries on the biological processes of vision may promote developments in various sectors of science and technology.

Lemgo, 27*th* of September 2015, Franziska Vieregge.

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Figures:

Fig. 1: http://www.bmb.leeds.ac.uk/illingworth/bioc3800/
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Fig. 2: http://droualb.faculty.mjc.edu/Course%20Materials/Physiology%20101/Chapter%20Notes/Fall%202011/chapter_10%20Fall%202011.htm
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