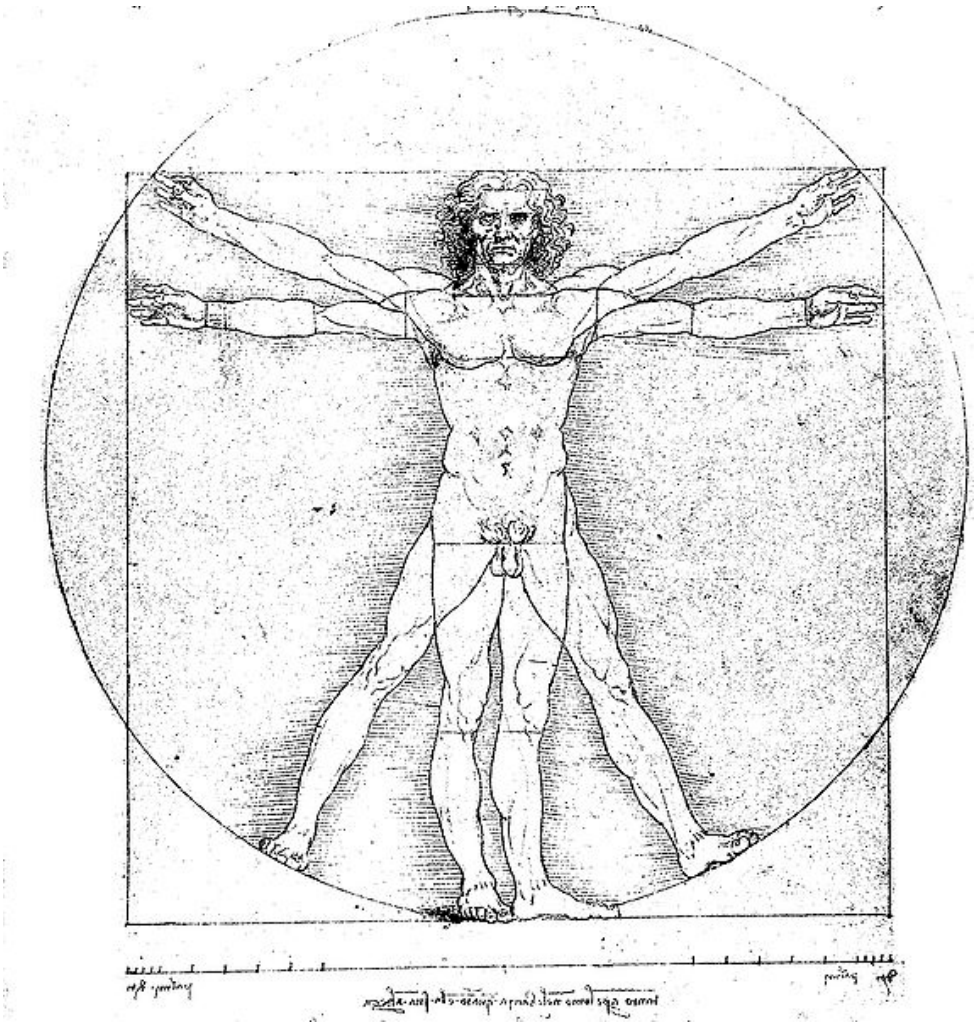
Biological Machines

The physiological basis of human sensory systems,
from an engineering point of view

28 Feb 2011, Ver 1.1



Contents

Articles

References

Article Licenses

Biological Machines/Introduction

While the human brain may make us what we are, our sensory systems are our windows and doors to the world. In fact they are our ONLY windows and doors to the world. So when one of these systems fails, the corresponding part of our world is no longer accessible to us. Recent advances in engineering have made it possible to replace sensory systems by mechanical and electrical sensors, and to couple those sensors electronically to our nervous system. While to many this may sound futuristic and maybe even a bit scary, it can work magically. For the auditory system, so called “cochlea implants” have given thousands of patients who were completely deaf their hearing back, so that they can interact and communicate freely again with their family and friends. Many research groups are also exploring different approaches to retinal implants, in order to restore vision to the blind. And in 2010 the first patient has been implanted with a “vestibular implant”, to alleviate defects in his balance system.

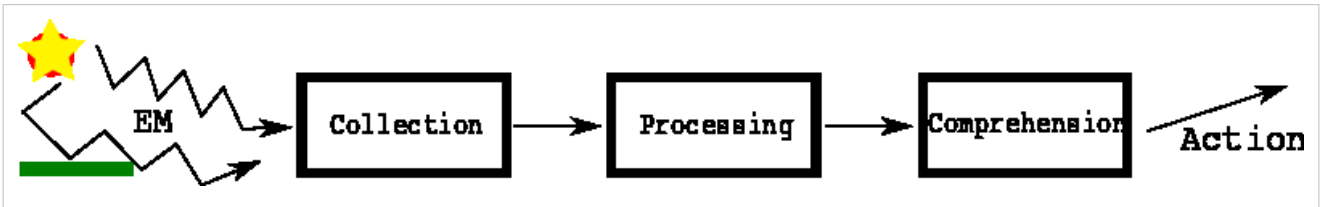
The wikibook “Biological Machines” wants to present our sensory system from an engineering and information processing point of view. On the one hand, this provides some insight in the sometimes spectacular ingenuity and performance of our senses. On the other hand, it provides some understanding of how our senses transduce external information into signals that our central nervous system can work with, and how – and how well - this process can be replaced by technical components.

Visual System

Biological Machines/Sensory Systems/Visual System

Introduction

Generally speaking, visual systems rely on Electromagnetic (EM) Waves to give an organism more information about its surroundings. This information could be regarding potential mates, dangers and sources of sustenance. Different organisms have different constituents that make up what is referred to as a visual system. A possible general pathway for what goes on in most visual systems can be seen in the following figure:



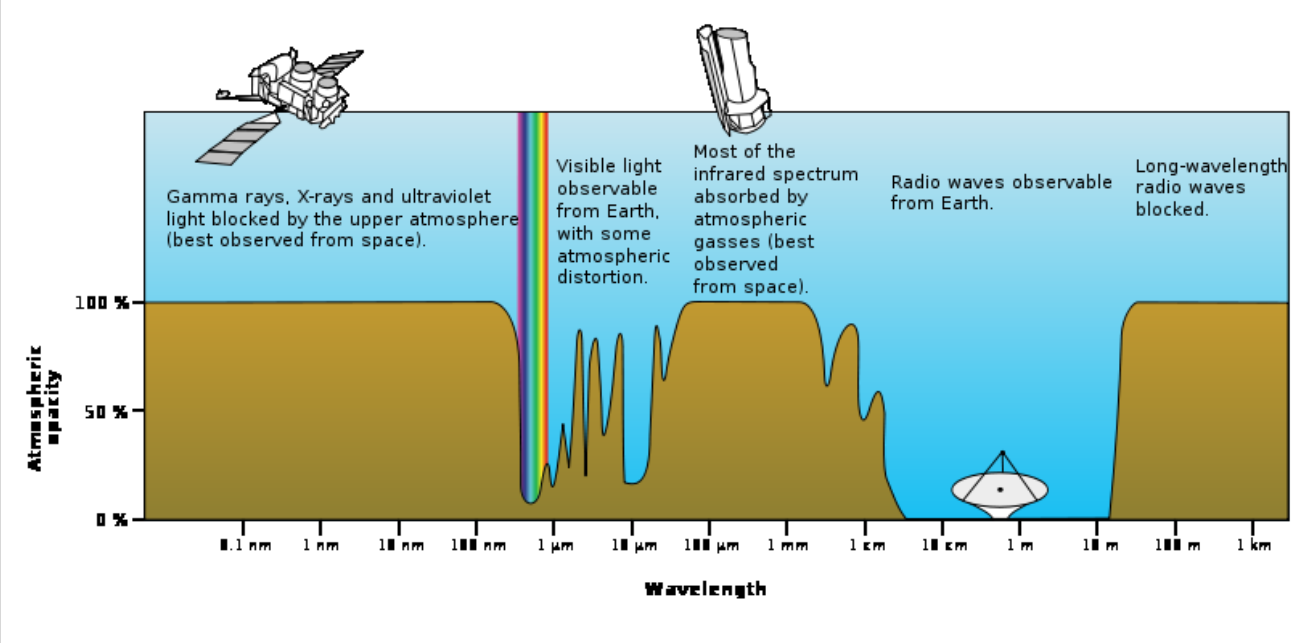
The EM waves are collected by visual system sensory organs and transduced by cells containing pigments that react to EM waves of a certain range of wavelengths. These photosensitive cells will change polarity/voltage when exposed to EM radiation, where the intensity of the EM waves is perceived as brightness, direction is discernible with accuracy based mostly on the complexity of the particular eye construction found in the organism. The complexity of eyes range from something as simple as an eye spot, which is nothing more than a collection of photosensitive cells, to a fully fledged camera eye. If an organism has different types of photosensitive cells, or cells sensitive to different wavelength ranges, the organism would theoretically be able to perceive colour or at the very least colour differences. Polarisation, another property of EM radiation, can be detected by some organisms, with insects and cephalopods having the highest accuracy.

Please note, in this text, the focus has been on using EM waves to see. Granted, some organisms have evolved alternative ways of obtaining sight or at the very least supplementing what they see with extra-sensory information. For example, whales or bats, which use echo-location. This may be seeing in some sense of the definition of the word, but it is not entirely correct. Additionally, vision and visual are words most often associated with EM waves in the visual wavelength range, which is normally defined as the same wavelength limits of human vision. Since some organisms detect EM waves with frequencies below and above that of humans a better definition must be made. We therefore define the visual wavelength range as wavelengths of EM between 300nm and 800nm. This may seem arbitrary to some, but selecting the wrong limits would render parts of some bird's vision as non-vision. Also, with this range of wavelengths, we have defined for example the thermal-vision of certain organisms, like for example snakes as non-vision. Therefore snakes using their pit organs, which is sensitive to EM between 5000nm and 30,000nm (IR), do not "see", but somehow "feel" from afar. Even if blind specimens have been documented targeting and attacking particular body parts.

Firstly a brief description of different types of visual system sensory organs will be elaborated on, followed by a thorough explanation of the components in human vision, the signal processing of the visual pathway in humans and finished off with an example of the perceptional outcome due to these stages.

Sensory Organs

Vision, or the ability to see depends on visual system sensory organs or eyes. There are many different constructions of eyes, ranging in complexity depending on the requirements of the organism. The different constructions have different capabilities, are sensitive to different wave-lengths and have differing degrees of acuity, also they require different processing to make sense of the input and different numbers to work optimally. The ability to detect and decipher EM has proved to be a valuable asset to most forms of life, leading to an increased chance of survival for organisms that utilise it. In environments without sufficient light, or complete lack of it, lifeforms have no added advantage of vision, which ultimately has resulted in atrophy of visual sensory organs with subsequent increased reliance on other senses (e.g. some cave dwelling animals, bats etc.). Interestingly enough, it appears that visual sensory organs are tuned to the optical window, which is defined as the EM wavelengths (between 300nm and 1100nm) that pass through the atmosphere reaching to the ground. This is shown in the figure below. You may notice that there exists other "windows", an IR window, which explains to some extent the thermal-"vision" of snakes, and a radiofrequency (RF) window, of which no known lifeforms are able to detect.



Through time evolution has yielded many eye constructions, and some of them have evolved multiple times, yielding similarities for organisms that have similar niches. There is one underlying aspect that is essentially identical, regardless of species, or complexity of sensory organ type, the universal usage of light-sensitive proteins called opsins. Without focusing too much on the molecular basis though, the various constructions can be categorised into distinct groups:

- Spot Eyes
- Pit Eyes
- Pinhole Eyes
- Lens Eyes
- Refractive Cornea Eyes
- Reflector Eyes
- Compound Eyes

The least complicated configuration of eyes enable organisms to simply sense the ambient light, enabling the organism to know whether there is light or not. It is normally simply a collection of photosensitive cells in a cluster in the same spot, thus sometimes referred to as spot eyes, eye spot or stemma. By either adding more angular

structures or recessing the spot eyes, an organisms gains access to directional information as well, which is a vital requirement for image formation. These so called pit eyes are by far the most common types of visual sensory organs, and can be found in over 95% of all known species.

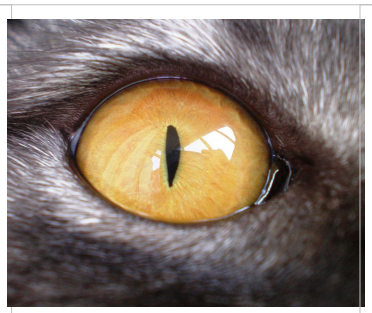
Pinhole eye

Taking this approach to the obvious extreme leads to the pit becoming a cavernous structure, which increases the sharpness of the image, alas at a loss in intensity. In other words, there is a trade-off between intensity or brightness and sharpness. An example of this can be found in the Nautilus, species belonging to the family Nautilidae, organisms considered to be living fossils. They are the only known species that has this type of eye, referred to as the pinhole eye, and it is completely analogous to the pinhole camera or the camera obscura. In addition, like more advanced cameras, Nautili are able to adjust the size of the aperture thereby increasing or decreasing the resolution of the eye at a respective decrease or increase in image brightness. Like the camera, the way to alleviate the intensity/resolution trade-off problem is to include a lens, a structure that focuses the light unto a central area, which most often has a higher density of photo-sensors. By adjusting the shape of the lens and moving it around, and controlling the size of the aperture or pupil, organisms can adapt to different conditions and focus on particular regions of interest in any visual scene. The last upgrade to the various eye constructions already mentioned is the inclusion of a refractive cornea. Eyes with this structure have delegated two thirds of the total optic power of the eye to the high refractive index liquid inside the cornea, enabling very high resolution vision. Most land animals, including humans have eyes of this particular construct. Additionally, many variations of lens structure, lens number, photosensor density, fovea shape, fovea number, pupil shape etc. exists, always, to increase the chances of survival for the organism in question. These variations lead to a varied outward appearance of eyes, even with a single eye construction category. Demonstrating this point, a collection of photographs of animals with the same eye category (refractive cornea eyes) is shown below.

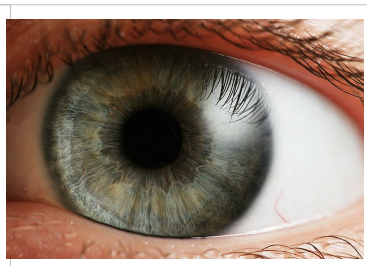
Refractive Cornea Eyes

Hawk Eye

Sheep Eye



Cat Eye



Human Eye

An alternative to the lens approach called reflector eyes can be found in for example mollusks. Instead of the conventional way of focusing light to a single point in the back of the eye using a lens or a system of lenses, these organisms have mirror like structures inside the chamber of the eye that reflects the light into a central portion, much like a parabola dish. Although there are no known examples of organisms with reflector eyes capable of image formation, at least one species of fish, the spookfish (Dolichopteryx longipes) uses them in combination with "normal" lensed eyes.

Compound eye

The last group of eyes, found in insects and crustaceans, is called compound eyes. These eyes consist of a number of functional sub-units called ommatidia, each consisting of a facet, or front surface, a transparent crystaline cone and photo-sensitive cells for detection. In addition each of the ommatidia are separated by pigment cells, ensuring the incoming light is as parallel as possible. The combination of the outputs of each of these ommatidia form a mosaic image, with a resolution proportional to the number of ommatidia units. For example, if humans had compound eyes, the eyes would have covered our entire faces to retain the same resolution. As a note, there are many types of compound eyes, but delving to deep into this topic is beyond the scope of this text.

Not only the type of eyes vary, but also the number of eyes. As you are well aware of, humans usually have two eyes, spiders on the other hand have a varying number of eyes, with most species having 8. Normally the spiders also have varying sizes of the different pairs of eyes and the differing sizes have different functions. For example, in jumping spiders 2 larger front facing eyes, give the spider excellent visual acuity, which is used mainly to target prey. 6 smaller eyes have much poorer resolution, but helps the spider to avoid potential dangers. Two photographs of the eyes of a jumping spider and the eyes of a wolf spider are shown to demonstrate the variability in the eye topologies of arachnids.

Eye Topologies of Spiders

Wolf Spider

Jumping Spider

Sensory Organ Components

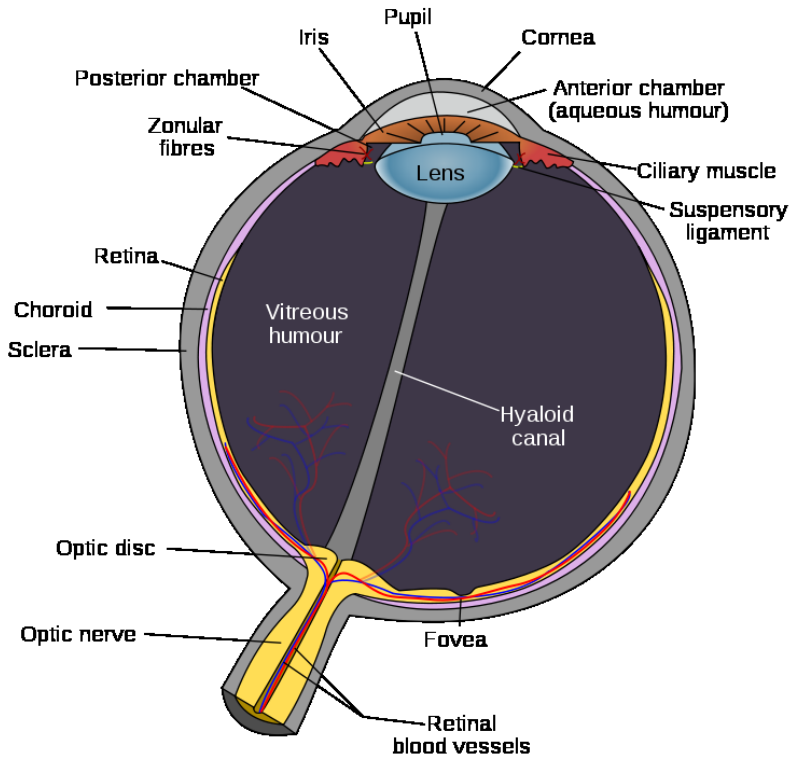
We humans are visual creatures, therefore our eyes are complicated with many components. In this chapter, an attempt is made to describe these components, thus giving some insight into the properties and functionality of human vision.

Getting inside of the eyeball - Pupil, iris and the lens

Light rays enter the eye structure through the black aperture or pupil in the front of the eye. The black appearance is due to the light being fully absorbed by the tissue inside the eye. Only through this pupil can light enter into the eye which means the amount of incoming light is effectively determined by the size of the pupil. A pigmented sphincter surrounding the pupil functions as the eye's aperture stop. It is the amount of pigment in this iris, that give rise to the various eye colours found in humans.

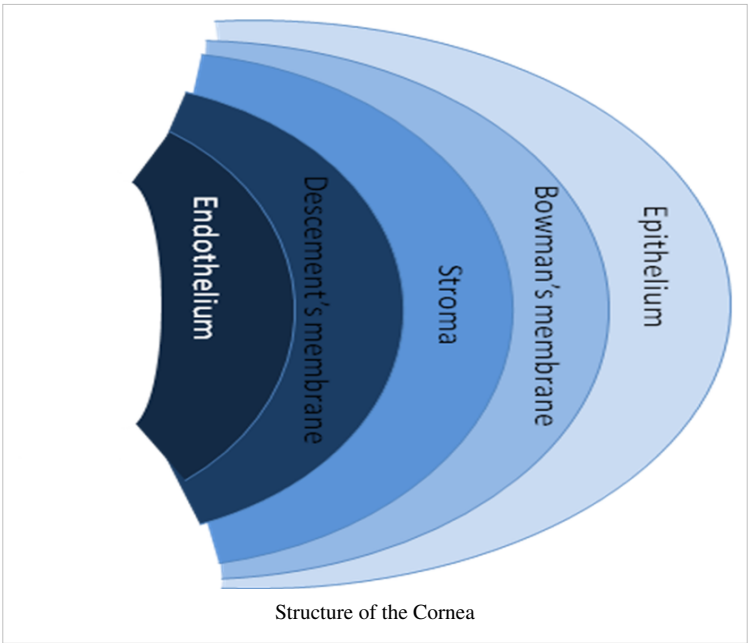
In addition to this layer of pigment, the iris has 2 layers of ciliary muscles. A circular muscle called the pupillary sphincter in one layer, that contracts to make the pupil smaller. The other layer has a smooth muscle called the pupillary dilator, which contracts to dilate the pupil. The combination of these muscles can thereby dilate/contract the pupil depending on the requirements or conditions of the person. The ciliary muscles are controlled by ciliary zonules, fibres that also change the shape of the lens and hold it in place.

The lens is situated immediately behind the pupil. Its shape and characteristics reveal a similar purpose to that of camera lenses, but they function in slightly different ways. The shape of the lens is adjusted by the pull of the ciliary zonules, which consequently changes the focal length. Together with the cornea, the lens can change the focus, which makes it a very important structure indeed, however only one third of the total optical power of the eye is due to the lens itself. It is also the eye's main filter. Lens fibres make up most of the material for the lense, which are long and thin cells void of most of the cell machinery to promote transparency. Together with water soluble proteins called crystallins, they increase the refractive index of the lens. The fibres also play part in the structure and shape of the lens itself.



Schematic diagram of the human eye

Beamforming in the eye – Cornea and its protecting agent - Sclera



Structure of the Cornea

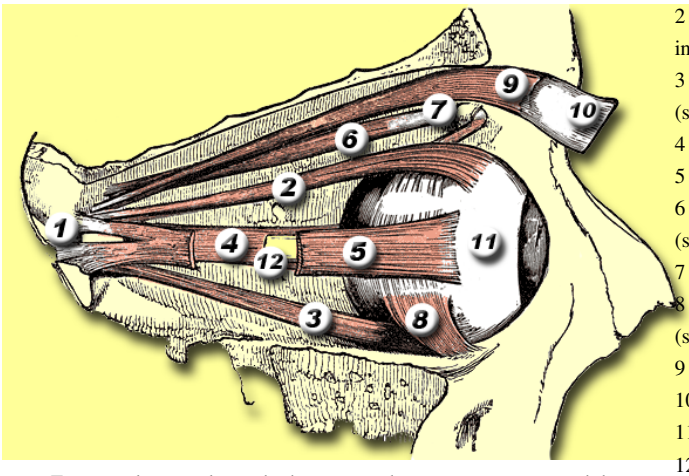
The cornea, responsible for the remaining 2/3 of the total optical power of the eye, covers the iris, pupil and lens. It focuses the rays that pass through the iris before they pass through the lens. The cornea is only 0.5mm thick and consists of 5 layers:

- Epithelium: A layer of epithelial tissue covering the surface of the cornea.
- Bowman's membrane: A thick protective layer composed of strong collagen fibres, that maintain the overall shape of the cornea.
- Stroma: A layer composed of parallel collagen fibrils. This layer makes up 90% of the cornea's thickness.
- Descemet's membrane and Endothelium: Are two layers adjusted to the anterior chamber of the eye filled with aqueous humor fluid produced by the ciliary body. This fluid moisturises the lens, cleans it and maintains the pressure in the eye ball. The chamber, positioned between cornea and iris, contains a trabecular meshwork body through which the fluid is drained out by Schlemm canal, through posterior chamber.

The surface of the cornea lies under two protective membranes, called the sclera and Tenon's capsule. Both of these protective layers completely envelop the eyeball. The sclera is built from collagen and elastic fibres, which protect the eye from external damages, this layer also gives rise to the white of the eye. It is pierced by nerves and vessels with the largest hole reserved for the optic nerve. Moreover, it is covered by conjunctiva, which is a clear mucous membrane on the surface of the eyeball. This membrane also lines the inside of the eyelid. It works as a lubricant and, together with the lacrimal gland, it produces tears, that lubricate and protect the eye. The remaining protective layer, the eyelid, also functions to spread this lubricant around.

Moving the eyes – extra-ocular muscles

The eyeball is moved by a complicated muscle structure of extra-ocular muscles consisting of four rectus muscles – inferior, medial, lateral and superior and two oblique – inferior and superior. Positioning of these muscles is presented below, along with functions:



Extra-ocular muscles and other some other components around the eye

1 = Annulus of Zinn – Muscle Attachment
2 = Superior rectus muscle - Elevation (primary function), intorsion (secondary), adduction (tertiary)
3 = Inferior rectus muscle – Depression (primary), extortion (secondary), adduction (tertiary)
4 = Medial rectus muscle – Adduction (primary)
5 = Lateral rectus muscle – Abduction (primary)
6 = Superior oblique muscle – Intorsion (primary), depression (secondary), abduction (tertiary)
7 = Trochlea of superior oblique - Pulley
8 = Inferior oblique muscle – Extortion (primary), elevation (secondary), abduction (tertiary)
9 = Levator palpebrae superioris muscle – Eyelid Movement
10 = Eyelid
11 = Eyeball
12 = Optic nerve

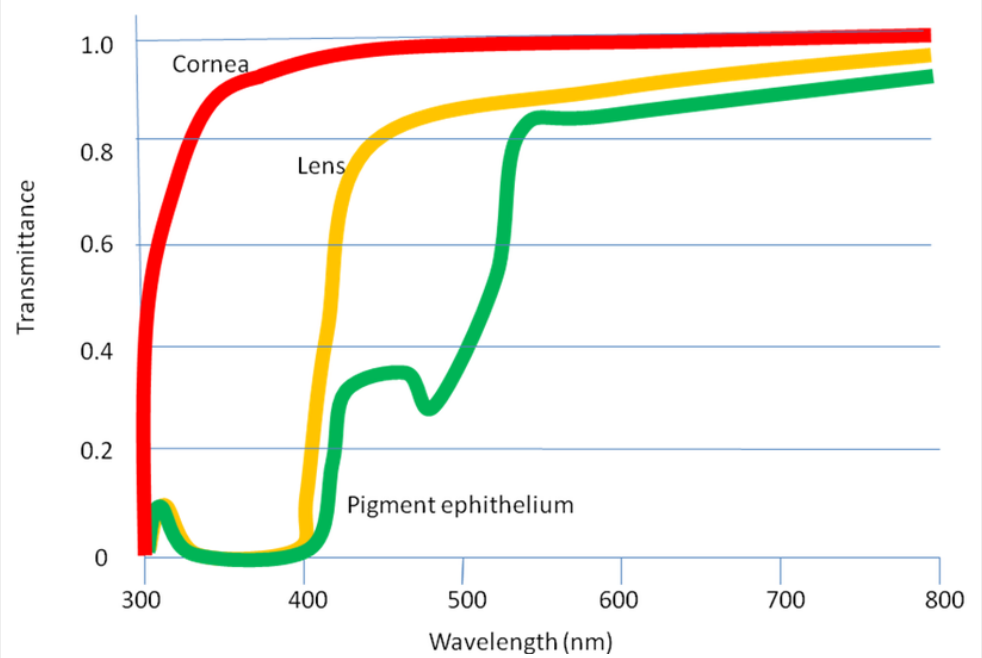
As you can see, the extra-ocular muscles (2,3,4,5,6,8) are attached to the sclera of the eyeball and originate in the annulus of Zinn, a fibrous tendon surrounding the optic nerve. A pulley system is created with the trochlea acting as a pulley and the superior oblique muscle as the rope, this is required to redirect the muscle force in the correct way. The remaining extra-ocular muscles have a direct path to the eye and therefore do not form these pulley systems. Using these extra-ocular muscles, the eye can rotate up, down, left, right and alternative movements are possible as a combination of these.

Other movements are also very important for us to be able to see. Vergence movements enable the proper function of binocular vision. Unconscious fast movements called saccades, are essential for people to keep an object in focus. The saccade is a sort of jittery movement performed when the eyes are scanning the visual field, in order to displace the point of fixation slightly. When you follow a moving object with your gaze, your eyes perform what is referred to as smooth pursuit. Additional involuntary movements called nystagmus are caused by signals from the vestibular system, together they make up the vestibulo-ocular reflexes.

The brain stem controls all of the movements of the eyes, with different areas responsible for different movements.

- Pons: Rapid horizontal movements, such as saccades or nystagmus
- Mesencephalon: Vertical and torsional movements
- Cerebellum: Fine tuning
- Edinger-Westphal nucleus: Vergence movements

Where the vision reception occurs – The retina



Filtering of the light performed by the cornea, lens and pigment epithelium

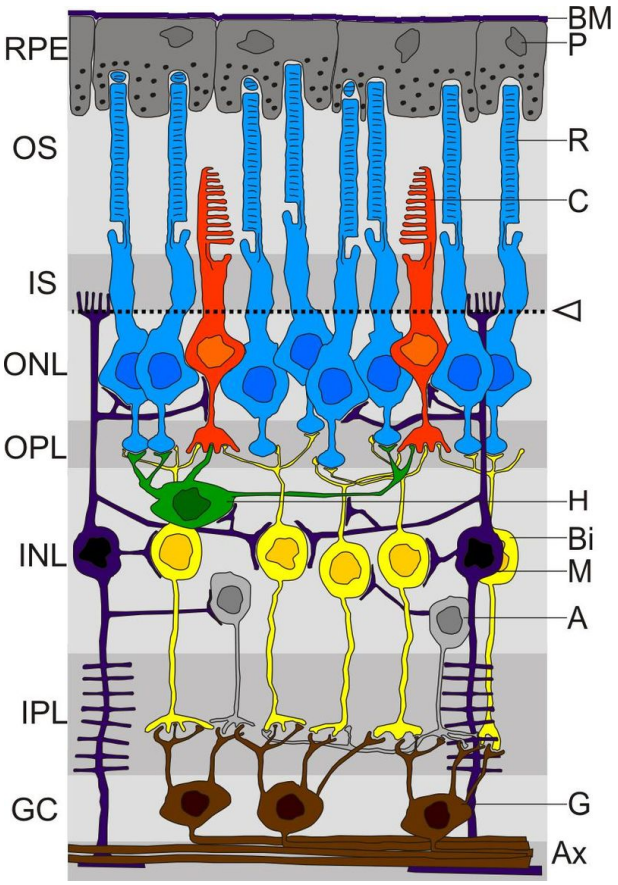
Before being transduced, incoming EM passes through the cornea, lens and the macula. These structures also act as filters to reduce unwanted EM, thereby protecting the eye from harmful radiation. The filtering response of each of these elements can be seen in the figure "Filtering of the light performed by cornea, lens and pigment epithelium". As one may observe, the cornea attenuates the lower wavelengths, leaving the higher wavelengths nearly untouched. The lens blocks around 25% of the EM below 400nm and more than 50% below 430nm. Finally, the pigment ephithelium, the last stage of filtering before the photo-reception, affects around 30% of the EM between 430nm and 500nm.

A part of the eye, which marks the transition from non-photosensitive region to photosensitive region, is called the ora serrata. The photosensitive region is referred to as the retina, which is the sensory structure in the back of the eye. The retina consists of multiple layers presented below with millions of photoreceptors called rods and cones, which capture the light rays and convert them into electrical impulses. Transmission of these impulses is nervously initiaed by the ganglion cells and conducted through the optic nerve, the single route by which information leaves the eye.

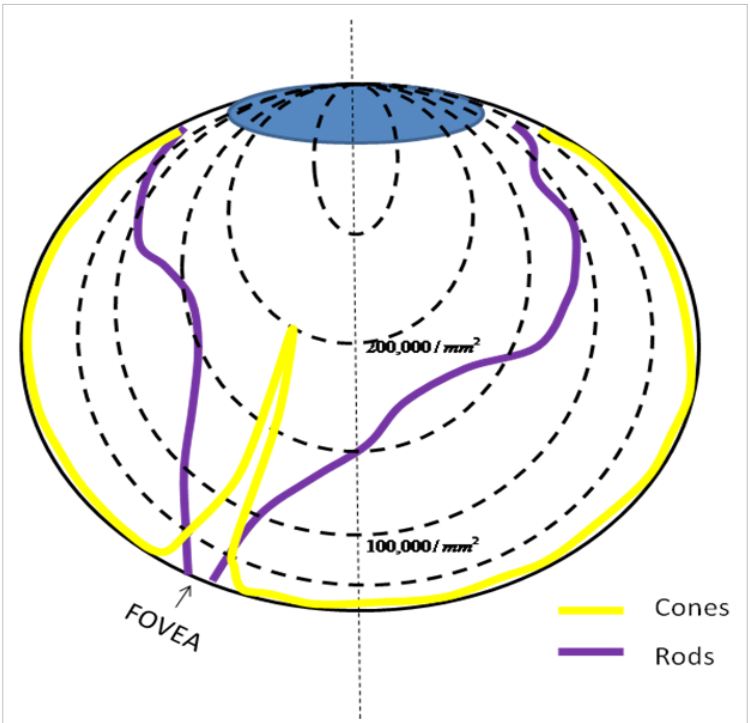
A conceptual illustration of the structure of the retina is shown on the right. As we can see, there are five main cell types:

- photoreceptor cells
- horizontal cells
- bipolar cells
- amecrine cells
- ganglion cells

Photoreceptor cells can be further subdivided into two main types called rods and cones. Cones are much less numerous than rods in most parts of the retina, but there is an enormous aggregation of them in the macula, especially in its central part called the fovea. In this central region, each photo-sensitive cone is connected to one ganglion-cell. In addition, the cones in this region are slightly smaller than the average cone size, meaning you get more cones per area. Because of this ratio, and the high density of cones, this is where we have the highest visual acuity.



Structure of retina including the main cell components: RPE: retinal pigment epithelium; OS: outer segment of the photoreceptor cells; IS: inner segment of the photoreceptor cells; ONL: outer nuclear layer; OPL: outer plexiform layer; INL: inner nuclear layer IPL: inner plexiform layer; GC: ganglion cell layer; P: pigment epithelium cell; BM: Bruch-Membran; R: rods; C: cones; H: horizontal cell; B: bipolar cell; M: Müller cell; A:amacrine cell; G: ganglion cell; AX: Axon; arrow: Membrane limitans externa.



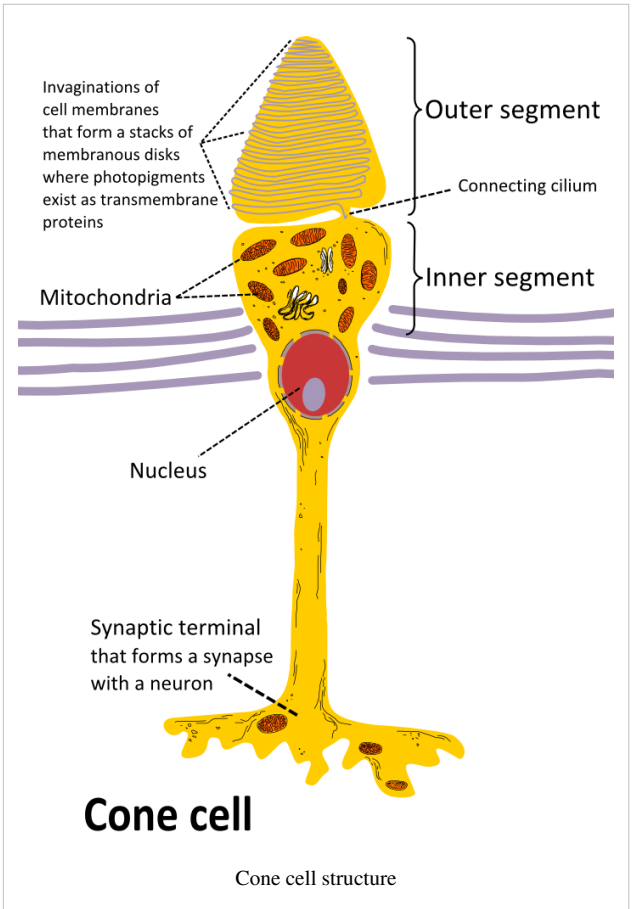
Density of rods and cones around the eye

There are 3 types of human cones, each of the cones responding to a specific range of wavelengths, because of three types of a pigment called photopsin. Each pigment is sensitive to red, blue or green wavelength of light, so we have blue, green and red cones, also called S-, M- and L-cones for their sensitivity to short-, medium- and long-wavelength respectively. It consists of protein called opsin and a bound chromphore called the reinal. The main building blocks of the cone cell are the synaptic terminal, the inner and outer segments, the interior nucleus and the mitochondria.

The spectral sensitivities of the 3 types of cones:

- 1. S-cones absorb short-wave light, i.e. blue-violet light. The maximum absorption wavelength for the S-cones is 420nm
- 2. M-cones absorb blue-green to yellow light. In this case The maximum absorption wavelength is 535nm
- 3. L-cones absorb yellow to red light. The maximum absorption wavelength is 565nm

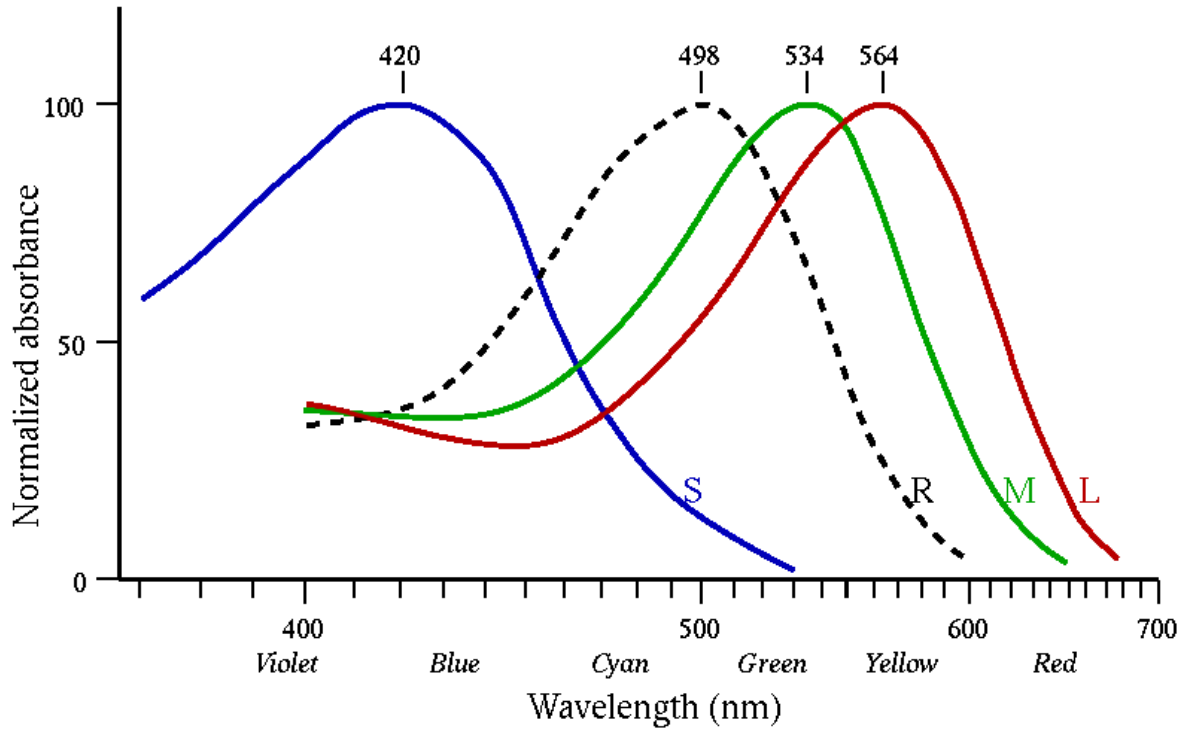
The inner segment contains organelles and the cell's nucleus and organelles. The pigment is located in the outer segment, attached to the membrane as trans-membrane proteins within the invaginations of the cell-membrane that form the membranous disks, which are clearly visible in the figure displaying the basic structure of rod and cone cells. The disks maximize the reception area of the cells. The cone photoreceptors of many vertebrates contain spherical organelles called oil droplets, which are thought to constitute intra-ocular filters which may serve to increase contrast, reduce glare and lessen chromatic aberrations caused by the mitochondrial size gradient from the periphery to the centres.



Cone cell structure

Rods have a structure similar to cones, however they contain the pigment rhodopsin instead, which allows them to detect low-intensity light and makes them 100 times more sensitive than cones. Rhodopsin is the only pigment found in human rods, and it is found on the outer side of the pigment epithelium, which similarly to cones maximizes absorption area by employing a disk structure. Similarly to cones, the synaptic terminal of the cell joins it with a bipolar cell and the inner and outer segments are connected by cilium.

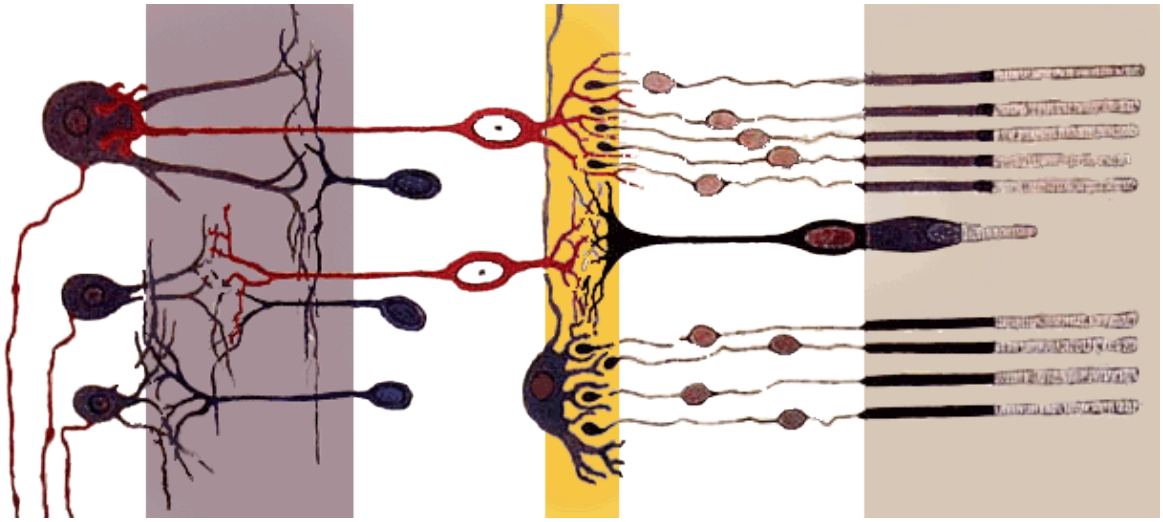
The pigment rhodopsin absorbs the light between 400-600nm, with a maximum absorption at around 500nm. This wavelength corresponds to greenish-blue light which means blue colours appear more intense in relation to red colours at night.



The sensitivity of cones and rods across visible EM

EM waves with wavelengths outside the range of 400 – 700 nm are not detected by either rods nor cones, which ultimately means they are not visible to human beings.

Horizontal cells occupy the inner nuclear layer of the retina. There are two types of horizontal cells and both types hyper-polarise in response to light i.e. they become more negative. Type A consists of a subtype called HII-H2 which interacts with predominantly S-cones. Type B cells have a subtype called HI-H1, which features a dendrite tree and an axon. The former contacts mostly M- and L-cone cells and the latter rod cells. Contacts with cones are made mainly by prohibitory synapses, while the cells themselves are joined into a network with gap junctions.



Cross-section of the human retina, with bipolar cells indicated in red.

Bipolar cells spread single dendrites in the outer plexiform layer and the perikaryon, their cell bodies, are found in the inner nuclear layer. Dendrites interconnect exclusively with cones and rods and we differentiate between one rod bipolar cell and nine or ten cone bipolar cells. These cells branch with amacrine or ganglion cells in the inner

plexiform layer using an axon. Rod bipolar cells connect to triad synapses or 18-70 rod cells. Their axons spread around the inner plexiform layer synaptic terminals, which contain ribbon synapses and contact a pair of cell processes in dyad synapses. They are connected to ganglion cells with AII amacrine cell links.

Amecrine cells can be found in the inner nuclear layer and in the ganglion cell layer of the retina. Occasionally they are found in the inner plexiform layer, where they work as signal modulators. They have been classified as narrow-field, small-field, medium-field or wide-field depending on their size. However, many classifications exist leading to over 40 different types of amecrine cells.

Ganglion cells are the final transmitters of visual signal from the retina to the brain. The most common ganglion cells in the retina is the midget ganglion cell and the parasol ganglion cell. The signal after having passed through all the retinal layers is passed on to these cells which are the final stage of the retinal processing chain. All the information is collected here forwarded to the retinal nerve fibres and optic nerves. The spot where the ganglion axons fuse to create an optic nerve is called the optic disc. This nerve is built mainly from the retinal ganglion axons and Portort cells. The majority of the axons transmit data to the lateral geniculate nucleus, which is a termination nexus for most parts of the nerve and which forwards the information to the visual cortex. Some ganglion cells also react to light, but because this response is slower than that of rods and cones, it is believed to be related to sensing ambient light levels and adjusting the biological clock.

Signal Processing

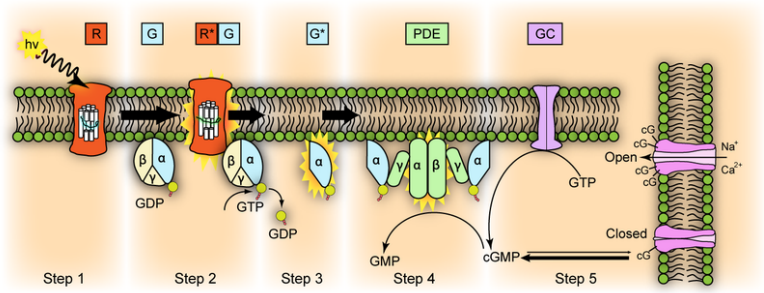
As mentioned before the retina is the main component in the eye, because it contains all the light sensitive cells. Without it, the eye would be comparable to a digital camera without the CCD (Charge Coupled Device) sensor. This part elaborates on how the retina perceives the light, how the optical signal is transmitted to the brain and how the brain processes the signal to form enough information for decision making.

Creation of the initial signals - Photosensor Function

Vision invariably starts with light hitting the photo-sensitive cells found in the retina. Light-absorbing visual pigments, a variety of enzymes and transmitters in retinal rods and cones will initiate the conversion from visible EM stimuli into electrical impulses, in a process known as photoelectric transduction. Using rods as an example, the incoming visible EM hits rhodopsin molecules, transmembrane molecules found in the rods' outer disk structure. Each rhodopsin molecule consists of a cluster of helices called opsin that envelop and surround 11-cis retinal, which is the part of the molecule that will change due to the energy from the incoming photons. In biological molecules, moieties, or parts of molecules that will cause conformational changes due to this energy is sometimes referred to as chromophores. 11-cis retinal straightens in response to the incoming energy, turning into retinal (all-trans retinal), which forces the opsin helices further apart, causing particular reactive sites to be uncovered. This "activated" rhodopsin molecule is sometimes referred to as Metarhodopsin II. From this point on, even if the visible light stimulation stops, the reaction will continue. The Metarhodopsin II can then react with roughly 100 molecules of a G_s protein called transducing, which then results in α_s and $\beta\gamma$ after the GDP is converted into GTP. The activated α_s-GTP then binds to cGMP-phosphodiesterase(PDE), suppressing normal ion-exchange functions, which results in a low cytosol concentration of cation ions, and therefore a change in the polarisation of the cell.

The natural photoelectric transduction reaction has an amazing power of amplification. One single retinal rhodopsin molecule activated by a single quantum of light causes the hydrolysis of up to 10^6 cGMP molecules per second.

Photo Transduction



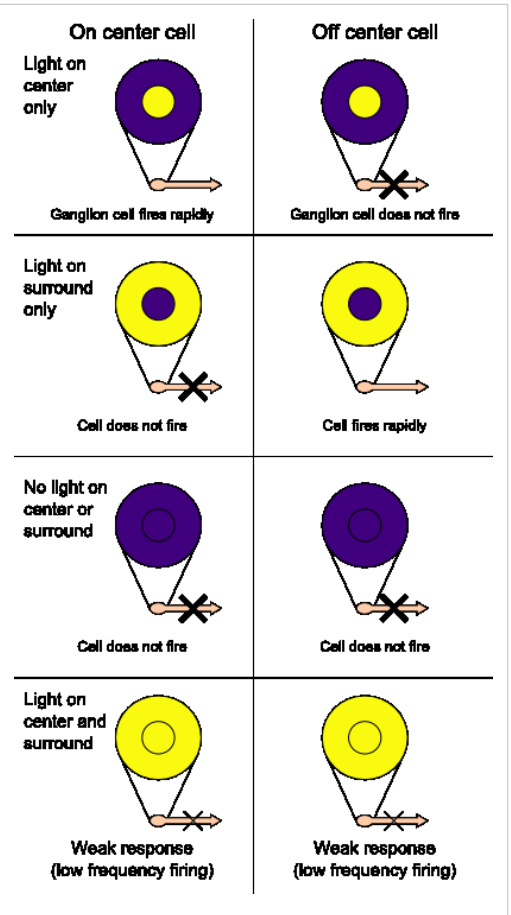
Representation of molecular steps in photoactivation (modified from Leskov et al., 2000). Depicted is an outer membrane disk in a rod. Step 1: Incident photon (hν) is absorbed and activates a rhodopsin by conformational change in the disk membrane to R*. Step 2: Next, R* makes repeated contacts with transducin molecules, catalyzing its activation to G* by the release of bound GDP in exchange for cytoplasmic GTP. The α and γ subunits Step 3: G* binds inhibitory γ subunits of the phosphodiesterase (PDE) activating its α and β subunits. Step 4: Activated PDE hydrolyzes cGMP. Step 5: Guanylyl cyclase (GC) synthesizes cGMP, the second messenger in the phototransduction cascade. Reduced levels of cytosolic cGMP cause cyclic nucleotide gated channels to close preventing further influx of Na+ and Ca2+.

1. A light photon interacts with the retinal in a photoreceptor. The retinal undergoes isomerisation, changing from the 11-*cis* to all-*trans* configuration.
2. Retinal no longer fits into the opsin binding site.
3. Opsin therefore undergoes a conformational change to metarhodopsin II.
4. Metarhodopsin II is unstable and splits, yielding opsin and all-*trans* retinal.
5. The opsin activates the regulatory protein transducin. This causes transducin to dissociate from its bound GDP, and bind GTP, then the alpha subunit of transducin dissociates from the beta and gamma subunits, with the GTP still bound to the alpha subunit.
6. The alpha subunit-GTP complex activates phosphodiesterase.
7. Phosphodiesterase breaks down cGMP to 5'-GMP. This lowers the concentration of cGMP and therefore the sodium channels close.
8. Closure of the sodium channels causes hyperpolarization of the cell due to the ongoing potassium current.
9. Hyperpolarization of the cell causes voltage-gated calcium channels to close.
10. As the calcium level in the photoreceptor cell drops, the amount of the neurotransmitter glutamate that is released by the cell also drops. This is because calcium is required for the glutamate-containing vesicles to fuse with cell membrane and release their contents.
11. A decrease in the amount of glutamate released by the photoreceptors causes depolarization of On center bipolar cells (rod and cone On bipolar cells) and hyperpolarization of cone Off bipolar cells.

Without visible EM stimulation, rod cells containing a cocktail of ions, proteins and other molecules, have membrane potential differences of around -40mV. Compared to other nerve cells, this is quite high (-65mV). In this state, the neurotransmitter glutamate is continuously released from the axon terminals and absorbed by the neighbouring bipolar cells. With incoming visble EM and the previously mentioned cascade reaction, the potential difference drops to -70mV. This hyper-polarisation of the cell causes a reduction in the amount of released glutamate, thereby affecting the activity of the bipolar cells, and subsequently the following steps in the visual pathway.

Similar processes exist in the cone-cells and in photosensitive ganglion cells, but make use of different opsins. Photopsin I through III (yellowish-green, green and blue-violet respectively) are found in the three different cone cells and melanopsin (blue) can be found in the photosensitive ganglion cells.

Processing Signals in the Retina

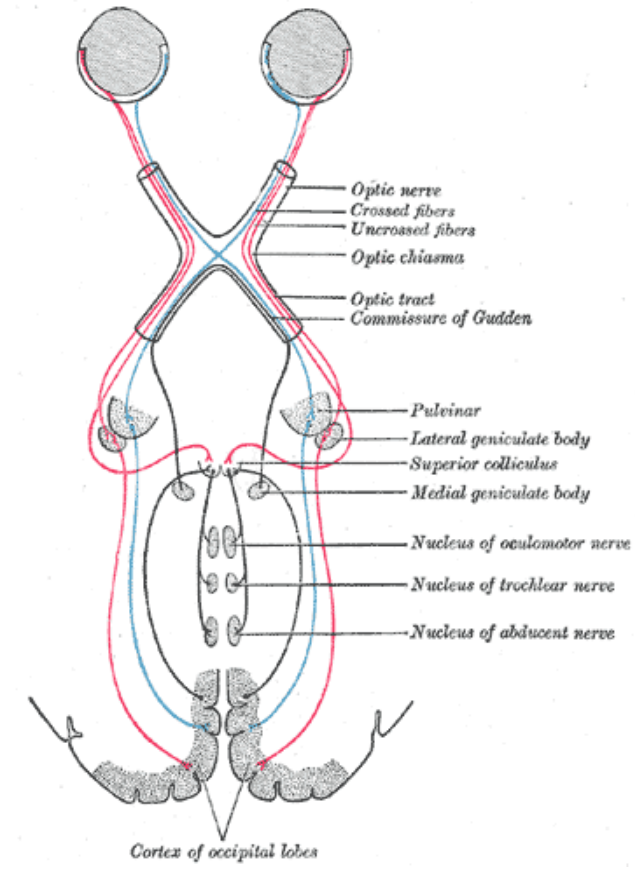


Different bipolar cells react differently to the changes in the released glutamate. The so called ON and OFF bipolar cells are used to form the direct signal flow from cones to bipolar cells. The ON bipolar cells will depolarise by visible EM stimulation and the corresponding ON ganglion cells will be activated. On the other hand the OFF bipolar cells are hyper polarised by the visible EM stimulation, and the OFF ganglion cells are inhibited. This is the basic pathway of the Direct signal flow. The Lateral signal flow will start from the rods, then go to the bipolar cells, the amacrine cells, and the OFF bipolar cells inhibited by the Rod-amacrine cells and the ON bipolar cells will stimulated via an electrical synapse, after all of the previous steps, the signal will arrive at the ON or OFF ganglion cells and the whole pathway of the Lateral signal flow is established.

When the action potential (AP) in ON, ganglion cells will be triggered by the visible EM stimulus. The AP frequency will increase when the sensor potential increases. In other words, AP depends on the amplitude of the sensor's potential. The region of ganglion cells where the stimulatory and inhibitory effects influence the AP frequency is called receptive field (RF). Around the ganglion cells, the RF is usually composed of two regions: the central zone and the ring-like peripheral zone. They are distinguishable during visible EM adaptation. A visible EM stimulation on the centric zone could lead to AP frequency increase and the stimulation on the periphery zone will decrease the AP frequency. When the light source is turned off the excitation occurs. So the name of ON field (central field ON) refers to this kind of region. Of course the RF of the OFF ganglion cells act the opposite way and is therefore called "OFF field" (central field OFF). The RFs are organised by the horizontal cells. The impulse on the periphery region will be impulsed and transmitted to the central region, and there the so-called stimulus contrast is formed. This function will make the dark seem darker and the light brighter. If the whole RF is exposed to light. the impulse of the central region will predominate.

Processing Signals in the Cortex

As mentioned previously, axons of the ganglion cells converge at the optic disk of the retina, forming the optic nerve. These fibres are positioned inside the bundle in a specific order. Fibres from the macular zone of the retina are in the central portion, and those from the temporal half of the retina take up the periphery part. A partial decussation or crossing occurs when these fibres are outside the eye cavity. The fibres from the nasal halves of each retina cross to the opposite halves and extend to the brain. Those from the temporal halves remain uncrossed. This partial crossover is called the optic chiasma, and the optic nerves past this point are called optic tracts, mainly to distinguish them from single-retinal nerves. The function of the partial crossover is to transmit the right-hand visual field produced by both eyes to the left-hand half of the brain only and visa versa. Therefore the information from the right half of the body, and the right visual field, is all transmitted to the left-hand part of the brain when reaches the posterior part of the fore-brain (diencephalon).



The pathway to the central cortex

The information relay between the fibres of optic tracts and the nerve cells occurs in the lateral genuculate bodies, the central part of the visual signal processing, located in the thalamus of the brain. From here the information is passed to the nerve cells in the occipital cortex of the corresponding side of the brain. The dorsal nucleus of the lateral geniculate body is composed of six layers. The crossed fibres go on in layers 1, 4 and 6, and the uncrossed fibres in layers 2, 3 and 5. From here the information from the right and left eye is separated.

Although human vision is combined by two halves of the retina and the signal is processed by the opposite cerebral hemispheres, the visual field is considered as a smooth and complete unit. Hence the two visual cortical areas are thought of as being intimately connected. This connection, called corpus callosum is made of neurons, axons and dendrites. Because the dendrites make synaptic connections to the related points of the hemispheres, electric simulation of every point on one hemisphere indicates simulation of the interconnected point on the other hemisphere. The only exception to this rule is the primary visual cortex.

The synapses are made by the optic tract in the respective layers of the lateral geniculate body. Then these axons of these third-order nerve cells are passed up to the calcarine fissure in each occipital lobe of the cerebral cortex. Because bands of the white fibres and axons pair from the nerve cells in the retina go through it, it is called the striate cortex, which incidentally is our primary visual cortex, sometimes known as V1. At this point, impulses from the separate eyes converge to common cortical neurons, which then enables complete input from both eyes in one region to be used for perception and comprehension. Pattern recognition is a very important function of this particular part of the brain, with lesions causing problems with visual recognition or blindsight.

Based on the ordered manner in which the optic tract fibres pass information to the lateral geniculate bodies and after that pass in to the striate area, if one single point stimulation on the retina was found, the response which produced electrically in both lateral geniculate body and the striate cortex will be found at a small region on the particular retinal spot. This is an obvious point-to-point way of signal processing. And if the whole retina is stimulated, the

responses will occur on both lateral geniculate bodies and the striate cortex gray matter area. It is possible to map this brain region to the retinal fields, or more usually the visual fields.

Any further steps in this pathway is beyond the scope of this book. Rest assured that, many further levels and centres exist, focusing on particular specific tasks, like for example colour, orientations, spatial frequencies, emotions etc.

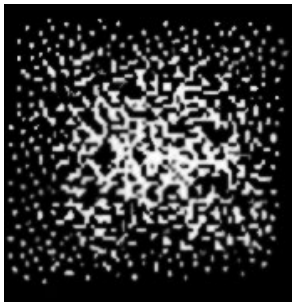
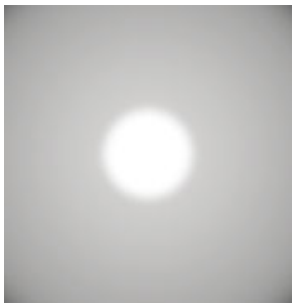
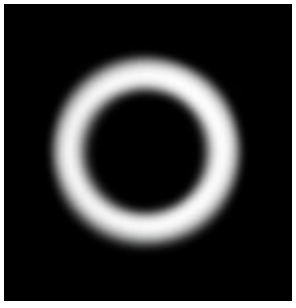
Visual Perception

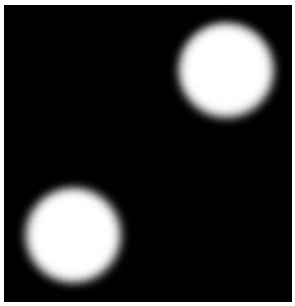
Equipped with a firmer understanding of some of the more important concepts of the signal processing in the visual system, comprehension or perception of the processed sensory information is the last important piece in the puzzle. Visual perception is the process of translating information received by the eyes into an understanding of the external state of things. It makes us aware of the world around us and allows us to understand it better. Based on visual perception we learn patterns which we then apply later in life and we make decisions based on this and the obtained information. In other words, our survival depends on perception.

Simulation of the Visual System

In this section an overview in the simulation of processing done by the early levels of the visual system will be given. The implementation to reproduce the action of the visual system will thereby be done with MATLAB and its toolboxes. The processing done by the early visual system was discussed in the section before and can be put together with some of the functions they perform in the following schematic overview. A good description of the image processing can be found in (Cormack 2000).

Schematic overview of the processing done by the early visual system

Structure	Operations	2D Fourier Plane
World	$I(x, y, t, \lambda)$	
Optics	Low-pass spatial filtering	
Photoreceptor Array	Sampling, more low-pass filtering, temporal lowhandpass filtering, λ filtering, gain control, response compression	
LGN Cells	Spatiotemporal bandpass filtering, λ filtering, multiple parallel representations	

Primary Visual Cortical Neurons: Simple & Complex	Simple cells: orientation, phase, motion, binocular disparity, & λ filtering	
	Complex cells: no phase filtering (contrast energy detection)	

On the left, are some of the major structures to be discussed; in the middle, are some of the major operations done at the associated structure; in the right, are the 2-D Fourier representations of the world, retinal image, and sensitivities typical of a ganglion and cortical cell. (From Handbook of Image and Video Processing, A. Bovik)

As we can see in the above overview different stages of the image processing have to be considered to simulate the response of the visual system to a stimulus. The next section will therefore give a brief discussion in Image Processing. But first of all we will be concerned with the Simulation of Sensory Organ Components.

Simulating Sensory Organ Components

Anatomical Parameters of the Eye

The average eye has an anterior corneal radius of curvature of r_C = 7.8 mm , and an aqueous refractive index of 1.336. The length of the eye is L_E = 24.2 mm. The iris is approximately flat, and the edge of the iris (also called limbus) has a radius r_L = 5.86 mm.

Optics of the Eyeball

The optics of the eyeball are characterized by its 2-D spatial impulse response function, the Point Spread Function (PSF)

$$h(r) = 0.95 \cdot \exp\left(-2.6 \cdot |r|^{1.36}\right) + 0.05 \cdot \exp\left(-2.4 \cdot |r|^{1.74}\right),$$

in which r is the radial distance in minutes of arc from the center of the image.

Practical implementation

Obviously, the effect on a given digital image depends on the distance of that image from your eyes. As a simple place-holder, substitute this filter with a Gaussian filter with height 30, and with a standard deviation of 1.5.

In one dimension, a Gaussian is described by

$$g(x) = a \cdot \exp\left(-\frac{x^2}{2\sigma^2}\right).$$

Activity of Ganglion Cells

Ignoring the

- temporal response
- effect of wavelength (especially for the cones)
- opening of the iris
- sampling and distribution of photo receptors
- bleaching of the photo-pigment

we can approximate the response of ganglion cells with a **Difference of Gaussians** (DOG, Wikipedia [1])

$$f(x;\sigma) = \frac{1}{\sigma_1\sqrt{2\pi}} \exp\left(-\frac{x^2}{2\sigma_1^2}\right) - \frac{1}{\sigma_2\sqrt{2\pi}} \exp\left(-\frac{x^2}{2\sigma_2^2}\right).$$

The values of $\sigma_1$and $\sigma_2$have a ratio of approximately 1:1.6, but vary as a function of eccentricity. For midget cells (or P-cells), the Receptive Field Size (RFS) is approximately

$$RFS \approx 2 \cdot \text{Eccentricity},$$

where the RFS is given in arcmin, and the Eccentricity in mm distance from the center of the fovea (Cormack 2000).

Activity of simple cells in the primary visual cortex (V1)

Again ignoring temporal properties, the activity of simple cells in the primary visual cortex (V1) can be modeled with the use of Gabor filters (Wikipedia [2]). A Gabor filter is a linear filter whose impulse response is defined by a harmonic function (sinusoid) multiplied by a Gaussian function. The Gaussian function causes the amplitude of the harmonic function to diminish away from the origin, but near the origin, the properties of the harmonic function dominate

$$g(x, y; \lambda, \theta, \psi, \sigma, \gamma) = \exp\left(-\frac{x'^2 + \gamma^2 y'^2}{2\sigma^2}\right) \cos\left(2\pi \frac{x'}{\lambda} + \psi\right),$$

where

$$x' = x\cos\theta + y\sin\theta\,,$$

and

$$y' = -x\sin\theta + y\cos\theta\,.$$

In this equation, λ represents the wavelength of the cosine factor, θ represents the orientation of the normal to the parallel stripes of a Gabor function (Wikipedia [3]), ψ is the phase offset, σ is the sigma of the Gaussian envelope and $\gamma$is the spatial aspect ratio, and specifies the ellipticity of the support of the Gabor function.

This is an example implementation in MATLAB:

```
function gb = gabor_fn(sigma,theta,lambda,psi,gamma)

  sigma_x = sigma;
  sigma_y = sigma/gamma;

  % Bounding box
  nstds = 3;
  xmax =
max(abs(nstds*sigma_x*cos(theta)),abs(nstds*sigma_y*sin(theta)));
  xmax = ceil(max(1,xmax));
  ymax =
max(abs(nstds*sigma_x*sin(theta)),abs(nstds*sigma_y*cos(theta)));
  ymax = ceil(max(1,ymax));
  xmin = -xmax;
  ymin = -ymax;
  [x,y] = meshgrid(xmin:xmax,ymin:ymax);

  % Rotation
  x_theta = x*cos(theta) + y*sin(theta);
  y_theta = -x*sin(theta) + y*cos(theta);

  gb = exp(-.5*(x_theta.^2/sigma_x^2+y_theta.^2/sigma_y^2)).*
cos(2*pi/lambda*x_theta+psi);
```

```
end
```

Image Processing

One major technical tool to understand is the way a computer handles images. We have to know how we can edit images and what techniques we have to rearrange images.

Image Representation

Grayscale

For a computer an image is nothing more than a huge amount of little squares. These squares are called "pixel". In a grayscale image, each of this pixel carries a number n, often it holds $0 \leq n \leq 255$. This number n, represents the exactly color of this square in the image. This means, in a grayscale image we can use 256 different grayscales, where 255 means a white spot, and 0 means the square is black. To be honest, we could even use more than 256 different levels of gray. In the mentioned way, every pixels uses exactly 1 byte (or 8 bit) of memory to be saved. (Due to the binary system of a computer it holds: 2^8=256) If you think it is necessary to have more different gray scales in your image, this is not a problem. You just can use more memory to save the picture. But just remember, this could be a hard task for huge images. Further quite often you have the problem that your sensing device (e.g. your monitor) can not show more than this 256 different gray colors.

Colour

Representing a colourful image is only slightly more complicated than the grayscale picture. All you have to know is that the computer works with a additive colour mixture of the three main colors **Red, Green** and **Blue**. This are the so called RGB colours.

Also these images are saved by pixels. But now every pixel has to know 3 values between 0 and 256, for every Color 1 value. So know we have 256^3= 16,777,216 different colours which can be represented. Similar to the grayscale images also here holds, that no color means black, and having all color means white. That means, the colour (0,0,0) is black, whereas (0,0,255) means blue and (255,255,255) is white.

Image Filtering

1D Filter

In many technical applications, we find some primitive basis in which we easily can describe features. In 1 dimensional cases filters are not a big deal, therefore we can use this filters for changing images. The so called "Savitzky- Golay Filter" allows to smooth incoming signals. The filter was described in 1964 by Abraham Savitzky and Marcel J. E. Golay. It is a impulse-respond filter (IR).

For better understanding, lets look at a example. In 1d we usually deal with vectors. One such given vector, we call x and it holds: $\mathbf{x} = (x_1, x_2, \ldots, x_n)\ with\ n\ \in \mathbb{N}$. Our purpose is to smooth that vector x. To do so all we need is another vector $(w) = (w_1, w_2, \ldots, w_m)\ with\ n > m\ \in \mathbb{N}$, this vector we call a weight vector.

With $y(k) = \sum_{i=1}^{m} w(i)x(k-m+i)$ we now have a smoothed vector y. This vector is smoother than the vector before, because we only save the average over a few entries in the vector. These means the newly found vectorentries, depends on some entries right left and right of the entry to smooth. One major drawback of this approach is, the the newly found vector y only has n-m entries instead of n as the original vector x.
Drawing this new vector would lead to the same function as before, just with less amplitude. So no data is lost, but we have less fluctuation.

2D Filter

Going from the 1d case to the 2d case is done by simply make out of vectors matrices. As already mentioned, a gray-level image is for a computer or for a softwaretool as MATLAB nothing more, than a huge matrix filled with natural numbers, often between 0 and 255.

The weight vector is now a weight-matrix. But still we use the filter by adding up different matrix-element-multiplications. $y(n,m) = \sum_{i=1}^{k} \sum_{j=1}^{l} w_{ij} \times x(n-1+i, m-1+j)$

Dilation and Erosion

For linear filters as seen before, it holds that they are commutativ. Cite from wikipedia: "One says that x commutes with y under $*$ if:

$$x * y = y * x$$"

In other words, it does not matter how many and in which sequence different linear filters you use. E.g. if a Savitzky-Golay filter is applied to some date, and then a second Savitzky-Golay filter for calculationg the first derivative, the result is the same if the sequence of filters is reversed. It even holds, that there would have been **one** filter, which does the same as the **two** applied.

In contrast **morphological operations** on an image are non-linear operations and the final result depends on the sequence. If we think of any image, it is defined by pixels with values x_{ij}. Further this image is assumed to be a black-and-white image, so we have

$$x_{ij} = 0 \; or \; 1, \forall i, j$$

To define a morphological operation we have to set a **structural element** SE. As example, a 3x3-Matrix as a part of the image.

The definition of **erosion** E says:

$$E(M) = \begin{cases} 0, \; if \sum_{i,j=0}^{3} (se)_{ij} < 9 \\ 1, \; else \end{cases} , with \; (se)_{ij}, M \in SE \, .$$

So in words, if **any** of the pixels in the structural element M has value 0, the erosion sets the value of M, a specific pixel in M, to zero. Otherwise E(M)=1

And for the **dilation** D it holds, if **any** value in SE is 1, the dilation of M, D(M), is set to 1.

$$D(M) = \begin{cases} 1, \; if \sum_{i,j=0}^{3} (se)_{ij} >= 1 \\ 0, \; else \end{cases} , with \; (se)_{ij}, M \in SE \, .$$

Compositions of Dilation and Erosion: Opening and Closing of Images

There are two compositions of dilation and erosion. One called **opening** the other called **closing**. It holds:

$$\begin{aligned} opening &= dilation \circ erosion \\ closing &= erosion \circ dilation \end{aligned}$$

Prostheses for the Visual System

Visual Implants

A **visual implant** or **visual prosthesis** is a form of neural prosthesis intended to partially restore lost vision or amplify existing vision. It usually takes the form of an externally-worn camera that is attached to a stimulator on the retina, optic nerve, or in the visual cortex, in order to produce perceptions in the visual cortex. A very good review of current approaches, and of the physiological-technical challenges involved, has been written by (Cohen 2007).

Patients

The ability to give sight to a blind person or to amplify existing perception of a person with amblyopia via a visual prosthesis depends on the circumstances surrounding the loss of sight or amblyopia respectively. Candidates for visual prosthetic implants can be patients which have:

- *Retinitis Pigmentosa*, a degeneration of the photo receptors in the retina, the rods and cones.
- *AMD* (Age-related Macula Degeneration), a disease in which abnormal blood vessels grow under the central retina, leak fluid and blood and eventually cause degeneration, and scarring. Nowadays the most common cause of blindness.

Approaches

To date at least 23 different groups are designing visual prostheses. Implants are tried out at different locations of our visual system:

- epiretinal
- subretinal
- suprachoroidal
- optic nerve
- visual cortex

Visual perceptions elicited by electrical stimulation are called "electrophosphenes". With all stimulation options, the effects of eye movements are a problem: stimulation at a constant site on the retina or on the cortex are perceived as moving stimuli when the eyes move!

Epiretinal Implants

Stimulate mainly the ganglion cells.

Advantages:

- Easy access, coming through the vitreous body.

Challenges:

- May stimulate axons, thereby becoming much less specific.

Active research group: e.g. EpiRet (Giessen, Germany).

Subretinal Implants

Already in 1997 implantable microchips containing an array of 5000 silicon microphotodiodes with electrodes were produced ("artificial silicon retina"). But passive subretinal implants may not be successful in generating sufficient current to activate local neurons in the retinal network using ambient light levels; so currently active implants are currently tried out.

Advantages:

- More natural stimulation of the ganglion cells, through direct depolarization of the remaining bipolar cells.

Challenges:

- The wires have to cope with ca. 100'000 eye movements / day.
- The blood supply may be negatively affected (since the implant forms a barrier between the choriocapillaris vasculature and the retina).

Active research group: e.g. IMI (Intelligent Medical Implants, Bonn, Germany).

Suprachoroidal Implants

Advantages:

- Little risk of retinal detachment.
- No occulusion of blood supply.
- Adjacent to the outer retina (i.e. the photo receptors)

Challenges:

- Require higher stimulation currents.

Stimulation of the Optic Nerve

With cuff-electrodes, typically with only a few segments.

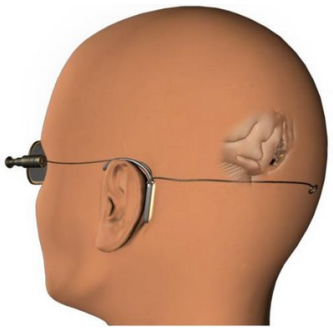
Advantages:

- Little trauma to the eye.

Challenges:

- Not very specific.

Cortical Implants



The Visual Cortical Implant

Dr. Mohamad Sawan [4], Professor and Researcher at Polystim neurotechnologies Laboratory [5] at the Ecole Polytechnique de Montreal, has been working on a visual prosthesis to be implanted into the human cortex. The basic principle of Dr. Sawan's technology consists in stimulating the visual cortex by implanting a silicium microchip on a network of electrodes made of biocompatible materials and in which each electrode injects a stimulating electrical current in order to provoke a series of luminous points to appear (an array of pixels) in the field of vision of the sightless person. This system is composed of two distinct parts: the implant and an external controller. The implant lodged in the visual cortex wirelessly receives dedicated data and energy from the external controller. This implantable part contains all the circuits necessary to generate the electrical stimuli and to oversee the changing microelectrode/biological tissue interface. On the other hand, the battery-operated outer control comprises a micro-camera which captures the image as well as a processor and a command generator which process the imaging data to select and translate the captured images and to generate and

manage the electrical stimulation process and oversee the implant. The external controller and the implant exchange data in both directions by a powerful transcutaneous radio frequency (RF) link. The implant is powered the same way. (Wikipedia [6])

Advantages:

- Much larger area for stimulation: 2° radius of the central retinal visual field correspond to 1 mm^2 on the retina, but to 2100 mm^2 in the visual cortex.

Challenges:

- Implantation is more invasive.
- Parts of the visual field lie in a sulcus and are very hard to reach.
- Stimulation can trigger seizures.

References

[1] http://en.wikipedia.org/wiki/Difference_of_gaussians
[2] http://en.wikipedia.org/wiki/Gabor_filter
[3] http://en.wikipedia.org/wiki/Gabor_function
[4] http://www.polymtl.ca/recherche/rc/en/professeurs/details.php?NoProf=108/
[5] http://www.polystim.ca/
[6] http://en.wikipedia.org/wiki/Visual_prosthesis

Auditory System

Biological Machines/Sensory Systems/Auditory System

Introduction

The sensory system for the sense of hearing is the auditory system. The ability to hear is not found as widely in the animal kingdom as other senses like touch, taste and smell. It is restricted mainly to vertebrates and insects. Within these, mammals and birds have the most highly developed sense of hearing. The table below shows frequency ranges of humans and some selected animals:

Humans	20-20'000 Hz
Whales	20-100'000 Hz
Bats	1'500-100'000 Hz
Fish	20-3'000 Hz

Mother and child

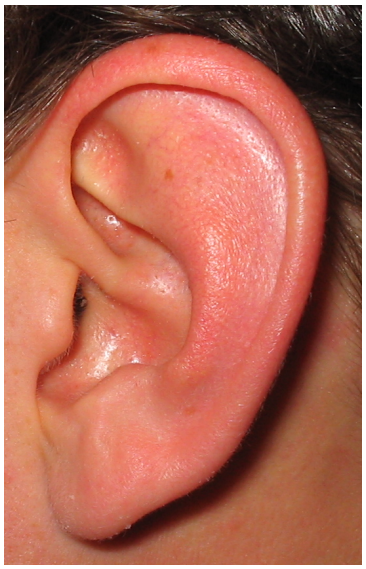
Humpback whales in the singing position

Big eared townsend bat

Hyphessobrycon pulchripinnis fish

Sensory Organs

The organ that detects sound is the ear. It acts as receiver in the process of collecting acoustic information and passing it through the nervous system into the brain. The ear includes structures for both the sense of hearing and the sense of balance. It does not only play an important role as part of the auditory system in order to receive sound but also in the sense of balance and body position.



Human (external) ear

Humans have a pair of ears placed symmetrically on both sides of the head which makes it possible to localize sound sources. The brain extracts and processes different forms of data in order to localize sound, such as:

- the shape of the sound spectrum at the tympanic membrane (eardrum)
- the difference in sound intensity between the left and the right ear
- the difference in time-of-arrival between the left and the right ear
- the difference in time-of-arrival between reflections of the ear itself (this means in other words: the shape of the pinna (pattern of folds and ridges) captures sound-waves in a way that helps localizing the sound source, especially on the vertical axis.

Healthy, young humans are able to hear sounds over a frequency range from 20 Hz to 20 kHz. We are most sensitive to frequencies between 2000 to 4000 Hz which is the frequency range of spoken words. The frequency resolution is 0.2% which means that one can distinguish between a tone of 1000 Hz and 1002 Hz. A sound at 1 kHz can be detected if it deflects the tympanic membrane (eardrum) by less than 1 Angstrom, which is less than the diameter of a hydrogen atom. This extreme sensitivity of the ear may explain, why it contains the smallest bone that exists inside a human body: the stapes (stirrup). It is 0.25 to 0.33 cm long and weighs between 1.9 and 4.3 mg.

Sensory Organ Components

The aim of this section is to explain the anatomy of the auditory system of humans. The chapter illustrates the composition of auditory organs in the sequence that acoustic information proceeds during sound perception.
Please note that the core information for “Sensory Organ Components” can also be found on the Wikipedia page “Auditory system”, excluding some changes like extensions and specifications made in this article. (see also: Wikipedia Auditory system [1])

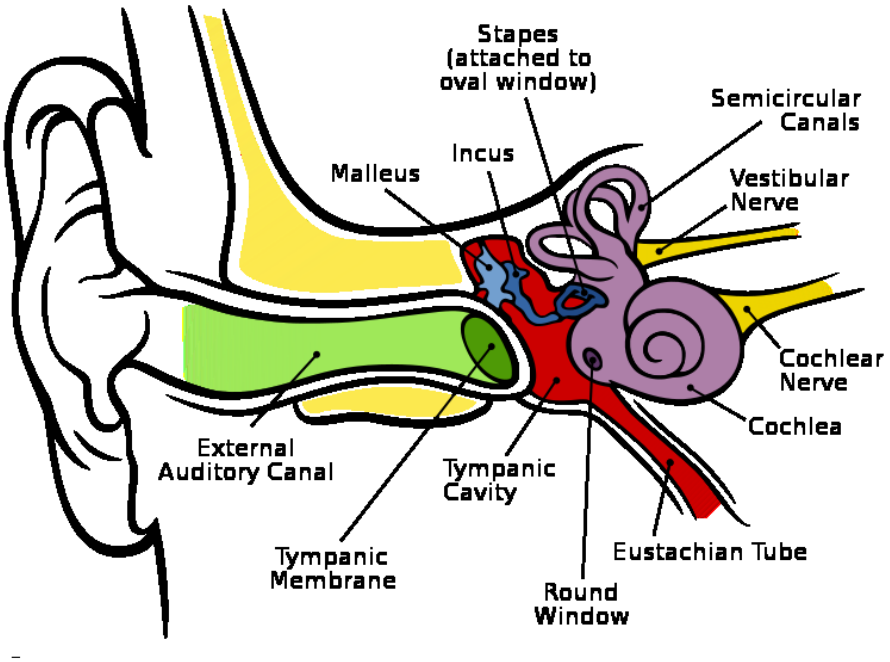
The auditory system senses sound waves, that are changes in air pressure, and converts these changes into electrical signals. These signals can then be processed, analyzed and interpreted by the brain. The pathways and conversion of the signals is treated more precisely in "Physiology of the Auditory System". For the moment, let's focus on the structure and components of the auditory system. The auditory system consists mainly of two parts:

- the ear and
- the auditory nervous system (central auditory system)

The ear

The ear is the organ where the first processing of sound occurs and where the sensory receptors are located. It consists of three parts:

- outer ear
- middle ear
- inner ear



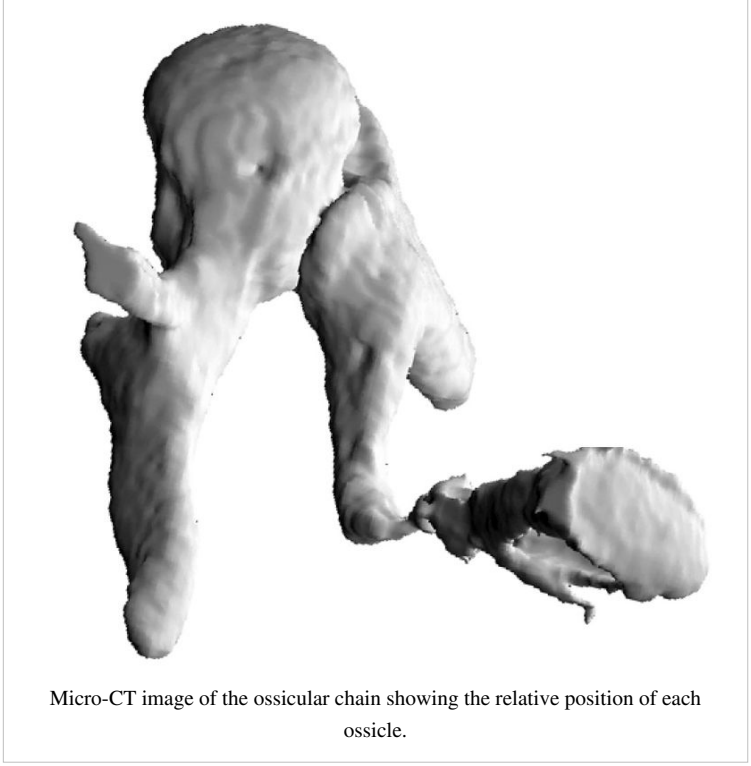
Anatomy of the human ear (green: outer ear / red: middle ear / purple: inner ear)

Outer ear

Function: Gathering sound energy and amplification of sound pressure.

The folds of cartilage surrounding the ear canal (external auditory meatus, external acoustic meatus) are called the pinna. It is the visible part of the ear. Sound waves are reflected and attenuated when they hit the pinna, and these changes provide additional information that will help the brain determine the direction from which the sounds came. The sound waves enter the auditory canal, a deceptively simple tube. The ear canal amplifies sounds that are between 3 and 12 kHz. At the far end of the ear canal is the tympanic membrane (eardrum), which marks the beginning of the middle ear.

Middle ear

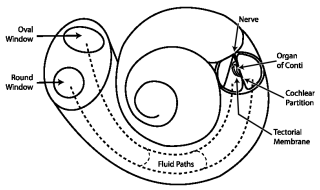
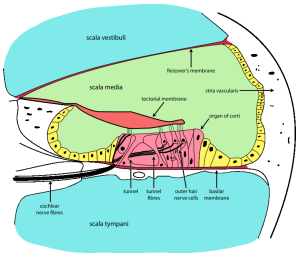


Micro-CT image of the ossicular chain showing the relative position of each ossicle.

Function: Transmission of acoustic energy from air to the cochlea.

Sound waves traveling through the ear canal will hit the tympanic membrane (tympanum, eardrum). This wave information travels across the air-filled tympanic cavity (middle ear cavity) via a series of bones: the malleus (hammer), incus (anvil) and stapes (stirrup). These ossicles act as a lever and a teletype, converting the lower-pressure eardrum sound vibrations into higher-pressure sound vibrations at another, smaller membrane called the oval (or elliptical) window, which is one of two openings into the cochlea of the inner ear. The second opening is called round window. It allows the fluid in the cochlea to move. The malleus articulates with the tympanic membrane via the manubrium, whereas the stapes articulates with the oval window via its footplate. Higher pressure is necessary because the inner ear beyond the oval window contains liquid rather than air. The sound is not amplified uniformly across the ossicular chain. The stapedius reflex of the middle ear muscles helps protect the inner ear from damage. The middle ear still contains the sound information in wave form; it is converted to nerve impulses in the cochlea.

Inner ear

Structural diagram of the cochlea	Cross section of the cochlea
	

Function: Transformation of mechanical waves (sound) into electric signals (neural signals).

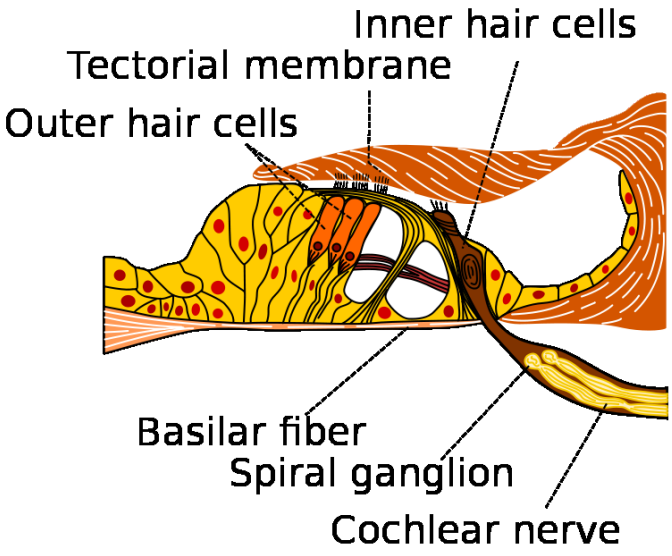
The inner ear consists of the cochlea and several non-auditory structures. The cochlea is a snail-shaped part of the inner ear. It has three fluid-filled sections: scala tympani (lower gallery), scala media (middle gallery, cochlear duct) and scala vestibuli (upper gallery). The cochlea supports a fluid wave driven by pressure across the basilar membrane separating two of the sections (scala tympani and scala media). The basilar membrane is about 3 cm long and between 0.5 to 0.04 mm wide. Reissner's membrane (vestibular membrane) separates scala media and scala vestibuli. Strikingly, one section, the scala media, contains an extracellular fluid similar in composition to endolymph, which is usually found inside of cells. The organ of Corti is located in this duct, and transforms mechanical waves to electric signals in neurons. The other two sections, scala tympani and scala vestibuli, are located within the bony labyrinth which is filled with fluid called perilymph. The chemical difference between the

two fluids endolymph (in scala media) and perilymph (in scala tympani and scala vestibuli) is important for the function of the inner ear.

Organ of Corti

The organ of Corti forms a ribbon of sensory epithelium which runs lengthwise down the entire cochlea. The hair cells of the organ of Corti transform the fluid waves into nerve signals. The journey of a billion nerves begins with this first step; from here further processing leads to a series of auditory reactions and sensations.

Transition from ear to auditory nervous system



Section through the spiral organ of Corti

Hair cells

Hair cells are columnar cells, each with a bundle of 100-200 specialized cilia at the top, for which they are named. These cilia are the mechanosensors for hearing. The shorter ones are called stereocilia, and the longest one at the end of each haircell bundlekinocilium. The location of the kinocilium determines the on-direction, i.e. the direction of deflection inducing the maximum hair cell excitation. Lightly resting atop the longest cilia is the tectorial membrane, which moves back and forth with each cycle of sound, tilting the cilia and allowing electric current into the hair cell.

The function of hair cells is not fully established up to now. Currently, the knowledge of the function of hair cells allows to replace the cells by cochlear implants in case of hearing lost. However, more research into the function of the hair cells may someday even make it possible for the cells to be repaired. The current model is that cilia are attached to one another by “tip links”, structures which link the tips of one cilium to another. Stretching and compressing, the tip links then open an ion channel and produce the receptor potential in the hair cell. Note that a deflection of 100 micrometers already elicits 90% of the full receptor potential.

Neurons

The nervous system distinguishes between nerve fibres carrying information *towards* the central nervous system and nerve fibres carrying the information *away* from it:

- *Afferent neurons* (also sensory or receptor neurons) carry nerve impulses from receptors (sense organs) *towards* the central nervous system
- *Efferent neurons* (also motor or effector neurons) carry nerve impulses *away* from the central nervous system to effectors such as muscles or glands (and also the ciliated cells of the inner ear)

Afferent neurons innervate cochlear inner hair cells, at synapses where the neurotransmitter glutamate communicates signals from the hair cells to the dendrites of the primary auditory neurons. There are far fewer inner hair cells in the cochlea than afferent nerve fibers. The neural dendrites belong to neurons of the auditory nerve, which in turn joins the vestibular nerve to form the vestibulocochlear nerve, or cranial nerve number VIII.

Efferent projections from the brain to the cochlea also play a role in the perception of sound. Efferent synapses occur

on outer hair cells and on afferent (towards the brain) dendrites under inner hair cells.

Auditory nervous system

The sound information, now re-encoded in form of electric signals, travels down the auditory nerve (acoustic nerve, vestibulocochlear nerve, VIIIth cranial nerve), through intermediate stations such as the cochlear nuclei and superior olivary complex of the brainstem and the inferior colliculus of the midbrain, being further processed at each waypoint. The information eventually reaches the thalamus, and from there it is relayed to the cortex. In the human brain, the primary auditory cortex is located in the temporal lobe.

Primary auditory cortex

The primary auditory cortex is the first region of cerebral cortex to receive auditory input. Perception of sound is associated with the right posterior superior temporal gyrus (STG). The superior temporal gyrus contains several important structures of the brain, including Brodmann areas 41 and 42, marking the location of the primary auditory cortex, the cortical region responsible for the sensation of basic characteristics of sound such as pitch and rhythm. The auditory association area is located within the temporal lobe of the brain, in an area called the Wernicke's area, or area 22. This area, near the lateral cerebral sulcus, is an important region for the processing of acoustic signals so that they can be distinguished as speech, music, or noise.

Physiology of the Auditory System

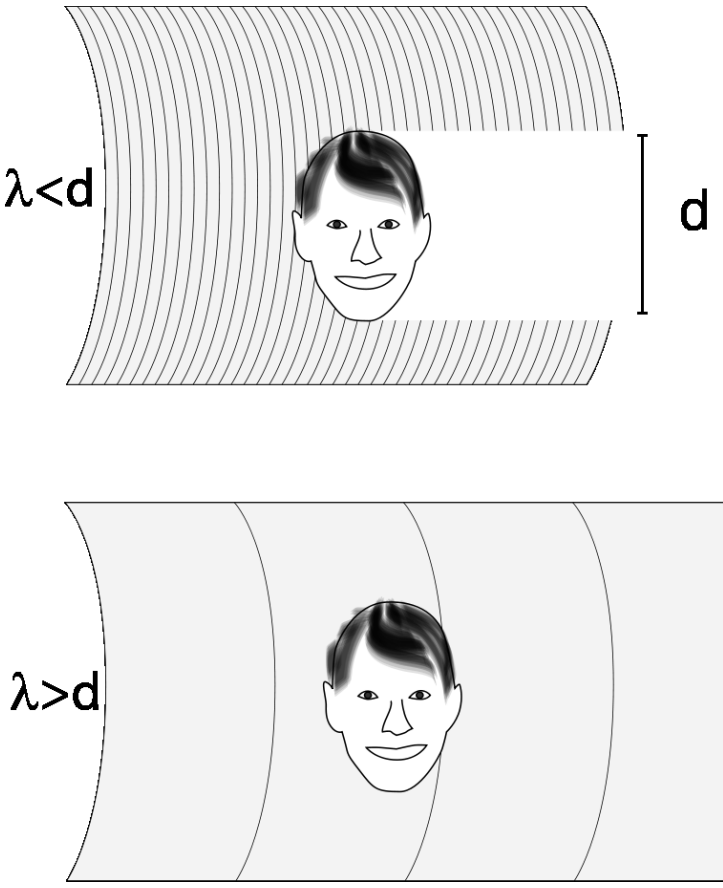
Now that the anatomy of the auditory system has been sketched out, this topic goes deeper into the physiological processes which take place while perceiving acoustic information and converting this information into data that can be handled by the brain.

Effect of the head

Sound waves with a wavelength shorter than the head produce a sound shadow on the ear further away from the sound source. When the wavelength is shorter than the head, diffraction of the sound leads to approximately equal sound intensities on both ears.

Sound reception at the pinna

The pinna collects sound waves in air affecting sound coming from behind and the front differently with its corrugated shape. Sound is then further modified by the outer ear canal. It acts as resonator amplifying the incoming frequencies.



Difference in loudness and timing help us to localize the source of a sound signal.

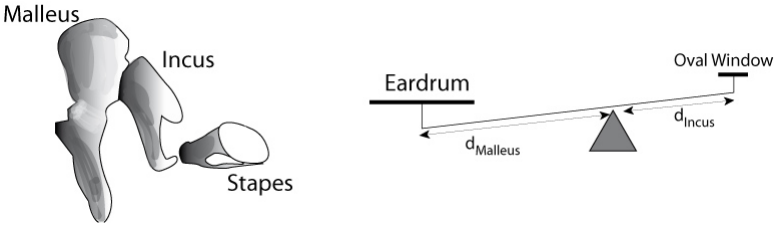
Sound conduction to the cochlea

Sound that entered the pinna in form of waves travels along the auditory canal until it reaches the beginning of the middle ear marked by the tympanic membrane (eardrum). Since the inner ear is filled with fluid, the middle ear is kind of an impedance matching device in order to solve the problem of sound energy reflection on the transition from air to the fluid. As an example, on the transition from air to water 99.9% of the incoming sound energy is reflected. This can be calculated using:

$$\frac{I_r}{I_i} = \left(\frac{Z_2 - Z_1}{Z_2 + Z_1}\right)^2$$

with I_r the intensity of the reflected sound, I_i the intensity of the incoming sound and Z_k the wave resistance of the two media (Z_{air} = 414 kg m^{-2} s^{-1} and Z_{water} = 1.48*10^6 kg m^{-2} s^{-1}). Three factors that contribute the impedance matching are:

- the relative size difference between tympanum and oval window
- the lever effect of the middle ear ossicles and
- the shape of the tympanum.



Mechanics of the amplification effect of the middle ear.

The longitudinal changes in air pressure of the sound-wave cause the tympanic membrane to vibrate which, in turn, makes the three chained ossicles malleus, incus and stirrup oscillate synchronously. These bones vibrate as a unit, elevating the energy from the tympanic membrane to the oval window. In addition, the energy of sound is further enhanced by the areal difference between the membrane and the stapes footplate. The middle ear acts as an impedance transformer by changing the sound energy collected by the tympanic membrane into greater force and less excursion. This mechanism facilitates transmission of sound-waves

in air into vibrations of the fluid in the cochlea. The transformation results from the pistonlike in- and out-motion by the footplate of the stapes which is located in the oval window. This movement performed by the footplate sets the fluid in the cochlea into motion.

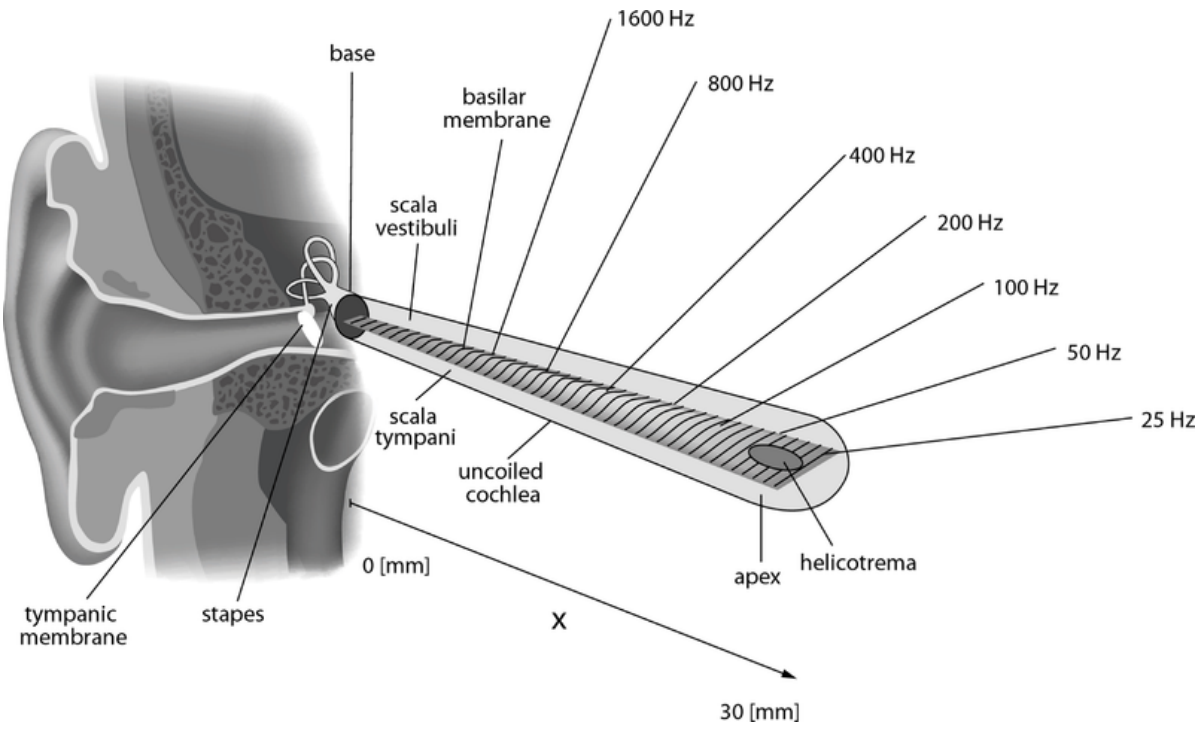
Frequency analysis in the cochlea

The three fluid-filled compartements of the cochlea (scala vestibuli, scala media, scala tympani) are separated by the basilar membrane and the Reissner's membrane. The function of the cochlea is to separate sounds according to their spectrum and transform it into a neural code. When the footplate of the stapes pushes into the perilymph of the scala vestibuli, as a consequence the membrane of Reissner bends into the scala media. This elongation of Reissner's membrane causes the endolymph to move within the scala media and induces a displacement of the basilar membrane. The separation of the sound frequencies in the cochlea is due to the special properties of the basilar membrane. The fluid in the cochlea vibrates (due to in- and out-motion of the stapes footplate) setting the membrane in motion like a traveling wave. The wave starts at the base and progresses towards the apex of the cochlea. The transversal waves in the basilar membrane propagate with

$$c_{trans} = \sqrt{\frac{\mu}{\rho}}$$

with μ the shear modulus and ρ the density of the material. Since width and tension of the basilar membrane change, the speed of the waves propagating along the membrane changes from about 100 m/s near the oval window to 10 m/s near the apex.

There is a point along the basilar membrane where the amplitude of the wave decreases abruptly. At this point, the sound wave in the cochlear fluid produces the maximal displacement (peak amplitude) of the basilar membrane. The distance the wave travels before getting to that characteristic point depends on the frequency of the incoming sound. Therefore each point of the basilar membrane corresponds to a specific value of the stimulating frequency. A low-frequency sound travels a longer distance than a high-frequency sound before it reaches its characteristic point. Frequencies are scaled along the basilar membrane with high frequencies at the base and low frequencies at the apex of the cochlea.



The position x of the maximal amplitude of the travelling wave corresponds in a 1-to-1 way to a stimulus frequency.

Sensory transduction in the cochlea

The sensory cells of the auditory system, known as hair cells, are located along the basilar membrane within the organ of Corti. The human cochlea has about 30'000 such cells. There are two anatomically and functionally distinct types of hair cells: the inner and the outer hair cells. Along the basilar membrane these two types are arranged in one row of inner cells and three to five rows of outer cells. Most of the afferent innervation comes from the inner hair cells while most of the efferent innervation goes to the outer hair cells. The inner hair cells influence the discharge rate of the individual auditory nerve fibres that connect to these hair cells. Therefore inner hair cells transfer sound information to higher auditory nervous centers. The outer hair cells, in contrast, amplify the movement of the basilar membrane by injecting energy into the motion of the membrane and reducing frictional losses but do not contribute in transmitting sound information. The motion of the basilar membrane deflects the stereocilias (hairs on the hair cells) and causes the intracellular potentials of the hair cells to decrease (depolarization) or increase (hyperpolarization), depending on the direction of the deflection. When the stereocilias are in a resting position, there is a steady state current flowing through the channels of the cells. The movement of the stereocilias therefore modulates the current flow around that steady state current.

Lets look at the modes of action of the two different hair cell types separately:

- Inner hair cells:

The deflection of the hair-cell stereocilia opens mechanically gated ion channels that allow small, positively charged potassium ions (K^+) to enter the cell and causing it to depolarize. Unlike many other electrically active cells, the hair cell itself does not fire an action potential. Instead, the influx of positive ions from the endolymph in scala media depolarizes the cell, resulting in a receptor potential. This receptor potential opens voltage gated calcium channels; calcium ions (Ca^{2+}) then enter the cell and trigger the release of neurotransmitters at the basal end of the cell. The neurotransmitters diffuse across the narrow space between the hair cell and a nerve terminal, where they then bind to receptors and thus trigger action potentials in the nerve. In this way, neurotransmitter increases the firing rate in the VIIIth cranial nerve and the mechanical sound signal is converted into an electrical nerve signal.
The repolarization in the hair cell is done in a special manner. The perilymph in Scala tympani has a very low concentration of positive ions. The electrochemical gradient makes the positive ions flow through channels to the perilymph. (see also: Wikipedia Hair cell [2])

- Outer hair cells:

In humans outer hair cells, the receptor potential triggers active vibrations of the cell body. This mechanical response to electrical signals is termed somatic electromotility and drives oscillations in the cell's length, which occur at the frequency of the incoming sound and provide mechanical feedback amplification. Outer hair cells have evolved only in mammals. Without functioning outer hair cells the sensitivity decreases by approximately 50 dB (due to greater frictional losses in the basilar membrane which would damp the motion of the membrane). They have also improved frequency selectivity (frequency discrimination), which is of particular benefit for humans, because it enables sophisticated speech and music. (see also: Wikipedia Hair cell [2])

With no external stimulation, auditory nerve fibres discharge action potentials in a random time sequence. This random time firing is called spontaneous activity. The spontaneous discharge rates of the fibers vary from very slow rates to rates of up to 100 per second. Fibers are placed into three groups depending on whether they fire spontaneously at high, medium or low rates. Fibers with high spontaneous rates (> 18 per second) tend to be more sensitive to sound stimulation than other fibers.

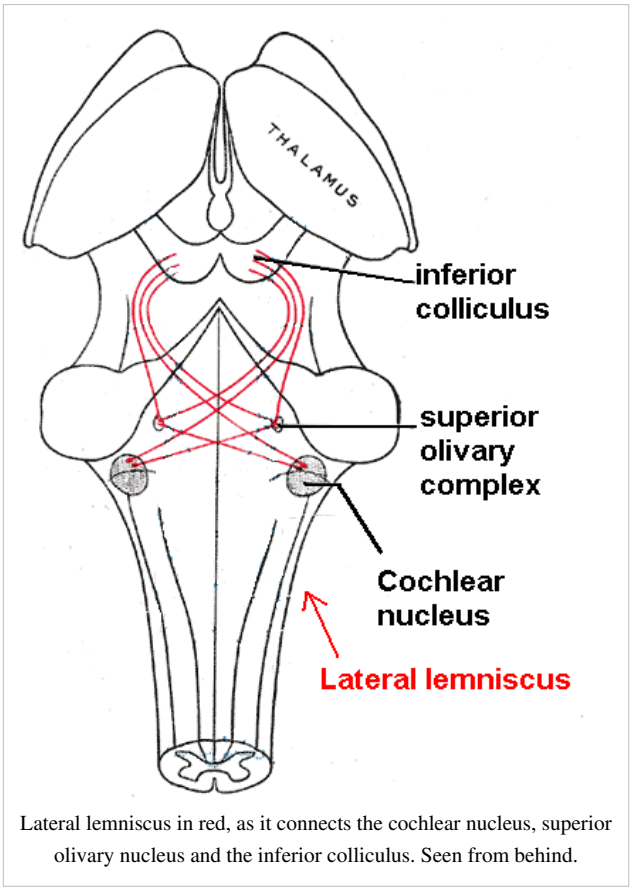
Auditory pathway of nerve impulses

So in the inner hair cells the mechanical sound signal is finally converted into electrical nerve signals. The inner hair cells are connected to auditory nerve fibres whose nuclei form the spiral ganglion. In the spiral ganglion the electrical signals (electrical spikes, action potentials) are generated and transmitted along the cochlear branch of the auditory nerve (VIIIth cranial nerve) to the cochlear nucleus in the brainstem.

From there, the auditory information is divided into at least two streams:

- Ventral Cochlear Nucleus:

One stream is the ventral cochlear nucleus which is split further into the posteroventral cochlear nucleus (PVCN) and the anteroventral cochlear nucleus (AVCN). The ventral cochlear nucleus cells project to a collection of nuclei called the superior olivary complex. There, the differences in time and loudness of the sound information in each ear are compared. Differences in sound intensity are processed in cells of the lateral superior olivary complex and timing differences (runtime delays) in the medial superior olivary complex. This comparison of sound information from both ears allows the determination of the direction where the sound came from. The superior olive is the first node where signals from both ears come together and can be compared. As a next step, the superior olivary complex sends information up to the inferior colliculus via a tract of axons called lateral lemniscus. The function of the inferior colliculus is to integrate information before sending it to the thalamus and the auditory cortex. It is interesting to know that the *superior* colliculus close by shows an interaction of auditory and visual stimuli.



Lateral lemniscus in red, as it connects the cochlear nucleus, superior olivary nucleus and the inferior colliculus. Seen from behind.

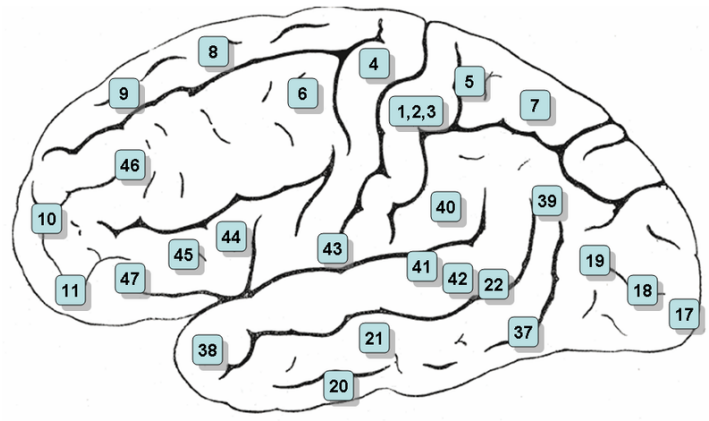
- Dorsal Cochlear Nucleus:

The dorsal cochlear nucleus (DCN) analyzes the quality of sound and projects directly via the lateral lemnisucs to the inferior colliculus.

From the inferior colliculus the auditory information from ventral as well as dorsal cochlear nucleus proceeds to the auditory nucleus of the thalamus which is the medial geniculate nucleus. The medial geniculate nucleus further transfers information to the primary auditory cortex, the region of the human brain that is responsible for processing of auditory information, located on the temporal lobe. The primary auditory cortex is the first relay involved in the conscious perception of sound.

Processing of sound information beyond the primary auditory cortex

Sound information that reaches the primary auditory cortex (Brodmann areas 41 and 42) is further passed to higher order auditory areas. Sounds that are words are processed by Wernicke's area (Brodmann area 22). This area is involved in understanding written and spoken language (verbal understanding). The production of sound (verbal expression) is linked to Broca's area (Brodmann areas 44 and 45). The muscles to produce the required sound when speaking are contracted by the facial area of motor cortex which are regions of the cerebral cortex that are involved in planning, controlling and executing voluntary motor functions.



Lateral surface of the brain with Brodmann's areas numbered.

Signal Processing

Hearing starts with pressure waves hitting the auditory canal and is finally perceived by the brain. This section details the process transforming vibrations into perception.

Outer and middle ear: Gating, reflection, attenuation and amplification

When hitting the pinna, the sound waves are reflected and attenuated or amplified. These changes will later help sound localization. In the external auditory canal, sounds between 3 and 12 kHz - a range crucial for human communication - are amplified. The middle ear has a gating function, it can protect the inner ear from damage through loud sounds.

Basilar membrane: Frequency splitting, loudness encoding

Most everyday sounds are composed of multiple frequencies. The brain processes the distinct frequencies, not the complete sounds. Due to its inhomogeneous properties, the basilar membrane is performing an approximation to a Fourier transform. The sound is thereby split into its different frequencies, and each hair cell on the membrane corresponds to a certain frequency. The loudness of the frequencies is encoded by the firing rate of the corresponding afferent fibre. This is due to the amplitude of the traveling wave on the basilar membrane, which depends on the loudness of the incoming sound.

Superior olivary complex: Sound localization

The superior olivary complex - a small mass of gray substance - is believed to be involved in the localization of sounds in the azimuthal plane (i.e. their degree to the left or the right). There are two major cues to sound localization: Interaural level differences (ILD) and interaural time differences (ITD). The ILD measures differences in sound intensity between the ears. This works for high frequencies (over 1.6 kHz), where the wavelength is shorter than the distance between the ears, causing a head shadow - which means that high frequency sounds hit the averted ear with lower intensity. Lower frequency sounds don't cast a shadow, since they wrap around the head. However, due to the wavelength being larger than the distance between the ears, there is a phase difference between the sound waves entering the ears - the timing difference measured by the ITD. This works very precisely for frequencies below 800 Hz, where the ear distance is smaller than half of the wavelength. Sound localization in the median plane (front, above, back, below) is helped through the outer ear, which forms direction-selective filters.

Primary auditory cortex and higher order auditory areas: Sound perception

The primary auditory cortex is the first relay involved in the conscious perception of sound. It is known to be tonotopically organized and performs the basics of hearing: pitch and volume. Depending on the nature of the sound (speech, music, noise), it will then be further processed by different areas in the brain.

Human Speech and Hearing Loss

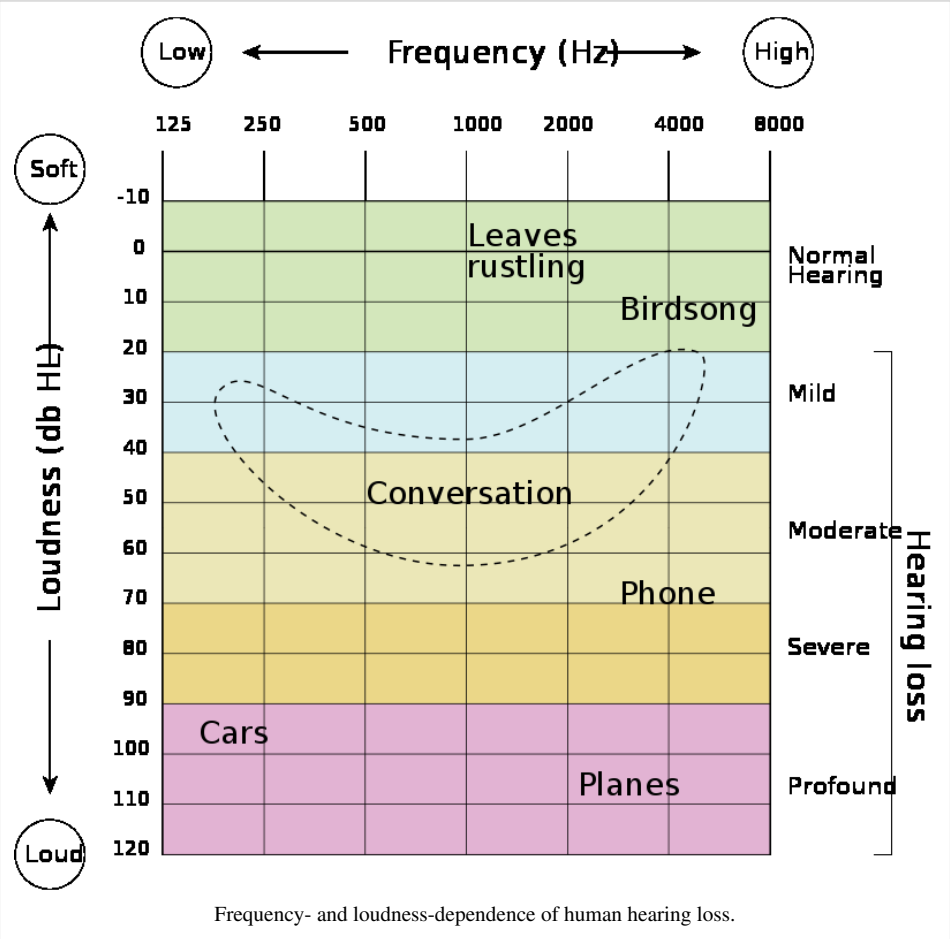
The intensity of sound is typically expressed in deciBel (dB), defined as

$$SPL = 20 * log\frac{p}{p_0}$$

where SPL = "sound pressure level" (in dB), and the reference pressure is $p_0 = 2x10^{-5} N/m^2$. Note that this is much smaller than the air pressure (ca. 105 N/m^2)! Also watch out, because sound is often expressed relative to "Hearing Level" instead of SPL.

- 0 - 20 dB SPL ... hearing level (0 dB for sinusoidal tones, from 1 kHz – 4 kHz)
- 60 dB SPL ... medium loud tone, conversational speech

Fundamental frequency, from the vibrations of the vocal cords in the larynx, is about 120 Hz for adult male, 250 Hz for adult female, and up to 400 Hz for children.



Frequency- and loudness-dependence of human hearing loss.

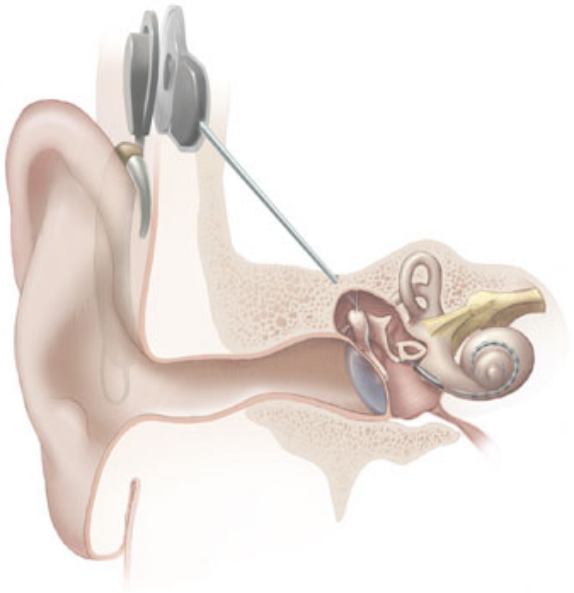
Formants

Formants are the dominant frequencies in human speech, and are caused by resonances of the signals from the vocal cord in our mouth etc. Formants show up as distinct peaks of energy in the sound's frequency spectrum. They are numbered in ascending order starting with the format at the lowest frequency.

Phonems

Speech is often considered to consist of a sequence of acoustic units called phons, which correspond to linguistic units called phonemes. Phonemes are the smallest units of sound that allows different words to be distinguished. The word "dog", for example, contains three phonemes. Changes to the first, second, and third phoneme respectively produce the words "log", "dig", and "dot". English is said to contain 40 different phonemes, specified as in /d/, /o/, /g/ for the word "dog".

Cochlear Implants



Cochlear implant

A cochlear implant (CI) is a surgically implanted electronic device that replaces the mechanical parts of the auditory system by directly stimulating the auditory nerve fibers through electrodes inside the cochlea. Candidates for cochlear implants are people with severe to profound sensorineural hearing loss in both ears and a functioning auditory nervous system. They are used by post-lingually deaf people to regain some comprehension of speech and other sounds as well as by pre-lingually deaf children to enable them to gain spoken language skills. A quite recent evolution is the use of bilateral implants allowing recipients basic sound localization.

Parts of the cochlear implant

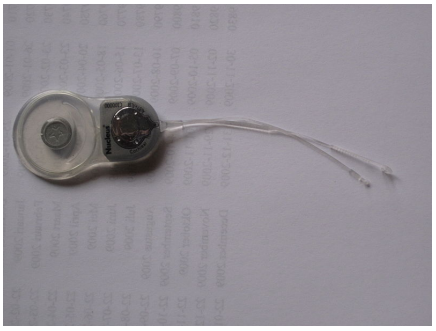
The implant is surgically placed under the skin behind the ear. The basic parts of the device include:

External:

- a microphone which picks up sound from the environment
- a speech processor which selectively filters sound to prioritize audible speech and sends the electrical sound signals through a thin cable to the transmitter,
- a transmitter, which is a coil held in position by a magnet placed behind the external ear, and transmits the processed sound signals to the internal device by electromagnetic induction,

Internal:

- a receiver and stimulator secured in bone beneath the skin, which converts the signals into electric impulses and sends them through an internal cable to electrodes,
- an array of up to 24 electrodes wound through the cochlea, which send the impulses to the nerves in the scala tympani and then directly to the brain through the auditory nerve system



The internal part of a cochlear implant (model Cochlear Freedom 24 RE)

Signal processing for cochlear implants

In normal hearing subjects, the primary information carrier for speech signals is the envelope, whereas for music, it is the fine structure. This is also relevant for tonal languages, like Mandarin, where the meaning of words depends on their intonation. It was also found that interaural time delays coded in the fine structure determine where a sound is heard from rather than interaural time delays coded in the envelope, although it is still the speech signal coded in the envelope that is perceived.

In order to incorporate the fine structure of auditory signals, some cochlear implant makers have modified their stimulation technique for low frequency signal components. A series of stimulation pulses is started at each positive-going zero crossing in a channel's band-pass filter's upper corner frequency. This so-called fine-structure processing is typically used on the lower 2 to 3 channels (300 to 500 Hz).

Current Developments

Multiple microphones

On its newest implants, the company Cochlea uses 3 microphones instead of one. The additional information is used for beam-forming, i.e. extracting more information from sound coming from straight ahead. This can improve the signal-to-noise ratio when talking to other people by up to 15dB, thereby significantly enhancing speech perception in noisy environments.

Integration CI – Hearing Aid

Preservation of low-frequency hearing after cochlear implantation is possible with careful surgical technique and with careful attention to electrode design. For patients with remaining low-frequency hearing, the company MedEl offers a combination of a cochlea implant for the higher frequencies, and classical hearing aid for the lower frequencies. This system, called EAS for electric-acoustic stimulation, uses with a lead of 18mm, compared to 31.5 mm for the full CI. (The length of the cochlea is about 36 mm.) This results in a significant improvement of music perception, and improved speech recognition for tonal languages.

Fine Structure

For high frequencies, the human auditory system uses only tonotopic coding for information. For low frequencies, however, also temporal information is used: the auditory nerve fires synchronously with the phase of the signal. In contrast, the original CIs only used the power spectrum of the incoming signal. In its new models, MedEl incorporates the timing information for low frequencies, which it calls fine structure, in determining the timing of the stimulation pulses. This improves music perception, and speech perception for tonal languages like Mandarin.

Virtual Electrodes

The numbers of electrodes available is limited by the size of the electrode (and the resulting charge and current densities), and by the current spread along the endolymph. To increase the frequency specificity, one can stimulate two adjacent electrodes. Subjects report to perceive this as a single tone at a frequency intermediate to the two electrodes.

Simulation of a cochlear implant

Sound processing in cochlear implant is still subject to a lot of research and one of the major product differentiations between the manufacturers. However, the basic sound processing is rather simple and can be implemented to gain an impression of the quality of sound perceived by patients using a cochlear implant. The first step in the process is to sample some sound and analyze its frequency. This is usually done using fast Fourier transform (FFT). The result of a FFT is the sound signal in frequency domain, namely information about the signal's frequencies and their intensity. The second step is to concentrate those intensities on a few distinct frequencies ("binning") and convert the signal back to spatial domain. The result is a sound signal consisting of a few distinct frequencies - the location of the electrodes in the simulated cochlea. The main parameters are the length of the sound signal used for the FFT integration, the number of electrodes used and their represented frequencies.

The following MATLAB function does sound processing on a given signal. Decisions about the length of the signal to be integrated (signal is a sound file in MATLAB representation, Fs its frame rate) and the properties of the implant (lowerFreq, upperFreq, nElectrodes) are done by the caller. The function returns a processed signal procSignal, which consists only of those few frequencies available. It relies on the built-in FFT implementation as well as on a custom binning function condensing the frequencies to the few available electrodes. The signal in time domain is written in lowercase (signal, procSignal), while its Fourier transform in frequency domain is written in capital letters (SIGNAL, procSIGNAL).

```
function procSignal = soundProcessor (signal, Fs, lowerFreq, upperFreq,
 nElectrodes)

    L = length(signal);
    nFFT = 2^nextpow2(L); % numbers of fft points
    SIGNAL = fft(signal, nFFT);
    procSIGNAL = binning(SIGNAL, Fs, lowerFreq, upperFreq,
nElectrodes);
    procSignal = ifft(procSIGNAL);

end
```

References

[1] http://en.wikipedia.org/wiki/Auditory_system
[2] http://en.wikipedia.org/wiki/Hair_cell

Vestibular System

Biological Machines/Sensory Systems/Vestibular System

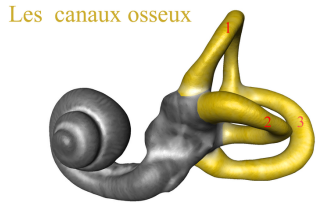
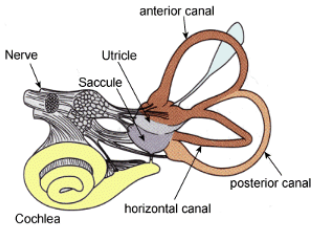
Introduction

The main function of the balance system, or vestibular system, is to sense head movements, especially involuntary ones, and counter them with reflexive eye movements and postural adjustments that keep the visual world stable and keep us from falling.

Sensory Organs

Together with the cochlea, the vestibular system is carried by a system of tubes called the *membranous labyrinth*. These tubes are lodged within the cavities of the bony labyrinth located in the inner ear. A fluid called *perilymph* fills the space between the bone and the membranous labyrinth, while another one called *endolymph* fills the inside of the tubes spanned by the membranous labyrinth. These fluids have a unique ionic composition suited to their function in regulating the electrochemical potential of hair cells, which are as we will later see the transducers of the vestibular system. The electric potential of endolymph is of about 80 mV more positive than perilymph.

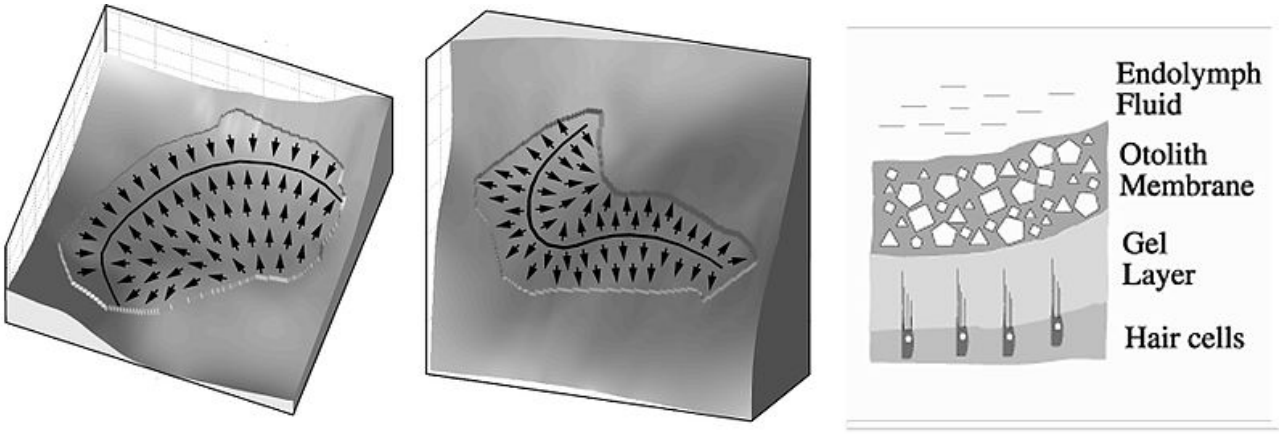
Since our movements consist of a combination of linear translations and rotations, the vestibular system is composed of two main parts: The otolith organs, which sense linear accelerations and thereby also give us information about the head's position relative to gravity, and the semicircular canals, which sense angular accelerations.

Human bony labyrinth (Computed tomography 3D)	**Internal structure of the human labyrinth**
	

Sensory Organ Components

Otoliths

The otolith organs of both ears are located in two membranous sacs called the *utricle* and the *saccule* which primary sense horizontal and vertical accelerations, respectively. They are located at the central part of the labyrinth, also called the *vestibule* of the ear. Both utricle and saccule have a thickened portion of the membrane called the *macula*. A gelatinous membrane called the *otolthic membrane* sits atop the macula, and microscopic stones made of calcium carbonate crystal, the otoliths, are embedded on the surface of this membrane. On the opposite side, hair cells embedded in supporting cells project into this membrane.



The otoliths are the human sensory organs for linear acceleration. The utricle (left) is approximately horizontally oriented; the saccule (center) lies approximately vertical. The arrows indicate the local on-directions of the hair cells; and the thick black lines indicate the location of the striola. On the right you see a cross-section through the otolith membrane. The graphs have been generated by Rudi Jaeger, while we cooperated on investigations of the otolith dynamics.

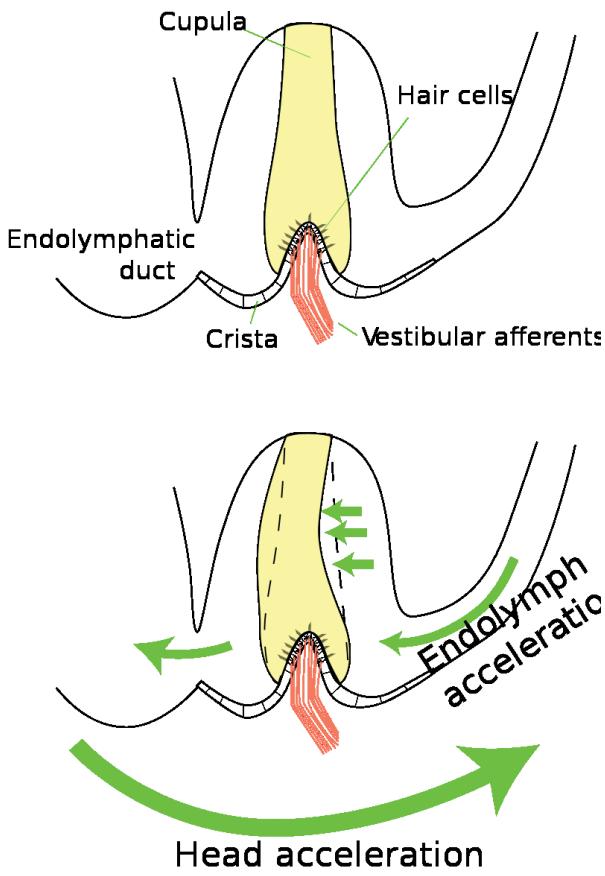
Semicircular Canals

Each ear has three semicircular canals. They are half circular, interconnected membranous tubes filled with endolymph and can sense angular accelerations in the three orthogonal planes. The canals on each side are approximately orthogonal to each other. The *anterior and posterior semicircular canals* are approximately vertical, and the *horizontal semicircular canals* approximately horizontal. Each canal presents a dilatation at one end, called the *ampulla*. Each membranous ampulla contains a saddle-shaped ridge of tissue, the *crista*, which extends across it from side to side. It is covered by neuroepithelium, with hair cells and supporting cells. From this ridge rises a gelatinous structure, the *cupula*, which extends to the roof of the ampulla immediately above it, dividing the interior of the ampulla into two approximately equal parts.

Haircells

The sensors within both the otolith organs and the semicircular canals are the *hair cells*. They are responsible for the transduction of a mechanical force into an electrical signal and thereby build the interface between the world of accelerations and the brain.

Hair cells have a tuft of *stereocilia* that project from their apical surface. The thickest and longest stereocilia is the *kinocilium*. Stereocilia deflection is the mechanism by which all hair cells transduce mechanical forces. Stereocilia within a bundle are linked to one another by protein strands, called *tip links*, which span from the side of a taller stereocilium to the tip of its shorter neighbor in the array. Under deflection of the bundle, the tip links act as gating springs to open and close mechanically sensitive ion channels. *Afferent nerve excitation* works basically the following way: when all cilia are deflected toward the kinocilium, the gates open and cations, including potassium ions from the potassium rich endolymph, flow in and the membrane potential of the hair cell becomes more positive (depolarization). The hair cell itself does not fire action potentials. The depolarization activates voltage-sensitive calcium channels at the basolateral aspect of the cell. Calcium ions then flow in and trigger the release of neurotransmitters, mainly glutamate, which in turn diffuse across the narrow space between the hair cell and a nerve terminal, where they then bind to receptors and thus trigger an increase of the action potentials firing rate in the nerve. On the other hand, *afferent nerve inhibition* is the process induced by the bending of the stereocilia away from the kinocilium (hyperpolarization) and by which the firing rate is decreased. Because the hair cells are chronically leaking calcium, the vestibular afferent nerve fires actively at rest and thereby allows the sensing of both directions (increase and decrease of firing rate). Hair cells are very sensitive and respond extremely quickly to stimuli. The quickness of hair cell response may in part be due to the fact that they must be able to release neurotransmitter reliably in response to a threshold receptor potential of only 100 µV or so.



Cross-section through ampulla. Top: The cupula spans the lumen of the ampulla from the crista to the membranous labyrinth. Bottom: Since head acceleration exceeds endolymph acceleration, the relative flow of endolymph in the canal is opposite to the direction of head acceleration. This flow produces a pressure across the elastic cupula, which deflects in response.

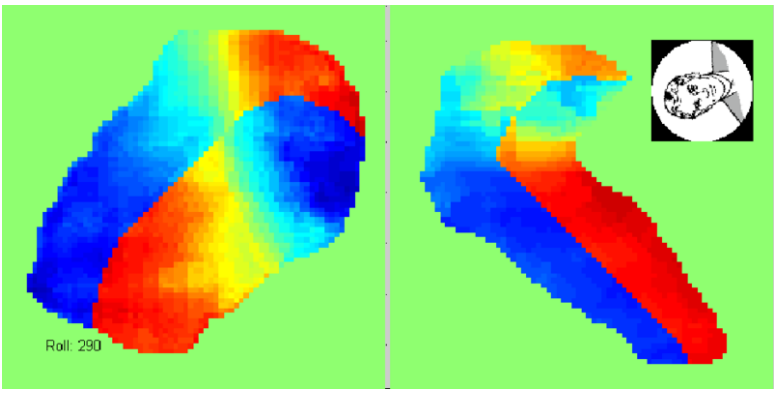
Transduction of Movement

Transduction of Movement

The hair cells of the otolith organs are responsible for the transduction of a mechanical force induced by linear acceleration into an electrical signal. Since this force is the product of gravity plus linear movements of the head

$$\vec{F} = \vec{F}_g + \vec{F}_{inertial} = m(\vec{g} - \frac{d^2\vec{x}}{dt^2})$$

it is therefore sometimes referred to as *gravito-inertial force*. The mechanism of transduction works roughly as follows: The *otoconia*, calcium carbonate crystals in the top layer of the otoconia membrane, have a higher specific density than the surrounding materials. Thus a linear acceleration leads to a displacement of the otoconia layer relative to the connective tissue. The displacement is sensed by the hair cells. The bending of the hairs then polarizes the cell and induces afferent excitation or inhibition.



Excitation (red) and inhibition (blue) on utricle (left) and saccule (right), when the head is in a right-ear-down orientation. The displacement of the otoliths was calculated with the finite element technique, and the orientation of the haircells was taken from the literature.

While each of the three semicircular canals senses only one-dimensional component of rotational acceleration, linear acceleration may produce a complex pattern of inhibition and excitation across the maculae of both the utricle and saccule. The saccule is located on the medial wall of the vestibule of the labyrinth in the spherical recess and has its macula oriented vertically. The utricle is located above the saccule in the elliptical recess of the vestibule, and its macula is oriented roughly horizontally when the head is upright. Within each macula, the kinocilia of the hair cells are oriented in all possible directions.

Therefore, under linear acceleration with the head in the upright position, the saccular macula is sensing acceleration components in the vertical plane, while the utricular macula is encoding acceleration in all directions in the horizontal plane. The otolthic membrane is soft enough that each hair cell is deflected proportional to the local force direction. If denotes the direction of maximum sensitivity or *on-direction* of the hair cell, and the gravito-inertial force, the stimulation by static accelerations is given by

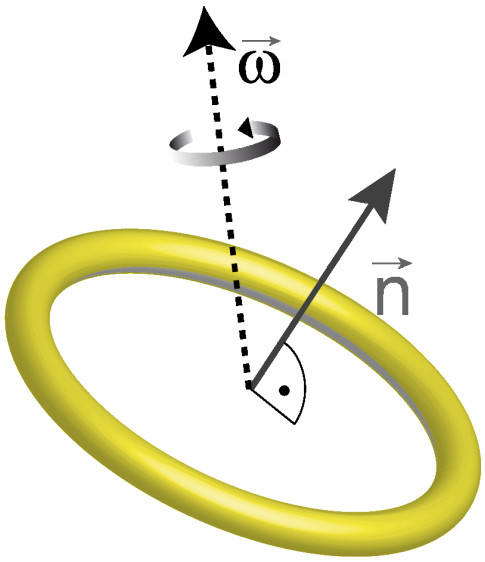
$$stim_{otolith} = \vec{F} \cdot \vec{n}$$

The direction and magnitude of the total acceleration is then determined from the excitation pattern on the otolith maculae.

Transduction of Angular Acceleration

The three semicircular canals are responsible for the sensing of linear accelerations. When the head accelerates in the plane of a semicircular canal, inertia causes the endolymph in the canal to lag behind the motion of the membranous canal. Relative to the canal walls, the endolymph effectively moves in the opposite direction as the head, pushing and distorting the elastic cupula. Hair cells are arrayed beneath the cupula on the surface of the crista and have their stereocilia projecting into the cupula. They are therefore excited or inhibited depending on the direction of the acceleration.

This facilitates the interpretation of canal signals: if the orientation of a semicircular canal is described by the unit vector $\vec{n}$, the stimulation of the canal is proportional to the projection of the angular velocity $\vec{\omega}$ onto this canal



The stimulation of a human semicircular canal is proportional to the scalar product between a vector n (which is perpendicular to the plane of the canal), and the vector omega indicating the angular velocity.

$$stim_{canal} = \vec{\omega} \cdot \vec{n}$$

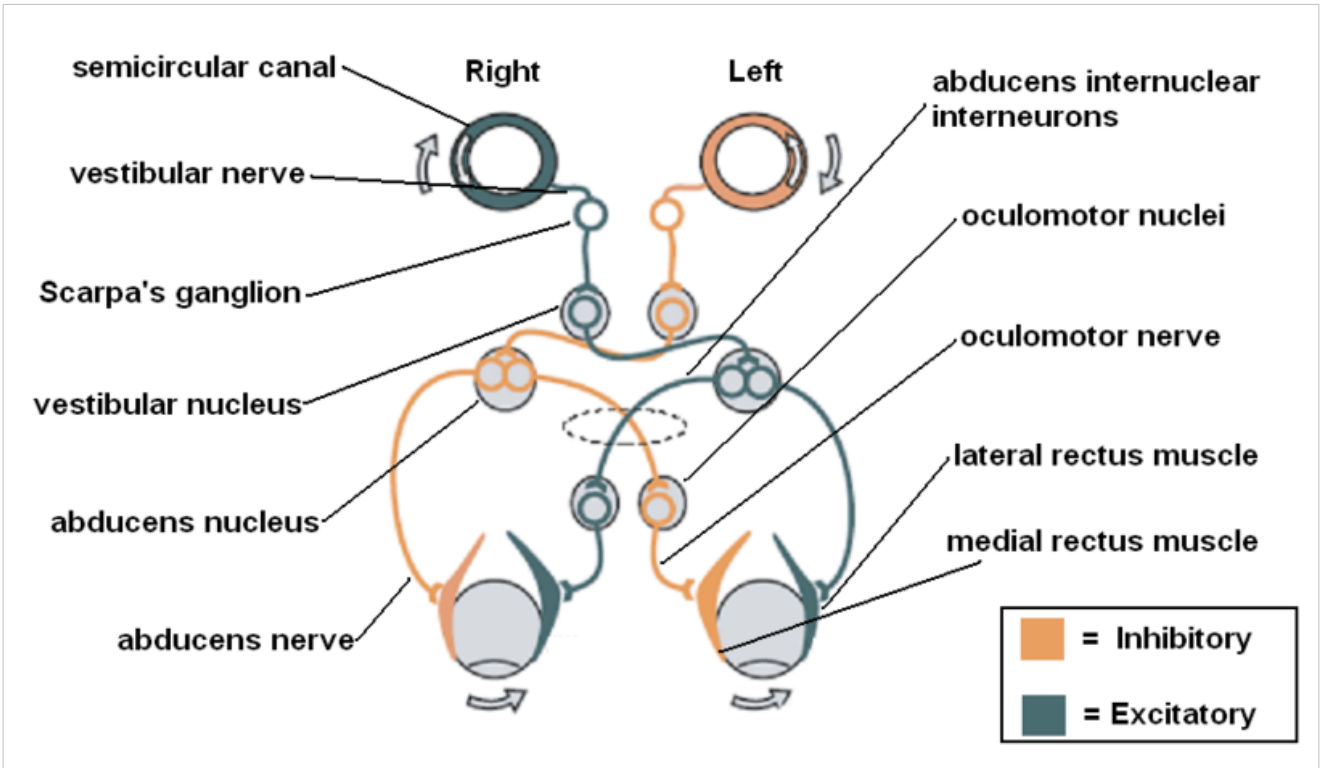
The horizontal semicircular canal is responsible for sensing accelerations around a vertical axis, i.e. the neck. The anterior and posterior semicircular canals detect rotations of the head in the sagittal plane, as when nodding, and in the frontal plane, as when cartwheeling.

In a given cupula, all the hair cells are oriented in the same direction. The semicircular canals of both sides also work as a push-pull system. For example, because the right and the left horizontal canal cristae are “mirror opposites” of each other, they always have opposing (*push-pull principle*) responses to horizontal rotations of the head. Rapid rotation of the head toward the left causes depolarization of hair cells in the left horizontal canal's ampulla and increased firing of action potentials in the neurons that innervate the left horizontal canal. That same leftward rotation of the head simultaneously causes a hyperpolarization of the hair cells in the right horizontal canal's ampulla and decreases the rate of firing of action potentials in the neurons that innervate the horizontal canal of the right ear. Because of this mirror configuration, not only the right and left horizontal canals form a push-pull pair but also the right anterior canal with the left posterior canal (RALP), and the left anterior with the right posterior (LARP).

Physiology of the Vestibular System

Central Vestibular Pathways

The information resulting from the vestibular system is carried to the brain, together with the auditory information from the cochlea, by the *vestibulocochlear nerve*, which is the eighth of twelve cranial nerves. The cell bodies of the bipolar afferent neurons that innervate the hair cells in the maculae and cristae in the vestibular labyrinth reside near the internal auditory meatus in the vestibular ganglion (also called Scarpa's ganglion, Figure Figure 10.1). The centrally projecting axons from the vestibular ganglion come together with axons projecting from the auditory neurons to form the eighth nerve, which runs through the internal auditory meatus together with the facial nerve. The primary afferent vestibular neurons project to the four vestibular nuclei that constitute the *vestibular nuclear complex* in the brainstem.



Vestibulo-Ocular Reflex (VOR)

An extensively studied example of function of the vestibular system is the *vestibulo-ocular reflex* (VOR). The function of the VOR is to stabilize the image during rotation of the head. This requires the maintenance of stable eye position during horizontal, vertical and torsional head rotations. When the head rotates with a certain speed and direction, the eyes rotate with the same speed but in the opposite direction. Since head movements are present all the time, the VOR is very important for stabilizing vision.

How does the VOR work? The vestibular system signals how fast the head is rotating and the oculomotor system uses this information to stabilize the eyes in order to keep the visual image motionless on the retina. The vestibular nerves project from the vestibular ganglion to the vestibular nuclear complex, where the vestibular nuclei integrate signals from the vestibular organs with those from the spinal cord, cerebellum, and the visual system. From these nuclei, fibers cross to the contralateral abducens nucleus. There they synapse with two additional pathways. One pathway projects directly to the lateral rectus muscle of eye via the abducens nerve. Another nerve tract projects from the abducens nucleus by the abducens interneurons to the oculomotor nuclei, which contain motor neurons that drive eye muscle activity, specifically activating the medial rectus muscles of the eye through the oculomotor nerve. This short latency connection is sometimes referred to as *three-neuron-arc*, and allows an eye movement within less than 10 ms after the onset of the head movement.

For example, when the head rotates rightward, the following occurs. The right horizontal canal hair cells depolarize and the left hyperpolarize. The right vestibular afferent activity therefore increases while the left decreases. The vestibulocochlear nerve then carries this information to the brainstem and the right vestibular nuclei activity increases while the left decreases. This makes in turn neurons of the left abducens nucleus and the right oculomotor nucleus fire at higher rate. Those in the left oculomotor nucleus and the right abducens nucleus fire at a lower rate. This results in the fact than the left lateral rectus extraocular muscle and the right medial rectus contract while the left medial rectus and the right lateral rectus relax. Thus, both eyes rotate leftward.

The *gain* of the VOR is defined as the change in the eye angle divided by the change in the head angle during the head turn

$$gain = \frac{\Delta_{Eye}}{\Delta_{Head}}$$

If the gain of the VOR is wrong, that is, different than one, then head movements result in image motion on the retina, resulting in blurred vision. Under such conditions, motor learning adjusts the gain of the VOR to produce more accurate eye motion. Thereby the cerebellum plays an important role in motor learning.

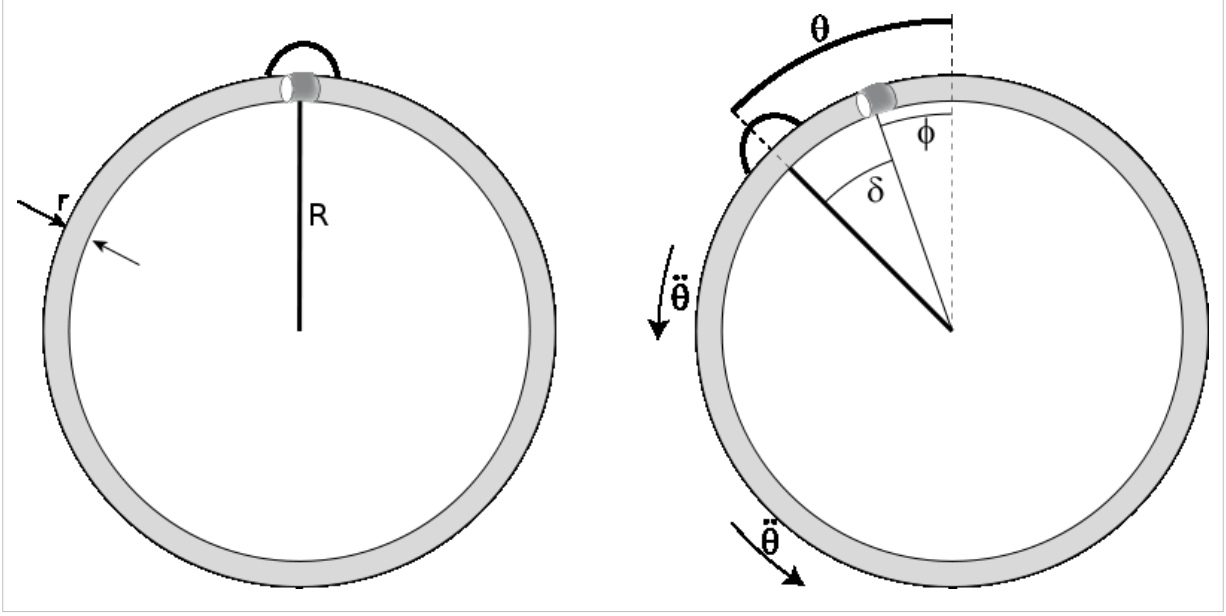
The Cerebellum and the Vestibular System

It is known that postural control can be adapted to suit specific behavior. Patient experiments suggest that the cerebellum plays a key role in this form of *motor learning*. In particular, the role of the cerebellum has been extensively studied in the case of adaptation of vestibulo-ocular control. Indeed, it has been shown that the gain of the vestibulo-ocular reflex adapts to reach the value of one even if damage occur in a part of the VOR pathway or if it is voluntary modified through the use of magnifying lenses. Basically, there are two different hypotheses about how the cerebellum plays a necessary role in this adaptation. The first from (Ito 1972;Ito 1982) claims that the cerebellum itself is the site of learning, while the second from Miles and Lisberger (Miles and Lisberger 1981) claims that the vestibular nuclei are the site of adaptive learning while the cerebellum constructs the signal that drives this adaptation. Note that in addition to direct excitatory input to the vestibular nuclei, the sensory neurons of the vestibular labyrinth also provide input to the Purkinje cells in the flocculo-nodular lobes of the cerebellum via a pathway of mossy and parallel fibers. In turn, the Purkinje cells project an inhibitory influence back onto the vestibular nuclei. Ito argued that the gain of the VOR can be adaptively modulated by altering the relative strength of the direct excitatory and indirect inhibitory pathways. Ito also argued that a message of retinal image slip going through the inferior olivary nucleus carried by the climbing fiber plays the role of an error signal and thereby is the modulating influence of the Purkinje cells. On the other hand, Miles and Lisberger argued that the brainstem neurons targeted by the Purkinje cells are the site of adaptive learning and that the cerebellum constructs the error signal that drives this adaptation.

Signal Processing and Mechanics

Semicircular Canals

Model without Cupula



Let us consider the mechanical description of the semi-circular canals (SCC). We will make very strong and reductive assumptions in the following description. The goal here is merely to understand the very basic mechanical principles underlying the semicircular canals.

The first strong simplification we make is that a semicircular canal can be modeled as a circular tube of "outer" radius R and "inner" radius r. (For proper hydro mechanical derivations see (Damiano and Rabbitt 1996) and Obrist (2005)). This tube is filled with endolymph.

The orientation of the semicircular canal can be described, in a given coordinate system, by a vector $\vec{n}$ that is perpendicular to the plane of the canal. We will also use the following notations:

θ Rotation angle of tube [rad]

$\dot{\theta} \equiv \frac{d\theta}{dt}$ Angular velocity of the tube [rad/s]

$\ddot{\theta} \equiv \frac{d^2\theta}{dt^2}$ Angular acceleration of the tube [rad/s^2]

ϕ Rotation angle of the endolymph inside the tube [rad], and similar notation for the time derivatives

$\delta = \theta - \phi$ movement between the tube and the endolymph [rad].

Note that all these variables are scalar quantities. We use the fact that the angular velocity of the tube can be viewed as the projection of the actual angular velocity vector of the head $\vec{\omega}$ onto the plane of the semicircular canal described by $\vec{n}$ to go from the 3D environment of the head to our scalar description. That is,

$$\dot{\theta} = \vec{\omega} \cdot \vec{n}$$

where the standard scalar product is meant with the dot.

To characterize the endolymph movement, consider a free floating piston, with the same density as the endolymph. Two forces are acting on the system:

1. The inertial moment $I\ddot{\phi}$, where I characterizes the inertia of the endolymph.
2. The viscous moment $B\dot{\delta}$, caused by the friction of the endolymph on the walls of the tube.

This gives the equation of motion

$$I\ddot{\phi} = B\dot{\delta}$$

Substituting $\phi = \theta - \delta$ and integrating gives

$$\dot{\theta} = \dot{\delta} + \frac{B}{I}\delta.$$

Let us now consider the example of a velocity step $\dot{\theta}(t)$ of of constant amplitude ω. In this case, we obtain a displacement

$$\delta = \frac{I}{B}\omega \cdot (1 - e^{-\frac{B}{I}t})$$

and for $t \gg \frac{I}{B}$, we obtain the constant displacement

$$\delta \approx \frac{I}{B}\omega .$$

Now, let us derive the time constant $T_1 \equiv \frac{I}{B}$. Fora thin tube, $r \ll R$, the inertia is approximately given by

$$I = ml^2 \approx 2\rho\pi^2 r^2 R^3.$$

From the Poiseuille-Hagen Equation, the force F from a laminar flow with velocity *v* in a thin tube is

$$F = \frac{8\bar{V}\eta l}{r^2}$$

where $\bar{V} = r^2\pi v$ is the volume flow per second, η the viscosity and $l = 2\pi R$ the length of the tube.

With the torque $M = F \cdot R$ and the relative angular velocity $\Omega = \frac{v}{R}$, substitution provides

$$B = \frac{M}{\Omega} = 16\eta\pi^2 R^3$$

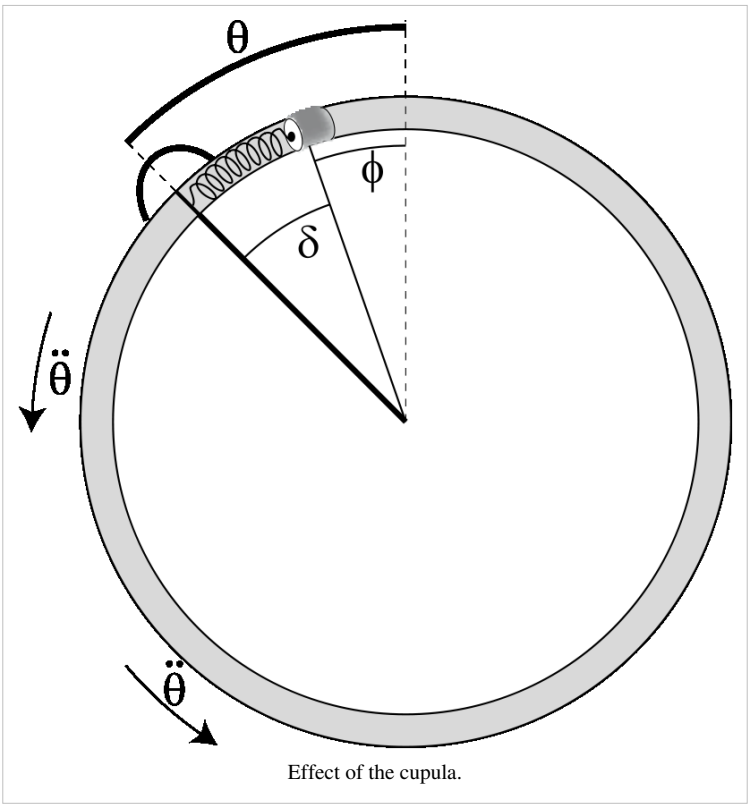
Finally, this gives the time constant T_1

$$T_1 = \frac{I}{B} = \frac{\delta r^2}{8\eta}$$

For the human balance system, replacing the variables with experimentally obtained parameters yields a time constant $T_1$of about 0.01 s. This is brief enough that in equation (10.5) the $\approx$ can be replaced by " = ". This gives a system gain of

$$G \equiv \frac{\delta}{\omega} = \frac{I}{B} = T_1$$

Model with Cupula



Effect of the cupula.

Our discussion until this point has not included the role of the cupula in the SCC: The cupula acts as an elastic membrane that gets displaced by angular accelerations. Through its elasticity the cupula returns the system to its resting position. The elasticity of the cupula adds an additional elastic term to the equation of movement. If it is taken into account, this equation becomes

$$\ddot{\theta} = \ddot{\delta} + \frac{B}{I}\dot{\delta} + \frac{K}{I}\delta$$

An elegant way to solve such differential equations is the *Laplace-Transformation*. The Laplace transform turns differential equations into algebraic equations: if the Laplace transform of a signal x(t) is denoted by X(s), the Laplace transform of the time derivative is

$$\frac{dx(t)}{dt} \xrightarrow{LaplaceTransform} s \cdot X(s) - x(0)$$

The term x(0) details the starting condition, and can often be set to zero by an appropriate choice of the reference position. Thus, the Laplace transform is

$$s^2\tilde{\theta} = s^2\tilde{\delta} + \frac{B}{I}s\tilde{\delta} + \frac{K}{I}\tilde{\delta}$$

where "~" indicates the Laplace transformed variable. With $T_1$from above, and T_2defined by

$$T_2 = \frac{B}{K}$$

we get the

$$\frac{\tilde{\delta}}{\tilde{\theta}} = \frac{T_1 s^2}{T_1 s^2 + s + \frac{1}{T_2}}$$

For humans, typical values for $T_2 = B/K$ are about 5 sec.

To find the poles of this transfer function, we have to determine for which values of s the denominator equals 0:

$$s_{1,2} = \frac{1}{T_1}\left(-1 \pm \sqrt{1 - 4\frac{T_1}{T_2}}\right)$$

Since $T_2 \gg T_1$, and since

$$\sqrt{1-x} \approx 1 - \frac{x}{2} for x \ll 1$$

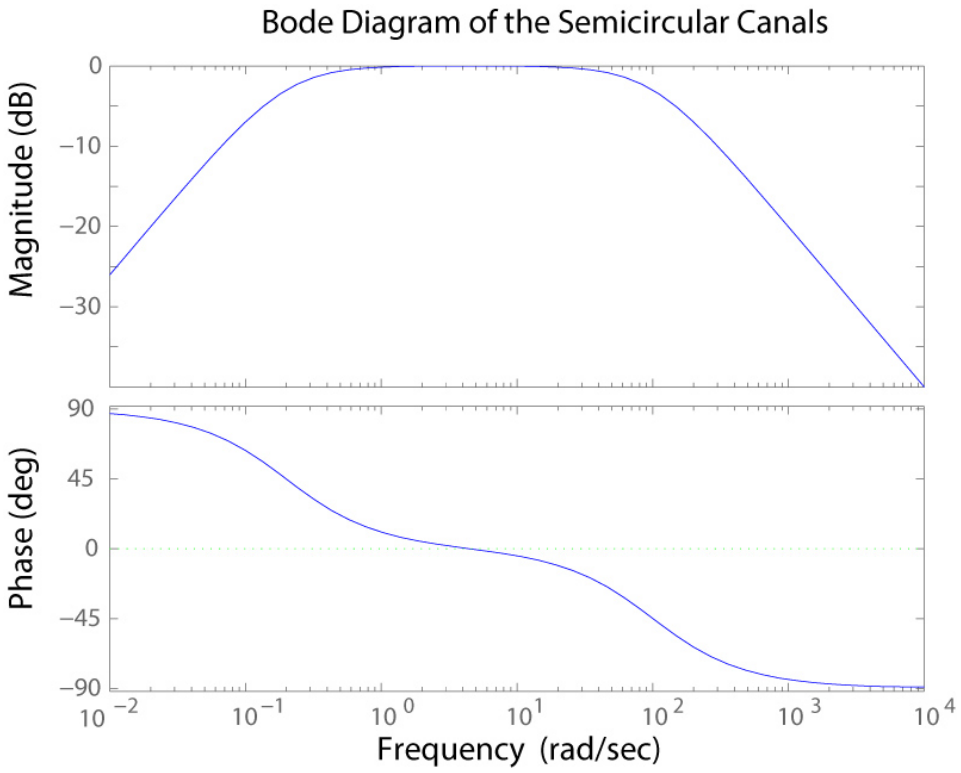
we obtain

$$s_1 \approx -\frac{1}{T_1}, and s_2 \approx -\frac{1}{T_2}$$

Typically we are interested in the cupula displacement δ as a function of head velocity $\dot{\theta} \equiv s\tilde{\theta}$:

$$\frac{\tilde{\delta}}{s\tilde{\theta}}(s) = \frac{T_1 T_2 s}{(T_1 s + 1)(T_2 s + 1)}$$

For typical head movements (0.2 Hz < f < 20Hz), the system gain is approximately constant. In other words, for typical head movements the cupula displacement is proportional to the angular head velocity!

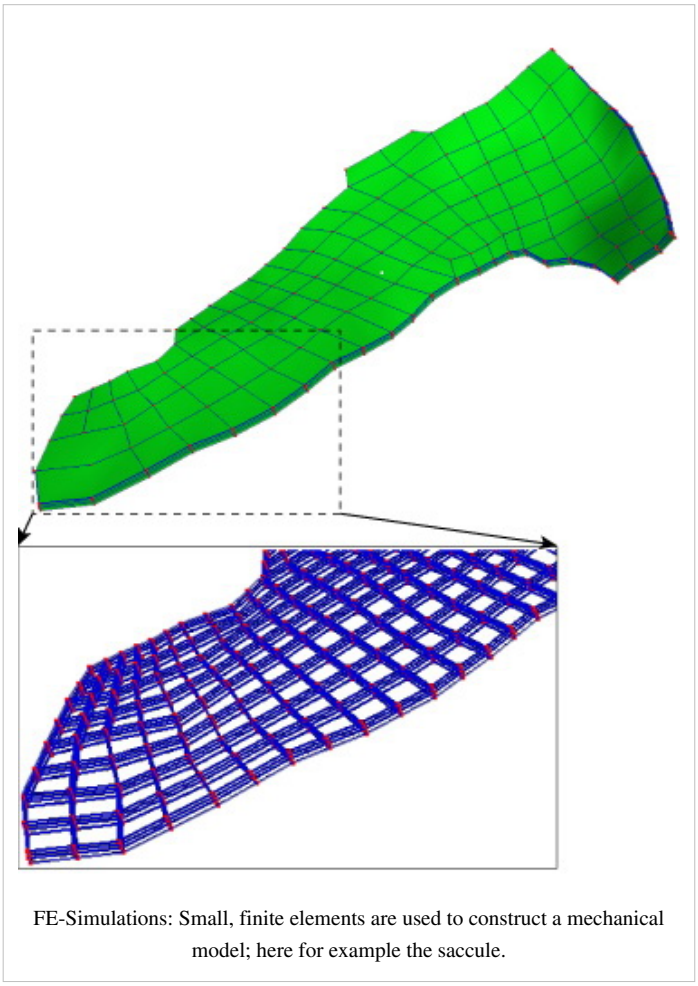


Bode plot of the cupula displacement of a function of head velocity, with T1 = 0.01 sec, T2 = 5 sec, and an amplification factor of (T1+ T2)/ (T1* T2) to obtain a gain of approximately 0 for the central frequencies.

Otoliths

Consider now the mechanics of the otolith organs. Since they are made up by complex, visco-elastic materials with a curved shape, their mechanics cannot be described with analytical tools. However, their movement can be simulated numerically with the finite element technique. Thereby the volume under consideration is divided into many small volume elements, and for each element the physical equations are approximated by analytical functions.

Here we will only show the physical equations for the visco-elastic otolith materials. The movement of each elastic material has to obey Cauchy's equations of motion:



FE-Simulations: Small, finite elements are used to construct a mechanical model; here for example the saccule.

$$\rho \frac{\partial^2 u_i}{\partial t^2} = \rho B_i + \sum_j \frac{\partial T_{ij}}{\partial x_j}$$

where ρ is the effective density of the material, u_i the displacements along the i-axis, B_i the i-component of the volume force, and T_{ij} the components of the Cauchy's strain tensor. x_j are the coordinates.

For linear elastic, isotropic material, *Cauchy's strain tensor* is given by

$$T_{ij} = \lambda e \delta_{ij} + 2\mu E_{ij}$$

where λ and μ are the *Lamé constants*; μ is identical with the shear modulus. $e = div(\vec{u})$, and E_{ij} is the stress tensor

$$E_{ij} = \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right).$$

This leads to Navier's Equations of motion

$$\delta \frac{\partial^2 u_i}{\partial t^2} = \rho B_i + (\lambda + \mu)\frac{\partial e}{\partial x_i} + \mu \sum_j \frac{\partial^2 u_i}{\partial x_j^2}$$

This equation holds for purely elastic, isotropic materials, and can be solved with the finite element technique. A typical procedure to find the mechanical parameters that appear in this equation is the following: when a cylindrical sample of the material is put under strain, the *Young coefficient E* characterizes the change in length, and the *Poisson's ratio* ν the simultaneous decrease in diameter. The Lamé constants λ and μ are related to E and ν by:

$$E = \frac{\mu(3\lambda + 2\mu}{\lambda + \mu}$$

and

$$\nu = \frac{\lambda}{2(\lambda + \mu)}$$

Olfactory System

Biological Machines/Sensory Systems/Olfactory System

Introduction

Probably the oldest sensory system in the nature, the **olfactory system** concerns the sense of smell. The olfactory system is physiologically strongly related to the gustatory system, so that the two are often examined together. Complex flavors require both taste and smell sensation to be recognized. Consequently, food may taste "different" if the sense of smell does not work properly (e.g. head cold).

Generally the two systems are classified as visceral sense because of their close association with gastrointestinal function. They are also of central importance while speaking of emotional and sexual functions.

Both taste and smell receptors are chemoreceptors that are stimulated by molecules soluted respectively in mucus or saliva. However these two senses are anatomically quite different. While smell receptors are distance receptors that do not have any connection to the thalamus, receptors pass up the brainstem to the thalamus and project to the postcentral gyrus along with those for touch and pressure sensibility for the mouth.

In this article we will first focus on the organs composing the **olfactory system**, then we will characterize them in order to understand their functionality and we will end explaining the transduction of the signal and the commercial application such as the eNose.

Sensory Organs

In vertebrates the main **olfactory system** detects odorants that are inhaled through the nose where they come to contact with the olfactory epithelium, which contains the olfactory receptors.

Olfactory sensitivity is directly proportional to the area in the nasal cavity near the septum reserved to the olfactory mucous membrane, which is the region where the olfactory receptor cells are located. The extent of this area is a specific between animals species. In dogs, for example, the sense of smell is highly developed and the area covered by this membrane is about $75 - 150\ cm^2$; these animals are called macrosmatic animals. Differently in humans the olfactory mucous membrane cover an area about $3 - 5\ cm^2$, thus they are known as microsmatic animals.

In humans there are about 10 million olfactory cells, each of which have 350 different receptor types composing the olfactory mucous membrane. The 350 different receptors are characteristic for only one odorant type. The bond with one odorant molecule starts a molecular chain reaction, which transforms the chemical perception into an electrical signal.

The electrical signal proceeds through the olfactory nerve's axons to the olfactory bulbs. In this region there are between 1000 and 2000 glomerular cells which combine and interpret the potentials coming from different receptors. This way it is possible to unequivocally characterise e.g. the coffee aroma, which is composed by about 650 different odorants. Humans can distinguish between about 10.000 odors.

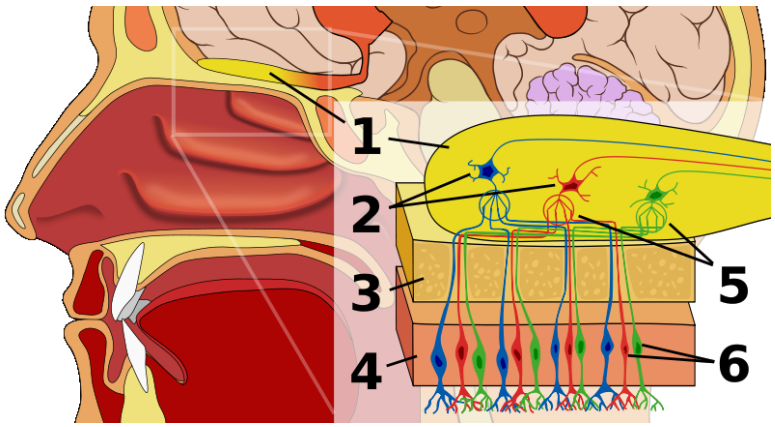
The signal then goes forth to the olfactory cortex where it will be recognized and compared with known odorants (i.e. olfactory memory) involving also an emotional response to the olfactory stimuli.

It is also interesting to note that the human genome has about $600 - 700$ genes (~2% of the complete genome) specialized in characterizing the olfactory receptors, but only 350 are still used to build the **olfactory system**. This is

a proof of the evolution change in the necessity of humans in using the olfaction.

Sensory Organ Components

Similar to other sensory modalities, olfactory information must be transmitted from peripheral olfactory structures, like the olfactory epithelium, to more central structures, meaning the olfactory bulb and cortex. The specific stimuli has to be integrated, detected and transmitted to the brain in order to reach sensory consciousness. However the **olfactory system** is different from other sensory systems in three fundamental ways as depicted in the book of Paxianos G. and Mai J.K., "The human Nervous System".



1: Olfactory bulb 2: Mitral cells 3: Bone 4: Nasal Epithelium 5: Glomerulus 6: Olfactory receptor cells

1. Olfactory receptor neurons are continuously replaced by mitotic division of the basal cells of the olfactory epithelium. The motivation of this is the high vulnerability of the neurons, which are directly exposed to the environment.
2. Because of phylogenetic relationship, olfactory sensory activity is transferred directly fro the olfactory bulb to the olfactory cortex, without a thalamic relay.
3. Neural integration and analysis of olfactory stimuli may not involve topographic organization beyond the olfactory bulb, meaning that spatial or frequency axis are not needed to project the signal.

Olfactory Mucous Membrane

The olfactory mucous membrane contain the olfactory receptor cells and in humans it covers an area about $3 - 5$ cm^2 in the roof of the nasal cavity near the septum. Because the receptors are continuously regenerated it contains both the supporting cells and progenitors cells of the olfactory receptors. Interspersed between these cells are $10 - 20$ millions receptor cells.

Olfactory receptors are infect neurons with a short and thick dendrites. Their extended end is called an olfactory rod, from which cilia project to the surface of the mucus. These neurons have a length of 2 micrometers and have between 10 and 20 cilia of diameter about 0.1 micrometers.

The axons of the olfactory receptor neurons go through the cribriform plate of the ethmoid bone and enter the olfactory bulb. This passage is in absolute the most sensitive of the **olfactory system**; the damage of the cribriform plate (e.g. breaking the nasal septum) can imply the destruction of the axons compromising the sense of smell.

A further particularity of the mucous membrane is that with a period of a few weeks it is completely renewed.

Olfactory Bulbs

In humans the olfactory bulb is located anteriorly with respect to the cerebral hemisphere and remain connected to it only by a long olfactory stalk. Furthermore in mammals it is separated into layers and consist of a concentric lamina structure with well-defined neuronal somata and synaptic neuropil.

After passing the cribriform plate the olfactory nerve fibers ramify in the most superficial layer (olfactory nerve layer). When these axons reach the olfactory bulb the layer gets thicker and they terminate in the primary dendrites of the mitral cells and tufted cells forming in this way the complex globular synapses called olfactory glomeruli. Both these cells send other axons to the olfactory cortex and appear to have the same functionality but in fact tufted cells are smaller and consequently have also smaller axons.

The axons from several thousand receptor neurons coverage on one or two glomeruli in a corresponding zone of the olfactory bulb; this suggest that the glomeruli are the unit structures for the olfactory discrimination.

In order to avoid threshold problems in addition to mitral and tufted cells, the olfactory bulb contains also two type of cells with inhibitory properties: periglomerular cells and granule cells. The first will connect two different glomeruli, the second, without using any axons, build a reciprocal synapses with the lateral dendrites of the mitral and tufted cells. By releasing GABA the granule cell on the one side of these synapse are able to inhibits the mitral (or tufted) cells, while on the other side of the synapses the mitral (or tufted) cells are able to excite the granule cells by releasing glutamate. Nowadays about 8.000 glomeruli and 40.000 mitral cells have been counted in young adults. Unfortunately this huge number of cells decrease progressively with the age compromising the structural integrity of the different layers.

Olfactory Cortex

The axons of the mitral and tufted cells pass through the granule layer, the intermediate olfactory stria and the lateral olfactory stria to the olfactory cortex. This tract forms in humans the bulk of the olfactory peduncle. As depicted in the book of Paxianos G. and Mai J.K., "The human Nervous System", the primary olfactory cortical areas can be easily described by a simple structure composed of three layers: a broad plexiform layer (first layer); a compact pyramidal cell somata layer (second layer) and a deeper layer composed by both pyramidal and nonpyramidal cells (third layer). Furthermore, in contrast to the olfactory bulb, only a little spatial encoding can be observed; “that is, small areas of the olfactory bulb virtually project the entire olfactory cortex, and small areas of the cortex receive fibers from virtually the entire olfactory bulb” [3].

In general the olfactory tract can be divided in five major regions of the cerebrum: Anterior olfactory nucleus, the olfactory tubercle, the piriform cortex, Anterior cortical nucleus of the amygdala and the entorhinal cortex.Olfactory information is transmitted from primary olfactory cortex to several other parts of the forebrain, including orbital cortex, amigdala, hippocampus, central striatum, hypothalamus and mediodorsal thalamus.

Interesting is also to note that in humans, the piriform cortex can be activated by sniffing, whereas the to activate the lateral and the anterior orbitofrontal gyri of the frontal lobe only the smell is required. This is possible because in general the orbitofrontal activation is grater on the right side than the left side, this directly imply an asymmetry in the corticals reception of the olfaction. A further implication of the emotional response to olfactory stimuli as olfactory memories can be assigned to the fibers projection to the amigdala of the the entorhinal cortex.

A good and complete description of the substructure of the olfactory cortex can be found in the book of Paxianos G. and Mai J.K., "The human Nervous System".

Signal Processing

Examples of olfactory thresholds from William, "Review of Medial Physiology".

Substance	mg/L of Ari
Ethyl ether	5.83
Chloroform	3.30
Pyridine	0.03
Oil of peppermint	0.02
lodoform	0.02
Butyric acid	0.009
Propyl mercaptan	0.006
Artificial musk	0.00004
Methyl mercaptan	0.0000004

Only substances which comes in contact with the olfactory epithelium can be excite the olfactory receptors. The right table shows some threshold for some representative substances. These values give an impression of the huge sensitivity of the olfactory receptors.

It is remarkable that humans can recognize more than 10'000 different odors but they should at least differ about the 30% before they can be distinguished. Compared to the visual system, such precision would mean a a 1% change in light intensity, where as compared to hearing the direction perception may be indicated by the slight difference in the time of arrival of odoriferous molecules in the two nostrils [4]. It is amazing how the same number of carbon atoms (normally between 3 and 20) in odors molecules can leads to different odors just by slightly change in the structural configuration.

Signal Transduction

An interesting feature of the olfactory system is how a simple sense organ that apparently lacks a high degree of complexity can mediate discrimination of more than 10'000 different odors. On the one hand this is made possible by the huge number of different odorant receptor. The gene family for the olfactory receptor is infect the largest family studied so far in mammals. On the other hand the neural net of the olfactory system's provide with their 1800 glomeruli a large two dimensional map in the olfactory bulb that is unique to each odorant. In addition, the extracellular field potential in each glomerulus oscillates, and the granule cells appear to regulate the frequency of the oscillation. The exact function of the oscillation is unknown, but it probably also helps to focus the olfactory signal reaching the cortex [3].

Smell measurement

Olfaction, as described in the research of R. Haddad et al., consists of a set of transforms from physical space of odorant molecules (olfactory physicochemical space), through a neural space of information processing (olfactory neural space), into a perceptual space of smell (olfactory perceptual space). The rules of these transforms depend on obtaining valid metrics for each of those spaces.

Olfactory perceptual space

As the perceptual space represent the “input” of the smell measurement, it’s aim is to describe the odors in the most simple possible way. Odor are infect ordered so that their reciprocal distance in space confers them similarity. This mean that odors the more two odors are near each other in this space the more are they expected to be similar. This space is thus defined by so called perceptual axes characterized by some arbitrarily chosen “unit” odors.

Olfactory neural space

As suggested by its name the neural spaces are generated from neural responses. This gives rise to an extensive database of odorant-induced activity, which can be used to formulate an olfactory space where the concept of similarity serves as a guiding principal. Using this procedure different odorant are than expected to be similar if they generate a similar neuronal response. This database can be navigated at the Glomerular Activity Response Archive [1].

Olfactory physicochemical space

The need of identify the molecular encryption of the biological interaction, make the physicochemical space the most complex one of the olfactory space described so far. R. Haddad suggest that one possibility is to span this space would to represent each odorant by a very large number of molecular descriptors by use either a variance metric or a distance metric. In his first description single odorants may have many physicochemical features and one expect these feature to present themselves at various probabilities within the world of molecules that have a smell. In such metric the orthogonal basis generated from the description of the odorant leads to represent each odorant by a single value. While in the second, the metric represents each odorant with a vector of 1664 values, on the basis of Euclidean distances between odorants in the 1664 physicochemical space. Whereas the first metric enabled the prediction of perceptual attributes, the second enabled the prediction of odorant-induced neuronal response patterns.

Electronic measurement of odors

Nowadays odors can be measured electronically in a huge amount of different way, some examples are: mass spectrography, gas chromatography, raman spectra and most recently electronic nose. In general they assume that different olfactory receptors have different affinities to specific molecular physicochemical properties, and that the different activation of these receptors gives rise to a spatio-temporal pattern of activity that reflects odors.

Electronic Nose

eNose are analytic devices for mimicking the principle of biological olfaction that have as main component an array of non specific chemical sensors. Combining electronics, path recognition and modern technology, the eNoses uses gas sensors to translate the chemical signal into an electrical signal when an odorant volatiles from samples reach the fas sensor array. Usually the pattern recognition is used to perform either the quantitative or the qualitative identification. In order to reproduce the olfactory epithelium a gas sensor array is sealed in a chamber of the eNose. A cross-sensitive chemical sensors will than act as olfactory neuron transferring the odor information from a chemical into an electric form similar to the one process which occur in the olfactory bulb where the signal is integrated and enhanced. The information is than elaborated by an artificial neuronal network, which provide coding, processing and storage. The gas sensor array transforms odor information from the sample space into a measurement space. This is a key procedure for information processing within an eNose. Gas sensors with different transduction

principles and different fabrication techniques provide various ways to obtain odor information. Commercially a lot of different sensor types are available the most frequently used sensor types include metal oxide semiconductors (MOS), quartz crystal microbalances (QCM), conducting polymers (CP) and surface acoustic wave (SAW) sensors. A big influence in the choice of the sensor is made by the fast response, reversibility, repeatability and high sensitivity of the sensor. While constructing the sensor array for a eNose the sensors are selected to be cross-selective to different odors, such that their sensitivity is overlapped with the same odor, to make the most of type-limited sensors for obtaining adequate odor information. In general the amount of raw data generated from the array of sensor's is huge, so that the information has to be transferred from a high dimensional space into a lower one. Pattern recognition are then needed to encode the signal into a so called classification space. Both are important and necessary for designing a powerful information processing algorithm and constructing an array with high quality gas sensors. Many pattern recognition methods have been introduced into eNose, including parameterized and non-parameterized multivariate statistical methods. Artificial neural network have various significant advantages: (i) Self-adaptive, (ii) capability of error tolerance and generalization suitable for treating the problems (iii) parallel processing and distributed storage.

References

1. Schmidt, Lang (2007). "Ohysiologie des Menschen", *Soringer*, 30. Auflage.
2. Faller A., Schünke M. (2008). "Der Körper des Menschen", *Thieme*, 15. Auflage.
3. Paxianos G., Mai J.K. (2004). "The human Nervous System", *Elsevier accademic press*, 2nd Edition.
4. William. "Review of Medial Physiology", *Lange*, 22th Edition.
5. Haddad R. ed al (2008). "Measuring smells", *Elsevier Ltd*, 18:438-444
6. Mamlouk A.M., Martinez T. (2004). "One dimensions of the olfatory perception space", *Elsevier B.V.*
7. >Guang L ed al (2009), "Progress in bionic information processing techniques for an electronic nose based on olfactory models", *Chinese Science Bulletin*, 54(4)521-53Z

References

[1] http://gara.bio.uci.edu/

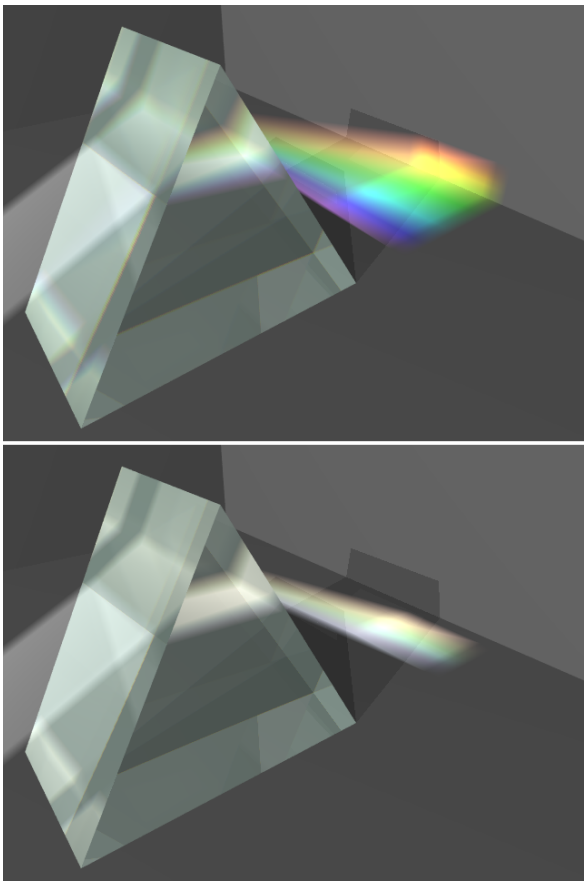
Biological Machines/Appendix

Spectrum

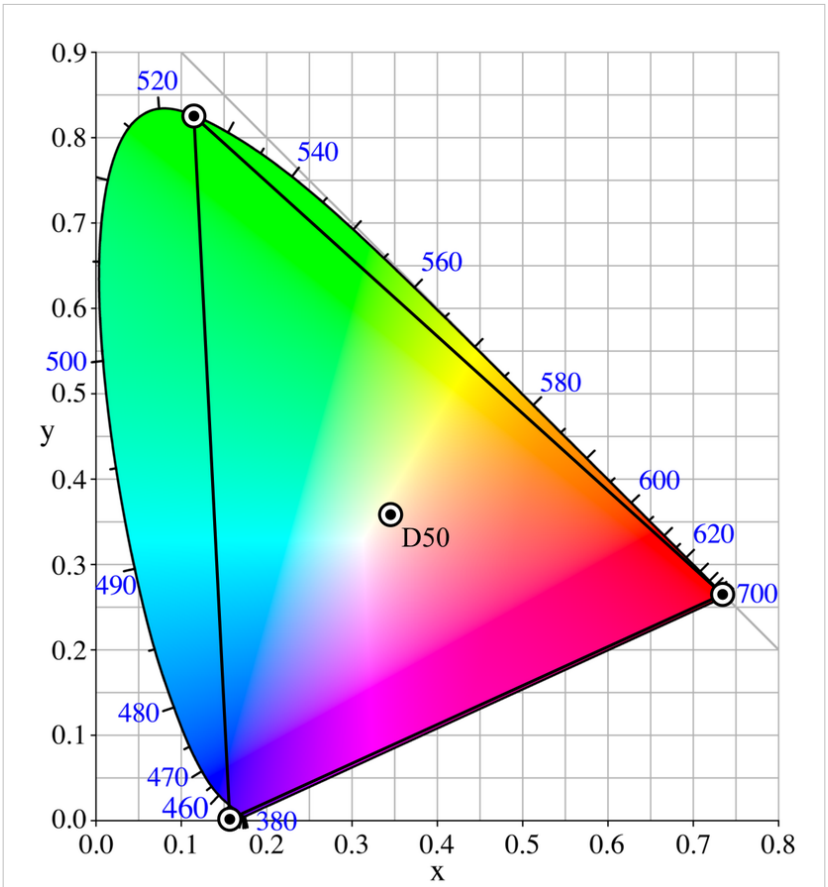
If light passes through a prism, a colour spectrum will be formed at the other end of the prism ranging from red to violet. The wavelength of the red light is from 650nm to 700nm, and the violet light is at around 400nm to 420nm. This is the EM range detectable for the human eye.

Colour Models

The colour triangle is often used to illustrate the colour-mixing effect. The triangle entangles the visible spectrum, and a white dot is located in the middle of the triangle. Because of additive colour mixing property of red (700nm), green(546nm) and blue(435nm), every colour can be produced by mixing those three colours.



Colour spectrum produced by a prism



The RGB color-triangle

History of *Biological Machines*

This Wikibook was started by engineers studying at ETH Zurich as part of the course Computational Simulations of Sensory Systems. The course combines physiology with an emphasis on the sensory systems, programming and signal processing. There is a plethora of information regarding these topics on the internet and in the literature, but there's a distinct lack of concise texts and books on the fusion of these 3 topics. The world needs a structured and thorough overview of biology and biological systems from an engineering point of view, which is what this book is trying to correct. We will start off with the Visual System, focusing on the biological and physiological aspects, mainly because this will be used in part to grade our performance in the course. The other part being the programming aspects have already been evaluated and graded. It is the authors' wishes that eventually information on physiology/biology, signal processing AND programming shall be added to each of the sensory systems. Also we hope that more sections will be added to extend the book in ways previously unthought of.

Biological Machines/Sources

Visual System

- http://www.yorku.ca/eye/
- http://www.eyedesignbook.com/ <-- Watch out, religious fanatic here.
- http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/
- http://www.physpharm.fmd.uwo.ca/undergrad/sensesweb/
- http://www.optometry.co.uk/articles/docs/0b3e55d71662f4e8381aea8637c48f4f_stafford20010112.pdfc
- Biology of Spiders by Rainer F. Foelix - Vision page 82-93
- Photoreceptors and light signalling by Alfred Batschauer, Royal Society of Chemistry (Great Britain), Published by Royal Society of Chemistry, 2003, ISBN 085404311X, 9780854043118
- http://emedicine.medscape.com/article/835021-overview
- http://www.stlukeseye.com/Anatomy/
- http://www.absoluteastronomy.com/topics/Rod_cell#encyclopedia
- http://hubel.med.harvard.edu/
- http://www.absoluteastronomy.com/topics/Photopsin
- Structural differences of cone 'oil-droplets' in the light and dark adapted retina of Poecilia reticulata P., Yvette W. Kunz and Christina Wise
- Advances in organ biology, Volume 10, Pages 1-395 (2005)
- <http://www.search.eb.com/eb/art-53283>"optic chiasm: visual pathways." Online Art. Encyclopaedia Britannica Online.
- Color atlas of physiology,Despopoulos, A. and Silbernagl, S.,2003, Thieme
- Neurotransmitter systems in the retina, Ehinger, B., Retina, 2-4, 305, 1982

Auditory System

- *Intraoperative Neurophysiological Monitoring*, 2nd Edition, Aage R. Møller, Humana Press 2006, Totowa, New Jersey, pages 55-70
- *The Science and Applications of Acoustics*, 2nd Edition, Daniel R. Raichel, Springer Science&Business Media 2006, New York, pages 213-220
- *Physiology of the Auditory System*, P. J. Abbas, 1993, in: *Cummings Otolaryngology: Head and Neck Surgery*, 2nd edition, Mosby Year Book, St. Louis
- http://thalamus.wustl.edu/course/audvest.html
- http://faculty.washington.edu/chudler/hearing.html
- *Computer Simulations of Sensory Systems*, Lecture Script Ver 1.3 March 2010, T. Haslwanter, Upper Austria University of Applied Sciences, Linz, Austria,

Biological Machines/Authors

This list contains the names of all the authors that have contributed to this text. If you have added, modified or contributed in any way, please add your name to this list.

Name	Institution
Thomas Haslwanter	Upper Austria University of Applied Sciences / ETH Zurich
Aleksander George Slater	Imperial College London / ETH Zurich
Piotr Jozef Sliwa	Imperial College London / ETH Zurich
Qian Cheng	ETH Zurich
Salomon Wettstein	ETH Zurich
Philipp Simmler	ETH Zurich
Renate Gander	ETH Zurich

Article Sources and Contributors

Biological Machines/Cover *Source*: http://en.wikibooks.org/w/index.php?oldid=1514748 *Contributors*: Skela

Biological Machines/Introduction *Source*: http://en.wikibooks.org/w/index.php?oldid=2054825 *Contributors*: Adrignola, Skela, Thomas.haslwanter

Biological Machines/Sensory Systems/Visual System *Source*: http://en.wikibooks.org/w/index.php?oldid=1539196 *Contributors*: Adrignola, Psimmler, Salomonw, Skela

Biological Machines/Sensory Systems/Auditory System *Source*: http://en.wikibooks.org/w/index.php?oldid=2060738 *Contributors*: Adrignola, Rega, Skela, Thomas.haslwanter, 34 anonymous edits

Biological Machines/Sensory Systems/Vestibular System *Source*: http://en.wikibooks.org/w/index.php?oldid=2060553 *Contributors*: Adrignola, Skela, Thomas.haslwanter, 15 anonymous edits

Biological Machines/Sensory Systems/Olfactory System *Source*: http://en.wikibooks.org/w/index.php?oldid=1971872 *Contributors*: Adrignola, Jomegat, Skela, Zurlos

Biological Machines/Appendix *Source*: http://en.wikibooks.org/w/index.php?oldid=2054821 *Contributors*: Adrignola, Skela, Thomas.haslwanter

Biological Machines/Sources *Source*: http://en.wikibooks.org/w/index.php?oldid=1931404 *Contributors*: A mu, Adrignola, Pole from sweden, Rega, Skela, 1 anonymous edits

Biological Machines/Authors *Source*: http://en.wikibooks.org/w/index.php?oldid=2030691 *Contributors*: Adrignola, Psimmler, Rega, Skela, Thomas.haslwanter

Image Sources, Licenses and Contributors

Image:Biological_machines_cover.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Biological_machines_cover.jpg *License*: Public Domain *Contributors*: Adrignola, Skela

Image:Generic_visual_system.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Generic_visual_system.svg *License*: Public Domain *Contributors*: Aleksander G. Slater

Image:Atmospheric_electromagnetic_opacity.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Atmospheric_electromagnetic_opacity.svg *License*: Public Domain *Contributors*: NASA (original); SVG by Mysid.

Image:Nautilus_pompilius_(head).jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Nautilus_pompilius_(head).jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Lycaon

File:Hawk_eye.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Hawk_eye.jpg *License*: Creative Commons Attribution 2.0 *Contributors*: Steve Jurvetson

File:Ewe sheep black and white.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Ewe_sheep_black_and_white.jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:George Gastin

File:Изображение_307.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Изображение_307.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: User:Zema zZz

File:Eye_iris.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Eye_iris.jpg *License*: Creative Commons Attribution-Sharealike 2.5 *Contributors*: User:Che

Image:Volucella_pellucens_head_complete_Richard_Bartz.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Volucella_pellucens_head_complete_Richard_Bartz.jpg *License*: Creative Commons Attribution-Sharealike 2.5 *Contributors*: User:Makro Freak, User:Richard Bartz

File:Wolf_eyes_for_guide.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Wolf_eyes_for_guide.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: User:Opoterser

File:Phidippus_pius_eyes.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Phidippus_pius_eyes.jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Opoterser

Image:Schematic_diagram_of_the_human_eye_en.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Schematic_diagram_of_the_human_eye_en.svg *License*: Public Domain *Contributors*: Rhcastilhos

Image:Structure_cornea1.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Structure_cornea1.png *License*: GNU Free Documentation License *Contributors*: Piotr Sliwa. Original uploader was A mu at en.wikibooks

Image:Eyemuscles.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Eyemuscles.png *License*: Public Domain *Contributors*: Alno, Edelhart, Kersti Nebelsiek, Lennert B, Lipothymia

Image:Filtering_em_eye.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Filtering_em_eye.png *License*: Public Domain *Contributors*: Piotr Sliwa

Image:Retina.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Retina.jpg *License*: GNU Free Documentation License *Contributors*: Peter Hartmann at de.wikipedia, edited by Marc Gabriel Schmid

Image:Density_rods_n_cones.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Density_rods_n_cones.png *License*: Public Domain *Contributors*: Piotr Sliwa. Original uploader was Skela at en.wikibooks

Image:Cone_cell_en.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Cone_cell_en.png *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Kruusamägi

File:Cone-response.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Cone-response.svg *License*: GNU Free Documentation License *Contributors*: User:Maxim Razin

Image:Fig_retine.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Fig_retine.png *License*: Public Domain *Contributors*: Chrkl, Diego UFCG, Drahkrub, Jarry1250, Lipothymia, 1 anonymous edits

Image:Phototransduction.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Phototransduction.png *License*: Creative Commons Attribution 3.0 *Contributors*: User:Caddymob

File:Receptive field.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Receptive_field.png *License*: Public Domain *Contributors*: User:Xoneca, user:delldot

File:Gray722.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Gray722.png *License*: unknown *Contributors*: Arcadian, Lipothymia, Was a bee

Image:2D_Fourier_Plane_01.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:2D_Fourier_Plane_01.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: Salomonw

Image:2D_Fourier_Plane_02.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:2D_Fourier_Plane_02.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: Salomonw

Image:2D_Fourier_Plane_03.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:2D_Fourier_Plane_03.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: Salomonw

Image:2D_Fourier_Plane_04.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:2D_Fourier_Plane_04.jpg *License*: Creative Commons Attribution 3.0 *Contributors*: Salomonw

Image:ImplantSawan.JPG *Source*: http://en.wikibooks.org/w/index.php?title=File:ImplantSawan.JPG *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: Mohamad Sawan

File:Mother-Child_face_to_face.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Mother-Child_face_to_face.jpg *License*: Creative Commons Attribution 2.0 *Contributors*: GeorgHH, Nihiltres, Widescreen, 1 anonymous edits

File:Sanc0602.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Sanc0602.jpg *License*: Public Domain *Contributors*: Achim Raschka, B.navez, Bricktop, Myself488, Viriditas, 1 anonymous edits

File:Big-eared-townsend-fledermaus.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Big-eared-townsend-fledermaus.jpg *License*: Public Domain *Contributors*: Eusebius, Furado, Liné1, Nordelch, 5 anonymous edits

File:Hyphessobrycon_pulchripinnis.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Hyphessobrycon_pulchripinnis.jpg *License*: Creative Commons Attribution 2.5 *Contributors*: User:Waugsberg

File:Ear.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Ear.jpg *License*: Creative Commons Attribution-Sharealike 2.0 *Contributors*: User:Dbenbenn

File: Anatomy_of_the_Human_Ear.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Anatomy_of_the_Human_Ear.svg *License*: Creative Commons Attribution 2.5 *Contributors*: Chittka L, Brockmann

File: Middle_Ear_Ossicles.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Middle_Ear_Ossicles.jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: Mattia Ferrazzini

File:Cochlea.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Cochlea.svg *License*: Public Domain *Contributors*: User:Fred the Oyster

File:Cochlea-crosssection.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Cochlea-crosssection.svg *License*: GNU Free Documentation License *Contributors*: User:Fred the Oyster

File:Organ_of_corti.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Organ_of_corti.svg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Madhero88

File: Sound_shadow.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Sound_shadow.svg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Thomas.haslwanter

File: MiddleEar Amplification.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:MiddleEar_Amplification.jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Thomas.haslwanter

File: Uncoiled cochlea with basilar membrane.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Uncoiled_cochlea_with_basilar_membrane.png *License*: Creative Commons Attribution 2.5 *Contributors*: Kern A, Heid C, Steeb W-H, Stoop N, Stoop R

File:Lateral_lemniscus.PNG *Source*: http://en.wikibooks.org/w/index.php?title=File:Lateral_lemniscus.PNG *License*: unknown *Contributors*: User:Mikael Häggström

File:Gray726-Brodman.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Gray726-Brodman.png *License*: unknown *Contributors*: Arcadian, Lipothymia, Magnus Manske, Was a bee

File:HearingLoss.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:HearingLoss.svg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Thomas.haslwanter

Image:Cochlear implant.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Cochlear_implant.jpg *License*: unknown *Contributors*: Inductiveload, Matt314, Maxim Razin, Nagy, Wst, 10 anonymous edits

Image:Cochearimplants.JPG *Source*: http://en.wikibooks.org/w/index.php?title=File:Cochearimplants.JPG *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Edwtie

File:Canaux osseux.png *Source*: http://en.wikibooks.org/w/index.php?title=File:Canaux_osseux.png *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: José Braga

File: VestibularSystem.gif *Source*: http://en.wikibooks.org/w/index.php?title=File:VestibularSystem.gif *License*: GNU Free Documentation License *Contributors*: user:Thomas.haslwanter

File: Otoliths w CrossSection.jpg *Source*: http://en.wikibooks.org/w/index.php?title=File:Otoliths_w_CrossSection.jpg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Thomas.haslwanter

File:Ampulla of SemicircularCanal.svg *Source*: http://en.wikibooks.org/w/index.php?title=File:Ampulla_of_SemicircularCanal.svg *License*: Creative Commons Attribution-Sharealike 3.0 *Contributors*: User:Thomas.haslwanter

License