Photic transduction

A. Process

Light path

Cornea, aqueous humour, lens, vitreous humour, retina (nervous coat), pigment epithelium (which absorbs any light not captured by the retina preventing back-reflection, and assists the photoreceptors metabolically). At the foveola, the centre of the fovea, the neural elements are shifted to one side so the light has a direct path to the photoreceptors.

The retina is part of the CNS, unlike all other sensory structures.

Photoreceptors

Photoreceptors are divided into rods and cones. Cones perform better than rods in all visual tasks except the detection of dim stimuli. **Rods are achromatic,** having only one pigment, **but are more sensitive than cones.** They amplify light signals more (one photon can evoke a response), but are saturated in daylight. Cones mediate colour vision (there are three subtypes with different pigments for red, green and blue). Although there are 20 rods for each cone the **cones provide better spatial resolution** for two reasons. Firstly, they are concentrated in the fovea where the image is least distorted. Secondly, rods are *convergent* in that many rods synapse on one target interneuron (a bipolar cell) where the signals reinforce, improving the ability of the brain to detect dim lights but degrading the ability to transmit spatial variations in the image. Only a few cones converge on each bipolar cell; cones in the foveola do not converge at all.

Photoreceptors do not fire action potentials; they respond to light with a graded change in membrane potential. Rods respond slowly, allowing the effects of photons 100ms apart to summate. This enables better detection of light but means they cannot detect flicker above 12Hz. Cones respond faster and can detect flicker up to 55 Hz. Therefore **cones provide greater temporal resolution.**

Photoreceptors contain (1) a region for phototransduction, the *outer segment*, closest to the outer, distal surface of the retina and on the side furthest from the lens; (2) the *inner segment*, containing the nucleus and biosynthetic machinery; (3) a *synaptic terminal* connected to the inner segment by a thin *stalk* or *cilium*. The outer segments are packed with membranous discs (free-floating in rods, invaginations of the cell surface in cones) which, in rods, develop at the base of the outer segment and migrate outwards to the tip (3 discs made per hour in rods) where the discarded tips are phagocytosed by pigment epithelial cells. Cones also undergo renewal and phagocytosis of the membranes, but renewal is not understood.

The discs contain pigment molecules. They are arranged with the flat surface perpendicular to the disc and are stacked to maximize light absorption. Rods contain 10^8 pigment molecules. Phototransduction proper is as follows.

1. Light activates pigment molecules in photoreceptors.

In rods: the visual pigment is rhodopsin. This is the protein opsin (embedded in the disc membrane) linked to retinal (the light-absorbing portion). Non-activated rhodopsin contains 11-*cis* retinal, which fits into a binding site in opsin. Light causes 11-*cis* retinal to become all-*trans* retinal (the more stable form). This is the only light-dependent step. This form of retinal no longer fits into the opsin binding site, so opsin undergoes a conformational change. Within 1ms rhodopsin has proceeded through several unstable intermediates to metarhodopsin II. This triggers the second step. It is short-lived; within minutes (i.e. too slow to inactivate the light response) the Schiff-base covalent linkage between opsin and retinal hydrolyses; the opsin and all-*trans* retinal diffuse away. The retinal is transported to the pigment epithelium by a retinal-binding protein (it is not very water-soluble) where it is reduced to all-*trans* retinol (vitamin A), the precursor for 11-*cis* retinal synthesis. This is used to regenerate rhodopsin. Vitamin A deficiency leads to night blindness and eventually to total blindness via the deterioration of receptor outer segments.

In cones: the pigment is cone opsin, again linked to 11-*cis* retinal. There are three types of cone opsin, which interact with the retinal in different ways and cause it to be sensitive to different parts of the visual spectrum.

2. These activated molecules cause the stimulation of cGMP phosphodiesterase, which reduces cytoplasmic cGMP concentration.

Cytoplasmic [cGMP] is a function of the balance between the activity of guanylate cyclase and cGMP phosphodiesterase. In the dark, there is little phosphodiesterase activity and [cGMP] is about 2 μM. Stimulation by light activates rhodopsin, which activates the G-protein transducin. This activates cGMP phosphodiesterase. Transducin has intrinsic GTPase activity, functioning as an off switch. There is tremendous amplification: one activated rhodopsin can diffuse within the disc membrane and activate hundreds of transducin molecules; each of these can activate a cGMP phosphodiesterase; each of these can hydrolyse 10^3 cGMP per second.

In addition to the processes mentioned that terminate the cascade, activated rhodopsin is a target for phosphorylation by opsin kinase. Phosphorylated rhodopsin interacts with a regulatory protein called arrestin, leading to its rapid inactivation.

3. The reduction in cGMP closes cGMP-gated ion channels in the plasma membrane, hyperpolarizing the cell.

The photoreceptor's membrane potential in the dark is determined by nongated (leakage) K^+ channels, which tend to drive the membrane potential to the potassium equilibrium potential of –70mV, and by open cGMP-gated channels which admit a *dark current* of about 50 pA (mainly Na^+). This current keeps the membrane potential at about –40 mV. The cGMP-gated channels are only found in the outer segment (and are the only channel there). The K^+ channels are confined to the inner segment. Therefore in darkness current flows into the outer segment and out of the inner segment (out because the cell is depolarized with respect to the potassium equilibrium potential). To compensate the cells have a high density of Na^+–K^+ pumps in the inner segment.

A bright light can cause the closure of all cGMP-gated channels, driving the membrane potential to –70 mV. Intermediate light intensities set the membrane potential to values between –40 and –70 mV.

Light adaptation is important in cones, such as when you walk into bright sunlight from a dark room. The light closes all cGMP-gated channels but within a few seconds the membrane potential rises and the photoreceptors are no longer saturated. This is a process dependent on calcium, which inhibits guanylate cyclase. Normally, calcium makes up one-seventh of the dark current, and its concentration in the outer segment is constant in the dark because it is extruded by a specialized carrier in the outer membrane. During prolonged illumination the cGMP-gated channels are closed, which leads to a drop in the level of calcium; this relieves the calcium inhibition of guanylate cyclase, so cGMP levels rise and the channels reopen, causing slow depolarization of the cone.

Light adaptation also involved a **desensitization** of the cone, not considered here.

Dark adaptation occurs over tens of minutes and involves several changes to rods.

Output from the retina

Ganglion cells are the output neurons of the retina. Their axons form the optic nerve. They transmit information as action potentials. Between the photoreceptors and the ganglion cells are three classes of interneuron: **bipolar, horizontal and amacrine cells,** which transmit information from photoreceptors to ganglion cells and combine it.

Ganglion cells show constant activity; light modulates this. Each cell responds to light directed at a specific area of the retina, called the **receptive field** of the cell. The fields are roughly **circular.** The fields are smallest at the fovea (centres only a few minutes of arc) and largest at the periphery (centres 3° to 5°. 1° on the retina is about 0.25mm). The receptive fields have a **centre and an antagonistic surround.**

There are two types of ganglion cell. **On-centre ganglion cells** are stimulated by light on their receptive field centre and inhibited by light to the surround. **Off-centre ganglion cells** do the opposite, and their firing rate is highest for a brief period when a light applied to the field centre is turned off. In both types of cell the response evoked by a ring of light to the surround almost completely cancels the response evoked by light to the centre, so diffuse illumination of the whole field evokes only a small response. After adaptation to extreme darkness or very dim light for over an hour, illumination of the surround ceases to inhibit the response to illumination of the centre. On- and off-centre ganglion cells are present in roughly equal numbers and provide parallel pathways for the processing of visual information: every photoreceptor sends outputs to both types of ganglion cell.

This system of field organization maximizes the detection of contrast, and since the retina does this the opportunity for signal corruption (before contrast detection occurs) is minimized. The two types of ganglion cell are specialized to signal rapid increases (on-centre) or decreases (off-centre) in illumination. On-centre neurons, for example, have a low rate of firing under dim illumination anyway, and therefore are ill-suited to signalling rapid drops in illumination but well-suited to signalling rises.

The retina is also involved in processing specific aspects of the visual image. Most ganglion cells of primates fall into two classes, M and P (also called Pα and Pβ). Both classes contain on- and off-centre ganglion cells. M cells have large cell bodies and a large dendritic arborization; the latter gives them a large receptive field, and they show a relatively transient response to sustained illumination. They respond to large objects, and movement. P cells are more numerous, have smaller receptive fields, are mostly wavelength-selective and are involved in colour vision. They are thought to be responsible for analysis of fine detail (though M cells may be involved here too).

A few ganglion cells do not have a centre-surround receptive field organization. For example, some response to changes in the overall luminance and are important in controlling pupillary reflexes.

Interneuron connections

The responses of the ganglion cells are a result of the 'wiring' of interneurons. Each type of interneuron plays a specific rôle in processing the signals from the photoreceptors.

Cone signals are conveyed to ganglion cells through direct or lateral pathways. Cones in the centre of a ganglion cell's receptive field synapse with bipolar cells that synapse with the ganglion cells (*direct* or *vertical pathways*). Signals from cones in the field surround reach the ganglion cell via horizontal and amacrine cells (*lateral pathways*). Horizontal cells transfer information from distant cones to nearby bipolar cells. Some types of amacrine cell transfer information from distant bipolar cells to ganglion cells.

This is reflected in retinal organization: there are nuclear layers, containing cell nuclei and plexiform layers, where most synapses are. They are

(1) the *outer nuclear layer*: photoreceptors
(2) the *outer plexiform layer*: processes of receptor, bipolar and horizontal cells
(3) the *inner nuclear layer*: bipolar, horizontal and amacrine cells
(4) the *inner plexiform layer*: processes of bipolar, amacrine and ganglion cells

(5) the *ganglion cell layer*: ganglion cells.

Horizontal and bipolar cells do not fire action potentials; they transmit signals passively but have short processes so signal reduction is insignificant. Ganglion cells fire action potentials, as do many amacrine cells.

Bipolar cells also have centre-surround receptive fields. Cones in the centre of a bipolar cell's receptive field are directly connected to the bipolar cell. They release glutamate continuously, less so when hyperpolarized by light. The glutamate hyperpolarizes on-centre bipolar cells (at some synapses by opening K^+ channels, at others by closing cGMP-gated Na^+ channels by stimulating cGMP phosphodiesterase indirectly) and depolarizes off-centre bipolar cells (by opening Na^+ channels), so on-centre bipolar cells are excited by light and vice versa. Cones in the field surround are connected to horizontal cells, which synapse onto cones in the field centre and depolarize them in response to light at the surround.

Each class of bipolar cells has excitatory connections with ganglion cells of the same class. It is possible that in mammals it also inhibits ganglion cells of the opposite class (this would obviously increase sensitivity). The responses of ganglion cells are largely determined by input from bipolar cells, but are also shaped by amacrine cells. There are over 20 types of amacrine cell using at least 8 neurotransmitters; some function similarly to horizontal cells (mediating antagonistic inputs to ganglion cells from bipolar cells in the ganglion cell's surround) while others may shape the complex receptive field properties of specific types of ganglion cells, such as the M-type ganglion cells that are orientation-specific.

Different pathways convey rod signals to ganglion cells in the moderately and extremely dark-adapted eye. In the moderately dark-adapted eye, rod signals can be transmitted directly to neighbouring cones via gap junctions. The signals are then relayed to ganglion cells as described. This means that the receptive field properties of ganglion cells do not change as the eye becomes moderately dark-adapted. In the extremely dark-adapted eye, ganglion cell sensitivity increases dramatically until they can detect the effects of individual photons absorbed by rods in their receptive field centre (one reason for this is the lack of inhibition from their surround). Here, ganglion cells cease to detect local contrast and act as simple light detectors. This change results from an alteration in the signal pathway. During prolonged adaptation, the rod-cone gap junctions close and signals are transferred to ganglion cells via *rod bipolar cells*, a subset of on-centre bipolar cells that receive input only from rods. They send outputs to AII amacrine cells, which communicate with off-centre ganglion cells and on-centre cone bipolar cells (which synapse onto on-centre ganglion cells).

Most synapses in the retina are chemical; there are electrical synapses (gap junctions) between photoreceptors and between horizontal cells (which can mediate lateral information transfer over long distances). In addition to conventional chemical synapses there are two types of synapse which photoreceptors use exclusively: *ribbon synapses* (one presynaptic specialization to more than one postsynaptic element, often a *triad* composed of two horizontal cell processes and a central on-centre bipolar cell process; this ensures simultaneous release of transmitter onto the three elements) which are also found between bipolar cells and postsynaptic amacrine/ganglion cells, and *basal synapses* (not found in rods, only synapse between cones and off-centre bipolar cells, calcium-independent nonvesicular release, mechanism unknown but might be voltage-dependent transport of glutamate out of cells by specific carrier proteins).

B. Control

Tracking of objects by eye/head movements

Visual, somatic and auditory information is projected to three sensory maps in the **superior colliculus,** where there is also a motor map. The sensory maps are spatially aligned with each other (visual more superficial, receiving input from the retina and visual cortex; deeper layers mostly concerned with auditory and somatic sensory systems but receiving some visual input from the superficial layers). The size of the representation of a somatic structure depends not on its importance as a tactile organ but on its distance from the eye (so the nose and face have relatively large areas). A given point in the superior colliculus represents a point in visual space. The motor map allows the colliculus to control **saccadic** (fast) eye movements to orient the eye to a stimulus, together with the **frontal eye fields.** The colliculus receives information about (1) motion in the visual field, (2) visual attentiveness, (3) broad outlines of objects. The frontal eye fields receive input from the primary visual cortex about fine visual discrimination, and generates saccadic movements in response to complex stimuli.

The superior colliculus projects to the regions of the brain stem that control eye movements. It also gives axons to the **tectospinal tract,** which is involved in the reflex control of neck and head movements (its axons cross the midline and run to the upper spinal cord where neck motor neurons are), and the **tectopontine tract,** which relays visual input to the cerebellum for further coordination of eye/head movements.

The vestibulo-ocular reflex uses vestibular input to hold images stable on the retina during brief or rapid head rotation. The semicircular canals of the vestibular labyrinth signal how fast the head is rotating, and the oculomotor system responds by rotating the eyes at an equal and opposite velocity. Vestibular nystagmus resets eye position during sustained rotation (slow phase tracking, quick phase reset). However, the semicircular canals respond poorly to very slow movements and habituate to repeated movement in the same direction with a time constant of about 5 seconds (brain stem circuitry effectively extends this to 25s). The reflex is coordinated in the brain stem and is modulated by the cerebellum.

The vestibulo-ocular reflex is suppressible and can be switched off voluntarily; for example, if you are watching something that is moving with you, you want the eyes to travel with the head and the reflex tries to make the eyes remain in their original spatial position.

The optokinetic system uses visual input to hold images stable on the retina during sustained or slow head rotation. While the vestibular system has short latency and slow delay, the optokinetic system has long latency and slow build-up. It drives the eyes in the direction of full-field motion (the direction the stable aspects of the environment move in the visual field) to oppose head movement. The system responds well to the slow visual motion that slow head movement causes: in fact it interprets visual movement as head movement (if a car next to you at traffic lights moves forward, you feel as if you are moving backward).

Both these systems are under adaptive control. It is desirable to have a gain of 1 in the system, to stabilize the image on the retina. The reflex is too fast to use closed-loop control; it uses open-loop control. It adapts in the long-term; for example, glasses for myopia reduce the size of the retinal image, so the gain of the reflex must be reduced below 1.

The smooth pursuit system holds the image of a moving target on the fovea. It *moves* the eyes in space to keep a target on the fovea, by calculating how fast the target is moving. It is voluntary and requires a moving stimulus to calculate the eye velocity. It requires attention to an object to pursue it. The maximum velocity of the movement is about 100°/s. The system requires the cerebral cortex, cerebellum and pons, and is organized in pontine and mesencephalic reticular centres (as is the saccadic system, below).

The saccadic system brings new objects of interest onto the fovea. If a target's image suddenly moves off the fovea, there is a 200ms pause after which the eyes move quickly to return the image to the fovea. The rapid eye movement is called a *saccade*. Accurate saccades do not require a visual stimulus. The velocity of saccades is determined by the distance of the target from the fovea and is involuntary (unlike the amplitude and direction). Saccades reach speeds of 900°/s so there is no time for feedback during its course; small saccades make corrections after the primary one. The system can adapt to changes in muscle function (a cerebellar function). Horizontal saccades are generated in the pontine reticular centre and vertical saccades in the mesencephalic.

The vergence system adjusts the eyes for different viewing distances in depth. This involves *disconjugate* eye movements, unlike the other systems described which move both eyes the same amount in the same direction. Vergence is triggered by *retinal disparity* (differences between the position of an object in one eye compared to the other) greater than a few minutes of arc (compare stereopsis, which can use disparities of a few tens of seconds of arc).

Targets approaching the eyes normally become blurred and are brought into focus by accommodation

Targets approaching the eyes normally become blurred and are brought into focus by accommodation. Accommodation is effected by contraction of the ciliary muscle, which changes the radius of curvature of the lens: contraction releases tension on the suspensory ligament of the lens, allowing it to thicken on its own. Accommodation is linked to vergence (the accommodation-convergence reflex); blur can induce convergence as well as accommodation, and vergence can induce accommodation even when there is no blur. The change in lens curvature is accompanied by pupillary constriction to sharpen the focus. Accommodation is a cortical reflex; it accompanies conscious vision. The accommodation pathway runs from the visual cortex to the frontal eye field, to the Edinger-Westphal nucleus and thence to the ciliary ganglion: it does not pass through the pretectal nucleus, unlike the pupillary light pathway described below.

Pupillary light reflexes

are mediated by retinal ganglion cells that respond to overall changes in illumination and project to the **pretectal area.** Cells there project *bilaterally* (hence the consensual as well as the direct response) to preganglionic parasympathetic neurons in the Edinger-Westphal (accessory oculomotor) nucleus, just adjacent to neurons of the oculomotor nucleus. Fibres from the Edinger-Westphal nucleus run to the ciliary ganglion, where postganglionic neurons innervate the smooth muscle of the pupillary sphincter.

Biochemical and interneuron control

See above.

Auditory transduction

Process

Sound causes the **tympanic membrane** to vibrate. The vibrations are passed down the **ossicles** (malleus, incus, stapes) to the **oval window** of the cochlea. The system of ossicles conducts sound from the outer to inner ear, amplifying the sound pressure at the oval window and providing impedance matching between air and ear fluids. The vibration of the oval window causes a similar **vibration in the fluid** of the scala vestibuli, that of the scala tympani and the round window, fluid being incompressible. The pressure waves also cause vibration of the scala media and its floor, the **basilar membrane.** When the basilar membrane vibrates, so do the hair cells on it, relative to the tectorial membrane.

The inner hair cells in the organ of Corti sit on the basilar membrane and are attached at their apical ends via stereocilia to the tectorial membrane. When the stereocilia are bent one way, they depolarize; the other way, they hyperpolarize. **Vibration of the basilar membrane therefore causes sinusoidal potential changes in the overlying inner hair cell** at the frequency of the vibration. **Depolarization of the hair cell causes neurotransmitter to be released** from its basal surface. This excites the peripheral terminal of a sensory bipolar neuron whose cell body lies in the spiral ganglion and whose central axon constitutes part of the **auditory nerve** (CN VIII).

A particular frequency will excite a particular area of the basilar membrane for two reasons. Firstly, the basilar membrane has cross striations much like piano strings. Secondly, its width varies along the cochlea: it is narrow and stiff near the oval window, and wide and flexible at the apex of the cochlea. Therefore the membrane at the base of the cochlea resonates to high frequencies (short stiff strings), about 15 kHz; the membrane at the apex resonates at about 100 Hz. Between these extremes there is a **spectrum of resonance,** in which **frequencies are logarithmically represented along the membrane.** However, a sound sets up a travelling wave along the cochlea and does not cause the resonance of only one region of the membrane. But different sounds produce different **travelling waves,** with peak amplitudes at different positions along the cochlea. At low frequencies the peak amplitude of membrane motion is at the apex of the cochlea (near the helicotrema). As the frequency increases, the peak moves closer to the base. At a given frequency, the peak displacement increases and a broader region of the membrane vibrates.

Furthermore, the **hair cells are mechanically tuned.** Cells near the base have short, stiff stereocilia; at the apex the stereocilia are more than twice as long and more flexible than those at the base. The **hair cells are also electrically tuned** to the frequency to which they are mechanically tuned. The mechanical stimulus depolarizes and hyperpolarizes the cell via a Ca^{2+} current, a Ca^{2+}-activated K^+ current and a voltage-sensitive delayed K^+ current. Calcium influx causes depolarization, countered by the calcium-activated K^+ current which is augmented by the voltage-gated K^+ current to repolarize the cell; as calcium is being sequestered, the potassium currents decrease. The interaction between currents causes spontaneous fluctuation of the membrane potential about its resting level, and different cells have different current kinetics causing different frequencies of oscillation. Also, the **auditory nerve fibres are electrically tuned** [at least in some species] to the frequency of their hair cell. These various tuning mechanisms sharpen the response to a given frequency.

Note firstly that the auditory nerve fibres cannot fire with each peak of stimulus at high frequencies: the 1ms refractory period limits their rate of firing to about 0.5 kHz (upper bound of human hearing about 20 kHz). Secondly, the rate of firing takes a while to build up in response to a tone and the pattern of response is not the same from one stimulus to the next. Thirdly, the auditory system contains systems to demodulate AM and FM components of biologically significant sounds (e.g. speech).

Auditory nerve fibres respond to brief tones in similar ways: there is an initial phasic increase in firing rate above the spontaneous level, followed by a tonic discharge for the duration of the tone. When the tone ceases, there is a drop below the spontaneous level and a gradual increase to it. This pattern is evident in response to evoked by sounds 20dB above threshold.

The fibres also show **phase locking:** they fire preferentially at a certain point in the sound cycle. This enables them to convey frequency information even if they cannot fire once per cycle. Phase locking has been observed up to 8 kHz.

It is possible that several fibres phase-locked to a stimulus could inform a central target in the brain in concert about each cycle of a high-frequency sound, the *volley principle*. Auditory fibres might be identified by the location of the hair cells they innervate, the *place principle*.

Speech detection is a special problem: the vibrations of mouth and tongue are around 10 Hz, below the lower limit of hearing. However, they modulate higher frequency sounds from the vocal cords, and the ear can demodulate these sounds. The sharp tuning of receptors and nerve fibres allows frequency analysis; also, an individual fibre may have spectral components of its firing pattern both at the frequency of vocal cord vibration and at the lower modulating frequency of mouth and tongue.

Briefly, sound localization is by 1) interaural time difference (up to about 50 μs), for brief sounds; 2) phase difference, for continuous tones below 1400 Hz; 3) interaural intensity difference, for high frequencies where the wavelength is shorter than the interaural distance (the head reflects and absorbs shorter wavelengths).

Bats echolocate by listening to reflected clicks: the Doppler shift in the constant frequency component gives them the prey's relative velocity, and the frequency modulated component is used for rangefinding by the time delay between emission and reflection. The amplitude of the echo gives the angle subtended by the target. Target size is determined by

range and subtended angle. Binaural cues (such as interaural time or amplitude differences) give target azimuth; reflections of sound within the pinna and tragus allow the bat to determine the target's elevation.

Control

The **tensor tympani** muscle (innervated by the mandibular n.) keeps the tympanic membrane tense. It arises from bony and cartilaginous parts of the auditory tube and inserts into the handle of the malleus, and draws it inwards, making the eardrum more concave and more tense. It has no opponent. It damps overvibration from low-frequency sounds.

The **stapedius** muscle (facial n.) activates when incoming sound is very loud, and partially withdraws the foot of the stapes from the oval window by tilting it. The reflex only functions when the loud sound is present for a while (gunshots are too fast for it to respond to, discos aren't). It arises from the interior of the hollow pyramid, inserts into the back of the neck of the stapes and has no opponent other than elastic recoil. It damps overvibration from low-frequency sounds.

Outer hair cells have motor innervation from the CNS and change their length in response to stimulation. They probably alter the sensitivity and/or tuning of a small area of the cochlea. [They cause otoacoustic emissions, in whole or in part, and OAEs closely match the input sound in a healthy cochlea.] This may provide a mechanism by which the brain can tune the cochlea to sounds of interest. The OHCs may also influence the tuning of the IHCs as they are mechanically coupled through their common insertion into the tectorial membrane.

There are also efferent fibres from the CNS that synapse on afferent fibres from the inner hair cells.

Tactile transduction

The dorsal root ganglion neuron is the sensory receptor in the somatic sensory system. Almost all *modality* (type of sensation) coding is by *labelled line codes*: individual receptors respond selectively to one type of stimulus. However, there is some rôle for *pattern codes*, where relatively nonspecialized receptors code different stimuli using temporal patterns. The terminal of the peripheral branch of the axon transduces stimulus energy; the remainder of the peripheral branch together with the central branch (known collectively as the *primary afferent fibre*) transmit the encoded information to the CNS.

Mechanoelectric transduction is produced by direct mechanical interaction of the stimulus with the membrane channel. The channel is cytoskeletally linked to the plasmalemma. Few channels are open in the unstimulated membrane, whereas mechanical stimulus deforms the membrane, opening channels. The influx of Na^+ and K^+ causes the receptor terminal to depolarize locally, producing the receptor potential.

Different sensory receptors have distinguishing anatomical features. The cutaneous and subcutaneous mechanoreceptors of primates are listed below. They are subdivided into two major functional groups: *slowly adapting* mechanoreceptors respond continuously to a persistent stimulus; *rapidly adapting* mechanoreceptors respond only at the onset and termination of a persistent stimulus. All fibres are type Aβ (small myelinated, diameter 6-12 μm, conduction velocity 35-75 m/s) except hair-down receptors which are type Aδ (smallest myelinated, diameter 1-5 μm, conduction velocity 5-30 m/s).

In glabrous (hairless) skin:

Meissner's corpuscles are located in the dermal papillae and transduce flutter. They are rapidly adapting. They are coupled to the surrounding tissue by thin strands of connective tissue. Receptive field small (2-4 mm).

Merkel's receptors are located in the dermal papillae and transduce steady skin indentation. They are slowly adapting. Thought that epithelial cells transduce mechanical stimuli and synapse with the neuron. Receptive field small (2-4 mm).

Bare nerve endings

In hairy skin:

Hair receptors are subdivided into hair-guard, hair-tylotrich and hair-down. They are the principal mechanoreceptor of hairy skin.

Merkel's receptors are slightly different from those in glabrous skin.

Bare nerve endings

Subcutaneous receptors (in glabrous and hairy skin):

Pacinian corpuscles transduce vibration. Rapidly adapting. Large receptive field. Terminal encased in connective tissue laminae; without them [experimentally!] it is slowly adapting.

Ruffini's corpuscles transduce steady skin indentation. Slowly adapting. Large receptive field

Sensory information is processed by a series of relay nuclei. The central branches of the dorsal root ganglion neurons ascend in the dorsal columns and synapse with neurons in the **dorsal column nuclei.** Axons of these neurons cross the midline in the medulla and ascend as the **medial lemniscus.** In the thalamus they synapse with third-order neurons in the **ventral posterior medial** and **ventral posterior lateral nuclei.** The third-order neurons send axons to the **primary somatic sensory cortex (S-I),** in the postcentral gyrus of the parietal lobe. This consists of Brodmann's areas 1, 2, 3a and 3b. Most thalamic fibres run to 3a and 3b; the cells there then project into 1 and 2. All four areas of S-I project to the **secondary somatic sensory cortex (S-II);** this projection is required for the perceptual function of S-II. Some thalamic fibres also project to 1, 2 and S-II, and some to the posterior parietal cortex (Brodmann's areas 5 and 7) which also receives input from S-I. So there are four representations of the body surface in S-I and one in S-II. This allows parallel processing of information in slightly different ways.

The relay nuclei are composed of *projection (relay) neurons* that send axons to the next relay nucleus. Each receives input from many afferent axons. However, in the dorsal column nuclei, for example, some projection neurons may be activated by a single afferent fibre, giving high-fidelity transmission. More commonly there is extensive convergence and divergence. In addition to activating relay neurons, afferent fibres activate interneurons (excitatory or inhibitory) that process information by modulating the activity of relay neurons.

There are three patterns of inhibitory pathway; there is no inhibition of the peripheral receptor in the somatic sensory system, but in all subsequent relay nuclei.. *Feed-forward (reciprocal) inhibition* allows one group of neurons to inhibit another. It permits "singleness of action": winner-takes-all. *Feedback (recurrent) inhibition* allows the most active neurons to inhibit less activate adjacent elements, enhancing contrast. Both these patterns create zones of contrast in the CNS and contribute to *selective perception*. Finally, *distal inhibition* is the inhibition of incoming information to the relay nuclei by distant sites such as the motor cortex and brain stem. In the dorsal column nuclei this is mainly by presynaptic terminals.

The body surface is spatially mapped to the somatic sensory cortex in an orderly fashion, with the most sensitive areas of tactile sensation (fingertips, lips) occupying the greatest area. This mapping is called **somatotopy.** Each central neuron has a specific receptive field, and shows little or no spontaneous activity. The size of the receptive field varies with the area of skin: there are most receptive fields per unit area in the areas for tongue and fingertips. The receptive field size in the sensory system, particularly in the cerebral cortex, can be altered by experience and injury.

The receptive fields have excitatory and inhibitory components. Both are greatest when excitatory/inhibitory stimulus is applied to the centre of the field, and the response diminishes with a gradient towards the edge of the field. The inhibitory field may be larger, giving rise to an inhibitory surround which sharpens the peak of activity. Excitation will supersede inhibition. Since excitation precedes inhibition, this chronological sequence is seen at the synapses of the centre of the receptive field.

Lateral inhibition can aid two-point discrimination. Without it, a single point stimulus would stimulate the centre of the receptive field in a given sensory cell population with high probability of excitation, and the edges with low probability of excitation (they fire fewer impulses with longer latency). Lateral inhibition in the form of the inhibitory surround summates when two stimuli are brought close together, so the two peaks of activity are sharper and better distinguished.

Neurons in the somatic sensory cortex are grouped along three axes: into 6 cellular layers distinguished by connections to other areas, into columns by submodality (skin/rapidly adapting receptors, skin/slowly adapting receptors, deep tissue/muscle and stretch receptors etc.) and along the third axis by location in/on the body. Thus layer 4 receives input from the thalamus, area 3b receives cutaneous receptor input and there is an area in the third axis for the back of the hand. The areas of submodality are of necessity involved in analysing different aspects of somatic sensation: area 1 receives input from rapidly-adapting receptors and therefore is involved in sensing texture; area 2 has a map of deep pressure receptors and is involved in sensing objects' size/shape (area 3a receives input primarily from muscle stretch receptors and 3b from cutaneous receptors as mentioned).

While sensation is faithfully reproduced in the early stages of processing by central neurons, in the later stages of cortical processing the neurons have complex feature-detecting properties and integrate various inputs. This is particularly the case in Brodmann's areas 1 and 2. There are motion-sensitive, orientation-sensitive and direction-sensitive neurons, and even more complex neurons that project to the motor cortex for sensory-motor integration. Finally, the somatosensory cortex projects to the posterior parietal cortex where integration with other senses occurs to form an overall picture of the body.

Olfactory transduction

Humans can distinguish thousands of odorants, at concentrations as low as a few parts per trillion. The olfactory epithelium, about $5cm^2$ in area and lying over the superior and part of the middle concha, contains receptor cells, supporting cells and basal cells. The receptors are bipolar neurons with a short peripheral and a long central process. The peripheral process expands in the mucosal surface into an **olfactory knob.** This gives rise to several immobile cilia that form a dense mat in the surface mucus, where they interact with odorants. The unmyelinated central process joins 10-100 others to form a bundle of axons that is surrounded by Schwann cell processes and passes through the cribriform plate of the ethmoid to the **olfactory bulb** on the underside of the frontal lobe. Unlike most neurons, they are regenerated from precursor basal cells (every 60 days). The new neurons must extend axons into the CNS and synapse with target mitral cells in the bulb. Those cells do not divide and must accept new synapses continually.

Odorants are absorbed into the mucous layer over the receptor. They then diffuse to the cilia or are presented attached to binding proteins in the mucosa. One such has been found: *olfactory binding protein*, which is secreted at the tip of the nasal cavity by the lateral nasal gland, is soluble and binds a wide variety of odorants. It carries small lipophilic molecules, and might trap odorants and deliver them to the receptor sites, or perhaps act as a sink or filter to protect olfactory neurons from exposure to excessive concentrations of odorant.

The receptor potential is due to the opening of Na^+ channels. One method of transduction probably involves an **increase in [cAMP]** by stimulation of adenylyl cyclase in the olfactory epithelium by the odorants - many do this, probably via olfactory receptors and the G-protein G_{olf}. Other organisms than humans (insects) have been shown to use an **IP_3** system for olfactory transduction; it is possible that the same organism may use a variety of second messengers.

Individual olfactory neurons respond to a variety of odorants. It is likely that there are hundreds of olfactory receptors, each recognising one or a few odorants; it is not known whether individual neurons have multiple receptor types or how narrowly tuned each is. It is likely that each neuron expresses only small numbers of distinct receptors.

There are regions of high sensitivity for individual odorants in the olfactory epithelium. Thus limonene preferentially activates neurons in the posterior mucosa, for example. Increased stimulus intensity can activate previously silent receptors in and around the area of maximum sensitivity, changing the overall firing pattern.

The sense of smell is unique in that its central connections project first to phylogenetically older portions of the cortex before reaching the thalamus and finally the neocortex. Smell and taste also have access to neural circuitry that controls emotional state and certain memories.

Within the olfactory bulb the primary axons synapse on the dendrites of large **mitral cells** and small **tufted cells** (the main output cells of the bulb) in synaptic areas called *glomeruli*. The axons of mitral and tufted cells project in the olfactory tract to the **secondary olfactory areas of the olfactory cortex.** This consists of 5 parts: (1) the anterior olfactory nucleus, which connects the two bulbs; (2) the olfactory tubercle; (3) the pyriform cortex, the main olfactory discrimination region; (4) the cortical nucleus of the amygdala; (5) the entorhinal area, which projects to the hippocampus.

There is no strict relationship between the arrangement of the projections of bulb neurons and the regions of mucosa from which they come. Therefore the olfactory bulb and higher centres must be able to distinguish different signals from the same region as different odours. Glomeruli seem to respond preferentially to certain odorants; at higher odorant concentration more glomeruli are activated, so the overall firing pattern carries information about the odour (just as in the mucosa).

The olfactory bulb actively processes information: periglomerular and granule neurons constitute local inhibitory circuits. As with other senses, information is eventually relayed through the thalamus to the neocortex. The olfactory tubercle projects to the medial dorsal nucleus of the thalamus, which projects to the **orbitofrontal cortex** where smell is consciously perceived. In addition **there are olfactory pathways to the limbic system** (amygdala and hippocampus): the amygdala connects the olfactory cortex to the hypothalamus and tegmentum of the midbrain and this pathway is thought to mediate the affective component of odours.

Not discussed here: the senses of balance, taste, proprioception, pain and thermal sensation.