

Systems Neuroscience – Daniel Kiper – 2022/2023

Lecture 1 – Visual System

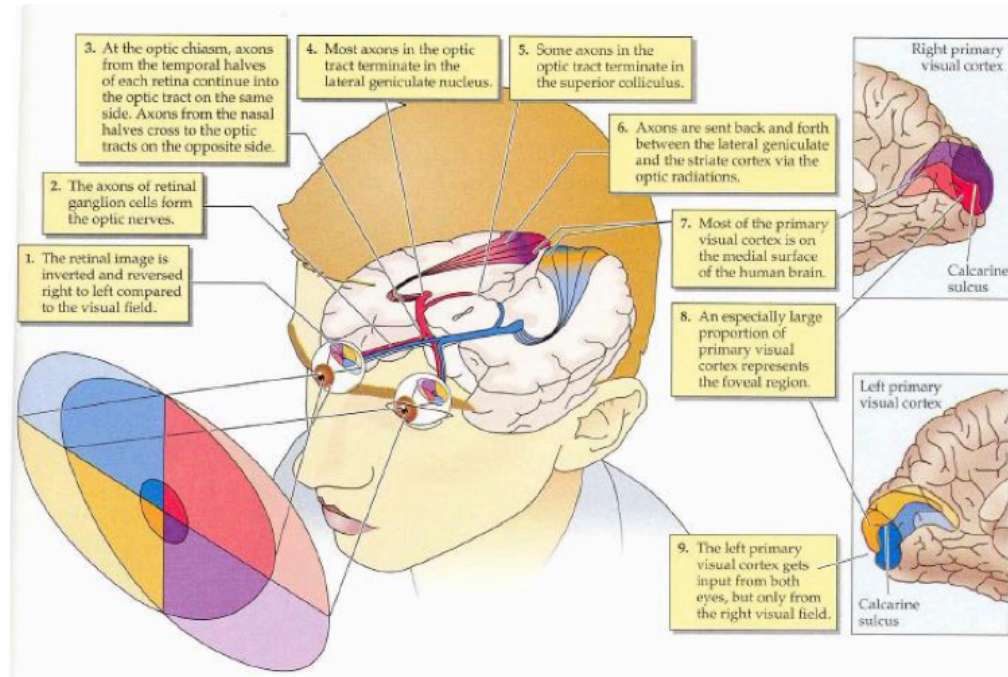
“All systems in the brain always interact. Every neuron can interact with any other neuron through no more than seven neurons.”

“Humans are “visual animals” (primates in general). Parts of visual cortex are easily accessible because they can be found at the outside/back of the cortex”

Retinocortical Pathways

The retinocortical pathways give rise to conscious vision

1. Visual field (approx. 180°). The same point is projected onto the nasal and the temporal part of the retina. The retinal image is inverted and reversed right to left compared to the visual field.
2. The axons of retinal ganglion cells form the optic nerves.

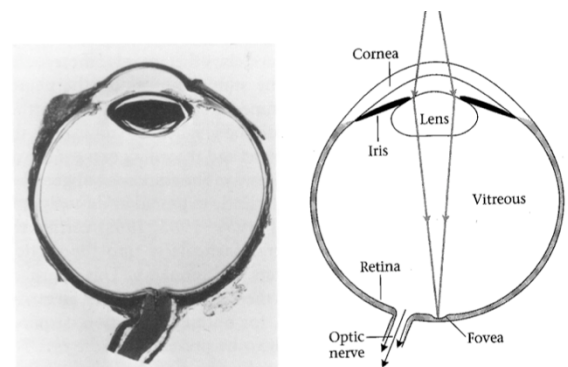


3. At the optic chiasm, axons from the temporal halves of each retina continue into the optic tract on the same side. Axons from the nasal halves cross to the optic tracts on the opposite side. The left hemisphere is analyzed in the right brain hemisphere and viceversa.
4. Most axons in the optic tract terminate in the lateral geniculate nucleus.
5. Some axons in the optic tract terminate in the superior colliculus.
6. Axons are sent back and forth between the lateral geniculate and the striate cortex via the optic radiations.
7. Most of the primary visual cortex is on the medial surface of the human brain. It is buried into the calcarine sulcus. And everything below the calcarine sulcus processes the lower quadrant of the visual field.
8. An especially large proportion of primary visual cortex represents the foveal region.
9. The left primary visual cortex gets input from both eyes, but only from the right visual field.

There is approximately a 40/50 ms delay until the visual signals/information is transmitted from the eye to the first neuron of the visual cortex.

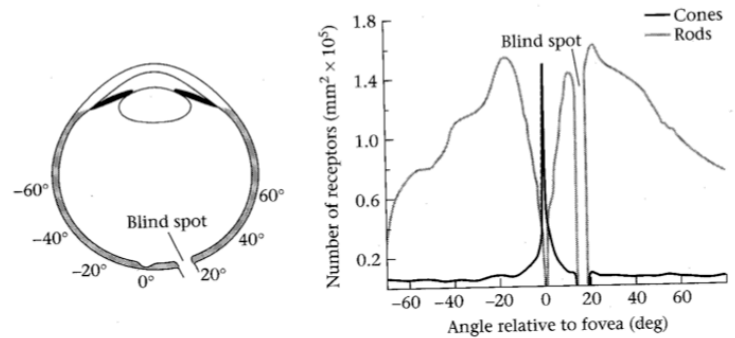
The Human Eye

The **optic nerve** represents a “blind spot” as there are no photoreceptors in its location. However, the brain compensates by “filling” the missing information. The **fovea** is involved in focused vision and allows only a few degrees of visual angle.



Distribution of Rods and Cones: a View from the Side

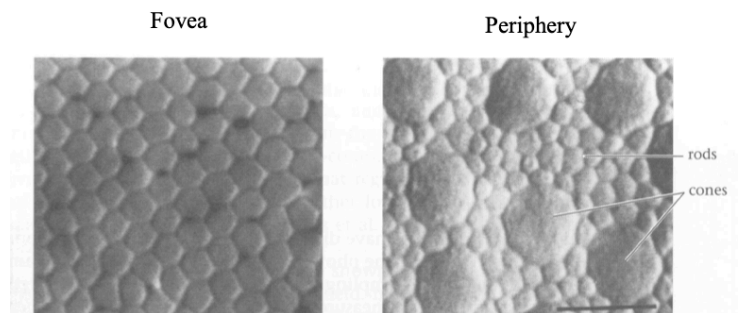
A different distribution of cones and rods is present on the retina. The **cones** work in day light (higher light levels) and are capable of color vision, while the **rods** are saturated during day time (low light levels), but they provide un-colored night vision. There exist 3 types of cones (short-wavelength sensitive, middle-wavelength sensitive and long-wavelength sensitive) and only 1 type of rods.



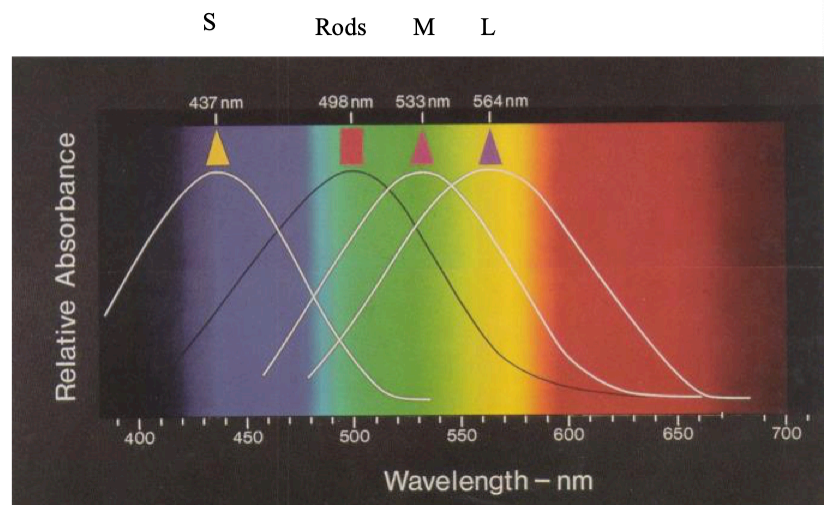
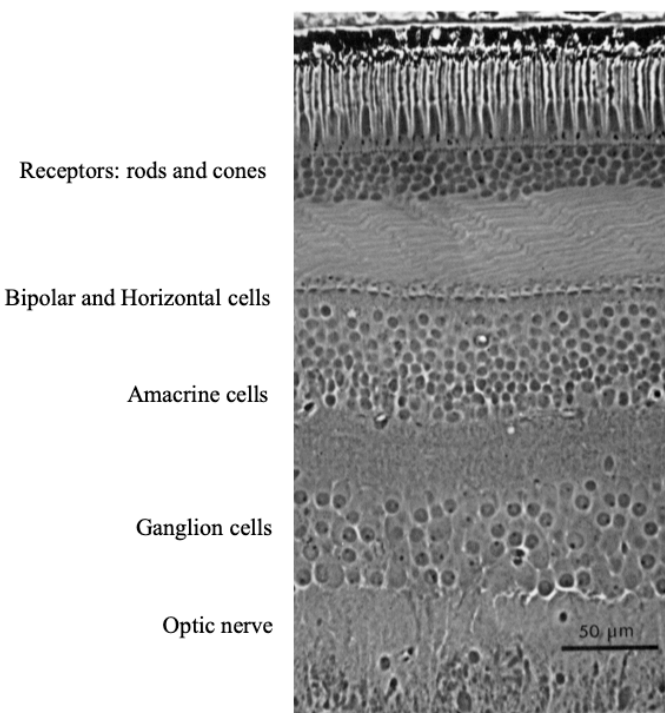
The figure shows the distribution of rods and cones in the retina. We can notice that the fovea is rod-free and has a very high density of cones. The density of cones falls off rapidly to a constant level at about 10-15 degrees from the fovea. Notice the blind spot which has no receptors. At about 15-20 degrees from the fovea, the density of the rods reaches a maximum.

Distribution of Rods and Cones: a View from the Front

As it can be seen from the picture, the fovea presents only rods, while in the periphery both cones and rods can be observed. In particular, cone density decreases with distance from the fovea.



Sensitivity for Wavelength of the 3 Types of Cones



A Section Through the Human Retina

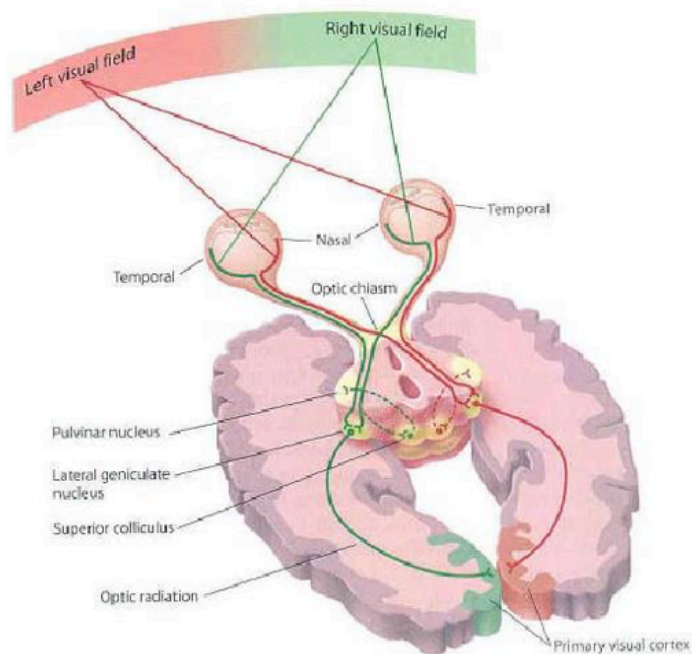
Horizontal cells modulate the output of photoreceptors and play many roles in early visual processing contributing to contrast enhancement, colour opponency, and the generation of center-surround receptive fields in cones. In the human retina there are approx. 1 million ganglion cells, which collect information about the visual world from bipolar and amacrine cells (retinal interneurons). There are many types of amacrine cells that are distinguished based on the way they

respond to visual inputs. Then the layer of photoreceptors responds to changes in membrane potential. Indeed, when the membrane changes potential, photoreceptors release neurotransmitters (they don't communicate through APs). Since they need nutrients, they are located closely to blood vessels, i.e., at the back of the eye in humans.

Basic Retinal Circuitry

The eye already processes the visual information before it sends it to the brain.

The Visual Pathways



Receptor terminals (RT)

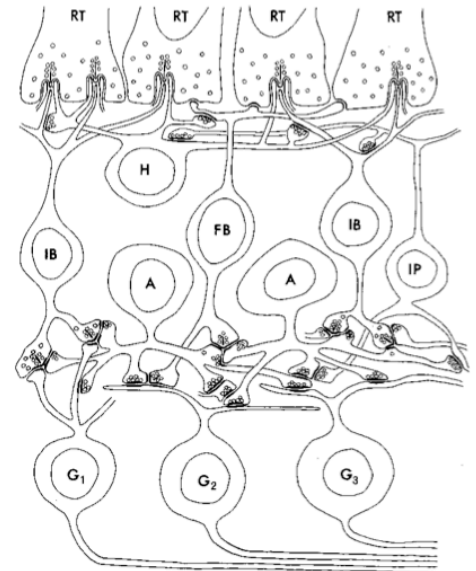
Horizontal cells (H)

Bipolar cells (B)

Amacrine cells (A)

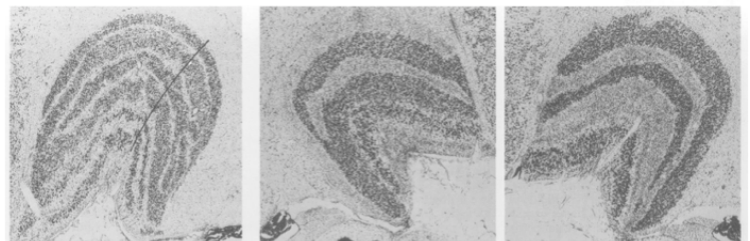
Ganglion cells (G)

Optic nerve



Within the visual pathways plays an important role the **Lateral Geniculate Nucleus (LGN)**, it belongs to the thalamus and it is composed of approx. a million of nerve nuclei. These cells respond more or less the same way ganglion cells do. Furthermore, each LGN receives signals from both eyes.

The Lateral Geniculate Nucleus (LGN)

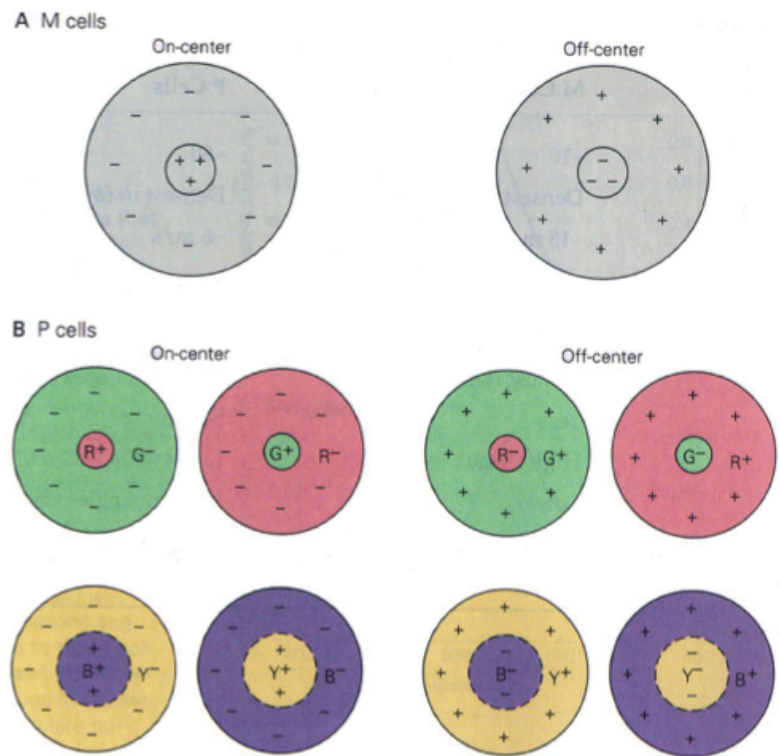


From this cross-section frame of LGN in a primate, it is possible to notice that it has a layer structure, where each layer receives input from one eye (three layers per eye), hence each layer is "monocular". The two bottom layers contain anatomically big cells: Magnocellular, Parvocellular and Koniocellular. M cells do not care about the color, but rather about light intensity differences. They are extremely contrast sensitive. P cells are less contrast sensitive, but they are sensitive to color and are more capable of discriminating fine details than their M counterparts. Finally, K cells deal with short wavelength information. Hence, there is an anatomical segregation according to the information treated.

Each cell in the visual pathway responds to just stuff happening in the receptive field of the cell. Each cell doesn't receive information from all the photoreceptors. It is important to notice that the receptive fields of ganglion cells are round.

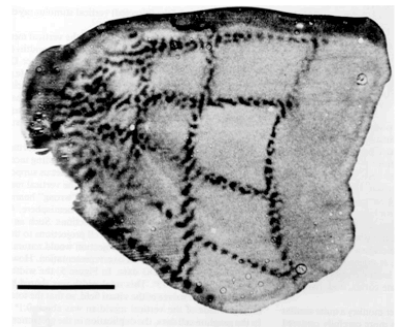
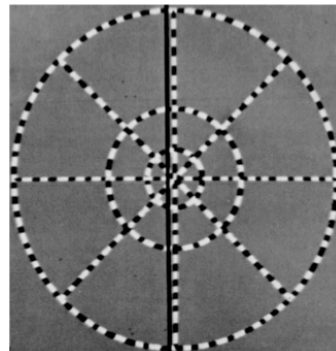
Receptive Fields of Ganglion Cells and LGN Neurons

Approximately 50% of Ganglion cells have an on-center, where the cell strongly responds to an increase of light intensity. While the other 50% shows off-center, where the cell strongly responds to a decrease in light intensity. This type of receptive field is great to detect contrast. The study of this structure provided insights on the process of adaption of the retina to the overall light level. While M-cells and Ganglion cells show very similar receptive fields, P-cells have round receptive fields that discriminate between middle and long wavelengths. Furthermore, the size of the centers of the receptive fields changes depending on the location of the cell in the retina. Finally, K-cells show again round receptive fields which distinguishes among short wavelengths.



Cortical Representation Measured with 2-Deoxy-Glucose

Part of a monkey left hemisphere cortex. The black regions show regions of the brain that have been activated by the visual input. In particular, it demonstrates the **retinotopic visualization**, i.e., a faithful projection of the image. Furthermore, we can notice the **cortical magnification**, i.e., in the cortex, the center of vision is “amplified” and a great percentage of brain tissue is dedicated to the center of vision.

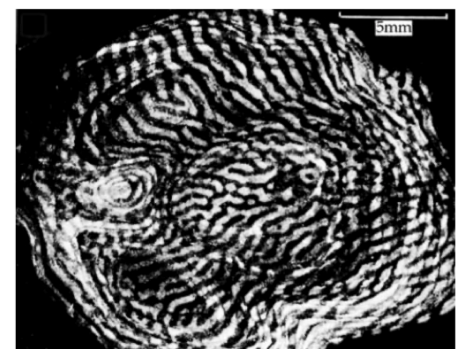


Hubel and Wiesel, circa 1969

They were performing an experiment, studying the receptive fields of cells located in the primary visual cortex of different animals. These two researchers understood what the primary visual cortex is doing. Current vision papers often still cite them and some of the questions they posed are still unanswered. The visual system is thanks to them one of the best understood system of the brain.

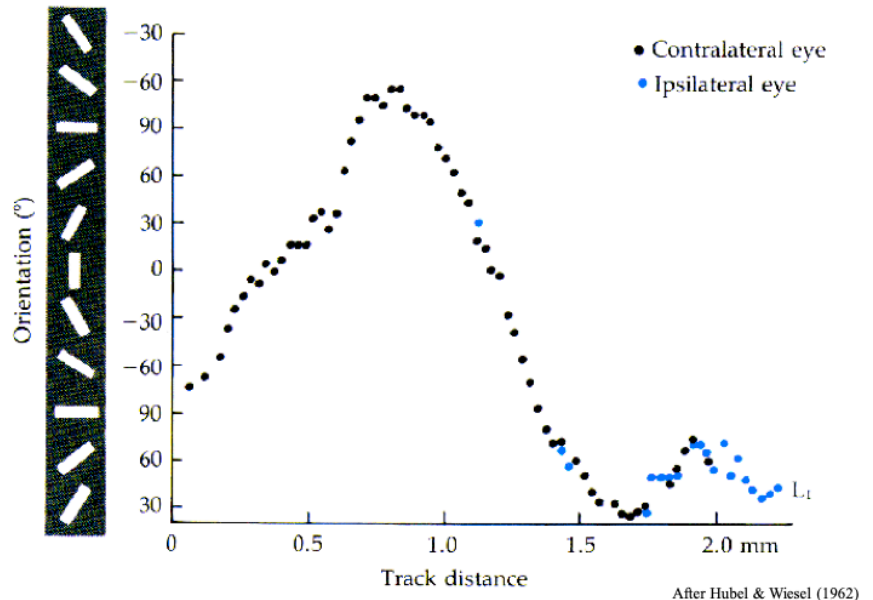
Ocular Dominance Columns Measured with Radioactive Proline

The picture shows a piece of V1, black bands respond to the left eye and white to the right eye. Contrary to what's happening in the LGN, here the vast majority of cells in the primary visual cortex are binocular, i.e., each cell receives inputs from both sides. For most cells one eye is more important than the other (**ocular dominance**). This was one of Hubel & Wiesel discoveries.



The second thing they discovered is that cells in the primary visual cortex are elongated, they are not round anymore. Which means that the best way to excite one of these cells is to use lines of lights rather than round dots. Individual cells are line detectors. And they also discovered that each cell has a preference over the orientation of the line. Each cell strongly responds to lines of a specific orientation (**orientation selectivity**). That's important because it gives real insights into what the visual cortex does, because it "looks in the image to see where there are edges and lines". Then they analyzed the orientation selectivity through the following experiment:

Each point represents the preferred orientation of a cell in the visual cortex as they are encountered by inserting an electrode in the visual cortex. It is peculiar that the preferred orientation changes smoothly as you go deeper, they realized that it depends on the oblique direction of penetration with the electrode. So, they moved from one "orientation column" to the other.

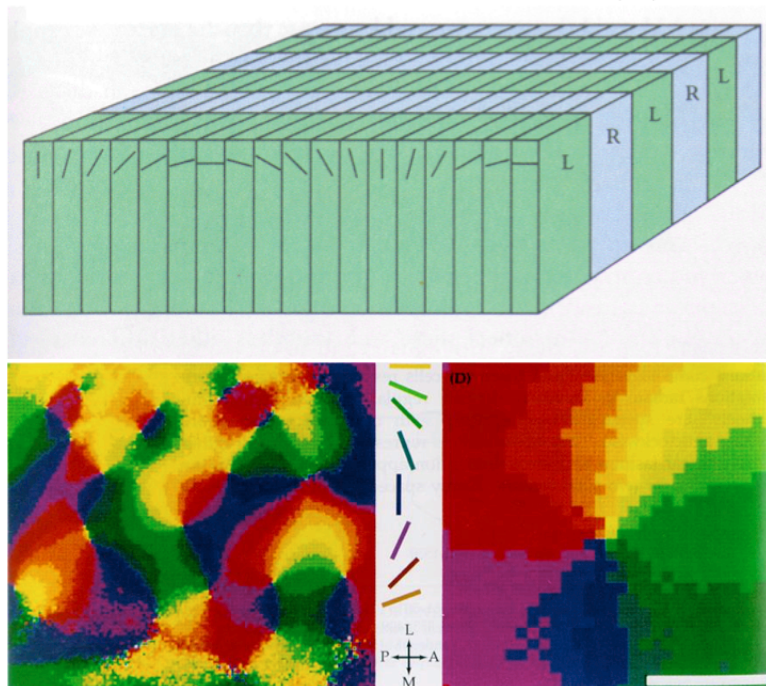
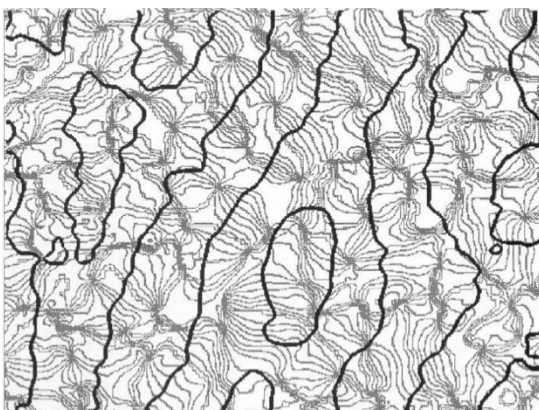


The "ice-cube" Model of Hubel and Wiesel

This is the proposal they made about the organization of the visual cortex. Within each band the cells prefer a specific orientation. In particular, each set of binocular bands analyze a specific part of the visual field. This organization is valid for humans and primates, but it's not true for all animals, e.g., rodents, indeed they do not present orientation columns.

Orientation Columns Measured with Optical Imaging

Each color represents a preference for a different orientation. This is a more accurate representation of the orientation columns.



This represents the relation between ocular dominance (thick black lines) columns and orientation columns (grey lines). It seems as intersecting with perpendicular lines.

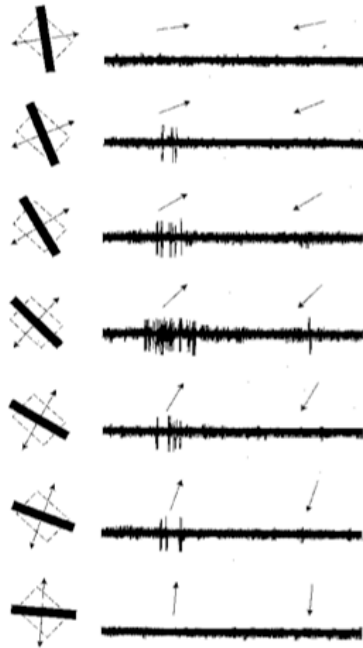
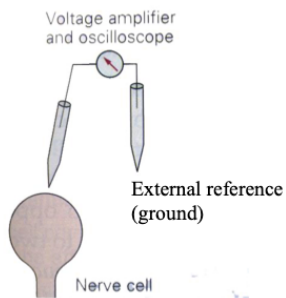
Receptive Fields of LGN and V1 Simple Cells

Taken from Hubel & Wiesel, we can see two examples of LGN receptive fields. Crosses are the on-centers, surrounded by off triangles. While LGN receptive fields are round. In V1, the on and off regions are elongated as shown in the picture.



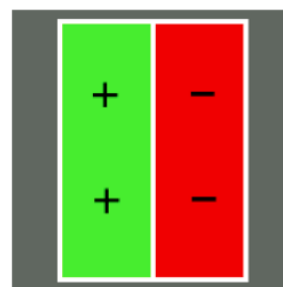
Extracellular Recordings

Selectivity for Stimulus Orientation and Direction in Area V1

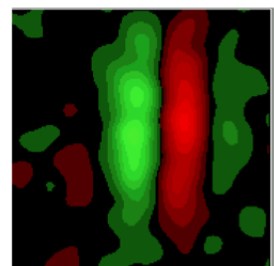


Receptive Field of a Simple Cell

The following pictures show the schematic example of on/off regions measured through reverse correlation, which allows to map spatial/temporal characteristics.



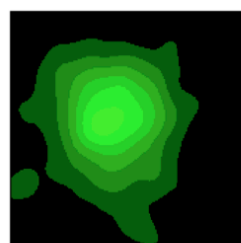
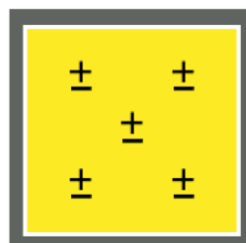
Schematic of the receptive field



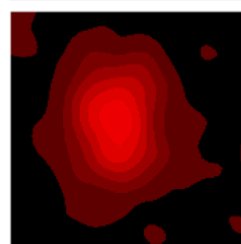
Responses to white dots - responses to black dots

Receptive Field of a Complex Cell

Sometimes cells have overlapping on and off regions, in such a case they are called **complex cells**. If you look at the receptive field, it's difficult to tell which preferred orientation they have, even though they are strongly orientation selective. The receptive field of complex cell is the result of summation and integration of the receptive fields of many input simple cells.



Responses to white dots



Responses to black dots

Schematic picture showing the right hemisphere of a macaque, with V1 represented by the big red area on the back (top left sketch), while at the bottom we can see the left hemisphere.

A lot of our cortex is dedicated to analyze visual signals. It's called Primary Visual Cortex because that's where most of the visual inputs end up first.

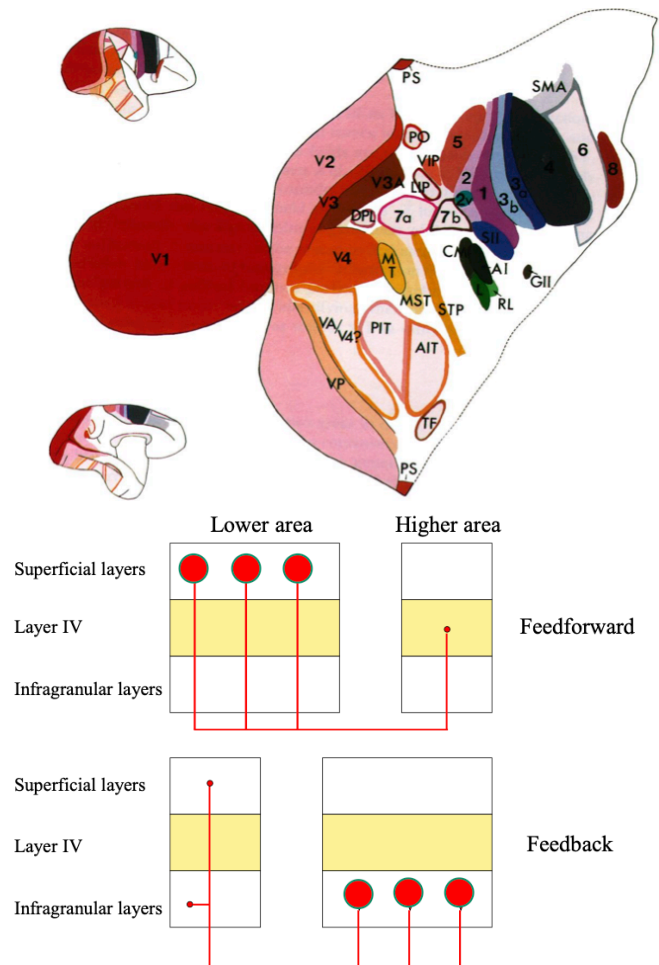
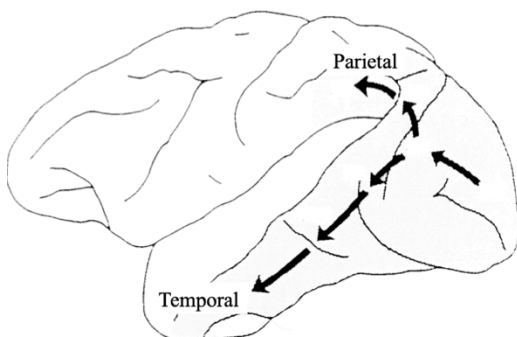
Just like monkeys, also Humans have many different visual areas

Lots of signals travel from the superficial layers of one region to the layer 4 of the next region, this sort of connection is called **feedforward** (it travels under infragranular layers).

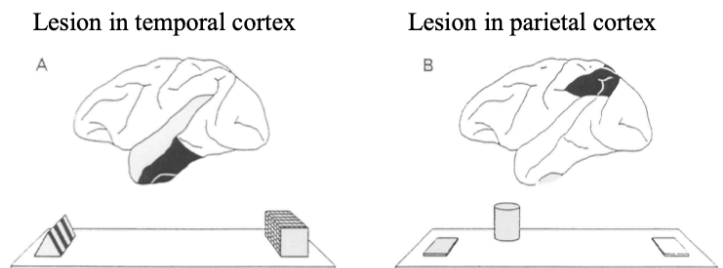
Other signals travel from the infragranular layers of one region to the superficial and infragranular layers of a different region, this is called a **Feedback**.

Two Cortical Functional Streams

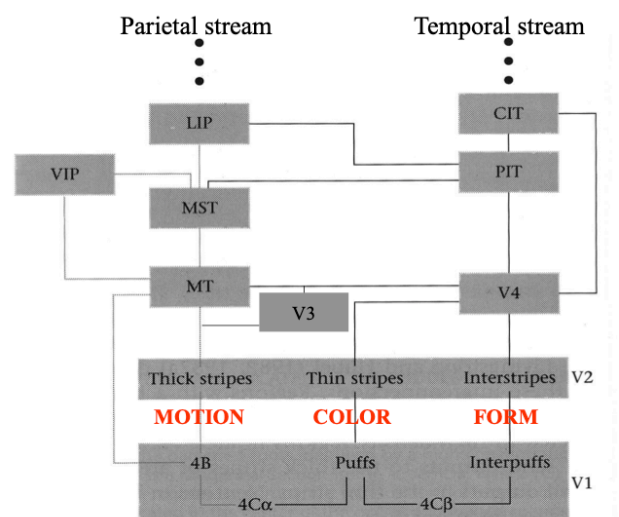
These two pathways are doing different things and it has been found through lesion studies.



Effects of Lesions in Two Cortical Regions



Monkeys with parietal cortex lesions were not able to perform tasks associated with object localization, but they were capable of object identification. On the contrary, monkeys with temporal cortex lesions were still capable of object localization but were defecting of object recognition skills. Hence, the conclusion that temporal and parietal cortices are both involved in processing visual information, but they have distinct roles. The **temporal cortex** is primarily involved in processing information about the **objects and scenes that we see**, while the **parietal cortex** is involved in **spatial processing**, including spatial attention and orientation.



Lecture 2 – Auditory System

The Physics of sound

Sound is a vibration that propagates as an acoustic wave through a transmission medium such as air. Audition is the ability of the organs evolved by humans to perceive these changes in air pressure which are then translated in our sensation of sounds.

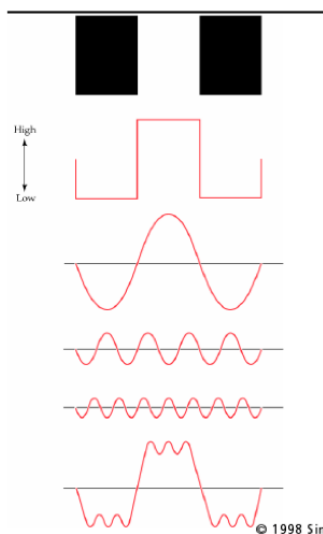
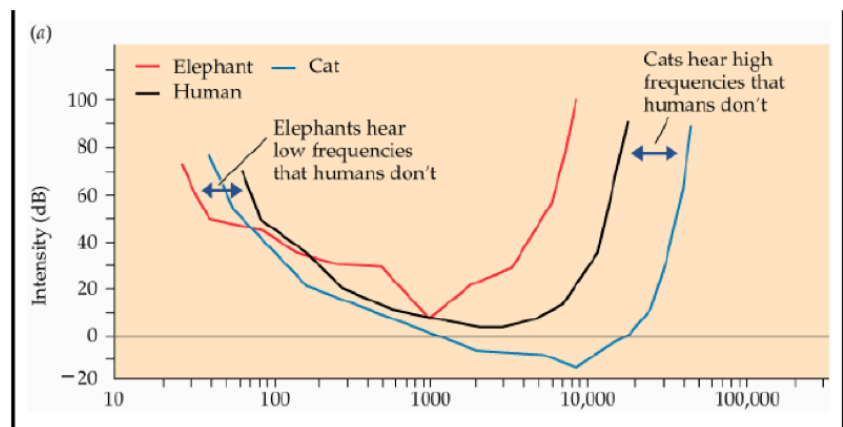
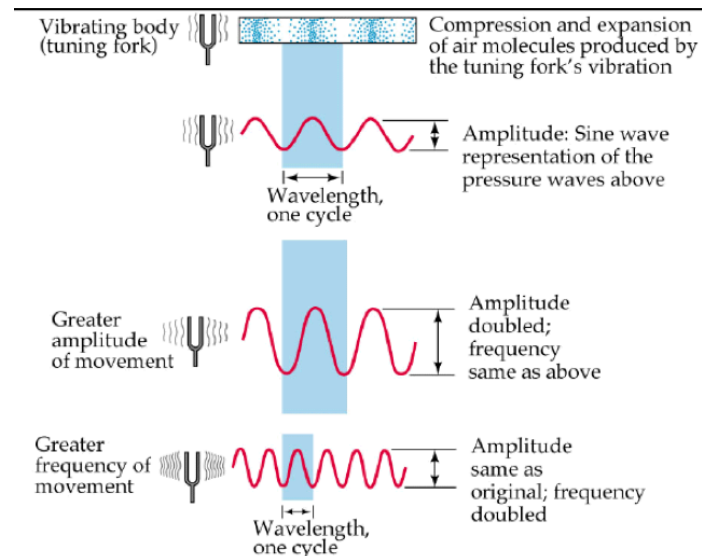
Amplitude and **Wavelength** are the parameters of the waves generated by the vibrating body.

Measuring Sound Intensity

Sound intensity is related to the changes of amplitude of the waves. And the Decibels are a perceptual measurement.

We are sensitive to an enormous range of intensities, so a logarithmic scale works well. Intensity in dB = $20 \times \log(P_1/P_2)$ where P_2 is 20 Micropascal, which is the **reference air pressure**, i.e., the minimal air pressure difference that humans can detect.

From the graph to the right, it can be noticed that cats need lower intensity to be able to hear sounds keeping frequency constant. In addition, the frequencies that require the lowest intensity to be heard in humans are those associated with human speech, because our ear is perfectly tuned for that.



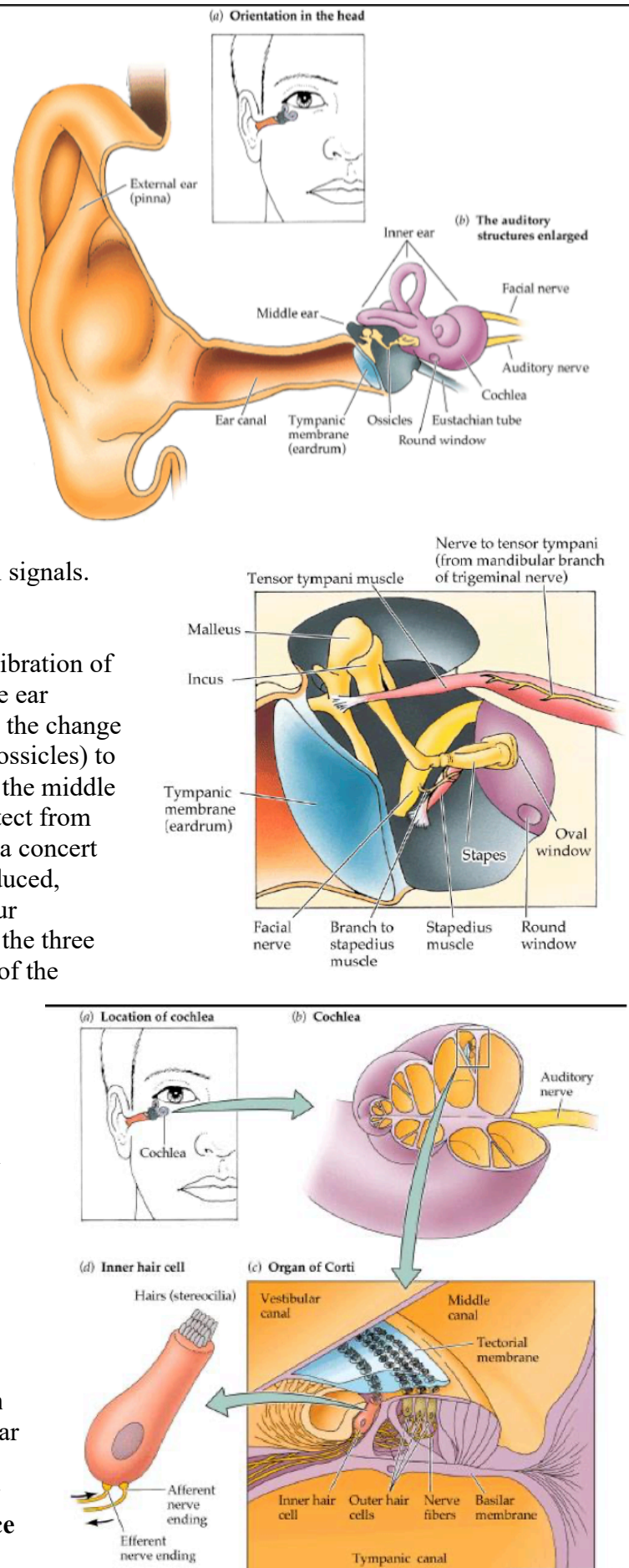
Fourier Analysis

“Any complex waveform can be represented as the sum of a series of sine waves of different frequencies and amplitudes”. This is very important to understand how the cochlea works because it seems to be performing a type of Fourier analysis, by decomposing the sound waves.

The Human Ear

Key parts:

- External Ear (pinna): it collects sound waves and channels them into the ear canal, where the sound is amplified.
- Tympanic Membrane
- Ossicles: the ossicle chamber is filled with air. Ossicles are malleus, incus and stapes. These three ossicles connect the tympanic membrane to the inner ear allowing for transmission of sound waves.
- Eustachian tube: equalizes the pressure
- Cochlea: it is filled with liquid. It transforms changes in pressure in electrical signals.



The Middle Ear

The whole job of these ossicles is to transmit the vibration of the tympanic membrane to the cochlea. The middle ear matches the impedance difference, which is due to the change from the air environment (tympanic membrane & ossicles) to the liquid environment of cochlea. The muscles in the middle ear limit the range of motion of the ossicles to protect from high intensity stimuli. That's why when you go to a concert then you feel like your auditive capabilities are reduced, because these muscles become stiff and reduce your sensibility. In particular, we can notice that one of the three ossicles, the stapes, presses onto the oval window of the cochlea to transmit changes in air pressure.

The Inner Ear

The key element of the inner ear is represented by the **Organ of Corti**, it is contained in the middle canal. This organ can be thought of as the retina in the visual system, it contains the nerve cells that will translate changes in pressures to electrical signals.

Tympanic Membrane & Ossicular System

Sound stimuli pass through pinna and exterior auditory canal to strike **Tympanic Membrane (TM)**, causing it to vibrate. The **Ossicular System** conducts sound from the TM through the middle ear to the cochlea. The faceplate of the stapes pushes forward on the cochlear fluid (oval window) every time the TM and malleus move inward. **Impedance matching** is provided by the ossicular system

between sound waves in air and sound vibration in the cochlear fluid (fluid has a greater inertia than air). Most amplification occurs because the area of the TM is 17x greater than the stapes/oval window surface area.

The Mechanics of the Basilar Membrane

The basilar membrane is inside the cochlea and vibrates to sound waves, it will vibrate differentially along its length depending on the frequency of the stimulus. It is broader and thinner at the end, while it is smaller and thicker at the beginning. In particular, low frequencies can be found at the end, while high frequencies are at the beginning. Hair cells at different positions respond to different frequencies (only because of their location) (Mechanical Fourier Analysis).

The **Organ of Corti** is the location where vibrations are translated into electrical signals. It is situated on top of the basilar membrane and contains **hair (auditory receptor) cells**, these generate **nerve impulses** in response to vibration of the basilar membrane. When the basilar membrane is vibrating, the tectorial membrane changes position, which makes hair cells move back and forth.

- **Inner Hair Cells:** single row, provide fine **auditory discrimination**. 90% of auditory nerve fibers innervate these cells.
- **Outer Hair Cells:** three rows, detect the **presence of sound**. (Less important for audition).

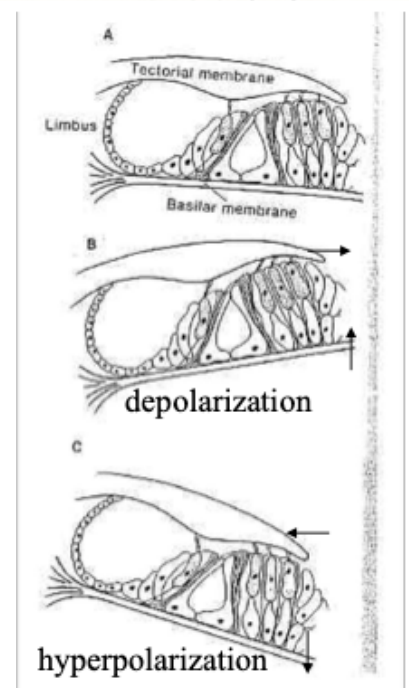
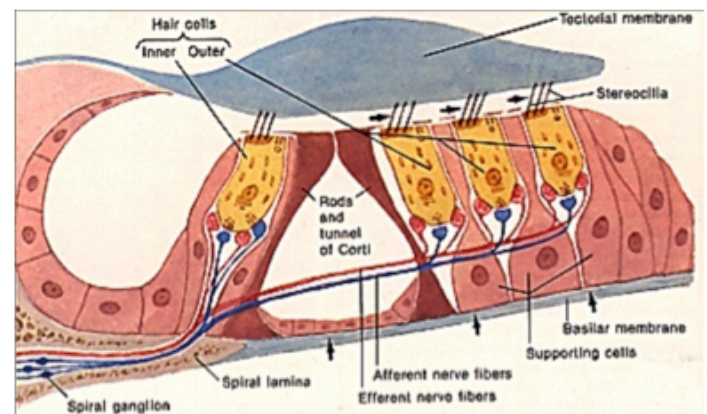
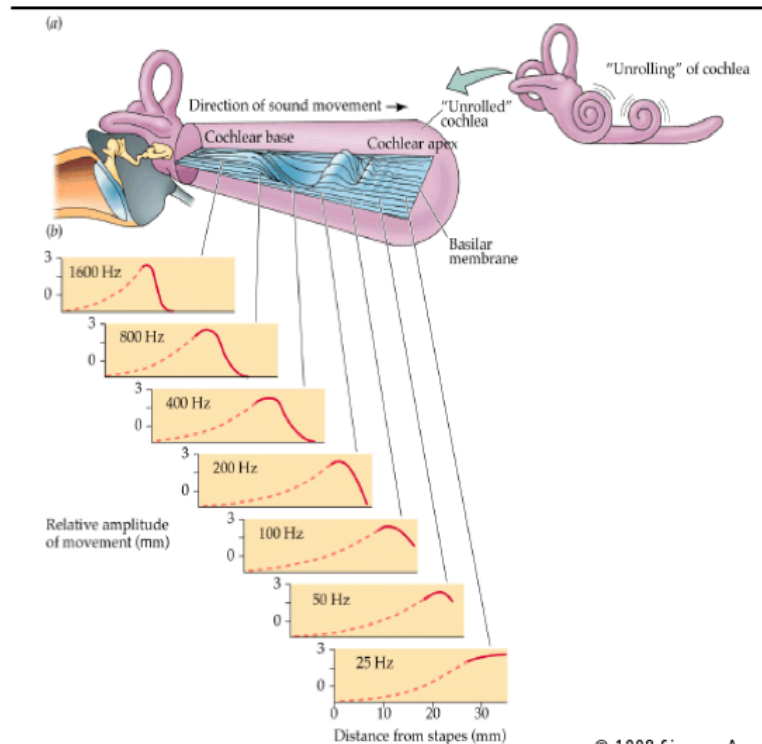
The hair cells contain **stereocilia**, which protrude into the overlying **tectorial membrane**.

Auditory Transduction

The **up-and-down** motion of the basilar membrane causes the Organ of Corti to vibrate up-and-down, which, in turn causes the stereocilia to bend **back-and-forth**.

Polarization of the Stereocilia

- (B) When the Organ of Corti moves **upward**, the stereocilia bend **away** from the limbus and they **depolarize**.
- (C) When the Organ of Corti moves **downward**, the stereocilia bend **toward** the limbus and they **hyperpolarize**.



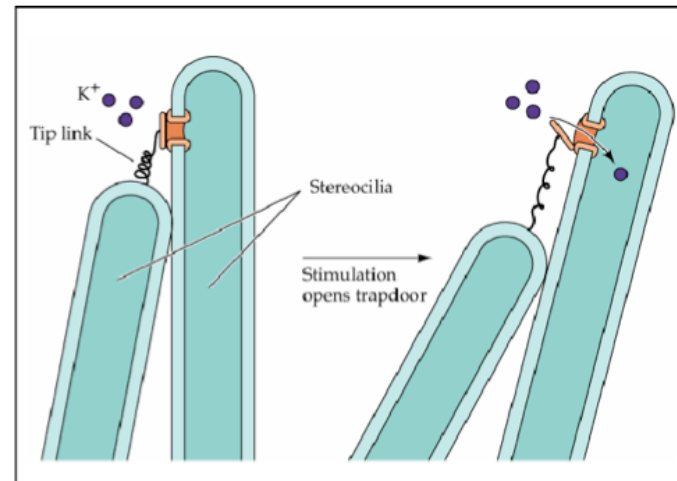
Transduction at Hair Cells

- High concentration of K^+ outside the cell.
- Then the channel opens.
- Causing a change in the membrane potential.

Receptor Potential

The hair cells are depolarized by the movement of K^+ ions into the cell:

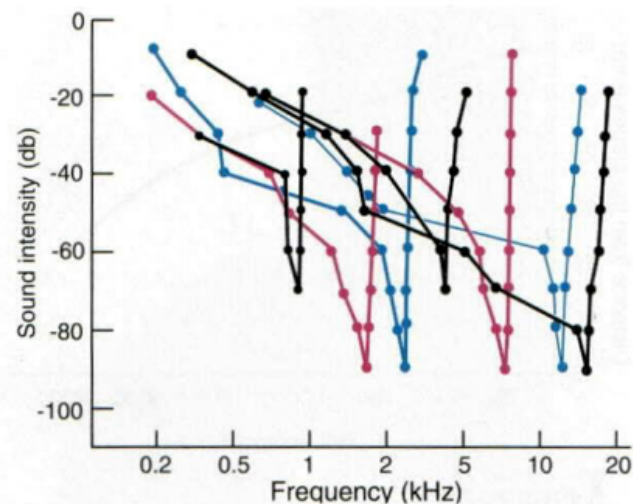
- The **endolymph** contains a high K^+ and is **electrically positive**. The **hair cells** also contain a high K^+ but are **electrically negative** (Na/K pumps) because their concentration is less than the outside. Hence, driving force for **K^+ into cells**.
- When the **stereocilia bend away** from the limbus, they cause K channels to **open**. K^+ then flows into the cell and the **hair cell depolarizes**.
- When the **stereocilia bend towards** the limbus, they cause K channels to **close** and the **hair cell hyperpolarizes**.



Release of Synaptic Transmitter

- When the hair cell depolarizes, a Ca channel opens, allowing **calcium** to enter the cell. Calcium initiates the release of synaptic transmitter, which stimulates the auditory nerve fiber.
- The cell bodies of the auditory nerve fibers are located within the **spiral ganglion**. Their axons join those from the vestibular apparatus to form the **vestibulocochlear nerve**.

The picture to the right shows the minimal sounds intensity for single units in the cochlear nerve to react. Individual fibers show frequency preferences.



Tuning curves of single units in the cochlear nerve. dB = decibel; kHz = kilohertz (1000 Hz).

(From Katsuki, Y. in *Sensory Communication*, edited by W.A. Rosenblith. Copyright 1961 by MIT Press.)

Encoding

How what we have seen so far translates into encoding of information? Neighboring cells in the cortex tend to prefer the same/neighboring frequencies.

- **Place principle of f determination:** the frequency (f) of a sound that activates a particular hair cells depends on the location of the hair cell along the basilar membrane. This spatial organization is maintained all the way to the cerebral cortex. The auditory cortex shows that specific brain neurons are activated by specific sound frequencies (**tonotopic organization**). The brain knows which frequencies compose the sound by the movements of hair cells in the cochlear.
- **Volley principle of f determination:** low frequencies are discriminated by firing of the auditory nerve fibers at the same frequency as the sound wave. The frequency of firing of the cell corresponds to the frequency of the sound. If the frequency of the sounds is too high, i.e., the neuron cannot fire so many APs in a second, 2 cells can coordinate and fire alternatively.

- **Loudness.** As the amplitude of vibration increases, a larger proportion of the basilar membrane vibrates, causing more and more of the hair cells to move. This leads to **spatial summation** of impulses and transmission through a greater number of nerve fibers.

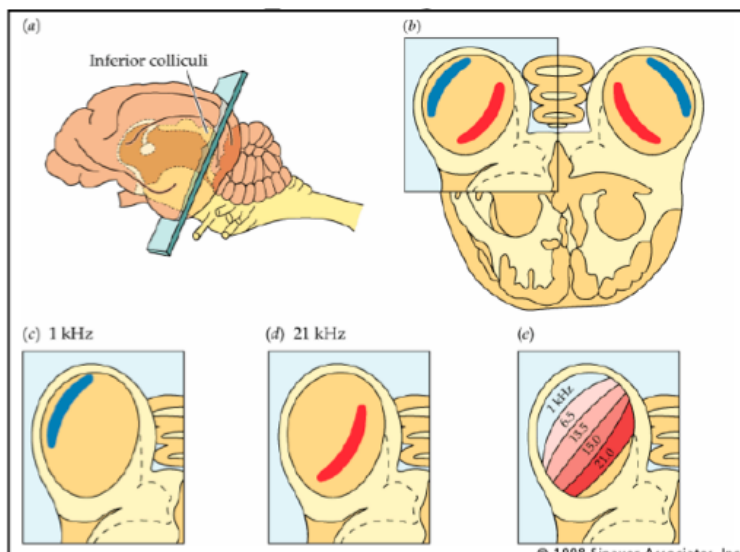
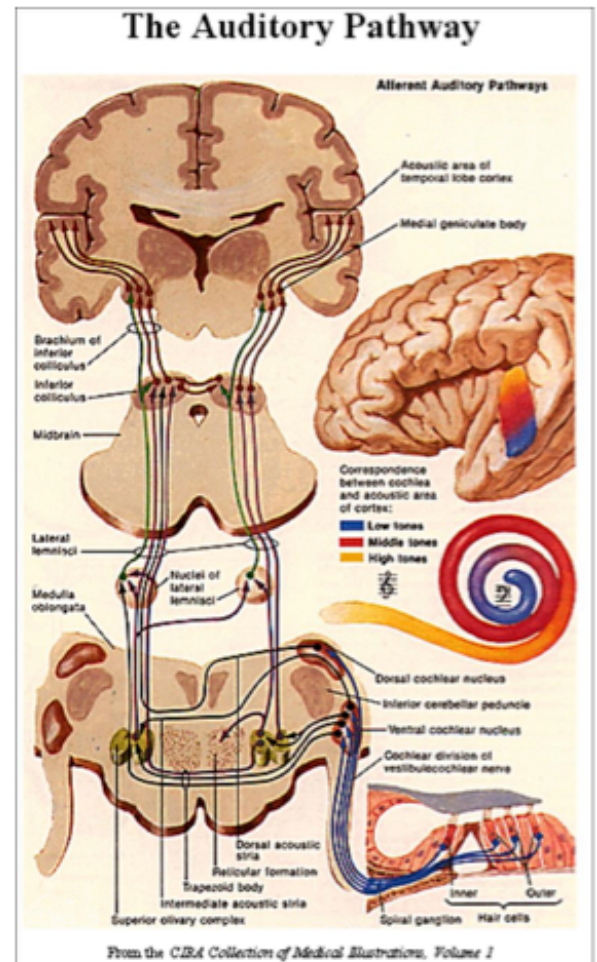
Signals from both ears are transmitted to both sides of the brain, with preponderance to contralateral pathway. Many collateral fibers to RAS of brain stem (loud sound).

Tonotopic organization is maintained from cochlea to auditory cortex. Where high frequency sounds excite neurons at one end, whereas low frequency sounds excite neurons at the opposite end. The first auditory cortex is excited by the MGN, whereas the auditory association areas are excited secondarily by impulses from the first auditory cortex.

The circuits are quite complex because we use these circuits for sound localization.

Tonotopic Organization

Different frequencies are organized in a regular fashion, which represents the tonotopical organization.



Discrimination of “Sound Patterns” by the First and Second Auditory Cortex

Destruction of both (but not one) first auditory cortices will reduce greatly one’s sensitivity to hearing. Interpretation of the meaning and sequence of sound tones in the auditory signals – second auditory cortex.

There is a close association between the areas involved in the processing of auditory information (**Auditory Cortex**) and those involved in processing language (**Wernicke’s Area**).

Physiology and Psychophysics

There is a complicated relation between the physics of the signals and what we perceive.

- Cochlea performs mechanical spectral analysis of sound signal.
- Pure tone induces traveling wave in basilar membrane, maximum mechanical displacement along membrane is function of frequency (place coding).
- Displacement of basilar membrane changes with compression and rarefaction (frequency coding).
- The pitch stay to frequency as loudness stays to intensity.



Perception of Pitch

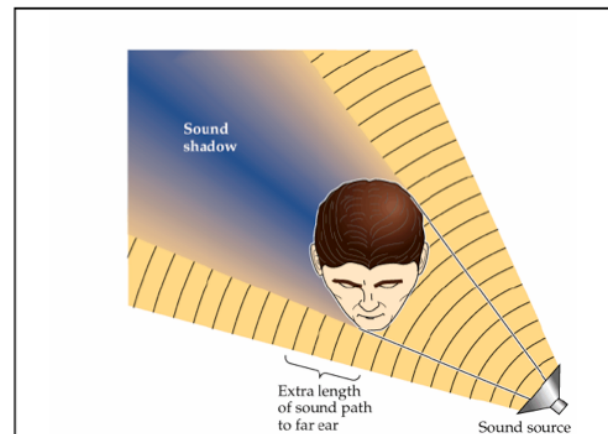
- Along the basilar membrane, hair cell response is tuned to frequency
 - Each neuron in the auditory nerve responds to acoustic energy near its preferred frequency.
 - Preferred frequency is place coded along the cochlea. Frequency coding believed to have a role at lower frequencies.
- Higher auditory centers maintain frequency selectivity and are “tonotopically mapped”.
- Pitch is related to frequency for pure tones.
- For periodic or quasi-periodic sounds the pitch typically corresponds to inverse of period.
- Some have no perceptible pitch (e.g., clicks, noise).
- Sounds can have same pitch but different spectral content, temporal envelope ... *timbre*. The timbre is what allows us to hear the difference between the same frequency played by different instruments.

Perception of Loudness

- Intensity is measured on a logarithmic scale in decibels.
- Range from threshold to pain is about 120 dB-SPL (Sound Pressure Level).
- Loudness is related to intensity but also depends on many other factors (attention, frequency, harmonics, ...). Attention because you can isolate particular frequencies and/or locations (e.g., trumpet in a band).

Spatial Hearing

- Auditory events can be perceived in all directions from observer.
- Auditory events can be localized internally or externally at various distances.
- Audition also supports motion perception
 - Change in direction
 - Doppler shift (A source coming towards you is perceived as having a higher pitch than a source getting away from you)



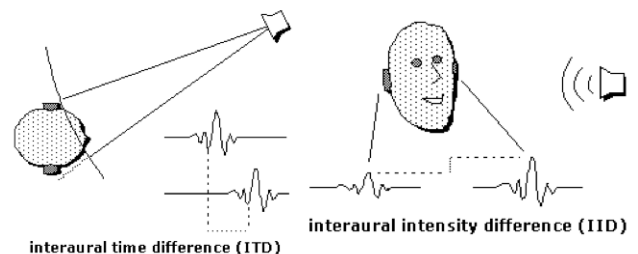
Cocktail Party Effect

- In environments with many sound sources it is easier to process auditory streams if they are separated spatially.
- Spatial sound techniques can help in sound discrimination, detection and speech comprehension in busy immersive environments.

Spatial Auditory Cues

Two basic types of head-centric direction cues

- Binaural cues
- Spectral cues (they are the cues that change in frequency depending on where the sound is coming from).



Binaural Directional Cues

- When a source is located eccentrically it is closer to one ear than the other
 - The sound arrives later and weaker to one ear, **Interaural Time Difference (ITD)**
 - The head “shadow” also weakens the sound that arrives from the opposite ear, **Interaural Intensity Difference (IID)**
- Binaural cues are robust but ambiguous.

Interaural Time Differences (ITD)

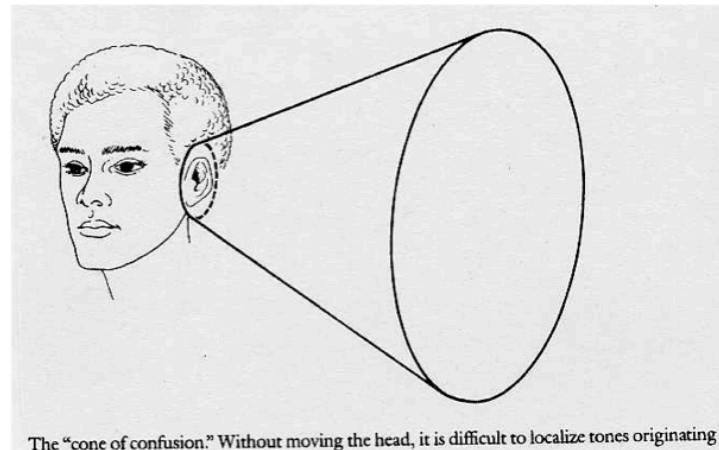
- ITD increase with directional deviation from the median plane. It is about $600\mu\text{s}$ for a source located directly to one side.
- Humans are sensitive to as little as $10\mu\text{s}$ as ITD. Sensitivity decreases with ITD.
- For a given ITD, phase difference is a linear function of frequency.
- For pure tones, phase based ITD is ambiguous (imagine listening to a sinusoidal wave with ITD between the two ear, it is difficult to “match the peaks” because on one ear they could either arrive early or late but it’s difficult to tell which of the two).
- At low to moderate frequencies phase difference can be detected. At high frequencies we can use ITD in signal envelope.
- ITD cues appear to be integrated over a window of 100-200ms (binaural sluggishness).

Interaural Intensity Differences (IID)

- With lateral sources head shadow reduces intensity at opposite ear.
- Effect of head shadow is most pronounced for high frequencies.
- IID cues are most effective above about 2000Hz.
- IID of less than 1dB are detectable. At 4000Hz a source located at 90 degrees gives about 30dB IID.

Ambiguity and Lateralization

- These binaural cues are ambiguous. The same ITD/IID can arise from sources anywhere along a “cone of confusion”.
- Spectral cues and changes in ITD/IID with observer/object motion can help disambiguate.
- When directional cues are used in headphone systems, sounds are *lateralized* left versus right but seem to emanate from inside the head (not localized).
- Also for near sources (less than 1m) there is significant IID due to differences in distance to each ear even at lower frequencies.
- Intersection of these “near field” IID curves with cones of confusion constrains them to toroids of confusion.



Spectral Cues

- Pinnae or outer ears and head shadow each ear and create frequency dependent attenuation of sounds that depend on direction of source.
- Pinnae are relatively small, spectral cues are effective predominately at higher frequency (i.e., above 6000 Hz).
- Direction estimation requires separation of spectrum of sound source from spectral shaping by the pinnae.
- Shape of the pinnae shows large individual differences which is reflected in differences in spectral cues.

Lecture 3 – Somatosensory System

The human skin is the largest organ of the human body.

Somatosensory System Functions

- **Exteroceptive Functions**
 - **Mechanoreception** – pressure or touch (**tactile** sensitivity)

- **Thermoreception** – temperature (**thermal** sensitivity)
- **Nociception** – noxious (damaging or potentially damaging) stimuli (**noxious** sensitivity). Noxious stimulus refers to the capacity of a stimulus of injuring our skin, regardless if it is painful or not.
- **Proprioceptive Functions (Kinaesthesia)** – information about position and movement of limbs and body in space.
- **Interoceptive Functions** – information from internal organs.

Mechanoreception

- **Form Perception** (pressure is part of form perception)
 - E.g., identification of objects by touch alone; Braille reading; measured experimentally in terms of “two-point threshold” (minimal distance between the stimuli need to feel that there are 2 pencils pressing on your skin).
 - Note (Huge) variation in sensitivity across skin surface.
- **Texture Perception**
 - Our ability to analyse surfaces by touching them which is closely associated with vibration perception. Texture perception is very important for rodents.
- **Vibration Perception**
 - Flutter (frequencies < 40 Hz)
 - Vibration (frequencies 40 – 400 Hz)

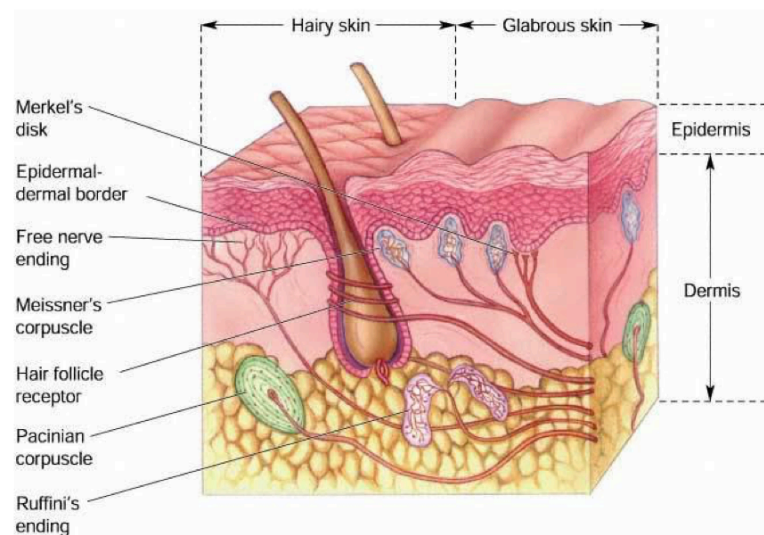
Skin and Skin Receptors

There are many different types of receptors in the skin (number is still debated), the skin is a huge organ (large surface) filled with receptors.

- Size of skin as receptor surface
- **Glabrous** (hairless) and **Hairy skin**.
- Distinctions between:
 - **Encapsulated** and **Unencapsulated** receptors
 - **Superficial (cutaneous)** and **Deep** receptors. (The location in the skin give them a different type of sensitivity.

At the base of the hair follicle, we have some nerves wrapped around the hair. Just below the epidermis, we have Merkel's disk, free nerve ending and Meissner's corpuscle. Deeper layers of the skin have the Pacinian corpuscle and Ruffini's endings.

- **Superficial Encapsulated Receptors:**
 - Merkel Receptor/Disk
 - Meissner Corpuscle
- **Deep Encapsulated Receptors:**
 - Ruffini Ending
 - Pacinian Corpuscle
- **Unencapsulated Receptors** – free nerve endings.



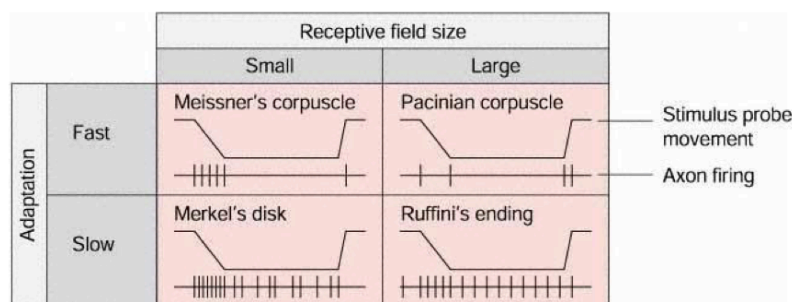
Because of their location in the skin and the nature of their specializations, different encapsulated receptor types have different forms of cutaneous sensitivity. This was first discovered not by looking at receptors themselves but by recording from **single Cutaneous Afferent Fibers** (can be

done in humans and in animals, e.g., Swedish researcher sticking electrodes in his arms). All of the mechanoreceptor afferent axons are medium diameter (6 – 12 μm), well-myelinated fibers with conduction velocities of 35-75 m/s. They are called **A β Fibers**.

Cutaneous Afferents

Some of these receptors quickly adapt, while others don't. Fibers are classified as either:

- **Rapidly Adapting (RAs)**
- **Slowly Adapting (SAs)**
- Also in terms of the size of their **Receptive Field** (The size of the area on the skin from which they can be activated) (it is also related to the position of the receptor, indeed superficial receptors tend to have smaller RF than deeper ones).



A **stimulus probe movement** consists of applying a pressure through a probe on the skin and subsequent release.

In the picture to the left, we can notice that the top row adapts very fast to the pressure stimulus and signal it. Ruffini's endings on the contrary never completely adapts to the new stimulus and doesn't stop firing.

Schematic Illustration of Determination of Receptive Field

As we can see from the picture, Meissner's corpuscles tend to have small RF. On the contrary, Pacinian corpuscles are relatively deep and have large receptive fields.

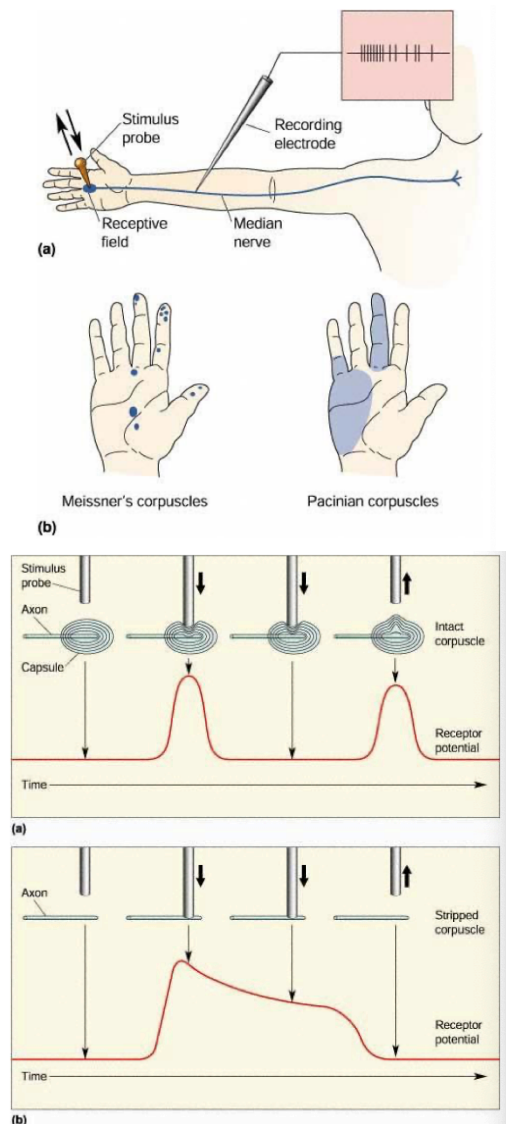
RAs respond only at the beginning and end of sustained displacements (i.e., to transients) but respond well to higher frequency vibrations. Two types:

- **RA I: Meissner Corpuscles** (10 – 200 Hz) (small RF)
- **RA II: Pacinian Corpuscles** (70 – 1000 Hz) (large RF)

SAs respond throughout sustained displacements of the skin, and are thus suited to coding the duration and magnitude of mechanical stimuli. Two types:

- **SA I: Merkel Receptors/Disks** (small RF)
- **SA II: Ruffini Endings** (large RF)

Encapsulation has a very important role to play. The sensitivity characteristics of a particular afferent fiber reflects the specialized nature of the encapsulated ending (e.g., If you dissect away the onion-like layers of a PC, the fiber from that PC becomes sensitive to sustained displacement) and its position on the skin. By removing the capsule and leaving only the axon, they realized that the receptor potential was relatively different, to the point of changing a fast-adapting receptor to a slowly adapting one. Papers show that these properties are due to the mechanical properties of this structure.



Summary Classification Table

	SUPERFICIAL (small RF)	DEEP (large RF)
RA	MEISSNER CORPUSCLE (RAI)	PACINIAN CORPUSCLE (PC)
SA	MERKEL DISK (SAI)	RUFFINI ENDING (SAII)

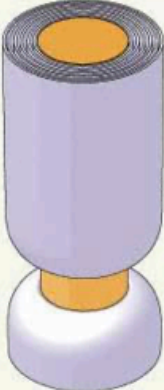
Hairy Skin

- Merkel disks, Pacinian corpuscles and free nerve endings as in glabrous skin. While Ruffini's endings and Meissner's corpuscles are less common in hairy skin.
- Innervation of hair follicles (by free nerve endings or more specialized endings).
- A recent discovery – hairy skin has “soft touch” receptors that project to cortical regions associated with emotion and sexual arousal.

Nociception

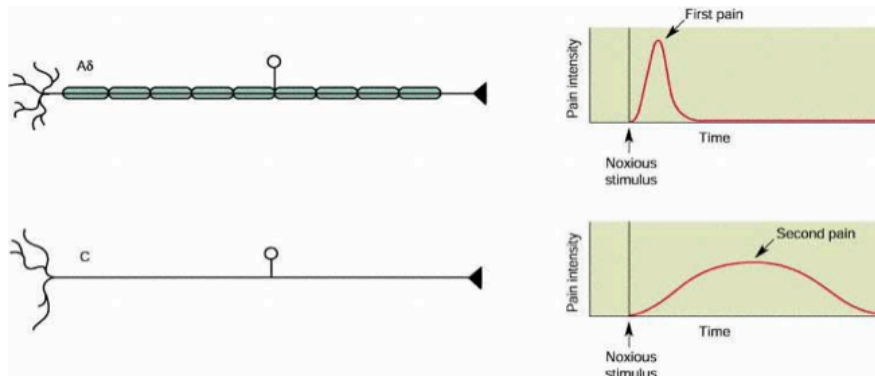
- Nociceptors respond to noxious mechanical and thermal stimuli (i.e., stimuli that produce or threaten to produce tissue damage) and also to chemicals released by damaged tissue (e.g., histamine, etc.).
- Note distinction between noxiousness as a quality of the stimulus and pain as perceptual and emotional response.
- Two types of nociceptor:
 - **High Threshold Mechanoreceptors**
 - **Polymodal Nociceptors**
- Receptors are **free nerve endings**.
- Afferent axons are of different types (which have very different conduction velocities):
 - **High Threshold Mechanoreceptors: A δ Fibers.**
 - **Polymodal Nociceptors: C Fibers.**

Axon types in nerves from skin and from muscles (Note different terminologies associated with different origins).

Axons from skin	A α	A β	A δ	C
Axons from muscles	Group I	II	III	IV
				
Diameter (μm)	13–20	6–12	1–5	0.2–1.5
Speed (m/sec)	80–120	35–75	5–30	0.5–2
Sensory receptors	Proprioceptors of skeletal muscle	Mechanoreceptors of skin	Pain, temperature	Temperature, pain, itch

Different fiber types give rise to different pain sensations:

- “First” or “Cutaneous Pricking” pain – mediated by **A δ Fibers**.
- “Second” or “Burning” pain – mediated by **C Fibers**.



Thermoreception

- Thermoreceptors: “**Warm**” fibers and “**Cold**” fibers.
- They respond to increase or decrease in temperature, respectively, from steady state and to maintained temperature.
- At intermediate skin temperatures (approx. 30-35 degrees) there is ongoing discharge in both warm and cold fibers, and a change in skin temperature reciprocally modifies the discharge in the two fiber types. At a lower adapting temperature (e.g., 26 degrees) only cold fibers are active, and an increase in temperature first decreases the discharge in cold fibers, and then – with larger increments – begin to engage the previously silent warm fibers.
- Large receptive fields, so temperature sensations are not well localized.
- Note relativity of thermal sensations (i.e., change in temperature is what is felt as warm or cold) and similar relativity of neuronal responses. (Three buckets of water experiment)
- Receptors are free/bare nerve endings.
- Afferent axons:
 - **Warm Fibers: C Fibers**
 - **Cold Fibers: A δ Fibers**

Proprioception (The Kinaesthetic Sense)

- Provides information about the position and movement of the limbs and body in space (e.g., limb movement without vision; passive movement).
- Proprioceptive information supplements “efference copy” (It refers to perform precise, well-coordinated movements) information from motor system.
- Information is provided by three classes of receptors:
 - **Cutaneous Mechanoreceptors**
 - **Joint Receptors**
 - **Muscle Spindles** (Muscle fibers that are measuring the state of tension of the muscle) and **Golgi Tendon Organs**

Cutaneous Mechanoreceptors and Joint Receptors

- **Cutaneous Mechanoreceptors**
 - Information about skin stretch from Ruffini/SAII afferents
 - Of different importance in different regions (important around hands, mouth and feet).
- **Joint Receptors**

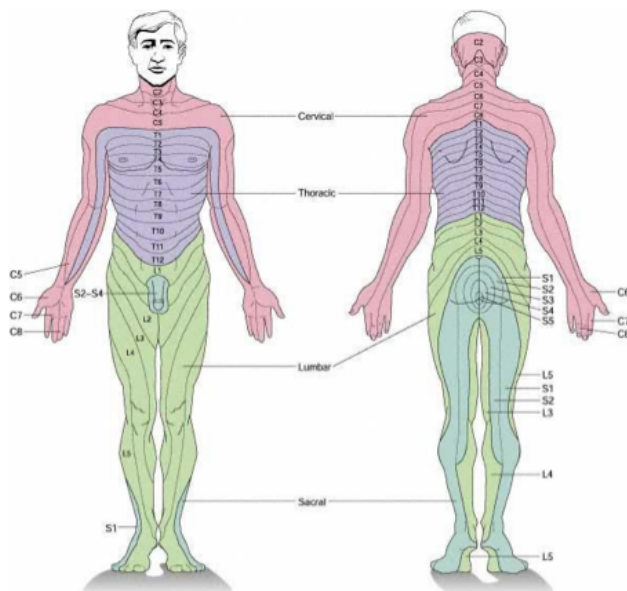
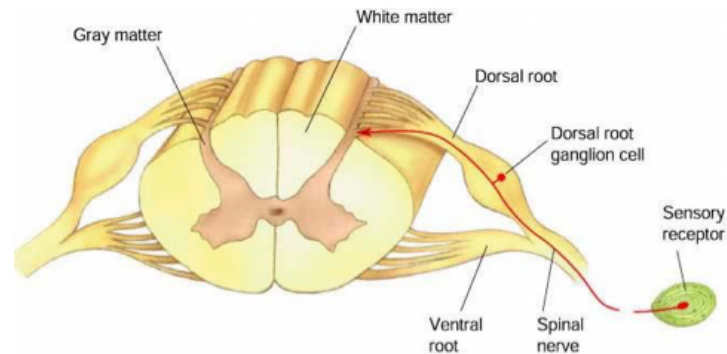
- Ruffini-type endings and Pacinian corpuscles in joint capsule.
- But not essential, because anesthesia or removal of joint capsules does not result in loss of limb position sense (they seem to be supplementary).

Muscle Spindles and Golgi Tendon Organs

- Golgi tendon organs (**Ib** fibers) respond to tendon stretch.
- Muscle spindles (type **Ia** and **II** axons) are coiled around intrafusal muscle fibers; respond to muscle stretch; type I axons constitute the sensory component of the knee-jerk reflex.

Dorsal Root Ganglia

All somatic fibers are the axons of dorsal root ganglion cells (or trigeminal ganglion cells in the case of the head and neck). DRG cells have no dendrite, but a single bifurcating axon – sends one process to the periphery and another to the CNS.



Dermatomes

The axons of individual dorsal root innervate a restricted region of skin that is the same in everyone – **dermatome**. A **dermatomal map** is a stereotyped pattern of dermatomes that allows for diagnosis of location of injury or infection of dorsal roots on basis of skin distribution of sensitivity (e.g., in shingles).

Modality Segregation

It is the basic principle of organization of the somatosensory system. Information from each class of receptors reaches a different group of neurons in the CNS and these neurons project to higher levels along segregated “parallel” pathways. This segregation begins with the place of termination of different classes of afferent axon in the spinal cord. It continues with two major ascending pathways:

- **The Dorsal Column – Medial Lemniscal Pathway**
- **The Spino – Thalamic Pathway** (pain & temperature information)

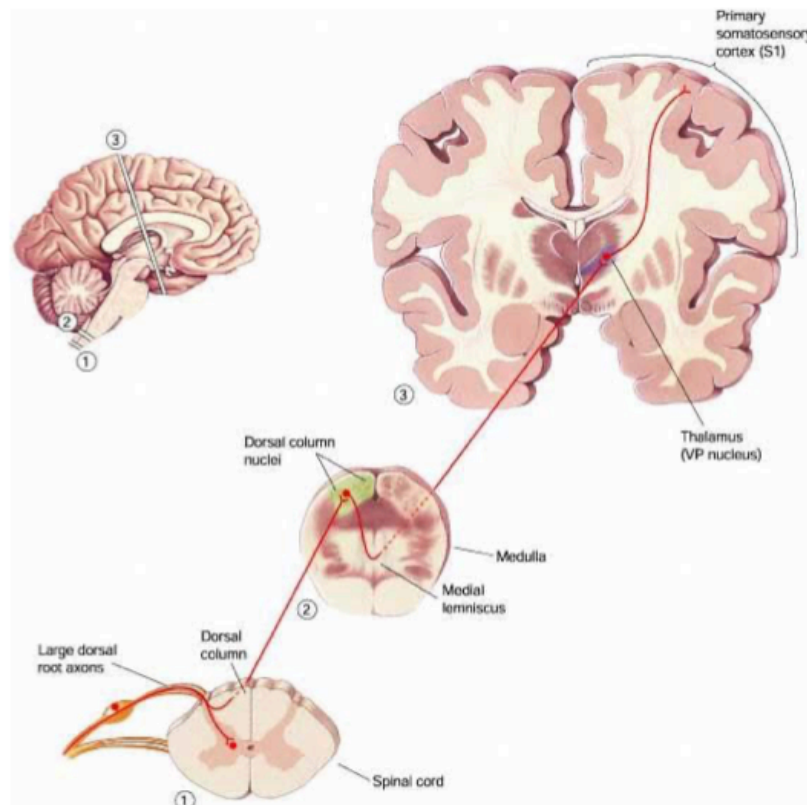
Segregation in Spinal Cord

- The spinal grey matter is divided into a number of layers (laminae); laminae I – VI comprise the dorsal horn.
- Aδ and C fibers terminate predominantly in layer I (the marginal layer) and layer II (the substantia gelatinosa).
- Aδ axons bifurcate, one branch ascending in the dorsal columns, the other terminating on cells in the deeper dorsal laminae.

The Dorsal Column – Medial Lemniscal Pathway

- The ascending branches of **A β axons** (conveying discriminative touch information, i.e., carrying mechanoreceptive information) ascend in the dorsal columns (the **gracile and cuneate fasciculi**), and synapse on cells in the **dorsal column nuclei (DCN)** in the medulla (the **gracile and cuneate nuclei**, respectively).
- The axons of DCN cells cross the midline and ascend in the **medial lemniscus** to the **lateral division of the ventro-posterior nucleus (VPL)** of the thalamus.
- **VPL** cells in turn project to the primary somatosensory cortex (**S1**).

The Dorsal Column System



Things to Note About Dorsal Column – Medial Lemniscal Pathway

- The **Gracile Fasciculus** extends the entire length of the spinal cord; it and the **Gracile Nucleus** contain a representation of the feet, legs, and lower trunk.
- The **Cuneate Fasciculus** begins at the cervical level; it and the **Cuneate Nucleus** contain a representation of the hands, arms, and upper trunk.
- The entire system is topographically organized (i.e., adjacent parts of the body surface are represented by adjacent neurons – **Somatotopy**).
- The decussation (crossing over) of the medial lemnisci results in a representation of the **contralateral** body surface on each side of the brain at levels above the DCN.

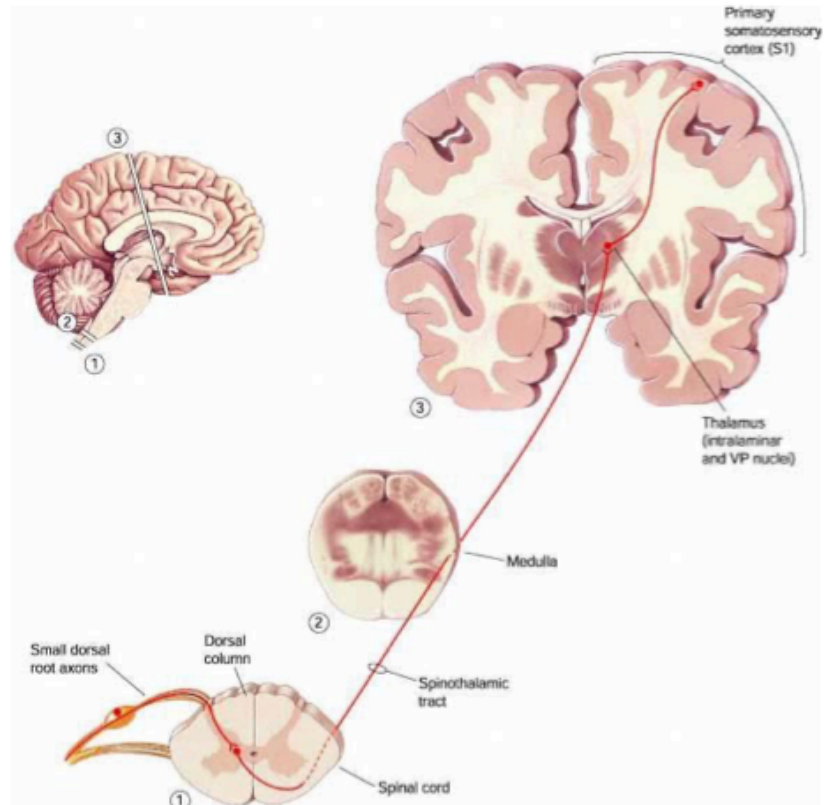
The Spino – Thalamic Pathway

- It represents the second-major pathway
- Small-diameter myelinated and unmyelinated axons (**A δ** and **C** fibers serving temperature sensitivity and nociception) terminate in the spinal cord itself.
- The axons of the spinal neurons then cross the midline and ascend as **the anterolateral system**.

- Most of these fibers (constituting the **spino-thalamic system**) terminate in VL and in the intralaminar and posterior groups of thalamic nuclei.
- Other ascending fibers terminate in the reticular formation (the **spino-reticular system**) and in the midbrain.
- The VPL neurons receiving spino-thalamic input are segregated from those receiving medial lemniscal input and project to both primary and secondary somatosensory cortex (**SI** and **SII**).

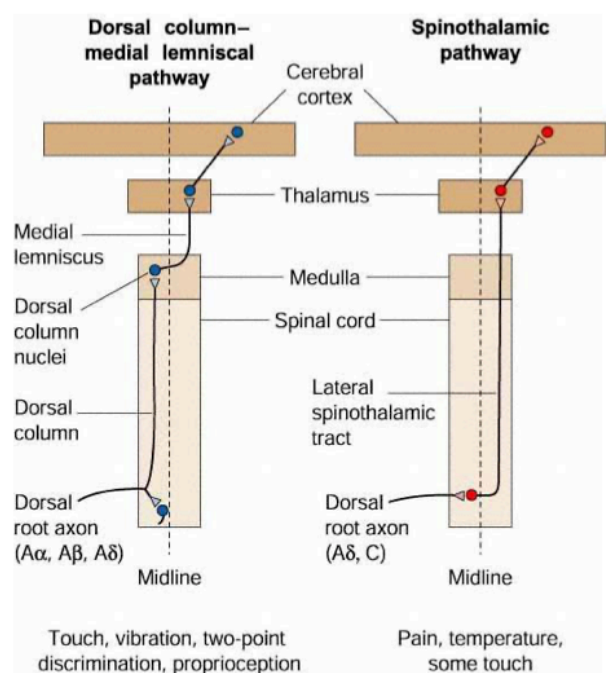
The Spino – Thalamic System

Note that the drawing is inaccurate with respect to the location of the cell body in the cord – it should be in lamina I or II.



Schematic Representation of Dorsal Column-Medial Lemniscal and Spino-Thalamic Pathways

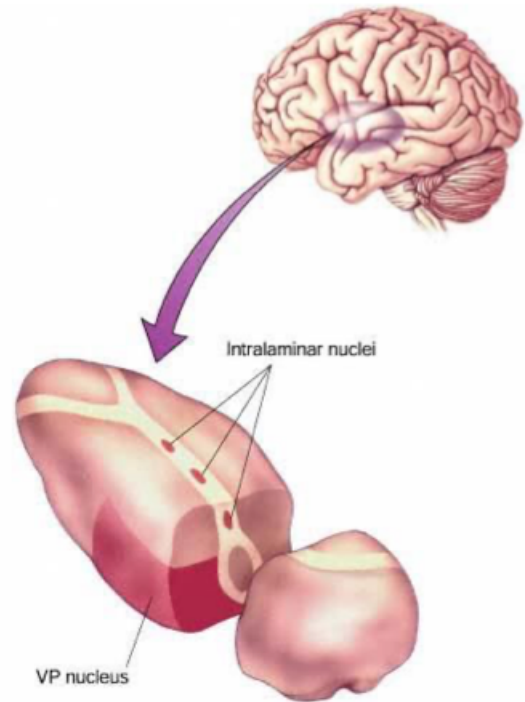
When people have lesions in the spinal cord, they will lose all the mechanoreceptive information associated with parts of the body below the lesion for Dorsal Column – Medial Lemniscal Pathway.



Schematic Illustration of the Location of the Major Thalamic Nuclei Involved in the Processing of Somatosensory Information

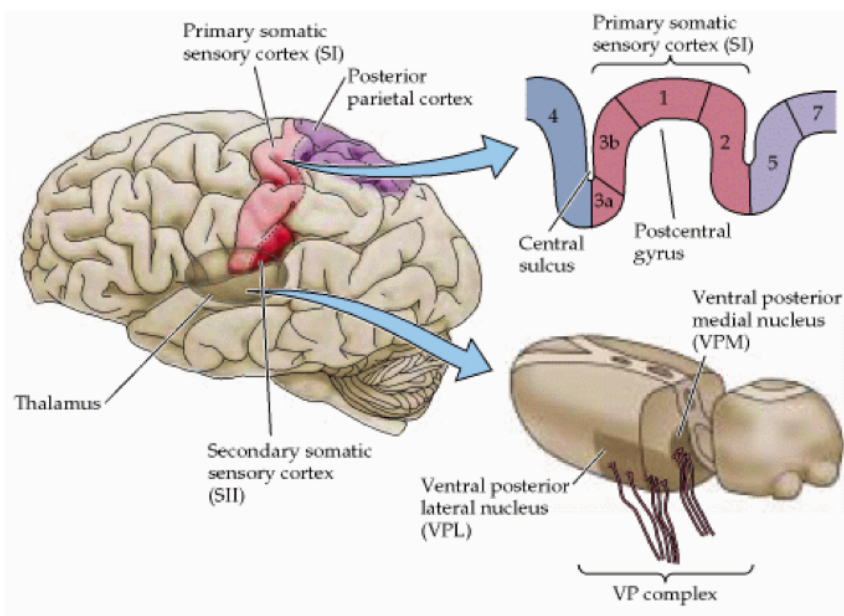
The Trigeminal System

- It is dedicated to the brain and the neck,
- Conveys somatosensory input from the face.
- Large-diameter myelinated axons of the trigeminal ganglion conveying discriminative touch information terminate in the principal trigeminal nucleus.
- The axons of these cells then cross the midline, join the medial lemniscus, and terminate in the **medial division of the Ventro-Posterior Nucleus (VPM)**.
- Small diameter lightly-myelinated and unmyelinated axons of the trigeminal ganglion conveying thermal and nociceptor information descend in the spinal trigeminal tract and terminate in the spinal trigeminal nucleus.
- The axons of these cells then project to VPM and to the posterior and intralaminar thalamic nuclei (i.e., rather like the anterolateral system).
- Hence, we have a separation again of mechanoreceptors from thermoreceptors.



The Somatosensory Thalamus

- The **ventrobasal** complex of the thalamus has the two major divisions previously described:
 - **VPL** (somatosensory information from the body)
 - **VPM** (somatosensory information from the face)
- Both are somatotopically organized
- Thalamic neurons have adaption properties (SA vs RA) like those of peripheral neurons, but the RFs are larger than those of dorsal root ganglion cells and are commonly concentric, with a central excitatory area and a surrounding inhibitory area.



Somatosensory Cortex

- Two major areas in primates
 - **SI** – on posterior bank of central sulcus and crown of post-central gyrus.
 - **SII** – on lip and upper bank of lateral fissure.
- SI contains 4 distinct areas (**3a, 3b, 1, and 2**) with different characteristics and functions:
 - Areas 3a and 3b receive most of the direct projections from the thalamus and in turn project to areas 1 and 2.
 - Areas 3b and 1 receive input from skin receptors.
 - Areas 3a and 2 receive input from joint and muscle receptors.
- Effects of cortical lesions:
 - Large lesions of all of SI produce deficits in position sense and in discrimination of size, texture and shape. They also produce motor deficits in hand function. (Link between somatosensory information and motor-commands).
 - Area 3b lesions result in severe deficits in tactile discrimination of texture, size and shape.
 - Area 1 lesions affect texture but not size discrimination.
 - Area 2 lesions affect size and shape but not texture discrimination.

Cortical Receptive Fields

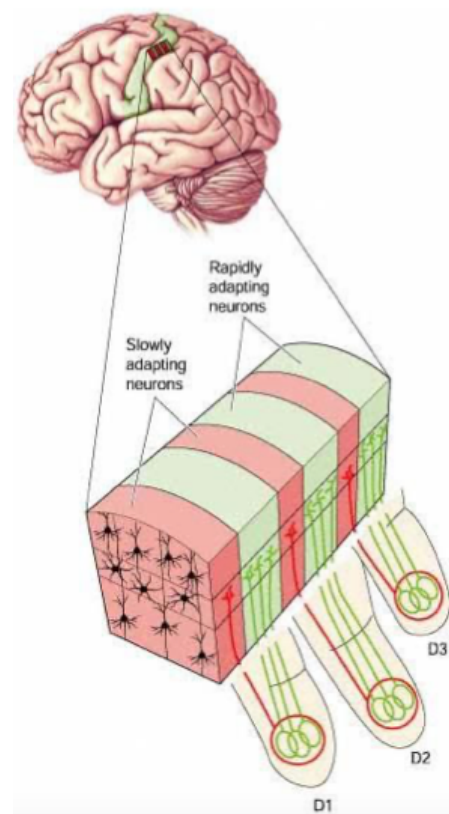
- Receptive fields in area 3b, like those in the thalamus, are larger than those of DRG neurons and typically have excitatory centre – inhibitory surround structure.
- Receptive fields in “higher” cortical areas are larger than those in 3b, and many are much more complex (e.g., sensitive to the orientation of an edge (cf. visual cortex), the direction of movement across the skin, or the surface curvature of objects).
- Some neurons in area 2 are selective for the 3-dimensional shape of objects.

Cortical Somatotopy

- Human somatotopy – classic map (“homunculus”) based on cortical stimulation (produced by Penfield).
- Distorted nature of homunculus.
- Differences between species (enlarged representation of face and facial vibrissae in rodents (the “musunculus”).
- Neurophysiological evidence in monkeys indicates that each of the 4 areas comprising SI is somatotopically organized (i.e., a “full homunculus” for each one of these regions).
- Note that multiple representations of the receptor surface are a common feature of all sensory cortices.
- Note that representations are commonly “mirror-reversed” across field boundaries.

Columnar Organization

- Neurons in a “column” running orthogonal to the cortical surface and through the cortical layers have very similar RFs and modality properties (including adaptation rate).
- A cortical column is approx. 300 – 600 μm in diameter.
- Columnar organization was first described in detail by Mountcastle and his colleagues in somatosensory cortex and is now recognized as one of the fundamental principles of the organization of sensory cortex.



Lecture 4 – Vestibular System

The vestibular system plays a central role in the maintenance of equilibrium and gaze stability. (It is also involved in keeping eye position). The vestibular system, by means of its receptors for the perception of linear and angular acceleration, plays a central role in **orientation**. It seems to be designed to answer two basic questions:

- Which way is up?
- In which direction am I moving?

It is very elusive to test, as it is difficult to reach and stick-in electrodes to study. It presents five peripheral “receptors” (three **Semicircular Canals**, **Utricule**, **Saccule**).

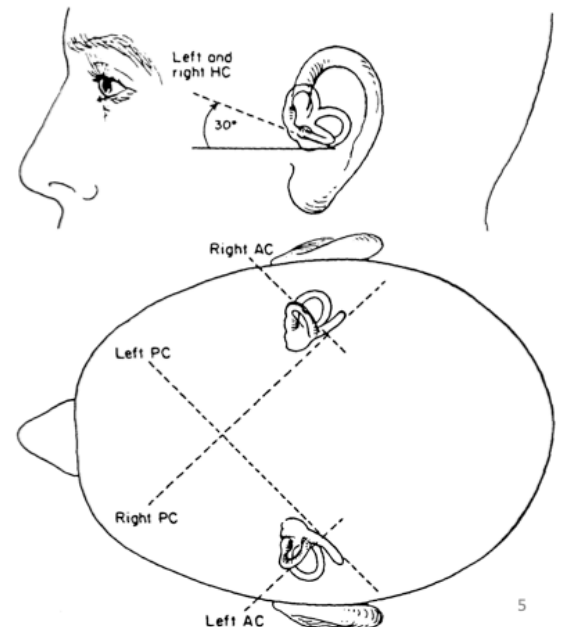
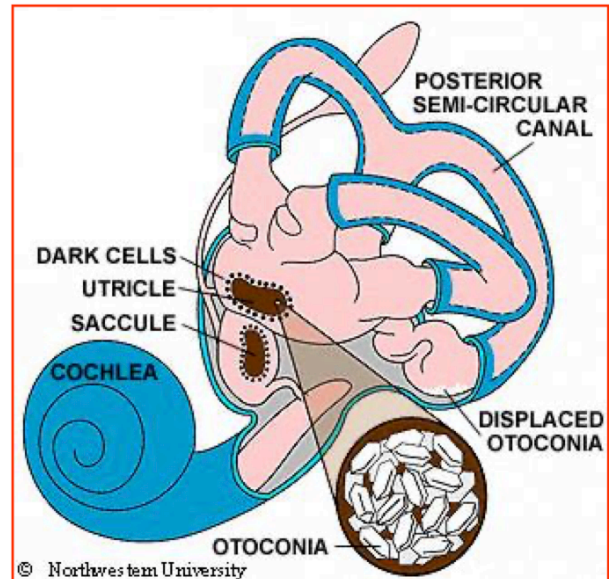
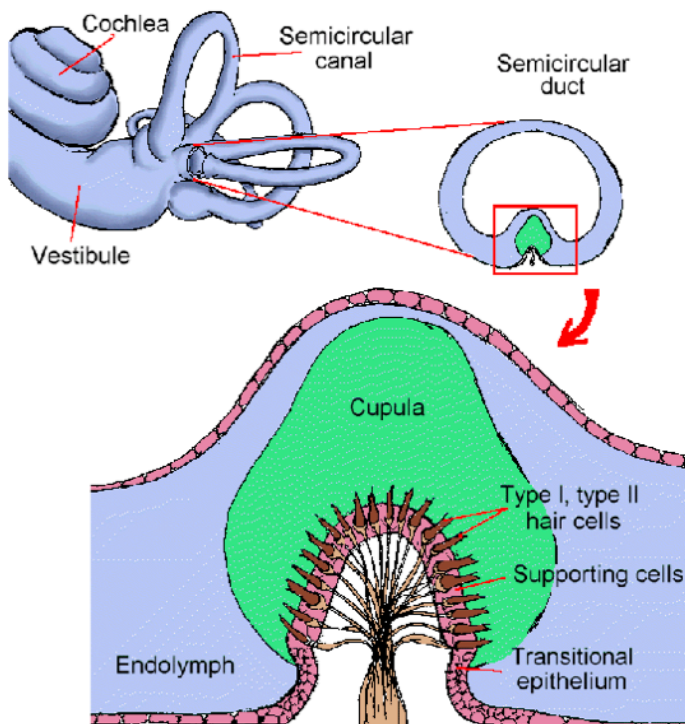
- **Semicircular Canals:** respond to rotation acceleration of the head.
- **Otolith Organs:** respond to linear acceleration and static position.
 - **Utricle**
 - **Saccule**

The Semicircular Canals

- Posterior canal shares plane with contralateral anterior canal.
- Horizontal canals share plane.
- These canals contain two types of hair cells

Vestibular Hair Cells

- **Type I (Inner)**
- **Type II (Outer)**



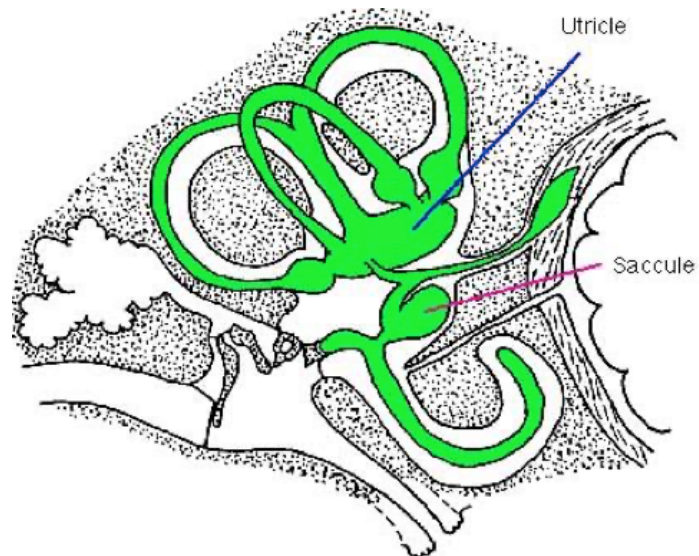
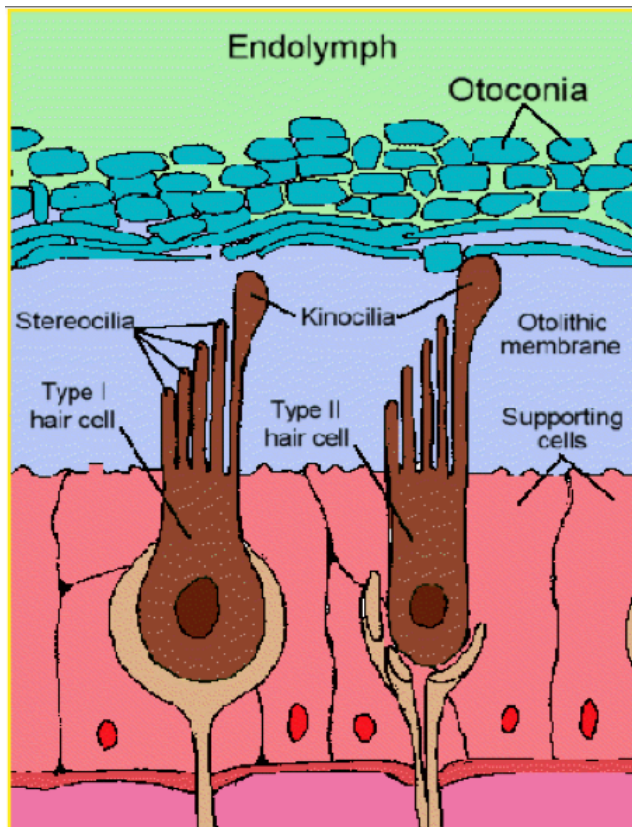
Responses of the Cristae

All Kinocilia are oriented in the same direction. Crista in each pair of canals respond inversely to each other.

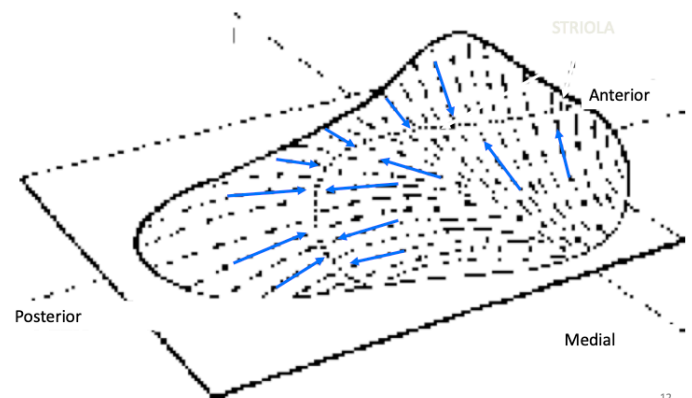
The **Cupula** presents a gelatinous structure, while the **Endolymph** is liquid. Once the liquid move, the Cupula bends in one or the other direction depending on the movement of the liquid, which in turn makes the cilia bending causing spikes elicitation. Hence, the cilia transform mechanical bending into electrical signals.

The Otolithic Organs

- **Saccul:** roughly vertical orientation, responds to acceleration components within the saggital plane.
- **Utricle:** horizontal (+ 30 degrees) orientation, responds to left-right acceleration.

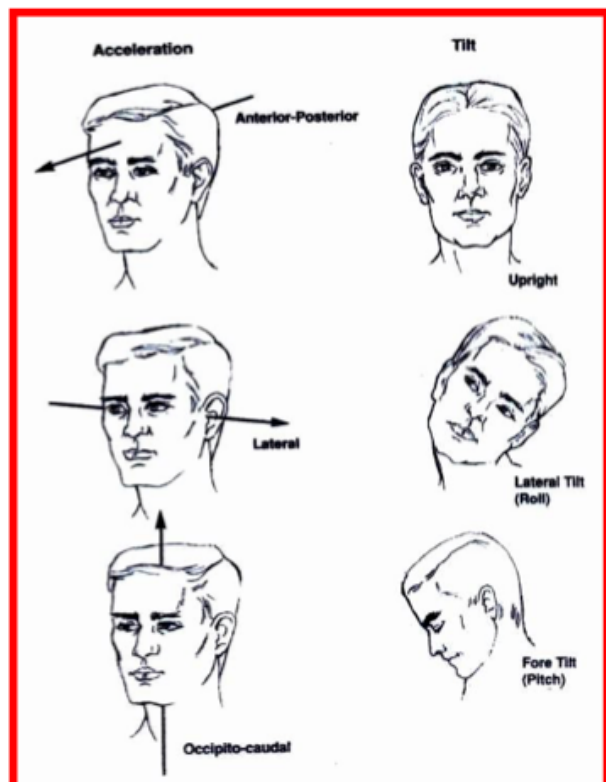


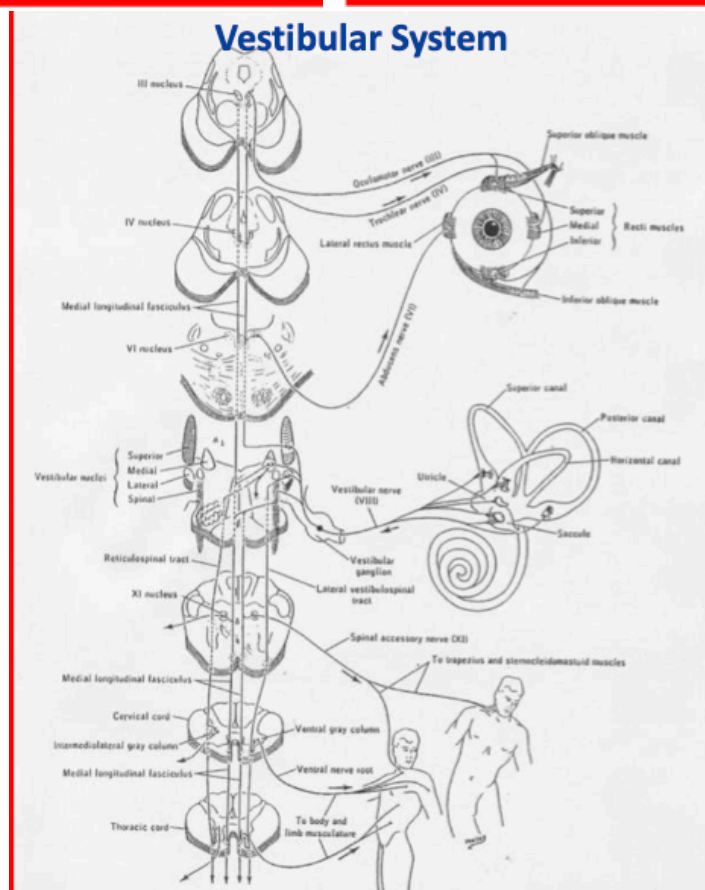
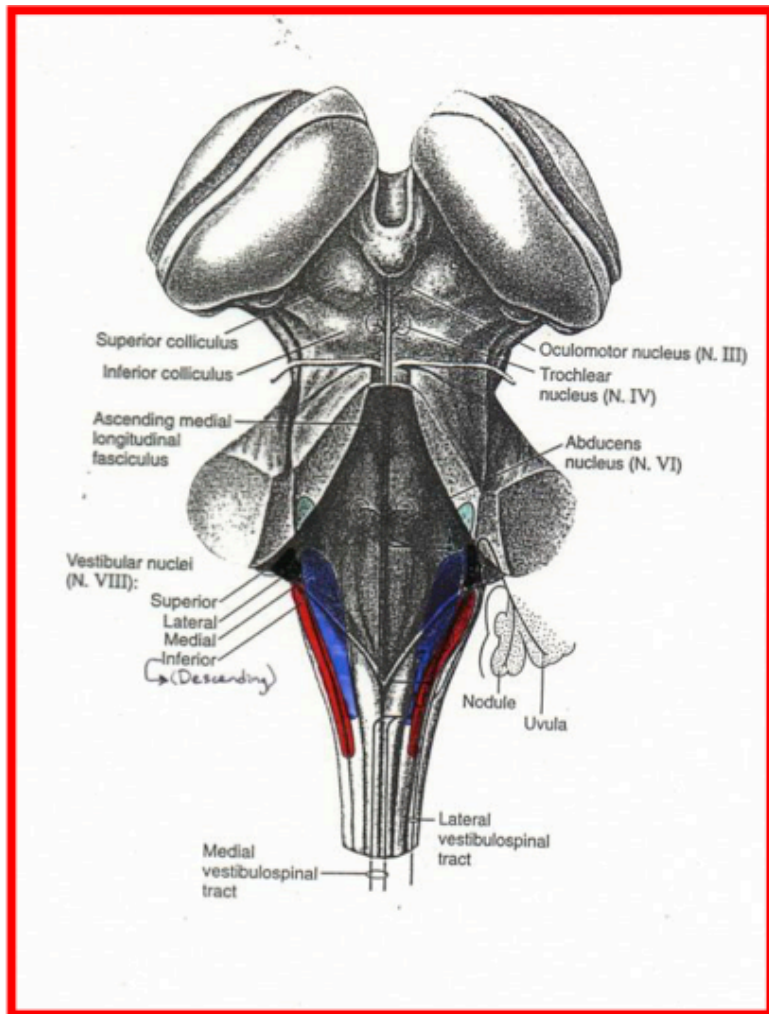
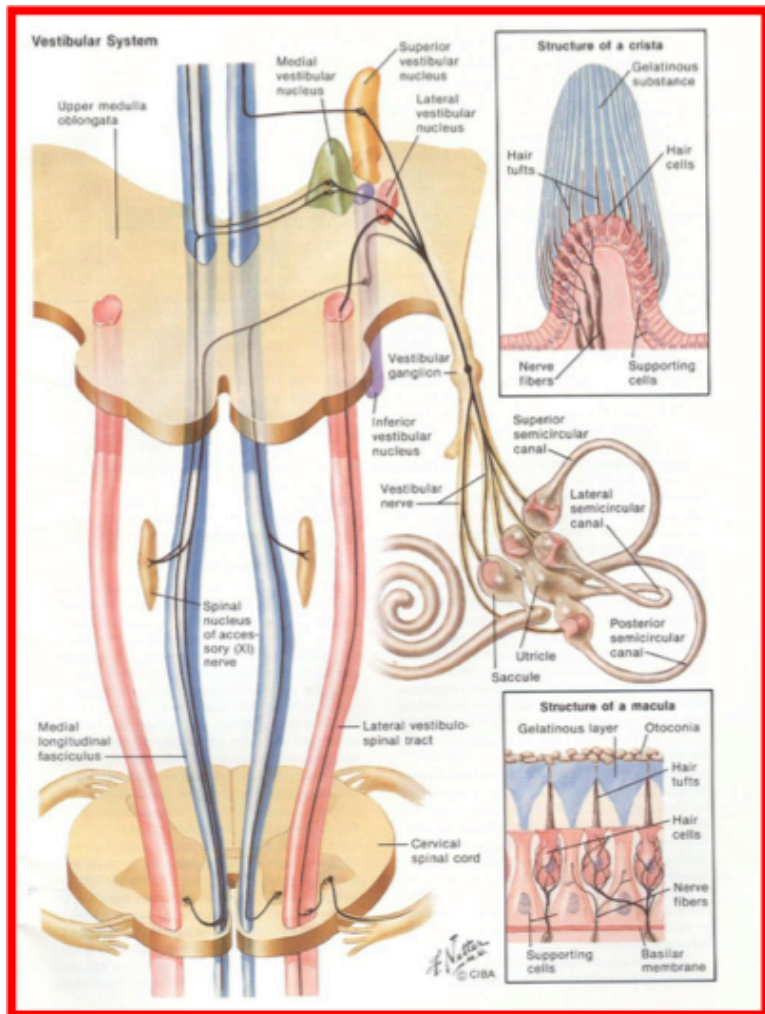
Excitation Patterns in the Utricle



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The Otoliths register linear acceleration and static tilt

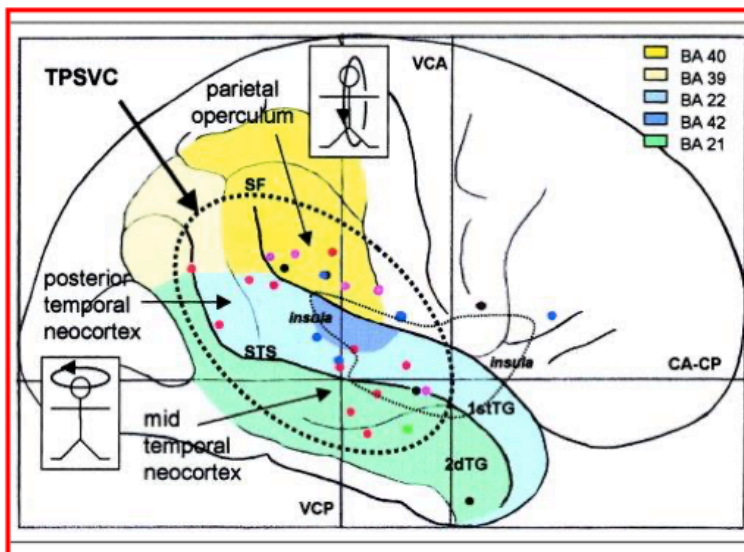




Vestibular Nuclei (VN)

Vestibular signals originating in the two labyrinths first interact with signals from other sensory systems in the VN. Only one fraction of the neurons in the VN receive direct vestibular input, and most neurons receive afferent input from other sensory systems (visual or proprioceptive) or regions of the CNS (cerebellum, reticular formation, spinal cord and contralateral VN). Consequently, the output of neurons from the VN reflects the interaction of many systems.

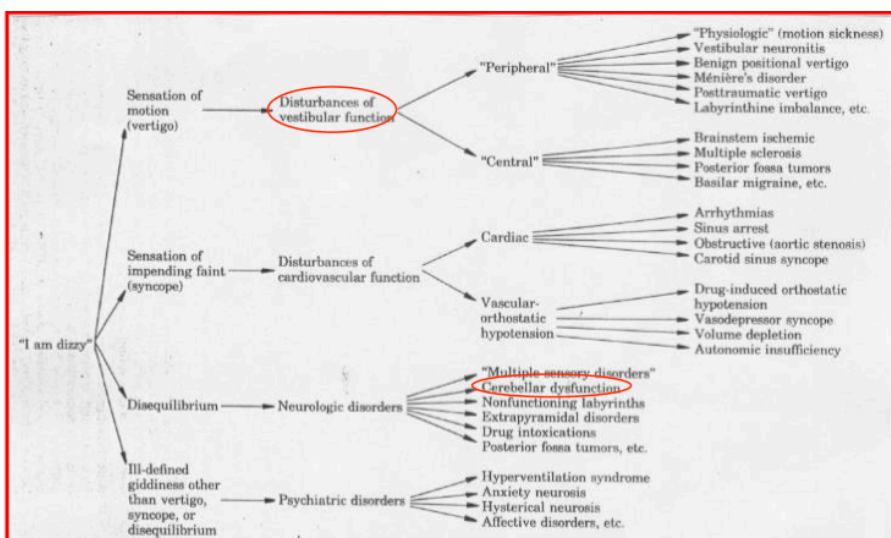
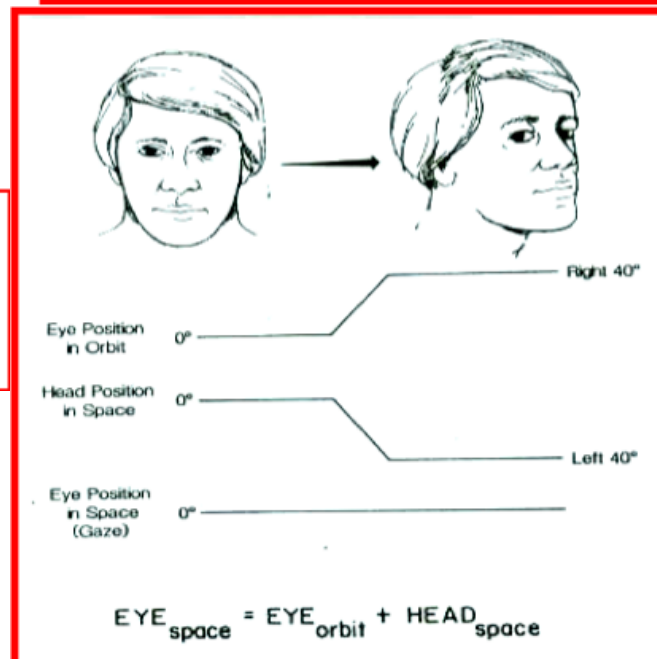
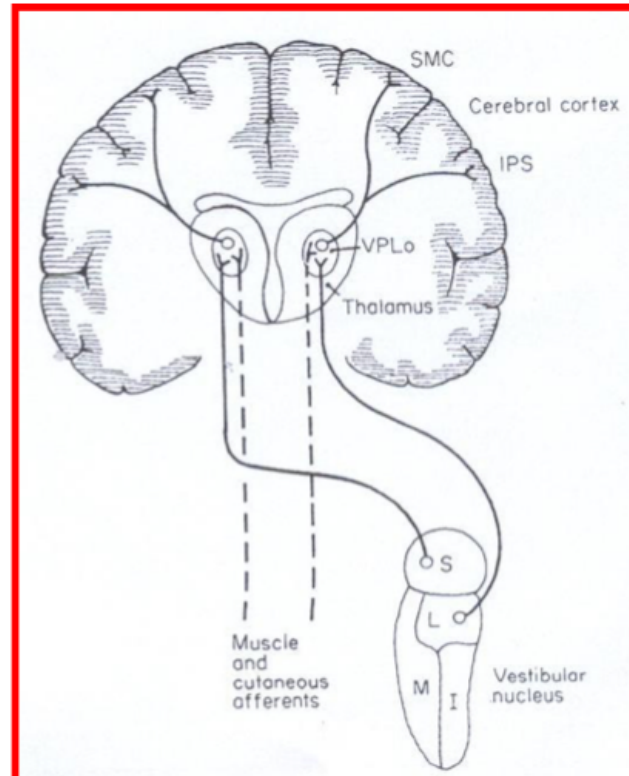
Vestibular Cortex



Schematic representation of the temporo-peri-Sylvian vestibular cortex (TPSVC). The vestibular sites located at the lateral aspect of the right or left hemispheres are projected on a lateral view of the right hemisphere normalized in the proportional stereotactic grid system of Talairach and Tournoux. BA = Brodmann area; CA-CP = anterior commissure-posterior commissure plane; VCA = vertical plane through CA; VCP = vertical plane through CP; SF = Sylvian fissure; STS = superior temporal sulcus; 1stTG = first (superior) temporal gyrus; 2dTG = second (mid) temporal gyrus. (red dots) Yaw plane illusions; (pink dots) pitch plane illusions; (blue dots) roll plane illusions; (green dots) translations; (black dots) indefinable sensations of body motion.

Vestibulo – Ocular Reflex (VOR)

To hold images of the seen world steady on the retina during brief head rotations.



Dizziness – Vertigo – Disequilibrium

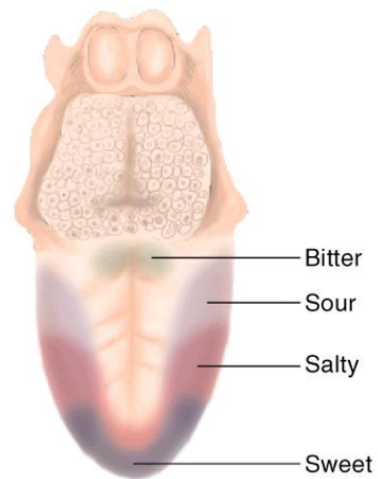
Lecture 5 – Auditory System

Brain Facts – Taste & Smell

- Average number of human taste buds = 5000.
- Number of human olfactory receptor cells = 40 Million.
- Number of dog olfactory receptor cells = 1 Billion. (Different dog species have different number of olfactory receptor cells).

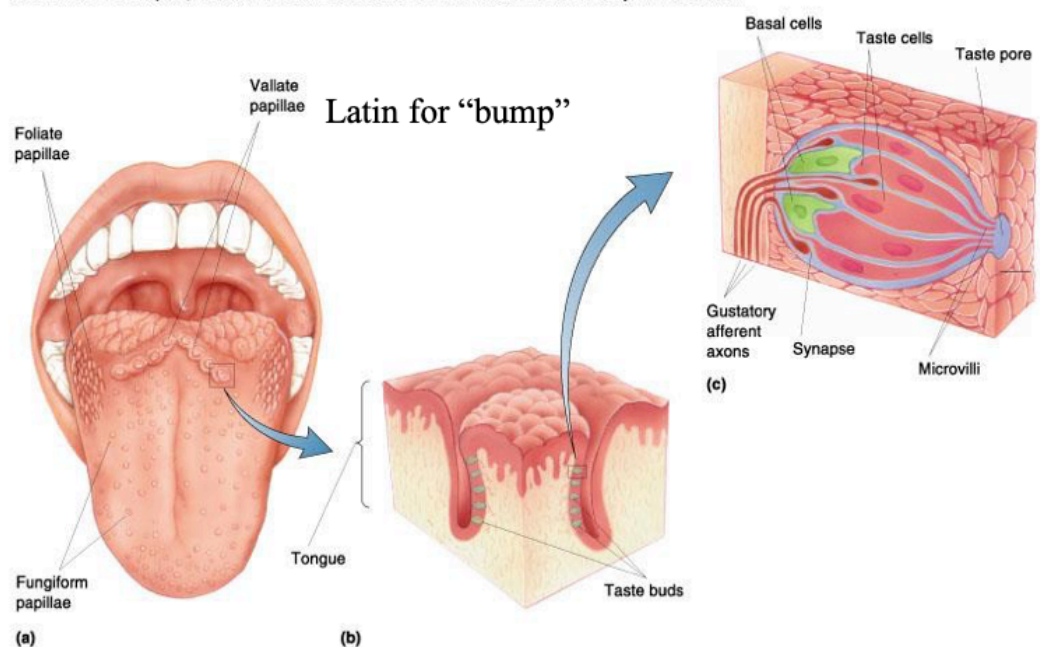
Sensitivity of Different Regions of the Tongue to Different Tastes

Most of the tongue is sensitive to all tastes. However, certain regions of the tongue are most sensitive to specific basic tastes. Any taste that we experience can be obtained as a combination of these four tastes (with the exception of fatty and Umami tastes).



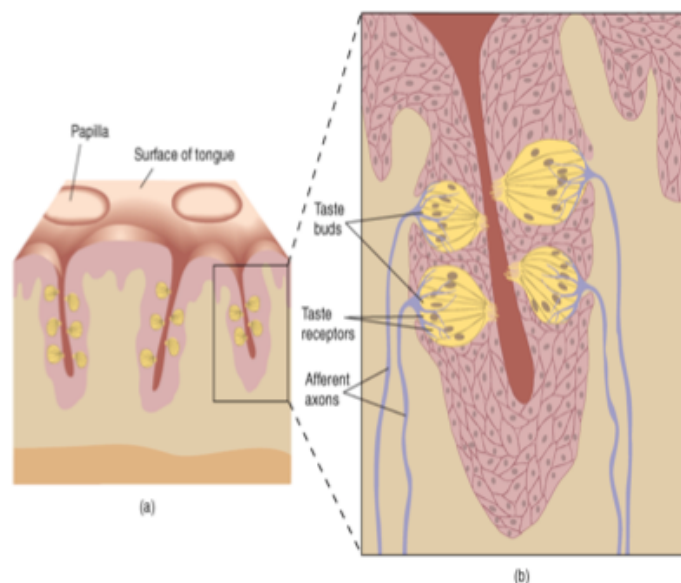
The papillae contain the taste buds, which in turn contain many cells. Each of these cells has access to the surface of the mouth through a “taste pore”, that’s where the molecules contained in the saliva and what we eat bind to particular receptors which evoke the sense of taste.

The tongue, its papillae, and its taste buds. (a) Papillae are the taste-sensitive structures. The largest and most posterior are the vallate papillae. Foliate papillae are elongated. Fungiform papillae are relatively large toward the back of the tongue and much smaller along the sides and tip. (b) Cross-sectional view of a vallate papilla showing the locations of taste buds (receptor cells), gustatory afferent axons and their synapses with taste cells, and basal cells. Microvilli at the apical end of the taste cells extend into the taste pore, the site where chemicals dissolved in saliva can interact directly with taste cells.



Taste

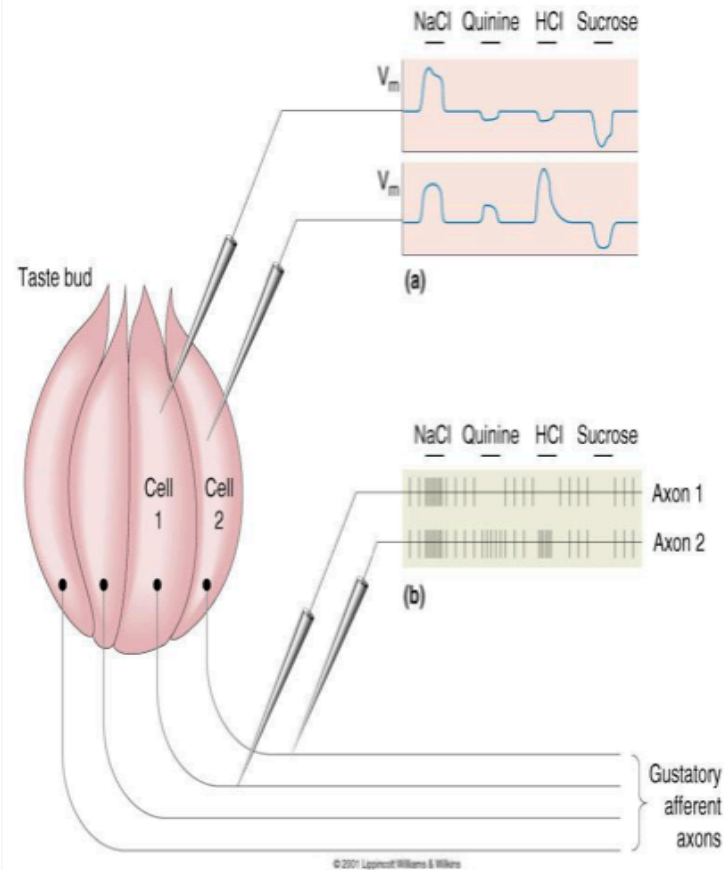
- **Papillae** – each one has several hundred taste buds – each having 50 – 150 receptor cells.
- An average person has 2000 – 5000 taste buds, although super-tasters have as many as 20000. And then there are the sorry bunch who only have 500.



Recordings made in the afferent fibers

Figure 8.4

Responsiveness of taste cells and gustatory axons. (a) Two different cells were exposed to salt (NaCl), bitter (quinine), sour (HCl), and sweet (sucrose) stimuli, and their membrane potential was recorded with electrodes. Notice the different sensitivities of the two cells. (b) In this case, the action potential discharge of the sensory axons was recorded. This is an example of extracellular recording of action potentials. Each vertical deflection in the record is a single action potential.



- Ill-colored food tastes “just not right”. (Blue fondue)
- Lumpy mashed potatoes, soggy bacon, celery, or carrots, smoothness of grapes.
- Lack of smell make it difficult to distinguish a bite of an apple vs. an onion.

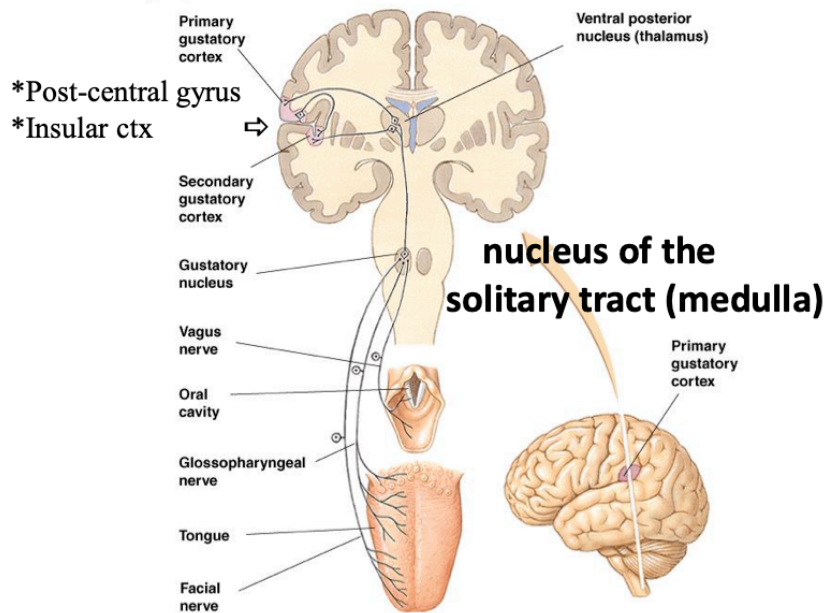
Capsaicin

- The active ingredient in spicy food.
- Releases substance P from certain nociceptors in the mouth.
- Substance P is a peptide synthesized by noci (pain) receptors that causes vasodilation and release of histamine and hyperalgesia (super sensitivity to pain).
- Be forewarned about the searing pain that comes from rubbing your eyes with chili-stained (capsaicin-coated) fingers.

Smell – Olfaction

- We can smell and differentiate between several hundred thousand substances, only about 20% are pleasant and only approx. 16 – 20 are identifiable.
- Anosmia – Odor blindness.
- Women are slightly better than men in both detecting and identifying odors.
- The ability to detect odors declines somewhat with age.
- Smokers show a dulled sense of smell (they found pleasant odors to be less pleasant and unpleasant odors to be less unpleasant).
- The olfactory system begins in the roof of the nasal cavity.

The Gustatory System



Where does that gourmet flavor come from?

- Flavor is a complex thing, it is not just the result of the receptors on the tongue. It is highly influenced by smell and vision.
- The color, texture, aroma, expectations, temperature and satiety all play a role in the perception of taste along with the direct activation of the primary tastes.
- Smell and taste are us. Secondary to visual capture.

- Olfactory receptors are ciliated epithelial cells capable of detecting thousands of different odors.
- Axons from the olfactory receptors project through the cribriform plate and synapse on dendrites of mitral cells in the olfactory bulb.
- There is **no direct** projection to the thalamus (unlike all the other sense we have discussed so far).

- **Primary olfactory cortex**
– ventral anterior temporal lobe (ipsilateral projection from each nostril **detect changes in odor**).

- **Secondary cortex** – lateral orbitofrontal cortex (**identifies smell**).

- Olfactory receptors continually die and regenerate in a cycle that lasts about 1-3 months.

- Mucus (snot) covers the epithelium, flows constantly & is replaced every 10 min. (contains antibodies to protect from virus; provides moisture and removes foreign material from inspired air, indeed if the mucus dries out, our risk of contracting infections increases).

- The strict connection with the limbic system (associated with emotions) explains why odors bring back memories of childhood as well as creating disgust reactions (e.g., those associated with foods that made you sick).

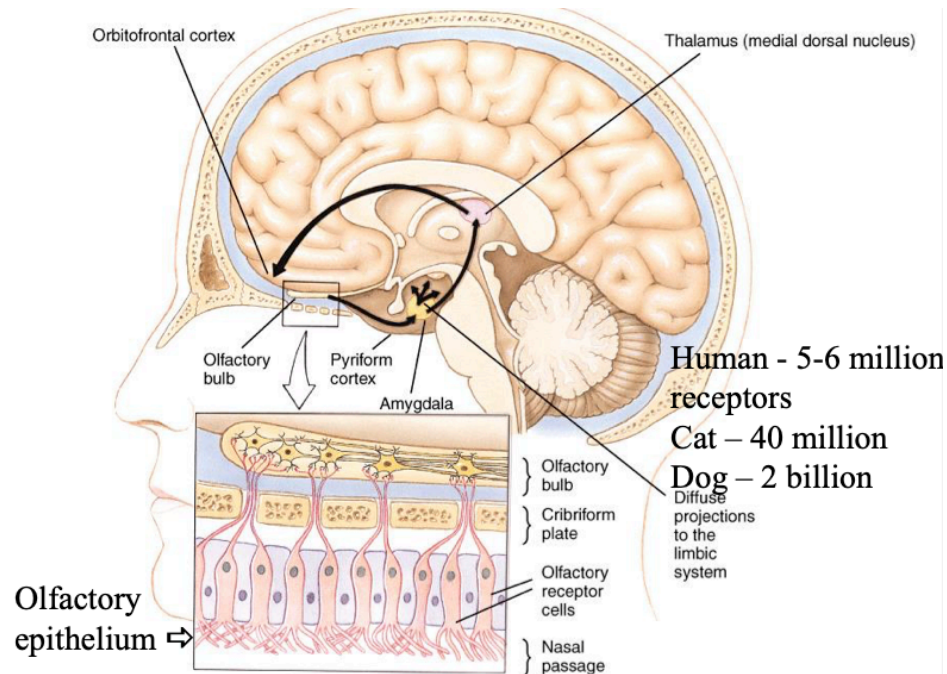
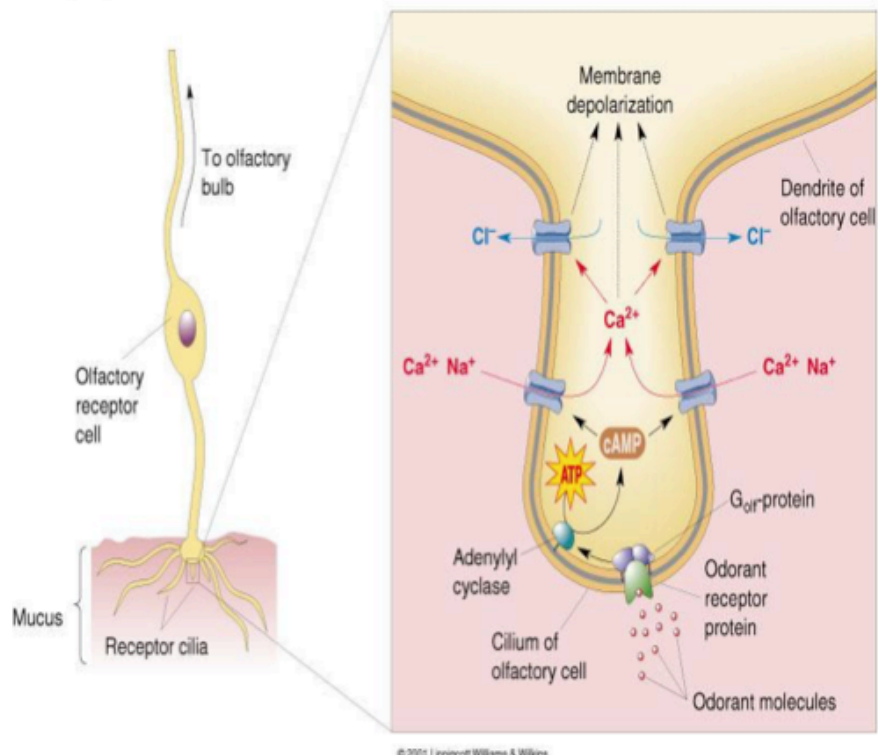


Figure 8.12
Transduction mechanisms of vertebrate olfactory receptor cells. This drawing shows a single cilium of an olfactory receptor cell and the signaling molecules of olfactory transduction that it contains. Golf is a special form of G-protein found only in olfactory receptor cells.

Transduction

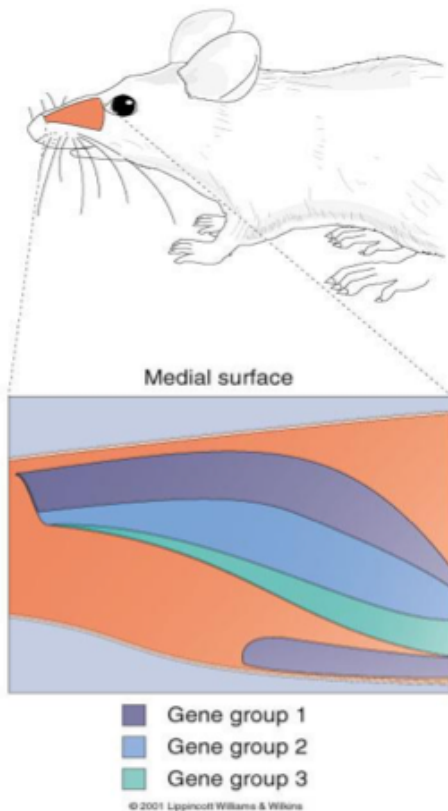
It occurs in the cilia, and it the process through which the odorants bind to the receptors:

- Odorant binds to the receptor
- Activates cAMP
- Influx of Na^+ and Ca^{2+}



- **Piriform Cortex (First)**
– Perception of Odor.
- **Orbitofrontal Cortex** –
Conscious Perception or
Identification of Odor.
- **Limbic System** –
Emotional, Appetitive,
and Reproductive
Aspects of Odor.

Figure 8.14
Maps of the expression of different olfactory receptor proteins on the olfactory epithelium of a mouse. Three groups of genes were mapped in this case, and each had a separate nonoverlapping zone of distribution. (Source: Adapted from Ressler et al., 1993, p. 602.)



► The Olfactory System

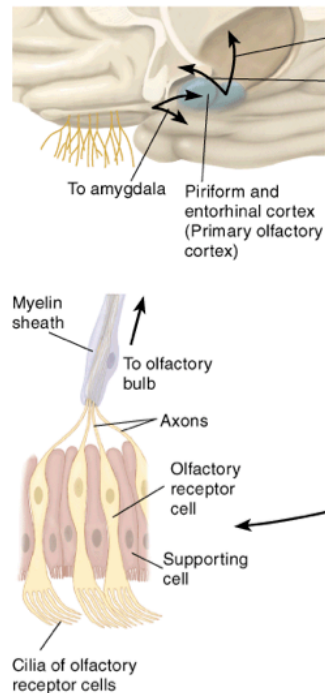
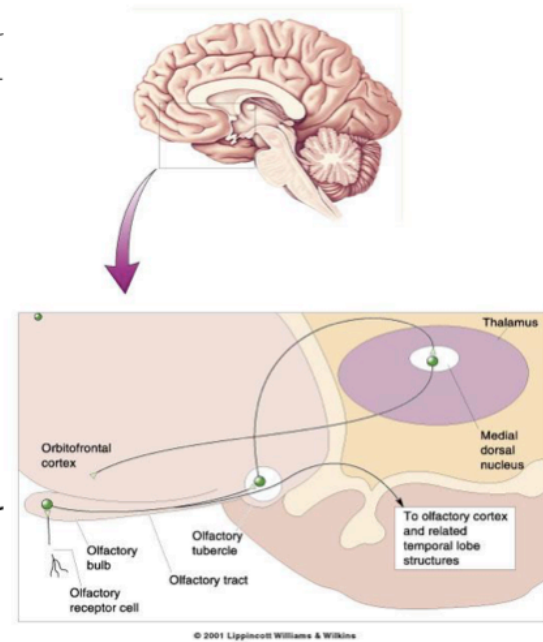


Figure 8.19
Central olfactory pathways. Axons of the olfactory tract branch and enter many regions of the forebrain, including the olfactory cortex. The neocortex is reached only by a pathway that synapses in the medial dorsal nucleus of the thalamus.



Pheromones

Airborne chemicals released from animals that have a physiological or behavioral effect on another (individuals of the same species).

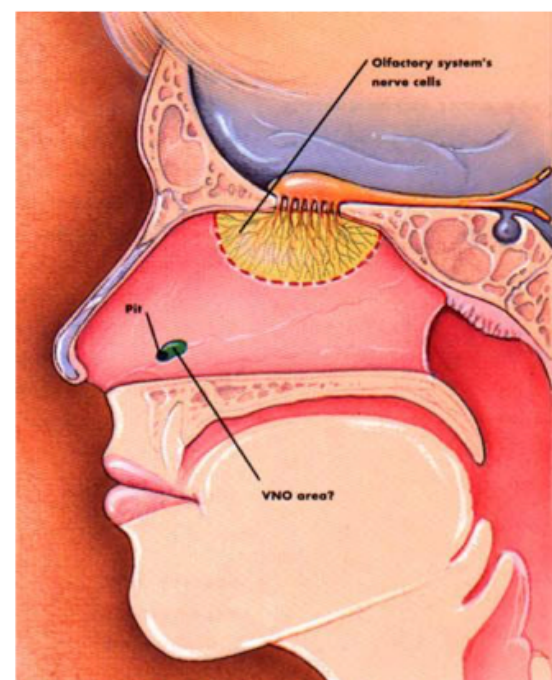
Vomerolnasal Organ (VMO) – ventromedial Hyp.

While the potency may not compare to the insect system, investigators are beginning to find evidence that many mammals ranging from pigs to elephants can have a pheromone-type response to a sniff of secretions. Yes, even humans appear to respond.

McClintock Effect – synchronization of menstrual cycles in women who live together:

- Cotton pads underneath the arms of donor women (8hrs) and then wiped underneath the noses of recipient women (did not wash face for 6 hrs.)
- The recipients were not told the source of the chemicals and did not consciously perceive any odors.
- Recipient's menstrual cycle either shortened or lengthened.

Researchers have found that female rodents share the same characteristic. Furthermore, chemicals emitted from a female rat during one part of its reproductive cycles will lengthen a fellow rodent's cycle. Chemicals from another part of the cycle will shorten the cycle.



- Isolated on a remote island for several weeks, a scientist notes that his beard sprouts at a pathetic rate. Back in the company of women, his whisker growth returns to a gallop.
- Male moths will detect the spray of a fertile female as far as a mile away. The pheromone causes them to drop all business and meet the female for mating.
- Bloodhounds have difficulty distinguishing between the smells of identical twins, but not fraternal siblings.
- Bruce Effect – a recently impregnated female mouse will abort fetus if encountered by a male mouse other than the one with which she mated.

Synesthesia

- Association between colors and number or between shapes and tastes by people. The capacity to join sensory experiences across sensory modalities.
- 1:25000 people (Cytowic, 1988).
- Genetic components in families, indeed a whole family might share this peculiar trait of associating multiple sense. However, the genetic component is still undetermined.
- Tasting shapes, colored hearing (speech and music have colors).

Lecture 6 – Motor System

Why Is the Motor System Important

The fact that we have a brain has to do with the fact that we move (counterexample, some animal in the ocean is capable of digesting its own brain as soon as he finds a stable spot to live).

- All observable behavior is directly related to activity in the motor system.
- Without the motor system we could experience sensation, think, reason, problem solve, read, write and do mental math, but we would not be able to communicate our thoughts and abilities to anyone.

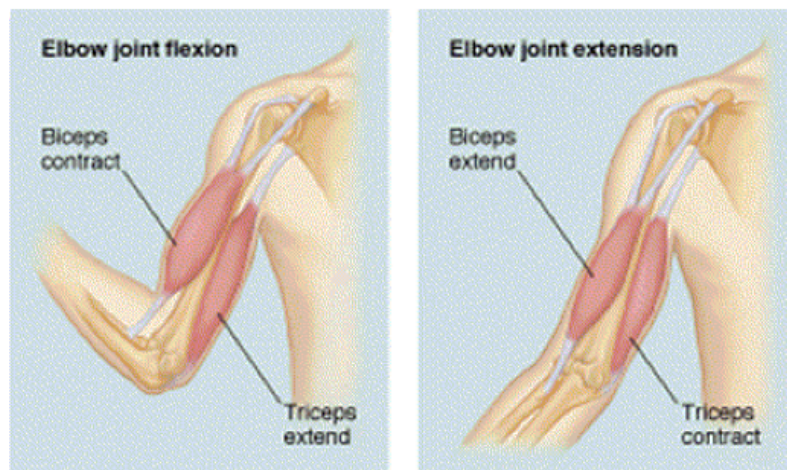
Overview of Motor System

- Spinal Reflexes
- Corticospinal and Corticobulbar Tracts
- Cortical-subcortical-thalamo-cortical systems
 - Involving Basal Ganglia
 - Involving Pons and Cerebellum

Skeletal Muscles (vs. Smooth Muscles)

Striated vs Smooth because the smooth muscles are the ones that control our internal organs.

- Striated (striped) appearance because they are comprised of muscle fibers.
- Move through a pull action (contraction)
- Work in pairs with a reciprocal muscles (bicep contracts & triceps relaxes)
- Stimulated by a Motor Neuron (neurons that bring the electrical pulses to muscles).

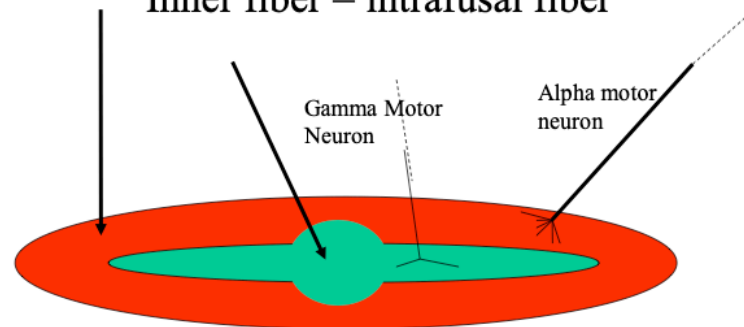


Anatomy of the Muscle

Striated muscles are made of muscle fibers that have two parts, **Outer** and **Inner**:
The following image represents only one muscle fiber – a muscle has many fibers

Outer fiber = extrafusal fiber

Inner fiber = intrafusal fiber

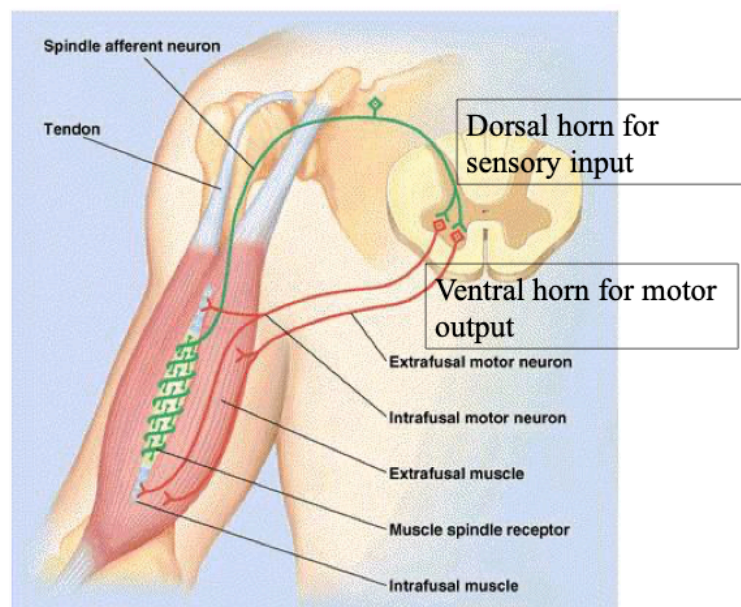


Wrapped around the intrafusal fiber, there is a sensory nerve that picks up the sensation of stretch. Good part of the innervation in the muscles senses the stretch of the muscles rather than controlling the muscle movements.

Each muscle fiber has a **Gamma Motor Neuron** that synapses on the intrafusal fiber. The **Alpha Motor Neuron** synapses on the extrafusal fibers. One alpha motor neuron can simulate numerous fibers. This is called **Motor Unit**. The neural link between the alpha motor neuron and the muscle fiber is called the **Neuromuscular Junction**.

The Muscle – Spindle Feedback Circuit

This loop is the basis of reflexes.



The ratio between the alpha motor neuron and the number of muscle fibers it innervates is associated with the degree of dexterity needed in the movement:

- **High Ratio** (1:150) = contraction of large muscles
- **Low Ratio** (1:10) = contraction of small muscles needed for fine movements (Finger, Lips)

Motor Homunculus is related to the number of alpha motor neurons needed to innervate muscles of various regions of our body.

Comparing the Anatomy of the CNS with the Anatomy of the Neuromuscular Junction

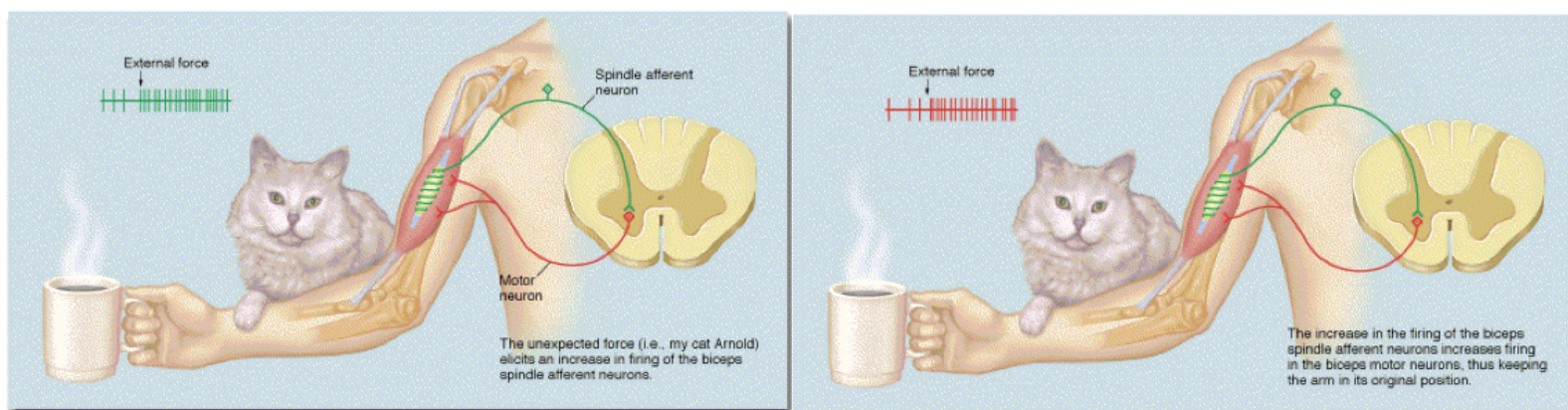
<u>Motor Unit</u>		<u>CNS Synapse</u>
• Alpha Motor Neuron	=	Presynaptic Neuron
• Muscle Fiber	=	Postsynaptic Neuron
• Endplate	=	Dendrite
• NT is Acetylcholine	=	Many different NTs
• Nicotinic Receptors	=	Many different receptors
• Calcium enters	=	Sodium enters
• Endplate Potential (EPP)	=	EPSP
• Muscle Contraction or Muscle Action Potential & movement	=	Action Potential & release of NT

How is Limb Position Maintained?

- **Involuntary Movement** (i.e., posture): continual contraction and relaxation of the muscles in our feet and calves.
- **Voluntary Movement**: stretch of the intrafusal fiber causes contraction of the extrafusal fiber via alpha motor neuron. Keeping the movement at this position requires a direct signal from the brain.

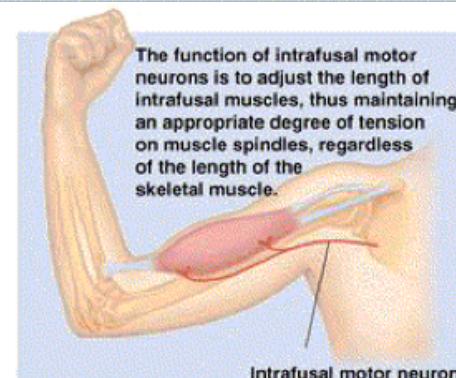
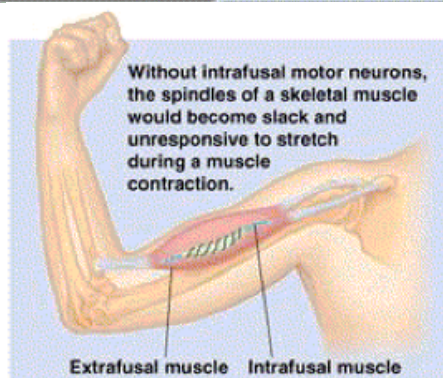
Automatic Maintenance of Limb Position

How is the position maintained with an external force? The intrafusal motor neuron (Gamma) signals the change, which is accounted for by the Extrafusal Motor Neuron (Alpha) by increased firing.



Intrafusal Motor Neurons

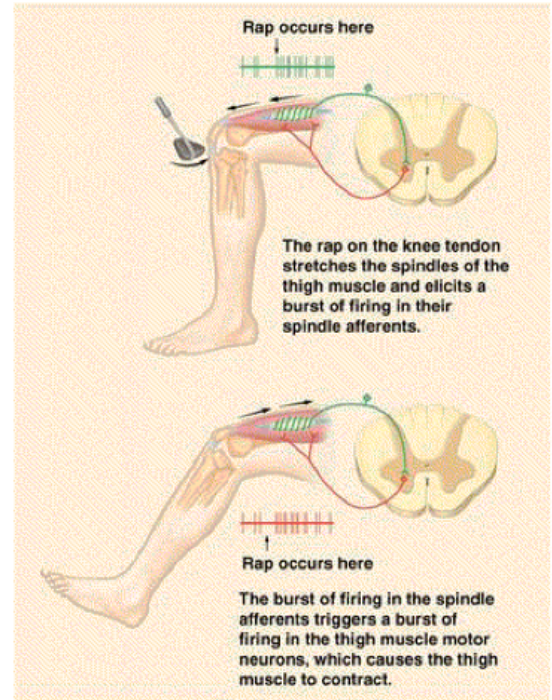
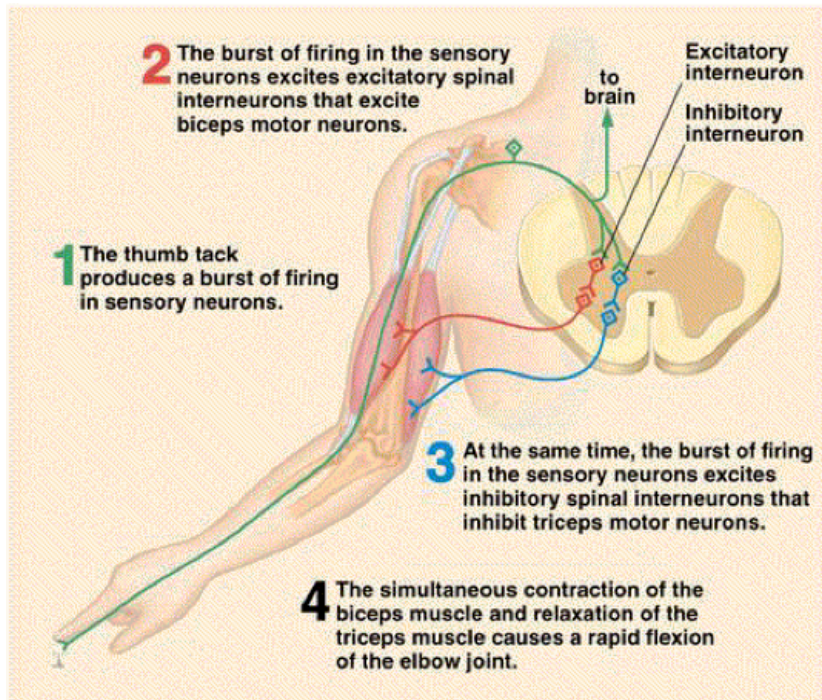
The Gamma Motor Neuron makes sure that the intrafusal muscles show always a state of tension to exert a reaction when needed (e.g., the previous cat).



Remember that muscles work in pairs, so if one contracts the other relaxes. This is referred to as **Reciprocal Innervation**. What if both muscles contracted at the same time?

Reciprocal Innervation of Antagonistic Muscles

The Elicitation of a Stretch Reflex



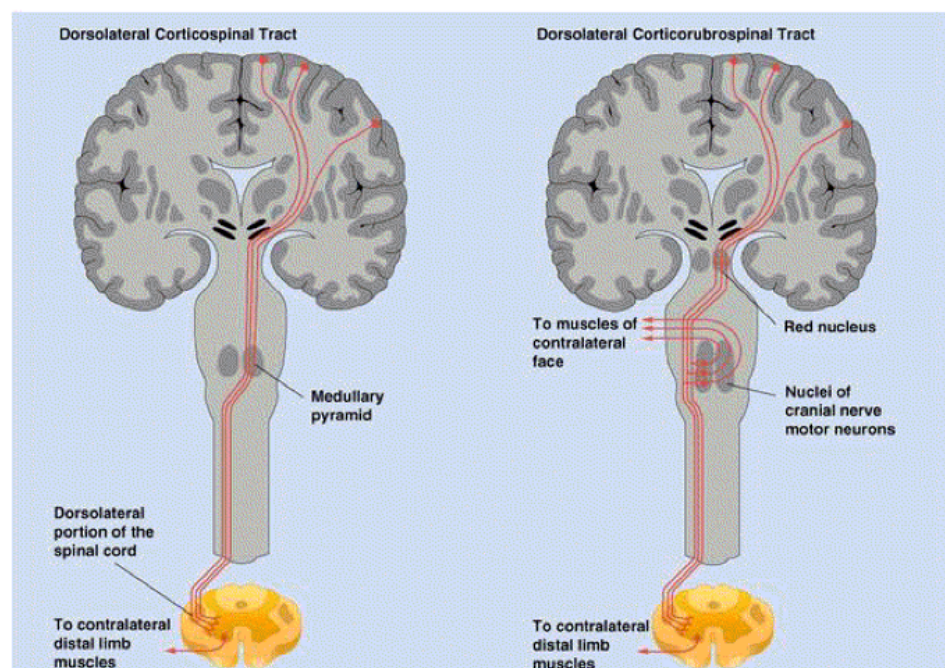
Neurologist often measure this reflex because the presence of such reflex indicates a functioning spinal cord.

Alpha Motor Neuron is the **Final Common Path** for all movements. Movement can be generated from:

- Sensory signals in the muscle spindle like the stretch reflex.
- Sensory signals from skin as in the pain withdrawal response.
- Involuntary signals from the brainstem for posture, keeping us upright without conscious attention.
- Signals from the brain for voluntary movement.

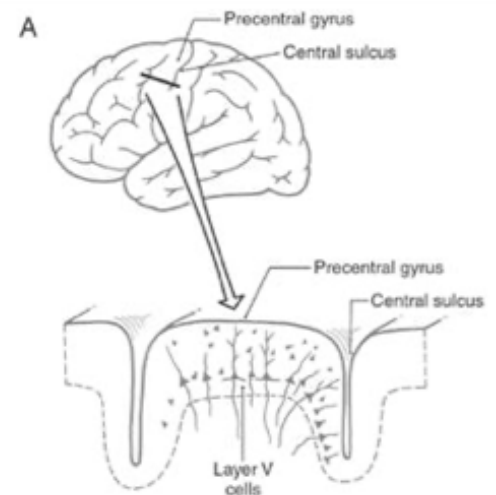
But, regardless of where the signal originates, all movement is the result of activity in the Alpha Motor Neuron – making this the **Final Common Path**.

The Two Divisions of the Dorsolateral Motor Pathway



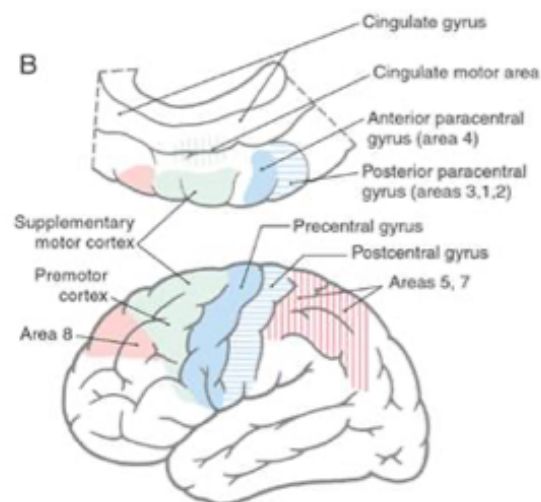
Corticospinal Tract

- Origins: Primary Motor Cortex (MI), Premotor Cortex, Supplemental Motor Cortex, Anterior Paracentral Gyrus, Parietal Lobe (including SI) and Cingulate Gyrus.
- Collaterals: Small percentage of Corticospinal Neurons
 - 1. Midbrain (primarily red nucleus)
 - 2. Trigeminal Nuclei
 - 3. Pontine Nuclei
- Termination is Spinal Cord: mostly laminae 3-7, few in ventral horn and laminae 1-2; mostly innervating interneurons, although some innervation of alpha motor neurons.
- Neurotransmitter: Glutamate and/or Aspartate.



Corticobulbar Tracts

- Control over facial muscles; bilateral input to motor neurons controlling muscles in upper face, but contralateral input to motor neurons controlling lower face (in humans, not sure about rodents).
- Control over muscles of mastication: motor trigeminal and RF. (Reticular Formation)
- Control over external eye muscles: input comes from frontal and parietal eye fields, rather than from MI; projection to midbrain and paramedian pontine RF
- Control over tongue: hypoglossal and RF
- Control over swallowing reflexes: nucleus ambiguus and RF.

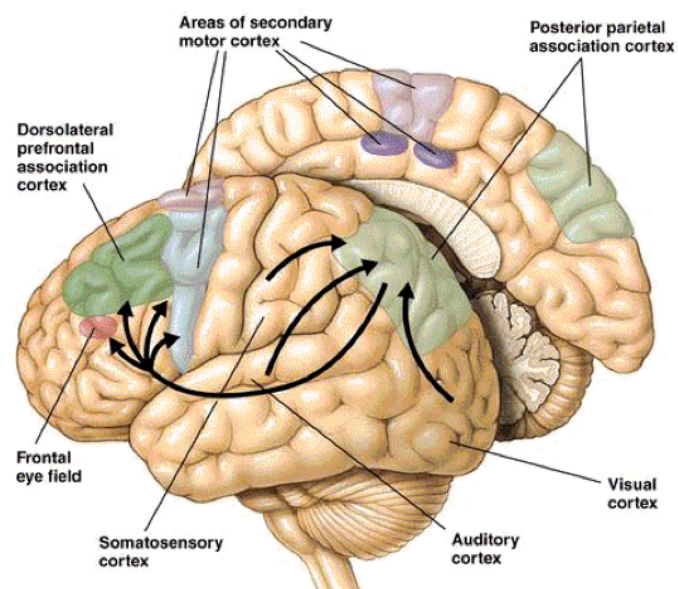


Pyramidal Tract Origin

Voluntary Movement: Instructions from Cerebral Cortex

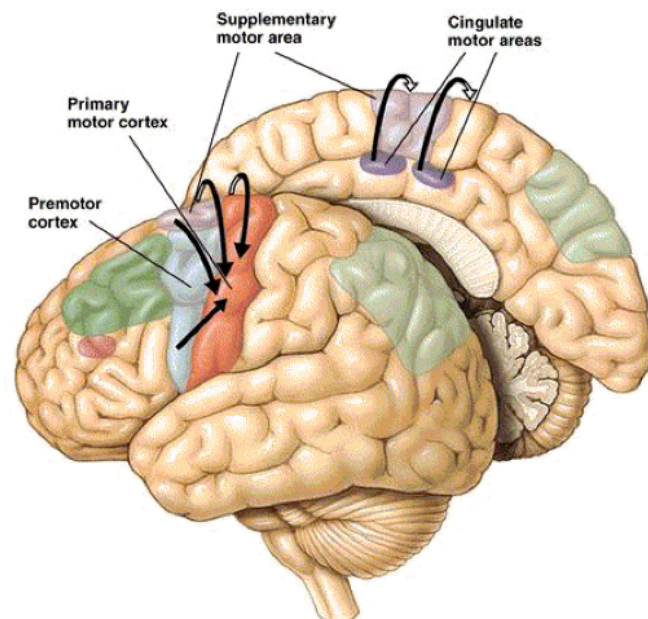
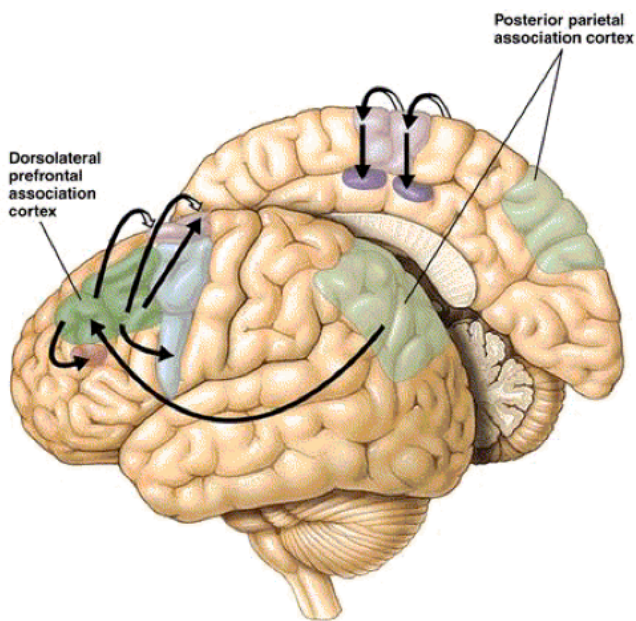
- Dorsolateral Prefrontal Cortex: directs movement of our limbs (as in reaching) and movements of our fingers.
- Actual signal for movement must go through pre-motor cortex, then motor cortex.
- From motor cortex, signal travels down spinal cord eventually reaching the alpha motor neuron.
- But, the instructions for this movement ultimately comes from our Parietal lobe, which receives sensory input.

► Cortical Input and Output Pathways



It is important to note in the picture that the **Posterior Parietal Association Cortex** is the location where all these sensory information are integrated, as well as the point of origin of the decision to perform a particular movement.

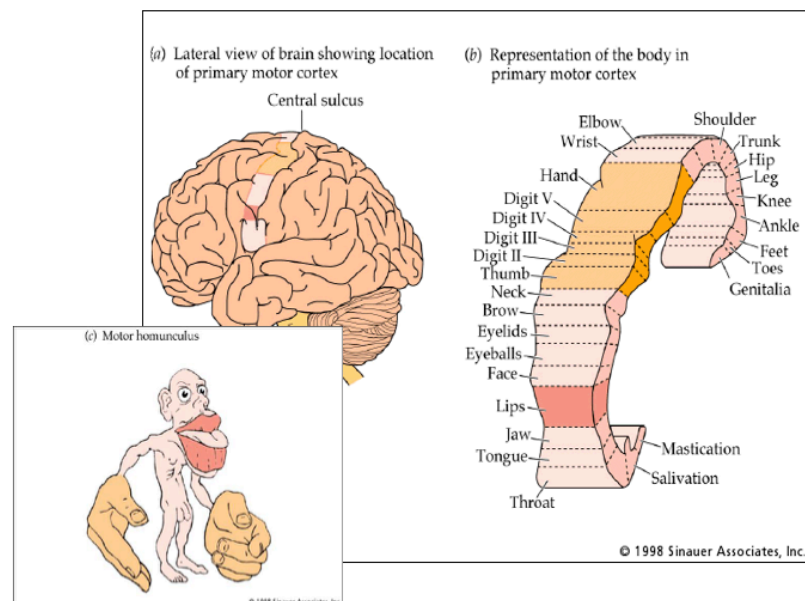
► Four Areas of the Secondary Motor Cortex



In the **Premotor Cortex** the sequence of muscles to be activated is planned. Then, in the **Primary Motor Cortex** all the muscles needed to perform a particular movement are “read” and the exact contractions and relaxation information are calculated.

Where is the best place to implant electrodes to read impulses and try to decode the intentions of an individual, which can be used to actuate prosthesis? There are **two school**:

- **Primary Motor Cortex** to read the output signals of the brain, but that's already very difficult as the inputs are already decomposed and spread around the area.
- **Parietal Cortex** in order to read the high-level commands of the movements that the individual would like to perform.



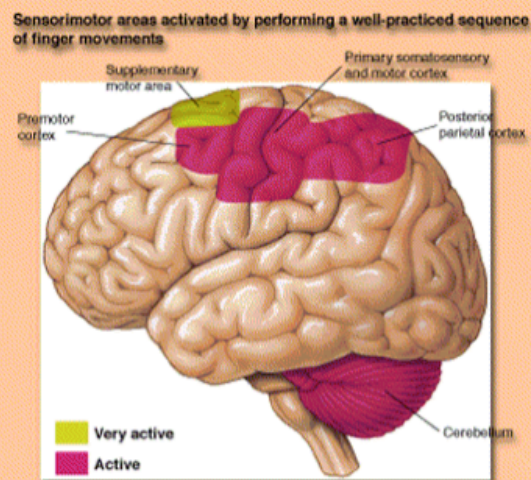
Control of Movement by Motor Cortex

- **Micro-stimulation Studies:** in MI movements of particular contralateral joints (e.g., distal finger) can be elicited by micro-stimulation; in MII contractions of groups of muscles sequentially to produce overall movements of limbs, often bilaterally.
- **Electrical Activity During Movement:** corticospinal neurons active just before initiation of a movement; activity related to amount of force necessary to produce movement; directionally-sensitive corticospinal neurons; higher-order motor cortex involved in calculating trajectories in space (probably in close communication with cerebellum) and in planning larger-scale movements (probably in close communication with the basal ganglia).
- **Imaging Studies in Humans:** random movements of digits activates MI (precentral gyrus); planned movements activate MI and supplemental motor cortex; thinking about planned movements activates supplemental motor cortex, but not MI.

There has been a lot of work done about thinking of movements, which leads to an activation of this area that are usually involved in planning. It involves mirror neurons, which is a population of neurons shown to be active in humans/animals when they observe someone else performing a particular movement, which are the same neurons that activate when someone plans the same movement. Hypothesis consider them involved in the process of learning by imitation and they are considered to be very important in the process of learning language.

Activation of different cortical areas involved in performing a sequence of actions that has been well practiced.

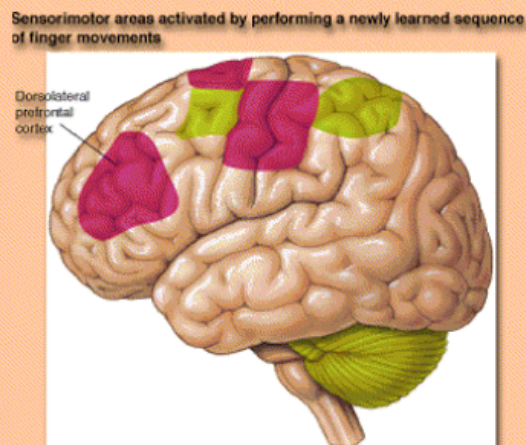
► Sequences of Finger Movements Recorded by a PET



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Compared to performing a sequence of actions that has not been extensively practiced

► Sequences of Finger Movements Recorded by a PET (continued)



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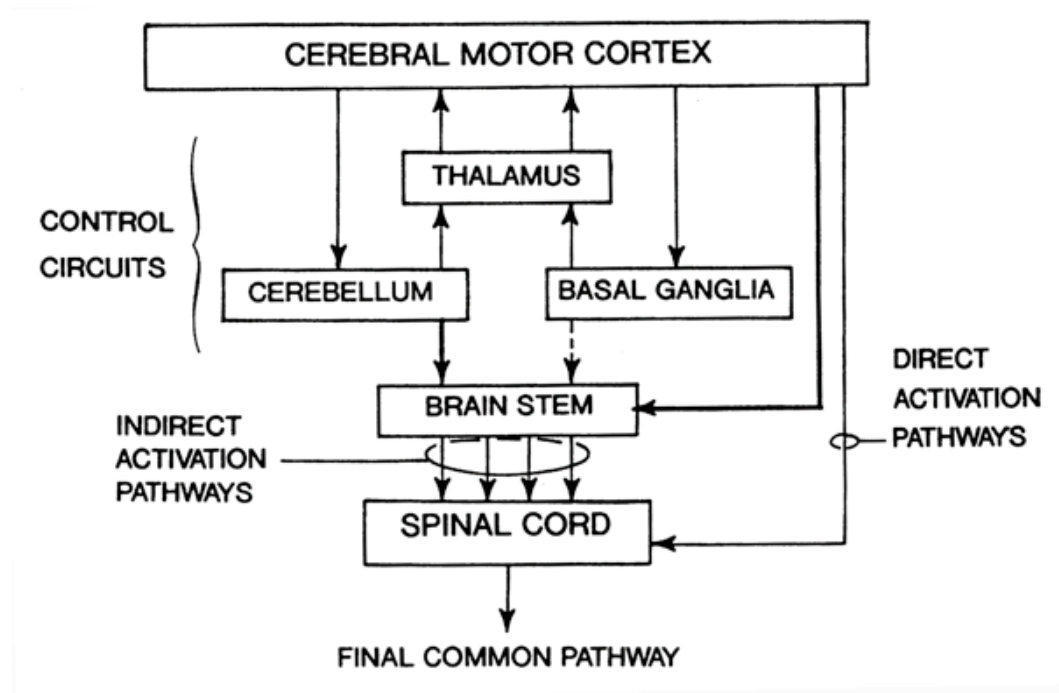
Of course, this is really too simple...

Other brain areas are involved in movement:

- Ventromedial Frontal Cortex – involved in body control, posture and whole body movements.
- Cerebellum
- Basal Ganglia
- Brainstem
- Frontal Eye Fields are involved in control of saccadic movements, and they can be found in the frontal part of the brain

In the end, all movement funnels through the alpha motor neuron (final common path).

Motor Hierarchy and Loops



Disorders of the Motor System

- **Amyotrophic Lateral Sclerosis** – motor neurons of the brainstem & spinal cord are destroyed.
- **Huntington's Disease** – progressive destruction of the basal ganglia (GABA).
- **Muscular Dystrophy** – biochemical abnormality affecting the utilization of Ca^{++} causing wasting away of muscles.
- **Myasthenia Gravis** – autoimmune disorder that destroys Ach receptors (starts with head as in drooping eyelids then progresses to swallowing & respiration).
- **Parkinson's Disease** – degeneration of neurons in the striatum due to loss of cells in the substantia nigra that synthesis/release dopamine.

Lecture 7 – Autonomic Nervous System

How is the organization of the autonomic nervous system different from that of the somatic nervous system?

Autonomic Nervous System (ANS) operates without conscious instruction.

Coordinates systems functions: Cardiovascular, Respiratory, Digestive, Urinary and Reproductive. (All these functions are to a large extent under ANS control)

Organization Similarities of SNS and ANS

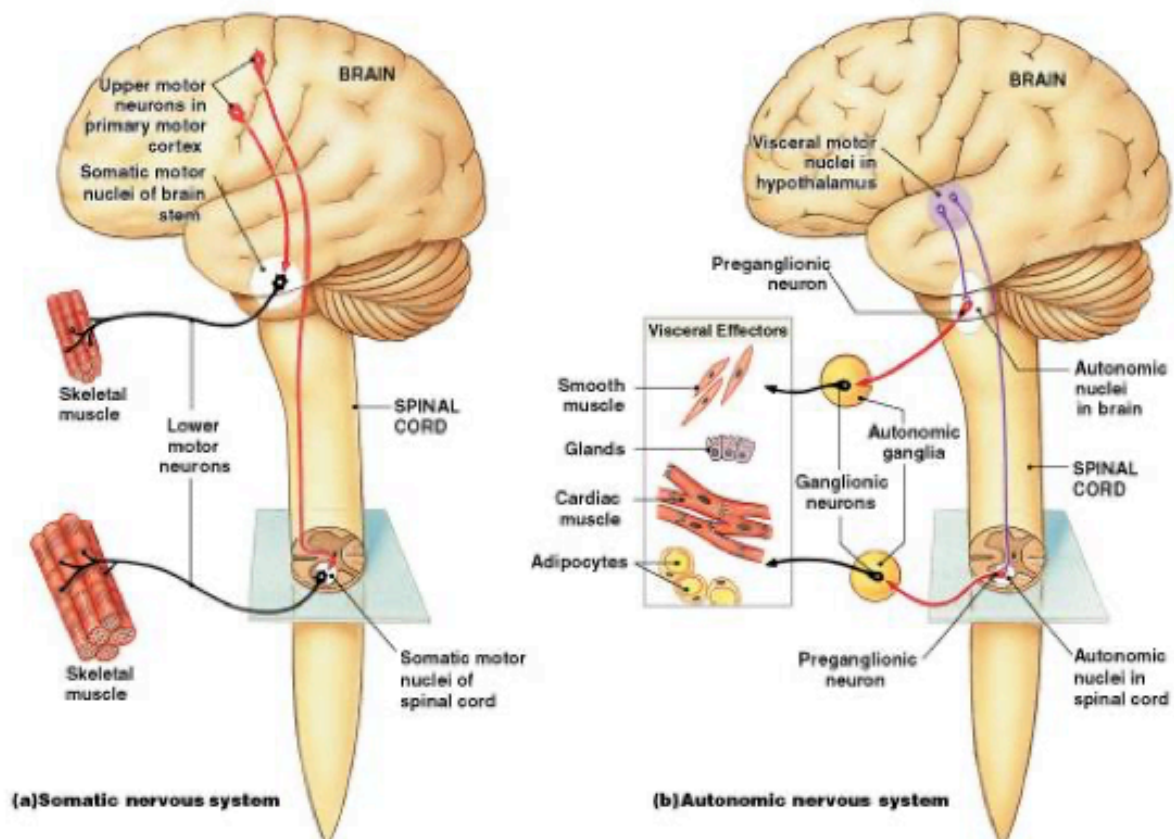
Are efferent divisions. Carry motor commands:

- SNS controls skeletal muscles
- ANS controls visceral effectors (Smooth musculature that is operating most of the organs. The heart is not made of smooth muscles but striate, however it still is under strong influence from ANS).

The ANS

Motor neurons synapse on visceral motor neurons in autonomic ganglia (small populations of neurons). Ganglionic neurons control visceral effectors.

Organization Similarities of SNS and ANS (to remember)



Preganglionic Fibers

Axons of preganglionic neurons leave CNS and synapse on ganglionic neurons.

Autonomic Ganglia

It is a peripheral Ganglia that contains many ganglionic neurons. Such ganglionic neurons innervate visceral effectors: cardiac muscle, smooth muscle, glands, adipose tissues

Postganglionic Fibers

Axons of ganglionic neurons begin at autonomic Ganglia and extend to peripheral target organs.

Somatic or Visceral Sensory Information

Trigger visceral reflexes (Set of sensors that sense things like blood oxygenation levels, the ANS would increase breath rate in case of oxygen lacks).

Motor commands of reflexes distributed by ANS.

What are the divisions and functions of the ANS?

All of the organs receive commands by both the innervations, which indeed work in a complementary manner.

- **Sympathetic Division:** “kicks in” only during exertion, stress, or emergency. It is the part of the nervous system that needs to be activated when your level of awareness needs to be increased.
- **Parasympathetic Division:** controls during resting conditions. It is the one involved when you are in a resting situation. For example allows for digestion, which it may be stopped by the sympathetic division when we suddenly face a stressing situation (e.g., catching a bus).

Divisions of the ANS

- 2 divisions may work independently: some structures innervated by only one of the two divisions.
- 2 divisions may work together: each controlling one stage of a complex process.

Sympathetic Division

- Preganglionic fibers (thoracic and superior lumbar) synapse in ganglia near spinal cord.
- Preganglionic fibers are short (they go from CNS to ganglia).
- Postganglionic fibers are long. (contained in the sympathetic ganglia).

Fight or Flight

Sympathetic division readies body for crisis. Increase in sympathetic activity:

- Stimulates tissue metabolism
- Increases alertness

Parasympathetic Division

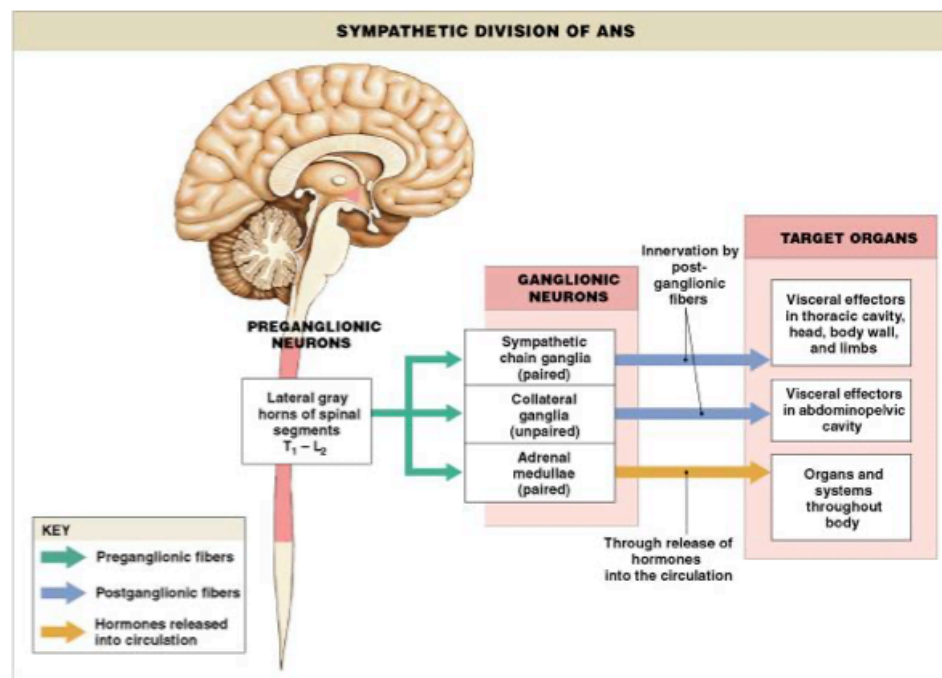
- Preganglionic fibers originate in brain stem and sacral segments of spinal cord.
- Synapse in ganglia close to (or within) target organs.
- Preganglionic fibers are long (they go all the way to the organs).
- Postganglionic fibers are short.

Rest and Repose

Parasympathetic division stimulates visceral activity. It conserves energy and promotes sedentary activities.

Enteric Nervous System (ENS)

- It is considered to be the third division of ANS.
- Extensive network in digestive tract walls.
- Complex visceral reflexes coordinated locally.
- Roughly 100 million neurons (It's very complex, yet it doesn't give rise to any conscious perception of its operations).
- All neurotransmitters are found in the brain.



Structure of the Sympathetic Division

- Preganglionic neurons located between segments T₁ and L₂ of spinal cord.
- Ganglionic neurons in ganglia near vertebral column.
- Cell bodies of preganglionic neurons in lateral gray horns.
- Axons enter ventral roots of segments.

SANS Ganglionic Neurons

Occur in three locations:

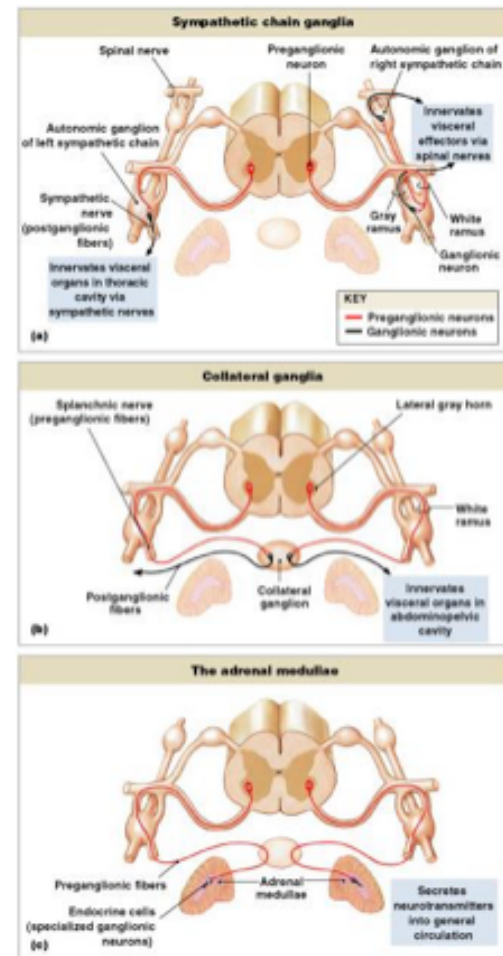
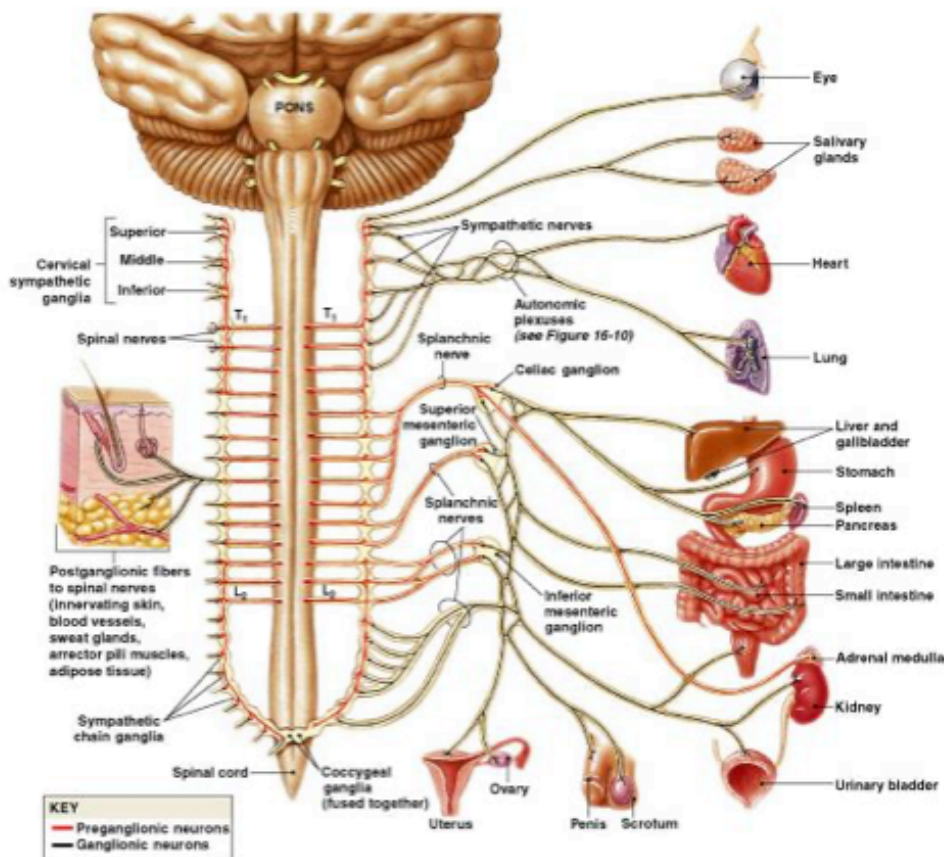
- Sympathetic Chain Ganglia
- Collateral Ganglia (innervate organs)
- Adrenal Medullae

Organization of Sympathetic Division

Ventral roots of spinal segments T₁ - L₂ contain sympathetic preganglionic fibers.

Sympathetic Innervation

The Sympathetic innervation is generally widespread, while the Parasympathetic one is generally much more local.



Adrenal Medulla

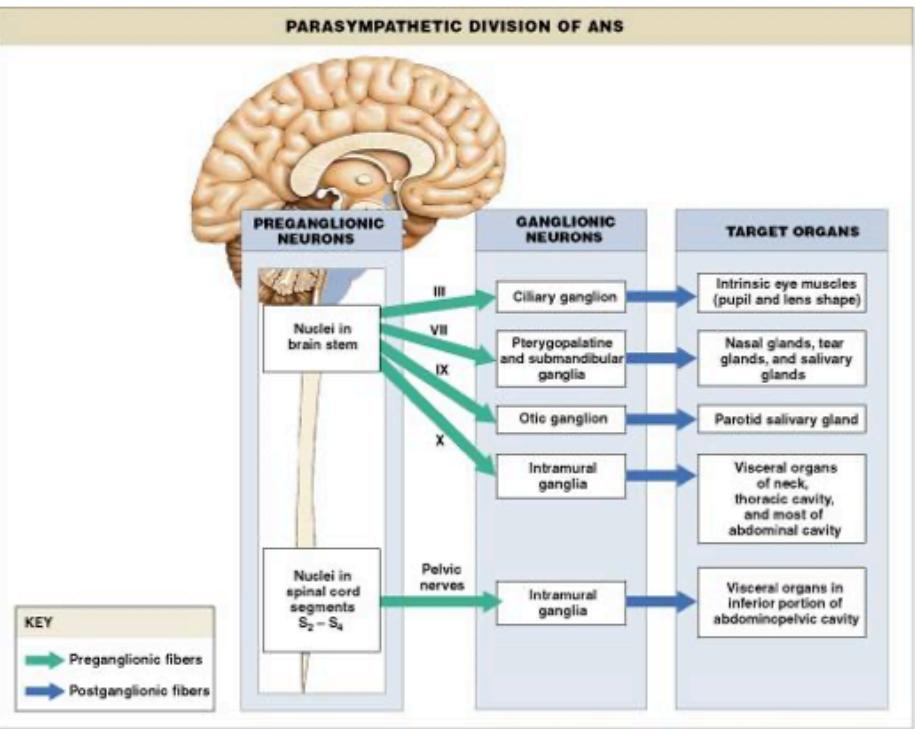
- Preganglionic fibers entering adrenal gland proceed to center (adrenal medulla).
- Modified sympathetic ganglion.
- Preganglionic fibers synapse on neuroendocrine cells.
- Specialized neurons secrete hormones into bloodstream.

Generalized Sympathetic Activation

- Release of Epinephrine (Adrenaline) by Adrenal Medulla.
- Affect alpha and beta receptors throughout body (these work through G Proteins).

What are the structures and functions of the parasympathetic division of the ANS?

The Parasympathetic Division



Autonomic Nuclei

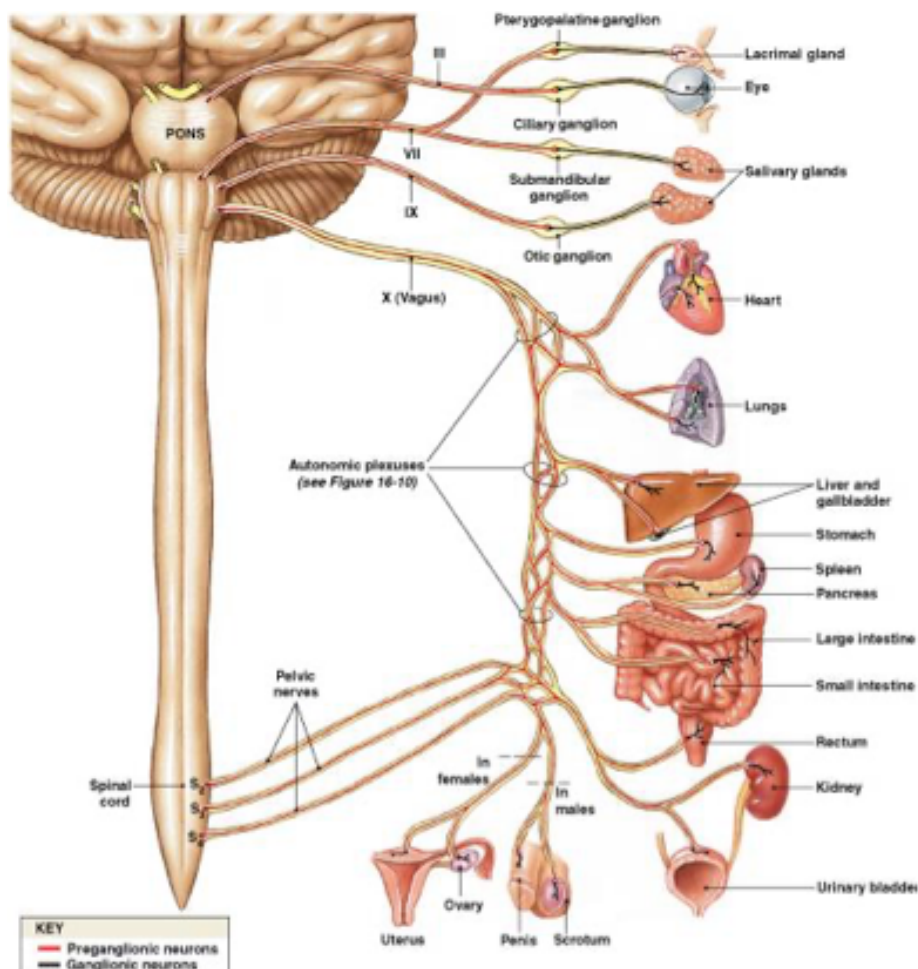
- Are contained in the mesencephalon, pons, and medulla oblongata: in lateral gray horns of spinal segments S₂ – S₄.

Ganglionic Neurons in Peripheral Ganglia

Preganglionic fiber synapses on 6-8 ganglionic neurons:

- Terminal ganglion (near target organ)
- Intramural ganglion (embedded in tissues of target organ).

Parasympathetic Innervation



Vagus Nerve

Often mentioned because of the vagus reflex, when you have a long sustained activation of the sympathetic division, then the vagus nerve is activated to bring back the body to a state of rest, reduce heartbeat (e.g., runners at the end of the marathon collapse because blood misses in the brain due to the vagus nerve reflex).

- It provides 75% of all parasympathetic outflow.
- Branches intermingle with fibers of sympathetic division.

What are the effects of parasympathetic neurotransmitters on target organs and tissues?

Parasympathetic Activation

- Centers on relaxation, food processing and energy absorption.
- Localized effects last a few seconds at most.

Parasympathetic Neurons

- All release ACh as neurotransmitter.
- Effects vary widely.

Adrenergic and Cholinergic Receptors (more detailed than necessary)

SUMMARY TABLE 16-1 ADRENERGIC AND CHOLINERGIC RECEPTORS OF THE ANS			
Receptor	Location[s]	Response[s]	Mechanism
ADRENERGIC			
α_1	Widespread, found in most tissues	Excitation, stimulation of metabolism	Enzyme activation; release of intracellular Ca^{2+}
α_2	Sympathetic neuromuscular or neuroglandular junctions Parasympathetic neuromuscular or neuroglandular junctions	Inhibition of effector cell Inhibition of neurotransmitter release	Reduction of cAMP concentrations
β_1	Heart, kidneys, liver, adipose tissue*	Stimulation, increased energy consumption	Enzyme activation
β_2	Smooth muscle in vessels of heart and skeletal muscle; smooth muscle layers in intestines, lungs, bronchi	Inhibition, relaxation	Enzyme activation
CHOLINERGIC			
Nicotinic	All autonomic synapses between preganglionic and ganglionic neurons; neuromuscular junctions of SNS	Stimulation, excitation; muscular contraction	Opening of chemically regulated Na^+ channels
Muscarinic	All parasympathetic and cholinergic sympathetic neuromuscular or neuroglandular junctions	Variable	Enzyme activation causing changes in membrane permeability to K^+

*Adipocytes also contain an additional receptor type, β_3 , not found in other tissues. Stimulation of β_3 receptors causes lipolysis.

Comparing Sympathetic and Parasympathetic Divisions

- **Sympathetic:**
 - Widespread impact.
 - Reaches organs and tissues throughout body.
- **Parasympathetic:**
 - Innervates only specific visceral structures.

Sympathetic and Parasympathetic Divisions

SUMMARY TABLE 16-2 A STRUCTURAL COMPARISON OF THE SYMPATHETIC AND PARASYMPATHETIC DIVISIONS OF THE ANS		
Characteristic	Sympathetic Division	Parasympathetic Division
Location of CNS visceral motor neurons	Lateral gray horns of spinal segments T ₁ –L ₂	Brain stem and spinal segments S ₂ –S ₄
Location of PNS ganglia	Near vertebral column	Typically intramural
Preganglionic fibers		
Length	Relatively short	Relatively long
Neurotransmitter released	Acetylcholine	Acetylcholine
Postganglionic fibers		
Length	Relatively long	Relatively short
Neurotransmitter released	Normally NE; sometimes NO or ACh	Acetylcholine
Neuromuscular or neuroglandular junction	Varicosities and enlarged terminal knobs that release transmitter near target cells	Junctions that release transmitter to special receptor surface
Degree of divergence from CNS to ganglion cells	Approximately 1 : 32	Approximately 1 : 6
General function(s)	Stimulates metabolism; increases alertness; prepares for emergency ("fight or flight")	Promotes relaxation, nutrient uptake, energy storage ("rest and repose")

What is the relationship between the two divisions of the ANS, and the significance of dual innervation?

Dual Innervation

- Most vital organs receive instructions from both sympathetic and parasympathetic divisions.
- The two divisions commonly have opposing effects.

Autonomic Tone

The fact that we have this constant influx of para and sympathetic innervations in the organs. It is an important aspect of ANS function:

- If nerve is inactive under normal conditions, can only increase activity.
- If nerve maintains background level of activity, can increase or decrease activity.

Somatic and Visceral Motor Pathways

- Many parallels in organization and function.
- Integration at brain stem.
- Both systems under control of higher centers.

Lecture 8 – Limbic System

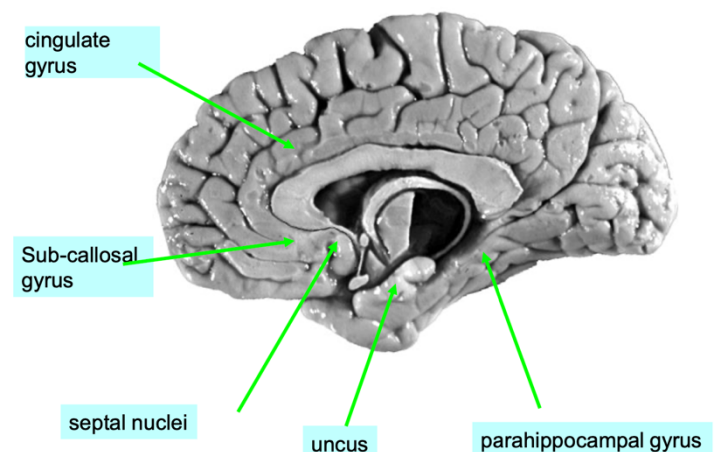
The term **limbic system** means the entire neuronal circuitry that controls **emotional behavior** and **motivational drives**.

What is the Limbic System?

Anatomically speaking:

- Hypothalamus
- Limbic lobe
- Hippocampus
- Amygdala

Limbic Lobe: C-Shape border of hemisphere



A major part of the limbic system is the hypothalamus with its related structures.

They control:

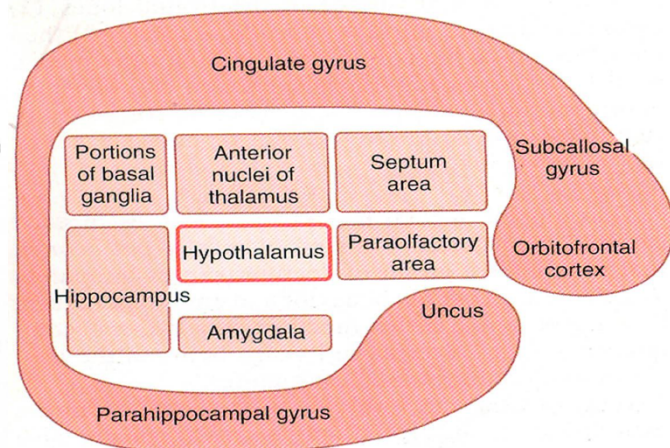
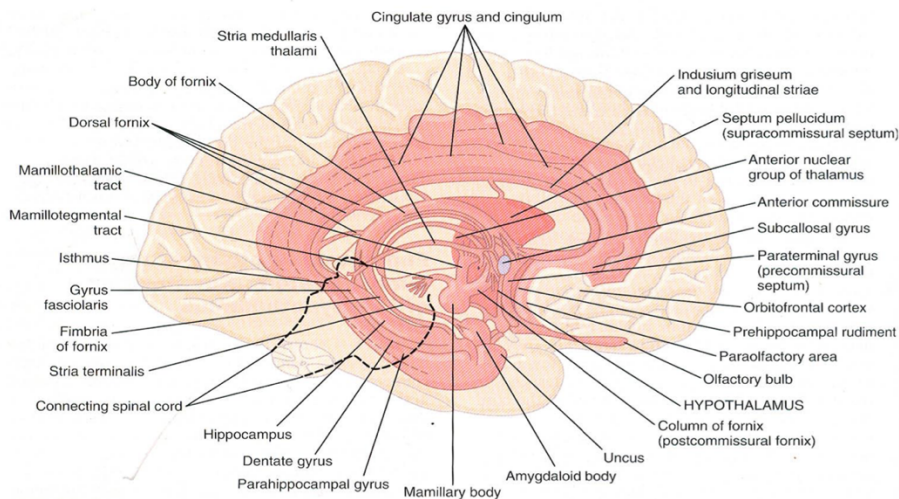
- Emotional behaviour
- Internal conditions of the body such as temperature, osmolality of the body fluids, and drives to eat and drink, and to control body weight.

These are collectively called **Vegetative Functions of the Brain**.

Functional Anatomy of the Limbic System: Key Position of the Hypothalamus (Not supposed to remember all of these names).

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Unit XI The Nervous System: C. Motor and Integrative Neurophysiology



Hypothalamus, a Major Control Headquarters for the Limbic System

From this view of a cut of the Hypothalamus, the functions of specific regions can be appreciated.

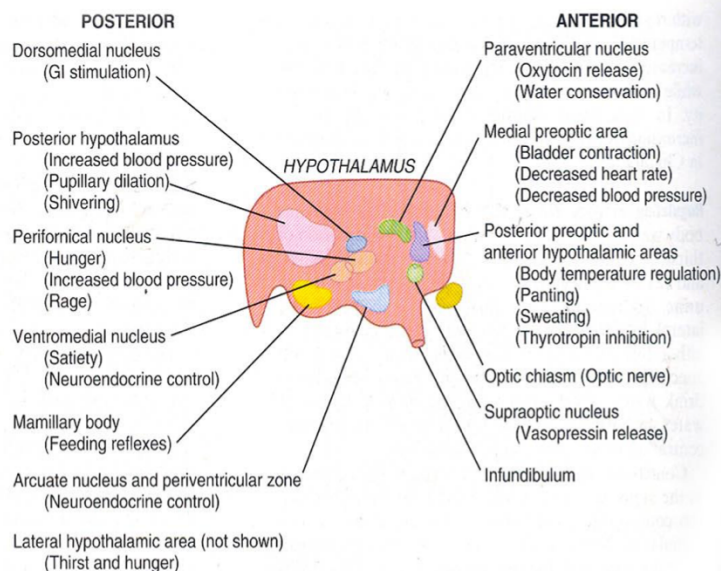


Figure 58-6

Control centers of the hypothalamus (sagittal view).

Hypothalamus represents less than 1% of the brain mass. It is one of the most important of the control pathways of the limbic system. It controls most of the **Vegetative and Endocrine Functions** of the body as well as many aspects of **Emotional Behaviour**.

Vegetative and Endocrine Control Functions of the Hypothalamus

- Cardiovascular Regulation
- Regulation of Body Temperature
- Regulation of Body water
- Regulation of Uterine Contractility and of Milk Ejection from the Breasts
- Gastrointestinal and Feeding Regulation
 - Stimulation of the lateral hypothalamic area results to extreme hunger, voracious appetite and intense desire for food.
 - Damage this area causes loss of desire for food, causing lethal starvation.

Hypothalamic Control of Endocrine Hormone Secretion by the Anterior Pituitary Gland.

Behavioral Functions of the Hypothalamus and Associated Limbic Structures

Effects Caused by Stimulation

- Stimulation of the lateral hypothalamus causes thirst and eating, increased general level of activity, leading to overt rage and fighting (strict connection with ANS).
- Stimulation of the ventromedial nucleus causes sense of satiety, decreased eating and tranquility.
- Stimulation of a thin zone of periventricular nuclei, leads to fear and punishment reactions.
- Sexual drive can be stimulated from several areas of the hypothalamus especially the anterior and most of the posterior portions of the hypothalamus.

Effects Caused by Hypothalamic Lesions

Cause effects opposite to those caused by stimulation.

“Reward” and “Punishment” Function of the Limbic System

The limbic structures are concerned with the affective nature of sensory sensations – that is, whether the sensations are pleasant or unpleasant or also called **reward or punishment or satisfaction or aversion**. (It is an important aspect, the hippocampus is associated with memory, indeed a strong way of remembering is by associating emotions to memories).

Reward Centers

- The major reward centers are located along the course of the media forebrain bundle (series of fibers that run along the C-Shape and connect the areas together), especially in the lateral and ventromedial nuclei of the hypothalamus.
- Weaker stimuli give a sense of reward, and stronger ones a sense of punishment.
- Less potent reward centers – septum, amygdala, certain areas of the thalamus and basal ganglia.
- Stimulation of these areas gives a sense of reward. When offered the choice of eating some delectable food, the animal often chooses the electrical stimulation.

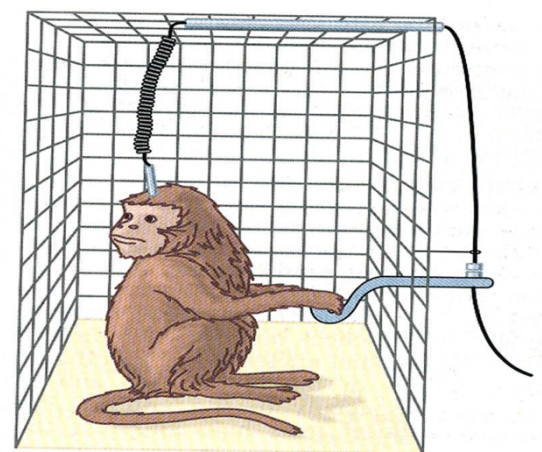


Figure 58-8

Technique for localizing reward and punishment centers in the brain of a monkey.

Punishment Centers

- Most potent areas have been found in the central gray area surrounding the Aqueduct of Sylvius in the mesencephalon.

- Less potent punishment areas are found in the amygdala and hippocampus.
- Stimulation in these areas causes the animal to show all **sign of displeasure, fear, terror, pain** and even **sickness**.

Rage – Its Association with Punishment Centers

Strong stimulation of the punishment centers, especially in the periventricular zone of the hypothalamus and the lateral hypothalamus causes the animal to:

- Develop a defense posture
- Extend its claws
- Lifts its tail
- Hiss
- Spit
- Growl
- Develop piloerection, wide-open eyes and dilated pupils

(All these body manifestations are carried out by the Sympathetic Nervous System).

Placidity and Tameness, exactly the opposite emotional behaviour patterns occur when the reward centers are stimulated.

Importance of Reward or Punishment in Behaviour

Almost everything that we do is related to reward and punishment. If we are doing something rewarding, we continue to do it; if it is punishing we cease to do it.

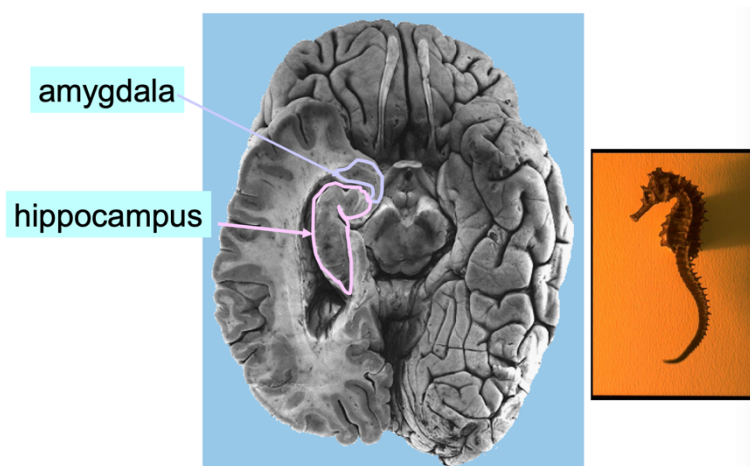
Reward and punishment centers constitute one of the most important of all the controllers of our bodily activities, our drives, our aversions, our motivations.

Importance of Reward or Punishment in Learning and Memory – Habituation vs Reinforcement

- If the sensory experience does not elicit a sense of either reward or punishment, repetition of the stimulus over and over leads to almost complete extinction of the cerebral cortical response, thus the animal becomes habituated to that specific sensory stimulus and thereafter **ignores** it.
- If the stimulus does cause either reward or punishment, the cerebral cortical response becomes progressively more and more intense during repeated stimulation and the response is said to be **reinforced**.

Medial Temporal Lobe: Hippocampus and Amygdala

Hereafter, two important structures of the limbic systems are highlighted: amygdala and hippocampus. The latter is involved in many functions like emotional behaviour and learning.



Specific Functions of Other Parts of the Limbic System

Role of the Hippocampus in Learning.

Effect of bilateral removal of the Hippocampus → Inability to learn.

Theoretical Function of the Hippocampus in Learning → Without the Hippocampus, consolidation of long-term memories of verbal or symbolic thinking type is poor or does not take place.

Hippocampus

It is part of the cortex and seems to be a particularly sensitive region of the brain. Often epileptic seizures start in the Hippocampus and often represents the first region where Alzheimer's disease symptom take place.

- Vulnerable to damage from anoxia, stress and environmental toxins.
- Often is epileptogenic focus.

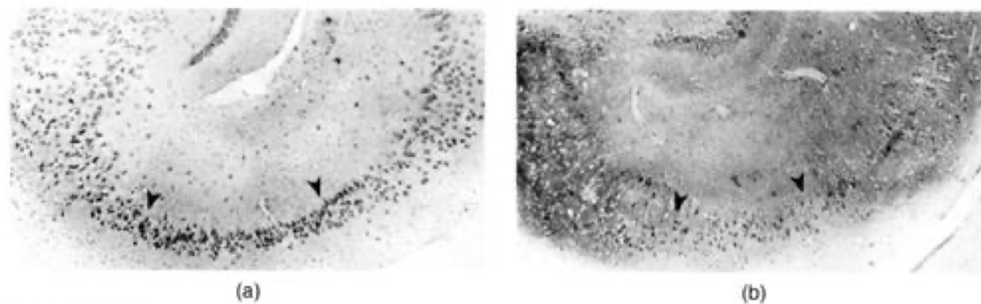


FIGURE 16.6

Photomicrographs showing brain damage caused by stress. (a) Section through the hippocampus of a normal monkey. (b) Section through the hippocampus of a monkey of low social status subjected to stress. Compare the regions between the arrowheads, normally filled with large pyramidal cells.

(From Uno, H., Tarara, R., Else, J. G., Suleman, M. A., and Sapolsky, R. M. *Journal of Neuroscience*, 1989, 9, 1706-1711. Reprinted by permission of the Journal of Neuroscience.)

HM: bilateral removal of Hippocampus

- Unable to lay down new declarative memories.
- Old memories intact.
- No change in intellect.
- No problems with procedural memory.

Amygdala

It is made of several nuclei and it is part of the temporal lobe of the brain rather than the cortex.

It receives neuronal signals from all portions of the limbic cortex. Because of its multiple connection, it is called the “**window**” through which the limbic system sees the place in the world.

It seems to be one of the gateways that allows sensation and perception to be associated with particular emotional connotations.

Amygdala: Function and Connections

- Highly processed sensory input.
- Widespread outputs to cortex, hippocampus, hypothalamus, brainstem.
- Responsible for learning and maintenance of link between a stimulus and its emotional value.
- Stimulation – fear and anxiety, déjà vu.
- Lesion – e.g., Kluver-Bucy syndrome (Lesions have been studied also in primates and humans, which lead to particular symptoms such as the Kluver-Bucy Syndrome, they studied the effects of mescaline on the brain, resulting in lesions of the amygdala).

Effects of Bilateral Removal of the Amygdala – Kluver-Bucy Syndrome

- Placid, flat affect.
- Fearless.
- Inappropriate social and sexual behaviour.
- Hyperoral and overly curious.

Amygdala: learning and memory of emotional significance of stimuli.

Overall Function of the Amygdala

It is the behavioral awareness areas that operate at a semiconscious level. The **amygdala** is believed to make the person's behavioral response appropriate for each occasion.

Functional roles

- Hippocampus: learning and declarative memory (memory for facts, events, faces, places, etc.).
- Amygdala: learning and memory of emotional significance stimuli.

Limbic Cortex

It is the least understood part of the brain. It functions as a cerebral association area for control of behavior. (Very few studies of electrical stimulation in the limbic cortex that tell us what it does, it seems to be related to motivational drive, emotions, sensations, coordinating behaviour and motivational drive. But it's still an open chapter as it is very poorly understood.

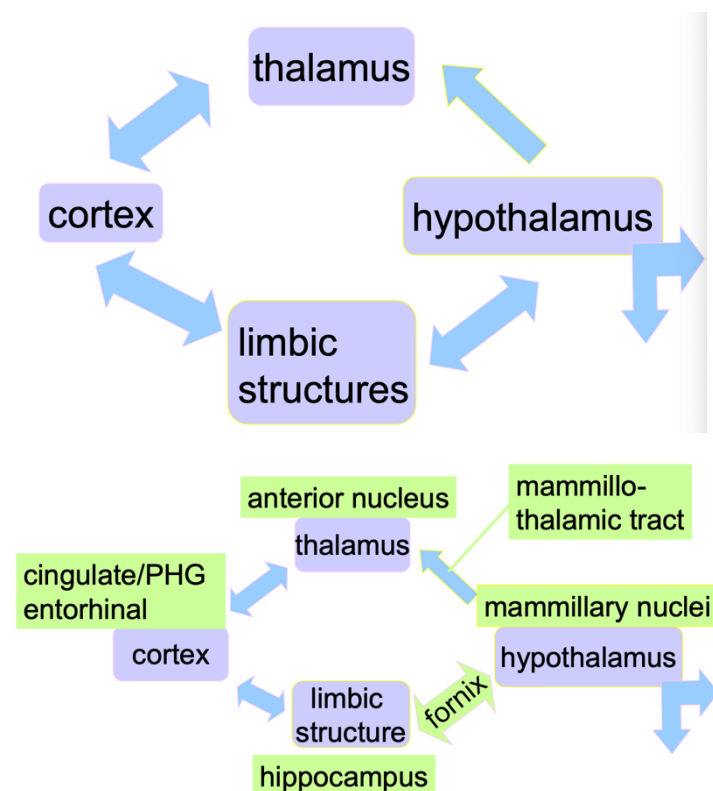
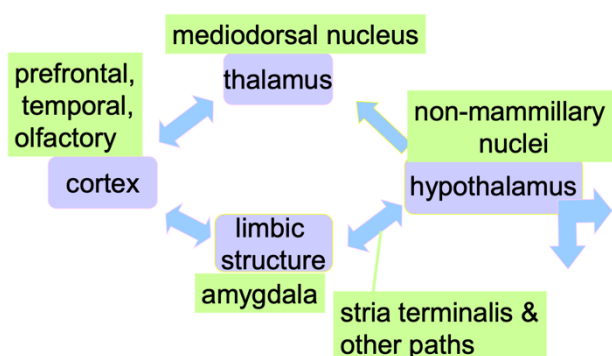
Basic Limbic Circuit: Loop!

It is a series of different systems that work together in this loop, this type of interconnection can be seen in a number of parallel circuits studied in the past as shown below.

Hippocampal Circuit

Papez: french researcher that described the first emotional circuit of the brain, which was the hippocampal circuit, it was considered the whole limbic system in the beginning until the discovery of additional parallel circuits such as the amygdala circuit.

Amygdala Circuit



Papez circuit!!

Sumamry

- Limbic structures and hypothalamus are highly interconnected with each other and with cortex and brainstem.
- Amygdala orchestrates emotional and drive-related behaviour through connections with brainstem, hypothalamus and spinal cord.
- Hippocampus is important for laying down new declarative memories.