Info-Bionics Engineering MSc, Specialization in Bionic Interfaces

FINAL EXAM QUESTIONS

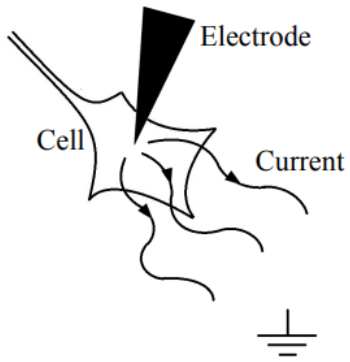
Made by Harascsák Ádám

Neural Interfaces and Prostheses

1. Characteristics of the electrodes used in electrophysiological measurements and stimulation

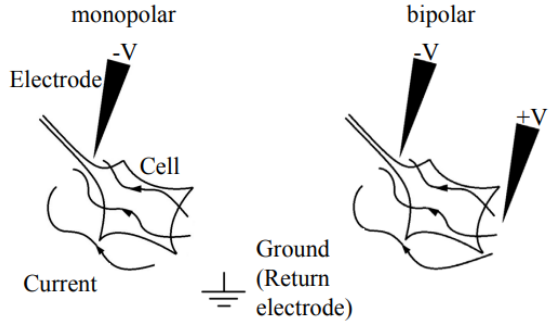
Electrodes are used to apply electricity into cells. This can be done in several ways:

1) INTRACELLULAR stimulation with electric current



In this case, we have an electrode that penetrates the cell thus we have direct control over all ion currents. But this technical implementation is hard because we have to use and put an electrode inside the cell, which is really hard.

2) EXTRACELLULAR stimulation with electric current

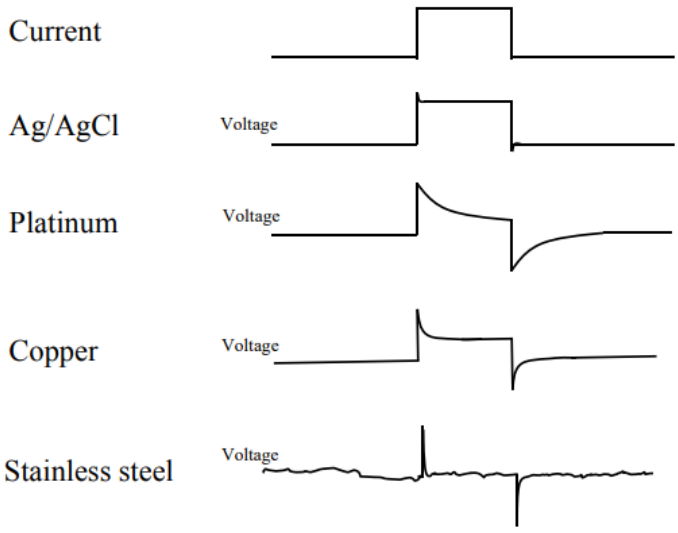


It has 2 ways of stimulation:

a) **Monopolar way:** when we insert the current very locally and we have a very large ground electrode.
b) **Bipolar way:** when we have two electrodes (similar to the monopolar electrode) for electrical stimulation and we put the electrodes in a small area close to each other.

Using extracellular stimulation we have just indirect control over all ionic currents but technical implementation is much more easier.

Since we have different types of electrodes we can characterise them to understand their effect for tissue and to understand how these electrodes record the voltage or deliver current in the tissue.

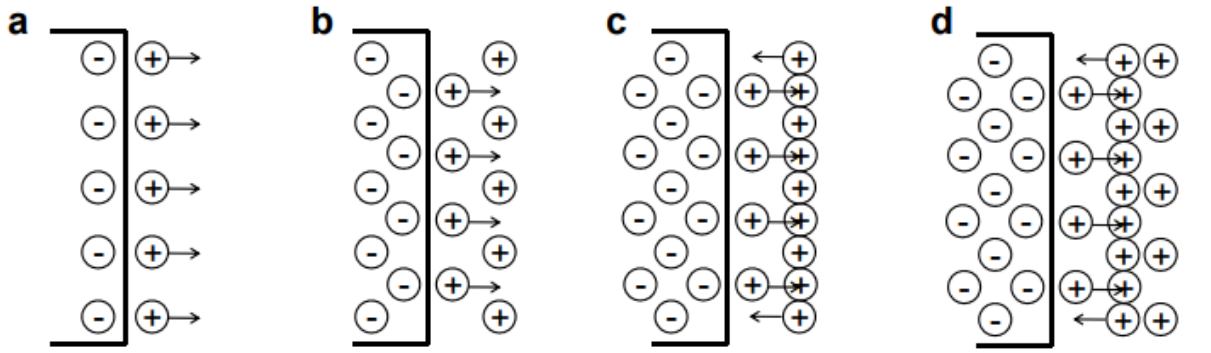


At the top of this figure, we can see the inserted squared shape current and under that, it's how goes through the different types of electrodes.

Metal composition is different.

This is because of the ELECTRICAL DOUBLE LAYER (DL).

Ion movement during metal-liquid contact → polarization → equilibrium



(a) Ionic flow into solution immediately after immersion,
(b) accumulation of ions in solution,
(c) ionic flow into and out of solution at different rates,
(d) equilibrium when rates are equal. (Cooper, 1962)

This is very similar to forming membrane potential, but instead of membrane, it has now metal-liquid demarcation.

Ion movement during metal-liquid contact causes polarization, so some of the positive ions from metal will go into the liquid but that will cause an electric field between the border of metal and liquid,

but some of them come back and there will be an equilibrium and one point the potential difference and cc. difference of ions will be equalised.

This equilibrium causes capacitance at the border, which so-called double layer and this capacitance is responsible for the drop of the voltage of the electrodes.

Polarisable electrodes show this type of electrical DL, and not-polarisable electrodes do not.

Polarizable electrodes: are metals, such as Ag, Au, Pt, etc.

- Amount of current depends on properties of DL (C, R)
- Current charges or discharges of the DL
- Current vs. voltage is non-linear
- DC impedance is big, and acts as capacitance, but can be decreased by increasing the surface.

Non-polarizable electrodes: Ag/Cl

- Current does not influence properties of DL
- Current flows freely on the DL
- Curren vs. voltage is linear
- Acts as resistance on DC

Metals more reactive than hydrogen	Potassium	K
	Sodium	Na
	Calcium	Ca
	Magnesium	Mg
	Aluminium	Al
	Zinc	Zn
	Iron	Fe
	Hydrogen	**H**
Metals less reactive than hydrogen	Copper	Cu
	Silver	Ag
	Platinum	Pt
	Gold	Au

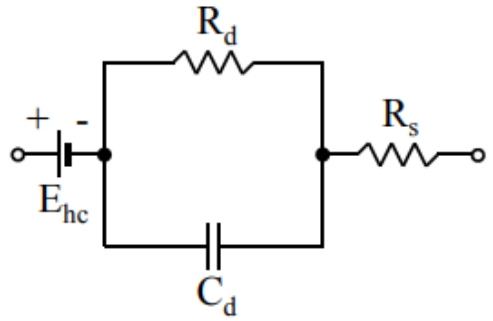
Decreasing chemical reactivity

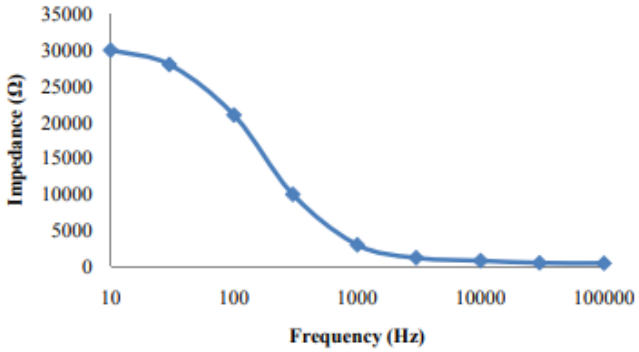
There are different metals, and in the case of metal-liquid-metal contact, they form a **galvanic cell**. Electrode potential is the potential difference relative to the standard hydrogen electrode.

Nobel metals: metals with positive potential.

Nobel metals: metals with positive potential.

Electrode-Electrolyte interface





E_{hc}: half-cell potential

Constant voltage generator

R_s: electrolyte resistance

R_d: interface resistance

$$Z_C = R_s + \frac{R_d \frac{1}{j \cdot \omega \cdot C}}{R_d + \frac{1}{j \cdot \omega \cdot C}}$$

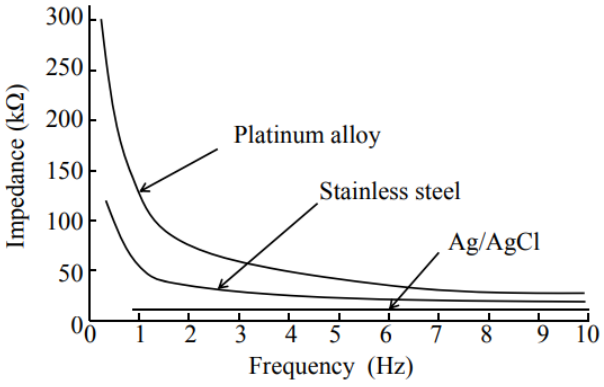
Z_C: electrode impedance

C: capacitance

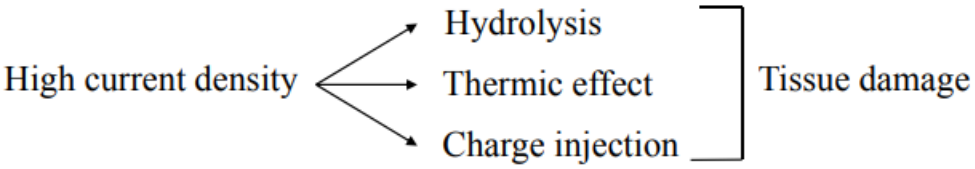
Freq dependence of Impedance graph:

At low freq- very high impedance and high freq – low impedance, those electrodes are very good to record high freq. activity but very bad at slow freq. activity.

Different metals ha different Impedance-freq. plot:



Using electrode and simply applying current causes tissue damage.



In order to avoid the harmful effects of these metal electrodes, there are 2 ways:

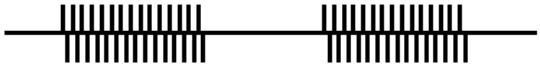
1) Use very short pulses of stimulation: **Monophasic repetitive stimulation**

An easier way to implement

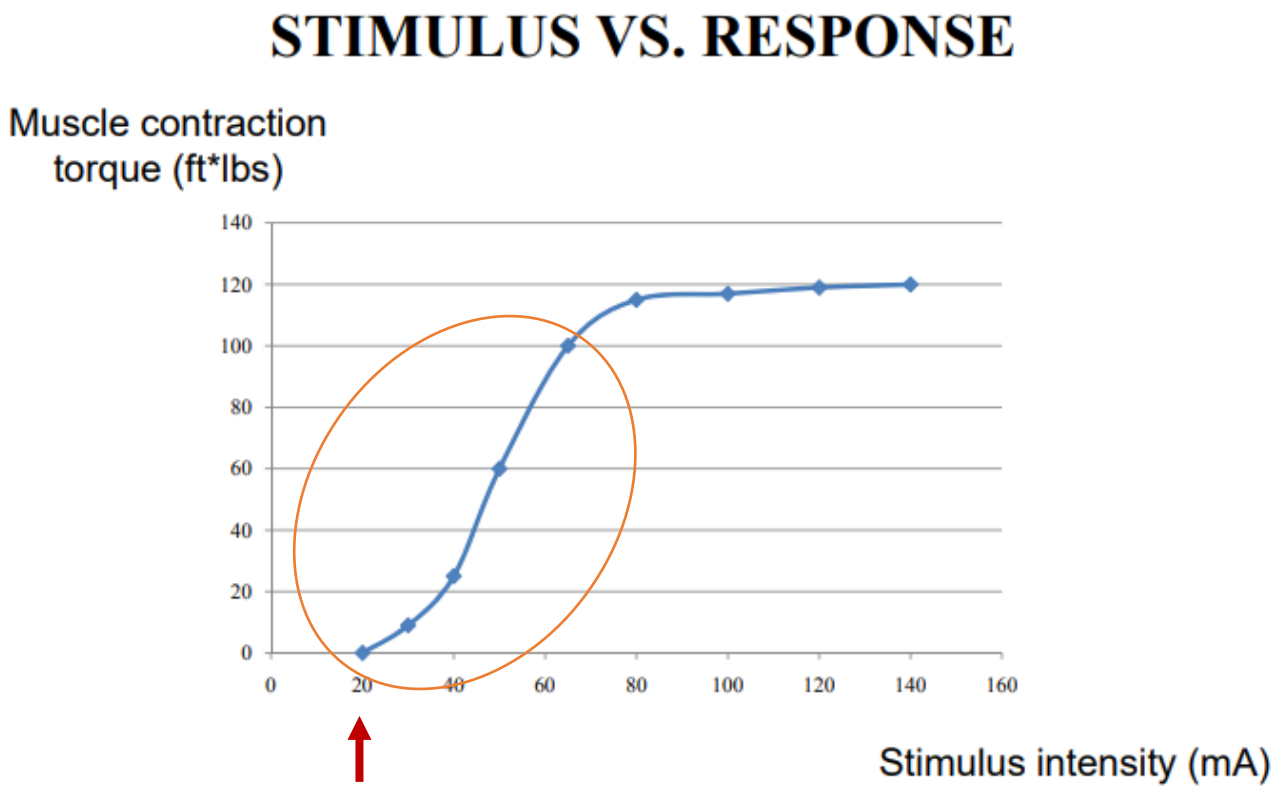
0.1-1 ms charge injections

2) But the best way in practice is to use **Biphasic repetitive stimulation**

First, inject in a very short pulse and then withdraw the current in the same place.



Stimulation has effects which can be measured



Threshold: Nothing happens under this.

Uprising phase: mostly, somewhat linear

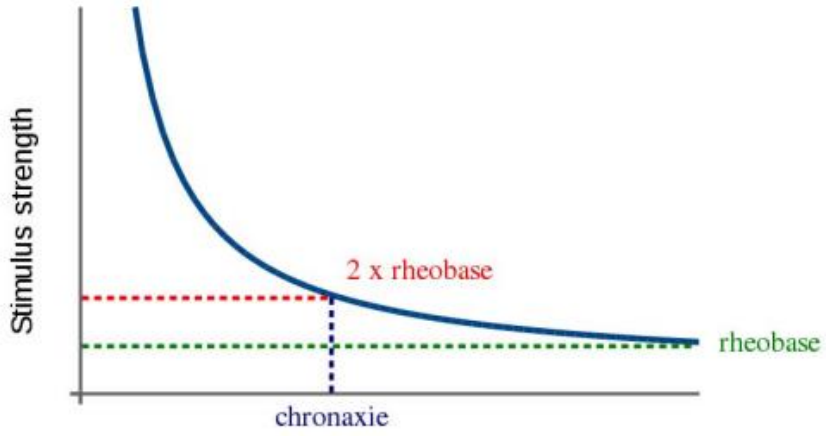
Abow some point, can not elicit bigger muscle responses

Sigmoid curve.

We can quantify some parameters during the stimuli, this is shown by the stimulus strength-duration curve.

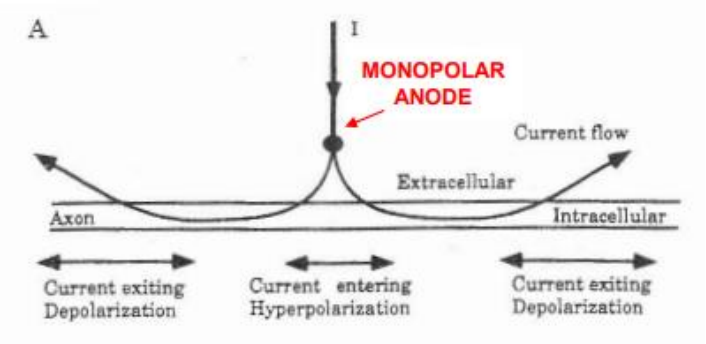
1) Rheobase: (Irh): the minimum current amplitude of infinite duration that results in an action potential.

2) Chronaxy (Chr): the minimum time over which an electric current double the strength of the rheobase needs to be applied, to generate an action potential.



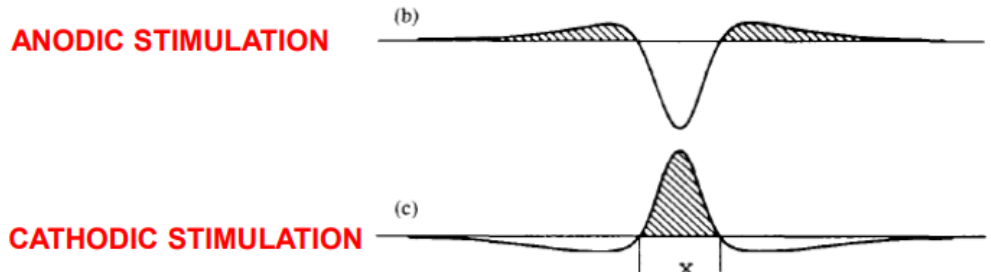
2. Functional electrical stimulation

EXTRACELLULAR STIMULATION



Stimulation with the positive electrode, so with ANODE, then we will have hyperpolarization in the axon under the stimulation (because if we have positive charges extracellularly then we will have more negative charges inside) then we will have an entering current which further exits the axon where that location we will have depolarization.

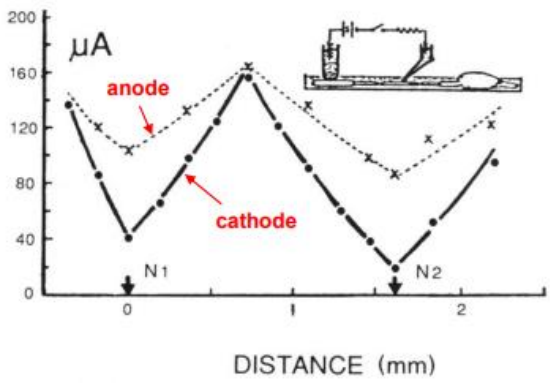
In the case of CATHODE, everything is the opposite, under the negative cathode electrode we will have depolarization and further away we will have hyperpolarization, where the current leaves the axon.



(This figure is not important, just illustrates the things)

The important difference between anodal and cathodal stimulation: The cathodal stimulation threshold current of -290 uA, on the other hand, the anodal stimulation threshold current is 1450 uA. It means if we want to monopolarly and extracellularly activate these devices we would choose CATHODAL stimulation because it has a lower threshold because of the depolarization of the electrode.

Minimum locations denote the Ranvier node positions.



1) **Rheobase: (Irh):** the minimum current amplitude of infinite duration that results in an action potential.
2) **Chronaxy (Chr):** the minimum time over which an electric current double the strength of the rheobase needs to be applied, in order to generate an action potential.

If we examine the Chronaxy time of different neuronal elements, it turns out that the myelinated nerve fiber has the lowest chronaxy time value, so it's easiest to stimulate. In this way, myelinated nerve fiber is a potential target for stimulation by the FES devices. Moreover, it is easiest to stimulate the thickest fibers (those with the largest diameters) and hardest to stimulate the thinnest fibers.

A: The ideal pulse duration for a single stimulus is around 0.1-0.2 ms. Everything above that has the same effect, and everything belongs that has a higher threshold.

C: Further we are from the fiber is higher the threshold current, thus we want to as close as put stimulation to the fiver as possible.

D: And also the higher fiber diameters have the lower threshold value and vice versa.

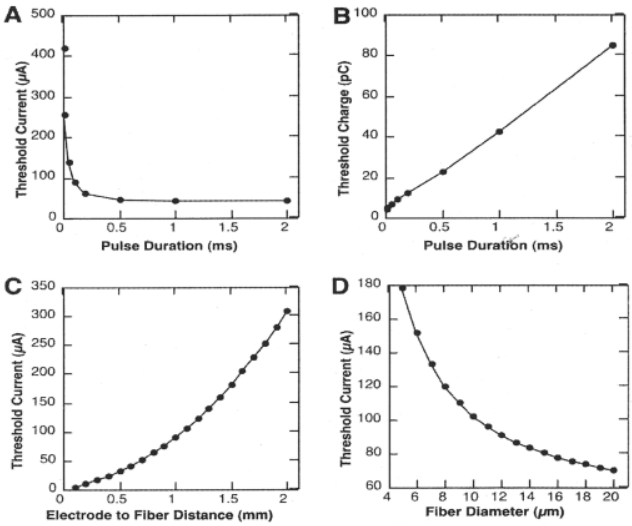
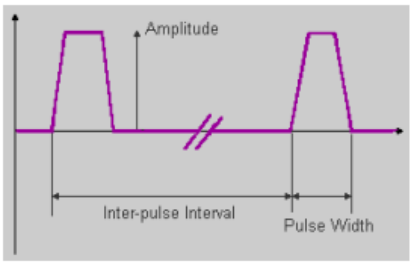
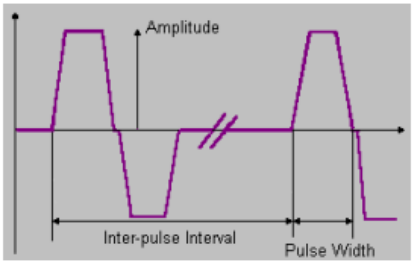


Fig. 6. Excitation properties of myelinated nerve fibers determined with a cable model. **(A)** The strength-duration curve describes the threshold current as a function of the stimulus duration. **(B)** The charge-duration curve describes the threshold charge as a function of the stimulus duration and is obtained by integration of the strength-duration relationship. **(C)** The current-distance curve describes the threshold current as a function of the electrode to nerve fiber distance. **(D)** The current-diameter curve describes the threshold current as a function of the nerve fiber diameter.

Stimulus pulse waveforms



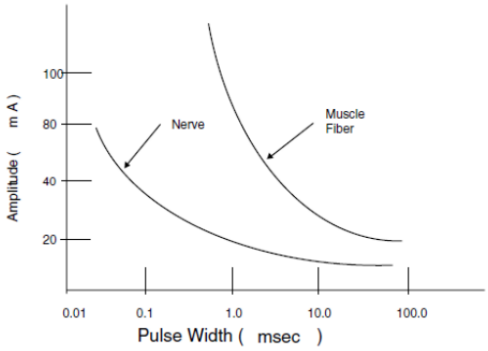
1) Monophasic waveform: it is not ideal because of the tissue reaction



2) Biphasic: charge-balanced pulses, so if we pumped charges into tissue we take them out so we do not damage the tissue, so in most cases, this technique is used.

ELECTRICAL STIMULATION PROCESS

At functional electric stimulation, not single fibers but peripheral nerves or muscles are stimulated! The concept of functional electrical stimulation (FES) is simple, but the realization is challenging!

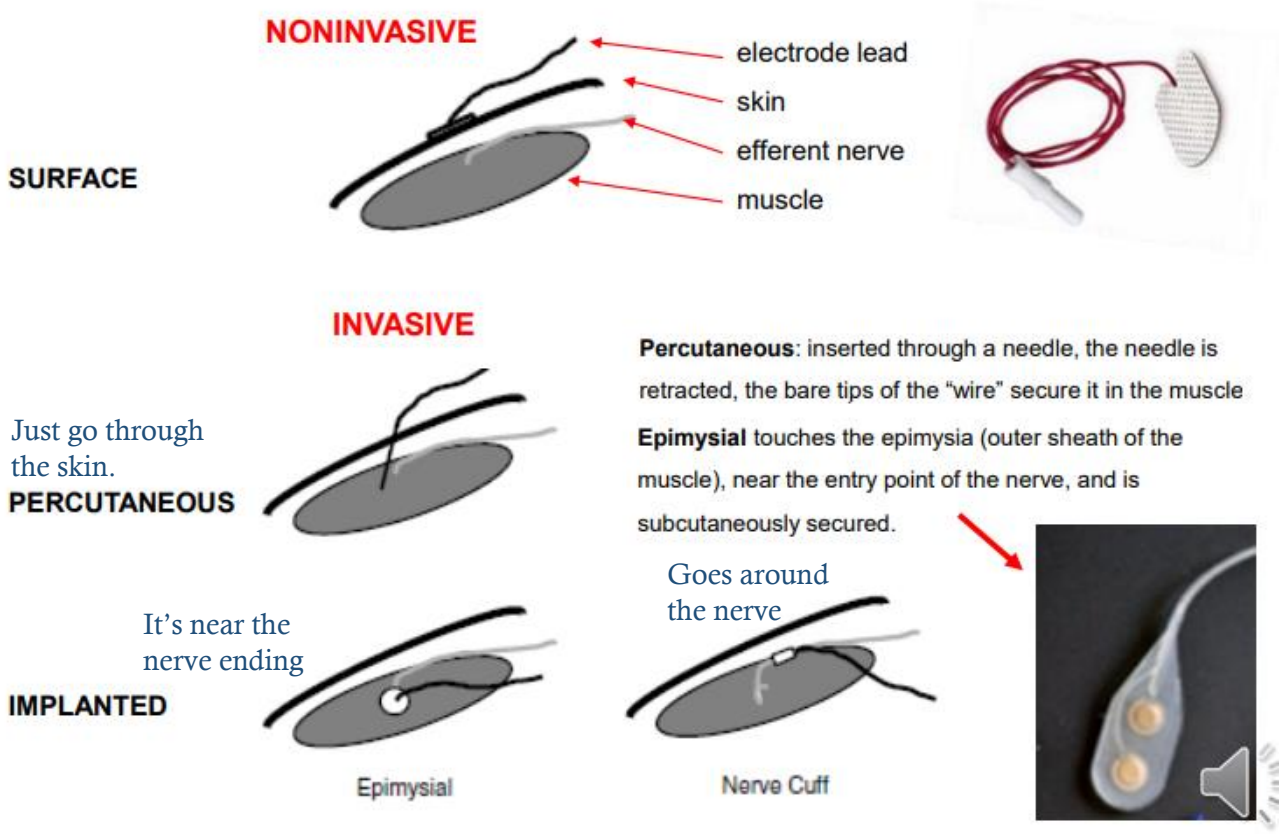


Charge production threshold for nerves and muscles: the threshold is much lower in nerves than in muscles.

The optimal number of stimuli of muscles in sec is 20-30 Hz.

(In higher stimuli muscles get tired quickly)

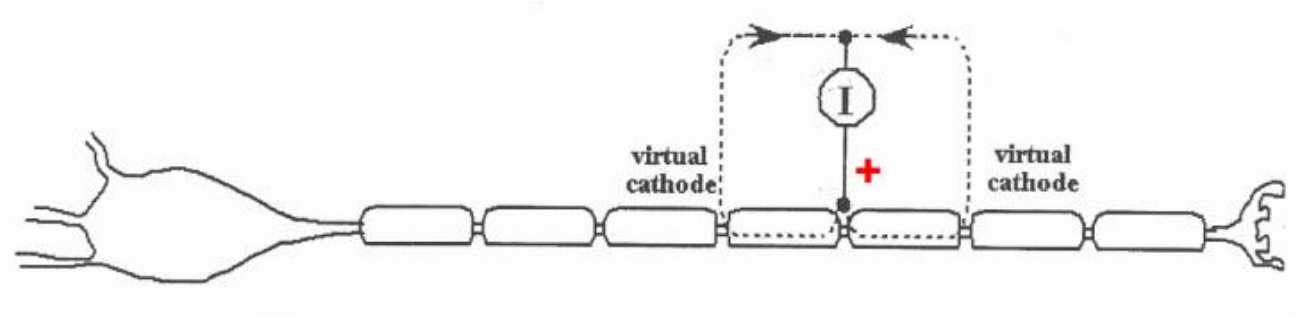
DIFFERENT TYPES OF ELECTRODES:



SURFACE ELECTRODES		IMPLANTED ELECTRODES	
Advantages	Disadvantages	Advantages	Disadvantages
Not permanent (nem állandó)	Hard to place exactly over the correct area	Does not require reapplication	Invasive
Good for short-term use	A hassle to put on all the time	Very precise muscle stimulation	Difficult to replace if required
Reusable	Difficult to simulate deep nerves	Good for long term use	Permanent
Good for nerves which are not deep	Precision is low		
Non-invasive	Can cause skin burn		
	Can stimulate pain feedback nerves		

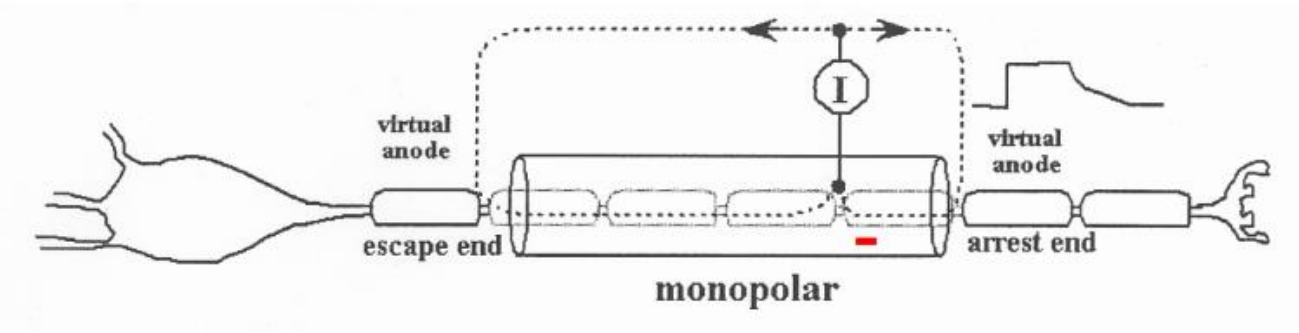
STIMULATION OF MYELINATED NERVE

1) Virtual cathode at the monopolar anode stimulation:



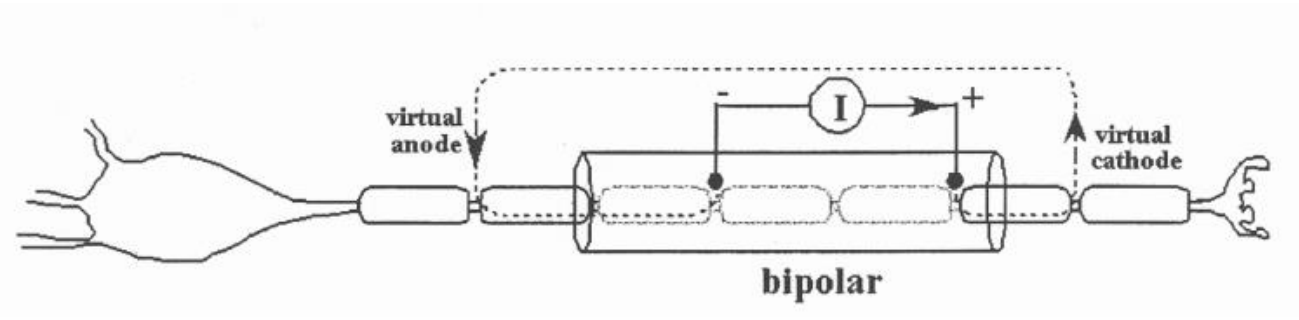
With anodal stimulation, we have hyperpolarization under the stimulation, and there are two sides where the circuit closes, so where current exit the nerve. Those are virtual cathodes because we have depolarization in the nerve. It means that it doesn't stimulate directly under the electrode, but it stimulates a little bit further the virtual cathode points.

2) How to use monopolar anodal stimulation to achieve unidirectional spread of action potential (ap):



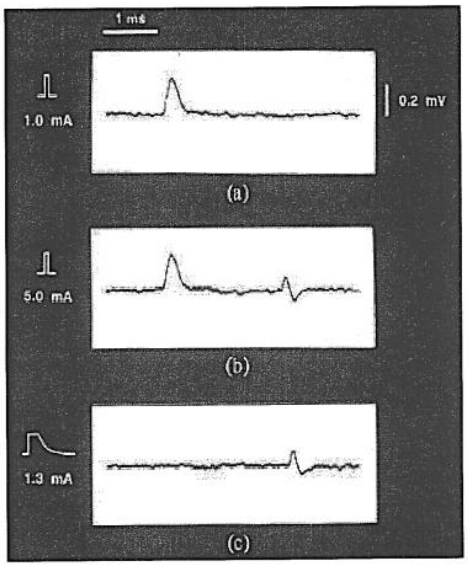
We apply monopolar cathodal stimulation which means there is depolarization right under the electrode and it has a virtual anode that closes the circuit and stops the effect of stimulation. If we do this asymmetrically (due to insulate a given part of the nerve and do not stimulate the middle but stimulate asymmetrically) at one and the anode will stop the stimulation propagation in one direction, but on the other side the anode is small enough to let run through the propagation.

3) It is possible to achieve better unidirectional spread of ap. by bipolar stimulation as well:



We apply a cathode (-) and an anode (+) and in this case, we will have a virtual cathode on one hand, and on the other hand, we will have an anode and which means the virtual cathode will stimulate and virtual anode will block the stimulation.

SELECTIVE STIMULATION OF LARGE AND SMALL DIAMETER NERVE FIBERS:



Small stimulus intensity, short pulse duration →**large nerve fibers**

High stimulus intensity, short pulse duration → **both** small and large nerves

Small intensity, long duration (with slow decreasing) → **small diameter nerves**, because of long duration blocks the propagation of high diameter nerves but it's not long enough to block propagation at small diameter nerve.

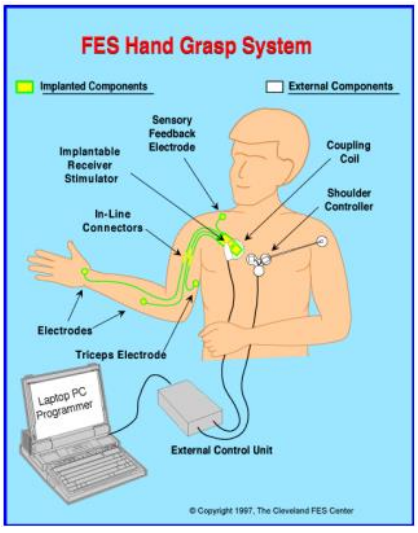
We always put the negative (-) electrode, the cathode in the **motor point**, so above motor endplates (motor endplates is where nerve endings connect to the nerve fiber).

And the other polarity electrode is away from there and in this set-up, we can achieve the lowest threshold stimulation.

FES SYSTEMS

I) *UPPER LIMB FES SYSTEMS*

1. **FREEHAND SYSTEM**



- Quite old, end of 90'

- Implentable, electrodes implented into the arm. There is a feedback electrode and a coupling coil which comunicates with computer and sends pulses to the electrodes.

- Epymisial electrodes (put in the nerve endings).

- Stimulatior implented in the chest.

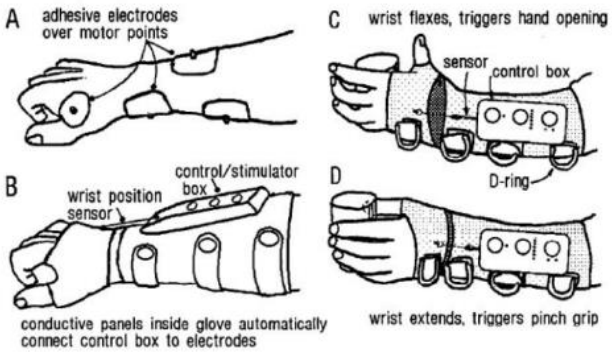
- To controll the freehand system a shoulder position sensor implanted into non-injured shoulder.

2. **BIONIC GLOVE**

Designed to enhance tenodesis grasp in patients that have control of wrist flexion and extension. It controls the wrist movement and stimulate the muscles to achive more precise and forceful to grasp an object

- External device

- Uses position transducer on wrist to detect wrist flection and extension.



- Three adhesive surface electrodes placed over motor points of target muscles.

- One reference (anode) electrode places proximal to the wrist crease (csukló hajlat).

- Old device.

3. NESS H200 System

Principle is to help people who have stills(??) of mevement in their hands but the force or precision is not setisfactory.

- Developed by NESS Ltd., Israel in 2004.

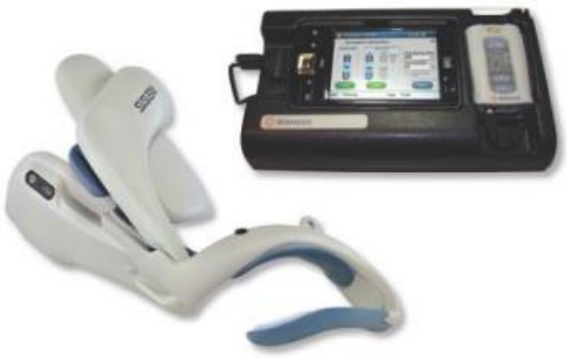
- Non-invasive prosthesis: no implanting operation needed.

- Two parts: orthosis and microprocessor.

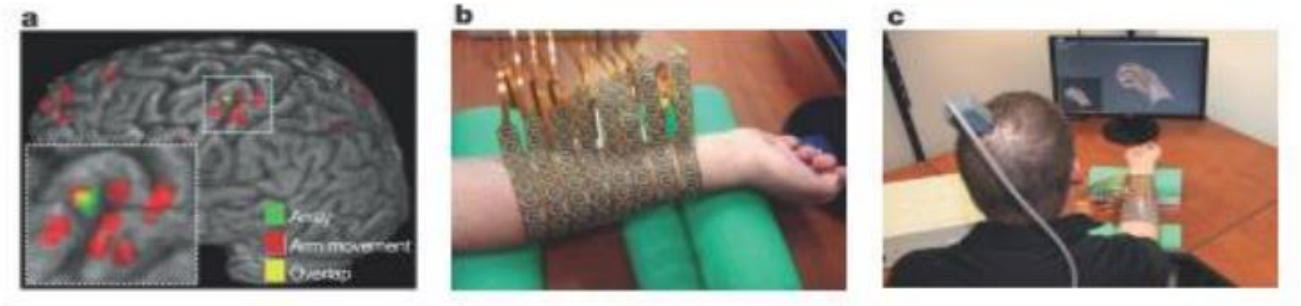
- Orthosis: external stimulating device applied on forearm and wrist.

- Stimulates four different muscles in forearm wrist through the skin.

- Microprocessor: computes stimulation patterns for different tasks.



4. NEURAL BYPASS SYSTEM



- Connected with BCI.

- Microelectrode array is implented into the motorcortex of brain.

- By wireing a computer controls stimulation of electrodes externaly connected to the arm of patient.

- So the patient selcontrols the orthosis, so the stimulatior ehich stimulates the arm by the the patient own brain signals.

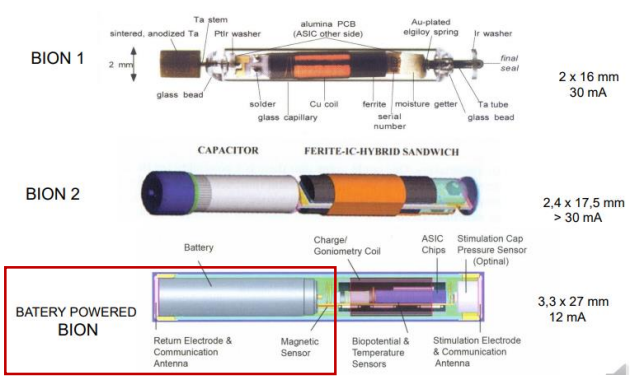
5. BION MICROSTIMULATOR

- Developed by Advanced Bionics Corporation in 2005

- Implantable, battery (aksi) powered microstimulator

- Small enough to be able to be implanted into a muscle or near a nerve

It has batery, most advanced!



- Recharging and communication through a magnetic transmission coil so it can be wierlessly recharged and communicate with computer.

- Several different uses: chronic pain, bladder function restoration, shoulder subluxation treatment:

  ▪ Shoulder subluxation: paralyzed shoulder joint (for example in stroke survivors) lets the humerus (felkarcsont) to leave the cotyle of shoulder which causes pain

  ▪ Stimulation of shoulder joint keeps humerus in the cotyle and reduces pain

  ▪ BION stimulator implanted into shoulder to provide stimulation

  ▪ Control through transmission coil

  ▪ 6 hours/day stimulation

6) EXOSKELETONS FOR REHABILITATION

- External orhoses which help to movement of budyparts

- „REHAB" finger exoskeleton for rehabilitation

- SOFT ROBOTIC GLOVE for combined assistance and at home rehab.

- MCP DRIVER™ FOR FINGER LOSS

II) *UPPER LIMB PROSTHESES AND EXOSKELETONS*

1) THOUGHT-CONTROLLED BIONIC ARM

- Developed at the Rehabilitation Institute of Chicago (RIC) in 1985-2006, Todd Kuiken

- Full arm prosthesis for upper limb amputees

- Prosthesis attached to the shoulder

- Loose ends of arm motor and sensory nerves re-innervated into chest using technique called targeted re-innervating

- Smarter control of prosthetic arm possible with regaining sense of touch: prosthetic arm moved with the movement of chest muscles and arm sensory nerves re-innervated into chest sensory nerves

- In summary: Arm nerves connected to chest muscles, and the activity of chest muscles is detected by EMG electodes and this signal is used to control robotic arm.

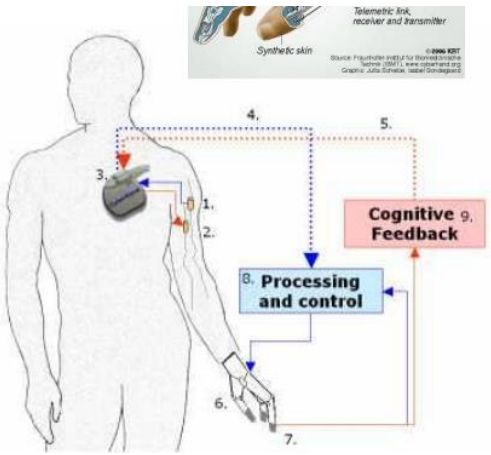
2) „CYBERHAND" PROJECT

- European research project

- It has impented and surface parts to control the prosthatic hand.

- Also use cognitive feedback using the stimulator implented into chest.

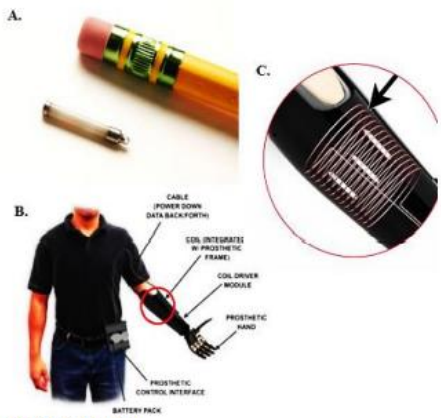
- Still under developement.



3) **„IMES System”** (implantable myoelectric sensor)

- Use several tiny implented electode, which detect the percise EMG information of arm and send information to the controller, which controls the robotic arm.

- Electrodes have very good spetial resolution.



The IMES® System
A Size example of an IMES® electrode.
B The IMES® System
C The magnetic coil built into the prosthetic frame that powers IMES® and receives EMG information

4) **„BEBIONIC” HAND PROSTHESIS**

1 Individual motors in each finger allow you to move the hand and grip in a natural, coordinated manner.

2 14 selectable grip patterns and hand positions let you perform a vast number of everyday activities with ease.

3 Foldaway fingers provide natural looking movement, and flex when you brush past people or bump into objects.

4 Soft finger pads and a wide thumb profile maximise the surface area and enhances your grip.

5 Powerful microprocessors continuously monitor the position of each finger, giving you precise, reliable control over hand movements.

6 Auto grip means no more accidents, as the bebionic automatically senses when a gripped item is slipping and adjusts the grip to secure it.

Developed by Stepper Co. (Leeds)

http://bebionic.com/the_hand

In February 2017 Otto Bock acquired Be Bionic

7 Proportional speed control gives you precision control over delicate tasks.

5) **OPEN BIONICS 3D PRTOSTHESIS**

- Making design and device construction more cost affordable.

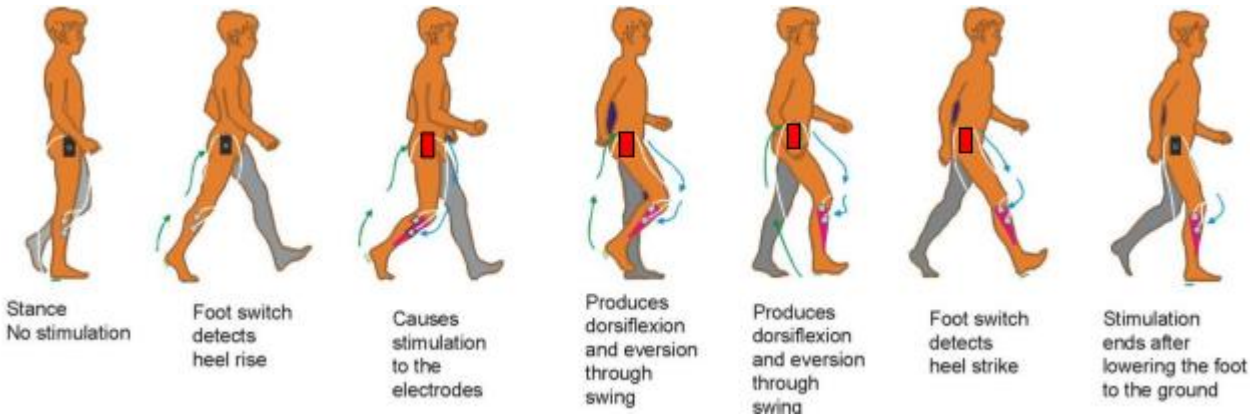
- Reproductable

- Trying to be aneable for as musch as people as possible.

III) *LOWER LIMB FES SYSTEMS*

1) **„Dual Implant Walking System" - STIMUSTEP™**

IMPLANTED DROPPED FOOT STIMULATOR



- It can help for patient who can not lift their foot while walking (just pull their feet on the floor but not able to lift from foor).

- There is a sensor in the shoe

-Patient tries to lift his/her foot, the switch closes the circuit which starts the stimulatior, stimulates the nerves and achives the foot to lifted from floor.

- When patients put their foot back on the floor, the swich is closed, its opens the circuits, so the stimulation stops.

- This is an implentable device, implented the simulatior near the nerve.

- Also there is an external part

- BIONESS company also has a wireless system

2) **PARASTEP I SYSTEM**

Parastep I™ System is a microcomputer controlled functional neuromuscular stimulation (FNS) system that enables independent, unbraced ambulation (i.e., standing and walking) by people with a spinal cord injury.

The Parastep is a non-invasive system and consists of the following components:

- a microcomputer controlled neuromuscular stimulation unit

- a battery activated power pack with recharger

- surface applied skin electrodes

- a control and stability walker with finger activated control switches.

III) *LOWER LIMB PROSTHESES AND EXOSKELETONS*

- BLUETOOTH controlled leg prosthesis (US army)
- RIC'S "Bionic leg" (controlled by patient neural signal)
- Bionic ANKLE–FOOT prosthesis

} PROSTHESIS

- HOCOMA: **Body Weight Supported Treadmill Training**

  Helps people to relearn walking by puting them into a spetial device which puts the patient in a kind of upright position and makes them walk by the trainer device and using the own body weight.

- Other devices using an exoskeleton the hepl peaople learn walking.
- And also posible to combine Exoskeleton and FES

  Relieves pain

} EXOSKELETONS

REQUIREMENTS OF A PRACTICAL FES SYSTEM (electrical orthosis)

1. Should be Simple to Put On and Put Off

This is vital as it will to a large extent determine the amount of use the patient will get out of their system. This will limit the number of connections and leads that are external to the body.

2. Function must be Relevant to the User

Some functions seem to have 'obvious' relevance to anyone. But even a function like standing may be of very little use to paraplegic in adapted accommodation.

3. System must Consistently Provide the Desired Function

The electrical orthosis must provide the desired function under a range of working conditions both external, eg. location, and internal, eg. electrode positioning.

4. The System must include the User

The condition of the user's muscles, bones, ligaments and cardiovascular performance are of vital importance in ensuring that the required function can be attained safely and repeatably.

5. User must be Aware of the Limitations of the System

It must be ensured that the user has realistic expectations. With open-loop systems the user should understand the problems that may occur, eg. with fatigue, and realize how these will affect the performance of the system.

6. User must Understand Commitment Required to Maximize the Benefits

Generally a long term commitment to a training program (>3 months for "sit to stand") is required.

7. System should Ideally be Fail Safe

This is not at present always possible, eg. how does one make an electrical stimulation only standing system fail safe! With open-loop systems the user should possess the strength/control to cope in the event of a systems failure. The degree to which failure is dangerous depends on the system - but the possibility of failure needs to be carefully considered in programming the stimulator.

BRINDLEY BLADDER CONTROL SYSTEM

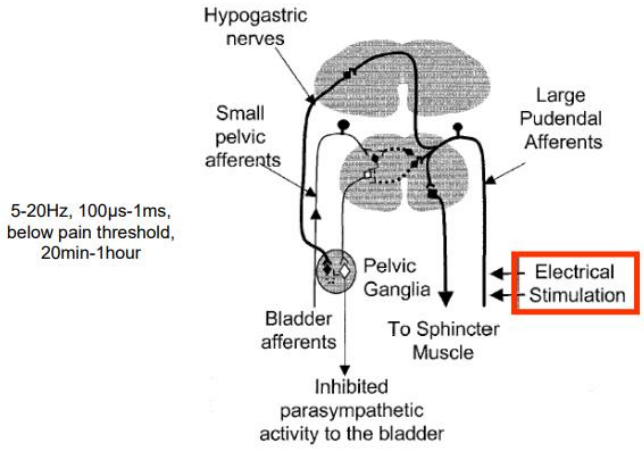
Electrode can be implented to stimulate the corresponding nerves to controll the bladder finction.

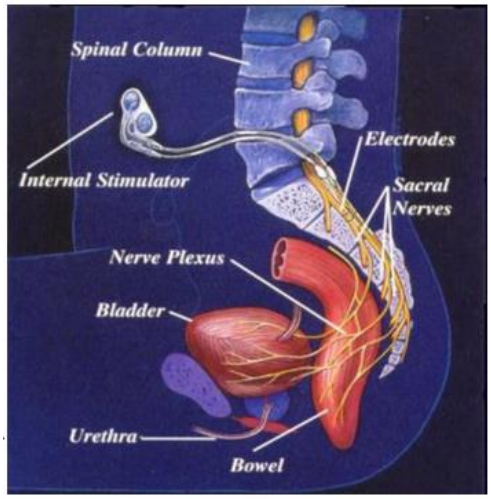
An internal stimulator and an external controller is needed to controll urination.

Internal electrode is placed into the sacral foramina S3. Spetial hooks can help to electrodes do not come out.

Initial costs is higher but the cumulative cost is lower then traditional ways.

Spinal reflex pathways controlling the lower urinary tract. Electrical stimulation of large pudendal afferents inhibits parasympathetic activity to the bladder. Such stimulation can be achieved by implanted electrodes (sacral afferent stimulation) or by transcutaneous electrical stimulation (anal and vaginal plug electrodes, dorsal penile or clitorial electrodes).





3. Stereotaxic technique and neuronavigation. Their application areas

STEREOTACTIC TECHNIQUE

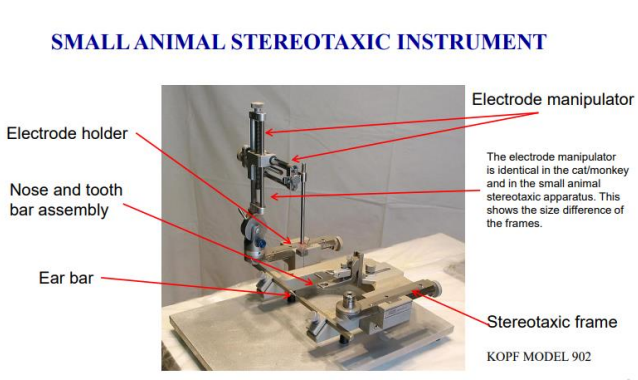
Stereotactic surgery or stereotaxy is a minimally invasive form of surgical intervention which makes use of a three-dimensional coordinate system to locate small targets inside the body and to perform on them some action (such as ablation, biopsy, lesion, injection, stimulation, implantation, radiosurgery, etc).

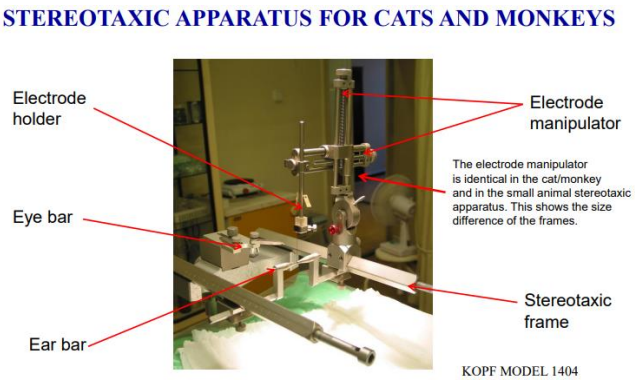
A method was needed to exactly localize these deep-seated nuclei. First device was developed by Horley and Clarke.

Definitions:

Stereotaxic apparatus consists of a metal frame that serves for rigid fixation of the head of the animal in reference to the coordinate system. In rodents the head is fixed by two ear bars inserted into the external auditory meati and the tooth bar over which the front teeth are placed. Reference points are also on the skull the bregma and lambda sutures. In cats two ear bars and two eye bars placed on the inferior orbital ridges are used. The frame also serves as the base for the manipulation of the positioners or electrode holders in the three dimensional coordinate system.

Stereotaxic atlas contains cell and fiber stained brain sections as well as schematic figures based on these sections. Sections are made in all three dimensions: front -rear direction, medial - lateral direction, dorsal - ventral direction.





Reference points in the case of rats: **Bregma and Lambda**, Bregma and Lambda are intersections of bone plates on the dorsal skull surface.

The Brain sizes approximately are the same in the case of all bigger and smaller rats.

Stereotaxic atlas (in the case of rats)

at the bottom, there are reference coordinates (e.g.: how much behind or in front of Bragma…)

than page of atlas, (right or left from the midline, and then how deep in the tissue)

Biphase stimulation and small tip size can achieve better results (small tip electrode: more current flux at the tip → More total neurons recruited and ect…)

PRACTICAL APPLICATION - I. ANIMALS

0) **Chronic electrode implementation in** rat

Chronic electrode implantation means that the animal recovers from the operation with the implanted electrodes fixed to its skull. After recovery, multiple recording or stimulation sessions can be performed with this animal.

- The operation is carried out with surgical anesthesia with sterilized instruments.
- Ear bars are attached and the nose is fixed by the nose bar and tooth bar.
- Then we open the skin and measure the coordinates to drill holes for the electrodes.
- And then electrodes can be inserted into the brain, attached to the electrode holder and The electrodes are fixed to the skull by light curing dental adhesive.
- Wound is closed, a connector is attached to the head → We can read the electrical signals from the brain.
- Couple of days after the implantation the rat is well and ready for the behavioral experiments.

The chronically implanted electrodes are usually thin enamel insulated tissue friendly stainless steel wires. Twisted wire electrodes are easy to fabricate. They are used for deep brain recording or stimulation, they cause relatively little harm to brain tissue and provide stable recordings for long time. The electrodes are fixed to the skull by dental filling and acrylic materials. For recording of brain electrical activity stainless screws are fixed into the skull as reference and ground electrodes. The electrodes are connected to miniature multicontact socket to which the multilead cable can be connected for the time of the experiments. Chronically implanted rat can be used in behavioral experiments for months.

1) **FEEDING AND ANGER REACTION EVOKED BY HYPOTHALAMIC STIMULATION**

- Walter Rudolf Hess: research for hypothalamic stimulation

- Different hypothalamic areas are stimulated electrically → those areas reactivated → different behavior reactions can be evoked (eating, anger …)

- Similar to this, sleep induced by low frequency stimulation of the thalamus

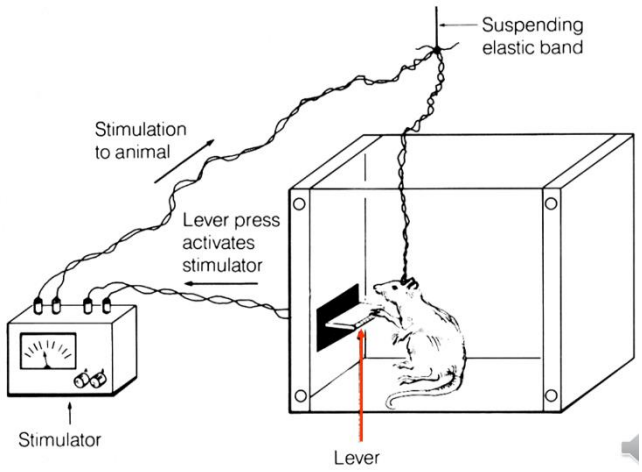
2) **SELF-STIMULATION IN THE RAT**

First, let implant electrodes into the hypothalamic of the rat.

Wires are connected to a stimulator, which is controlled by a lever inside the rat cage (controlled by the rat).

The stimulation produces a very pleasant (**reward**) feeling for the animal (Even if the animal is hungry the animal won't eat due to the stimulation). And even food shock can not cause to stop the stimulation.

Self-s stimulation is proportional to the stimulus intensity, but there is a threshold which above the feeling is not pleasant.

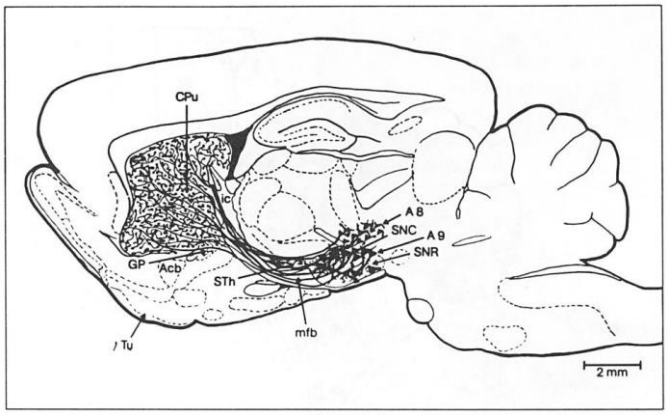


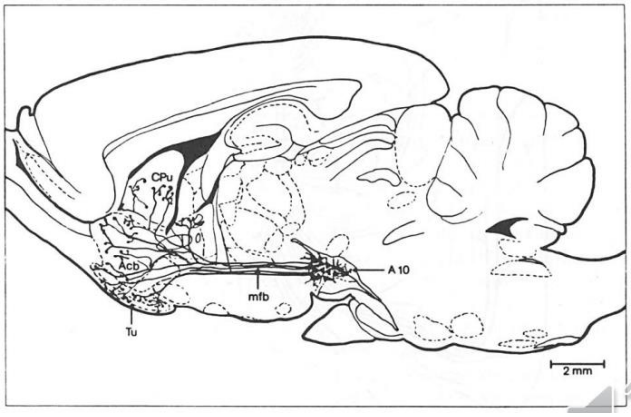
Why it has such a strong effect?

There are 2 dopaminergic pathways:

1. **Motion pathway:** From Substantial Nagra and going to Staetum, the internal capsula and Globus pallidus, control motion.

2. **<u>Mesolimbic pathway:</u>** medial forebrain bundle (MFB). The MFB is a part of the reward system, involved in the integration of reward and pleasure. This pathway is controlled by self stimulation.





1. 2.

PRACTICAL APPLICATION - II. HUMANS

Neuronavigation: Minimal invasive neurosurgery is becoming more and more standard in neurosurgical procedures. Neuronavigation is important technique in this.

- **Sterotactic neurosurgery** represent the „**frame based**" neuronavigation.
- The other method is the **„frameless"** neuronavigation.

Both methods are based on brain imaging like MR, CT and PET!!!

STEREOTAXIC TECHNIQUE IN HUMAN

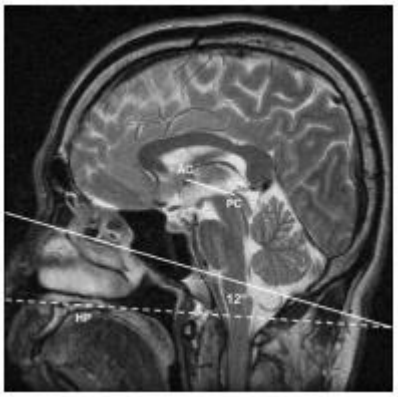
Modern neurosurgery dates back to the period of Harvey Cushing (1869-1939). Stereotaxic method was rarely used since the Horsley -Clarke apparatus could not be adapted for humans because there were no good reference points. Only modern imaging techniques solved this problem.

The up to date human stereotactic method was developed by American (Ernest A. Spiegel and Henry T. Wycis, 1947) and Swedish (Lars Leksell, 1949) neurosurgeons. They used intracerebral reference points, Spiegel and Wycis used traditional Cartesian coordinates while Leksell introduced the polar coordinate system that easier can be calibrated in the operating room.

Nowadays Leksell stereotaxic system is more used. The problem in the case of humans is that a stereotaxic atlas can not be used, because in the case of humans the is a big variability between brain sizes, location and regions, but medical imaging can help.

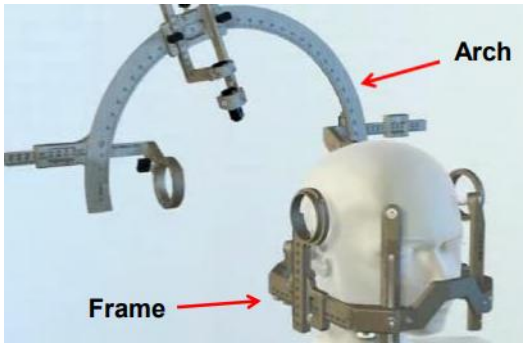
TALAIRACH COORDINATES

Jean Talairach (1911-2007) French neurosurgeon and Gabor Szikla (1928-1983) developed the human brain coordinate system, named after Talairach. It uses intracerebral reference points. They are the horizontal line connecting the anterior and posterior commissures serving a vertical zero. The midsagittal plane through these points serves the vertical coordinate. The rostral-caudal coordinates are measured from the anterior commissure. The limitation of this atlas is that there are large size differences in the human brains.



LEKSELL STEREOTACTIC SYSTEM®

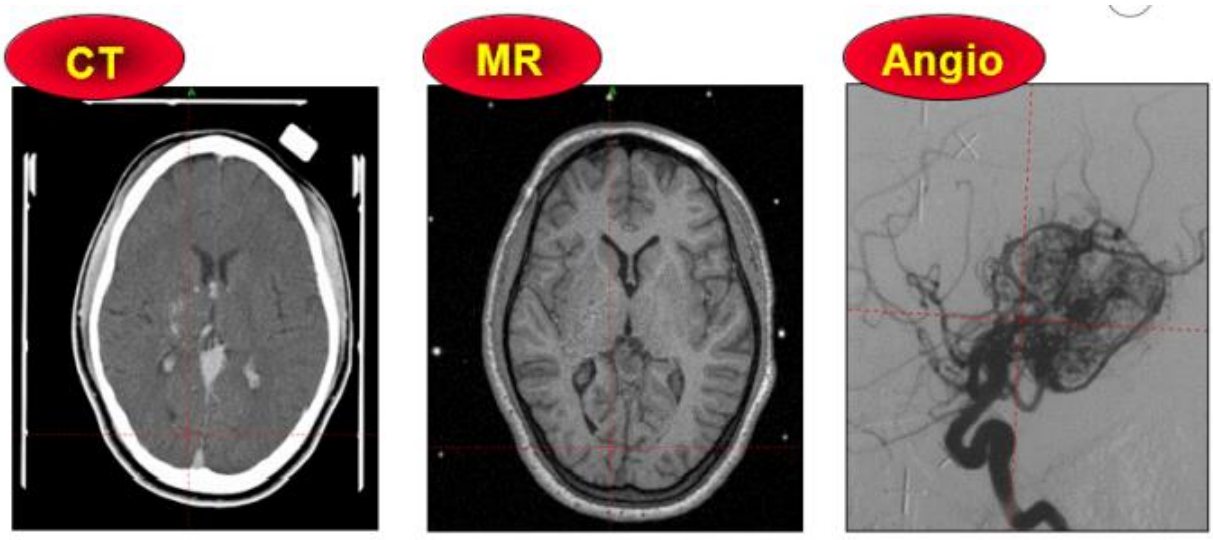
Teher is a head holder, a head frame that is attached to the head during local anesthesia, and there is an arch that can be attached to the frame, and polar coordinates can be shown in the frame and in the arch as well. Also, there is an electrode manipulator which helps to precisely plan to introduce electrodes.



The Frame is fixed to the patient's head with four screws in local anesthesia. **MRI, CT or Angiography can be made while the frame is attached. The indicator box generates positional marks during scanning.**

The Frame serves as the base of the coordinate system. The target point can be determined in relation to the AC- PC line. The positioner attached to the Arch can reach any structure in the cerebrum.

Leksell SurgiPlan® is an advanced image-based neurosurgical planning software, specifically designed for Leksell Stereotactic System®. Combines the following images:



- CT: white bars (shadows of stereotaxic frame), not a very nice image from the brain but a nice image of the skull.
- MR: reflective dots for reference planning on the MR image, nice image of the brain
- Angiographic images: blood vessels

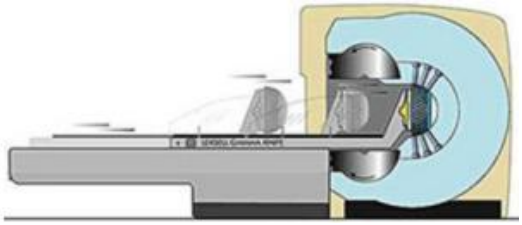
Important to use imaging during the surgery, this software also can help with that. Integrate real-time imaging.

NEUROSURGICAL APPLICATION OF STEREOTACTIC TECHNIQUE

1) **Leksell Gamma Knife ®**

Non-invasive

The principle of gamma surgery is that high intensity gamma radiation kills cancer cells and shrinks tumors. The aim is to focus a series of low intensity gamma radiation becams to one single point in the brain where the tumor or malformation is. This is done by the Gamma knife.



The radiation beams converge with high accuracy on the target. Each individual beam has low intensity and therefore does not affect the tissue through which it passes on its way to the target. The beams converge in an isocenter where the cumulative radiation intensity becomes extremely high. The extreme precision of Leksell Gamma Knife, better than 0.5 mm, makes it possible to administer a high radiation dose to the lesion with minimal risk of damaging healthy tissue.

With very few exceptions, Gamma Knife surgery is given on a single occasion and without general anesthesia. During the procedure the patient can communicate with the Gamma Knife team through a video and audio connection.

2) **ROSA SURGICAL ROBOT**

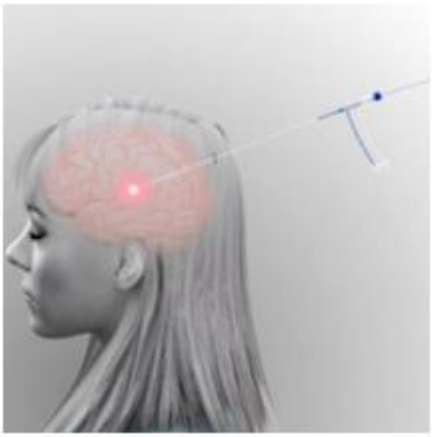
High precision surgical robot for various applications. Can be used for Electrical Stimulation

Uses stereotaxy, multimodal brain imaging and laser scanning for neuronavigation before and during surgery.

Available in Hungary (since 2018 at the National Institute of Clinical Neurosciences Budapest.)

3) **MRI-GUIDED LASER ABLATION TECHNOLOGY** FOR MINIMALLY INVASIVE NEUROSURGERY

- Not use electrical stimulation



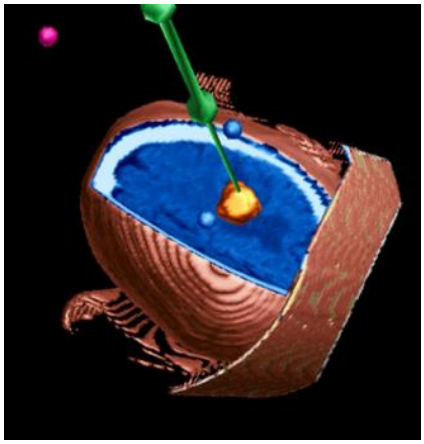
- Use MRI-guided laser ablation tech. to get rid of tumors deep inside the brain.

- A guide tube has to be inserted into the brain and use heating 44°-59°C. So stereotaxically implantable optical fiber for delivery of laser energy, which is enclosed in an internally cooling catheter.

  Different tips of laser ablation fiber: Fully open tip (larger area quickly) or small directional tip (more precisely tiny area)

- And the whole tech. is guided by real-time MRI tech. → precise guiding

4) **FRAMELESS NEURONAVIGATION**



- Don't have to attach the neural navigation frame on the head, but have to attach reflective reference points on the head, which reflect the coming radiation (either ultrasound or radio freq.) from a frameless radiation device.

- Reflections go back to the detectors and the surgeon can see where the device is in the brain

- **Frameless neuronavigation also uses imaging tech. for planning!**

4. Deep brain stimulation (DBS)

DISEASES, WHICH TYPICALLY CAN BE TREATED WITH DBS. (MAYBE NOT NECESSARY)

1) **PARKINSON'S** DISEASE

1817: James Parkinson describes the disease

Four cardinal signs of Parkinson's:

- Tremor (resting state)
- Rigidity
- Bradykinesia: (The condition is characterised by the slowness of voluntary movements, which not only slow down but also become difficult to start and stop. The patient's posture becomes stooped.)
- Instability

Other signs: Problems in cognition, behavior, senses, sleep and mood (loss of smell, which may appear years earlier than the cardinal symptoms.)

Cause: death of dopamine-containing neurons in the substantia nigra projecting to the basal ganglia = nigrostriatal pathway, the motion control dopaminergic pathway. The cause of this cell death is unknown. It's interesting, cell dies just in the substantia nigra, reward behavior is not affected.

When the first motion symptoms appear, 90% of substantia nigra dopaminergic cells are died → High plasticity of this pathway

In Hungary: 200-400 patients / 100.000 pers., appr. 20-30 thousand patients in total

Treatment: Levodopa: giving precursors of dopamine, dopamine agonists: medication which dopamine receptor agonist, so enhance the remaining dopamine functions

During treatment, the effect of medications gets shorter and dyskinesia (motion problems get worse) may develop.

2) **ESSENTIAL TREMOR**

- Rhythmic (4-12 Hz) tremor **during voluntary moves**

- Mostly affected: arms, head, face

- Unknown origin, the cerebellum-brainstem-thalamus-cortex network may play a role.

- No dedicated medication

- Prevalence: 0,3-5,6%

3) **DYSTONIA**

- **Involuntary, sustained** (tartós)**, repetitive and often painful moves with various extents** (single muscle, limb or whole body)

- Alters body posture and moving

- Secondary effects: disturbed sleep, exhaustion, mental stress, difficulties in concentration

- Unknown origin

- No dedicated medication

4) TOURETTE-SYNDROME

- Described by Georges Gilles de la Tourette

- Begins in childhood, hereditary

- **Repetitive, strong motor and vocal tics, sometimes swear-words**

- No dedicated medication, the applied medications have several side effects

DBS SYSTEMS

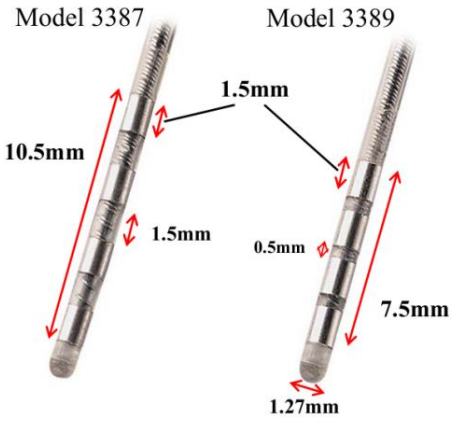
Concept of DBS: „The main concept (of DBS) is that delivery of high frequency electrical current in a very specific area of the brain, alters the faulty circuitry of the brain and minimizes certain symptoms of the disorder."

Important to note that, DBS never heels the patient, it is just a treatment zhat makes symptoms get better, and makes the symptoms less bearable.

DBS systems have 4 components:

- Electrode
- Lead (connects electrodes and simulator)
- Stimulator
- Programming device

DBS electrode and lead



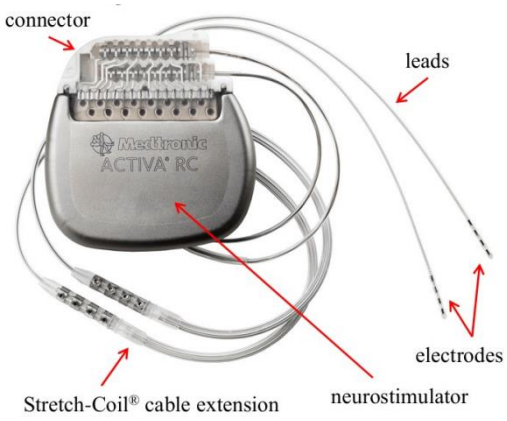
• DBS electrode is implanted into the target brain area for stimulation

• Thin, insulated wire or small ring, stimulation contacts at the tip, usually 4 contacts in a row

• Size and distance between stimulation contacts may vary. Electrode surface (1.5 mm is quite high → low impedance → low current intensity to achieve stimulation

• The lead connects the electrode with the stimulator under the skin

DBS stimulator



• The DBS stimulator is a pacemaker-like, titanium covered device producing the stimuli coming out from the DBS electrode.

• Consists of a battery and microelectronic components

• Implanted under the skin in the chest, usually under the clavicle

•Programmable externally, very flexible device in terms of programming and setting stimulation

- Two different stimulation site configurations, amplitudes and pulse widths are programmable for each electrode. Set by the doctor based on patient reflections.

DBS programming

• Therapist sets range of user actions:

– Basically, only for monitoring stimulation, only programmable by the therapist

– By the therapist's decision, the patient can choose from pre-set stimulation configurations according to the patient's actual state. The therapist's control is necessary in this case too.

DBS SURGERY

1. Preoperative examination

DBS indications

In the **"On" state**: when the medication is ON and it works and the patient has fewer symptoms. (Medication effect is on); severe dyskinesia and other non-motoric symptoms

In the **"Off" state**: when the medication is OFF or the medication is don't work and the patient has several symptoms, (Medication effect is off);

- Severe tremor, rigidity, akinesia/bradykinesia or
- Random on/off fluctuations or
- Medication-resistant tremor

2. DBS surgery in two steps:

- Implanting stimulation electrodes using stereotaxic technique
- Implanting stimulator under chest skin and connecting it to the electrodes

3. The operation itself

• Beginning of surgery: fixing stereotaxic frame to head
• MRI imaging and determining stereotaxic coordinates with the planning software
• Attaching electrode to manipulator
• Drilling holes in the skull
• Precisely determining target area by microelectrode recording and stimulation
• Stereotaxic electrode implantation
• Test stimulation for fine tuning stimulation parameters: best effect without side effects
• After confirming its position, the electrode fixed to the skull
• MRI validation of electrode placement and lack of bleeding

• Implanting stimulator in the chest in general anesthesia
• Connecting stimulator to electrodes with lead under the skin

2.1. **Electrophysiological identification** of the target area by using an acute electrode during the surgery before implanting the final chronic electrode because there is a typical firing of the subthalamic nucleus (STN) in Parkinson's:

- Asymmetric, high frequency, burst firing synchronized to tremor; easily can be identify
- Responds to contralateral limb movement

Apply the first Microstimulation: setting therapy and avoiding side effects

After finding the correct position and stimulation parameters, the final electrode is implanted

DBS TARGET AREAS – BASAL GANGLIA

Target areas are all in the Basal ganglia which is a tiny are deep in the brain controlling voluntary and involuntary movements.

There are also excitatory connections and inhibitory connections as well, and each of tiny ganglia in the basal ganglia is a target area for different diseases treatments using DBS

Parkinson's disease: main target area is the **subthalamic nucleus (STN)**
Stimulation parameters: 130-185 Hz frequency, 60-150 μs pulse width, 1-2,5 V intensity

Dystonia and torticollis (wry neck): globus pallidus internus (GPi) Stimulation parameters: 200-400 μs pulse width, 2,2-7 V intensity

Essential tremor: electrode implanted into the **ventrolateral nucleus of the thalamus (Vim)**

Physiology of DBS

• Partial knowledge: clinical application ahead of research

• Intensive research for understanding DBS

• Difficulty: no experiments on humans. Results from animal experiments can only be used with restrictions.

• Most information comes from modeling studies.

• DBS effect depends on several factors:

– Geometric configuration of stimulating electrodes *

– Electric properties of brain tissue **

• Brain tissue reaction after electrode implantation electrode impedance increases

• High frequency stimulation applied in DBS counteracts impedance increase due to tissue reaction to a certain extent.

THE DBS PARADOXON

Paradoxon: therapeutic stimulation has the same effect as lesioning the target area

4 different hypotheses:

1. **Depolarization block**: strong depolarization evoked by DBS prevents repolarization and thus action potential generation.

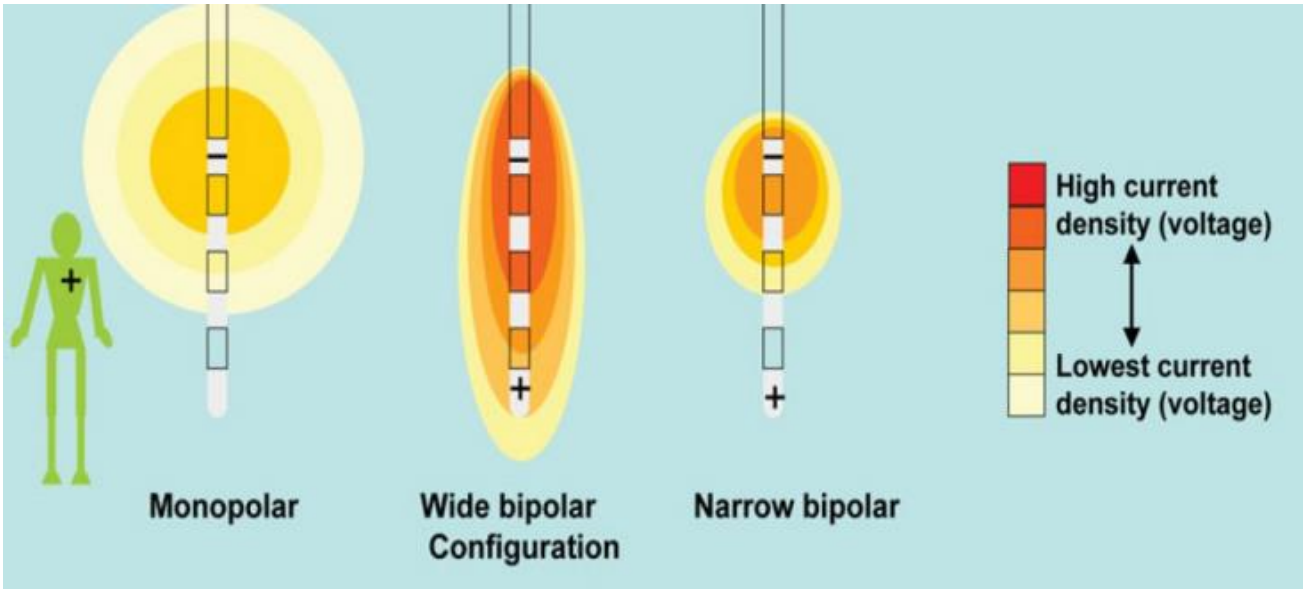
2. **Inhibition of local neuronal elements:** DBS selectively stimulates inhibitory afferent fibers.

3. **Synaptic depression**: DBS inhibits synaptic transmission in the target area by vesicular depletion of neurotransmitters

4. **Modulation of pathological activity**: high frequency DBS disrupts abnormal neural rhythm in the target area

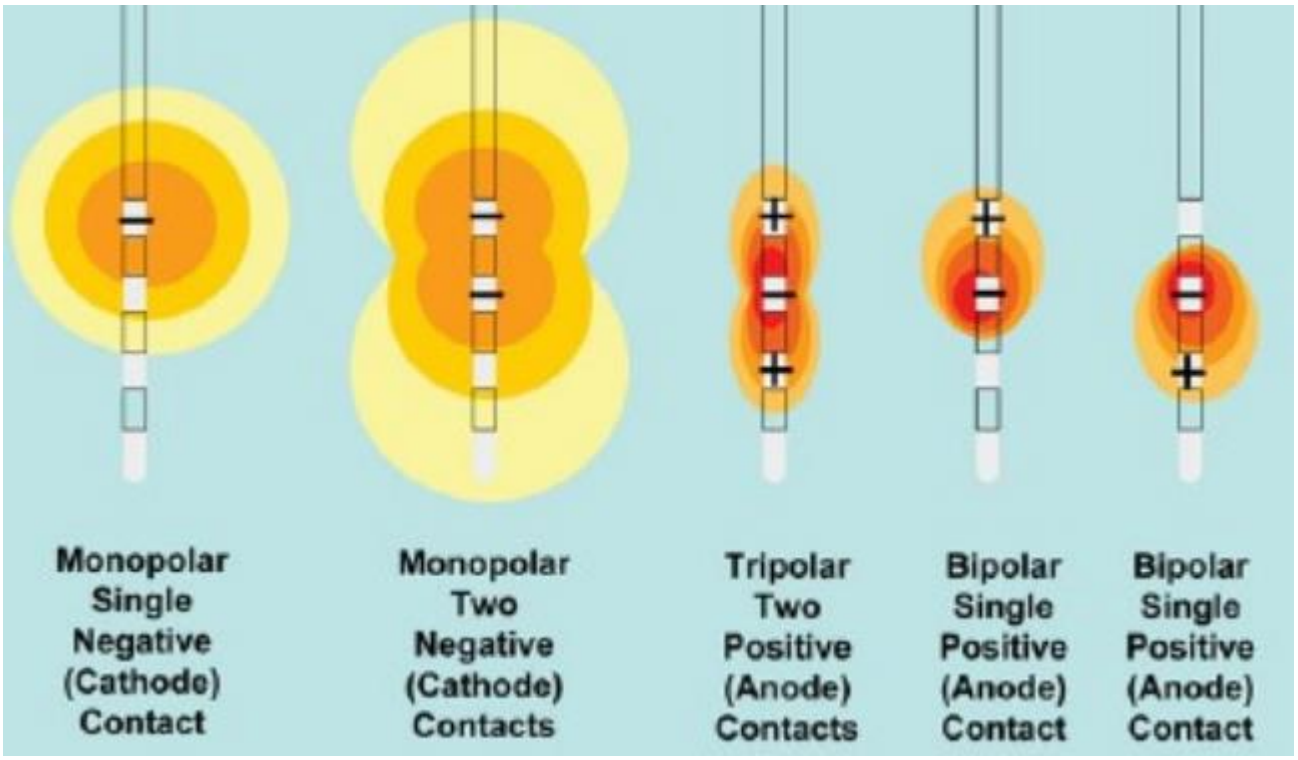
+1 : **Antidromic blockade of slow axons:** DBS frequency is set to block signals in 1 μm or smaller diameter axons. Thus, delays longer than 2-3 ms are blocked in the cortex-basal ganglia-cortex loop, ameliorating symptoms.

Geometric configuration of stimulating electrodes *



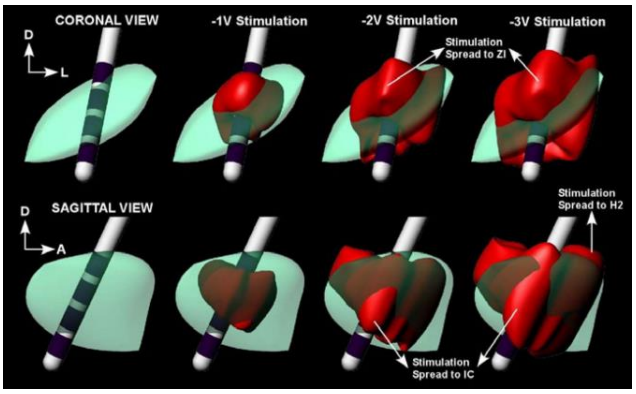
Monopolar stimulation: large area current distribution, low current density

Bipolar stimulation: current distribution confined in a small area, high current density setting the proper extent of the stimulated area by configuring stimulation electrode polarity.



Setting the proper extent of the stimulated area by configuring stimulation electrode polarity.

Brain tissue electric properties **



Different neural elements have different electric properties

• Stimulation threshold characterised by **chronaxy**

- Myelinated axons: 30-200 μs (lowest)
- Dendrites: 1-10 ms

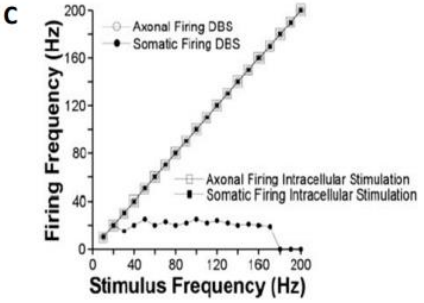
• Brain tissue: **inhomogeneous conductor**

• Electric stimulation: complex three-dimensional extracellular potential field

• Effect on brain tissue characterized by the second spatial derivative.

• Stimulation affects both local and distally (távoli) projecting elements, direction dependent (anisotropy)

• Finite element models describe the electric field of stimulation and the extent of stimulated tissue



We can also modelling DBS on neuronal level

- Axon is able to follow DBS stimulation but the soma is not.
- (Somatic firing is blocked)

FURTHER DBS APPLICATIONS

• Chronic pain: ventral caudal thalamus, periaqueductal/periventricular gray matter, subthreshold motor cortex stimulation

• Epilepsy: anterior and centromedial thalamus, STN

• Depression: subcallosal gyrus cinguli, Brodmann area 25

• Obsessive-compulsive disorder (OCD): nucleus accumbens, Capsula interna anterior

Psychological area can be treated by DBS but it is a hard difficult area, (high risk, highly complicated)

Risks of DBS surgery

• General risks of surgery

• Brain bleeding, infection

• Device failure

• Suboptimal electrode placement causing problems: dysarthria, hypophonia, dysphagia, paraesthesia, eyelid-opening apraxia

• Most often: speech disorder

5. Transcranial magnetic and electric stimulation

1965 - First to stimulate the human nerves magnetically using harmonic magnetic fields.
1985 - Non-invasive, painless, cortical stimulation with magnetic fields.

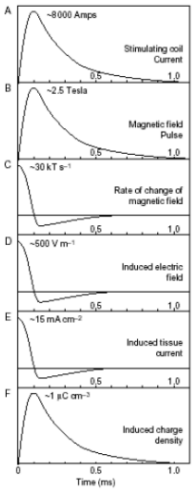
TRANSCRANIAL MAGNETIC STIMULATION (TMS)

Transcranial magnetic stimulation (TMS): is a non-invasive method to cause depolarization in the neurons of the brain. TMS uses electromagnetic induction to induce weak electric currents using a rapidly changing magnetic field; this can cause activity in specific or general parts of the brain with minimal discomfort, allowing the functioning and interconnections of the brain to be studied.

A variant of TMS, **repetitive transcranial magnetic stimulation (rTMS)** has been tested as a treatment tool for various neurological psychiatric disorders including migraines, strokes, Parkinson's disease, dystonia, tinnitus, depression and auditory hallucinations.

Principles: we have a Thyristor trigger circuit that is able to generate high intensity, short duration magnetic pulses in the coil. Magnetic field generated by rapidly changing current in the coil (purple lines) and blue lines indicate the evoked electric field in the brain that is evoked by the magnetic field of the coil.

In this way, a non-attenuated, noninvasive stimulation of the brain can be achieved.



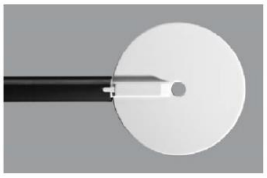
Timing of magnetic stimulation (all necessary to know :c)

A: Stimulating coil current	~	8000 A (very high)
B: Magnetic field pulse	~	2.5 T
C: Rate of change of magnetic field	~	30 kT/s (extremely high)
D: Induced electric field	~	500 V/m
E: Induced tissue current	~	15 mA/cm^2
F: Induced charge density	~	1 uC/cm^3

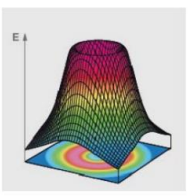
The importance of magnetic stimulation is that it's achieved by rapidly changing current in the coil, it generates the magnetic field which generates the secondary electric field in the brain.

Stimulation patterns:

1) - **Round coil:** quietly wild spread charge is generated



Round coil



2) - **Figure-8/Butterfly coil**: very nicely focused localised in the brain

- Practically most of the application use this type of coil

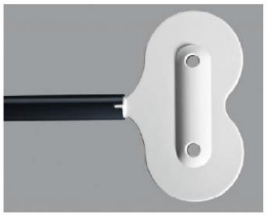
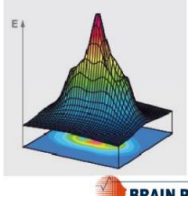


Figure-8 (butterfly) coil



Also, there are different coil types:

- Multilayer cylinder coil
- Flat single layer coil
- Flat multilayer coil

Depth profile: The actual stimulation depth is around 5 cm, so it can not go deeper than 3-5 cm, which means that Deep brain stimulation can not be achieved by magnetic stimulation, but Cortical stimulation can be achieved (very useful for research and treatment field) (The evoked electric field is not strong enough to evoke electrical changes in the deeper brain parts.)

Small and large coils have a similar effect, so not the coil size that affects the stimulation. The coil shape is more important.

APPLICATION OF TMS

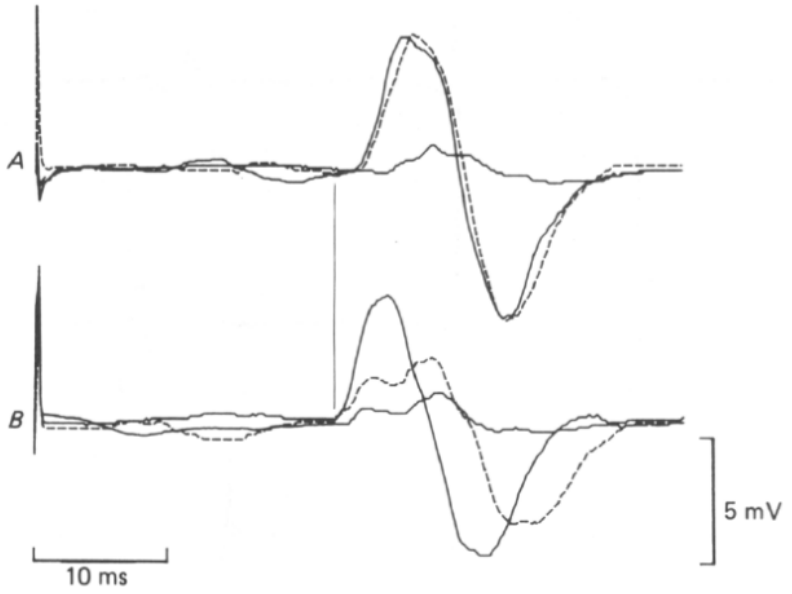
1) Motor potential evoked by stimulating motor cortex: Pheriferic, so limb movements can be evoked by stimulation both by magnetic and electric stimulation.

magnetic stimulation

To stimulate the brain

electric stimulation

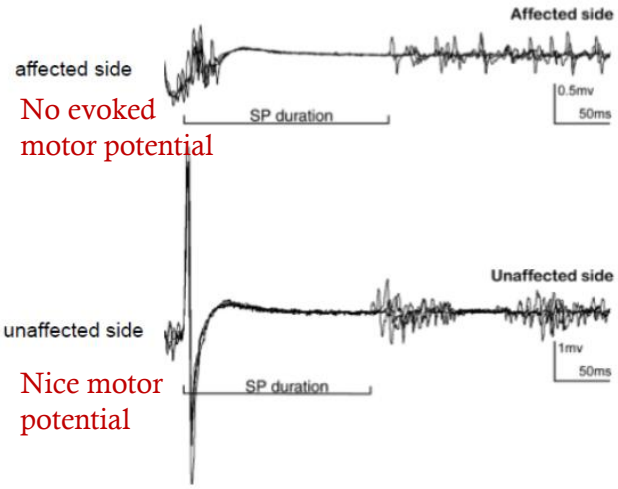
To stimulate the nerve



The time difference is the time which takes the stimulus from the central nervous system, so the central conduction time (because the magnetic stim. stimulates the brain itself while electrical stim. stimulates the nerves, so in case of elec. stim. the evoked potential starts earlier.)

2) Silent period phenomenon: Repetitive stimulation of the cortex is applied, there is a „silent" period when the stimulation does not evoke muscle movement. It can be studied in the case of stroke patients.

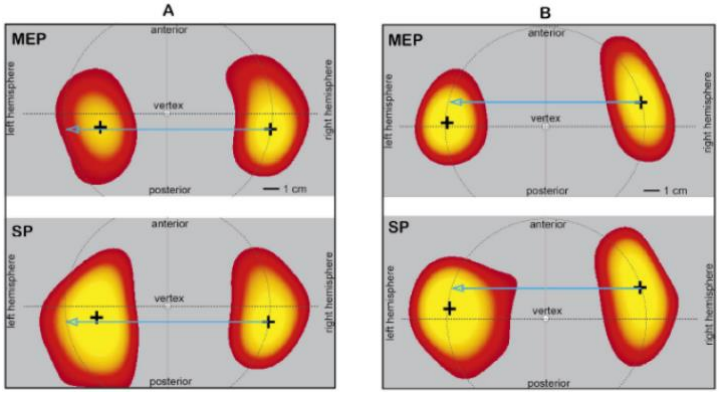
Silent period is still there, because other neural elements still working → stroke is local, not all of brain areas are affected



3) **Measure of center of evoked motor potentials by TMS (in stroke patient)**

Let's measure the potential changes which responsible for the limb movements in the brain.

In case of stroke, these areas are shifted because stroke effected sides can not generate potential to control the muscles anymore so other brain area takes over and shift (done by TMS and EEG)



Pros and Cons:

Advantages:

- painless
- central motor conduction time can be measured fast, without pain
- suitable for surgical monitoring

Contraindicated with:

- pacemaker
- focal epilepsy
- metal in the brain

RESARCH APPLICATION

TMS also can inhibit the brain, its depending on timing.

1) **VISUAL SEARCH task:** It was harder to find the target (or report that no target) if TMS was applied

rTMS can be easily used for inhibition.

2) **LETTER IDENTIFICATION task:** During TMS hard to count letters, but visual mask less confusing.
3) **Effect of rTMS on MOTOR CORTEX EXCITABILITY**: rTMS was applied 25 min and than TMS cortex stimulation
   - rTMS has longar lasting effect, and effect time and application time is proportional
   - TMS has no lasting effect
4) **Effect of TMS on brain activation during BRAILLE READING in blind subjects**:
   - Sencory motor cortex stimulation: Error rates of sited (megvakult vakok) is much higher than blind people (akik így születtek vakok)
   - Visual cortex stimulation: Originaly blind peoples error rates is higher, because their visual cortex area are taken over by other (sensory) procces function areas

COMMERCIAL APPLICATION DEVICES

5) **MAGNETIC SIZURE THERAPY IN DEPRESSION**
   - Not very acceppted that magnetic stimulation is usful to depression treatment.
   - Also exist rTMS version

tDCS AND tACS (Transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS))

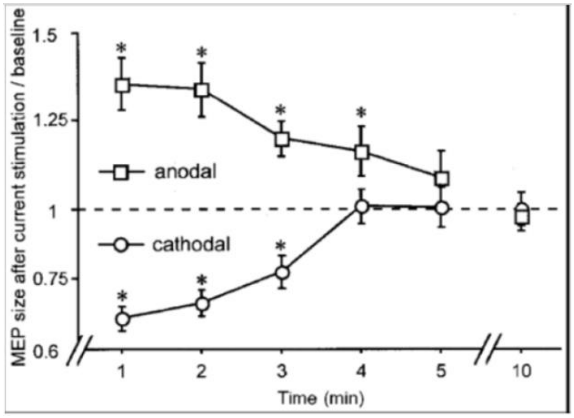
tDCS: Direct current application through relatively large surface electrodes placed on scalp. The current is gradually increased and reduced, so it has no direct effect even in a long lasting application. (~ 30 min.)

tACS oscillates a sinusoidal current at a chosen frequency to interact with the brain's endogenous cortical oscillations.

Depending on where we put the electrode for tDCS, it evokes different effects, so lacation and depth in brain also change

How to modulate brain activity:

Anodal tDCS enhances the responses while Cathodal decreases it. **So compleatly opposit than in case of FES**. The reason is the destance between the electrode and nerves, so in case of DC electrodes is much much further than FES. Moreover these are not an impulses.



Anodal: engance the ability of to be stimulatied, so decrease the stimulation threshold.

Cathodal: Not blocks the stimulation, just increases the stimulation threshold so makes difficult the nerves to be stimulated.

DC stimulation has after effect, which is proportional the stimulation duration. Similar phenomenon in case of rTMS.

tDCS could be effect the motor cortex, or visual cortex

- Cathodal tDCS can reduces the visual evoked potentials (in case of anodal stimulation increases)
- Finger movment task: Cathodal ipsilateral reduces the movement accuracy an anodla increases. Contralaterally the situation is the opposit, cathodal increases and anodal decreases the accuracy of finger movements.

This type of stimulation modulates the brain activity, does not have immediate effect.

The effect of visual cortex tDCS and rTMS onphosphene realization threshold.

Interesting field could be to study The effect of tDCS and rTMS on social cognition.

COMPERSION

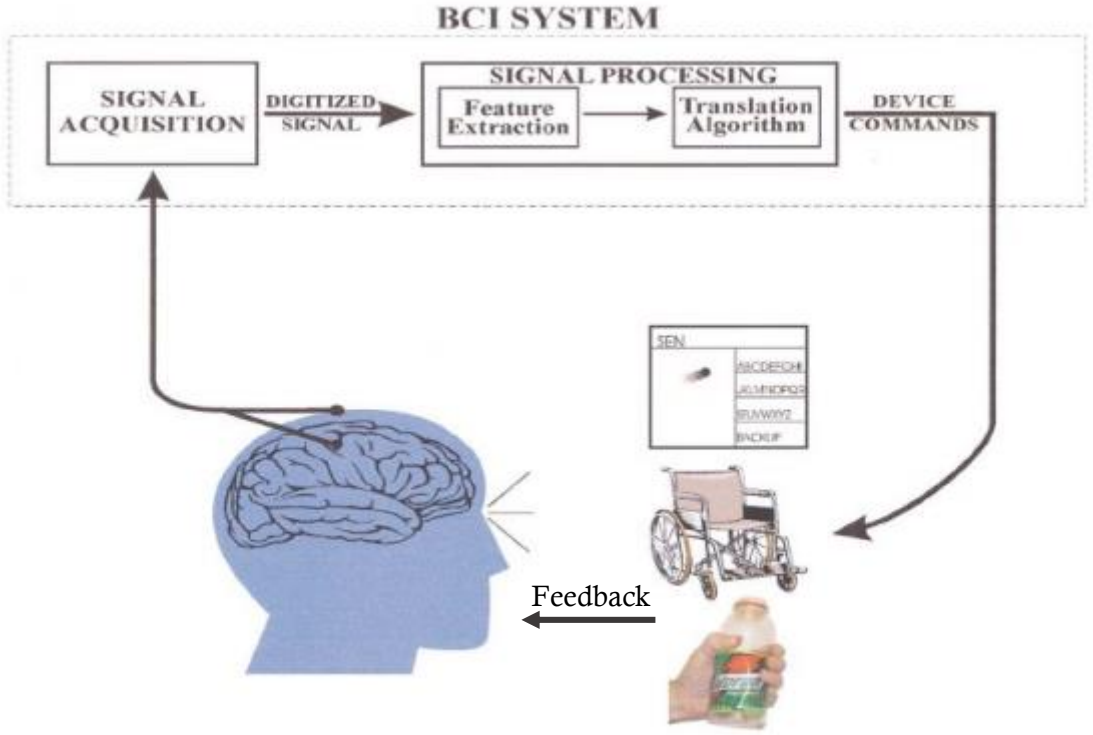
	tDCS	**rTMS**
Quality of sensation	No sound	Sound, loud click
Focality of stimulation	Less focal	More focal
Cost	Lower	Higher

COMMERCIALLY APPLICATIONS:

There are several commercial applications of tDCS that promise to enhance memory, cognitive abilities, sports abilities

6. Application of EEG signals for brain computer interfaces

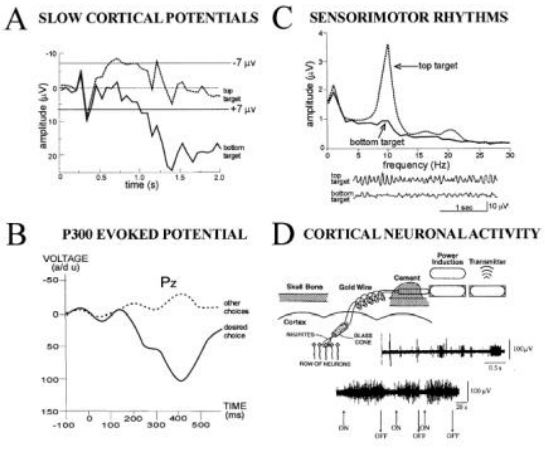
Basic design and operation of any BCI system. Signals from the brain are acquired by electrodes on the scalp or in the head and processed to extract specific signal features (e.g. amplitudes of evoked potentials or sensorimotor cortex rhythms, firing rates of cortical neurons) that reflect the user's intent. These features are translated into commands that operate a device (e.g. a simple word processing program, a wheelchair, or a neuroprosthesis). Success depends on the interaction of two adaptive controllers, user and system. The user must develop and maintain good correlation between his or her intent and the signal features employed by the BCI; and the BCI must select and extract features that the user can control and must translate those features into device commands correctly and efficiently. So system components: record the signal, process the signal where we extract the features and than translate the features to commands to controll the device. The patient get fededback from device (either patient see, the chaire mooving etc.)



Classification of BCI: it has 2 groups invasive and noninvasive.

Noninvasive BCI systems use signals recorded outside the brain. Most noninvasive methods are based on EEG. It provides a solution for paralyzed people for simple communications with the outside world. However neural signals have limited bandwidth. From EEG we can use different components:

- Slow cortical potentials (SCP)
- Oscillatory EEG activity
- Event-related synchronizations, ERS and desynchronizations, ERD,
- Event-related brain potentials, ERP, eg. P300, SSVEP,



APPLICATIONS

1) THOUGHT TRANSLATION DEVICE

• Birbaumer and colleagues were the first who developed BCI system for ALS patients. Their system used slow potential changes.

- **Amyotrophic lateral sclerosis (ALS)** is a progressive motor neuron disease of unknown origin. **Motor neurons in the central and peripheric motor nervous system die**, while sensory and cognitive systems are unaffected. There is no known medication for ALS. Patients affected can decide, if they accept artificial respiration and feeding, or die from respiratory failure. The last motor function to remain is usually eye movement. The state developed is called completely locked-in state (CLIS), if at least a single muscle function remains, it is called locked-in state (LIS).

• **Slow cortical potentials (SCP)** are low frequency potentials (e.g., less than 1 Hz) recorded from the scalp and are associated with various cognitive or sensory-motor events. Decreased cortical activation is associated with scalp positivity and increased activation is associated with negativity.

• Patients are trained to modify SCPs based on feedback and use this paradigm for BCI-based communication (Thought Translation Device).

• TTD is a Brain-Computer Interface for the completely paralyzed (CLIS) patients using slow-cortical potentials (SCP) to move a cursor on a monitor to select letters. TTD is a feedback device that enables people to respond by voluntary SCP changes.

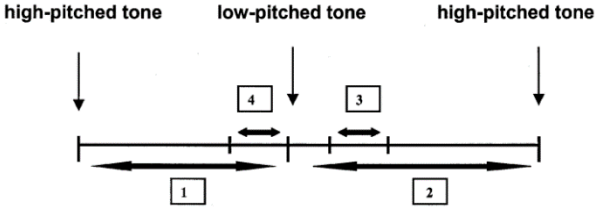
• During the training phase, the self-regulation of SCPs is learned through visual-auditory (or tactile) feedback and positive reinforcement. During the spelling phase, patients select letters or words with their SCPs.

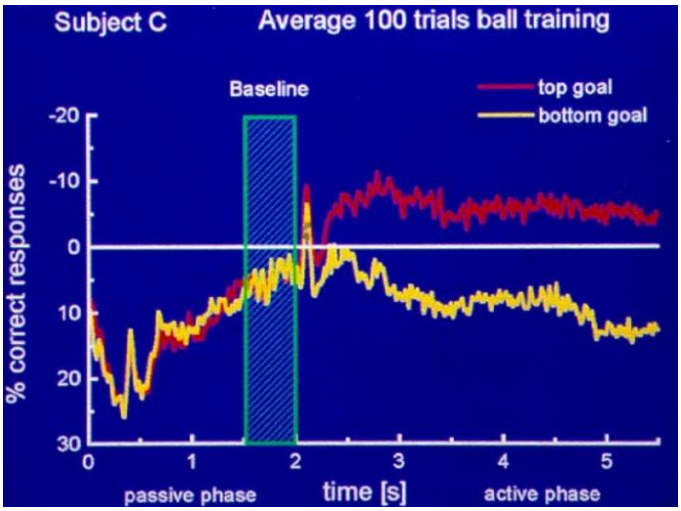
• A psychophysiological system for detection of cognitive functioning in completely paralyzed patients is an integral part of the TTD.

There is a **SUPPORT LANGUAGE PROGRAM** attached, which could help the patient to communicate with the world. (Sentences, words or single letters)

The first patient gets the tone: signal for selection cycle is starting. Then passive phase is following while patient has to relax, because after that the detection will come and end of passive phase happening at the baseline measuring (against which the comparison will be made). After that active phase is followed, while detection and feedback are carried out. So Here detect the change and moves the cursor on the screen and a new high-pitched tone sign that the cycle is ended.

Slow process, it could take 5-15 sec.





1	passive phase:	2 seconds
2	active (feedback) phase:	2 to 6 seconds
3	cursor movement:	0.5 seconds to 6 seconds
4	baseline	0.5 seconds

How it works? Binary selection task, first put almost one-half of the ABC, and the respons is positive if the set contains the desired letter or the response is negative if it does not. The new cycle will contain the quater of ABS (half of half ABC). So select just one letter is a realy long proccess.

Learning phase takes a lot of time, and the key element for learning is the motivation for training. → Psiyhology work.

7. Application of event related potentials for brain computer interfaces

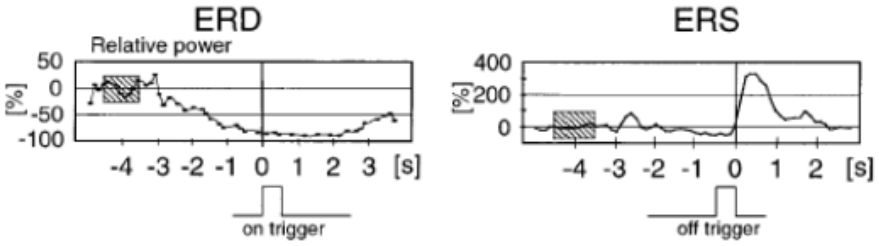
EVENT-RELATED DESYNCHRONIZATION (ERD)

EVENT-RELATED SYNCHRONIZATION (ERS)

A new device, that uses **Alpha band for desynchronisation** and **Betha band for synchronization** in response to different movements.

Alpha ERD and beta ERS to repeated flexion of the index finger. ERD appears before and during movement, ERS appears after the termination of the movement.

Easily can be detected by EEG (and fMRI).



ERS/ERD Localization in the cortex

The localization of ERD as well as the ERS corresponds to the cortical representation of the given movement.

ERD/ERS appear not only to the execution of a movement but also to the movement imagination. This means that it can be used in totally paralyzed patients as input to BCI systems.

How to use for BCI

The patient is trained to imagine foot and hand movements, they get feedback, and these imaginary movements can be used for e.g.: robotic hand/exoskeleton control, open or close robotic hand.

Training is needed.

These were Event Related Potential, not Evoked Potential, because not evoked by sensory stimulation, its evoked by imaginary movements.

BCI BASED ON MU RHYTHM

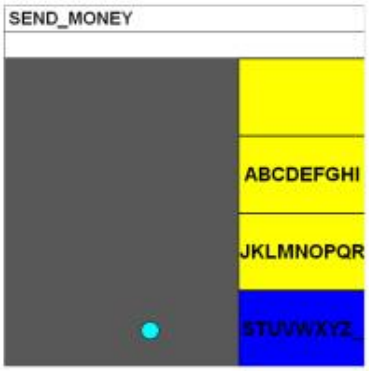
Some BCI methods were developed based on using the mu rhythm of the EEG. Mu rhythm is an 8-14 Hz "idling" rhythm found over the primary motor/somatosensory cortex. These areas are located around the central sulcus. The mu rhythm is largest over central sites such as C3, Cz, or C4. Mu rhythm is often called sensorimotor rhythm (SMR).

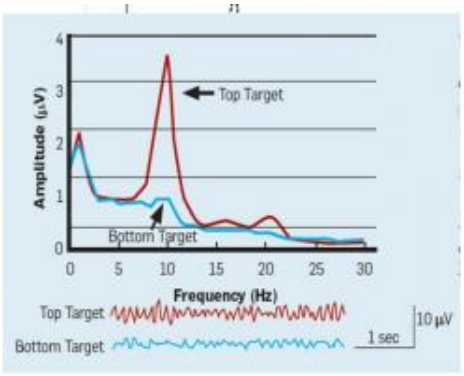
Mu activity is visible before a voluntary movement, sometimes 2 seconds before it begins. So it can be voluntarily controlled by the patient.

Mu activity reflects movement planning and execution. Mu activity can be voluntarily controlled by movement related imagery. This becomes easier in trained subjects. With continued practice, this control tends to become automatic, as is the case with many motor skills and imagery becomes unnecessary.

Mu rhythm is basically the alpha band, the difference is the alpha band is in the occipital cortex, while mu rhythm is in motor/somatosensory cortexes.

1) BCI BASED ON MU RHYTHM





BCI letter speller the users directed a ball by the mu rhythm. The ball was moving through the screen and the user had to move it up or down, pointing to the letter string containing the selected letter.

The mu rhythm and the ERD/ERS BCI are similar but ERD/ERS is elicited by external stimuli while mu rhythm is modulated spontaneous activity.

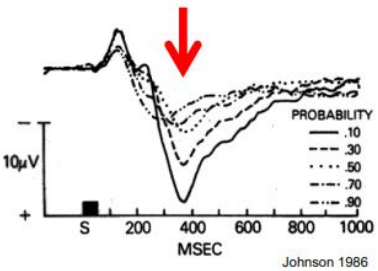
A binary selection task, tt doesn't use the slow-cortical potential it uses mu rhythm, which is easy to detect (has high intensity and high power).

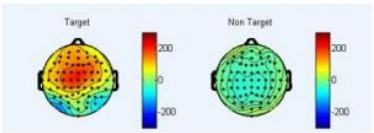
Still needs training.

2) BCI BASED ON P300 RESPONSE

This type of BCI uses the **P300** component of event-related brain potential.

P300: Active oddball paradigm, when we have a sequence of standard signals and then we have a deviant signal, and if the deviant signal is detected a nice 300 ms latency positive deviation in the EEG.



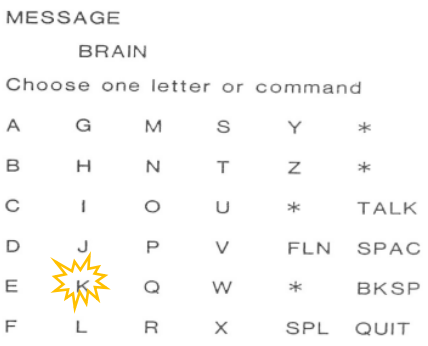


Amplitude of P300 is sensitive to stimulus probability, meaning of the stimulus, and the psychological resources allocated to the processing of it. Low probability stimulus has higher amplitude and vice-versa. The more complex the stimuli to be processed the longer the latency of the P300. The P300 has a distinct scalp distribution. It is typically the largest over the Pz site. P300 BCIs require no training. Nice scalp distribution, so it is easy to find the spot to measure it, but the spot changes with the paradigm.

The P300 BCI system consists of a matrix of letters or other symbols on the monitor. Rows or columns of the matrix are flashing randomly in rapid succession.

The flashing letter or symbol that the user wants to select produces a P300 potential. By detecting this P300 potential, the BCI system can determine the user's choice.

Doesn't need training!



And an average signal is needed! → Slow, takes more time for average

Average P300 signals can be detected for target and near-target as well, which means further complication.

30 sec/character, to improve that it could use predictive speller, to speed up the system to 7 selections per min.

3) BCI BASED ON STEADY STATE VISUAL EVOKED POTENTIALS (SSVEP)

This response is evoked by flickering lights in the range of 4-40 Hz.

> **Steady state response**: If we have a periodic signal either visually or auditory then the brain signals will take the same period. (e.g.: 4 Hz flickering visual stimulus → 4 Hz EEG oscillation on visual cortex). It's automatic, and „works always".

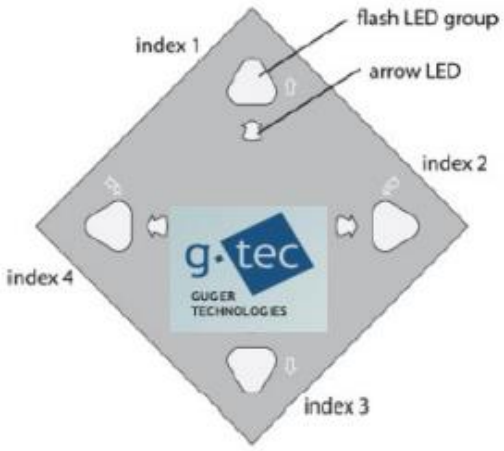
Steady state response (SSR) is sine wave like oscillation with frequency of the repetitive stimuli. It can be studied in the frequency domain (FFT). It may also be elicited by auditory and somatosensory stimuli. Nearly all subjects seem to have this activity.

SSVEP requires no training. Selective attention can enhance SSVEP.

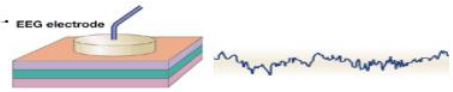
How is that for BCI?

Two or more light source flashing with different repetition rates can be used to elicit SSVEPs with increased amplitude in the frequency of the attended light source.

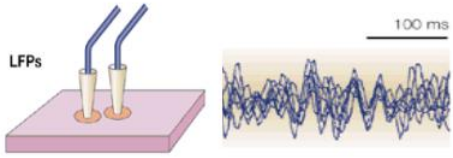
The Patient can decide which concentrate on, and the focused signal freq. will appear on EEG. Doesn't need to move the eyes, concentration is enough!



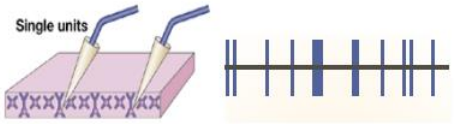
8. Application of single unit recording techniques for brain computer interfaces



The limitations of noninvasive EEG-based BCI systems are the distances between the recording electrodes on the scalp and the underlying cortical tissue. This is why the signal amplitude is small the bandwidth is limited and S/N ratio is low.

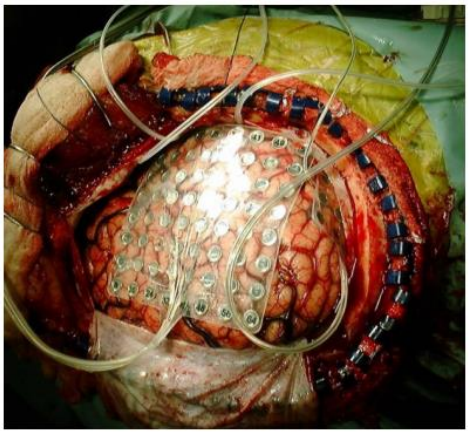


The advantage of invasive techniques is that the recording electrodes are on the surface of the neocortex or in the neural tissue. The ECoG is often called semi-invasive because the electrodes are not inserted into the tissue. Better special resolution, better S/N ratio and higher amplitude signal.



Signals of what can be used for BCI: for e.g.: EcoG can be used if put electrodes on the brain surface, if you sting (or stick szúrni) electrodes of the brain surface then we have LFPs (The Local Field Potential (LFP) is the electric potential recorded in the extracellular space in brain tissue) or even we can measure single units.

BCI BASED ON ELECTROCORTICOGRAM (ECOG)



BCIs based on ECoG are working on the same principles as the EEG BCIs. ECoG BCI research has almost exclusively been performed on epilepsy patients, in whom subdural grids are clinically placed over suspected epileptogenic foci.

The advantage of ECoG-based is that electrodes are on the cortical surface, yielding a much finer spatial resolution on the order of mm as well as the ability to record higher-frequency (10–200 Hz) content in the signal.

It was found that patients could quickly learn to modulate high-frequency gamma rhythms in both motor cortical areas and in Broca's speech area to control a one-dimensional computer cursor in real time.

1. NEUROTROPHIC ELECTRODE (Historically important, end of '90s)

There was developed a special glass microelectrode for chronic recording of neuronal activity. Researchers cortically implanted these microelectrodes filled with neurotrophic growth factor (there are substances in the electrodes that attract neurons so neurons grow into the electrode so really close to the recording electrode and with it it can record nice high quality signals.) first into animals. The axon of the neurons targeted by the electrodes grows into them and allows recording of the spike activity.

After a series of successful animal experiments, they implant the neurotropic electrode into the brains of several ALS patients. This implantation requires major surgery lasting about 10 hours.

Neural activity has been recorded with this type of electrodes in ALS patients for five years.

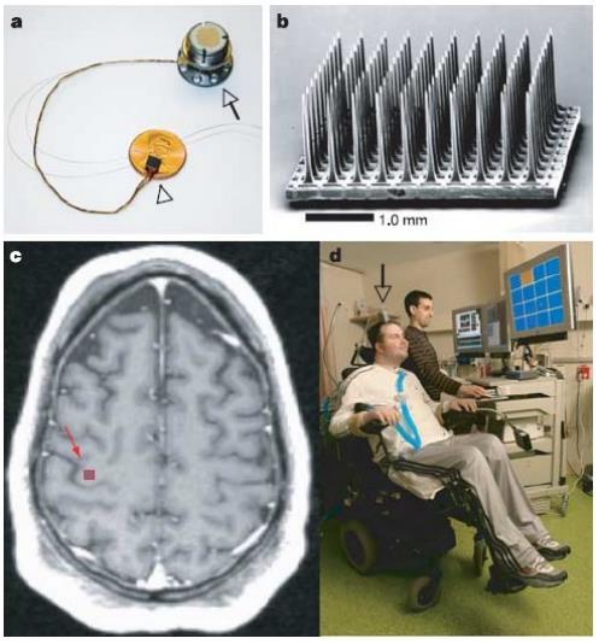
The only problem is that it works nicely in theory, it was promising but don't do this anymore.

1) HUMAN IMPLANTED ELECTRODE MATRIX/BRAIN GATE SYSTEM

It's silicone probes, Si needle array that each needle has single recording content at the tip.

Very t iny chip that can be implanted into the brain, Connector is needed and can't be implanted forever because it has to be taken out because of the infection risks.

Currently, the system consists of a „**sensor**" (a device implanted in the brain, into the motor cortex, that records signals directly related to imagined limb movement); a „**decoder**" (extracts the features and then a set of computers and embedded software that turns the brain signals into a useful command for an external device); and, the „**external device**" – which could be a standard computer desktop or another communication device, a powered wheelchair, a prosthetic or robotic limb.



Also needs training!

4) FUTURE DEVICES

How a fully-implantable BMI could restore limb mobility in paralyzed subjects or amputees. Although the details of this system have to be worked out through future research, it is clear that the BMI for human clinical applications **should be encased in the patient's body as much as possible. Wireless** telemetry offers a viable solution for this purpose. The prosthesis not only should have the functionality of the human arm in terms of power and accuracy of the actuators, **but also should be equipped with the sensors of touch and position from which signals can be transmitted back to the subject's brain.**

5) COMMERCIAL BCI FOR HEALTHY PEOPLE

EMOTIV EPOC NEUROHEADSET – Playing computer games without touching the mouse or keyboard. (Detecting brain signals, eye movement, face muscle signals…)

EMOTION READING

WAKE UP when it's optimal

9. Correction of conduction hearing diseases by prostheses

CHARACTERISTICS OF THE SOUND (maybe not necessary)

Sound is periodic pressure waves of compression and expansion of the air. Sound propagates in the air as a longitudinal „compression wave" with a speed of 343 m/s, **1230 km/h**.

1) Freq

- Human audible **frequency range**: 20 – 20,000 Hz
- **Pitch** is the quality that makes it possible to judge sounds as "higher" and "lower" in the sense associated with musical melodies. (So the pitch is not really the freq. itself, but the perception of lower or higher sound)
- Our subjective perception is a logarithmic function of the frequency as a physical variable. "Equal" intervals actually multiply. (We say we hear equal intervals but those are exponentially increasing intervals)

2) Loudness (intensity, what we hear)

- Our subjective perception of loudness is also a logarithmic function of the intensity as a physical variable.
- **Sound Pressure Level (SPL)** is a logarithmic measure of the effective pressure of a sound relative to a reference value: dB=20 x logPn / 20μP. (20 micro Pascal)
- Clinicians measure sound intensity in **dB HL (deciBel Hearing Level)**, i.e. dB relative to the quietest sounds that a young healthy individual ought to be able to hear.
- Around 100 dB level is the maximum that we hear without completely damaging.

Natural sounds:

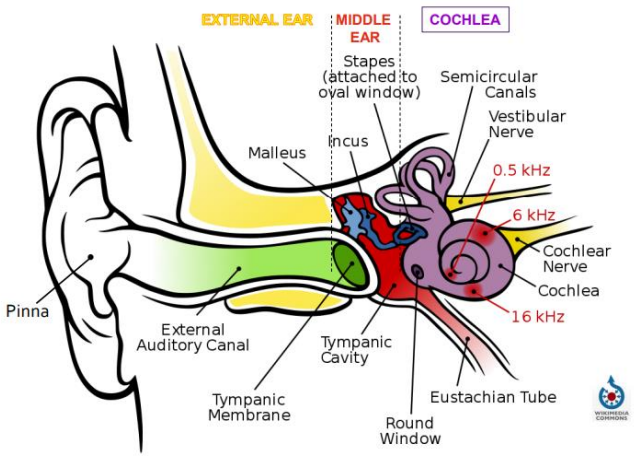
▪ multiple frequencies (music: piano chords, hitting keys simultaneously; speech). We hear it as a "whole" not parts.
▪ natural speech is about 100 – 10 kHz
▪ constantly changing (prosody in speech; trills in bird song)

The spectra of the vowels ah-oh-ee-oo are shown. The peaks in the spectra are called **„formants".** The formant frequencies are different for each vowel and these bands are what determine the phonetic quality of the vowel.

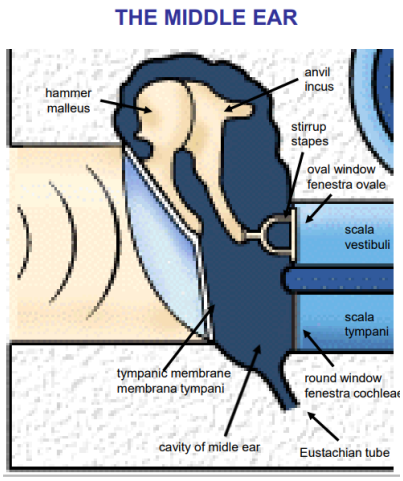
THE HEARING ORGAN

The hearing organ can be divided 3 parts:

- External ear
  - ear that we see
  - External auditory canal, that leads to the
  - Tympanic membrane
- Middle ear
  - Tympanic membrane connects from the inner side to the 3 middle ear bones, which conduct sound from Tympanic membrane to the Oval window and these 3 bones has amplification function as well



    - Malleus/Hammer/Kalapács
    - Incus/Anvil/Üllő
    - Stapes/Stirrup/Kengyel
    - Tympanic cavity
- Inner ear or Cochlea
    - Oval window
    - double helix of cochlea
    - Round window
    - Semicircular canals, which are responsible for balance
    - Cochlear nerve
    - Vestibular nerve



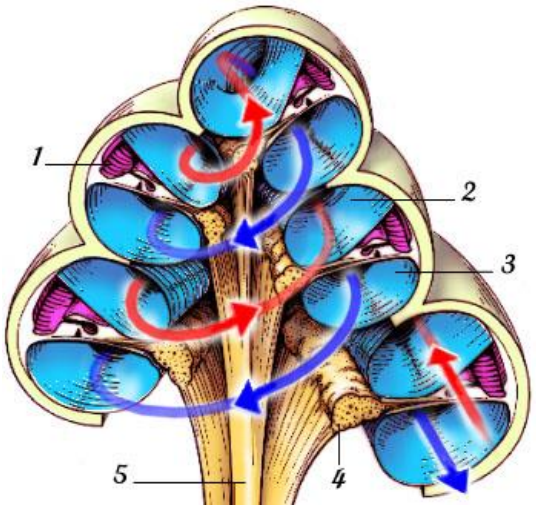
The middle ear

- Works as a transmitter, transmits vibrations from air to fluid inside the cochlea.

- Σ >17x amplification = 25-30 dB pressure increase, because of Tympanic membrane area is much larger than the Oval window and this area difference ration is actually serves as an amplification of the pressure. Trasmitter and amplifire

- Movement of the tympanic membrane is extremely tiny:
2 dB whisper = 10-7 mm (?)
threshold of pain = 0,1 mm

Inner ear/Cochlea



The cochlea contains the sensory end-organ of the auditory system. It resembles a snail shell (Greek word: kokhilas) and spirals.

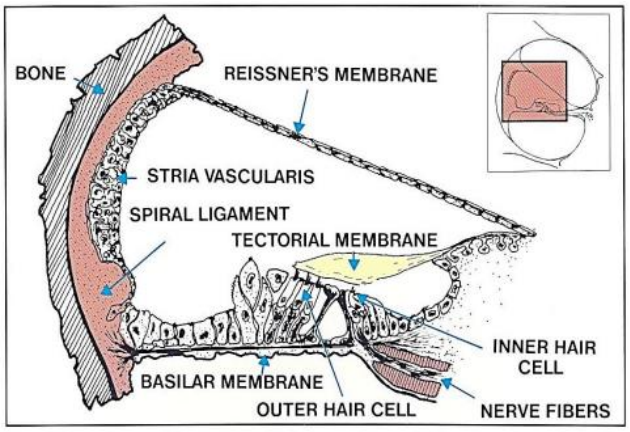
The cochlea has an osseous (csontos) capsule and a membraneous part that contains three fluid-filled canals:

- Scala Vestibuli (red arrow)
- Scala Tympani (blue arrow)
- Scala Media (purple)

The s. vestibuli is closed by the oval window, against which the stapes push in response to sound. The s. tympani is closed by the round window, a thin flexible membrane.

The Scala media contains the sensory organ, the **organ of Corti**.

SCALA MEDIA (ORGAN OF CORTI)

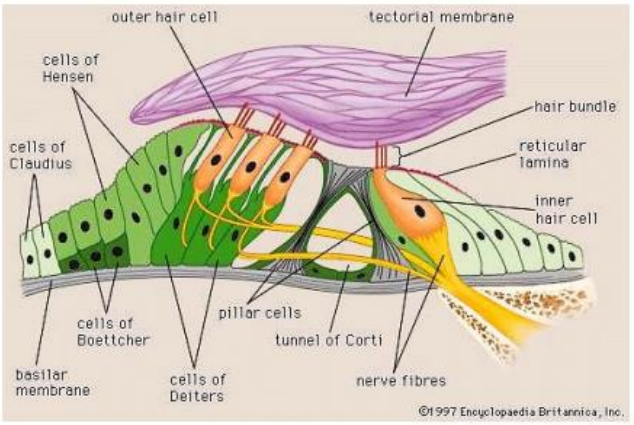


The organ of Corti contains the hair cells and supporting cells. The organ of Corti rests on the basilar membrane and is covered by the gelatinous tectorial membrane. The tectorial membrane's tapered distal edge forms a fragile *(törékeny, sérülékeny)* connection with the organ of Corti. There are one row of inner hair cells and three rows of outer hair cells.

~15.000 hair cells: ~ 3.500 inner hair cells, ~12.000 outer hair cells.

1) Inner hair cell

- Hearing depends entirely on the sensory receptors of the inner ear known as hair cells. Hair cells are extremely vulnerable and can be affected by disease, aging and over-exposure to loud noise. Once destroyed, they do not regenerate. It can be thought of as a **biological microphone**.



- The apical end of the hair cells is specialized for the reception and translation of mechanical energy into receptor currents.

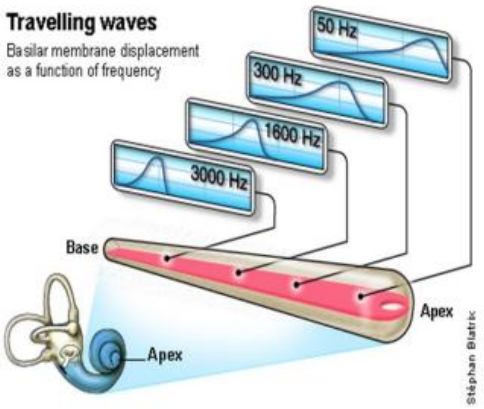
- 10-300 stereocilia per hair cells
- Length of the stereocilia: 1-10 µm
- Diameter of the stereocilia: ~0.4 µm

- Stereocilia of inner hair cells are arranged linearly, that of the outer hair cells are in V configuration.

2) Outer hair cell

The apical surface of inner support cells, one row of inner hair cells (i: IHCs), 3 rows of outer hair cells (o: OHCs)

BASILAR MEMBRANE



Piston *(dugattyú)* like oscillatory movement of the stapes at the oval window induces pressure oscillation in the incompressible fluids of the cochlea. The mechanical properties of the basilar membrane are the key to the cochlea's operation:

- the basilar is membrane elastic
- the membrane is wider at its apex (0.5mm) compared to the base (0.1mm)
- it decreases in stiffness from base to apex, the base being 100 times stiffer

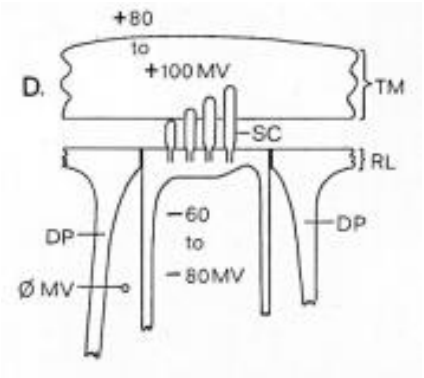
As a result the sound-driven vibrations travel as waves along the basilar membrane. High-frequency sounds moving only a small region of the basilar membrane near the stapes, whereas low frequencies cause almost the entire membrane to move. As shown in this schematic drawing, as the frequency varies from high to low, the site of maximum displacement of the basilar membrane shifts toward the apex. This passive tonotopy (freq. distribution) was described by Georg von Békésy.

Electrical potential relations in the inner ear

The cochlear canals contain two types of fluid: perilymph and endolymph.

Perilymph has a similar ionic composition as extracellular fluid found elsewhere in the body and fills the scalae vestibuli and tympani. (Rich Na^{2+}, low K^{+} level)

Endolymph, found inside the cochlear duct (scala media), has a unique composition: very rich in potassium K^{+} (150mM), very poor in sodium Na^{2+}(1mM) almost completely lacking in calcium Ca^{2+} (20-30 μM).



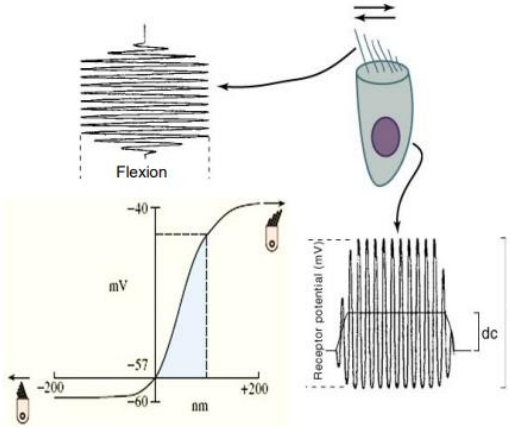
Hair cells conduct two very different fluid media → helps to generate fast potential changes.

Resting potential of the hair cells: -60 - -80 mV.
15% of the channels are open
endolymph – perilymph = +80 - +100 mV
endolymph – intracellular space = ~160 mV

Receptor potential
100 nm displacement (movement) of a stereocilium equals 90% of its total operating range.

Normal sound intensity: ~ ±1° displacement
Hearing threshold: ±0,3 nm → 100 μV receptor pot.
Brownian motion of stereocilia: 3 nm.

Receptor potential, also known as a generator potential, is a graded potential change in the receptor cells caused by the specific sensory stimulus. Its amplitude is proportional with the intensity of the stimulus and its waveform is a replica of that of the sensory stimulus.



The figure shows sigmoidal input-output function of hair cells. Symmetrical sinusoidal displacement of stereocilia produces an asymmetrical response that includes AC and DC receptor potential components. The AC component is electrical copy of the sound stimulus causing the mechanical displacement of the stereocilium.

Since the waveform pattern of the sound vibration arriving the ear (e.g. speech) and that of the AC component of the receptor potential are identical the receptor potential of the ear is called **cochlear microphonic potential**.

- The receptor potential is an electrical copy of the sound pattern and corresponds to its physical parameters.
- Since the waveform pattern of the sound vibration arriving the ear (e.g. speech) and that of the AC component of the receptor potential are identical the receptor potential of the ear is called cochlear microphonic potential.
- The cochlear microphonic potential can be recorded by electrode placed to the round window.
- The cochlear microphonic potential can be used in human to diagnose cochlear damage: electrocochleography.
- Transmit mechanical liquid movement into elecrtical potential changes.

Displacement of the hair bundle towards the tallest stereocilium increase of the proportion of open channels, thereby a depolarizing voltage change, a receptor potential is generated. Bundle movement away from the tallest stereocilium hyperpolairze the hair cell. The hair cells have synaptic contacts at their base with the bipolar nerve cells of the ganglion spirale. The nerve cells of the ganglion spirale have a unique feature: they have spontaneous activity even in silence. The receptor potential changes of the inner hair

cells modify the spontaneous activity of the acoustic nerve, the depolarization increases, hyperpolarization decreases the impulse frequency.

Air pressure waves → Fluid pressure waves → Receptor potential → Action potential changes of auditory nerve fibers

OUTER HAIR CELLS

Active amplification

The active mechanism of the outer hair cells shifts the place of the maximum and increases its amplitude.

Tip links are filamentous connections between two stereocilia. Displacement of the stereocilia towards the tall edge opens additional mechanically activated channels and the resultant influx of K+ and later Ca++ ions depolarize the cell by as much as tens of mV. The displacement of the stereocilia towards the short edge shuts the channels hyperpolarizes the cell. During cell depolarization ionic current flows in through the mechanoelectrical transducer channels. The outer hair cell responds by changing length so that the cells pull the basilar membrane closer to the tectorial membrane (which can bend the stereocilia of inner hair cells) and they execute the amplification function.

OTO-ACOUSTIC emission

- OHC contractions-elongations themselves vibrate cochlear fluids and the middle ear conducting mechanism transfers this vibration back to the air of the external auditory canal: there, the emissions can be registered by a microphone.
- OHC is a diagnostic tool to evaluate cochlear function.

I think the topic itself starts on the next page, but who knows? ¯_(ツ)_/¯

TYPES OF HEARING LOSS:

Conductive hearing loss: otitis media, otosclerosis, tympanic membrane perforation. It affects the tympanic membrane and middle ear (e.g.: Middle ear bones are fixed together or tympanic membrane is perforated.)

Sensorineural hearing loss: damage of the hair cells, congenital, pre-lingual, post-lingual, NOISE

Mixed hearing loss: combination of both conductive and sensorineural hearing loss

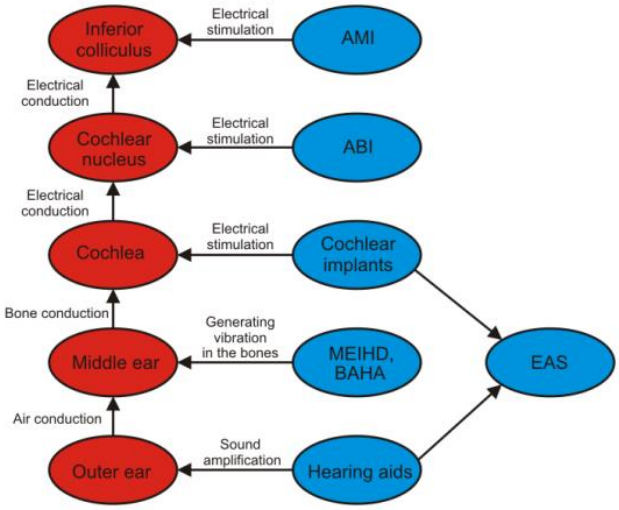
Neural hearing loss: damage of the auditory nerve or other brain structures of the auditory pathway

Depending on the level of exposure, damage to hair cells may:

- only involve stereocilia, and some repair mechanisms are possible, or
- involve the entire hair cell, which undergoes apoptosis and dies.

MIDDLE EAR MECHANICAL IMPLANTS

- Bone-anchored hearing apparatus (BAHA)
- Middle ear implantable hearing devices (MEHID)

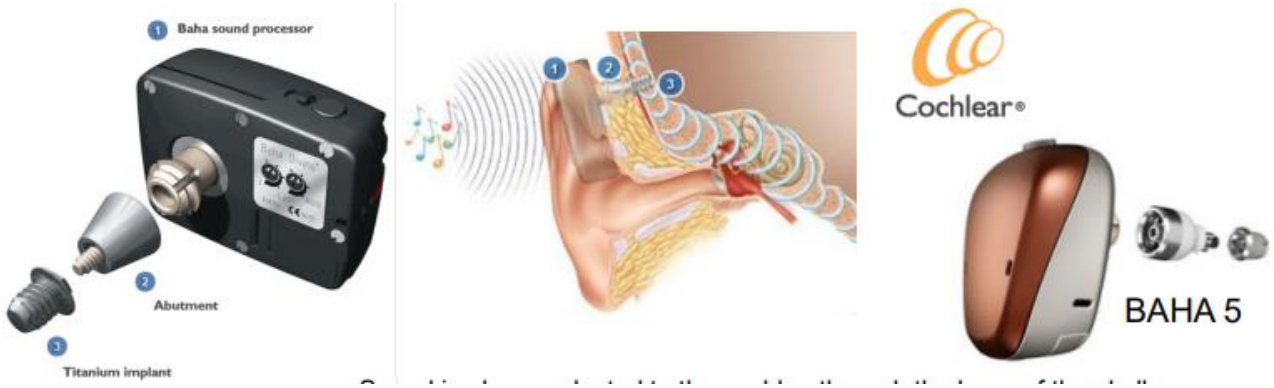


EAS – Electric Acoustic Stimulation
BAHA - Bone anchored hearing apparatus
MEIHD - Middle ear implantable hearing devices
ABI - Auditory brainstem implants
AMI - Auditory midbrain implants

Targets (red) of different types of hearing aids (blue). On the horizontal arrows the method of signal generation of the respective hearing aid is presented. Next to the vertical arrows, the ways of transmitting the sound signals originating from the outside world are shown.

HEARING DEVICES

1) **BONE-ANCHORED HEARING APPARATUS (BAHA)**



Sound is also conducted to the cochlea through the bone of the skull. Bone conduction bypasses the middle ear the vibrations directly reach the cochlea. The Baha device (Cochlear Corporation) is a percutaneous

implantable device primarily used for conductive hearing loss, or more recently, for single-sided sensorineural hearing loss.

A titanium screw of a few millimeters in length is placed into the mastoid bone, it also transmits the vibration (3). BAHAs are composed of two components: the fixture anchored to the bone, onto which the abutment *(alátámasztás)* (2), which sticks out of the skin, is affixed. The microphone and the sound processor (1) are connected to the abutment. In this way, the sound, transformed into processed vibrations, is transmitted directly to the inner ear via the abutment and the screw.

2) MIDDLE EAR IMPLANTABLE HEARING DEVICE (MEIHD)

MEIHDs were developed to treat conductive or sensorineural hearing loss with a degree from mild to severe. They can be partially-implanted or totally-implanted. Totally-implanted solutions, where the device is completely concealed in the body, are fully functioning also during swimming or bathing, and there is no occlusion effect present (Occlusion effect: when an object fills the ear canal, and the person perceives "hollow" or "booming" echo-like sounds of their own voice. It is mostly experienced in case of traditional hearing aids). MEIHDs directly stimulate the ossicles in the middle ear, and because the sensor and the driver are uncoupled, the feedback (which is another annoying effect of conventional aids) is almost completely eliminated.

TWO TYPES OF MEIHDs:

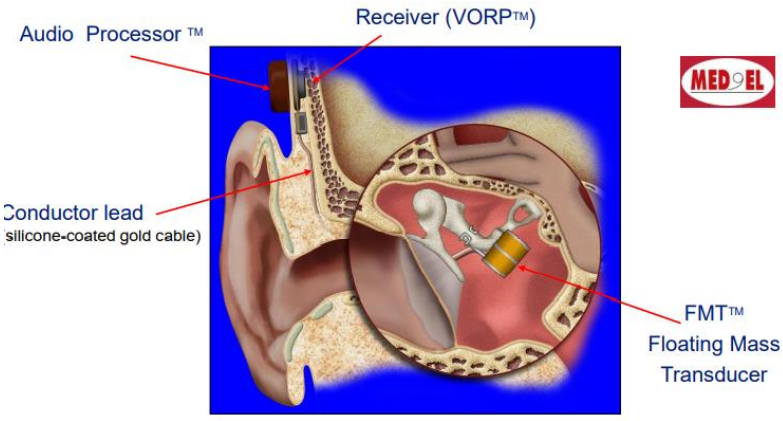
a) **Electromagnetic hearing devices** function by passing an electric current into a coil, which creates a fluctuating magnetic field (corresponding to the acoustic input). This causes a small magnet (samarium cobalt or neodymium iron boron), which is attached to the vibratory structures of the middle ear, to vibrate. This vibration, in turn, causes the movement of these structures resulting in the sensation of hearing. The coil may be separate from the magnet or integrated with it. The coil and magnet must be close, because the power is decreased by the square of the distance between them.
b) **Piezoelectric devices** operate by passing an electric current into a piezoceramic crystal, which changes its volume (by deformation or bending). This deformation provides the mechanical energy to stimulate the ossicular chain or inner ear, it produces a vibratory signal. The power output is directly related to the size of the crystal.

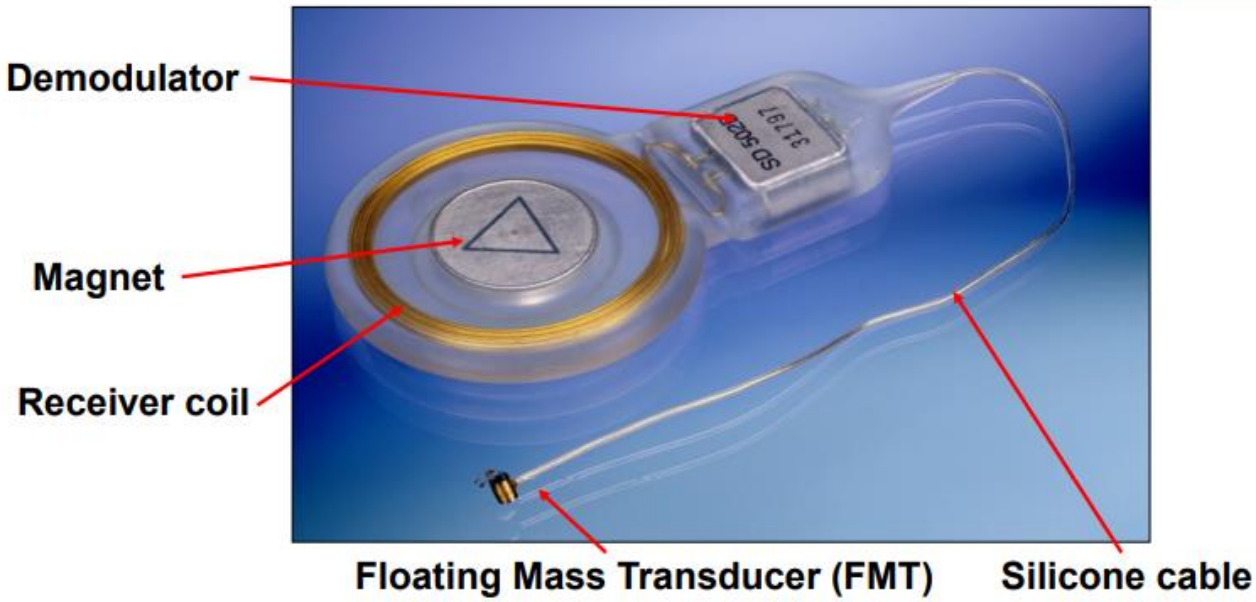
CONCRETE EXAMPLES

1) VIBRANT® SOUNDBRIDGE® product by MED-EL company from Austria !

Partially implanted electromagnetic hearing device. The VSB comprised two parts: the internal, surgically implanted receiver/demodulator, also known as the "Vibrating Ossicular Prosthesis" (VORP), and the external audioprocessor, which is placed onto the scalp and remains in place by magnetic attraction between the two parts.

Conductor leads to the midle ear where conducted to the Floating Mass Transducer (FMT). FMT is moving according to the sound recived and it moves the incus and stapes which trasmit the information/sound to the oval window and the cochlea.

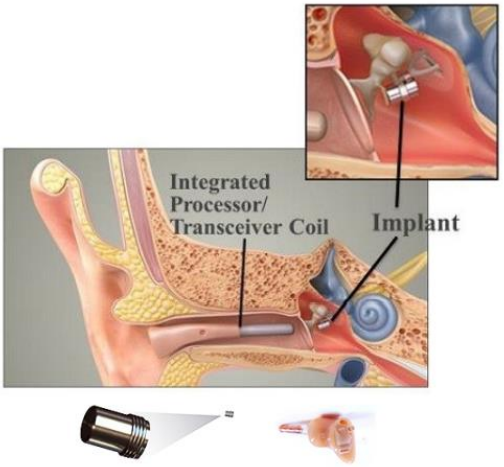




FMT:

- The electromagnetic transducer that generates the vibratory motion.
- FMT reproduces and amplifies the natural movement of the ossicular chain.
- The FMT should be in close contact and parallel to the stapes.
- Also can be placed directly to the round window

2) MAXUM HEARING AID by Ototronix Co. USA



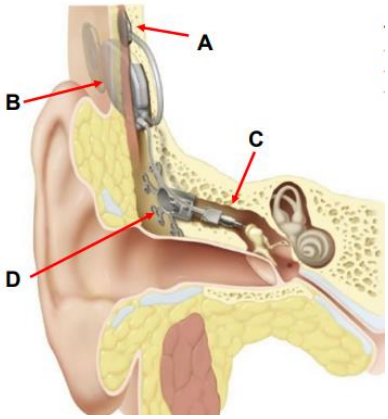
Partially implanted electromagnetic hearing device.

The difference is that it do not use a wire, because they place the FMT and Transceiver Coil close to each other because they place the Integrated Processor in the external auditory canal.

Advantage: no implanted wire under the skin

Disadvantage: Some side effect can occuar.

3) CARINA® MIDDLE-EAR IMPLANT by Cochlear Australia !



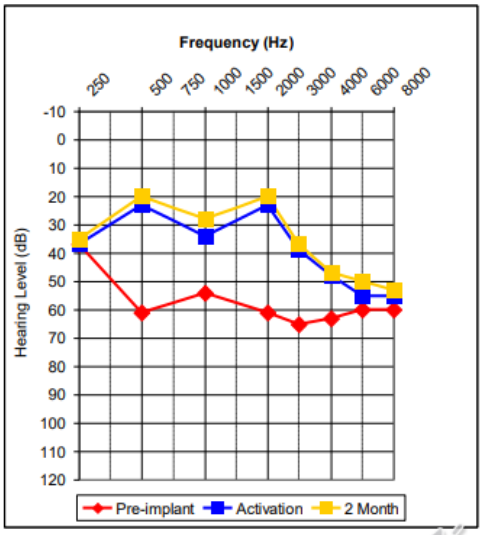
Totally implanted piezoelectric device

1.The microphone (A) under the skin captures sound and sends it to the implant via a lead.

2.The implant (B) processes the sound and sends it to the actuator.

3.The actuator (C) converts analogue electrical signal into mechanical vibrations and transfers to the ossicles.

4.The actuator is kept firmly to the temporal bone using a special fixation system (D).
The piezoelectric device is implanted near to the malleus, so when the sound is proccessed the electric changes in the actuator makes the piezoelectric cristal to elongate and to compressed and this makes moving the malleus and generate sound signal.



With this hearing aids, the hearing level does not reach the quality of a young hearing individual. But much better result can be achived by these devices than before implantation.

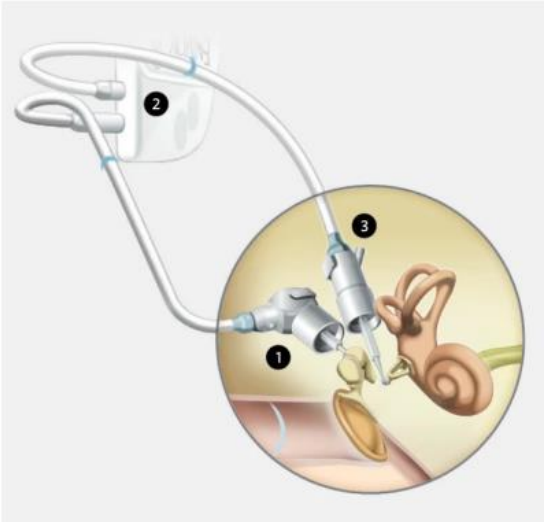
Better in case of low-frequences → This is enough to spech understanding.

Devices by Cochlear company can be modified depending on the condition of the patient. Actuator can be placed near the malleus, it can move the stapes directle, or the oval window and round window diectly. → flexible device

4) ESTEEM® TOTALLY IMPLANTABLE MIDDLE EAR IMPLANT (Envoy Medical Corporation USA)

Totally implanted double piezoelectric device

Sensor and Driver are both piezoelectric transducers.



1. The Esteem Sensor then converts the vibrations into electrical signals that are sent to the implanted Esteem Sound Processor.

2. The Esteem Sound Processor receives, adjusts and intensifies the signals to fit your unique hearing needs.

3. The Esteem Driver translates these customized signals to intensified vibrations. The vibrations are transferred to the inner ear where the cochlea cells are stimulated, causing you to hear more natural sound.

5) MED-EL BoneBridge BONE CONDUCTION IMPLANT

The BONEBRIDGE is a semi-implantable system consisting of an implantable part, the Bone Conduction Implant (including the Bone Conduction - Floating Mass Transducer, the BC-FMT), and the externally worn SAMBA audio processor. The BC-FMT vibrates the bone, the bone carries the vibration to the inner ear, where it is processed like normal sound.

6) BAHA® ATTRACT SYSTEM by Cochlear

Baha® Attract System is reinventing bone conduction. Titanium housed implanted magnet fixed into the bone. The external sound processor is connected to the implanted magnet by another external magnet. Baha SoftWear Pad on the external magnet is designed for higher patient comfort and less risk of soft tissue irritations. No directly connected part.

7) ADHERE SYSTEM by MED-EL

Non-implanted bone conduction device

Use not a magnet than a skin adhesive *(ragasztó)*

ADHEAR system has two parts: the adhesive adapter and the audio processor. The thin adhesive adapter sticks to the skin just behind the ear, the audio processor clicks onto this adapter. Its microphones pick up the sounds and then it vibrates the adapter

10. Working principle of the cochlear implants

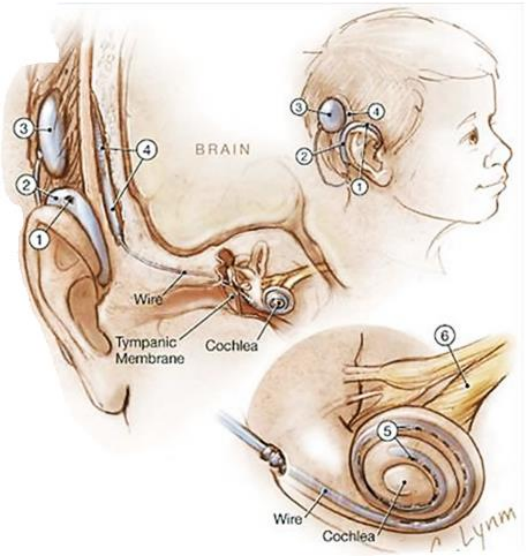
Hearing devices based on ELECTRICAL STIMULATION

- Cochlear implant (CI)
- Auditory brainstem implant (ABI)
- Auditory midbrain implant (AMI)

Cochlear implant

THE MAIN PARTS

1) **Microphone:** receives sound
2) **Speech processor:** process sound into digital information
3) **Transmitter:** relays informations to the implant
4) **Implant:** receives information and sends it as a pattern of electrical impulses through a wire
5) **Electrodes:** at the end of wire stimulate nerve cells inside the cochlea.
    a. It's implanted into the scala tympany through the round window
    b. Stimulate the auditory nerve endings directly
6) **Auditory nerve** sends signal to the brain, which interprets nerve signals as sound



THE ELECTRODE ARRAY

It's not able to go all the way until the end of apex ➔ Lowest frequency parts of the cochlea are not stimulated ➔ Low-freq. hearing is lost. :c / and also has speech understanding disorders/issues.

Properties:

- Length: 20-31.5 mm
- No. of contacts: 22 or higher; no more because of cross-talk and also if electrode size is smaller, it needs current intensity increasing which is not possible beyond a limit. (physical and physiological limiting factors) → Software tricks is needed to achieve better resolution.
- Contact spacing: 0.75-2.4 mm

Stylet technique is used during the implantation, so the damage to the cochlea and pressure for the cochlea walls are minimised.

The implantation is flexible so it can follow the curve of cochlea.

EXTERNAL UNIT (**SPEECH PROCESSOR**)

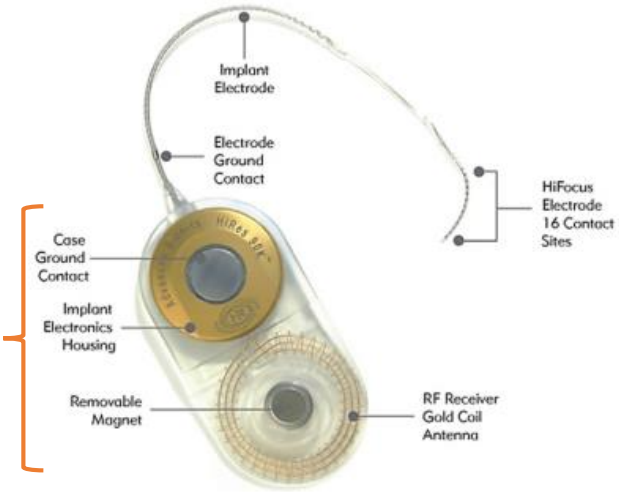
The external unit takes its input from a microphone. It has 3 main components:

- Digital signal processing (DSP) unit
- Power amplifier
- Radio frequency (RF) transmitter, (wireless)

INTERNAL UNIT/**IMPLANT**

- Receiver coil (RF receiver)
- Decoder
- Charge delivery system (stimulator)

This part is implanted behind the ear under the skin.



SAFETY ISSUES

- Power consumption is between 13 and 250 mW (speech processor 10%, RF link 70%, implanted internal unit 20%)

- Power sources: short service life, recharging of batteries on a daily basis

- Normal hearing has a 120 dB dynamic range, 200 discriminable steps and loudness grows as a power function of intensity. A cochlear implant user has a 10-20 dB dynamic range, 20 discriminable steps and loudness grows as an exponential function of electric currents.
Consequence: exposure to loud sound is can be really painful and soft sounds can be impossible to understand.

- Safety issues:

- Sterilization to eliminate infection
- Mechanical design with its potential to cause structural tissue damage
- Using biocompatible and non-toxic materials

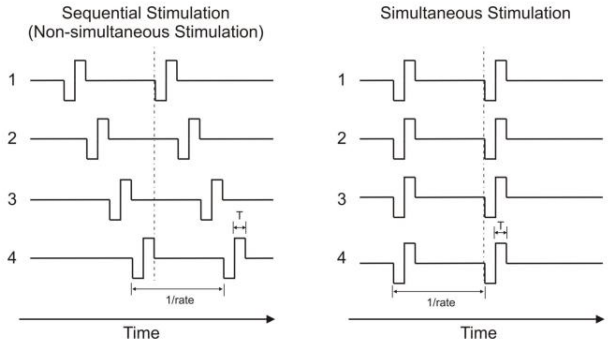
- Electronics and software considerations

11. Stimulation strategies used in cochlear prostheses

ELECTRICAL STIMULATION STRATEGIES

0.1) INTERLEAVED PULSES STIMULATION

Since speech consists of several frequencies → we want to stimulate all of those areas which correspond to the frequencies. (Processor makes freq. decomposition, and sends simultaneous information which electrodes have to be stimulated)



It's an ideal situation but the problem is cross-talk: The electrodes are really close to each other, and there is not enough space for the current to dissipate and not stimulate the nerve endings between the electrodes. In this way, the patient does not hear and understand the speech, just a whole cachofonial frequency.

Solution: Apply a non-simultaneous sequential stimulation with high enough pulse-rate → Brain and nerves will recognise this as would happen at the same time. → rid-off cross-talk.

0.2) STIMULUS PULSE WAVEFORMS

Various signal shapes can be used for electrical stimulation with difference in the amplitude or duration time. Biphasic pulses are the common signal shapes used for stimulation of cochlear implant electrodes to avoid charge accumulation. We don't use monophasic stimulation due to its tissue damaging problems. But instead of biphasic stimulation, it could be triphasic symmetric or triphasic precision stimulation as well.

ELECTRICAL STIMULATION STRATEGIES

Coding temporal information into electrical waveforms:

1. **Analog waveforms** - The acoustic signal is filtered, amplitude compressed and transmitted as an analog signal. Very simple, microphone receives the sound and transforms the signal to the voltage levels, and these voltage levels are the output of the electrodes and that's it. Problem is cross-talk.

2. **Pulse trains/pulse modulation** – The frequency of the pulses corresponds to some frequency in the acoustic signal. Uses interleaved sampling

3. **Amplitude-modulated pulse trains** – The rate of the pulse train is fixed and components of the acoustic signal are selected to modulate the amplitude of the pulse train.

The envelope of the sound is petrically presented by train of pulses in an amplitude modulated way. This is not used currently.

Pulse-width modulated pulse trains

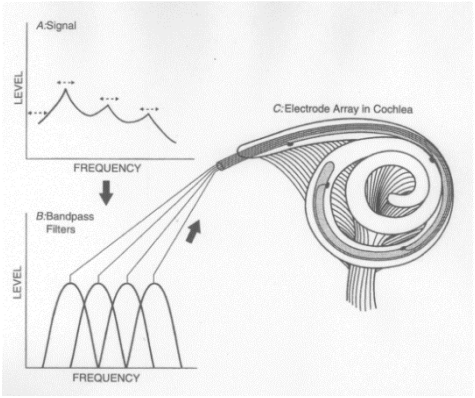
Analog waveform carries the most information. Some temporal detail is lost in the two pulsatile strategies, but they have the advantage that different channels can be stimulated at different times (no problems with current interaction on adjacent channels).

1) SIMULTANEOUS ANALOG STIMULATION (**SAS**)

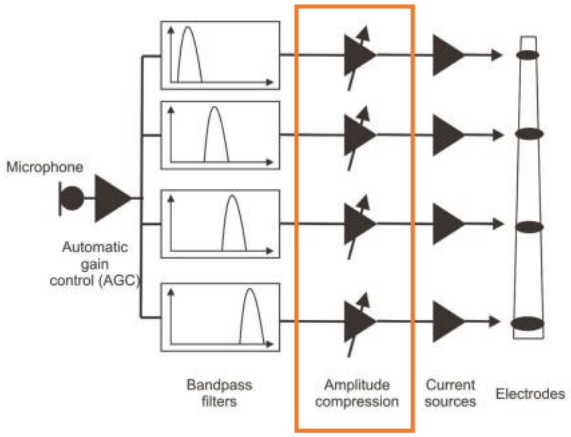
We get the analog input signal and that's put directly to the output, to the electrodes. Do some bandpass filtering to determine which electrodes have to stimulate. The problem is cross-talk.

2) COMPRESSED ANALOG (**CA**) STRATEGY (amplitude compression)

The cross-talk problem is the same in this case as well. It is the very same as SAS just in this case it an amplitude compression step between bandpass filtering and stimulation.



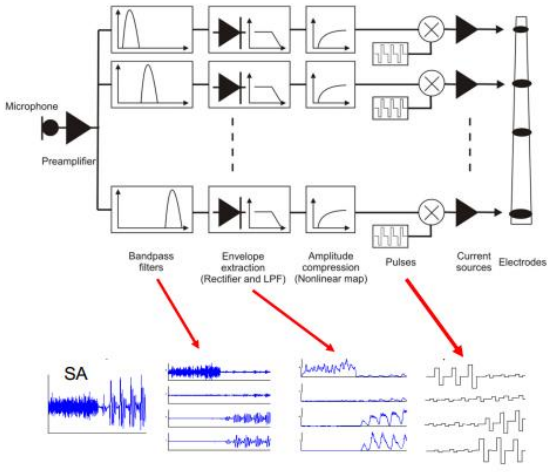
SAS



CA

3) CONTINUOUS INTERLEAVED SAMPLING (**CIS**) STRATEGY

Do bandpass filtering, then envelope extraction and some amplitude compression so let the current stimulation is not too high and it does interleaving of stimuli and it stimulates accordingly. Interleaving: pulses do not come simultaneously at the same time, they interleaved related to each other à cross-talk is minimised. (Simple bandpass filtering end envelope extraction)



4) **F0/F1/F2** STRATEGY

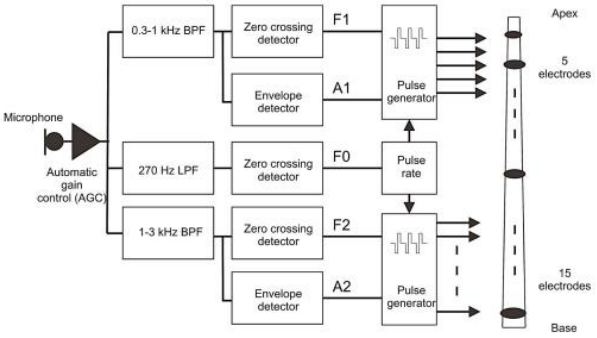
Designed for speech understanding.

In the F0/F1/F2 strategy spectral peaks or formants. (Formants build up the actual speech sound.)

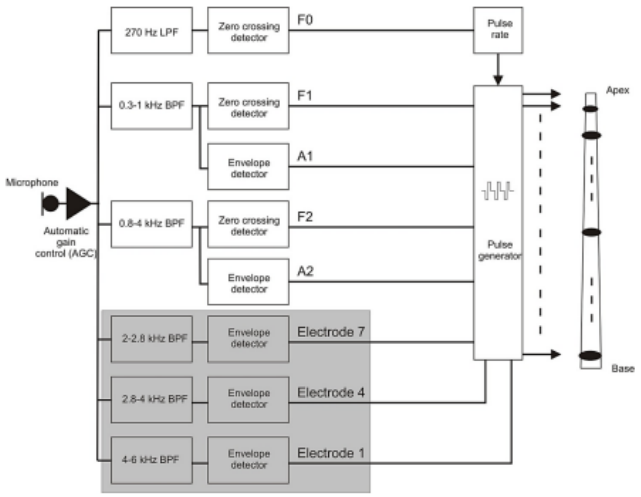
F1 and F2 formants are used for actual electrode determination, which electrodes have to stimulate.

F0: to determine pulse rate because F0 (which is under 270 Hz) can not be stimulated by cochlear implant because can not go high enough. Very useful, because it's a natural weight/property of the sound.

Lags the very high frequencies components of sound



5) MULTIPEAK (MPEAK) STRATEGY



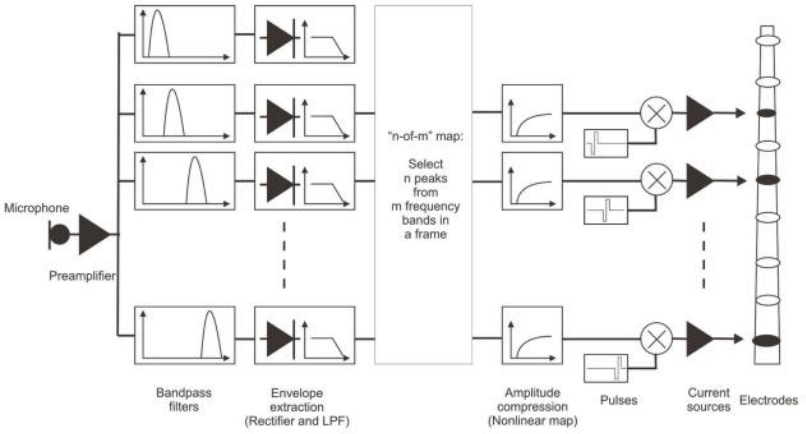
The MPEAK strategy is an improved version of the F0/F1/F2 strategy.

Adds high frequency detectors and stimulations to F0/F1/F2.

This part stimulates the first couple of electrodes, because these are the closest to the base which is the high freq. of cochlea.

Makes speech understanding better.

6) THE **„N-OF-M" STRATEGY** Channel-Picking (CP) strategy



Kind of generalised version of CIS.

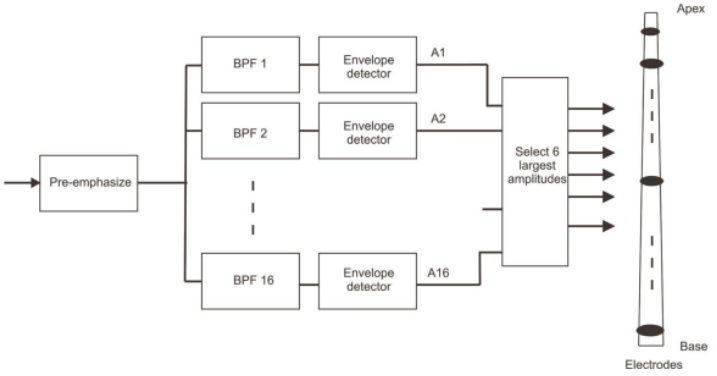
Higher number of bandpass filter is used compared to CIS. The process is similar but it has a threshold to select the „n number" of the highest intensity freq. bands and only stimulate those. Kind of picks the ideal channels to stimulate.

And also use continuous interleaving sampling as discussed before.

7) SPECTRAL MAXIMA SOUND PROCESSOR (**SMSP**) STRATEGY

Kind of n-of-m.

The SMSP strategy analyses **the speech waveform** instead of extracting features from the signal. It uses **16 band-pass filters** and a spectral maxima detector. Sound signal is processed through the bank of 16 band-pass filters. After envelope detection the **six largest envelope** outputs are selected for stimulation. The selected amplitudes are logarithmically compressed and transmitted to the six selected electrodes through the RF link. The largest envelopes are not

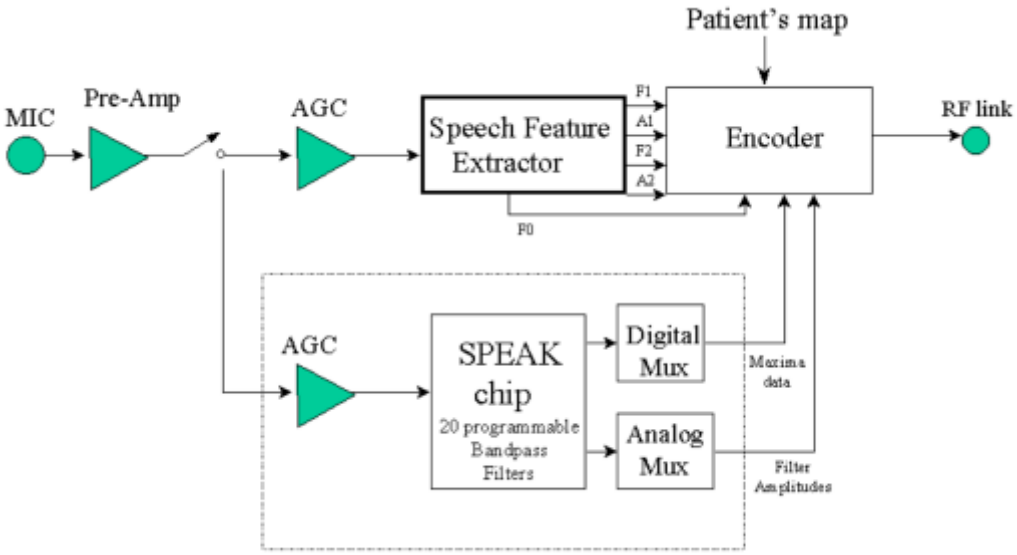


necessarily the spectral peaks, several „maxima" may come from a single spectral peak. Six interleaved (non-simultaneous) biphasic pulses are delivered to the selected electrodes.

Uses 16 bandpass filters, then detect envelope and selects the 6 largest amplitude. So it only has a difference in numbers compared to the n-of-m (n-of-m uses more bandpass filter and the output is also more).

All of these strategies are implemented in a general cochlear implant and these can be dynamically changed based on user experiences.

8) SPECTRAL PEAK (SPEAK) STRATEGY



Several chips.

Speech Feature Extractor: this is very similar to the filter banks in the case of F0/F1/F2 or Multi Peak.

Then programable bandpass filter in the peak that put in the Encoder that builds a map of the patient. ??

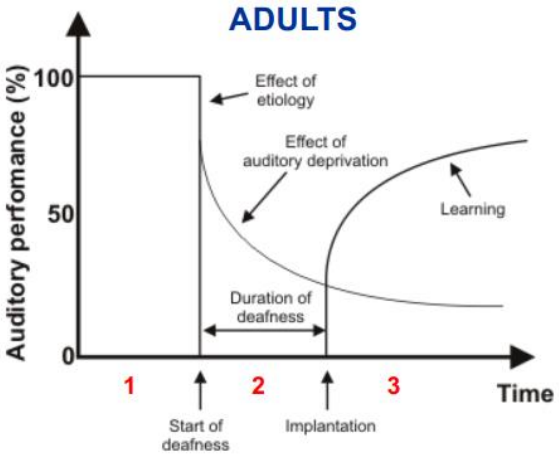
So SPEAK has not fix bandpass filtering, continously computes the bandpass filter boundaries according to the incoming sound. It can dynamically adapt to the stimulus.

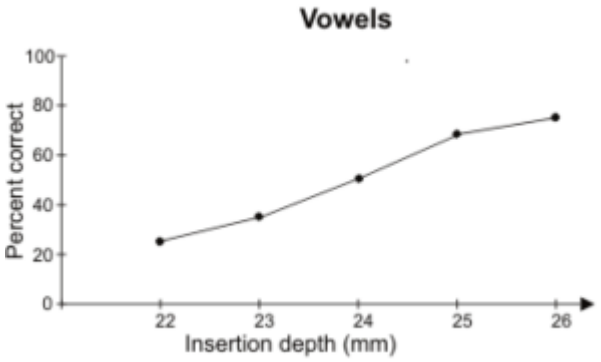
Kind of adapting filter bank that is what spectral peak uses.

And then 5-10 selected spectro maxima is used for stimulation.

AUDITORY PERFORMANCE

Several factors are involved in the performance of the implant users. The three-stage model of auditory performance (AP) for postlingually deafened adults. Stage 1 begins after normal language development. (AP around 100%) Stage 2 begins at the onset of deafness. (immediate drop in the AP and a further decrease until implantation) Stage 3 begins with the implantation (increase in the AP, and rises further as a result of learning and experience).





The most difficult task is to understand vowels, because it has low freq. components, so the F0 part/ first formant is a low freq. component that standard electrodes are sometimes unable to stimulate.

Company Name	Company Headquarters
Cochlear	Australia
Med-El	Austria
Advanced Bionics	USA

SPEECH PERCEPTION IN CHILDREN

Age is extremely crucial for the child's language and cognitive development, therefore implantations in childhood have very good results. It helps the children to be able to speak clearly and able to understand speech. Both prelingually and postlingually deafened children benefit from CI. Prelingually deafened children acquire speech production and speech perception skills at a slower rate. Children have already experienced hearing before they start to speak.

MUSIC RECOGNITION WITH COCHLEAR IMPLANT

Music understanding is much more difficult with CI.

- Rhythm: is easy to understand and hear
- Melodies: It's more difficult than rhythm, but it somewhat can be understood
- Chords: Very difficult to understand
- Instruments: Very difficult to understand

It's because of limited number of electrodes. Music is composed very high number of freq.s.

By ADVANCED BIONICS company has a solution (HiRes 120): They would like to increase the resolution of stimulation without increasing the number of electrodes. And the way that they do this is that interleave sampling is achieved by overlapping stimulations with different amplitudes. So they don't just only turn on and off the electrodes but it's kind of modulating amplitude of the stimulation also. And sometimes neighboring electrodes are stimulated which could lead to cross-talk, but they balance the stimulation intensity correctly and it aids to resolution instead of cross-talk. → Better experience.

FUTURE PROSPECTS

- Use of otoprotective drugs (against electrode insertion trauma, cellular, molecular damage, necrosis, apoptosis)
- Improvements in electrode design
- Improvements in sound processing strategies
- Use of stem cells to replace lost sensory hair cells and neural structures in the cochlea
- Gene therapy - recruits undamaged endogenous cells at the location of damage within the cochlea to develop into hair cell like cells
- Optical stimulation of the auditory nerve

OPTICAL STIMULATION OF THE AUDITORY NERVE

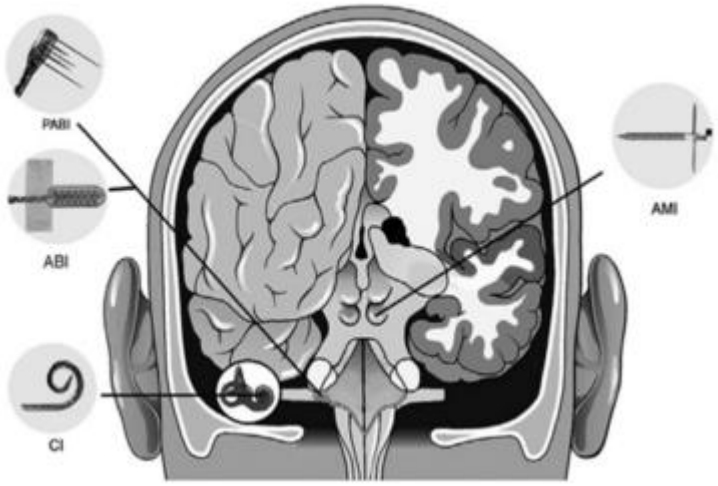
Implant infrared LED array and the long wavelength infrared light induce temperature changes that actually stimulate the cells in the cochlea. In this way, we can achieve high resolution and precise stimulation. It is proved in several animal species, but not yet in humans.

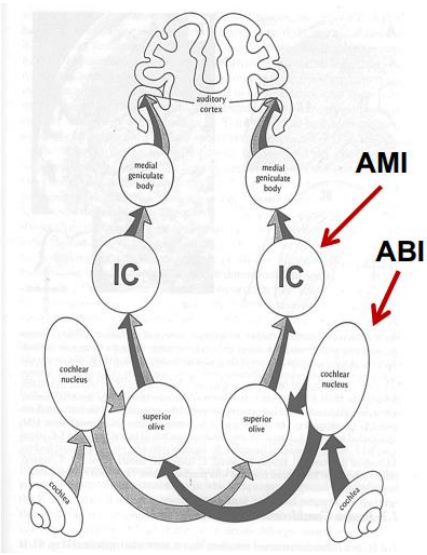
Different auditory neural prosthetics are used in patients for hearing restoration.

CI: Cochlear Implant, which consists of an electrode array that is implanted in the cochlea and used for auditory nerve stimulation.

ABI: Auditory Brainstem Implant that is used for surface stimulation of the cochlear nucleus.

AMI: Auditory Midbrain Implant that is used for penetrating stimulation of the auditory midbrain (i.i.: the inferior colliculus).





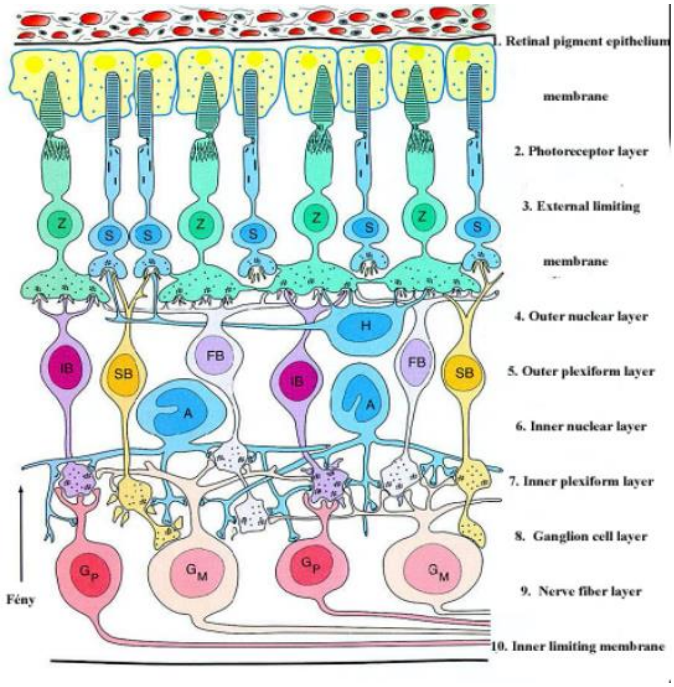
In cases when there is a tumor in/near the auditory nerve or in the auditory midbrain the cochlear implants are useless. Even the stimulation of the tumor presses the nerve and it's unable the transmit the stimulation to higher brain areas.

12. Retinal prostheses

BIOLOGICAL BASICS[1]

1) The Structure of the Eye

Most important part of the eye is the retina, which is the inner layer of the eyeball. From the retina, optic nerves get information and leads to this information for the central nervous system.



Several different layers:

- photoreceptor layer maintains the neurons which are sensitive to the light, the layer that captures the photons, it transforms the information into electrical and chemical signals.
- outer nuclear layer
- outer plexiform layer
- inner nuclear layer
- inner plexiform layer
- ganglion cell layer

Cell types:

- light sensitive photoreceptors
  - **Cones:** they can differentiate between colors
    - blue cone
    - green cone
    - red cone
  - **Rods:** more sensitive than cones, is responsible for ensuring that we can see in low light
- interneurons of the retina
  - bipolar cells: they connect the photoreceptors directly to the ganglion cells and transmit information between them.
  - horizontal cells: they have laterally running dendritic fibers connecting the photoreceptors, they are inhibitory interneurons (they connect to retinal cells in one half of the retina) connecting to cells of the outer retina.
  - amacrine cells: inhibitory interneurons with laterally running dendrites, connecting to cells of the inner retina.
- ganglion cells ("output neurons")

Fovea: region which has high density of rods and cones, it is responsible for sharp vision.

Blind spot: where the optic nerve escapes the eyeball (no cones, no rods)

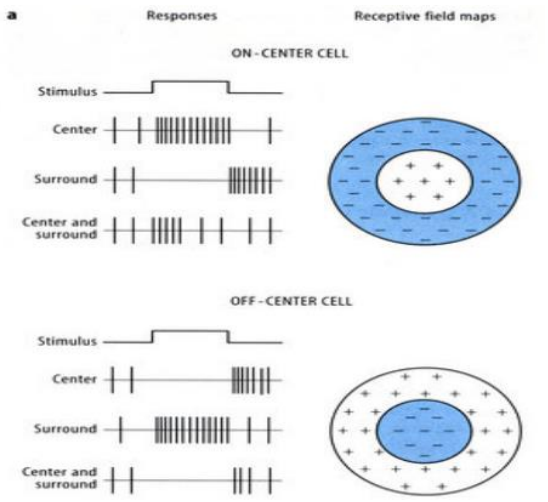
Macula: dense with cones and rods.

Light has to travel through all the cell layers because photoreceptor cells are in the backside of the retina.

1 Based on **Introduction to Functional Neurobiology** notes by Csomai Borbála and Kastal Csilla Noémi

Several cell layers are used to extract cellular features of the visual input. (Ganglion cells transmit these extracted features to the brain.)

For example ON- and OFF-BIPOLAR cells.



- Ganglion cells inherit the receptive field from the direct connection to bipolar cells
- On-centre ganglion cells
  - if light stimulation occurs in the center receptive field, it will activate the ganglion cell
- off-center ganglion cells
  - when there is light in the center, we expect inactivation
- the contrast detection, which is created by the bipolar cells is inherited by certain ganglion cells

Some of them respond to light stimuli with increasing cell activity while others respond to light increasing with decreasing activity.

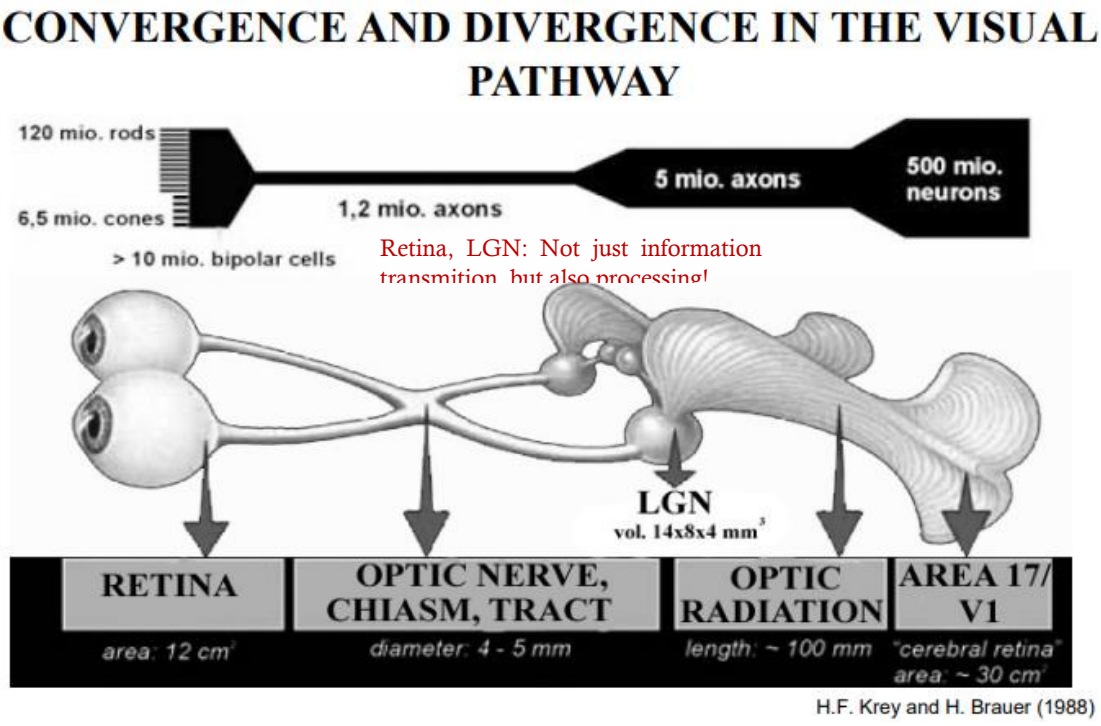
It is used when the stimuli are moving from one spot to the other the activity of these cells is changing so the information of illumination changing can be detected by these cells and information can be transmitted by the ganglion cells of the brain.

Retina does not only transmit visual information, it also does processing!

2) The visual pathway

eye → retina → optic nerve → Lateral Geniculate Nucleus (LGN) (6 layers) → visual cortices → higher order cortices

Some visual information from the eyes is crossed in the optic chiasm but others are not.



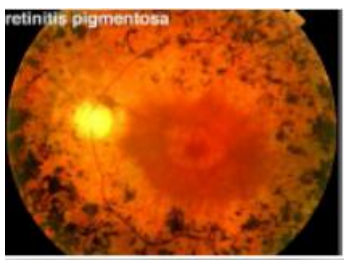
H.F. Krey and H. Brauer (1988)

RETINAL DISEASES AND DEGENERATIONS

Age-related macula degeneration (AMD),

- Light dots can be seen on the macula region
- Central sharp vision is gone, peripheral vision remains, impact for life quality

Retinitis pigmentosa (RP),



- Progressive loss of rod photoreceptor cells that line the retina of the eyeball.
- Black dots around the retina
- Peripheral vision is gone and some central vision remains,
- From the outside spreads towards inside
- Both can lead total blindness

Choroideremia

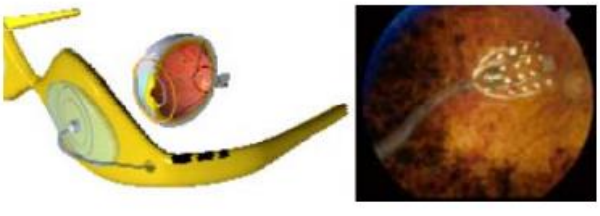
VISUAL IMPLANTS

- Retinal prostheses
  - Epiretinal
  - Subretinal
- Cortical implants
- Optic nerve
- Other solutions

EPIRETILAN IMPLANTS

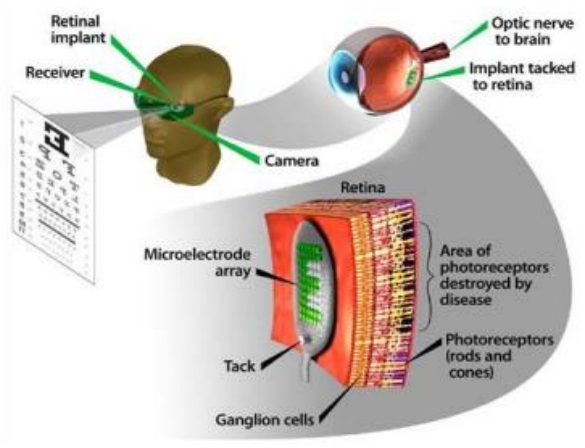
Epiretinal implants are put on the ganglion cell layer, so the inner side of the retina. Does not use the computational power of the retina itself → when designing the stimulation this should be taken into account.

There is a camera that puts on the glasses, that the patient wear. The camera records the visual stimulus, and there is also a computer worn by the patient, which computes the stimulation parameters from the inputs.



There is a wireless transmitter that transmits the actual power and stimulus pattern to the epiretinal implant.

1) **Second sight ARGUS** is the most widespread.



USA

Extra-ocular processing; only electrode array inside the eye:

Based on proven cochlear implant technology

- Six patients implanted with 4x4 array
- External camera and image processor
- Psychophysics in progress
- Today: 60 electrodes on a single chip

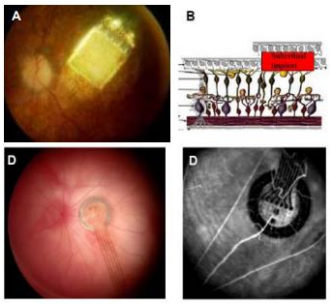
2) THE EPIRET TRIAL (P Walter, Mokwa, Schanze), Aachen, Giessen, Germany.

Only have 25 electrodes and it was only implanted in 6 blind volunteers.

SUBRETINAL IMPLANTS

The devices themselves are put behind the retina, next to the bipolar cells. Uses the whole retina computation power, a much more developed solution. It has much better resolution than epiretinal ones, more than 1500 pixels.

1) RETINA IMPLANT PILOT STUDY (E Zrenner), Tübingen Germany

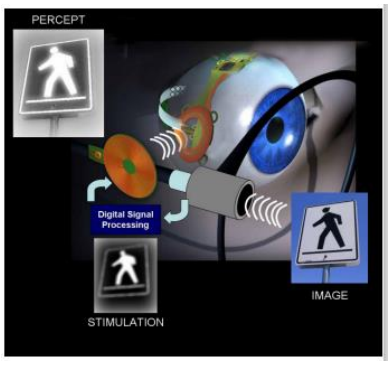


from 2005: 11 patients implanted.

– Resolution: 1520 pixels (40x38)

– Result: lines, lights, visual feeling, more grey tone, moving-, and some daily stuff were recognized.

2) BOSTON RETINA IMPLANT (J. Rizzo) Boston, USA



It has a receiver in the eyeball and an implant behind the retina. Use a camera also to record the image, and then the recorded information is sent to the receiver coil which stimulates the implant.

Needle-like electrodes stimulate the retina.

Wireless receiver on the eye .

Transimt power also from the external stimulator devices to this receiver coil, not just stimulation pattern.

3) PIXIUM VISION (Paris, France)

Produces both epiretinal and Subretinal implants.

Epiretinal:

- Epi-retinal implant (attached to the surface of the retina)
- 150 electrodes
- Designed for explantability
- Bioinspired camera sensor

Subretinal:

A tiny wireless photovoltaic implant, comprising 378 electrodes, each with its own local return circuit potentially enabling higher resolution.

Photovoltaic means using the power of light to stimulate the retina, it works more or less, it also needs external power.

	EPIRETINAL	SUBRETINAL
Pros	• Stimulating close to the photoreceptors so one can take advantage of native processing power in thalamus and cortex. • Surgical complications not necessarily as significant as cortical approach.	• Stimulating closest to the photoreceptors so one can take advantage of retinal, thalamic and cortical signal processing. • If bipolar cells can be directly stimulated, retinotopic organization should be preserved. • Surgical complications not necessarily as significant as cortical approach.
Cons	• Requires functional optic nerve pathway. • May stimulate optic nerve fibers rather than cell bodies: this will greatly complicate visuotopic organization. • Hard to imagine how saccadic eye motions will not cause very high sheer loads on implanted arrays (and eventual dislodging of array). • Difficult surgical access. • Difficult to adhere electrode array to retina.	• Requires functional optic nerve pathway to convey signals to cortex. • Blockage of nutrients from choroid to remnant retina by the implant. • Very complex surgical access. • Can't stimulate cells passively with micro implants (requires external power).

CORTICAL IMPLANTS

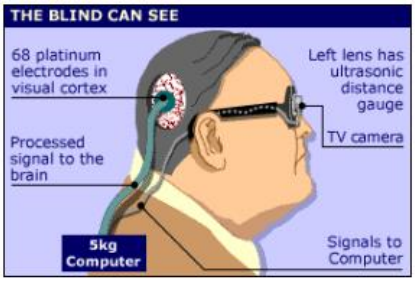
Very complex processes and computation going along through the visual pathway until it reaches the visual cortex.

The cortical map is completely distorted compared to the retinal percept. Realy carefully have to design the stimulation pattern.

The concept is to stimulate the primary visual cortex and all the other computations can be done already by the brain itself („where and what pathway")

The Two Streams hypothesis is a widely accepted, but still controversial, account of visual processing. As visual information exits the occipital lobe, it follows two main channels, or "streams". The ventral travels to the temporal lobe and is involved with object identification. The dorsal stream (or, "where pathway") terminates in the parietal lobe and processes spatial locations.

1) Cortical implants by William Dobelle



Also used camera and a computer and a wire goes into the brain through the skin and skull connecting to the stimulator electrodes put on the primary visual cortex.

Nobody could repeat his results.

2) Second Sight Orion I visual cortex implant

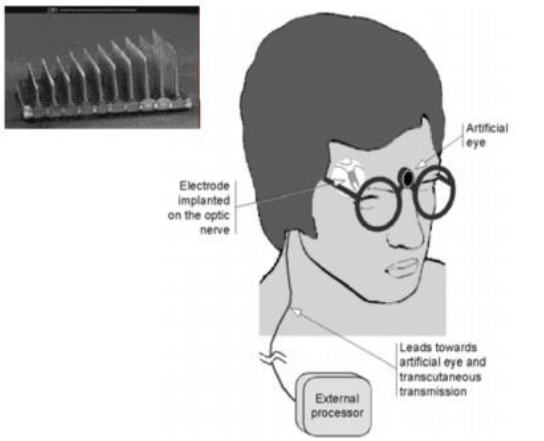
- 60 channels

- Implanted between the two visual cortices → two sides can be stimulated

- Uses wireless power transmission → Decrease infection risk.

OTHER SOLUTIONS:

1) Concept of the optic nerve stimulation



Variation of Utah electrode array

Around 100 electrodes, just the high of the needle is different from each other. Each row is a bit longer than the previous one so nicely can fit to the optic nerve.

Whole stimulation process is similar, so:

- Camera
- External processor
- Wired or wireless stimulator on the optic nerve

Other devices:

4-8 electrodes in he cuff around the optic nerve

Light-dark, direction, and stimulus strength can be learned → limited capacity

2) BRAINPORT

Tongue stimulator

Non-invasive

Use brain plasticity