Brain-Computer Interfacing and Applications

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Brain–Computer Interface

A **brain–computer interface** (**BCI**), sometimes called a **direct neural interface** or a **brain–machine interface**, is a direct communication pathway between a brain and an external device. BCIs are often aimed at assisting, augmenting or repairing human cognitive or sensory-motor functions.

Research on BCIs began in the 1970s at the University of California Los Angeles (UCLA) under a grant from the National Science Foundation, followed by a contract from DARPA. The papers published after this research also mark the first appearance of the expression *brain–computer interface* in scientific literature.

The field of BCI research and development has since focused primarily on neuroprosthetics applications that aim at restoring damaged hearing, sight and movement. Thanks to the remarkable cortical plasticity of the brain, signals from implanted prostheses can, after adaptation, be handled by the brain like natural sensor or effector channels. Following years of animal experimentation, the first neuroprosthetic devices implanted in humans appeared in the mid-nineties.

BCI versus neuroprosthetics

Neuroprosthetics is an area of neuroscience concerned with neural prostheses—using artificial devices to replace the function of impaired nervous systems and brain related problems or sensory organs. The most widely used neuroprosthetic device is the cochlear implant, which, as of 2006, has been implanted in approximately 100,000 people worldwide. There are also several neuroprosthetic devices that aim to restore vision, including retinal implants.

The differences between BCIs and neuroprosthetics are mostly in the ways the terms are used: neuroprosthetics typically connect the nervous system to a device, whereas BCIs usually connect the brain (or nervous system) with a computer system. Practical neuroprosthetics can be linked to any part of the nervous system—for example, peripheral nerves—while the term "BCI" usually designates a narrower class of systems which interface with the central nervous system.

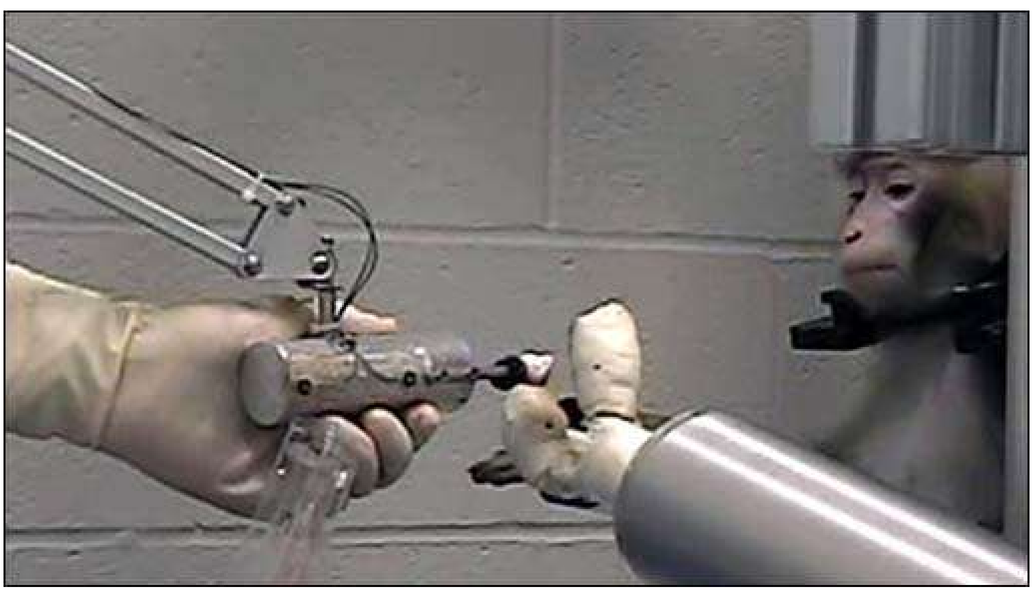
The terms are sometimes used interchangeably. Neuroprosthetics and BCIs seek to achieve the same aims, such as restoring sight, hearing, movement, ability to communicate, and even cognitive function. Both use similar experimental methods and surgical techniques.

Animal BCI research

Rats implanted with BCIs in Theodore Berger's experiments

Several laboratories have managed to record signals from monkey and rat cerebral cortices in order to operate BCIs to carry out movement. Monkeys have navigated computer cursors on screen and commanded robotic arms to perform simple tasks simply by thinking about the task and without any motor output. In May 2008 photographs that showed a monkey operating a robotic arm with its mind at the Pittsburgh University Medical Center were published in a number of well known science journals and magazines. Other research on cats has decoded visual signals.

Early work



Monkey operating a robotic arm with brain–computer interfacing

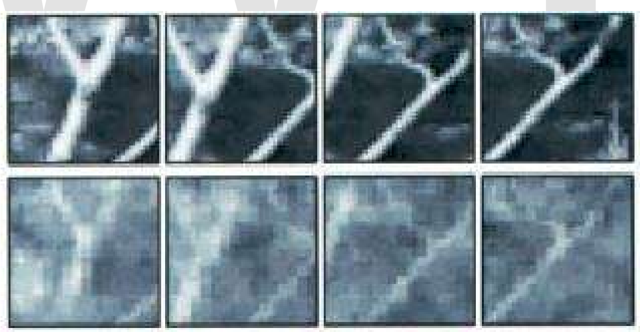
The operant conditioning studies of Fetz and colleagues first showed that monkeys could learn to control the deflection of a biofeedback meter arm with neural activity . Such work in the 1970s established that monkeys could quickly learn to voluntarily control the firing rates of individual and multiple neurons in the primary motor cortex if they were rewarded for generating appropriate patterns of neural activity.

Studies that developed algorithms to reconstruct movements from motor cortex neurons, which control movement, date back to the 1970s. In the 1980s, Apostolos Georgopoulos at Johns Hopkins University found a mathematical relationship between the electrical responses of single motor-cortex neurons in rhesus macaque monkeys and the direction that monkeys moved their arms (based on a cosine function). He also found that dispersed groups of neurons in different areas of the brain collectively controlled motor commands but was only able to record the firings of neurons in one area at a time because of technical limitations imposed by his equipment.

There has been rapid development in BCIs since the mid-1990s. Several groups have been able to capture complex brain motor centre signals using recordings from neural ensembles (groups of neurons) and use these to control external devices, including research groups led by Richard Andersen, John Donoghue, Phillip Kennedy, Miguel Nicolelis, and Andrew Schwartz.

Prominent research successes

Phillip Kennedy and colleagues built the first intracortical brain–computer interface by implanting neurotrophic-cone electrodes into monkeys.



Yang Dan and colleagues' recordings of cat vision using a BCI implanted in the lateral geniculate nucleus (top row: original image; bottom row: recording)

In 1999, researchers led by Yang Dan at University of California, Berkeley decoded neuronal firings to reproduce images seen by cats. The team used an array of electrodes embedded in the thalamus (which integrates all of the brain’s sensory input) of sharp-eyed cats. Researchers targeted 177 brain cells in the thalamus lateral geniculate nucleus area, which decodes signals from the retina. The cats were shown eight short movies, and their neuron firings were recorded. Using mathematical filters, the researchers decoded the signals to generate movies of what the cats saw and were able to reconstruct recognizable scenes and moving objects. Similar results in humans have been since then achieved by researchers in Japan.

Miguel Nicolelis has been a prominent proponent of using multiple electrodes spread over a greater area of the brain to obtain neuronal signals to drive a BCI. Such neural ensembles are said to reduce the variability in output produced by single electrodes, which could make it difficult to operate a BCI.

After conducting initial studies in rats during the 1990s, Nicolelis and his colleagues developed BCIs that decoded brain activity in owl monkeys and used the devices to reproduce monkey movements in robotic arms. Monkeys have advanced reaching and grasping abilities and good hand manipulation skills, making them ideal test subjects for this kind of work.

By 2000, the group succeeded in building a BCI that reproduced owl monkey movements while the monkey operated a joystick or reached for food. The BCI operated in real time and could also control a separate robot remotely over Internet protocol. But the monkeys could not see the arm moving and did not receive any feedback, a so-called open-loop BCI.

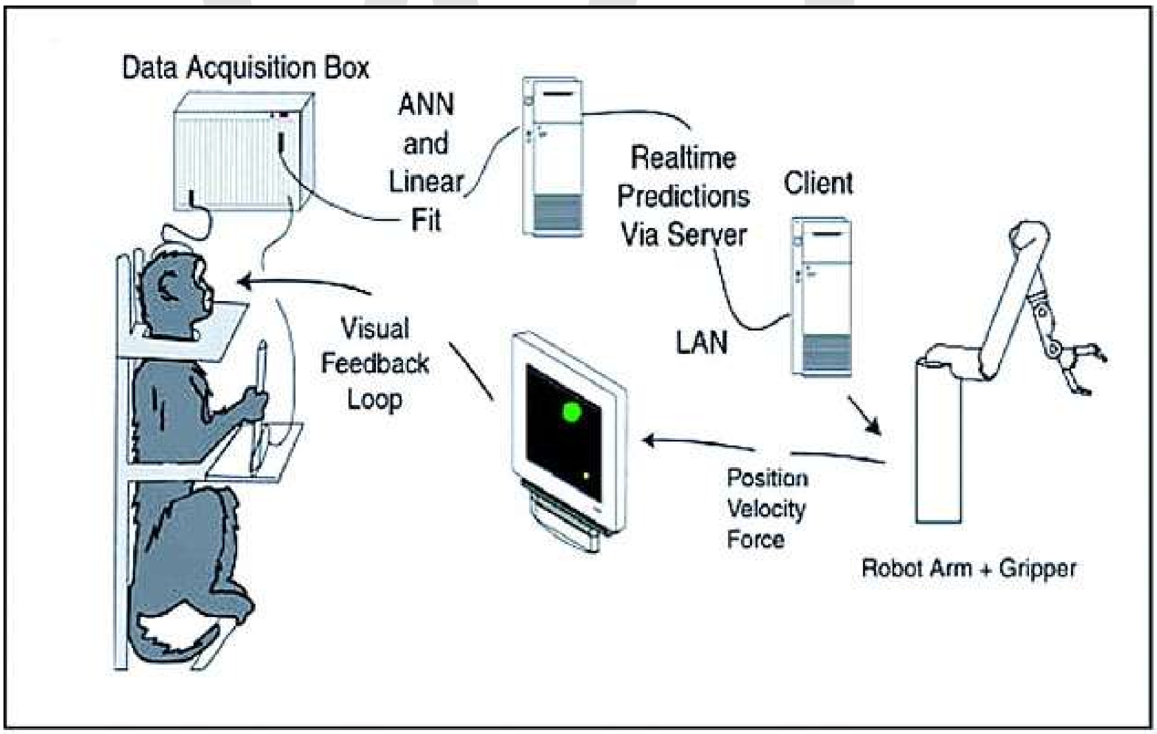


Diagram of the BCI developed by Miguel Nicolelis and colleagues for use on Rhesus monkeys

Later experiments by Nicolelis using rhesus monkeys, succeeded in closing the feedback loop and reproduced monkey reaching and grasping movements in a robot arm. With their deeply cleft and furrowed brains, rhesus monkeys are considered to be better models for human neurophysiology than owl monkeys. The monkeys were trained to reach and grasp objects on a computer screen by manipulating a joystick while corresponding movements by a robot arm were hidden. The monkeys were later shown the robot directly and learned to control it by viewing its movements. The BCI used velocity predictions to control reaching movements and simultaneously predicted hand gripping force.

Other labs that develop BCIs and algorithms that decode neuron signals include John Donoghue from Brown University, Andrew Schwartz from the University of Pittsburgh and Richard Andersen from Caltech. These researchers were able to produce working BCIs even though they recorded signals from far fewer neurons than Nicolelis (15–30 neurons versus 50–200 neurons).

Donoghue's group reported training rhesus monkeys to use a BCI to track visual targets on a computer screen with or without assistance of a joystick (closed-loop BCI). Schwartz's group created a BCI for three-dimensional tracking in virtual reality and also reproduced BCI control in a robotic arm. The group created headlines when they demonstrated that a monkey could feed itself pieces of zucchini using a robotic arm controlled by the animal's own brain signals.

Andersen's group used recordings of premovement activity from the posterior parietal cortex in their BCI, including signals created when experimental animals anticipated receiving a reward.

In addition to predicting kinematic and kinetic parameters of limb movements, BCIs that predict electromyographic or electrical activity of muscles are being developed. Such BCIs could be used to restore mobility in paralyzed limbs by electrically stimulating muscles.

Miguel Nicolelis *et al.* showed that activity of large neural ensembles can predict arm position. This work made possible creation of brain–machine interfaces — electronic devices that read arm movement intentions and translate them into movements of artificial actuators. Carmena et al. programmed the neural coding in a brain–machine interface allowed a monkey to control reaching and grasping movements by a robotic arm, and Lebedev *et al.* argued that brain networks reorganize to create a new representation of the robotic appendage in addition to the representation of the animal's own limbs.

The biggest impediment of BCI technology at present is the lack of a sensor modality that provides safe, accurate, and robust access to brain signals. It is conceivable or even likely that such a sensor will be developed within the next twenty years. The use of such a sensor should greatly expand the range of communication functions that can be provided using a BCI.

Development and implementation of a Brain–Computer Interface (BCI) system is complex and time consuming. In response to this problem, Dr. Gerwin Schalk has been developing a general-purpose system for BCI research, called BCI2000. BCI2000 has been in development since 2000 in a project led by the Brain–Computer Interface R&D Program at the Wadsworth Center of the New York State Department of Health in Albany, New York, USA.

A new 'wireless' approach uses light-gated ion channels such as Channelrhodopsin to control the activity of genetically defined subsets of neurons in vivo. In the context of a simple learning task, illumination of transfected cells in the somatosensory cortex influenced the decision making process of freely moving mice.

Human BCI research

Invasive BCIs

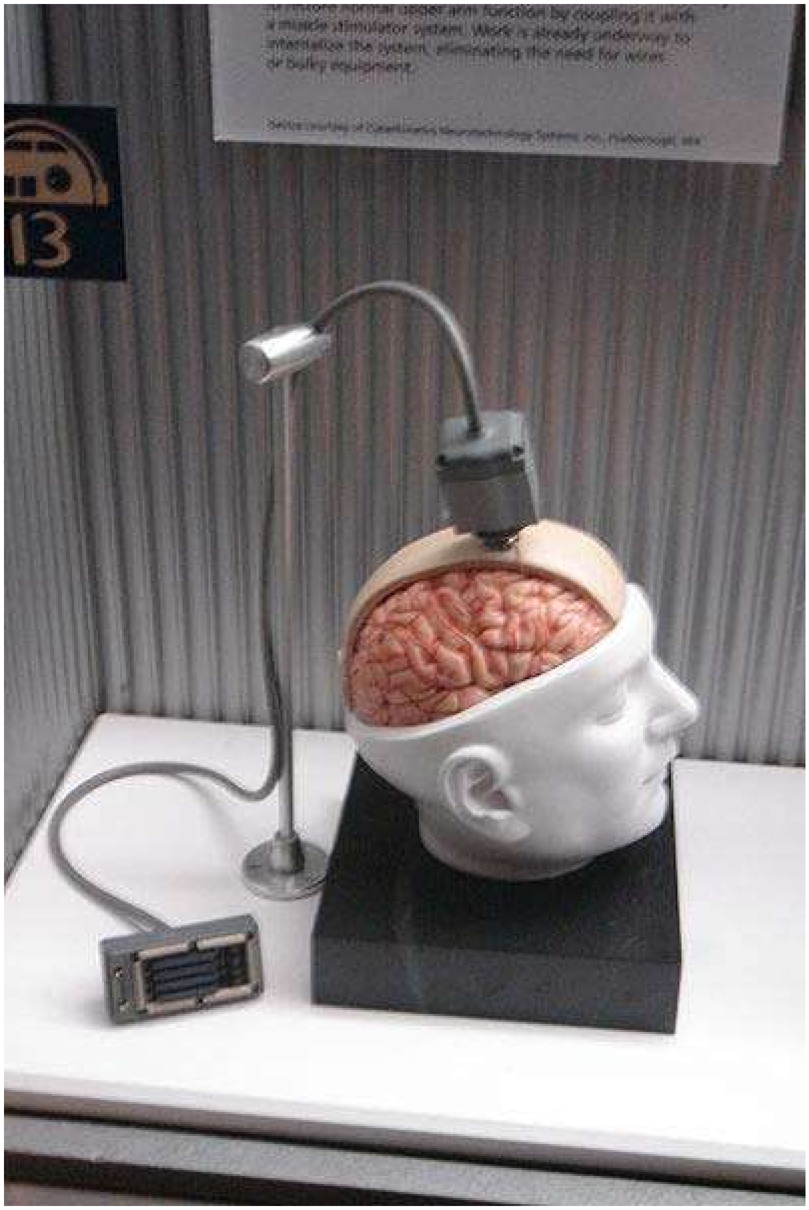
Invasive BCI research has targeted repairing damaged sight and providing new functionality to persons with paralysis. Invasive BCIs are implanted directly into the grey matter of the brain during neurosurgery. As they rest in the grey matter, invasive devices produce the highest quality signals of BCI devices but are prone to scar-tissue build-up, causing the signal to become weaker or even lost as the body reacts to a foreign object in the brain.

Jens Naumann, a man with acquired blindness, being interviewed about his vision BCI on CBS's The Early Show

In *vision science*, direct brain implants have been used to treat non-congenital (acquired) blindness. One of the first scientists to come up with a working brain interface to restore sight was private researcher William Dobelle.

Dobelle's first prototype was implanted into "Jerry", a man blinded in adulthood, in 1978. A single-array BCI containing 68 electrodes was implanted onto Jerry’s visual cortex and succeeded in producing phosphenes, the sensation of seeing light. The system included cameras mounted on glasses to send signals to the implant. Initially, the implant allowed

Jerry to see shades of grey in a limited field of vision at a low frame-rate. This also required him to be hooked up to a two-ton mainframe, but shrinking electronics and faster computers made his artificial eye more portable and now enable him to perform simple tasks unassisted.



Dummy unit illustrating the design of a BrainGate interface

In 2002, Jens Naumann, also blinded in adulthood, became the first in a series of 16 paying patients to receive Dobelle's second generation implant, marking one of the earliest commercial uses of BCIs. The second generation device used a more sophisticated implant enabling better mapping of phosphenes into coherent vision. Phosphenes are spread out across the visual field in what researchers call the starry-night effect. Immediately after his implant, Jens was able to use his imperfectly restored vision to drive slowly around the parking area of the research institute.

BCIs focusing on *motor neuroprosthetics* aim to either restore movement in individuals with paralysis or provide devices to assist them, such as interfaces with computers or robot arms.

Researchers at Emory University in Atlanta led by Philip Kennedy and Roy Bakay were first to install a brain implant in a human that produced signals of high enough quality to simulate movement. Their patient, Johnny Ray (1944–2002), suffered from 'locked-in syndrome' after suffering a brain-stem stroke in 1997. Ray's implant was installed in 1998 and he lived long enough to start working with the implant, eventually learning to control a computer cursor; he died in 2002 of a brain aneurysm.

Tetraplegic Matt Nagle became the first person to control an artificial hand using a BCI in 2005 as part of the first nine-month human trial of Cyberkinetics Neurotechnology's BrainGate chip-implant. Implanted in Nagle's right precentral gyrus (area of the motor cortex for arm movement), the 96-electrode BrainGate implant allowed Nagle to control a robotic arm by thinking about moving his hand as well as a computer cursor, lights and TV. One year later, professor Jonathan Wolpaw received the prize of the Altran Foundation for Innovation to develop a Brain Computer Interface with electrodes located on the surface of the skull, instead of directly in the brain.

Partially-invasive BCIs

Partially invasive BCI devices are implanted inside the skull but rest outside the brain rather than within the grey matter. They produce better resolution signals than non-invasive BCIs where the bone tissue of the cranium deflects and deforms signals and have a lower risk of forming scar-tissue in the brain than fully-invasive BCIs.

Electrocorticography (ECoG) measures the electrical activity of the brain taken from beneath the skull in a similar way to non-invasive electroencephalography (see below), but the electrodes are embedded in a thin plastic pad that is placed above the cortex, beneath the dura mater. ECoG technologies were first trialed in humans in 2004 by Eric Leuthardt and Daniel Moran from Washington University in St Louis. In a later trial, the researchers enabled a teenage boy to play Space Invaders using his ECoG implant. This research indicates that control is rapid, requires minimal training, and may be an ideal tradeoff with regards to signal fidelity and level of invasiveness.

(Note: These electrodes were not implanted in the patients for BCI experiments. The patient was suffering from severe epilepsy and had the electrodes temporarily implanted to help his physicians localize seizure foci; the researchers simply took advantage of this.)

Light Reactive Imaging BCI devices are still in the realm of theory. These would involve implanting a laser inside the skull. The laser would be trained on a single neuron and the neuron's reflectance measured by a separate sensor. When the neuron fires, the laser light pattern and wavelengths it reflects would change slightly. This would allow researchers to monitor single neurons but require less contact with tissue and reduce the risk of scar-tissue build-up.

This signal can be either subdural or epidural, but is not taken from within the brain parenchyma itself. It has not been studied extensively until recently due to the limited access of subjects. Currently, the only manner to acquire the signal for study is through the use of patients requiring invasive monitoring for localization and resection of an epileptogenic focus.

ECoG is a very promising intermediate BCI modality because it has higher spatial resolution, better signal-to-noise ratio, wider frequency range, and lesser training requirements than scalp-recorded EEG, and at the same time has lower technical difficulty, lower clinical risk, and probably superior long-term stability than intracortical single-neuron recording. This feature profile and recent evidence of the high level of control with minimal training requirements shows potential for real world application for people with motor disabilities.

Non-invasive BCIs

As well as invasive experiments, there have also been experiments in humans using non-invasive neuroimaging technologies as interfaces. Signals recorded in this way have been used to power muscle implants and restore partial movement in an experimental volunteer. Although they are easy to wear, non-invasive implants produce poor signal resolution because the skull dampens signals, dispersing and blurring the electromagnetic waves created by the neurons. Although the waves can still be detected it is more difficult to determine the area of the brain that created them or the actions of individual neurons.

EEG

Recordings of brainwaves produced by an electroencephalogram

Electroencephalography (EEG) is the most studied potential non-invasive interface, mainly due to its fine temporal resolution, ease of use, portability and low set-up cost. But as well as the technology's susceptibility to noise, another substantial barrier to using EEG as a brain–computer interface is the extensive training required before users can work the technology. For example, in experiments beginning in the mid-1990s, Niels Birbaumer of the University of Tübingen in Germany trained severely paralysed people to self-regulate the *slow cortical potentials* in their EEG to such an extent that these signals could be used as a binary signal to control a computer cursor. (Birbaumer had earlier trained epileptics to prevent impending fits by controlling this low voltage wave.) The experiment saw ten patients trained to move a computer cursor by controlling their brainwaves. The process was slow, requiring more than an hour for patients to write 100 characters with the cursor, while training often took many months.

Another research parameter is the type of waves measured. Birbaumer's later research with Jonathan Wolpaw at New York State University has focused on developing technology that would allow users to choose the brain signals they found easiest to operate a BCI, including *mu* and *beta* rhythms.

A further parameter is the method of feedback used and this is shown in studies of P300 signals. Patterns of P300 waves are generated involuntarily (stimulus-feedback) when people see something they recognize and may allow BCIs to decode categories of thoughts without training patients first. By contrast, the biofeedback methods described above require learning to control brainwaves so the resulting brain activity can be detected.

Lawrence Farwell and Emanuel Donchin developed an EEG-based brain–computer interface in the 1980s. Their "mental prosthesis" used the P300 brainwave response to allow subjects, including one paralyzed Locked-In syndrome patient, to communicate words, letters, and simple commands to a computer and thereby to speak through a speech synthesizer driven by the computer. A number of similar devices have been developed since then. In 2000, for example, research by Jessica Bayliss at the University of Rochester showed that volunteers wearing virtual reality helmets could control elements in a virtual world using their P300 EEG readings, including turning lights on and off and bringing a mock-up car to a stop.

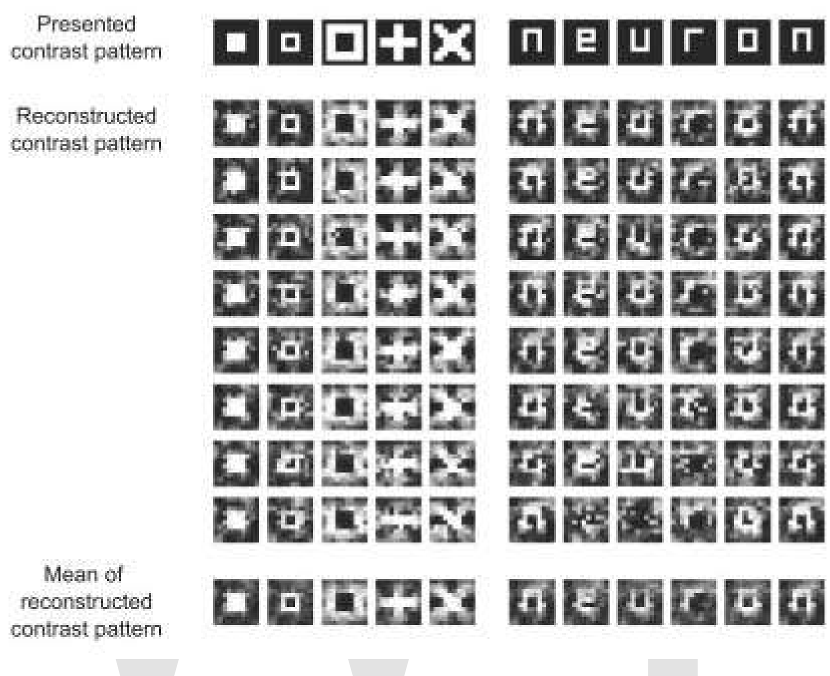
In the early 90s Babak Taheri, at UC DAVIS demonstrated the first single and also multichannel dry active electrode arrays using micro-machining. The single channel dry EEG electrode construction and results were published in 1994. The arrayed electrode was also demonstrated to perform well compared to Ag/AgCl electrodes. The device consisted of four sites of sensors with integrated electronics to reduce noise by impedance matching. The advantages of such electrodes are: (1) no electrolyte used, (2) no skin preparation, (3) significantly reduced sensor size, and (4) compatibility with EEG monitoring systems. The active electrode array is an integrated system made of an array of capacitive sensors with local integrated circuitry housed in a package with batteries to power the circuitry. This level of integration was required to achieve the functional performance obtained by the electrode. The electrode was tested on an electrical test bench and on human subjects in four modalities of EEG activity, namely: (1) spontaneous EEG, (2) sensory event-related potentials, (3) brain stem potentials, and (4) cognitive event-related potentials. The performance of the dry electrode compared favorably with that of the standard wet Ag/AgCl electrodes in terms of skin preparation, no gel requirements (dry), and higher signal-to-noise ratio. In 1999, researchers at Case Western Reserve University led by Hunter Peckham, used 64-electrode EEG skullcap to return limited hand movements to quadriplegic Jim Jatich. As Jatich concentrated on simple but opposite concepts like up and down, his beta-rhythm EEG output was analysed using software to identify patterns in the noise. A basic pattern was identified and used to control a switch: Above average activity was set to on, below average off. As well as enabling Jatich to control a computer cursor the signals were also used to drive the nerve controllers embedded in his hands, restoring some movement.

Electronic neural networks have been deployed which shift the learning phase from the user to the computer. Experiments by scientists at the Fraunhofer Society in 2004 using neural networks led to noticeable improvements within 30 minutes of training.

Experiments by Eduardo Miranda aim to use EEG recordings of mental activity associated with music to allow the disabled to express themselves musically through an encephalophone.

The Emotiv company has been selling a commercial video game controller, known as the Epoc, since December 2009. The Epoc uses electromagnetic sensors.

MEG and MRI



ATR Labs' reconstruction of human vision using fMRI (top row: original image; bottom row: reconstruction from mean of combined readings)

Magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) have both been used successfully as non-invasive BCIs. In a widely reported experiment, fMRI allowed two users being scanned to play Pong in real-time by altering their haemodynamic response or brain blood flow through biofeedback techniques.

fMRI measurements of haemodynamic responses in real time have also been used to control robot arms with a seven second delay between thought and movement.

More recently, research developed in the Advanced Telecommunications Research (ATR) Computational Neuroscience Laboratories in Kyoto, Japan allowed the scientists to reconstruct images directly from the brain and display them on a computer. The article announcing these achievements was the cover story of the journal Neuron of 10 December 2008, While the early results are limited to black and white images of 10x10 squares (pixels), according to the researchers further development of the technology may make it possible to achieve color images, and even view or record dreams.

Commercialization and companies

John Donoghue and fellow researchers founded Cyberkinetics. The company markets its electrode arrays under the BrainGate product name and has set the development of practical BCIs for humans as its major goal. The BrainGate is based on the Utah Array developed by Dick Normann.

Philip Kennedy founded Neural Signals in 1987 to develop BCIs that would allow paralysed patients to communicate with the outside world and control external devices. As well as an invasive BCI, the company also sells an implant to restore speech. Neural Signals' Brain Communicator BCI device uses glass cones containing microelectrodes coated with proteins to encourage the electrodes to bind to neurons.

Although 16 paying patients were treated using William Dobelle's vision BCI, new implants ceased within a year of Dobelle's death in 2004. A company controlled by Dobelle, Avery Biomedical Devices, and Stony Brook University are continuing development of the implant, which has not yet received Food and Drug Administration approval in the United States for human implantation.

Ambient, at a TI developers conference in early 2008, demoed a product they have in development call The Audeo. The Audeo is being developed to create a human–computer interface for communication without the need of physical motor control or speech production. Using signal processing, unpronounced speech representing the thought of the mind can be translated from intercepted neurological signals.

Mindball is a product developed and commercialized by Interactive Productline in which players compete to control a ball's movement across a table by becoming more relaxed and focused. Interactive Productline is a Swedish company whose objective is to develop and sell easy understandable EEG products that train the ability to relax and focus.

An Austrian company, Guger Technologies, g.tec, has been offering Brain Computer Interface systems since 1999. The company provides base BCI models as development platforms for the research community to build upon, including the P300 Speller, Motor Imagery, and mu-rhythm. They commercialized a Steady State Visual Evoked Potiential BCI solution in 2008 with 4 degrees of machine control.

A Spanish company, Starlab, has entered this market in 2009 with a wireless 4-channel system called Enobio. Designed for research purposes the system provides a platform for application development.

There are three main consumer-devices commercial-competitors in this area (launch date mentioned in brackets) which have launched such devices primarily for gaming- and PC-users:

- Neural Impulse Actuator (April, 2008)
- Emotiv Systems (December, 2009)

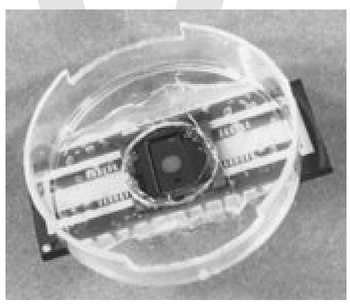
- NeuroSky (MindSet – June, 2009; Uncle Milton Force Trainer – Fall 2009, Mattel MindFlex – Summer, 2009)

Synthetic telepathy

Research is ongoing into synthetic or computer-mediated telepathy which would allow user-to-user communication through analysis of neural signals. The research aims to detect and analyze the word-specific neural signals, using EEG, which occur before speech is vocalized, and to see if the patterns are generalizable. As of 2009, the research is focused on military uses.

Cell-culture BCIs

Researchers have built devices to interface with neural cells and entire neural networks in cultures outside animals. As well as furthering research on animal implantable devices, experiments on cultured neural tissue have focused on building problem-solving networks, constructing basic computers and manipulating robotic devices. Research into techniques for stimulating and recording from individual neurons grown on semiconductor chips is sometimes referred to as neuroelectronics or neurochips.



World first: Neurochip developed by Caltech researchers Jerome Pine and Michael Maher

Development of the first working neurochip was claimed by a Caltech team led by Jerome Pine and Michael Maher in 1997. The Caltech chip had room for 16 neurons.

In 2003, a team led by Theodore Berger at the University of Southern California started work on a neurochip designed to function as an artificial or prosthetic hippocampus. The neurochip was designed to function in rat brains and is intended as a prototype for the eventual development of higher-brain prosthesis. The hippocampus was chosen because it is thought to be the most ordered and structured part of the brain and is the most studied area. Its function is to encode experiences for storage as long-term memories elsewhere in the brain.

Thomas DeMarse at the University of Florida used a culture of 25,000 neurons taken from a rat's brain to fly a F-22 fighter jet aircraft simulator. After collection, the cortical neurons were cultured in a petri dish and rapidly began to reconnect themselves to form a living neural network. The cells were arranged over a grid of 60 electrodes and used to control the pitch and yaw functions of the simulator. The study's focus was on understanding how the human brain performs and learns computational tasks at a cellular level.

Ethical considerations

There has not been a vigorous debate about the ethical implications of BCIs, even though there are several commercially available systems such as brain pacemakers used to treat neurological conditions, and could theoretically be used to modify other behaviours.

Important topics in the neuroethical debate are: 1) obtaining informed consent from people who have difficulty communicating, 2) risk/benefit analysis 3) shared responsibility of BCI teams (e.g. how to ensure that responsible group decisions can be made), 4) the consequences of BCI technology for the quality of life of patients and their families, 5) side-effects (e.g. neurofeedback of sensorimotor rhythm training is reported to affect sleep quality) 6) personal responsibility and its possible constraints (e.g. who is responsible for erroneous actions with a neuroprosthesis), 7) issues concerning personality and personhood and its possible alteration, 8) therapeutic applications and their possible exceedance, 9) questions of research ethics that arise when progressing from animal experimentation to application in human subjects, 10) mind-reading and privacy, 11) mind-control, 12) selective enhancement and social stratification and 13) communication to the media.

Emory University neuroscience professor Michael Crutcher has expressed concern about BCIs, specifically ear and eye implants: "If only the rich can afford it, it puts everyone else at a disadvantage." Clausen concluded in 2009 that “BCIs pose ethical challenges, but these are conceptually similar to those that bioethicists have addressed for other realms of therapy”. Moreover, he suggests that bioethics is well-prepared to deal with the issues that arise with BCI technologies. Haselager and colleagues pointed out that expectations of BCI efficacy and value play a great role in ethical analysis and the way BCI scientists should approach media. Furthermore, standard protocols can be implemented to ensure ethically sound informed-consent procedures with locked-in patients.

Researchers are well aware that sound ethical guidelines, appropriately moderated enthusiasm in media coverage and education about BCI systems will be of utmost importance for the societal acceptance of this technology. Thus, recently more effort is made inside the BCI community to initiate the development of ethical guidelines for BCI research, development and dissemination.

BCI based toys

Recently a number of companies have scaled back medical grade EEG technology (and in one case, NeuroSky, rebuilt the technology from the ground up) to create inexpensive BCIs. This technology has been built into toys and gaming devices; some of these toys have been extremely commercially successful like the NeuroSky and Mattel MindFlex.

- In 2006 Sony patented a neural interface system allowing radio waves to affect signals in the neural cortex.
- In 2007 NeuroSky released the first affordable consumer based EEG along with the game NeuroBoy. This was also the first large scale EEG device to use dry sensor technology.
- In 2008 OCZ Technology developed device for use in video games relying primarily on electromyography.
- In 2008 the Final Fantasy developer Square Enix announced that it was partnering with NeuroSky to create a game, Judecca.
- In 2009 Mattel partnered with NeuroSky to release the Mindflex, a game that used an EEG to steer a ball through an obstacle course. By far the best selling consumer based EEG to date.
- In 2009 Uncle Milton Industries partnered with NeuroSky to release the Star Wars Force Trainer, a game designed to create the illusion of possessing the force.
- In 2009 Emotiv released the EPOC, a 14 channel EEG device. The EPOC is the first commercial BCI to not use dry sensor technology, requiring users to apply a saline solution on the sensors.
- In 2010 NeuroSky added an electromyography function for recognising eye blink to the MindSet.

Chapter- 2

Neuroprosthetics

Neuroprosthetics (also called **neural prosthetics**) is a discipline related to neuroscience and biomedical engineering concerned with developing neural prostheses. Neural prostheses are a series of devices that can substitute a motor, sensory or cognitive modality that might have been damaged as a result of an injury or a disease. Cochlear implants provide an example of such devices. These devices substitute the functions performed by the ear drum and Stapes, while simulating the frequency analysis performed in the cochlea. A microphone on an external unit gathers the sound and processes it; the processed signal is then transferred to an implanted unit that stimulates the auditory nerves through a microelectrode array.

The development of such devices has had a profound impact on the quality of human life, and research in this field intends to resolve disabilities.

There is another side to the application of neural prostheses. These implantable devices can also be used in animal experiments as a tool for neuroscientists to develop a better understanding of how the brain works. Wireless electrical recording from the brain of awake, freely behaving animals can open many important doors into understanding how the brain handles different functions. Accurately probing and recording the electrical signals in the brain would help better understand the relationship among a local population of neurons that are responsible for a specific function. In order to substitute sensory, motor or cognitive modalities, we need to first understand which part of the brain is responsible for those modalities and how those functions are performed. Neuroprosthetics and neuro science have a very intertwined relationship. Neuroprostheses contribute to better understanding of the neural system and this better understanding helps develop better, more application-specific neural prostheses.

There are many challenges which must be overcome in order to develop these devices. Any implanted device has to be very small to be to minimally invasive, especially in the brain, eye or cochlea. Also this implant would have to communicate with the outside world wirelessly. This bidirectional wireless communication requires a high bandwidth for real-time data transmission; this is a great challenge considering that this data link has to operate through the skin. The minimal size of the implant means no battery can be embedded in the implant. Instead, the implant works on wireless power transmission through the skin. This is just as challenging as the data transmission. The tissue surrounding the implant is usually very sensitive to temperature rise so the implant must have very low power consumption in order to assure it won't harm the tissue. Another very important issue is the bio compatibility of the material that the implants are coated with. The more biocompatible these materials are, the less tissue reaction they will cause thus resulting less implant risk and longer implant period.

Gradually as these devices become safer and the our understanding of how the brain works enhances the use of these devices will become more and more common and help people with severe disabilities live a normal life. The neuroprosthetic seeing the most widespread use is the cochlear implant, with approximately 100,000 in use worldwide as of 2006.

Today, the use of cochlear implants and pacemakers has become an undeniable fact of life. The future holds an exciting prospect for the every day use of a variety of neural prostheses.

History

The first cochlear implant dates back to 1957. Other landmarks include the first motor prosthesis for foot drop in hemiplegia in 1961, the first auditory brainstem implant in 1977 and a peripheral nerve bridge implanted into spinal cord of adult rat in 1981. Paraplegics were helped in standing with a lumbar anterior root implant (1988) and in walking with Functional Electrical Stimulation (FES).

Regarding the development of electrodes implanted in the brain, an early difficulty was reliably locating the electrodes, originally done by inserting the electrodes with needles and breaking off the needles at the desired depth. Recent systems utilize more advanced probes, such as those used in deep brain stimulation to alleviate the symptoms of Parkinson's Disease. The problem with either approach is that the brain floats free in the skull while the probe does not, and relatively minor impacts, such as a low speed car accident, are potentially damaging. Some researchers, such as Kensall Wise at the University of Michigan, have proposed tethering 'electrodes to be mounted on the exterior surface of the brain' to the inner surface of the skull. However, even if successful, tethering would not resolve the problem in devices meant to be inserted deep into the brain, such as in the case of deep brain stimulation (DBS).

Sensory prosthetics

Visual prosthetics

A visual prosthesis can create a sense of image by electrically stimulating neurons in the visual system. A camera would wirelessly transmit to an implant, the implant would map the image across an array of electrodes. The array of electrodes has to effectively stimulate 600-1000 locations, stimulating these optic neurons in the retina thus will create an image. The stimulation can also be done anywhere along the optic signal's path way.

The optical nerve can be stimulated in order to create an image, or the visual cortex can be stimulated, although clinical tests have proven most successful for retinal implants.

A visual prosthesis system consists of an external (or implantable) imaging system which acquires and processes the video. Power and data will be transmitted to the implant wirelessly by the external unit. The implant uses the received power/data to convert the digital data to an analog output which will be delivered to the nerve via micro electrodes.

Photoreceptors are the specialized neurons that convert photons into electrical signals. They are part of the retina, a multilayer neural structure about 200 um thick that lines the back of the eye. The processed signal is sent to the brain through the optical nerve. If any part of this path way is damaged blindness can occur.

Blindness can result from damage to the optical pathway (cornea, aqueous humor, crystalline lens, and vitreous). This can happen as a result of accident or disease. The two most common retinal degenerative diseases that result in blindness secondary to photoreceptor loss is age related macular degeneration (AMD) and retinitis pigmentosa (RP).

The first clinical trial of a permanently implanted retinal prosthesis was a device with a passive microphotodiod array with 3500 elements. This trial was implemented at Optobionics, Inc., in 2000. In 2002, Second Sight Medical Products, Inc. (Sylmar, CA) began a trial with a prototype epiretinal implant with 16 electrodes. The subjects were six individuals with bare light perception secondary to RP. The subjects demonstrated their ability to distinguish between three common objects (plate, cup, and knife) at levels statistically above chance. An active sub retinal device developed by Retina Implant GMbH (Reutlingen, Germany) began clinical trials in 2006. An IC with 1500 microphotodiods was implanted under the retina. The microphotodiods serve to modulate current pulses based on the amount of light incident on the photo diode.

The seminal experimental work towards the development of visual prostheses was done by cortical stimulation using a grid of large surface electrodes. In 1968 Giles Brindley implanted an 80 electrode device on the visual cortical surface of a 52-year-old blind woman. As a result of the stimulation the patient was able to see phosphenes in 40 different positions of the visual field. This experiment showed that an implanted electrical stimulator device could restore some degree of vision. Recent efforts in visual cortex prosthesis have evaluated efficacy of visual cortex stimulation in a non-human primate. In this experiment after a training and mapping process the monkey is able to perform the same visual saccade task with both light and electrical stimulation.

The requirements for a high resolution retinal prosthesis should follow from the needs and desires of blind individuals who will benefit from the device. Interactions with theses patients indicate that mobility without a cane, face recognition and reading are the main necessary enabling capabilities.

The results and implications of fully-functional visual prostheses are exciting. However, the challenges are grave. In order for a good quality image to be mapped in the retina a high number of micro-scale electrode arrays are needed. Also, the image quality is dependent on how much information can be sent over the wireless link. Also this high amount of information must be received and processed by the implant without much power dissipation which can damage the tissue. The size of the implant is also of great concern. Any implant would be preferred to be minimally invasive.

With this new technology, several scientists, including Karin Moxon at Drexel, John Chapin at SUNY, and Miguel Nicolelis at Duke University, started research on the design of a sophisticated visual prosthesis. Other scientists have disagreed with the focus of their research, arguing that the basic research and design of the densely populated microscopic wire was not sophisticated enough to proceed.

Auditory prosthetics

Cochlear implants (CIs), auditory brainstem implants (ABIs), and auditory midbrain implants (AMIs) are the three main categories for auditory prostheses. CI electrode arrays are implanted in the cochlea, ABI electrode arrays stimulate the cochlear nucleus complex in the lower brain stem, and AMIs stimulates auditory neurons in the inferior colliculus. Cochlear implants have been very successful among these three categories. Today Advanced Bionics and Medtronic are the major commercial providers of cochlea implants.

In contrast to traditional hearing aids that amplify sound and send it through the external ear, cochlear implants acquire and process the sound and convert it into electrical energy for subsequent delivery to the auditory nerve. The microphone of the CI system receives sound from the external environment and sends it to processor. The processor digitizes the sound and filters it into separate frequency bands that are sent to the appropriate tonotonic region in the cochlea that approximately corresponds to those frequencies.

In 1957, French researchers A. Djourno and C. Eyries, with the help of D. Kayser, provided the first detailed description of directly stimulation the auditory nerve in a human subject. The individuals described hearing chirping sounds during simulation. In 1972, the first portable cochlear implant system in an adult was implanted at the House Ear Clinic. The U.S. Food and Drug Administration (FDA) formally approved the marketing of the House-3M cochlear implant in November 1984.

Improved performance in cochlea implants not only depends on understanding the physical and biophysical limitations of implant stimulation but also on an understanding of the brain's pattern processing requirements. Modern signal processing represents the most important speech information while also providing the brain the pattern recognition information that it needs. Pattern recognition in the brain is more effective than algorithmic preprocessing at identifying important features in speech. A combination of engineering, signal processing, biophysics, and cognitive neuroscience was necessary to produce the right balance of technology to maximize the performance of auditory prosthesis.

Since the early 2000s FDA has been involved in a clinical trial of device termed the "Hybrid" by Cochlear Corporation. This trial is aimed at examining the usefulness of cochlea implantation in patients with residual low-frequency hearing. The "Hybrid" utilizes a shorter electrode than the standard cochlea implant, since the electrode is shorter it stimulates the basil region of the cochlea and hence the high-frequency tonotopic region. In theory these devices would benefit patients with significant low-frequency residual hearing who have lost perception in the speech frequency range and hence have decreased discrimination scores.

Prosthetics for pain relief

The SCS (Spinal Cord Stimulator) device has two main components: an electrode and a generator. The technical goal of SCS for neuropathic pain is to mask the area of a patient's pain with a stimulation induced tingling, known as "paresthesia", because this overlap is necessary (but not sufficient) to achieve pain relief. Paresthesia coverage depends upon which afferent nerves are stimulated. The most easily recruited by a dorsal midline electrode, close to the pial surface of spinal cord, are the large dorsal column afferents, which produce broad paresthesia covering segments caudally.

In ancient times the electrogenic fish was used as a shocker to subside pain. Healers had developed specific and detailed techniques to exploit the generative qualities of the fish to treat various types of pain, including headache. Because of the awkwardness of using a living shock generator, a fair level skill was required to deliver the therapy to the target for the proper amount of time. (Including keeping the fish alive as long as possible) Electro analgesia was the first deliberate application of electricity. By the nineteenth century, most western physicians were offering their patients electrotherapy delivered by portable generator. In the mid-1960s, however, three things converged to insure the future of electro stimulation.

1. Pacemaker technology, which had it start in 1950, became available.

2. Melzack and Wall published their gate control theory of pain, which proposed that the transmission of pain could be blocked by stimulation of large afferent fibers.

3. Pioneering physicians became interested in stimulating the nervous system to relieve patients from pain.

The design options for electrodes include their size, shape, arrangement, number, and assignment of contacts and how the electrode is implanted. The design option for the pulse generator include the power source, target anatomic placement location, current or voltage source, pulse rate, pulse width, and number of independent channels. Programming options are very numerous (a four-contact electrode offers 50 functional bipolar combinations). The current devices use computerized equipment to find the best options for use. This reprogramming option compensates for postural changes, electrode migration, changes in pain location, and suboptimal electrode placement.

Motor prosthetics

Devices which support the function of autonomous nervous system include the implant for bladder control. In the somatic nervous system attempts to aid conscious control of movement include Functional electrical stimulation and the lumbar anterior root stimulator.

Bladder control implants

Where a spinal cord lesion leads to paraplegia, patients have difficulty emptying their bladders and this can cause infection. From 1969 onwards Brindley developed the sacral anterior root stimulator, with successful human trials from the early 1980s onwards. This device is implanted over the sacral anterior root ganglia of the spinal cord; controlled by an external transmitter, it delivers intermittent stimulation which improves bladder emptying. It also assists in defecation and enables male patients to have a sustained full erection.

The related procedure of sacral nerve stimulation is for the control of incontinence in able-bodied patients.

Motor prosthetics for conscious control of movement

Researchers are attempting to build motor neuroprosthetics that will help restore movement and the ability to communicate with the outside world to persons with motor disabilities such as tetraplegia or amyotrophic lateral sclerosis.

To capture electrical signals from the brain, scientists have developed microelectrode arrays smaller than a square centimeter that can be implanted in the skull to record electrical activity, transducing recorded information through a thin cable. After decades of research in monkeys, neuroscientists have been able to decode neuronal signals into movements. Completing the translation, researchers have built interfaces that allow patients to move computer cursors, and they are beginning to build robotic limbs and exoskeletons that patients can control by thinking about movement.

The technology behind motor neuroprostheses is still in its infancy. Investigators and study participants continue to experiment with different ways of using the prostheses. Having a patient think about clenching a fist, for example, produces a different result than having him or her think about tapping a finger. The filters used in the prostheses are also being fine-tuned, and in the future, doctors hope to create an implant capable of transmitting signals from inside the skull wirelessly, as opposed to through a cable.

Preliminary clinical trials suggest that the devices are safe and that they have the potential to be effective. Some patients have worn the devices for over two years with few, if any, ill effects.

Prior to these advancements, Philip Kennedy (Emory and Georgia Tech) had an operable if somewhat primitive system which allowed an individual with paralysis to spell words by modulating their brain activity. Kennedy's device used two neurotrophic electrodes: the first was implanted in an intact motor cortical region (e.g. finger representation area) and was used to move a cursor among a group of letters. The second was implanted in a different motor region and was used to indicate the selection.

Developments continue in replacing lost arms with cybernetic replacements by using nerves normally connected to the pectoralis muscles. These arms allow a slightly limited range of motion, and reportedly are slated to feature sensors for detecting pressure and temperature.

Dr. Todd Kuiken at Northwestern University and Rehabilitation Institute of Chicago has developed a method called targeted reinnervation for an amputee to control motorized prosthetic devices and to regain sensory feedback.

Sensory/motor prosthetics

In 2002 an array of 100 electrodes was implanted directly into the median nerve fibers of the scientist Kevin Warwick. The recorded signals were used to control a robot arm developed by Warwick's colleague, Peter Kyberd and was able to mimic the actions of Warwick's own arm. Additionally, a form of sensory feedback was provided via the implant by passing small electrical currents into the nerve. This caused a contraction of the first lumbrical muscle of the hand and it was this movement that was perceived.

Cognitive prostheses

Cognitive prostheses seek to restore cognitive function to individuals with brain tissue loss due to injury, disease, or stroke by performing the function of the damaged tissue with integrated circuits. The theory of localization states that brain functions are localized to a specific portion of the brain. However, recent studies on brain plasticity suggest that the brain is capable of rewiring itself so that an area of the brain traditionally associated with a particular function (i.e. auditory cortex) can perform functions associated with another portion of the brain. (i.e. auditory cortex processing visual information). Implants could take advantage of brain plasticity to restore cognitive function even if the native tissue has been destroyed.

Applications

Alzheimer's Disease

Alzheimer's Disease is projected to affect more than 107 million people worldwide by the year 2050. Due to increased life spans, more and more people are being affected by Alzheimer's disease. Alzheimer's disease renders individuals incapable of supporting themselves. Many of the more severe cases of Alzheimer's patients end up in nursing homes. Even a small measure of success by cognitive implants would help keep Alzheimer's patients out of nursing homes.

Hippocampal Deficits

Dr. Theodore Berger at the University of Southern California is developing a prosthetic for treatments of hippocampal detriments including Alzheimer's. Degenerative hippocampal neurons are the root cause of the memory disorders that accompany Alzheimer's disease. Also, hippocampal pyramidal cells are extremely sensitive to even brief periods of anoxia, like those that occur during stroke. Loss of hippocampal neurons in the dentate gyrus, an area associated with new memory formation has been attributed to blunt head trauma. Hippocampal dysfunction has also been linked to epileptic activity. This demonstrates the wide scope of neural damage and neurodegenerative disease conditions for which a hippocampal prosthesis would be clinically relevant.

Traumatic Brain Injury

More than 1.4 million people in the United States suffer traumatic brain injury. Orthosis for TBI patients to control limb movement via devices that read neurons in brain, calculate limb trajectory, and stimulate needed motor pools to make movement. (Anderson Paper, Cole at NIH - specifically "Computer software as an orthosis for Brain Injury",

Parkinson's Disease

Nearly 1 million people in the United States are affected by Parkinson's Disease. Deep Brain Stimulation relieves symptoms of Parkinson's Disease for numerous patients. Parkinson's Disease patients could benefit from a cortical device that mimics the natural signals needed to promote dopamine production. Another possible avenue for mitigation of PD is a device that supplements dopamine when given specific neuronal inputs which would let the body regulate dopamine levels with its intrinsic sensors.

Speech Deficits

Approximately 7.5 million people in the United States have trouble speaking. Many of these can be attributed to aphasias. The success of cochlear implants suggest that cortical implants to the speech areas of the brain can be developed to improve speech in such patients.

Paralysis

According to the Christopher and Dana Reeve Foundation's Paralysis Resource Center, approximately 6 million people are living with paralysis in the United States. Paralysis results from many sources, stroke, traumatic brain injury, neurodegenerative diseases like multiple sclerosis and Lou Gehrig's Disease, and congenital sources. Many patients would benefit from a prosthetic device that controls limb movement via devices that read neurons in brain, calculate limb trajectory, and stimulate the needed motor pools to make movement. This technology is being developed at the Andersen Lab, located at the California Institute of Technology. The goal is to develop a device to enable locked in patients, those without the ability to move or speak, to communicate with others.

Societal Impact/Market Information

Nearly 1 million people in the United States are affected by Parkinson's Disease.

Alzheimer's Disease is projected to affect more than 107 million people worldwide by the year 2050.

Just these two diseases indicate that there is already a large market for cognitive neural prosthetics, with more potential markestspace revealed in traumatic brain injury and speech problems (particularly damage to Broca's or Wernicke's areas).

More than 1.4 million people in the United States suffer traumatic brain injury.

Approximately 7.5 million people in the United States have trouble speaking. Many of these can be attributed to aphasias.

More than 6.5 million people in the United States have suffered stroke.

Obstacles

Mathematical Modeling

Accurate characterization of the nonlinear input/output (I/O) parameters of the normally functioning tissue to be replaced is paramount to designing a prosthetic that mimics normal biologic synaptic signals. Mathematical modeling of these signals is a complex task "because of the nonlinear dynamics inherent in the cellular/molecular mechanisms comprising neurons and their synaptic connections." The output of nearly all brain neurons are dependent on which post-synaptic inputs are active and in what order the inputs are received. (spatial and temporal properties, respectively).

Once the I/O parameters are modeled mathematically, integrated circuits are designed to mimic the normal biologic signals. For the prosthetic to perform like normal tissue, it must process the input signals, a process known as transformation, in the same way as normal tissue.

Size

Implantable devices must be very small to be implanted directly in the brain, roughly the size of a quarter. One of the example of microimplantable electrode array is the Utah array.

Wireless Controlling Devices can be mounted outside of the skull and should be smaller than a pager.

Power Consumption

Power consumption drives battery size. Optimization of the implanted circuits reduces power needs. Implanted devices currently need on-board power sources. Once the battery runs out, surgery is needed to replace the unit. Longer battery life correlates to fewer surgeries needed to replace batteries. One option that could be used in the medical field to recharge implant batteries without surgery or wires is being used in powered toothbrushes. These devices make of inductive coupling to recharge batteries. Another strategy is to convert electromagnetic energy into electrical energy, as in radio frequency identification tags.

Bio Compatibility

Cognitive prostheses are implanted directly in the brain, so biocompatibility is very important obstacle to overcome. Materials used in the housing of the device, the electrode material (such as iridium oxide), and electrode insulation must be chosen for long term implantation. Subject to Standards: ISO 14708-3 2008-11-15, Implants for Surgery - Active implantable medical devices Part 3: Implantable neurostimulators.

Crossing the Blood Brain Barrier can introduce pathogens or other materials that may cause an immune response. The brain has its own immune system that acts differently than the immune system of the rest of the body.

Questions to answer:How does this affect material choice? Does the brain have unique phages that act differently and may affect materials thought to be bio compatible in other areas of the body?

Data Transmission

Wireless Transmission is being developed to allow continuous recording of neuronal signals of individuals in their daily life. This allows physicians and clinicians to capture more data, ensuring that short term events like epileptic seizures can be recorded, allowing better treatment and characterization of neural disease.

A small, light weight device has been developed that allows constant recording of primate brain neurons at Stanford University. This technology also enables neuroscientists to study the brain outside of the controlled environment of a lab.

Methods of data transmission must be robust and secure. Neurosecurity is a new issue. Makers of cognitive implants must prevent unwanted downloading of information or thoughts from and uploading of detrimental data to the device that may interrupt function.

Correct Implantation

Implantation of the device presents many problems. First, the correct presynaptic inputs must be wired to the correct postsynaptic inputs on the device. Secondly, the outputs from the device must be targeted correctly on the desired tissue. Thirdly, the brain must learn how to use the implant. Various studies in brain plasticity (int link) suggest that this may be possible through exercises designed with proper motivation.

Current Developments

Andersen Lab

The Andersen Lab builds on research done previously by Musallam and show that high-level cognitive signals in the post parietal cortex, or PPC, can be used to decode the target position of reaching motions. Signals like these could be used to directly control a prosthetic device. Functionally speaking, the PPC is situated between sensory and motor areas in the brain. It is involved in converting sensory inputs into plans for action, a phenomenon known as sensory – motor integration.

Within the PPC is an area known as the post parietal reach region, or PRR for short. This area has been shown to be most active when an individual is planning and executing a movement. The PRR receives direct visual information, indicating that vision may be the primary sensory input. The PRR encodes the targets for reaching in visual coordinates relative to the current direction of gaze AKA retinal coordinates. Because it is coding the goal of the movement and not all the different variables required for the limb to contact the target, the planning signals of the PRR are considered cognitive in nature. Decoding these signals is important to help paralyzed patients, especially those with damage to areas of the brain that calculate limb movement variables, or relay this information to motor neurons. Perhaps the most astonishing possibility is utilizing these signals to provide 'locked in' individuals, those without the ability to move or speak, an avenue of communication.

First, Andersen and colleagues placed electrode arrays onto the dorsal premotor cortex, the PRR, and medial interparietal area (MIP) of monkeys to record signals made by these regions while the monkeys looked at a computer screen. After the monkeys touched a central cue spot on the screen and looked at a central fixation point (red), another cue (green) popped up briefly then disappeared. The monkeys were given a juice reward if they reached to where the newly vanished target was at the end of a short memory period, about 1.5 seconds. The recordings were made when the monkeys were planning movement, but sitting motionless in the dark absent of eye movements, ensuring that motor and sensory information were not influencing the planning activity.

Next, the researchers conducted brain-control trials using neural activity data recorded from 2 tenths of a second to 1 second of the memory period to decode the intended reach destination. A brain-machine interface used the decoded data to move a cursor to the spot on the screen where the monkeys planned to move, without using their limbs. Monkeys were rewarded with juice if the correct target was decoded and the cue was flashed again, providing visual reinforcement. After a month or two of training, the monkeys were much better at hitting the target. This learning is a testament to the brain's natural plasticity, and creates an opportunity for patients to improve how they operate the prosthesis with training. Each time the patient uses the prosthetic system, the brain could automatically make subtle adjustments to the input signal recorded by the system.

Finally, the researchers used reach trials to decode intentions in healthy monkeys. However, paralyzed patients cannot perform reach trials for the scientists to record reach intention data. Adaptive databases overcome this scenario. Each time a reach decoding is successful, it is added to the database. If the number of database entries is kept constant, one trial, (a less successful one) must be deleted. Eventually the database will contain only successful decodes, making the system work better each time the patient uses it. This suggests a FIFO, or first-in, first-out, setup. The oldest data drops out first. Initially filling the database will be difficult, but with rigorous training and many trials, the system will be able to accurately discern the user's intentions. This process, along with the brain's plasticity, should enable people to control a myriad of prostheses, and perhaps even motorized wheel chairs. Furthermore, in the future precision devices such as surgical tools could be controlled directly by the brain instead of controls manipulated by the motor system.

Hippocampal Prosthetic

Dr. Theodore Berger's research lab at the University of Southern California seeks to develop models of mammalian neural systems, currently the hippocampus, essential for learning and memory. The goal is to make an implantable device that replicates the way living hippocampal neurons behave and exchange electrical signals. If successful, it would be a large step towards a biomedical solution for Alzheimer's symptoms. Complications from brain injury to motor areas of the brain like reduced coordination could be improved. Speech and language problems caused by stroke could be reversed. To accomplish this, the device will listen for neuronal signals going to the hippocampus with implanted electrode arrays, calculate what the outgoing response of normal hippocampus neurons would be, and then to stimulate neurons in other parts of the brain, hopefully just like the tissue did before damage or degeneration.

Technologies Involved

Local Field Potentials

Local field potentials (LFPs) are electrophysiological signals that are related to the sum of all dendritic synaptic activity within a volume of tissue. Recent studies suggest goals and expected value are high-level cognitive functions that can be used for neural cognitive prostheses.

- explain how they are used
- how they are better than other methods

Automated Movable Electrical Probes

One hurdle to overcome is the long term implantation of electrodes. If the electrodes are moved by physical shock or the brain moves in relation to electrode position, the electrodes could be recording different nerves. Adjustment to electrodes is necessary to maintain an optimal signal. Individually adjusting multi electrode arrays is a very tedious and time consuming process. Development of automatically adjusting electrodes would mitigate this problem. Anderson's group is currently collaborating with Yu-Chong Tai's lab and the Burdick lab (all at Cal Tech) to make such a system that uses electrolysis-based actuators to independently adjust electrodes in a chronically implanted array of electrodes.

MRI

Used for imaging to determine correct positionings

Imaged Guided Surgical Techniques

Image-Guided Surgery is used to precisely position brain implants.

Future Directions

Self-charging implants that use bioenergy to recharge would eliminate the need for costly and risky surgeries to change implant batteries.

Memory/Brain off-loading and subsequent uploading to learn new information quickly. Researchers at the Georgia Institute of Technology are researching mammalian memory cells to determine exactly how we learn. The techniques used in the Potter Lab can be used to study and enhance the activities of neural prosthetics devices.

Controlling complex machinery with thoughts instead of converting motor movements into commands for machines would allow greater accuracy and enable users to distance themselves from hazardous environments.

Other future directions include devices to maintain focus, to stabilize/induce mood, to help patients with damaged cortices feel and express emotions, and to enable true telepathic communication, not simply picking up visual/auditory cues and guessing emotional state or subject of thought from context.

Chapter- 3

Hippocampus Prosthesis

Hippocampus Prosthesis is a type of cognitive prosthesis. A cognitive prosthesis is a prosthesis implanted into the nervous system in order to improve or replace the function of damaged brain tissue. This is especially difficult because any other kind for prosthesis who use plasticity of the brain to adapt to the requirement of the prosthesis, thus allowing the user to "learn" the use of his new body part, a cognitive prosthesis require the device to be able to fully replace the function of a small section of the nervous system. In order to achieve this we need a deep understanding of the functioning of the nervous system, a reliable mathematical model as well as the technology in order to properly manufacture and intall a cognitive prostesis. The primary goal of an artificial hippocampus is to provide a cure for the Alzheimer diesis and hippocampus related problem . To do so the prosthesis has to be able to receive information directly from the brain, analyse the information and give an appropriate output to the cerebral cortex. In other words being able to behave just like a natural hippocampus, also the artificial organ has to be completely autonomous since any exterior power source will greatly increases risk of infection.

Hippocampus

Role

The hippocampus is part of the human Limbic system, by interacting with the Neocortex and other part of the brain the limbic system produce emotions. Being a part of the limbic system, the hippocampus play its part in formation of emotion in addition of its other role such as consolidation of new memories, navigation and spacial orientation. The hippocampus is important in the sense that it is responsible for the formation of long term recognition memories, in other words this is the part of the brain that allow us to associate a face with a name. Because of its close relation with memory formation, Hippocampal damage is closely related to Alzheimer diesis.

Anatomy

The hippocampus is situated under the neocortex, it is "composed of several different subsystem that form a closed feedback loop, with input from the neocortex entering via the entorhinal cortex, propagating throught the intrinsic subregions of the hippocampus and the return to the neo cortex" In a electronic sense, the hippocampus is composed of slice of parallel circuits.

Essential Requirements

Biocompatibility

Since the prosthesis will be permanently implanted inside the brain, long term biocompatibility is required. Also we must also take into account the tendency for supporting braincells Astrocyte like to encapsulate the implant(This is a natural response for braincell, in order to protects neurons), thus impairing its function.

Bio-mimetic

Being biomimetic means that the implant must be able to fulfill the properties a real biological neuron. To do so we must have a depth understanding of the neuron behavior to build a solid mathematical model to be based upon. First we must take into account that like most of biological process the behaviors of neuron are highly nonlinear and depends on many factors: input frequency pattern etc. Also a good model must take into account the fact that the expression of a single nerve cell is negligible since the process are carried by group of neurons interacting in network. Once installed the device must assume all(or at least most) of the function of the damaged hippocampus for a prolonged period of time. First the Artificial neurons must be able to work together in network just like real neurons. Then, they must be able working and effective synaptic connection with the existing neurons of the brain; therefore a model for silicon/neurons interface will be required.

Size

The implant must be small enough to be implantable while minimizing collateral damages during and after the implantation.

Bidirectional communication

In order to fully assume the function of the damaged hippocampus the prosthesis must be able to communicate with the existing tissue in a bidirectional manner. in other words the implant must be able to receive information from the brain and give an appropriate and compressible feedback to the surrounding nerve cell.

Personalized

The structural and functional characteristic of the brain varies greatly between individual; therefore any neural implant has to be specific to each individual. Which require precise model of the hippocampus and the use of advanced brain imagery to determine individual variance.

Surgical Requirement

Since the prosthesis will be installed inside the brain, the operation itself will be much like a tumor removal operation. Although, collateral damage will be inevitable the effect on the patient will be minimal.

Model

"In order to incorporate the nonlinear dynamics of biological neurons into neuron models to develop a prosthesis, it is first necessary to measure them accurately. We have developed and applied methods for quantifying the nonlinear dynamics of hippocampal neurons (Berger et al., 1988a,b, 1991, 1992, 1994; Dalal et al., 1997) using principles of nonlinear systems theory (Lee and Schetzen, 1965; Krausz, 1975; P. Z. Marmarelis and Marmarelis, 1978; Rugh, 1981; Sclabassi et al., 1988). In this approach, properties of neurons are assessed experimentally by applying a random interval train of electrical impulses as an input and electrophysiologically recording the evoked output of the target neuron during stimulation (figure 12.2A). The input train consists of a series of impulses (as many as 4064), with interimpulse intervals varying according to a Poisson process having a mean of 500 ms and a range of 0.2–5000 ms. Thus, the input is ‘‘broadband’’ and stimulates the neuron over most of its operating range; that is, the statistical properties of the random train are highly consistent with the known physiological properties of hippocampal neurons. Nonlinear response properties are expressed in terms of the relation between progressively higher-order temporal properties of a sequence of input events and the probability of neuronal output, and are modeled as the kernels of a functional power series."

Technology involved

Imaging

Technology such as EEG, MEG, fMRI and other type of imaging technology are essential to the installation of the implant, which require a high precision in order to minimize collateral damage(since the hippocampus is situated inside the cortex)as well as the proper function of the device.

Silicon/Neuron interface

A silicon/neuron interface will be needed for the proper interaction of the silicons neurons of the prosthesis and the biological neurons of the brain.

Neuron network processor

In the brain, tasks are carried out by groups of interconnected neuronal network rater than a single cell, which means that any prosthesis must be able to simulate this network behavior. To do so we will need high number and density of silicon neuron to produce an effective prosthesis; therefore, a *High-density Hippocampal Neuron Network Processor* will be required in order for the prosthesis to carries out the task of a biological hippocampus. In addition a Neuron/Silicon interface will be essential to the bidirectional communication of the implanted prosthesis. The choice of material and the design must ensure long therm viability and bio compatibility while ensuring the density and the specificity of the interconnections.

Power Supply

Appropriate power supply is still a major issue for any neural implant, because the prosthesis are implanted inside the brain, long term biocompatibility aside, the power supply will require several specification. First the power supply must be self recharging. Unlike other prosthesis infection is a much greater issue for neural implant due to the sensitivity of the brain; therefore an external power source is not envisagable. Because the brain is also highly heat sensitive the power and the device itself must not generate to much heat to not disrupt brain function.

Recent development

Theodore Berger and his colleagues at the University of Southern California in Los Angeles have developed a working hippocampal prosthesis that has just passed the live tissue test, implantation in live rat then monkey are planned in the near future. The prosthesis is in the form of two electrode plate on both side of the damaged hippocampus, the input is gathered and analyzed by a external chips then an appropriate feedback will be computed and remitted to the brain so that the prosthesis function like a real hippocampus.

Chapter- 4

Cultured Neuronal Network

A **cultured neuronal network** is a cell culture of neurons that is used as a model to study the central nervous system, especially the brain. Often, cultured neuronal networks are connected to an input/output device such as a multi-electrode array (MEA), thus allowing two-way communication between the researcher and the network. This model has proved to be an invaluable tool to scientists studying the underlying principles behind neuronal learning, memory, plasticity, connectivity, and information processing.

Cultured neurons are often connected via computer to a real or simulated robotic component, creating a hybrot or animat, respectively. Researchers can then thoroughly study learning and plasticity in a realistic context, where the neuronal networks are able to interact with their environment and receive at least some artificial sensory feedback. One example of this can be seen in the Multielectrode Array Art (MEART) system developed by the Potter Research Group at the Georgia Institute of Technology in collaboration with the Symbi-oticA Research Group at the University of Western Australia. Another example can be seen in the neurally controlled animat.

Use as a Model

Advantages

The use of cultured neuronal networks as a model for their *in vivo* counterparts has been an indispensable resource for decades. It allows researchers to investigate neuronal activity in a much more controlled environment than would be possible in a live organism. Through this mechanism researchers have gleaned important information about the mechanisms behind learning and memory.

A cultured neuronal network allows researchers to observe neuronal activity from several vantage points. Electrophysiological recording and stimulation can take place either across the network or locally via an MEA, and the network development can be visually observed using microscopy techniques. Moreover, chemical analysis of the neurons and their environment is more easily accomplished than in an *in vivo* setting.

Disadvantages

Cultured neuronal networks are by definition disembodied cultures of neurons. Thus by being outside their natural environment, the neurons are influenced in ways that are not biologically normal. Foremost among these abnormalities is the fact that the neurons are usually harvested as neural stem cells from an embryo and are therefore disrupted at a critical stage in network development. When the neurons are suspended in solution and subsequently dispensed, the connections previously made are destroyed and new ones formed. Ultimately, the connectivity (and consequently the functionality) of the tissue is changed from what the original template suggested.

Another disadvantage lies in the fact that the cultured neurons lack a body and are thus severed from sensory input as well as the ability to express behavior – a crucial characteristic in learning and memory experiments. It is believed that such sensory deprivation has adverse effects on the development of these cultures and may result in abnormal patterns of behavior throughout the network.

Cultured networks on traditional MEAs are flat, single-layer sheets of cells with connectivity only two dimensions. Most *in vivo* neuronal systems, to the contrary, are large three-dimensional structures with much greater interconnectivity. This remains one of the most striking differences between the model and the reality, and this fact probably plays a large role in skewing some of the conclusions derived from experiments based on this model.

Growing a Neuronal Network

Neurons Used

Because of their wide availability, neuronal networks are typically cultured from dissociated rat neurons. Studies commonly employ rat cortical, hippocampal, and spinal neurons, although lab mouse neurons have also been used. Currently, relatively little research has been conducted on growing primate or other animal neuronal networks. Harvesting neural stem cells requires sacrificing the developing fetus, a process considered too costly to perform on many mammals that are valuable in other studies.

One study, however, did make use of human neural stem cells grown into a network to control a robotic actuator. These cells were acquired from a fetus that spontaneously aborted after ten weeks in gestation

Long-Term Culture

One of the most formidable problems associated with cultured neuronal networks is their lack of longevity. Like most cell cultures, neuron cultures are highly susceptible to infection. They are also susceptible to hyperosmolality from medium evaporation. The long timelines associated with studying neuronal plasticity (usually on the scale of months) makes extending the lifespan of neurons *in vitro* paramount.

One solution to this problem involves growing cells on an MEA inside a sealed chamber. This chamber serves as a non-humidified incubator that is enclosed by a fluorinated ethylene propylene (FEP) membrane that is permeable to select gases (i.e. gases necessary for metabolism) but impermeable to water and microbes. Other solutions entail an incubator with an impermeable membrane that has a specific mix of gases (air with 5% CO_2 is typical) sealed inside.

Multi-electrode Arrays (MEAs)

A multi-electrode array (MEA), also commonly called a microelectrode array, is a patterned array of electrodes laid out in a transparent substrate used for communication with neurons in contact with it. The communication can be, and usually is, bidirectional; researchers can both record electrophysiological data from a live network and stimulate it with a number of patterns.

This device has been an essential biosensor for more than thirty years. It has been used not only in the study of neuronal plasticity and information processing but also in drug and toxin effects on neurons. Additionally, when coupled with a sealed incubation chamber this device greatly reduces the risk of culture contamination by nearly eliminating the need to expose it to air.

Currently, commonly used MEAs have relatively poor spatial resolution. They employ approximately sixty electrodes for recording and stimulation in varying patterns in a dish with a typical culture of 50,000 cells or more (or a density of 5,000 cells/mm^2). It follows that each electrode in the array services a large cluster of neurons and cannot provide resolute information regarding signal origin and destination; such MEAs are only capable of region-specific data acquisition and stimulation.

Ideally it would be possible to record and stimulate from a single or a few neurons at a time. Indeed, companies such as Axion Biosystems are working to provide MEAs with much higher spatial resolution to this end (a maximum of 768 input/output electrodes). Another study investigates establishing a stable one-to-one connection between neurons and electrodes. The goal was to meet the ideal interface situation by establishing a correspondence with every neuron in the network. They do so by caging individual neurons while still allowing the axons and dendrites to extend and make connections. Neurons are contained within ‘’neurocages’’, and the device itself is referred to as the caged neuron MEA or neurochip.

Other research suggests alternative techniques to stimulating neurons *in vitro*. One study investigates the use of a laser beam to free caged compounds such as neurotransmitters and neuromodulators. A laser beam with wavelength in the UV spectrum would have extremely high spatial accuracy and, by releasing the caged compounds, could be used to influence a very select set of neurons.

Network Behavior

Spontaneous Network Activity

Spontaneous network bursts are a commonplace feature of neuronal networks both *in vitro* and *in vivo*. *In vitro*, this activity is particularly important in studies on learning and plasticity. Such experiments look intensely at the network-wide activity both before and after experiments in order to discern any changes that might implicate plasticity or even learning. However, confounding this experimental technique is the fact that normal neuronal development induces change in array-wide bursts that could easily skew data. *In vivo*, however, it has been suggested that these network bursts may form the basis for memories.

Depending on experimental perspective, network-wide bursts can be viewed either positively or negatively. In a pathological sense, spontaneous network activity can be attributed to the disembodiment of the neurons; one study saw a marked difference between array-wide firing frequency in cultures that received continuous input versus those that did not. To eliminate abhorrent activity, researchers commonly use magnesium or synaptic blockers to quiet the network. However, this approach has great costs; quieted networks have little capacity for plasticity due to a diminished ability to create action potentials. A different and perhaps more effective approach is the use of low frequency stimulation that emulates sensory background activity.

In a different light, network bursts can be thought of as benign and even good. Any given network demonstrates non-random, structured bursts. Some studies have suggested that these bursts represent information carriers, expression of memory, a means for the network to form appropriate connections, and learning when their pattern changes.

Array-Wide Burst Stability

Stegenga et al. set out to establish the stability of spontaneous network bursts as a function of time. They saw bursts throughout the lifetime of the cell cultures, beginning at 4–7 days *in vitro* (DIV) and continuing until culture death. They gathered network burst profiles (BPs) through a mathematical observation of array-wide spiking rate (AWSR), which is the summation of action potentials over all electrodes in an MEA. This analysis yielded the conclusion that, in their culture of Wistar rat neocortical cells, the AWSR has long rise and fall times during early development and sharper, more intense profiles after approximately 25 DIV. However, the use of BPs has an inherent shortcoming; BPs are an average of all network activity over time, and therefore only contain temporal information. In order to attain data about the spatial pattern of network activity they developed what they call phase profiles (PPs), which contain electrode specific data.

Data was gathered using these PPs on timescales of milliseconds up through days. . Their goal was to establish the stability of network burst profiles on the timescale of minutes to hours and to establish stability or developmental changes over the course of days. In summary, they were successful in demonstrating stability over minutes to hours, but the PPs gathered over the course of days displayed significant variability. These finding imply that studies of plasticity of neurons can only be conducted over the course of minutes or hours without bias in network activity introduced by normal development .

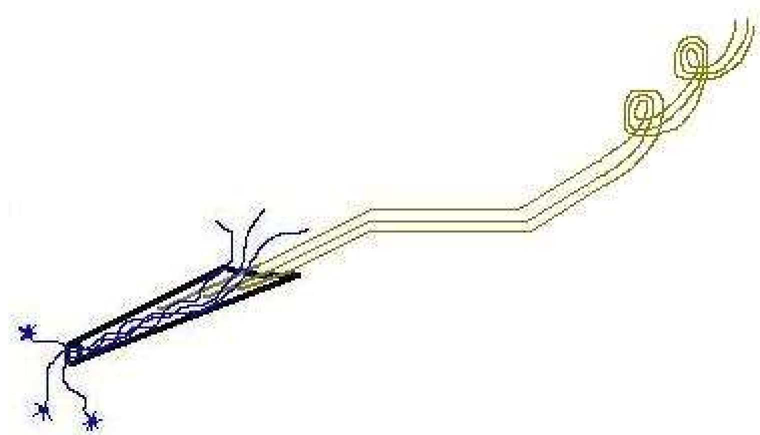
Learning vs. Plasticity

There is much controversy in the field of neuroscience surrounding whether or not a cultured neuronal network can learn. A crucial step in finding the answer to this problem lies in establishing the difference between learning and plasticity. One definition suggests that learning is “the acquisition of novel behavior through experience”. Corollary to this argument is the necessity for interaction with the environment around it, something that cultured neurons are virtually incapable of without sensory systems. Plasticity, on the other hand, is simply the reshaping of an existing network by changing connections between neurons: formation and elimination of synapses or extension and retraction of neurites and dendritic spines. But these two definitions are not mutually exclusive; in order for learning to take place, plasticity must also take place.

In order to establish learning in a cultured network, researchers have attempted to re-embody the dissociated neuronal networks in either simulated or real environments. Through this method the networks are able to interact with their environment and, therefore, have the opportunity to learn in a more realistic setting. Other studies have attempted to imprint signal patterns onto the networks via artificial stimulation. This can be done by inducing network bursts or by inputing specific patterns to the neurons, from which the network is expected to derive some meaning (as in experiments with animats, where an arbitrary signal to the network indicates that the simulated animal has run into a wall or is moving in a direction, etc.). The latter technique attempts to take advantage of the inherent ability of neuronal networks to make sense of patterns. However, experiments have had limited success in demonstrating a definition of learning that is widely agreed upon. Nevertheless, plasticity in neuronal networks is a phenomenon that is well-established in the neuroscience community, and one that is thought to play a very large role in learning.

Chapter- 5

Neurotrophic Electrode



The neurotrophic electrode: teflon-coated gold wires extend from the back of the glass cone, while neurites (shown in blue) grow through it.

The **neurotrophic electrode** is an intracortical device designed to read the electrical signals that the brain uses to process information. It consists of a small, hollow glass cone attached to several electrically conductive gold wires. The term *neurotrophic* means "relating to the nutrition and maintenance of nerve tissue" and the device gets its name from the fact that it is coated with Matrigel and nerve growth factor to encourage the expansion of neurites through its tip. It was invented by neurologist Dr. Philip Kennedy and was successfully implanted for the first time in a human patient in 1996 by neurosurgeon Roy Bakay.

Background

Motivation for development

Victims of locked-in syndrome are cognitively intact and aware of their surroundings, but cannot move or communicate due to near complete paralysis of voluntary muscles. In early attempts to return some degree of control to these patients, researchers used cortical signals obtained with electroencephalography (EEG) to drive a mouse cursor. However, EEG lacks the speed and precision that can be obtained by using a direct cortical interface.

Patients with other motor diseases, such as amyotrophic lateral sclerosis and cerebral palsy, as well as those who have suffered a severe stroke or spinal cord injury, also stand to benefit from implanted electrodes. Cortical signals can be used to control robotic limbs, so as the technology improves and the risks of the procedure are reduced, direct interfacing may even provide assistance for amputees.

Design development

When Dr. Kennedy was designing the electrode, he knew he needed a device that would be wireless, biologically compatible, and capable of chronic implantation. Initial studies with Rhesus monkeys and rats demonstrated that the neurotrophic electrode was capable of chronic implantation for as long as 14 months (human trials would later establish even greater robustness). This longevity was invaluable for the studies because while the monkeys were being trained at a task, neurons that were initially silent began firing as the task was learned, a phenomenon that would not have been observable if the electrode was not capable of long term implantation.

Components

Glass cone

The glass cone is only 1–2 mm long, and is filled with trophic factors in order to encourage axons and dendrites to grow through its tip and hollow body. When the neurites reach the back end of the cone, they rejoin with the neuropil on that side, which anchors the glass cone in place. As a result, stable and robust long-term recording is attainable. The cone sits with its tip near layer five of the cortex, among corticospinal tract cell bodies, and is inserted at an angle of 45° from the surface, about 5 or 6 mm deep.

Gold wires

Three or four gold wires are glued to the inside of the glass cone and protrude out the back. They record the electrical activity of the axons that have grown through the cone, and are insulated with Teflon. The wires are coiled so as to relieve strain because they are embedded in the cortex on one end and attached to the amplifiers, which are fixed to the inside of the skull, on the other. Two wires are plugged into each amplifier to provide differential signalling.

Wireless transmitter

One of the greatest strengths of the neurotrophic electrode is its wireless capability, because without transdermal wiring, the risk of infection is significantly reduced. As neural signals are collected by the electrodes, they travel up the gold wires and through the cranium, where they are passed on to the differential amplifiers. The amplified signals are sent through a switch to a transmitter, where they are converted to FM signals and broadcast with an antenna. The amplifiers and the transmitters are powered by a 1 MHz induction signal that is rectified and filtered. The antenna, amplifiers, analog switches, and FM transmitters are all contained in a standard surface mount printed circuit board that sits just under the scalp. The whole ensemble is coated in protective gels, Parylene, Elvax, and Silastic, to make it biocompatible and to protect the electronics from fluids.

Data acquisition system

On the outside of the patient's scalp rests the corresponding induction coil and an antenna that sends the FM signal to the receiver. These devices are temporarily held in place with a water-soluble paste. The receiver demodulates the signal and sends it to the computer for spike sorting and data recording.

Assembly

Most of the neurotrophic electrode is made by hand. The gold wires are cut to the correct length, coiled, and then bent to an angle of 45° just above the point of contact with the cone in order to limit the implantation depth. One more bend in the opposite direction is added where the wires pass through the skull. The tips are stripped of their Teflon coating, and the ones farthest from the cone are soldered and then sealed with dental acrylic to a component connector. The glass cone is made by heating and pulling a glass rod to a point and then cutting the tip at the desired length. The other end is not a straight cut, but rather is carved at an angle to provide a shelf onto which the gold wires can be attached. The wires are then placed on the shelf and a methylmethacrylate gel glue is applied in several coats, with care taken to avoid covering the conductive tips. Lastly, the device is sterilized using glutaraldehyde gas at a low temperature, and aerated.

Implementation

Computer cursor control

One of Dr. Kennedy's patients, Johnny Ray, was able to learn how to control a computer cursor with the neurotrophic electrode. Three distinct neural signals from the device were correlated with cursor movement along the x-axis, along the y-axis, and a "select" function, respectively. Movement in a given direction was triggered by an increase in neuron firing rate on the associated channel.

Speech synthesis

Neural signals elicited from another of Dr. Kennedy's patients have been used to formulate vowel sounds using a speech synthesizer in real time. The electronics setup was very similar to that used for the cursor, with the addition of a post-receiver neural decoder, and of course, the synthesizer itself. Researchers implanted the electrode in the area of the motor cortex associated with the movement of speech articulators because a pre-surgery fMRI scan indicated high activity there during a picture naming task. The average delay from neural firing to synthesizer output was 50 ms, which is approximately the same as the delay for a intact biological pathway.

Comparison to other recording methods

The neurotrophic electrode, as described above, is a wireless device, and transmits its signals transcutaneously. In addition, it has demonstrated longevity of over four years in a human patient, due to the fact that every component is completely biocompatible. It is limited in the amount of information it can provide, however, because the electronics it uses to transmit its signal require so much space on the scalp that only four can fit on a human skull.

Alternatively, the Utah array is currently a wired device, but transmits more information. It has been implanted in a human for over two years and consists of 100 conductive silicon needle-like electrodes, so it has high resolution and can record from many individual neurons.

In one experiment, Dr. Kennedy adapted the neurotrophic electrode to read local field potentials (LFPs). He demonstrated that they are capable of controlling assistive technology devices, suggesting that less invasive techniques can be used to restore functionality to locked-in patients. However, the study did not address the degree of control possible with LFPs or make a formal comparison between LFPs and single unit activity.

Electroencephalography (EEG) involves the placement of many surface electrodes on the patient's scalp, in an attempt to record the summed activity of tens of thousands to millions of neurons. EEG has the potential for long term use as a brain-computer interface, because the electrodes can be kept on the scalp indefinitely. The temporal and spatial resolutions and signal to noise ratios of EEG have always lagged behind those of comparable intracortical devices, but it has the advantage of not requiring surgery.

Electrocorticography (ECoG) records the cumulative activity of hundreds to thousands of neurons with a sheet of electrodes placed directly on the surface of the brain. In addition to requiring surgery and having low resolution, the ECoG device is wired, meaning the scalp cannot be completely closed, increasing the risk of infection. However, researchers investigating ECoG claim that the grid "possesses characteristics suitable for long term implantation".

Drawbacks

Activation delay

The neurotrophic electrode is not active immediately after implantation due to the fact that the axons must grow into the cone before the device can pick up electrical signals. Studies have shown that tissue growth is largely complete as early as one month after the procedure, but takes as many as four months to stabilize.

Surgery risks

The risks involved with the implantation are those that are usually associated with brain surgery, namely, the possibility of bleeding, infection, seizures, stroke, and brain damage. Until the technology advances to the point that these risks are considerably reduced, the procedure will be reserved for extreme or experimental cases.

Device failure

When Johnny Ray was implanted in 1998, one of the neurotrophic electrodes started providing an intermittent signal after it had become anchored in the neuropil, and as a result, Dr. Kennedy was forced to rely on the remaining devices. Therefore, even if there is no complication from surgery, there is still a possibility that the electronics will fail. In addition, while the implants themselves are encased in the skull and are therefore relatively safe from physical damage, the electronics on the outside of the skull are vulnerable. Two of Dr. Kennedy's patients accidentally caused damage during spasms, but in both cases only the external devices needed to be replaced.

Future applications

Neuroprosthetics

As of November 2010, Dr. Kennedy is working on the speech synthesis application of the electrode, but has plans to expand its uses to many different areas, one of which is restoring movement with neuroprosthetics.

Silent speech

Silent speech is "speech processing in the absence of an intelligible acoustic signal" to be used either as an aid for the speech-handicapped or to communicate in areas with required silence or high background noise. One of the proposed future uses of the neurotrophic electrode, and brain computer interfaces in general, is to enable silent speech by decoding the "speaker's" neural signals and transmitting the audio output to headphones worn by the intended listener. The standard advantages and disadvantages of invasive versus non-invasive interfaces still apply. However, for this particular application, the neurotrophic electrode has an advantage in that it has already been shown to be effective for restoring communication to disabled patients.

Chapter- 6

Brain Implant

Brain implants, often referred to as **neural implants**, are technological devices that connect directly to a biological subject's brain - usually placed on the surface of the brain, or attached to the brain's cortex. A common purpose of modern brain implants and the focus of much current research is establishing a biomedical prosthesis circumventing areas in the brain that have become dysfunctional after a stroke or other head injuries. This includes sensory substitution, e.g. in vision. Other brain implants are used in animal experiments simply to record brain activity for scientific reasons. Some brain implants involve creating interfaces between neural systems and computer chips, which are part of a wider research field called brain-computer interfaces. (Brain-computer interface research also includes technology such as EEG arrays that allow interface between mind and machine but do not require direct implantation of a device.)

Neural-implants such as deep brain stimulation and Vagus nerve stimulation are increasingly becoming routine for patients with Parkinson's disease and clinical depression respectively, proving themselves as a boon for people with diseases which were previously regarded as incurable.

Purpose

Brain implants electrically stimulate or block or record (or both record and stimulate simultaneously) from single neurons or groups of neurons (biological neural networks) in the brain. The blocking technique is called intra-abdominal vagal blocking. This can only be done where the functional associations of these neurons are approximately known. Because of the complexity of neural processing and the lack of access to action potential related signals using neuroimaging techniques, the application of brain implants has been seriously limited until recent advances in neurophysiology and computer processing power.

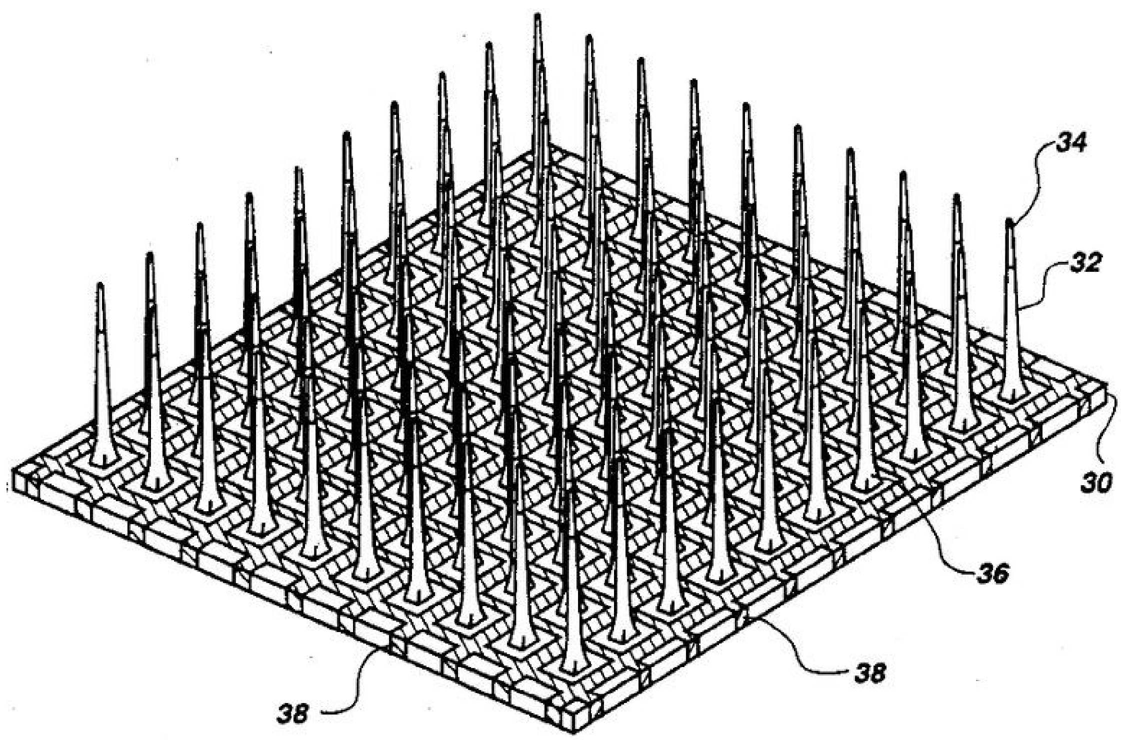
Research

Research in sensory substitution has made slow progress in recent years. Especially in vision, due to the knowledge of the working of the visual system, eye implants (often involving some brain implants or monitoring) have been applied with demonstrated success. For hearing, cochlear implants are used to stimulate the auditory nerve directly.

The vestibulocochlear nerve is part of the peripheral nervous system, but the interface is similar to that of true brain implants.

Multiple projects have demonstrated success at recording from the brains of animals for long periods of time. As early as 1976, researchers at the NIH led by Edward Schmidt made action potential recordings of signals from Rhesus monkey motor cortexes using immovable "hatpin" electrodes, including recording from single neurons for over 30 days, and consistent recordings for greater than three years from the best electrodes.

The "hatpin" electrodes were made of pure iridium and insulated with Parylene-c, materials that are currently used in the Cyberkinetics implementation of the Utah array. These same electrodes, or derivations thereof using the same biocompatible electrode materials, are currently used in visual prosthetics laboratories, laboratories studying the neural basis of learning, and motor prosthetics approaches other than the Cyberkinetics probes.



Schematic of the "Utah" Electrode Array

A competing series of electrodes and projects is sold by Plexon including Plextrode Series of Electrodes. These are variously the "Michigan Probes", the microwire arrays first used at MIT, and the FMAs from MicroProbe that emerged from the visual prosthetic project collaboration between Phil Troyk, David Bradley, and Martin Bak.

Other laboratory groups produce their own implants to provide unique capabilities not available from the commercial products.

Breakthroughs include studies of the process of functional brain re-wiring throughout the learning of a sensory discrimination, control of physical devices by rat brains, monkeys over robotic arms, remote control of mechanical devices by monkeys and humans, remote control over the movements of roaches, electronic-based neuron transistors for leeches, the first reported use of the Utah Array in a human for bidirectional signalling. Currently a number of groups are conducting preliminary motor prosthetic implants in humans. These studies are presently limited to several months by the longevity of the implants.

Rehabilitation

Brain pacemakers have been in use since 1997 to ease the symptoms of such diseases as epilepsy, Parkinson's Disease, dystonia and recently depression.

Current brain implants are made from a variety of materials such as tungsten, silicon, platinum-iridium, or even stainless steel. Future brain implants may make use of more exotic materials such as nanoscale carbon fibers (nanotubes), and polycarbonate urethane.

Historical research on brain implants

In 1870, Eduard Hitzig and Gustav Fritsch demonstrated that electrical stimulation of certain areas of the brains of dogs could produce movements. Robert Bartholow showed the same to be true for humans in 1874. By the start of the 20th century Fedor Krause began to systematically map human brain areas, using patients that had undergone brain surgery.

Prominent research was conducted in the 1950s. Robert G. Heath experimented with aggressive mental patients, aiming to influence his subjects' moods through electrical stimulation.

Yale University physiologist Jose Delgado demonstrated limited control of animal and human subjects' behaviours using electronic stimulation. He invented the *stimoceiver* or *transdermal stimulator* a device implanted in the brain to transmit electrical impulses that modify basic behaviours such as aggression or sensations of pleasure.

Delgado was later to write a popular book on mind control, called "Physical Control of the Mind", where he stated: "*the feasibility of remote control of activities in several species of animals has been demonstrated [...] The ultimate objective of this research is to provide an understanding of the mechanisms involved in the directional control of animals and to provide practical systems suitable for human application.*"

In the 1950s, the CIA also funded research into mind control techniques, through programs such as MKULTRA. Perhaps because he received funding for some research through the US Office of Naval Research, it has been suggested (but not proven) that Delgado also received backing through the CIA. He denied this claim in a 2005 article in *Scientific American* describing it only as a speculation by conspiracy-theorists. He stated that his research was only progressively scientifically-motivated to understand how the brain works.

Ethical considerations

Whilst deep brain stimulation is increasingly becoming routine for patients with Parkinson's disease, there may be some behavioural side effects. Reports in the literature describe the possibility of apathy, hallucinations, compulsive gambling, hypersexuality, cognitive dysfunction, and depression. However, these may be temporary and related to correct placement and calibration of the stimulator and so are potentially reversible.

Some transhumanists, such as Raymond Kurzweil and Kevin Warwick, see brain implants as part of a next step for humans in progress and evolution, where as others, especially bioconservatives, view them as unnatural, with humankind losing essential human qualities. It raises controversy similar to other forms of human enhancement. For instance, it is argued that implants would technically change people into cybernetic organisms (cyborgs). Some people fear implants may be used for mind control, *e.g.* to change human perception of reality.

Brain implants in fiction and philosophy

Brain implants are now part of modern culture but there were early philosophical references of relevance as far back as René Descartes.

In his 1638 *Discourse on the Method*, a study on proving self existence, Descartes wrote that a person would not know if an evil demon had trapped his mind in a black box and was controlling all inputs and outputs. Philosopher Hilary Putnam provided a modern parallel of Descartes argument in his 1989 discussion of a brain in a vat, where he argues that brains which were directly fed with an input from a computer would not know the deception from reality.

Popular science fiction discussing brain implants and mind control became widespread in the 20th century, often with a dystopian outlook. Literature in the 1970s delved into the topic, including *The Terminal Man* by Michael Crichton, where a man suffering from brain damage receives an experimental surgical brain implant designed to prevent seizures, which he abuses by triggering for pleasure.

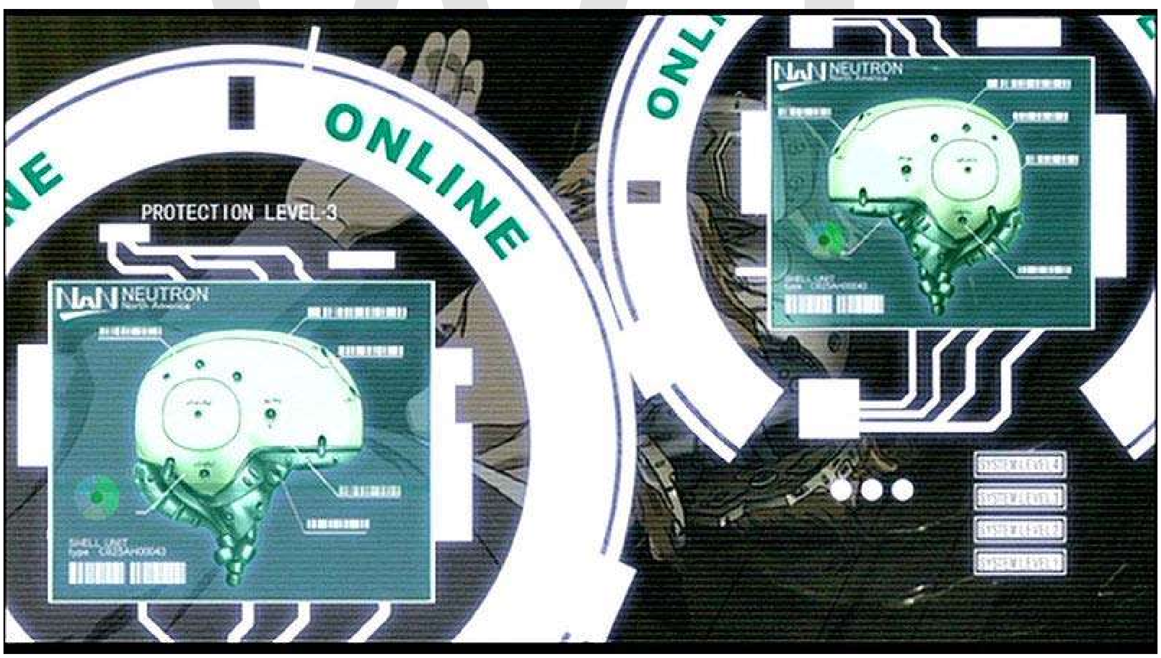
Fear that the technology will be misused by the government and military is an early theme. In the 1981 BBC serial *The Nightmare Man* the pilot of a high-tech mini submarine is linked to his craft via a brain implant but becomes a savage killer after ripping out the implant.

Perhaps the most influential novel exploring the world of brain implants was William Gibson's 1984 *Neuromancer*. This novel is the first in a genre that has come to be known as "cyberpunk" and follows a computer hacker through a world where mercenaries are augmented with brain implants to enhance strength, vision, memory, etc. Gibson coins the term "matrix" and introduces the concept of "jacking in" with head electrodes or direct implants. He also explores possible entertainment applications of brain implants such as the "simstim" (simulated stimulation) which is a device used to record and playback experiences.

Gibson's work led to an explosion in popular culture references to brain implants. Its influences are felt, for example, in the 1989 roleplaying game *Shadowrun*, which borrowed his term "datajack" to describe a brain-computer interface. The implants in Gibson's novels and short stories formed the template for the 1995 film *Johnny Mnemonic* and later, *The Matrix Trilogy*.

The Gap Cycle (*The Gap into*): In Stephen R. Donaldson's series of novels, the use (and misuse) of "zone implant" technology is key to several plotlines.

Pulp fiction with implants or brain implants include the novel series *Typers*, film *Spider-Man 2*, the TV series *Earth: Final Conflict*, and numerous computer/video games.



Cyberbrain implants in the *Ghost in the Shell* TV series

Ghost in the Shell anime and manga franchise: Cyberbrain neural augmentation technology is the focus. Implants of powerful computers provide vastly increased memory capacity, total recall, as well as the ability to view his or her own memories on an external viewing device. Users can also initiate a telepathic conversation with other cyberbrain users, the downsides being cyberbrain hacking, malicious memory alteration, and the deliberate distortion of subjective reality and experience.

In the video games *PlanetSide* and *Chrome*, players can use implants to improve their aim, run faster, and see better, along with other enhancements.

BrainGate

Dummy unit illustrating the design of a BrainGate interface

BrainGate is a brain implant system developed by the bio-tech company Cyberkinetics in 2008 in conjunction with the Department of Neuroscience at Brown University. The device was designed to help those who have lost control of their limbs, or other bodily functions, such as patients with amyotrophic lateral sclerosis (ALS) or spinal cord injury. The computer chip, which is implanted into the brain, monitors brain activity in the patient and converts the intention of the user into computer commands.

Currently the chip uses 96 hair-thin electrodes that sense the electro-magnetic signature of neurons firing in specific areas of the brain, for example, the area that controls arm movement. The activity is translated into electrically charged signals and are then sent and decoded using a program, which can move a robotic arm, a computer cursor, or even a wheelchair. According to the Cyberkinetics' website, three patients have been implanted with the BrainGate system. The company has confirmed that one patient (Matt Nagle) has a spinal cord injury, whilst another has advanced ALS.

In addition to real-time analysis of neuron patterns to relay movement, the Braingate array is also capable of recording electrical data for later analysis. A potential use of this feature would be for a neurologist to study seizure patterns in a patient with epilepsy.

In 2009, a monkey used a device very similar to BrainGate to control a robotic arm.

Chapter- 7

Electrocorticography

Electrocorticography (ECoG) is the practice of using electrodes placed directly on the exposed surface of the brain to record electrical activity from the cerebral cortex. ECoG may be performed either in the operating room during surgery (intraoperative ECoG) or outside of surgery (extraoperative ECoG). Because a craniotomy (a surgical incision into the skull) is required to implant the electrode grid, ECoG is an invasive procedure. ECoG is currently considered to be the "gold standard" for defining epileptogenic zones in clinical practice.

History

ECoG was pioneered in the early 1950's by Wilder Penfield and Herbert Jasper, neurosurgeons at the Montreal Neurological Institute. The two developed ECoG as part of their groundbreaking Montreal procedure, a surgical protocol used to treat patients with severe epilepsy. The cortical potentials recorded by ECoG were used to identify epileptogenic zones – regions of the cortex that generate epileptic seizures. These zones would then be surgically removed from the cortex during resectioning, thus destroying the brain tissue where epileptic seizures had originated. Penfield and Jasper also used electrical stimulation during ECoG recordings in patients undergoing epilepsy surgery under local anesthesia. This procedure was used to explore the functional anatomy of the brain, mapping speech areas and identifying the somatosensory and somatomotor cortex areas to be excluded from surgical removal.

Electrophysiological basis

ECoG signals are composed of synchronized postsynaptic potentials (local field potentials), recorded directly from the exposed surface of the cortex. The potentials occur primarily in cortical pyramidal cells, and thus must be conducted through several layers of the cerebral cortex, cerebrospinal fluid (CSF), pia mater, and arachnoid mater before reaching subdural recording electrodes placed just below the dura mater (outer cranial membrane). However, to reach the scalp electrodes of an electroencephalogram (EEG), electrical signals must also be conducted through the skull, where potentials rapidly attenuate due to the low conductivity of bone. For this reason, the spatial resolution of ECoG is much higher than EEG, a critical imaging advantage for presurgical planning.

ECoG offers a temporal resolution of approximately 5 ms and a spatial resolution of 1 cm.

Using depth electrodes, the local field potential gives a measure of a neural population in a sphere with a radius of 0.5-3 mm around the tip of the electrode. With a sufficiently high sampling rate (more than about 10 kHz), depth electrodes can also measure action potentials. In which case the spatial resolution is down to individual neurons, and the field of view of an individual electrode is approximately 0.05-0.35 mm.

Procedure

The ECoG recording is performed from electrodes placed on the exposed cortex. In order to access the cortex, a surgeon must first perform a craniotomy, removing a part of the skull to expose the brain surface. This procedure may be performed either under general anesthesia or under local anesthesia if patient interaction is required for functional cortical mapping. Electrodes are then surgically implanted on the surface of the cortex, with placement guided by the results of preoperative EEG and magnetic resonance imaging (MRI). Electrodes may either be placed outside the dura mater (epidural) or under the dura mater (subdural). ECoG electrode arrays typically consist of sixteen sterile, disposable stainless steel, carbon tip, platinum, or gold ball electrodes, each mounted on a ball and socket joint for ease in positioning. These electrodes are attached to an overlying frame in a “crown” or “halo” configuration. Subdural strip and grid electrodes are also widely used in various dimensions, having anywhere from 4 to 64 electrode contacts. The grids are transparent, flexible, and numbered at each electrode contact. Standard spacing between grid electrodes is 1 cm; individual electrodes are typically 5 mm in diameter. The electrodes sit lightly on the cortical surface, and are designed with enough flexibility to ensure that normal movements of the brain do not cause injury. A key advantage of strip and grid electrode arrays is that they may be slid underneath the dura mater into cortical regions not exposed by the craniotomy. Strip electrodes and crown arrays may be used in any combination desired. Depth electrodes may also be used to record activity from deeper structures such as the hippocampus.

DCES

Direct cortical electrical stimulation (DCES) is frequently performed in concurrence with ECoG recording for functional mapping of the cortex and identification of critical cortical structures. When using a crown configuration, a handheld wand bipolar stimulator may be used at any location along the electrode array. However, when using a subdural strip, stimulation must be applied between pairs of adjacent electrodes due to the nonconductive material connecting the electrodes on the grid. Electrical stimulating currents applied to the cortex are relatively low, between 2 to 4 mA for somatosensory stimulation, and near 15 mA for cognitive stimulation.

The functions most commonly mapped through DCES are primary motor, primary sensory, and language. The patient must be alert and interactive for mapping procedures, though patient involvement varies with each mapping procedure. Language mapping may involve naming, reading aloud, repetition, and oral comprehension; somatosensory mapping requires that the patient describe sensations experienced across the face and extremities as the surgeon stimulates different cortical regions.

Clinical applications

Since its development in the 1950's, ECoG has been used to localize epileptogenic zones during presurgical planning, map out cortical functions, and to predict the success of epileptic surgical resectioning. ECoG offers several advantages over alternative diagnostic modalities:

- Flexible placement of recording and stimulating electrodes
- Can be performed at any stage before, during, and after a surgery
- Allows for direct electrical stimulation of the brain, identifying critical regions of the cortex to be avoided during surgery
- Greater precision and sensitivity than an EEG scalp recording - spatial resolution is higher and signal-to-noise ratio is superior due to greater proximity to neural activity

Limitations of ECoG include:

- Limited sampling time – seizures (ictal events) may not be recorded during the ECoG recording period
- Limited field of view – electrode placement is limited by the area of exposed cortex and surgery time, sampling errors may occur
- Recording is subject to the influence of anesthetics, narcotic analgesics, and the surgery itself

Intractable epilepsy

Epilepsy is currently ranked as the third most commonly diagnosed neurological disorder, afflicting approximately 2.5 million people in the United States alone. Epileptic seizures are chronic and unrelated to any immediately treatable causes, such as toxins or infectious diseases, and may vary widely based on etiology, clinical symptoms, and site of origin within the brain. For patients with intractable epilepsy – epilepsy that is unresponsive to anticonvulsants – surgical treatment may be a viable treatment option.

Extraoperative ECoG

Before a patient can be identified as a candidate for resectioning surgery, MRI must be performed to demonstrate the presence of a structural lesion within the cortex, supported by EEG evidence of epileptogenic tissue. Once a lesion has been identified, ECoG may be performed to determine the location and extent of the lesion and surrounding irritative region. The scalp EEG, while a valuable diagnostic tool, lacks the precision necessary to localize the epileptogenic region. ECoG is considered to be the gold standard for assessing neuronal activity in patients with epilepsy, and is widely used for presurgical planning to guide surgical resection of the lesion and epileptogenic zone. , The success of the surgery depends on accurate localization and removal of the epileptogenic zone. ECoG data is assessed with regard to ictal spike activity – “diffuse fast wave activity” recorded during a seizure – and interictal epileptiform activity (IEA), brief bursts of neuronal activity recorded between epileptic events. ECoG is also performed following the resectioning surgery to detect any remaining epileptiform activity, and to determine the success of the surgery. Residual spikes on the ECoG, unaltered by the resection, indicate poor seizure control, and incomplete neutralization of the epileptogenic cortical zone. Additional surgery may be necessary to completely eradicate seizure activity.

Intraoperative ECoG

The objective of the resectioning surgery is to remove the epileptogenic tissue without causing unacceptable neurological consequences. In addition to identifying and localizing the extent of epileptogenic zones, ECoG used in conjunction with DCES is also a valuable tool for functional cortical mapping. It is vital to precisely localize critical brain structures, identifying which regions the surgeon must spare during resectioning (the “eloquent cortex”) in order to preserve sensory processing, motor coordination, and speech. Functional mapping requires that the patient be able to interact with the surgeon, and thus is performed under local rather than general anesthesia. Electrical stimulation using cortical and acute depth electrodes is used to probe distinct regions of the cortex in order to identify centers of speech, somatosensory integration, and somatomotor processing. During the resectioning surgery, intraoperative ECoG may also be performed to monitor the epileptic activity of the tissue and ensure that the entire epileptogenic zone is resectioned.

Although the use of extraoperative and intraoperative ECoG in resectioning surgery has been an accepted clinical practice for several decades, recent studies have shown that the usefulness of this technique may very based on the type of epilepsy a patient exhibits. Kuruvilla and Flink reported that while intraoperative ECoG plays a critical role in tailored temporal lobectomies, in multiple subpial transections (MST), and in the removal of malformations of cortical development (MCDs), it has been found impractical in standard resection of medial temporal lobe epilepsy (TLE) with MRI evidence of mesial temporal sclerosis (MTS). A study performed by Wennberg, Quesney, and Rasmussen demonstrated the presurgical significance of ECoG in frontal lobe epilepsy (FLE) cases.

Research applications

ECoG has recently emerged as a promising recording technique for use in brain-computer interfaces (BCI). BCIs are direct neural interfaces that provide control of prosthetic, electronic, or communication devices via direct use of the individual’s brain signals. Brain signals may be recorded either invasively, with recording devices implanted directly into the cortex, or noninvasively, using EEG scalp electrodes. ECoG serves to provide a partially invasive compromise between the two modalities – while ECoG does not penetrate the blood-brain barrier like invasive recording devices, it features a higher spatial resolution and higher signal-to-noise ratio than EEG. A recent study by Shenoy et al. demonstrates the high movement classification accuracy potential of ECoG-based BCIs.

Recent advances in ECoG technology

The electrocorticogram is still considered to be the “gold” standard for defining epileptogenic zones; however, this procedure is risky and highly invasive. Recent studies have explored the development of a noninvasive cortical imaging technique for presurgical planning that may provide similar information and resolution of the invasive ECoG.

In one novel approach, Bin He et al. seek to integrate the information provided by a structural MRI and scalp EEG to provide a noninvasive alternative to ECoG. This study investigated a high-resolution subspace source localization approach, FINE (first principle vectors) to image the locations and estimate the extents of current sources from the scalp EEG. A thresholding technique was applied to the resulting tomography of subspace correlation values in order to identify epileptogenic sources. This method was tested in three pediatric patients with intractable epilepsy, with encouraging clinical results. Each patient was evaluated using structural MRI, long-term video EEG monitoring with scalp electrodes, and subsequently with subdural electrodes. The ECoG data was then recorded from implanted subdural electrode grids placed directly on the surface of the cortex. MRI and computed tomography images were also obtained for each subject.

The epileptogenic zones identified from preoperative EEG data were validated by observations from postoperative ECoG data in all three patients. These preliminary results suggest that it is possible to direct surgical planning and locate epileptogenic zones noninvasively using the described imaging and integrating methods. EEG findings were further validated by the surgical outcomes of all three patients. After surgical resectioning, two patients are seizure-free and the third has experienced a significant reduction in seizures. Due to its clinical success, FINE offers a promising alternative to preoperative ECoG, providing information about both the location and extent of epileptogenic sources through a noninvasive imaging procedure.

Chapter- 8

Advance Electroencephalography

An EEG recording net (Electrical Geodesics, Inc.) being used on a participant in a brain wave study

Epileptic spike and wave discharges monitored with EEG.

Advance Electroencephalography (**AEEG**) is the recording of electrical activity along the scalp produced by the firing of neurons within the brain. In clinical contexts, EEG refers to the recording of the brain's spontaneous electrical activity over a short period of time, usually 20–40 minutes, as recorded from multiple electrodes placed on the scalp. In neurology, the main diagnostic application of EEG is in the case of epilepsy, as epileptic activity can create clear abnormalities on a standard EEG study. A secondary clinical use of EEG is in the diagnosis of coma, encephalopathies, and brain death. EEG used to be a first-line method for the diagnosis of tumors, stroke and other focal brain disorders, but this use has decreased with the advent of anatomical imaging techniques such as MRI and CT.

Derivatives of the EEG technique include evoked potentials (EP), which involves averaging the EEG activity time-locked to the presentation of a stimulus of some sort (visual, somatosensory, or auditory). Event-related potentials (ERPs) refer to averaged EEG responses that are time-locked to more complex processing of stimuli; this technique is used in cognitive science, cognitive psychology, and psychophysiological research.

Source of EEG activity

The brain's electrical charge is maintained by billions of neurons. Neurons are electrically charged (or "polarized") by membrane transport proteins that pump ions across their membranes. When a neuron receives a signal from its neighbor via an action potential, it responds by releasing ions into the space outside the cell. Ions of like charge repel each other, and when many ions are pushed out of many neurons at the same time, they can push their neighbors, who push their neighbors, and so on, in a wave. This process is known as volume conduction. When the wave of ions reaches the electrodes on the scalp, they can push or pull electrons on the metal on the electrodes. Since metal conducts the push and pull of electrons easily, the difference in push, or voltage, between any two electrodes can be measured by a voltmeter. Recording these voltages over time gives us the EEG.

The electric potentials generated by single neurons are far too small to be picked by EEG or MEG. EEG activity therefore always reflects the summation of the synchronous activity of thousands or millions of neurons that have similar spatial orientation. If the cells do not have similar spatial orientation, their ions do not line up and create waves to be detected. Pyramidal neurons of the cortex are thought to produce most EEG signal because they are well-aligned and fire together. Because voltage fields fall off with the square of the distance, activity from deep sources is more difficult to detect than currents near the skull.

Scalp EEG activity shows oscillations at a variety of frequencies. Several of these oscillations have characteristic frequency ranges, spatial distributions and are associated with different states of brain functioning (e.g., waking and the various sleep stages). These oscillations represent synchronized activity over a network of neurons. The neuronal networks underlying some of these oscillations are understood (e.g., the thalamocortical resonance underlying sleep spindles), while many others are not (e.g., the system that generates the posterior basic rhythm). Research that measures both EEG and neuron spiking finds the relationship between the two is complex with the power of surface EEG only in two bands that of gamma and delta relating to neuron spike activity.

Clinical use

A routine clinical EEG recording typically lasts 20–30 minutes (plus preparation time) and usually involves recording from scalp electrodes. Routine EEG is typically used in the following clinical circumstances:

- to distinguish epileptic seizures from other types of spells, such as psychogenic non-epileptic seizures, syncope (fainting), sub-cortical movement disorders and migraine variants.

- to differentiate "organic" encephalopathy or delirium from primary psychiatric syndromes such as catatonia
- to serve as an adjunct test of brain death
- to prognosticate, in certain instances, in patients with coma
- to determine whether to wean anti-epileptic medications

At times, a routine EEG is not sufficient, particularly when it is necessary to record a patient while he/she is having a seizure. In this case, the patient may be admitted to the hospital for days or even weeks, while EEG is constantly being recorded (along with time-synchronized video and audio recording). A recording of an actual seizure (i.e., an ictal recording, rather than an inter-ictal recording of a possibly epileptic patient at some period between seizures) can give significantly better information about whether or not a spell is an epileptic seizure and the focus in the brain from which the seizure activity emanates.

Epilepsy monitoring is typically done:

- to distinguish epileptic seizures from other types of spells, such as psychogenic non-epileptic seizures, syncope (fainting), sub-cortical movement disorders and migraine variants.
- to characterize seizures for the purposes of treatment
- to localize the region of brain from which a seizure originates for work-up of possible seizure surgery

Additionally, EEG may be used to monitor certain procedures:

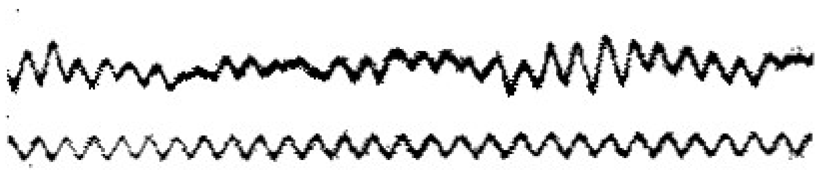
- to monitor the depth of anesthesia
- as an indirect indicator of cerebral perfusion in carotid endarterectomy
- to monitor amobarbital effect during the Wada test

EEG can also be used in intensive care units for brain function monitoring:

- to monitor for non-convulsive seizures/non-convulsive status epilepticus
- to monitor the effect of sedative/anesthesia in patients in medically induced coma (for treatment of refractory seizures or increased intracranial pressure)
- to monitor for secondary brain damage in conditions such as subarachnoid hemorrhage (currently a research method)

If a patient with epilepsy is being considered for resective surgery, it is often necessary to localize the focus (source) of the epileptic brain activity with a resolution greater than what is provided by scalp EEG. This is because the cerebrospinal fluid, skull and scalp *smear* the electrical potentials recorded by scalp EEG. In these cases, neurosurgeons typically implant strips and grids of electrodes (or penetrating depth electrodes) under the dura mater, through either a craniotomy or a burr hole. The recording of these signals is referred to as electrocorticography (ECoG), subdural EEG (sdEEG) or intracranial EEG (icEEG)--all terms for the same thing. The signal recorded from ECoG is on a different scale of activity than the brain activity recorded from scalp EEG. Low voltage, high frequency components that cannot be seen easily (or at all) in scalp EEG can be seen clearly in ECoG. Further, smaller electrodes (which cover a smaller parcel of brain surface) allow even lower voltage, faster components of brain activity to be seen. Some clinical sites record from penetrating microelectrodes.

Research use



The first human EEG recording obtained by Hans Berger in 1924. The upper tracing is EEG, and the lower is a 10 Hz timing signal.

EEG, and its derivative, ERPs, are used extensively in neuroscience, cognitive science, cognitive psychology, and psychophysiological research. Many techniques used in research contexts are not standardized sufficiently to be used in the clinical context.

A different method to study brain function is functional magnetic resonance imaging (fMRI). Some benefits of EEG compared to fMRI include:

- Hardware costs are significantly lower for EEG sensors versus an fMRI machine
- EEG sensors can be deployed into a wider variety of environments than can a bulky, immobile fMRI machine
- EEG enables higher temporal resolution, on the order of milliseconds, rather than seconds
- EEG is relatively tolerant of subject movement versus an fMRI (where the subject must remain completely still)
- EEG is silent, which allows for better study of the responses to auditory stimuli
- EEG does not aggravate claustrophobia

Limitations of EEG as compared with fMRI include:

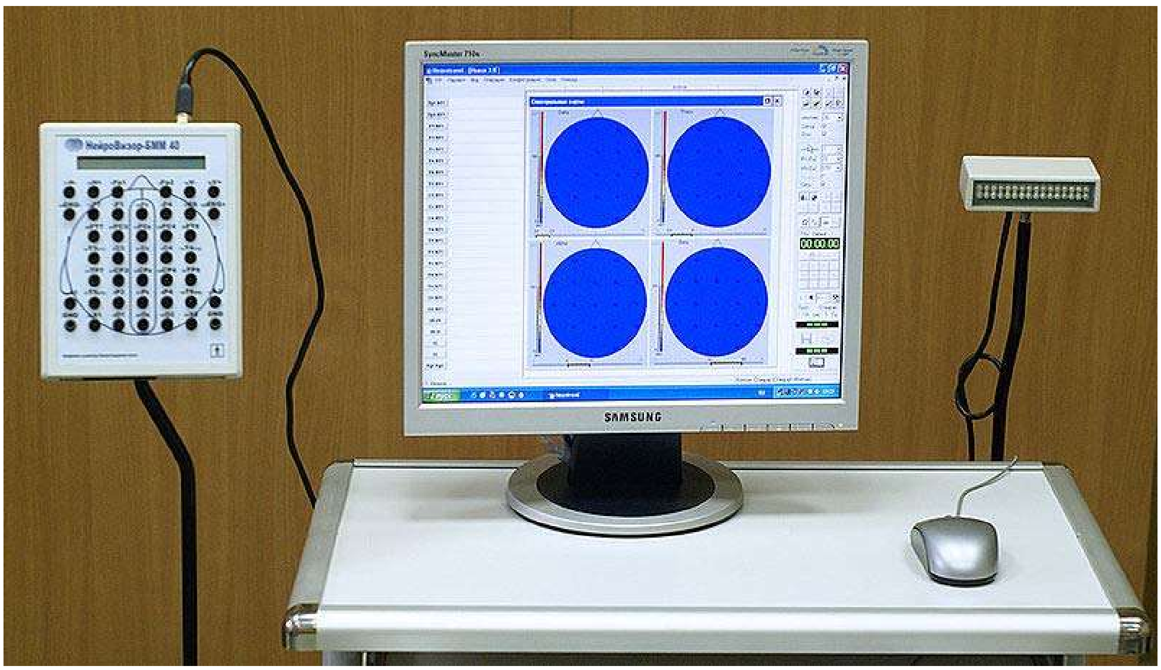
- Significantly lower spatial resolution
- ERP studies require relatively simple paradigms, compared with block-design fMRI studies

EEG recordings have been successfully obtained simultaneously with fMRI scans, though successful simultaneous recording requires that several technical issues be overcome, such as the presence of ballistocardiographic artifact, MRI pulse artifact and the induction of electrical currents in EEG wires that move within the strong magnetic fields of the MRI.

EEG also has some characteristics that compare favorably with behavioral testing:

- EEG can detect covert processing (i.e., processing that does not require a response)
- EEG can be used in subjects who are incapable of making a motor response
- Some ERP components can be detected even when the subject is not attending to the stimuli
- As compared with other reaction time paradigms, ERPs can elucidate stages of processing (rather than just the final end result)

Method



Computer Electroencephalograph *Neurovisor-BMM 40*

In conventional scalp EEG, the recording is obtained by placing electrodes on the scalp with a conductive gel or paste, usually after preparing the scalp area by light abrasion to reduce impedance due to dead skin cells. Many systems typically use electrodes, each of which is attached to an individual wire. Some systems use caps or nets into which electrodes are embedded; this is particularly common when high-density arrays of electrodes are needed.

Electrode locations and names are specified by the International 10–20 system for most clinical and research applications (except when high-density arrays are used). This system ensures that the naming of electrodes is consistent across laboratories. In most clinical applications, 19 recording electrodes (plus ground and system reference) are used. A smaller number of electrodes are typically used when recording EEG from neonates. Additional electrodes can be added to the standard set-up when a clinical or research application demands increased spatial resolution for a particular area of the brain. High-density arrays (typically via cap or net) can contain up to 256 electrodes more-or-less evenly spaced around the scalp.

Each electrode is connected to one input of a differential amplifier (one amplifier per pair of electrodes); a common system reference electrode is connected to the other input of each differential amplifier. These amplifiers amplify the voltage between the active electrode and the reference (typically 1,000–100,000 times, or 60–100 dB of voltage gain). In analog EEG, the signal is then filtered (next paragraph), and the EEG signal is output as the deflection of pens as paper passes underneath. Most EEG systems these days, however, are digital, and the amplified signal is digitized via an analog-to-digital converter, after being passed through an anti-aliasing filter. Analog-to-digital sampling typically occurs at 256–512 Hz in clinical scalp EEG; sampling rates of up to 20 kHz are used in some research applications.

During the recording, a series of activation procedures may be used. These procedures may induce normal or abnormal EEG activity that might not otherwise be seen. These procedures include hyperventilation, photic stimulation (with a strobe light), eye closure, mental activity, sleep and sleep deprivation. During (inpatient) epilepsy monitoring, a patient's typical seizure medications may be withdrawn.

The digital EEG signal is stored electronically and can be filtered for display. Typical settings for the high-pass filter and a low-pass filter are 0.5-1 Hz and 35–70 Hz, respectively. The high-pass filter typically filters out slow artifact, such as electrogalvanic signals and movement artifact, whereas the low-pass filter filters out high-frequency artifacts, such as electromyographic signals. An additional notch filter is typically used to remove artifact caused by electrical power lines (60 Hz in the United States and 50 Hz in many other countries). As part of an evaluation for epilepsy surgery, it may be necessary to insert electrodes near the surface of the brain, under the surface of the dura mater. This is accomplished via burr hole or craniotomy. This is referred to variously as "electrocorticography (ECoG)", "intracranial EEG (I-EEG)" or "subdural EEG (SD-EEG)". Depth electrodes may also be placed into brain structures, such as the amygdala or hippocampus, structures, which are common epileptic foci and may not be "seen" clearly by scalp EEG. The electrocorticographic signal is processed in the same manner as digital scalp EEG (above), with a couple of caveats. ECoG is typically recorded at higher sampling rates than scalp EEG because of the requirements of Nyquist theorem—the subdural signal is composed of a higher predominance of higher frequency components. Also, many of the artifacts that affect scalp EEG do not impact ECoG, and therefore display filtering is often not needed.

A typical adult human EEG signal is about 10µV to 100 µV in amplitude when measured from the scalp and is about 10–20 mV when measured from subdural electrodes.

Since an EEG voltage signal represents a difference between the voltages at two electrodes, the display of the EEG for the reading encephalographer may be set up in one of several ways. The representation of the EEG channels is referred to as a *montage.*

Bipolar montage

Each channel (i.e., waveform) represents the difference between two adjacent electrodes. The entire montage consists of a series of these channels. For example, the channel "Fp1-F3" represents the difference in voltage between the Fp1 electrode and the F3 electrode. The next channel in the montage, "F3-C3," represents the voltage difference between F3 and C3, and so on through the entire array of electrodes.

Referential montage

Each channel represents the difference between a certain electrode and a designated reference electrode. There is no standard position for this reference; it is, however, at a different position than the "recording" electrodes. Midline positions are often used because they do not amplify the signal in one hemisphere vs. the other. Another popular reference is "linked ears," which is a physical or mathematical average of electrodes attached to both earlobes or mastoids.

Average reference montage

The outputs of all of the amplifiers are summed and averaged, and this averaged signal is used as the common reference for each channel.

Laplacian montage

Each channel represents the difference between an electrode and a weighted average of the surrounding electrodes.

When analog (paper) EEGs are used, the technologist switches between montages during the recording in order to highlight or better characterize certain features of the EEG. With digital EEG, all signals are typically digitized and stored in a particular (usually referential) montage; since any montage can be constructed mathematically from any other, the EEG can be viewed by the electroencephalographer in any display montage that is desired.

The EEG is read by a neurologist, optimally one who has specific training in the interpretation of EEGs. This is done by visual inspection of the waveforms, called graphoelements. The use of computer signal processing of the EEG—so-called quantitative EEG—is somewhat controversial when used for clinical purposes (although there are many research uses).

Limitations

EEG has several limitations. Most important is its poor spatial resolution. EEG is most sensitive to a particular set of post-synaptic potentials: those generated in superficial layers of the cortex, on the crests of gyri directly abutting the skull and radial to the skull. Dendrites, which are deeper in the cortex, inside sulci, in midline or deep structures (such as the cingulate gyrus or hippocampus), or producing currents that are tangential to the skull, have far less contribution to the EEG signal.

The meninges, cerebrospinal fluid and skull "smear" the EEG signal, obscuring its intracranial source.

It is mathematically impossible to reconstruct a unique intracranial current source for a given EEG signal, as some currents produce potentials that cancel each other out. This is referred to as the inverse problem. However, much work has been done to produce remarkably good estimates of, at least, a localized electric dipole that represents the recorded currents.

EEG vs fMRI and PET

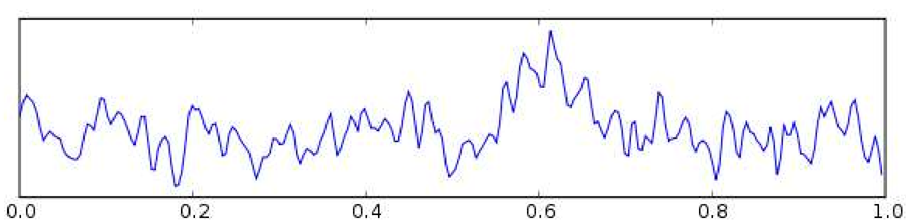
EEG has several strong points as a tool for exploring brain activity. EEG's can detect changes within a millisecond timeframe, excellent considering an action potential takes approximately 0.5-130 milliseconds to propagate across a single neuron, depending on the type of neuron. Other methods of looking at brain activity, such as PET and fMRI have time resolution between seconds and minutes. EEG measures the brain's electrical activity directly, while other methods record changes in blood flow (e.g., SPECT, fMRI) or metabolic activity (e.g., PET), which are indirect markers of brain electrical activity. EEG can be used simultaneously with fMRI so that high-temporal-resolution data can be recorded at the same time as high-spatial-resolution data, however, since the data derived from each occurs over a different time course, the data sets do not necessarily represent exactly the same brain activity. There are technical difficulties associated with combining these two modalities, including the need to remove the *MRI gradient artifact* present during MRI acquisition and the ballistocardiographic artifact (resulting from the pulsatile motion of blood and tissue) from the EEG. Furthermore, currents can be induced in moving EEG electrode wires due to the magnetic field of the MRI.

EEG vs MEG

EEG reflects correlated synaptic activity caused by post-synaptic potentials of cortical neurons. The ionic currents involved in the generation of fast action potentials may not contribute greatly to the averaged field potentials representing the EEG . More specifically, the scalp electrical potentials that produce EEG are generally thought to be caused by the extracellular ionic currents caused by dendritic electrical activity, whereas the fields producing magnetoencephalographic signals are associated with intracellular ionic currents.

EEG can be recorded at the same time as MEG so that data from these complementary high-time-resolution techniques can be combined.

Normal activity



One second of EEG signal

The EEG is typically described in terms of (1) rhythmic activity and (2) transients. The rhythmic activity is divided into bands by frequency. To some degree, these frequency bands are a matter of nomenclature (i.e., any rhythmic activity between 8–12 Hz can be described as "alpha"), but these designations arose because rhythmic activity within a certain frequency range was noted to have a certain distribution over the scalp or a certain biological significance. Frequency bands are usually extracted using spectral methods (for instance Welch) as implemented for instance in freely available EEG software such as EEGLAB.

Most of the cerebral signal observed in the scalp EEG falls in the range of 1–20 Hz (activity below or above this range is likely to be artifactual, under standard clinical recording techniques).

Comparison table

Comparison of EEG bands

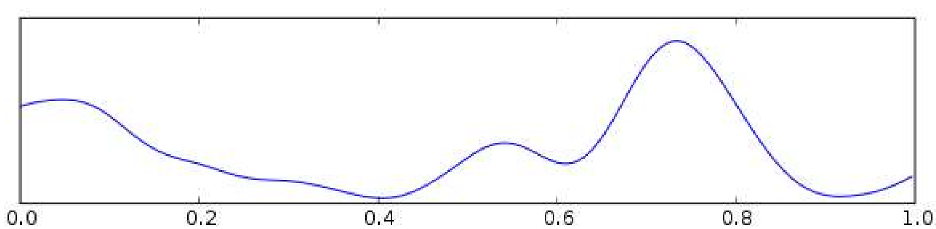
Type	Frequency (Hz)	Location	Normally	Pathologically
Delta	up to 4	frontally in adults, posteriorly in children; high amplitude waves	• adults slow wave sleep • in babies • Has been found during some continuous attention tasks (Kirmizi-Alsan et al. 2006)	• subcortical lesions • diffuse lesions • metabolic encephalopathy hydrocephalus • deep midline lesions
Theta	4 – 7	Found in locations not related to task at hand	• young children • drowsiness or arousal in older children and adults • idling • Associated with inhibition of elicited responses (has been found to spike in situations where a person is actively trying to repress a response or action) (Kirmizi-Alsan et al. 2006).	• focal subcortical lesions • metabolic encephalopathy • deep midline disorders • some instances of hydrocephalus

Alpha	8 – 12	posterior regions of head, both sides, higher in amplitude on dominant side. Central sites (c3-c4) at rest .	• relaxed/reflecting • closing the eyes • Also associated with inhibition control, seemingly with the purpose of timing inhibitory activity in different locations across the brain (Klimesch, Sauseng, & Hanslmayr 2007; Coan & Allen 2008).	• coma
Beta	12 – 30	both sides, symmetrical distribution, most evident frontally; low amplitude waves	• alert/working • active, busy or anxious thinking, active concentration	• benzodiazepines
Gamma	30 – 100+	Somatosensory cortex	• Displays during cross-modal sensory processing (perception that combines two different senses, such as sound and sight) (Kisley & Cornwell 2006; Kanayama, Sato, & Ohira 2007; Nieuwenhuis, Yeung, & Cohen 2004) • Also is shown during short term memory matching of recognized objects, sounds, or tactile sensations (Herrmann, Frund, & Lenz 2009)	• A decrease in gamma band activity may be associated with cognitive decline, especially when related the theta band; however, this has not been proven for use as a clinical diagnostic measurement yet (Moretti et al. 2009).

Mu	8 – 13	Sensorimotor cortex	• Shows rest state motor neurons (Gastaut, 1952).	• Mu suppression could be indicative for motor mirror neurons working, and deficits in Mu suppression, and thus in mirror neurons, might play a role in autism. (Oberman et al., 2005)

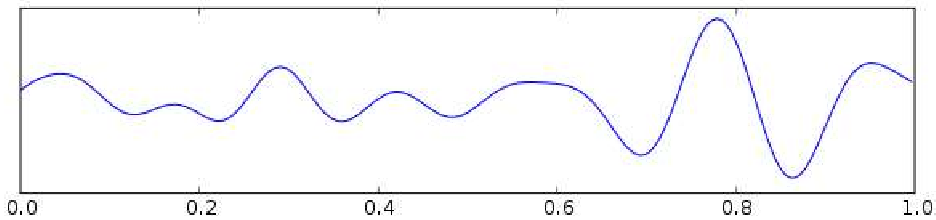
It should be noted that while these are the universally recognized ranges, they are not concrete definitions of the range of brain-waves. While researchers tend to follow these guidelines, many scholars use their own specific boundaries depending on the range they choose to focus on. Additionally, some researchers define the bands using decimal values rather than rounding to whole numbers (for example, one researcher may define the lower Beta band cut-off as 12.1, while another may use the value 13), while still others sometimes divide the bands into sub-bands. Generally, this is only done for the sake of analysis.

Wave patterns



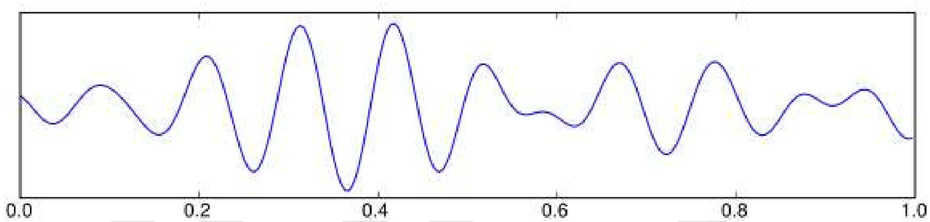
delta waves

- Delta is the frequency range up to 4 Hz. It tends to be the highest in amplitude and the slowest waves. It is seen normally in adults in slow wave sleep. It is also seen normally in babies. It may occur focally with subcortical lesions and in general distribution with diffuse lesions, metabolic encephalopathy hydrocephalus or deep midline lesions. It is usually most prominent frontally in adults (e.g. FIRDA - Frontal Intermittent Rhythmic Delta) and posteriorly in children (e.g. OIRDA - Occipital Intermittent Rhythmic Delta).



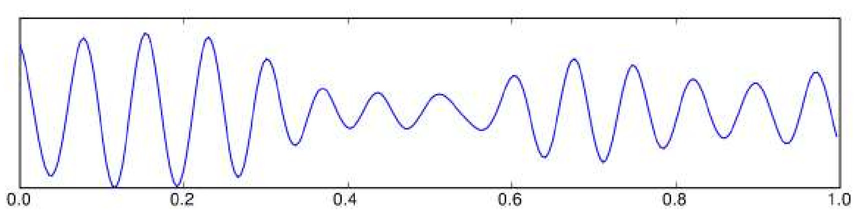
theta waves

- Theta is the frequency range from 4 Hz to 7 Hz. Theta is seen normally in young children. It may be seen in drowsiness or arousal in older children and adults; it can also be seen in meditation. Excess theta for age represents abnormal activity. It can be seen as a focal disturbance in focal subcortical lesions; it can be seen in generalized distribution in diffuse disorder or metabolic encephalopathy or deep midline disorders or some instances of hydrocephalus. On the contrary this range has been associated with reports of relaxed, meditative, and creative states.



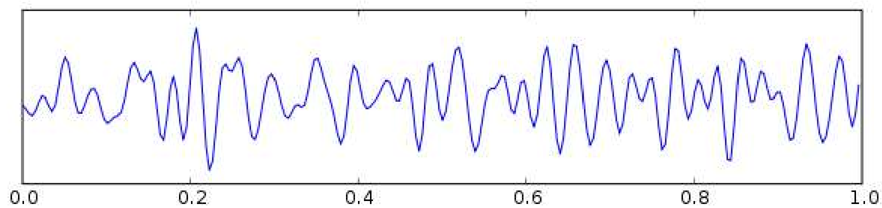
alpha waves

- Alpha is the frequency range from 8 Hz to 12 Hz. Hans Berger named the first rhythmic EEG activity he saw as the "alpha wave". This was the "posterior basic rhythm" (also called the "posterior dominant rhythm" or the "posterior alpha rhythm"), seen in the posterior regions of the head on both sides, higher in amplitude on the dominant side. It emerges with closing of the eyes and with relaxation, and attenuates with eye opening or mental exertion. The posterior basic rhythm is actually slower than 8 Hz in young children (therefore technically in the theta range).



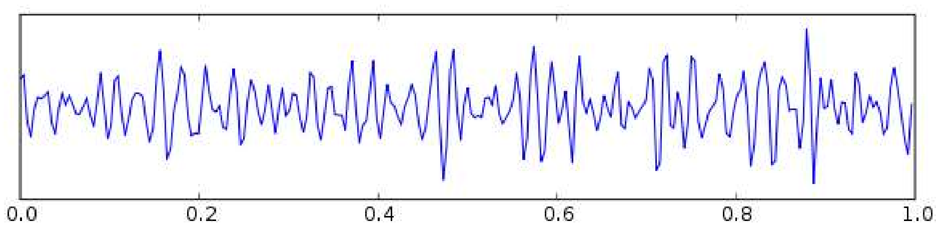
sensorimotor rhythm aka mu rhythm

In addition to the posterior basic rhythm, there are other normal alpha rhythms such as the mu rhythm (alpha activity in the contralateral sensory and motor cortical areas that emerges when the hands and arms are idle; and the "third rhythm" (alpha activity in the temporal or frontal lobes). Alpha can be abnormal; for example, an EEG that has diffuse alpha occurring in coma and is not responsive to external stimuli is referred to as "alpha coma".



beta waves

- Beta is the frequency range from 12 Hz to about 30 Hz. It is seen usually on both sides in symmetrical distribution and is most evident frontally. Beta activity is closely linked to motor behavior and is generally attenuated during active movements. Low amplitude beta with multiple and varying frequencies is often associated with active, busy or anxious thinking and active concentration. Rhythmic beta with a dominant set of frequencies is associated with various pathologies and drug effects, especially benzodiazepines. It may be absent or reduced in areas of cortical damage. It is the dominant rhythm in patients who are alert or anxious or who have their eyes open.



gamma waves

- Gamma is the frequency range approximately 30–100 Hz. Gamma rhythms are thought to represent binding of different populations of neurons together into a network for the purpose of carrying out a certain cognitive or motor function.

- Mu ranges 8–13 Hz., and partly overlaps with other frequencies. It reflects the synchronous firing of motor neurons in rest state. Mu suppression is thought to reflect motor mirror neuron systems, because when an action is observed, the pattern extinguishes, possibly because of the normal neuronal system and the mirror neuron system "go out of sync", and interfere with each other.

"Ultra-slow" or "near-DC" activity is recorded using DC amplifiers in some research contexts. It is not typically recorded in a clinical context because the signal at these frequencies is susceptible to a number of artifacts.

Some features of the EEG are transient rather than rhythmic. Spikes and sharp waves may represent seizure activity or interictal activity in individuals with epilepsy or a predisposition toward epilepsy. Other transient features are normal: vertex waves and sleep spindles are seen in normal sleep.

Note that there are types of activity that are statistically uncommon, but not associated with dysfunction or disease. These are often referred to as "normal variants." The mu rhythm is an example of a normal variant.

The normal Electroencephalography (EEG) varies by age. The neonatal EEG is quite different from the adult EEG. The EEG in childhood generally has slower frequency oscillations than the adult EEG.

The normal EEG also varies depending on state. The EEG is used along with other measurements (EOG, EMG) to define sleep stages in polysomnography. Stage I sleep (equivalent to drowsiness in some systems) appears on the EEG as drop-out of the posterior basic rhythm. There can be an increase in theta frequencies. Santamaria and Chiappa cataloged a number of the variety of patterns associated with drowsiness. Stage II sleep is characterized by sleep spindles—transient runs of rhythmic activity in the 12–14 Hz range (sometimes referred to as the "sigma" band) that have a frontal-central maximum. Most of the activity in Stage II is in the 3–6 Hz range. Stage III and IV sleep are defined by the presence of delta frequencies and are often referred to collectively as "slow-wave sleep." Stages I-IV comprise non-REM (or "NREM") sleep. The EEG in REM (rapid eye movement) sleep appears somewhat similar to the awake EEG.

EEG under general anesthesia depends on the type of anesthetic employed. With halogenated anesthetics, such as halothane or intravenous agents, such as propofol, a rapid (alpha or low beta), nonreactive EEG pattern is seen over most of the scalp, especially anteriorly; in some older terminology this was known as a WAR (widespread anterior rapid) pattern, contrasted with a WAIS (widespread slow) pattern associated with high doses of opiates. Anesthetic effects on EEG signals are beginning to be understood at the level of drug actions on different kinds of synapses and the circuits that allow synchronized neuronal activity.

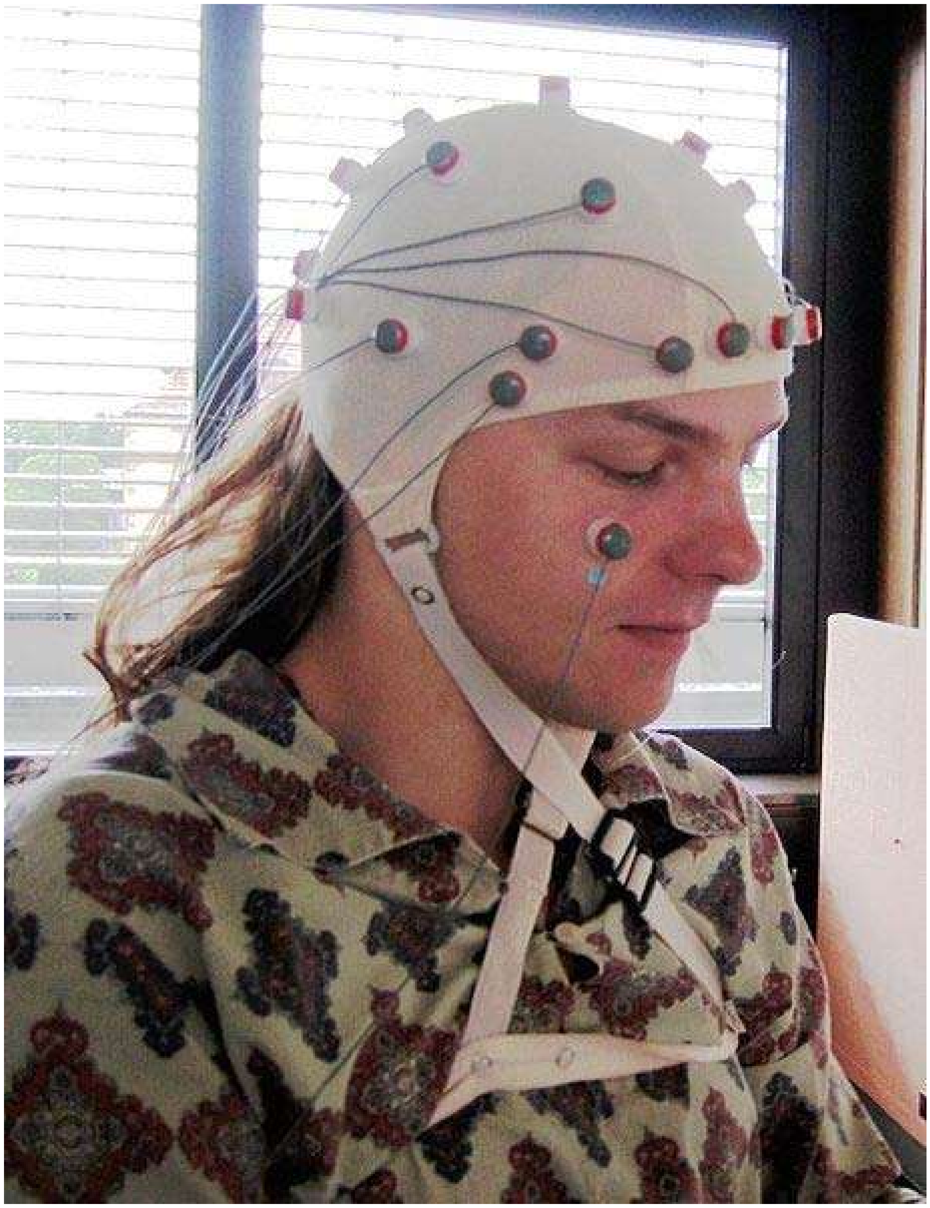
Artifacts

Biological artifacts

Electrical signals detected along the scalp by an EEG, but that originate from non-cerebral origin are called artifacts. EEG data is almost always contaminated by such artifacts. The amplitude of artifacts can be quite large relative to the size of amplitude of the cortical signals of interest. This is one of the reasons why it takes considerable experience to correctly interpret EEGs clinically. Some of the most common types of biological artifacts include:

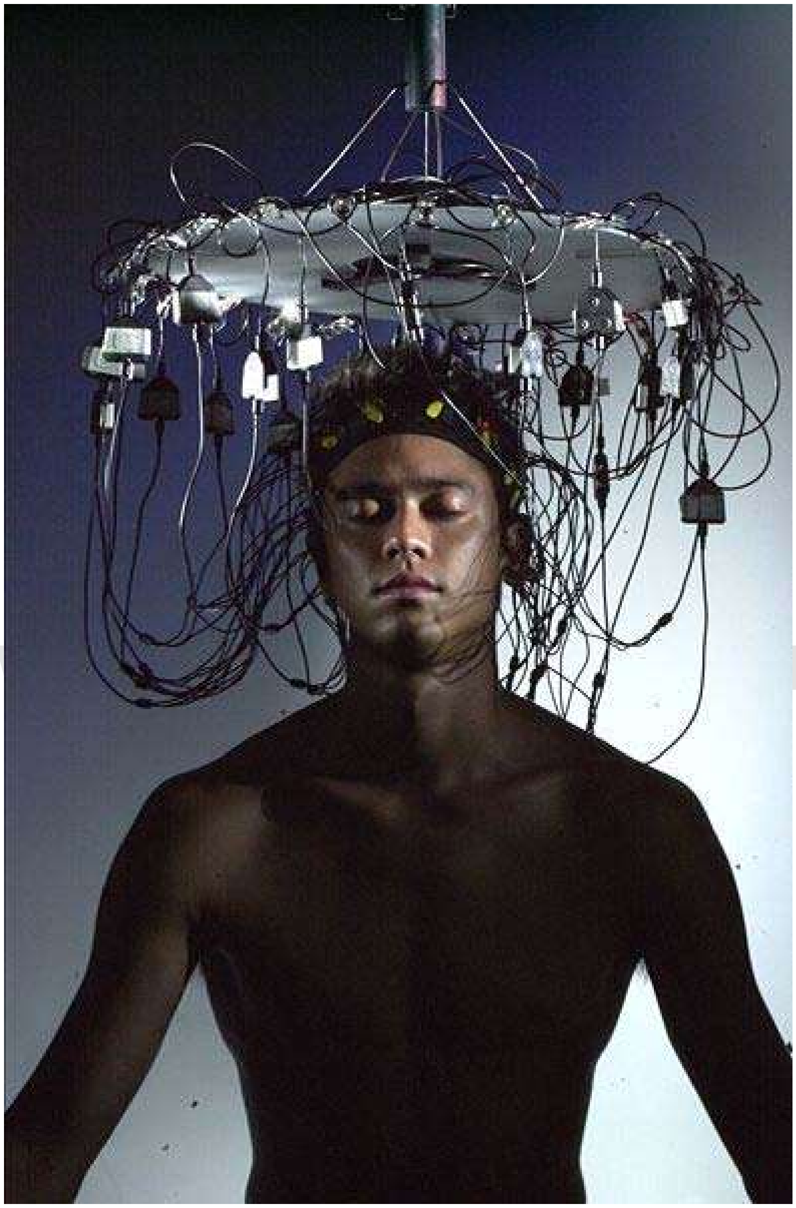
- Eye-induced artifacts (includes eye blinks, eye movements and extra-ocular muscle activity)
- EKG (cardiac) artifacts
- EMG (muscle activation)-induced artifacts
- Glossokinetic artifacts

The most prominent eye-induced artifacts are caused by the potential difference between the cornea and retina, which is quite large compared to cerebral potentials. When the eyes and eyelids are completely still, this corneo-retinal dipole does not affect EEG. However, blinks occur several times per minute, the eyes movements occur several times per second. Eyelid movements, occurring mostly during blinking or vertical eye movements, elicit a large potential seen mostly in the difference between the Electrooculography (EOG) channels above and below the eyes. An established explanation of this potential regards the eyelids as sliding electrodes that short-circuit the positively charged cornea to the extra-ocular skin. Rotation of the eyeballs, and consequently of the corneo-retinal dipole, increases the potential in electrodes towards which the eyes are rotated, and decrease the potentials in the opposing electrodes. Eye movements called saccades also generate transient electromyographic potentials, known as saccadic spike potentials (SPs). The spectrum of these SPs overlaps the gamma-band, and seriously confounds analysis of induced gamma-band responses, requiring tailored artifact correction approaches. Purposeful or reflexive eye blinking also generates electromyographic potentials, but more importantly there is reflexive movement of the eyeball during blinking that gives a characteristic artifactual appearance of the EEG.



Person wearing electrodes for EEG

Portable recording device for EEG



EEG electroencephalophone used during a music performance in which bathers from around the world were networked together as part of a collective musical performance, using their brainwaves to control sound, lighting, and the bath environment

Eyelid fluttering artifacts of a characteristic type were previously called Kappa rhythm (or Kappa waves). It is usually seen in the prefrontal leads, that is, just over the eyes. Sometimes they are seen with mental activity. They are usually in the Theta (4–7 Hz) or Alpha (8–13 Hz) range. They were named because they were believed to originate from the brain. Later study revealed they were generated by rapid fluttering of the eyelids, sometimes so minute that it was difficult to see. They are in fact noise in the EEG reading, and should not technically be called a rhythm or wave. Therefore, current usage in electroencephalography refers to the phenomenon as an eyelid fluttering artifact, rather than a Kappa rhythm (or wave).

Some of these artifacts can be useful in various applications. The EOG signals, for instance, can be used to detect and track eye-movements, which are very important in polysomnography, and is also in conventional EEG for assessing possible changes in alertness, drowsiness or sleep.

EKG artifacts are quite common and can be mistaken for spike activity. Because of this, modern EEG acquisition commonly includes a one-channel EKG from the extremities. This also allows the EEG to identify cardiac arrhythmias that are an important differential diagnosis to syncope or other episodic/attack disorders.

Glossokinetic artifacts are caused by the potential difference between the base and the tip of the tongue. Minor tongue movements can contaminate the EEG, especially in parkinsonian and tremor disorders.

Environmental artifacts

In addition to artifacts generated by the body, many artifacts originate from outside the body. Movement by the patient, or even just settling of the electrodes, may cause *electrode pops*, spikes originating from a momentary change in the impedance of a given electrode. Poor grounding of the EEG electrodes can cause significant 50 or 60 Hz artifact, depending on the local power system's frequency. A third source of possible interference can be the presence of an IV drip; such devices can cause rhythmic, fast, low-voltage bursts, which may be confused for spikes.

Artifact correction

Recently, independent component analysis techniques have been used to correct or remove EEG contaminates. These techniques attempt to "unmix" the EEG signals into some number of underlying components. There are many source separation algorithms, often assuming various behaviors or natures of EEG. Regardless, the principle behind any particular method usually allow "remixing" only those components that would result in "clean" EEG by nullifying (zeroing) the weight of unwanted components. Fully automated artifact rejection methods, which use ICA, have also been developed.

Abnormal activity

Abnormal activity can broadly be separated into epileptiform and non-epileptiform activity. It can also be separated into focal or diffuse.

Focal epileptiform discharges represent fast, synchronous potentials in a large number of neurons in a somewhat discrete area of the brain. These can occur as interictal activity, between seizures, and represent an area of cortical irritability that may be predisposed to producing epileptic seizures. Interictal discharges are not wholly reliable for determining whether a patient has epilepsy nor where his/her seizure might originate.

Generalized epileptiform discharges often have an anterior maximum, but these are seen synchronously throughout the entire brain. They are strongly suggestive of a generalized epilepsy.

Focal non-epileptiform abnormal activity may occur over areas of the brain where there is focal damage of the cortex or white matter. It often consists of an increase in slow frequency rhythms and/or a loss of normal higher frequency rhythms. It may also appear as focal or unilateral decrease in amplitude of the EEG signal.

Diffuse non-epileptiform abnormal activity may manifest as diffuse abnormally slow rhythms or bilateral slowing of normal rhythms, such as the PBR.

Intracortical Encephalogram electrodes and sub-dural electrodes can be used in tandem to discriminate and discretize artifact from epileptiform and other severe neurological events.

More advanced measures of abnormal EEG signals have also recently received attention as possible biomarkers for different disorders such as Alzheimer's disease.

History

A timeline of the history of EEG is given by Swartz. Richard Caton (1842–1926), a physician practicing in Liverpool, presented his findings about electrical phenomena of the exposed cerebral hemispheres of rabbits and monkeys in the British Medical Journal in 1875. In 1890, Polish physiologist Adolf Beck published an investigation of spontaneous electrical activity of the brain of rabbits and dogs that included rhythmic oscillations altered by light.

In 1912, Russian physiologist, Vladimir Vladimirovich Pravdich-Neminsky published the first animal EEG and the evoked potential of the mammalian (dog). In 1914, Napoleon Cybulski and Jelenska-Macieszyna photographed EEG-recordings of experimentally induced seizures.

German physiologist and psychiatrist Hans Berger (1873–1941) recorded the first human EEG in 1924. Expanding on work previously conducted on animals by Richard Caton and others, Berger also invented the electroencephalogram (giving the device its name), an invention described "as one of the most surprising, remarkable, and momentous developments in the history of clinical neurology". His discoveries were first confirmed by British scientists Edgar Douglas Adrian and B. H. C. Matthews in 1934 and developed by them.

In 1934, Fisher and Lowenback first demonstrated epileptiform spikes. In 1935 Gibbs, Davis and Lennox described interictal spike waves and the 3 cycles/s pattern of clinical absence seizures, which began the field of clinical electroencephalography. Subsequently, in 1936 Gibbs and Jasper reported the interictal spike as the focal signature of epilepsy. The same year, the first EEG laboratory opened at Massachusetts General Hospital.

Franklin Offner (1911–1999), professor of biophysics at Northwestern University developed a prototype of the EEG that incorporated a piezoelectric inkwriter called a Crystograph (the whole device was typically known as the Offner Dynograph).

In 1947, The American EEG Society was founded and the first International EEG congress was held. In 1953 Aserinsky and Kleitman describe REM sleep.

In the 1950s, William Grey Walter developed an adjunct to EEG called EEG topography, which allowed for the mapping of electrical activity across the surface of the brain. This enjoyed a brief period of popularity in the 1980s and seemed especially promising for psychiatry. It was never accepted by neurologists and remains primarily a research tool.

Various uses

The EEG has been used for many purposes besides the conventional uses of clinical diagnosis and conventional cognitive neuroscience. Long-term EEG recordings in epilepsy patients are used for seizure prediction. Neurofeedback remains an important extension, and in its most advanced form is also attempted as the basis of brain computer interfaces. The EEG is also used quite extensively in the field of neuromarketing. There are many commercial products substantially based on the EEG.

Honda is attempting to develop a system to move its Asimo robot using EEG, a technology it eventually hopes to incorporate into its automobiles.

EEGs have been used as evidence in trials in the Indian state of Maharastra.

EEG and Telepathy

DARPA budgeted $4 million in 2009 to investigate technology to enable soldiers on the battlefield to communicate via computer-mediated telepathy. The aim is to analyse neural signals that exist in the brain before words are spoken.