Neural implants: A review of current trends and future perspectives

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Abstract

Recent progress in microfabrication technique allowed the rapid development of neural implants. They are getting categorized as effective tools for clinical practice, especially to treat traumatic and neurodegenerative disorders. Microelectrode arrays already have been used in numerous neural interface devices. Basically, almost all neural implants have been developed based on BCI (Brain Computer Interface) system. When BCI system falls under invasive technique, it is referred as BMI or Brain Machine Interface. BMIs hold promises for neurorehabilitation of motor and sensory function, cognitive state evaluation and treatment of neurological chaos. A directed overview of the field of neural implants is discussed in this article. The aim of this review is to give a brief introduction of neural prosthetics as well as their exciting applications in treating neurological disorders and a deep discussion on their functionality are mentioned. BCI system and their different types, their functionality, their pros and cons, how other neural implants developed, and their present status have been covered. Different possibilities and possible future of deep brain stimulation (DBS), Neuralink, motor and sensory neural prosthetics are further discussed.

Keywords: Neuroprosthetics, Brain Computer Interface, Neural Implants, Deep Brain Stimulation

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1. Introduction:

Bioimplants has come to humanity as a blessing. It has a significant role in increasing the longevity and quality of human life by providing numerous solutions to various health problems. The uses of biomaterials for implantation are not new. It all began about four millennia ago when Egyptians and Romans both employed wood for toe replacements and gold and iron for dental uses [1,2] Over the past few decades, the use of artificial device has seen an upsurge to control the activity and functioning of various parts in a human being, which has led researchers to contemplations and skepticism [3] Among all type of implants brain implants, also referred as a neural implant, has opened a magical door in the history of bioimplants. Neural implants are some sort of medical tools which is amazingly powerful and placed on the surface or attached to the cortex of the brain. These implants interact with the brain by sending electrical impulses to neurons or by transmitting electrical signals from the brain to the computer or from the computer to the brain via a chip [3,4]. The journey of brain machine implants started back in 1780, with the discovery of stimulation of a dead frog's muscle by using an electrical spark, which has been discovered by Luigi Galvani [5]. Then in 1870 and 1924 Edward Hitzig and Gustav causes muscles movements through the electrical stimulation of specific parts of a dog's brain and Hanns Berger uses an EEG - (Electroencephalography) to record electrical activity from a human brain for the very first time respectively [6,7]. The first cochlear implant had implanted in 1969 which helped to restore a sense of sound and demonstrated the possibilities of neural implants. After 1969, advancement in neural implants has never stopped. In 1996 neurotrophic electrodes are implanted in a paralyzed man enabling him to control a computer cursor. Elon Musk launched Neuralink in 2016 with the intention of developing an ultra-high bandwidth brain-

machine interface, and till today they are developing their technology.

Implants like Deep Brain Stimulation (DBS), Brain Chip Interface and other Motor and Sensory Neural Prostheses have increasingly become a tentative treatment method for patients with various diseases such as Parkinson's Disease (PD), Spinal Injuries, Paraplegia, OCD, Depression and Anxiety, Loss of Vision, Hearing Problem, Loss of Limbs, Bell's Palsy, Alzheimer's Disease, Epilepsy and so on.

The existence of neural implants has led to a renaissance in modern neurosurgery and undoubtedly led to the refinement in treatment of complex problem [3]. Although there are some challenges and limitations in using bioelectronics equipment to treat neurological disorders, but rapid development of bioelectronics has subsided those limitations. With the advancement of neural prostheses, living in a Sci-fi world will not be a dream anymore.

2. Brain Computer Interface (BCI):

Brain Computer Interface (BCI) is a rapidly expanding field of research that uses signals which are recorded from the brain to allow communication and control applications with malfunctioned functions [8,9]. BCI can sometimes referred as (BMI) Brain Machine Interface. BCIs contributions are not only in medical field, but also in education, security, production, and gaming. The main function of BCI is it can measure brain signals and converts them into artificial output that can replace, repair, augment, or improve genuine output of CNS (Central Nervous System) [8,10]. BCI technology has helped in restoring the movement ability for individual who lost their motor functionality [9]. As mentioned, BCI do not play significant role only in medical field, but also normal individuals can use BCI as a novel input hand free device [9,11,12]. It has endless applications

[4]. The components of BCI system, their application, challenges, and their tentative solutions are described briefly in the subsections below.

2.1. BCI System Components:

The essential components of a BCI system are signal acquisition, signal preprocessing, feature extraction and classification [9].

Signal acquisitions record the brain waves, to enhance and to reduce the noise they send them to preprocessor component. The feature extraction component produces distinguish features for improved signal and tends to minimize the quantity of the data utilized by the classification component [9]. The produced features are translated into device commands by classifiers [9,13]. The important part of BCI based system is measuring brain generated oscillation. Signal acquisition methods depends on BCI application and the intended group of users [9]. As shown in Fig 1, there are mainly two signal acquisition method. One is invasive and other one is noninvasive.

Figure 1: Signal Acquisition Method in BCI

2.2. Noninvasive Technique:

The brain activity is measured with external sensors in noninvasive technology. Noninvasive methods such as electroencephalography (EEG), magnetoencephalography (MEG) or

functional magnetic resonance imaging (fMRI) are commonly used in neuroimaging studies of human cognitive, sensory, and motor functions [14]. The noninvasive technique does not provide adequate resolution for most BMI (Brain Machine Interface) applications [15]. These methods lack great temporal or spatial resolution, as well as a low signal to noise ratio, and limited high frequency sensitivity [14]. EEG is the recording of electrical activity which induced by the passage of electric currents during synaptic excitations of the dendrites in the neurons and it is particularly sensitive to secondary current effects [9,16,17]. Its temporal resolution has increased over time. Its signal to noise ratio and spatial resolution, however, are still limited. But their unique usability makes them preferable for commercial use. EEG record system contain electrodes, amplifiers, A/D converter and a recording device [16]. Electrodes are attached to a cap like device; thus, they provide poor quality signal as they need to cross many other layers [9,16]. However, to suffice low spatial resolution, noise ratio, signal localization problem many solutions have proposed. The distance between successive pairs of electrodes is either 10% or 20% of the scalp diameter, according to an international electrode placing approach [9]. BCI based applications began lowering the quantity of utilized electrodes while preserving the signal to noise ratio [9].

2.3. Invasive Technique:

By implanting electrodes on the brain's surface, invasive recording methods assess electrical activity in the cerebral cortex [16]. They provide high temporal and spatial resolution than other noninvasive techniques. It generates brain signals with a greater signal to noise ratio and lower sensitivity to artifact than EEG [14]. But this method suffers from lots of limitations. Following subsections will give brief description about ECoG and Intracortical

acquisition which mostly use invasive techniques.

2.3.1. Intracortical:

Intracortical acquisition is implanted under the cortex surface of the brain as the name implies [9]. To monitor the action impulses of individual neurons, only single electrode or array of electrodes are sufficient [9]. Its high spatial resolution creates a challenge with source localization. They may, however, have long term signal variability, which could be caused by neuronal cell loss or an increased tissue resistance [9]. Moreover, when the system includes a stimulation to activate any disabled limb, then a significant noise effect can be generated by that additional stimulus [9]. According to recent research, a patient with Amyotrophic lateral sclerosis was capable of moving a cursor on a computer screen to pick displayed things after a single electrode was implanted into the motor cortex [9].

2.3.2. Electrocorticography (ECoG):

Electrocorticography is an electrophysiological recording procedure that record electrical potentials from the cerebral cortex's surface [9,15]. Because the implant in ECoG, does not need to penetrate the cortex, it has the potential for greater signal consistency and higher signal resolution than EEG [15]. For generating a better amplitude signal, it is less impacted by the interference and artifacts caused by muscle engagement [9]. ECoG can monitor brain activity extremely precisely since the electrodes are positioned beneath the skull and near to the cortical surface. As a result, much recent research has started using ECoG to investigate the core mechanisms of cortical processes [18], and these benefits make ECoG a viable solution for seizure localization [9].

Although ECoG is gaining popularity in a verity of BMI application today's clinical ECoG implants are big and have poor spatial resolution [15]. To overcome these

limitations, 64 channel wireless micro electrodes bring ray of hope to minimize them [15]. Their wireless powering and readout paired with a microfabricated antenna and electrode grid with >10 times the electrode density of standard clinical ECoG arrays, allowing for spatial sampling of cortical function and volitional decoupling in BMI or BCI [19]. Due to the low power consumption of the integrated circuit (IC), it allows remote powering at a power level three times lower than set safety standards [15]. In case of using invasive technique usability issue always rise, however, small size and the flexibility of this micro electrode help to minimize the foreign body response [15].

In most situations, implanted devices have been used in patients for brief experiments of time. To address and alleviate this issue, CEA/LETI/CLINATEC have conducted a project to develop Wireless Implantable Multi Channel Acquisition system for capturing ECoG signals on 64 electrodes for long term human implantation [15]. The design of this device facilitated the surgical procedure and removes the risk for any infection [15].

People with variety of neurological disorders may get benefit from brain machine interfaces [20]. However, clinical BMIs have failed to gain widespread acceptance due to its modest channel counts limitations.

3. Brain Chip Interface (BCHI):

Brain chip interfaces are hybrid entities that can be implanted in the human brain as its parts that can imitate all the brain's operations, mathematically record them, and transport data in one or both directions [4,21]. Brain chips are made through nano technology with the purpose of converting a human being into a superhuman [4].

It is widely used by patients who lost body movement due to some neurological damage of brain. It also serves in military

purposes. Basically, to process human activities, the brain relies on neural networks, which collect information from each cell body and connect it to other neural network [4], this is how brain works. Some elementary parts of brain chip are the pedestal with chip, fiber optic cable, neural signal interpreter and the computer.

The chip is usually implanted in the human brain. The chip's extension wire is connected to a pedestal connector, whose duty is to record all of the patterns created by neural connections that regulate all of the brain's actions [4]. Fiber optic cable transfer all the signals to neural signal interpreter. The brain signal is then decoded into digital signal and transfer to the computer by the neural signal interpreter. Then the computer simulates all brain functions and sends them to a prosthetic device, allowing patients to move the damaged area of their body simply by thinking about it [4]. The neural network is directly linked to the brain chips electrically. Brain cells can be cultured directly on top of a chip and the fascinating thing is that they can grow on the chip with a tight electrical coupling [4].

Applications of Brain chip are so many, some of these are:

- Movement of paralyzed patients
- Remote controlled animals
- Telepathy
- Robotic Arms
- Bionic Face
- Prosthetic Device

Brain chip implant is the revolution in the field of engineering and neuroscience. Despite the risk of surgery and other issues, the result of using brain chip is undoubtedly amazing and unbelievable. As technology advances throughout the world, we may anticipate chips with nano technology to allow researchers to produce smaller and more superior chips to reduce other problems and to make brain chip interfaces less burdensome and more reliable options for individuals [4].

4. Deep Brain Stimulation (DBS):

Deep Brain Stimulators (DBSs) are a kind of implantable medical equipment that employs electrical stimulation to treat neurological problems [22]. DBS is a popular and effective neurosurgical method that permits for targeted circuit-based neuromodulation [22,23]. These devices are commonly used to treat Parkinson's Disease, essential tremor, and dystonia, movement disorders, epilepsy, and psychiatric disorder [22]. DBS has a long record of use in mental disorders and pain [23]. In 1948, Lawrence Pool, a Columbia University neurosurgeon was the first to describe the usage of subcortically inserted electrodes for therapeutic chronic stimulation [23]. And till today it is going through developments. Medtronic developed the first implanted pulse generator (IPG) for DBS, which had a maximum frequency of 130Hz, which is the quantity utilized in most modern DBS applications [24]. First dual channel IPG had the capabilities to deliver a current with a frequency of up to 250Hz [23]. Due to the stimulation of the subthalamic nucleus in PD, it turned out the most widely utilized IPG universally [23]. As time goes on, various advancements in this sector have been developed, including segmented leads, directional stimulation, better battery life, greater stability in determining stimulation parameters, and remote internet-based programming [23]. Current directionality with electrode segmentation, greater parameter space for programming (shorter pulse widths (10 μ s) and frequencies up to 10,000 Hz) and improved neural recording capabilities are among the most recent improvements in DBS [23]. DBS is mainly made up of 3 parts. IPG, Electrode and an extension. In current DBS system single or bilateral electrodes are implanted into the brain and is linked to an Implanted Pulse Generator (IPG) over the chest via extension wires. IPG carries a lithium battery which is placed in a titanium box and the life of that lithium battery is 3-5 years. Although DBS is a notable method

to treat Parkinson's Disease, psychiatric disease, and other chronic diseases but they are also responsible to create trouble such as heating of DBS system during MRI Scans. Furthermore, infection rates in chronic DBS patients vary from 5 to 10% [23]. However, researchers discovered that using antibacterial envelopes can help to prevent cardiac pacemaker infection [23]. They also believe that using antimicrobial coating in neurostimulation systems might help avoid infection, although further research is needed [23]. Also, researchers assume if they can eliminate those extension cables in DBS system then it will not make any trouble during MRI also will be less troublesome. Predicted future DBS system will contain a IPG and Electrodes. Implanted Pulse Generator would be:

- Small and carnialized
- It will be coupled to Wi-fi
- Performance of the battery will be longer and
- Will be energy harvesting

Electrodes:

- Multiple leads
- Sensing and stimulating abilities
- Adaptive or closed loop design

There will be no extension cables. We can forecast the future since electrode design, IPG capabilities, programming and stimulating techniques will all improve. Neuromodulation will be much safer, less intrusive, more precise and effective, and will be used on a considerably large number of patients for whom existing treatments are ineffective [23].

4.1. DBS and Parkinson's Disease: DBS is widely used to treat Parkinson Disease. This system has an effective impact on patients to alleviate from their symptoms. The loss of dopaminergic neurons in the substantia nigra compacta (SNC) causes Parkinson's Disease [24]. The damage of neurons in this SNC region causes an inequality between the direct and indirect pathways resulting in PDs symptoms such

as tremor, stiffness and walking difficulties, as well as akinesia, and bradykinesia [24]. A pulse generator in DBS system provides electrical current to the surgical target, generally the Subthalamic Nucleus (SNT), through a series of electrodes, assisting in the restoration of normal function [23,24]. Bidirectional connection of deep brain electrodes could be made with a computer to monitor electrical stimulation of the brain, that is how an understanding on inherent problem can be obtained [24]. To get warning signals before parkinsonian tremor begins, researchers use artificial intelligence. Those stimulators only need to generate signals occasionally rather than continuously [24]. It was discovered utilizing AI techniques that there are many forms of PD depending on the type of electrical impulses in the brain [23,24]. In addition, tracking brain impulses in real time and feeding them into a computer becomes easier. The computers then evaluate the data and synthesize other signals to transmit back to the brain, ensuring that the individual in question continues to operate [24]. The approach that has mentioned above can be used to manage other problems include clinical depression (Electrodes must be placed in the subgenual cingulate), epilepsy and Tourette's syndrome.

4.2. Biocompatibility:

The neural interfaces communicate with the neurological system using implantable electrodes [25]. There are some primary requirements of these electrodes. These electrodes must interact with as many individual neurons as possible with a greater signal to noise ratio, which drives them to develop novel electrode materials, that are physiologically transparent, biocompatible [26] and long lasting [25]. Some modern production technique, film printing contributes in increasing flexibility of electrode design, but they also create worries about the long-lasting performance and safety of novel materials, however this

can be solved using nanocoating [23,27,28]. In DBS system an interface develops between brain tissue and electrodes after implantation, which changes over time [23]. Chronic implantation of electrodes causes inflammatory foreign body reaction into the brain [23,29]. During implantation, chronically implanted leads showed a multinucleate giant cell reaction, which might be a response to the polyurethane element of the electrode's surface coating [23,30]. Although the data suggests long term DBS is fairly safe but further studies on those reactions needed [23].

5. Neuralink:

As the days are passing by, the use of artificial intelligence is increasing to ease our usage of the device [31]. Brain computer interfaces plays a promising role in neurorehabilitation of sensory and motor disabilities [32], exoskeleton, neurocommunication, cognitive state evaluation [33]. However, lack in recording from large number of neurons has narrowed the development of BMI (Brain Machine Interface). The average of millions of neurons can be recorded noninvasively via the skull, but the signal is distorted since it must pass through numerous layers [20]. Invasive electrodes can record useful signals as their electrodes are placed into the cortex, however they average the action of thousands of neurons and are unable to record deep brain impulses [20]. Invasive neuroimaging methods cannot offer high resolution cerebral activity recording for medical reasons in drug resistant patients, limiting the use of brain machine interfaces in clinical settings [33]. A brain machine interface for patients with drug resistant epilepsy is one of the most notable clinical applications of Neuralink technology. Neuralink will significantly improve seizure prediction.

When it comes to spatially localized neuronal activity, noninvasive techniques can't discern distinct features of neurophysiological illness in real time, thus

electrodes must be placed into specific brain regions [33]. BCI can predict a seizure onset, it is associated with a system that interferes with the signals that causes seizures [33]. Predicting seizures remains an uncertain problem, due to a lack of information regarding neurological processes in the onset brain region [33].

The following subsection will discuss about Neuralink's initial steps towards a scalable high bandwidth and high channel count BMI system [20].

5.1. About Neuralink:

Elon Musk came up with Neuralink in 2016, and it was unveiled to the public in 2017. It establishes a link between our brain's neurons and a machine, as the name implies [31]. Neuralink's high bandwidth channels makes them advanced technology to treat clinical disorders. This device has flexible electrode thread arrays with up to 3072 electrodes per array, distributed over 96 threads [20,33]. They created a neurosurgical robot that can implant 6 threads (192 electrodes) each minute with a millimeter spatial accuracy, avoiding surgical restrictions, surface vasculature and targeting particular brain regions [20]. They crammed electrode arrays into an implantable device with custom circuits for low power onboard amplification and digitalization [20]. A single USB-C Cable allows full speed data streaming from the device, as well as simultaneous recording from all channels [20]. Using this platform in a freely moving rat, a spiking yield up to 85.5% can be achieved [20,33]. Multi electrode polymer probes are thin, smaller in size, flexible and offer greater biocompatibility [20]. Polymer probes, on the other hand, are not firm enough, so they developed a neurosurgical robot that can implant polymer probes much more quickly and safely.

Neuralink is made up of three basic parts:

- Probes made of Ultra-fine polymer

- A neurosurgical robot and
- Custom high-density electronics

5.1.1. Neuralink's Function:

Neuralink will follow five major steps:

- Making of threads
- Threads are stitched into the tissues
- Reading and clearing the signals
- Signal transmission to the amplifier
- Signal amplification and transmission to the machine.

A USB-C port is built within a chip, which allows for amplification and transmission [31]. This USB-C port, coupled with a sensory device, and is implanted into the subject's brain [31]. However, it intends to offer a wireless option for the same. This is referred to as "N1 Sensors" by Neuralink which was unveiled in 2019. These sensors will be implanted in the skull and wirelessly linked to a gadget situated behind our ear that can be connected to iPhones via an app [31]. Neuralink made remarkable progress within a year, and on August 28th, 2020 they announced that the N1 implant they displayed in 2019, had been reduced to the size of a coin and that pod like device that nestled behind the ear had been removed. The new version of this Neuralink chip implant is called "Link V0.9", its 23mm×8mm size allows it to fit perfectly and flush within the skull, making it virtually unnoticeable, Fig 2 is showing a clear view of Link V0.9 chip. In order to reduce tissue damage and to avoid drilling holes in the skull, Neuralink intends to employ laser technology [31].

5.1.2. Applications of Neuralink:

a) For Visual Prosthesis: The people with blindness or retinal damage might benefit from Neuralink's visual prosthesis.

b) Disease Prediction:

Neuralink claimed to be able to detect chemical signals in the brain and thereby prevent the illness beforehand.

c) Eliminate Pain:

There are several disorders that might cause a great deal of pain. Neuralink device can play crucial role in eliminating pain.

d) AI Symbiosis:

Neuralink aspires to fill the void left by AI's ability to activate all of our brain's functions, allowing the human brain to cope with AI [31,34].

e) Neuroprosthesis:

The Neuralink device has the ability to control the movement of an exoskeleton or other robotics with the mind, as well as to assist people with medical limitations such as locked in syndrome and loss of neuronal connection to communicate. Neuralink device also monitors and train human physiological states and cognitive abilities and help to get rid of seizures for drug resistant epileptic patients.

If everything goes well then, Neuralink might be one of the most important innovations of the century.

Figure 2 "Link V0.9" that fits perfectly within the skull [35,36]

6. Brain Gate:

Brain Gate was developed via the bio-tech organization Cyber kinetics in 2003 [37]. It

is also known as Utah Array. This system was developed to help people who lost their body's control and movement. After being implanted below the skull, the Brain Gate has 100 tiny spikes, that will extend down roughly one millimeter into the brain to track the activity of a tiny group of neurons [37]. Patients with spinal cord injuries may now send brain signals to implanted sensors, which will generate electrical impulses, indicating their intention to move their paralyzed limbs [37]. These impulses assist users in controlling mechanical devices using a computer cursor.

There are some essential hardware components and software tools that Brain Gate contain.

6.1. Hardware Components Used:

- **The Chip:** Because the Brain Gate's electrodes are connected to platinum wires, it can monitor cerebral activity as well as deliver stimulating currents in both directions [24]
- **The Connector:** This is fixed in the brain's motor cortex.
- **The Converter:** The signal passes via an amplifier, where it is converted to digital data before being redirected to a computer via fiber optic cable [37].
- **The Computer:** The signal is processed by the computer, which then utilizes it to carry out activities such as communication and environmental management [37].

The array was recently fired into human brain or nervous system in a recent experiment [24]. The array was first assigned to a purely recording duty for therapeutic outcome [24]. The array electrodes have monitored electrical activity from neurons. Located in the motor cortex, this impulse has been converted into an impulse that allows a critical paralyzed patient to move a cursor on a computer screen utilizing neural impulses and visual

feedback [24]. This same technique has used again on a paralyzed individual to operate a robotic arm, even they had been able to learn feeding themselves with sufficient control over the arm. The key to this accomplishment is the capacity to monitor and understand motor cortical brain activity, as well as use the output to regulate prosthetic devices properly [24]. The entire technique is predicated on comprehending the neural coding of movement direction in the motor cortex [38]. However, because each motor neuron is tuned to just one way, the direction of movement may be anticipated using the right population of motor cortex neurons [24].

A paralyzed individual can also restore some control over their own arm by using Brain Gate. In this scenario, impulses from the person's motor cortex were used to stimulate the muscles of the wrists and hands through a cuff worn around the person's arm [23]. This is a sort of bi-pass function, of the nonfunctioning nervous system. As a result, each unique receiver has been able to produce solitary finger movements as well as six various wrist and hand motions [23].

7. Neural Sensory Prosthetics

7.1. Visual Prosthetics:

Visual prostheses are medically implanted devices that can restore some vision to people who are blind [39]. Retinal prostheses system has been developing several different surgical and engineering approaches. The loss of photoreceptor cells (PR) occurs in retinitis pigmentosa (RP) which is a hereditary retinal disease, or in degenerative conditions such as age-related macular degeneration (AMD) [40,41]. There are currently no therapeutic options available for either of these conditions. So, in such cases there are no other way but to use retinal prostheses. There are still various complex engineering and biological barriers to overcome in order to close the

gap between artificial and natural eyesight [42]. Improved image processing algorithms and data transfer system, as well as nanofabrication and polymerization processes, all indicate to a bright and inventive future for retinal prosthesis [42].

Charles Le Roy ran an electrical impulse over the ocular surface of a blind patient, in 1755, and the patient saw a flashlight [42], which was the first instance of electrically generated visual percepts or “phosphenes” [42]. Brindley and Lewin then employed an 80 electrode that was persistently inserted prosthesis to administer electrical stimulation to the visual cortex and produce phosphenes that were synchronized with the retinotopic map [42–44]. Potts and Inoue established shortly after, that electrical current applied over the globe of RP (retinal prosthesis) patients might generate subjective phosphenes and elicit noticeable responses from electrodes positioned across the occipital scalp [42]. Advances in materials and microelectronics manufacturing spurred research in the field of retinal prosthetics in the 1980s; alternative techniques include intracranial stimulation devices that work on the cortical or thalamic visual pathways, as well as optic nerve prosthesis [42,45]. In the next paragraph, certain technologies that are designed to offer direct stimulation to remaining retinal neurons, specifically those that have proceeded to the point of human testing, will be addressed.

7.2. Epiretinal Prosthesis:

Epiretinal prosthesis are medical devices that are implanted on the surface of the neurosensory retina, next to nerve fiber and ganglion layers, to recover partial vision for blind people [42]. This device has both pros and cons. The microelectrode arrays are tacked to the retinal surface, which is a benefit [42]. Moreover, locating the device and carrying out routine vitreoretinal surgery is a familiar approach to surgeons. The device’s placement in the vitreous cavity also allows for safe heat dispersion [42]. Direct activation of retinal ganglion

cells has certain drawbacks, such as bypassing the remaining intraretinal processing system, which limits their capacity to reconstruct the normal retinal topographic structure. Furthermore, due to the presence of epiretinal devices, ectopic visual percepts from accidental axonal stimulation may occur, resulting in a loss in spatial resolution and distortion of the planned stimulation pattern [42].

7.2.1. Argus II Retinal Prosthesis System:

The Argus II epiretinal prosthesis was the first device which has been approved by European Union back in 2011 and got FDA approval in 2013 [39,42]. This system consists of an implanted and external component [42]. An external component is a glass mounted camera that is connected to a transportable visual processing unit that analyzes the picture for transmission to an external communication coil. This glass mounted coil offers power induction as well as data transfer to an internal matching coil through wireless radiofrequency (RF) telemetry. A silicone scleral buckle secures the internal matching coil to the sclera [42]. Once the signal is received, the RF signal is converted to an electrical signal and the output command is set by an application specific internal circuit (ASIC) [42]. It goes straight to the 60 microelectrode arrays of the intraocular retinal stimulator. The internal circuit is hermetically sealed and has a lifetime of over 10 years in accelerated aging testing [39].

7.2.2. EPI-RET3 Retinal Implant System:

The EPI-RET3 implant’s internal component is totally intraocular. It contains a chip and receiver coil. These are found in the aphakic capsular bag. The epiretinal stimulation array is directly linked to the retinal stimulator [42]. A physical transscleral cable is not required with this procedure. instead relying on inductive linkages to provide implant energy or data, lowering the danger of infection or erosion [42]. EPI-RET3 is made up of an external

camera and visual processor that wirelessly delivers the computed spatiotemporal pattern of stimulation pulses to the inner part [46]. This system employs ultra-high frequency pulsed charge-controlled stimulation to eliminate significant stimulation artifacts and permits bilateral stimulation and recording by the electrodes [42]. By adopting a bidirectional enhancement system to accommodate inherent activity of retinal neurons, it is feasible to classify response types from particular retinal locations and adapt stimulation algorithms to produce more noticeable stimulation patterns [42,47]. The construction of a very big electrode array (VLARS) for epiretinal stimulation has been the focus of future advancements for EPI-RET3 [42].

7.3. Subretinal Prosthesis:

Subretinal prosthesis are located closer to the target retina which favors them by performing natural retinal signal amplification and necessitating lower stimulation levels [42]. Unless this system has built-in photosensitivity and amplification capability, it will need a power supply and a data transmission link [42]. In terms of surgery, subretinal implantation is more challenging.

7.3.1. Alpha IMS and AMS:

The Alpha IMS is the earliest and only subretinal implant to get CE certification approval, which was achieved 2013 [42]. It contains a photovoltaic array, also known as multiphotodiode array (MPDA), with 1500 discrete photodiode amplifier electrode units on a 3-mm² microchip [42]. They all will transform surrounding luminance into an electrical signal [42]. IMS is an active device that amplifies the signal using an external power source. This power is provided via a silicone supply cord that is attached to a fixation pad wrapped beneath the orbit, travelling subcutaneously and then through the temporal muscle to a subdermal coil that is secured to the postauricular cranial bone [42]. A magnetically attached detachable external

coil magnetically connects to the subdermal coil, allowing electromagnetic power induction and adjustment of contrast intensity and luminance via a portable device [48,49]. RPE degradation and retinal adhesion can make sub foveal device insertion more difficult. These challenges may lead to increased reported rates of device relocation, replacement surgery, and device malfunction [42,50,51].

The Alpha AMS is a bigger model with 1600 photodiode complexes that got CE clearance in 2016. It is likewise comparable to IMS in terms of functionality. To extend the functional life of this new Alpha device, a minor change was made, which included:

- Altering a monophasic pulse to a biphasic pulse [52].
- The chip is new and slightly larger
- A broader polyimide in order to fit the new chip [52].

The primary distinction between Alpha devices and other implants is that Alpha devices have a photodiode array in the subretinal space, whereas other implants have an epiretinal array on the retina's surface [53]. Another distinction is that Alpha implant detects light and transfers it to the overlying inner retina, whereas other implants employ a digital camera mounted on a spectacle to detect light and wirelessly transfer it to the implant's receiver [53].

7.4. Suprachoroidal Prostheses:

This technology is less intrusive and more easily repairable or replaceable. However, because the suprachoroidal area is extremely vascular, there is a danger of bleeding and fibrosis post implantation. As it placed away from the neurosensory retina, it requires greater stimulation power to elicit visual percepts [42]. Some examples of suprachoroidal prostheses are “Bionic Vision Australia”, and “Suprachoroidal transretinal stimulation”.

There are more retinal implants such as intelligent retinal implant system II, Boston retinal implant (development is ongoing),

artificial silicon retina (the company has closed and no more results published from this group), photovoltaic retinal implant bionic vision system (this gadget has progressed to the stage of human trials).

Retinal implants have already shown substantial success, and other visual prosthesis systems will make great advances in the upcoming years as technical, surgical, and other approaches improve [39]. There are, however, certain limits. It is believed that advancements in medical technology, neurology, electronics, and material science would encourage the invention and improvement of an easily accessible system for restoring a functional vision to many blind people [39].

7.5. Auditory Prostheses:

In 1950s, electrical stimulation was first used to restore hearing function in France. A surgeon and an engineer collaborated to implant a cable into deaf patients' inner ear [54,55]. Since then, constant development is occurring in the auditory prostheses field. By the 1970s, numerous companies in Europe began manufacturing cochlear implant. Over the next 20 years patient results improved dramatically due to the improvement in electrode design and signal processing [56–58]. Today cochlear implants are recognized as a trustworthy technology for restoring hearing in people with severe to profound hearing loss, and they have been authorized as a therapeutic technique since the mid-1980s [59].

Internal and exterior components make up a cochlear implant. The external system is worn behind the ear, in a pocket or with a harness, while the internal system is surgically placed into the auditory system [59]. A microphone, a speech processor, a transmitter, and a magnet are all part of the external system. The exterior components' job is to capture the noises from the environment, process them, transform the auditory signals, and send them to the

internal component [59]. A receiver, electrode system, stimulator, and magnet are included in the internal component. Its job is to receive the electrical impulses from the outer section of the cochlea and pass them to the auditory nerve fibers. The exterior components are held in place by a magnet. Cochlear implants work by electrically stimulating the acoustic nerves within the auditory system, bypassing the outer and middle ear. This distinguishes them from other hearing aids [59]. Cochlear implants have progressed from cumbersome, body worn single electrode technology to today's multi-channel ear level or single unit devices after more than two decades of research and development [59,60]. Current technologies, on the other hand, have a limited ability to enjoy music and function poorly in noisy environment [60]. The goal of future technical advancement is to give hearing outcomes that are equal to normal hearing from a completely implanted gadget that allows for both 'continuous' and 'hidden' hearing. Due to the exorbitant cost of existing technologies, a high quality, low costs implant is urgently needed [60]. If we can combine this technology with speech processing software that can be programmed remotely, we will be able to provide more effective hearing rehabilitation [60]. Although reaching this aim would be extremely difficult.

8. Neural Motor Prosthetics

8.1. Bionic Limbs:

Loss of limbs can be devastating. Due to the need to improve the lives of crippled people, the history of the prosthetic limbs began with Hooks and other prosthetic replacements in the Middle Ages and extended through Ambrose Pare's mechanical hand, to current robotic, osteointegrated [61] bionic limbs [62–69]. Bionic limbs or prosthetic limbs are an electromechanical device that attaches to the human body and mimic the functions of natural arms. The field of neuroprostheses

has been evolving and advancing Over the last few decades, the area of neuroprosthetics has evolved and progressed as a consequence of both medical and technical advancements [69,70]. Replantation is always the primary choice of treatment after a severe amputation [69]. However, prostheses are still a superior option since reconstructable limbs are common in traffic accidents, malignancies, and severe diabetic patients [69]. Limb prostheses are expected to be a limb replacement that simulates a wide range of typical limb functions while also seeming surprisingly lifelike [62]. Since the beginning prosthetic limbs progressed a lot, but the patient's control and putting "feeling" of this feigned replacement is still so complicated [69]. As a result, various research projects have been launched in attempt to reclaim the device's motor function and sensory transmission from the prosthesis to the body. The advantages of recovering prosthetic feedback and motor function in upper and lower limb amputees have been demonstrated by researchers [61,65] [71–75]. These methods make it possible to replace an entire limb with an operational sensorized prosthetic device that mimics the limb's near natural motor and sensory function [69]. These innovations helped to develop 'Bionic Limbs' and represented the newest achievement in prosthetics.

Bionic limbs are prosthetic implement that have a direct link with the remaining neurological or neuromuscular system of individuals who have lost their limbs. Before discussing their function and controlling process, the functional difference between upper limbs and lower limbs are briefly discussed.

The function of upper limbs (UL) and lower limbs (LL) differs. Upper limb amputation is the most complex [69]. Our hands regulate almost 40 muscles, and their involvement in the cortex's huge surface area demonstrates their vital role in human activity. However, current commercially

available prostheses are unable of simulating such actuation or sensory control [69,76,77].

On the contrary lower limbs are used for waking, standing, and maintaining balance and stability. After a transtibial amputation, these tasks were largely recreated using below the knee prostheses [69]. These individuals are able to walk, dance, and participate in sports at a near normal pace [69]. Due to its increased weight, high transfemoral amputations have a difficult time restoring normal stride and balance and are at danger of falling. Individuals who used them report several long-term problems [78,79]. Therefore, this implant is still under development.

8.1.1. Control Systems:

Electric impulses from muscles or neurons beyond the level of amputation are used to operate a bionic limb [69]. Bilateral communication among electronic signals and ionic currents within living beings is enabled through biological residuum and electronic device interfaces [80]. Bidirectional control is achieved by sensation restoration, which involves connecting the residual neurons or muscles exceeding the amputation level to the prosthetic device sensors [69]. As a result, current hand prosthesis offers intuitive control as well as regular flow of sensation from the bionic arm to the consumer. They are controlled by sophisticated motors and allow the recovery of complex hand motions using direct muscle impulses [81,82]. New surgical approaches have increased the effectiveness of these technologies' interactions with a variety of muscle [83–85] and neurological tissues [86,87] in a more intimate manner [69]. These allow for a direct muscle approach through tiny implant injections, nerve rerouting for muscular reinnervation [82,88,89] and nerve interfacing around or within the fascicular structure [69]. By encoding sensory algorithms applied on a system controller, the impulses from tactile

and position sensors included in the prosthesis are translated into electrical impulses to record the sensory information flow [69]. Stimulations are administered to the nerve via a neural stimulator, which is made up of microelectrodes that were previously implanted into or around the somatosensory nerves, allowing users to feel sensations directly on the phantom limb [69].

8.1.2. Methods of Interface:

To achieve neural signal pickup, natural nerve motor signal from the neuromuscular junction needs to be obtained. Therefore, recording electrode should be placed on the surface of the muscle [90] (intramuscular EMG). In addition, motor intentions might be captured directly from the peripheral nerves [69,91,92] (electroneurography (EEG)). The kind of tissue interfaced can be split into three major groups based on the implant used:

I. Nerve and Muscle Transferring: The residual nerves (e.g., median, and ulnar nerve) of the severed stumps are transferred to accessible muscles (e.g., chest muscles) and neural control signals are amplified using natural muscular amplifiers in Targeted Muscular Reinnervation (TMR) [69]. As a result, signals are registered and sent to the prosthesis, allowing it to control its action [69].

Recently an interface that permits proprioceptive impulses from both muscles to be delivered to the central nervous system was established, re-creating the dynamic muscle contact that occurred prior to amputation anatomy [69]. It is referred to as the agonist-antagonist myoneural interface (AMI).

II. Direct Muscle Interfacing: It is referred to as the second type of bionic limbs. Here, direct intramuscular implants are used to gather signals from the remaining muscular tissue. Intramuscular implant-based control entails inserting a

small recording device into the remaining muscle to capture muscular contractions, which are subsequently recorded wirelessly using a coil placed in the socket [69]. This is how muscular contractions activate the movement of prosthesis. However, sensory feedback is not available with this system.

III. Direct Nerve Interfacing: This third technique is based on the direct connection of residual nerves through the use of implanted peripheral neural interfaces [69]. Neural electrodes travel around or through the nerve in this arrangement, increasing the potential of controlling the device or conveying a sensation from the device [93,94]. The sensation of the missing limbs via electrodes placed invasively in the residual nerves that innervate the Upper Limbs (UL) or Lower Limbs (LL) is the third type of bionic limbs [69]. Electrodes are inserted and positioned intraneurally through the fascicles [69,95] or around the nerves by means of an epineural cuff to enhance and regain sensibility of bionic limb[96] [69]. In certain experiments, patients were given intraneural implants with external cables that link to unreal touch sensors and a bionic limb neural stimulator [69]. These patients have shown remarkable dexterity, and even texture recognition [69,97]. Another advantage is that phantom pain is reduced as a result of the physiologically realistic afferent drive restoration [69,98–100].

Bionic limb replacement has the potential to be completely insertable, bilateral device for the upper limb that uses invasive electrodes to get muscle or nerve impulses, as well as sensory input via nerve stimulation. In order to apply this bionic technology to lower limb amputees, more research and study are required. To improve quality-of-life, more study into the durable existence of electrodes, their attachment, cable fixation and entirely implanted and transportable devices is still needed [69].

9. Discussion:

Since the beginning researchers have been working on brain to understand its function and monitor brain's electrical signals to research, diagnose and treatment of neurological disorder, as well as to control artificial limbs by utilizing these signals. Neural interfaces have been playing a significant role in the field of neural implants [101] such as researchers have implemented robotic limbs [102] speech synthesizer [103] human neuroprosthetic control of human cursor [104–106] auditory prosthesis, retinal prosthesis etc. Neural interfaces allow for the recording and activation of neural tissue, allowing the peripheral and central nervous systems to be successfully connected to the outside world [107]. All of these strategies, however, have a number of flaws. For example, contemporary visual prosthetic systems still lack the vision that they potentially restore [39]. The essential stipulation for neural visual prosthetic is that it should make functional contact with still functioning neural elements [39]. Recent visual neural prosthesis, however, only allow patients to feel light spots and better contrast edges and do not provide sufficiently high resolution or clarity for them to restore a functional sense of vision. As we've mentioned before about the ARGUS II and Alpha IMS, in clinical testing their best visual grating acuities were 20/1260 and 20/546 respectively [49,108] what is not even close as the required visual acuity to recognize shapes, objects and letters. For every neural implant, designing microelectrodes are very important. Individual neuron-stimulating microelectrodes must be positioned extremely near to the targeted cells and have the same size as the neurons they are seeking to activate [39]. They can't be too tiny since their impedances would be too high, causing them to completely miss adjacent neurons. Furthermore, when electrode area increases, the quantity of safe charge area decreases. The long-term survival of stimulating electrodes, which is

harmed by electrolytic degradation and glial scarring is another restriction [109–111]. Recent used biomaterials are regarded to be biocompatible in the sense that may be tolerated by the body; yet they cause biological responses and some amount of encapsulation, which is why they are not completely biocompatible. As a result, scientists are considering inventing new materials to preserve electronics over lengthy periods of time. According to a recent study, liquid crystal polymers exhibit a molecular arrangement close to that of a solid while maintaining the fluidity of liquid, which helped them improve several unique qualities such as low water permeability, chemical inertness, and mechanical durability [107]. A recent on liquid crystal elastomers, a subclass of LCPs, has shown that it is possible to construct devices with features that deploy away from a central insertion point to link with tissue volume while minimizing tissue injury [107]. There are limitations in electrical stimulation too, researchers are reconsidering using optogenetic tools as a stimulation method to bypass these all limitations [112]. This approach has demonstrated to be effective in blind animal models of Retinitis Pigmentosa, and human trials for retinal prosthesis are already underway [113–116]. Neural implants are trying to improve quality of life, but they are costly. For example, the current cost of DBS device is \$10,000 per unit [117]. DBS is an invasive surgical procedure, there are some surgical complications. A report stated that 3.9% of patients have faced intracranial hemorrhage [118]. Additional outpatient surgery is also needed because replacement of battery is required after every 3-5 years. Hardware related issues are also included in DBS device. Thereby, the main advantage of DBS is maintenance cost. BCI or BMI which is known as heart of neural implants, also have some obstacles in their way of development. They usually face usability challenges, technical challenges which include training process, information rate, non-linearity

rate, nonstationarity and noise, small training set, high dimensionality curse etc. To eradicate these issues researchers proposed some tentative solutions such as decreasing noise ratio by using temporal based preprocessing also frequency band filtering to remove noise and artifacts. Machine learning may be used to address some of the drawbacks of short training sets and single trials. The support vector machine classification method which use supervised learning to distinguish between two types of data. It has strong generalization properties and is resistant to overtraining and the dimensionality curse [9]. Although BCI still suffering from some complications but it's contribution in neurotech is mind blowing. Researchers already developed prosthetic limbs which can restore sensory properties as well by using invasive BCI system. However, there are still some features that users wish to have such as ability to move individual fingers and thumbs, less weight, less visualization, increase movement speed, adaptability of grip strength etc. However, there are ethical issues what remains as big concern for making progress in the field of neural implants. There are mainly two types of technique, invasive and noninvasive. In invasive technique electrodes need to implant into deep brain structure which require some serious surgery and have surgical risk including hemorrhage and infection, these surgical risks are associated with ethical issues. Not only should surgical risk be considered, but all brain implants should address the possible ramifications for each individual's autonomy, privacy, accountability, consent, integrity, and dignity. Privacy should be maintained in devices like Neuralink, cause hackers can take control over its chip which may create catastrophic situation. So, researchers should take proper measures to minimize these issues. All these issues impose unique constraints on the advancement of any neural prosthesis. Although researchers proposed solutions to minimize them still further studies and

knowledge are required to make them effective.

10. Conclusion:

Neurological disorders will benefit greatly from the development of neural implants. Rapid advances in the past two decades have led to neural prosthetics becoming a standard of care in various diseases like from epilepsy to Parkinson's disease, even psychiatric disorders. Their constant contribution improved patient's life who has lost their limbs. Even they make life easier who has lost their vision and who has other sensory circuit disorders. They've already shown a ton of potential, and it's fair to predict that in the upcoming years, all neural prosthetic systems will make substantial development as surgical, technical, and rehabilitative approaches all evolve. We anticipate that advances in medical technology, cognitive science, electronic goods, material science and bioinformatics will enhance the intellect of these neural prosthetic devices, promoting the development of new and upgrading custom-tailored neuroprosthetic systems to improve wellbeing of all individuals.

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