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NEUROSCIENCE AND BRAIN-COMPUTER-INTERFACE: BRIDGING MEDICINE AND TECHNOLOGY FOR ADVANCING PATIENTS CARE

Mohammed Matoog Karami[1*]

1. ***Department of Clinical Physiology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.***

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ABSTRACT

This article presents an overview of the evolution and the current landscape of Brain-Machine Interfaces (BMI), focusing on technological innovations and implementations. There has been a significantly increasing interest in BMI driven by the advance in technology, and by research conducted by academic institutes and private companies. The historical evolution of BMI can be traced back to the work in the 1920s that laid the foundation for modern electroencephalogram (EEG). Early experiments started with monkeys and aimed to record their brains' activity. Nowadays, implanted brain ships have been shown to enable humans to control robotic limbs, browse emails and type words, only by thoughts. The brain has an intricate physiology with its 120 billion interconnected neurons. Invasive approaches to implant probes in brain tissue proves to be superior in data collection. Among the available invasive probes, Neuralink showcase the cutting-edge developments in the field with their robotic insertion methods, flexible high-throughput electrodes, and costume integrated circuit. The Neuropixels probe has emerged as a notable competitor to Neuralink probes. Neuropixels probe addresses key BMI requirements such as high-density recording sites and narrow cross-sectional area to minimize brain damage. More importantly, in contrast to Neuralink probes, Neuropixels is readily available for researchers and has been employed in neuroscience laboratories. Despite exciting proof-of-concept demonstrations, the article acknowledges challenges in the field such as power requirements, biocompatibility and durability. However, the transformative potential of BMI in advancing healthcare and improving the quality of life necessitates more efforts and research.

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Introduction

The past few decades have witnessed an increasing interest in brain-machine interface (BMI). It is considered one of the most exciting and promising interdisciplinary fields of medicine and technology [1, 2]. Brain-machine interface refers to the neurotechnology that monitors and records electrical activities within the brain and consequently decodes the obtained data to extract useful information [3]. The information could be subsequently used for various purposes, such as controlling external software/hardware, or for research purposes to get a better understanding of brain physiology. According to PubMed timeline results, the annual average results number for a query with the key phrase "brain-machine interface" was 126 for the years between 2003 – 2012 [4]. This number jumped to 655 for the years 2013 – 2022 [5] (https://pubmed.ncbi.nlm.nih.gov/). This increase in interest is significantly attributed to the advances in computer science and technology, and to the work conducted by research institutes and pioneering private companies such as Neuralink, Blackrock Neurotech, and others.

Historically, the German scientist Hans Berger was the first to detect electrical currents in the human brain via scalp electrodes [6, 7]. His work in the 1920s set the base for the modern electroencephalogram (EEG), which is a pivotal tool in neurology and neuroscience. In the 1960s, Kamiya was able to determine certain features in EEG recording that could be purposely controlled by the human volunteer [7, 8]. The first experiment to utilize electrical brain activity to command an external device was performed in monkeys a few years later [9]. Afterward, EEG allowed patients to control a cursor on a screen using only their minds [10]. This led to the emergence of the term "brain-computer interface (BCI)", which is usually replaced by the term "brain-machine interface (BMI)" in invasive studies where the recording electrode is placed inside the skull.

Corresponding Author: Mohammed Matoog Karami; Department of Clinical Physiology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia. E-mail: mkarami@kau.edu.sa.

More recently, researchers have been experimenting with bidirectional BMI, which is a new approach that integrates sensory feedback with motor signals. For example, when a person touches an object using a prosthetic limb that is controlled by the person's brain, special sensors at the edge of the prosthetic limb can send back signals via the brain-machine interface. These signals stimulate the sensory cortex of the person and simulate the feeling of touch perception.
Nowadays, there are various approaches to monitor brain activity including the well-known noninvasive EEG, which is routinely used in medical centers. When combined with transcranial magnetic stimulation (TMS), EEG has the potential to treat several brain-related conditions such as depression and obsessive-compulsive disorder [11, 12]. Other currently available techniques to monitor brain activity include electrocorticography (ECoG), which is an invasive intracranial EEG, magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), functional near infra-red spectroscopy (fNIRS) and positron emission tomography (PET). Occasionally, researchers use multiple approaches to get a better understanding of brain physiology.
The brain-machine interface market was estimated to reach $1.46B by 2020, with a compound annual growth rate (CAGR) of 11.5% between 2014 to 2020 [13]. A comparable prediction of $1.72B with a CAGR of 11.5% between 2012 and 2022 was made by [14]. Much of this growth is attributed to non-invasive technologies [15]. Non-invasive approaches received increased attention because they are easier to apply and significantly safer in comparison to invasive approaches. Despite these advantages, invasive approaches are superior in terms of spatial and temporal resolution and signal-to-noise ratio (SNR). Therefore, there has been a recent increasing interest in invasive BCIs, driven by the advance in technology, and by research conducted by major institutes and companies such as Neuralink and Synchron. It is widely believed that innovative and unique application of BMI could be only achieved via invasive approaches due to the aforementioned reasons. Therefore, only invasive approaches will be reviewed in this article.

Basic Physiology of Brain and Neurons

The brain is probably the most complex organ in the human body. It contains more than 120 billion intricately connected neurons, as well as supportive non-excitable glial cells, which are significantly higher in number when compared to neurons [16]. The structure of a Neuron is typically consisting of the soma (the cell body), dendrites, and an axon. electrochemical signals (impulses) travel through the dendrites and soma of the neuron, toward the axon, which transmits the electrical signal to the dendrites of the next neurons. The majority of brain volume consists of myelinated neuron axons, given their whitish color, and hence called the white matter of the brain. The outer folded crust of the brain consists of neuronal cell bodies, given it a grayish color hence called the gray matter of the brain. Additionally, there are small groups of gray matter masses buried deep within the white matter of the brain. Collectively, they are referred to as basal ganglia. They are connected to various other gray matter of the brain and have an important role in motor control. The significant difference in size between white and gray matter (40% to 60%) reflects the intricate connectivity between all brain neurons which is critical for brain physiology [12].
Neurons communicate with each other's via the secretion of chemical molecules called neurotransmitters. Neurotransmitters deliver the signals from one neuron to another by passing the synaptic cleft (the physical space between the axon terminal of the first neuron and the dendrite of the second neuron). The generation and transmission of the signal within the neuron itself is mediated via the opening and closing of ion channels that control the flow of ions across the neuron's membrane. The rapid change in ion concertation between the inside and the outside of the neuron induces electrochemical changes and produces the signal (also referred to as the impulse or action potential) [17]. Since ions carry charges, this event is accompanied by a detectable rapid and transient change in voltage, which can be detected via electrodes attached to a voltmeter. This is basically how researchers monitor neuronal brain activity.
Action potential appears as spikes in electrode recording charts. The flow of spikes over time is referred to as spike train, which represents the raw data fed into most BMIs. These spikes are usually filtered at 40 kHz and represent the membrane potential of neurons near the electrode. When multiple electrodes are used, the subsequent spike-sorting algorithm can identify the membrane potential time series of each neuron [18]. An alternative low pass filtering (<300 Hz) can be applied to raw electrode recordings followed by downsampling to 1 kHz to obtain Local Field Potentials (LFP) [19]. This potential represents the sum of the potential of thousandths of neurons around the electrode. Notably, in a non-invasive approach where electrodes are placed externally on the head such as ECG, the presence of noise, muscle contraction, skin, bones, and other interference significantly decreases the quality of recording. When certain types of electrodes are used in an invasive approach, it is possible to record single neuron activity. However, since individual neuron responses fluctuate within and between task trials, the use of recording the sum of a population of neurons results in a more reliable BMI [20]. In conventional BMI, the cerebral cortex is usually targeted for data acquisition/stimuli delivery. However, other parts of the brain have arguably equal if not higher importance in the field of BMI, such as basal ganglia, cerebellum, hippocampus, and Amygdala. These parts play a key role in motor control, action selection, memory, and emotions [20].

Invasive BMI in Human

Utah Electrode

The first human experiment with invasive implantable BMI was performed in 2004 using a Utah electrode array from Cyberkinetics Inc. [21]. Early results from a tetraplegic patient showed the ability to control a computer cursor to perform

various tasks. For example, the patient was able to open e-mail and control a television with his mind, even while he was talking with the researchers. The patient was also able to control the movement of the robotic arm and, open and close a prosthetic hand [21].

The Utah intracortical microelectrode array was originally developed by researchers at the University of Utah as a successor to the planar electrode arrays [22]. The planar electrode array has a two-dimensional planar shape with a single shaft (‘pitch fork’ geometry) [23]. The Utah intracortical microelectrode array was developed to enable the closing of the skulls of experimental animals after the implantation, which was not possible with the planar electrode array. This feature is crucial for long-term chronic monitoring. The Utah array consists of 100 micro-needles (1.5 mm long) that protrude from a miniscule base (4 mm × 4 mm × 0.2 mm). The silicon microneedle tips are coated with iridium oxide allowing them to be used as microelectrodes [24].

Utah electrode array was initially commercialized by Cyberkinetics Inc. Afterward, all Cyberkinetics work was handled by Blackrock Microsystems LLC for hardware manufacturing, and by Braingate Inc for clinical development [3]. Many institutes used the Blackrock device in human BMIs such as Battelle/Ohio State University, CalTech, Johns Hopkins, Thomas Jefferson University, and the University of Pittsburg. In addition, Braingate Inc. has been working with implantable BMI and demonstrated various capabilities of BMI. For example, there was a trial to decode spoken English using intracortical electrode arrays implanted in the dorsal precentral gyrus. The decoders were trained to differentiate between 39 English phonemes and to vocalize speech via a neural pattern-matching method. With the use of a recurrent neural network (RNN) classifier, the researchers were able to achieve 33.9% accuracy [25]. Nonetheless, this attempt is promising for speech BCIs, which could be life-changing for patients with speech disorders.

Recently, Francis and his colleagues established a BMI that predicted the outcome of handwriting movements based on the recordings of the activity of the motor cortex [26]. They used this approach to translate handwriting movement into matching text on the screen in real-time. To achieve this, they trained RNN to transform the recorded neural activity into mathematical probabilities to determine the likelihood of each character at a time. This probability was either determined in real-time (online decoding) or was subjected to comprehensive processing (offline decoding) via the use of a large-vocabulary language model to autocorrect mistakes. This BMI eventually allowed a hand-paralyzed patient to type texts at a speed of 90 characters per minute with 94.1% raw accuracy. When offline decoding was used, the accuracy increased to 99% [26].

The standard cabled BrainGate iBMI (intra-cortical brain-machine interface) uses hardware/software from Blackrock Microsystems to monitor neural activity. The system involves a NeuroPort Patient Cable that connects head-mounted pedestals to hardware that filters and digitizes the recorded signals on each of the microelectrodes [27]. Recently, this system was replaced by a Pedestal-Mounted Wireless Transmitter (BWD) in two tetraplegic patients. Upon testing, wireless transition configuration proved to be as effective as wired transmission about bitrate. The patients were able to control a standard tablet computer to browse the web and navigate through several applications [27].

The Utah Array is the only intracortical electrode array that received commercial FDA clearance for short-term monitoring of brain activity (30 days or less). Blackrock is applying for long-term clearance, which will enable the merchandising of brain-machine interfaces in clinical therapy [24].

Michigan Probe

Utah array is capable of acquiring signals from almost any cortical area. However, it can’t reach deep structures within the brain. This limitation could be overcome with the use of the Michigan probe. The first model of this multi-channel depth probe was developed in the 1970s, before Utah arrays [28]. Michigan electrode length is ten times longer than the Utah electrode (15 mm vs 1.5 mm), which allows the probes to reach deeper brain structures [29]. Preclinical research showed that the Michigan probe can be used to measure neural activity, provide electrical stimulation, and study the control of emotions and memories [29]. Due to the inherent risk in delivering electrode tips to the targeted location, human research has been scarce. However, the importance of this direction in the field of neuroscience and BMI is undoubted since deep brain structures are involved in various poorly understood cognitive functions such as emotions and memory. Currently, Deep brain stimulation (DBS), which is a neurosurgical procedure that delivers electrical impulses to modulate the neurocircuitry of beep brain structures, is a standard of care in Parkinson's disease, essential tremor, and dystonia [30]. There is evidence that DBS might help patients with major depressive disorder and Alzheimer's disease [30].

Electrocorticography (ECoG)

ECoG is a human-tested invasive BMi technology. Occasionally, ECoG is also called intracranial electroencephalography (iEEG) as it is very similar to ECG except that the electrodes are placed inside the skull. Therefore, craniotomy is needed to implant the electrodes and that is why it is classified as an invasive BMI. Nonetheless, many consider ECoG as semi or partially-invasive BMI. ECoG provides more accurate neural signals in comparison to EEG because there is direct close contact with brain tissue. When compared to invasive BMI such as Utah array or other neural probes, ECoG induces minute or no brain scarring since the electrodes do not penetrate brain tissue. On the other hand, ECoG relies on local field potentials (LFPs) and can’t attain single-unit activity [29]. Unlike other invasive BMI, ECoG strips and grids have been used routinely in clinical practice to locate epileptic focus in drug-resistant patients. This allows the surgeon to remove or disrupt the brain tissue where epileptic seizures are initiated. All surgical workflow including pre and post-operative protocols are already established, which highly encourages researchers to experiment ECoG based BMIs in humans.

Most of what we know about ECoG signals came from patients with epilepsy who underwent surgery. The implanted ECoG electrodes are usually kept for a week for monitoring. During this period, many patients voluntarily enrolled in studies that correlate the real-time recorded signals with specific actions or tasks. Commercial ECoG arrays for clinical use as well as BMI-related items are available from various companies such as NeuroPace, Medtronic, and PMT Corp [31]. Standard clinical ECoG arrays consist of 2.3 mm-diameter electrodes that are spaced 1 cm apart [31]. Researchers have been working to enhance the spatiotemporal resolution of ECoG. For example, it was possible to increase the number of channels of the ECoG electrode grid from 32 to 252 using MEMS fabrication techniques. Other techniques have been also used to develop ECoG with narrow spacing including laser-based high-speed and high-resolution fabrication methods, and oxygen plasma etching [29].
Current ECoG-based BMI Studies show that it is possible to deduce information from various cortical areas and use them for multiple applications. Several groups demonstrated proof-of-concept experiments where a computer cursor could be moved via patient thought. For example, an ALS patient was able to communicate using a commercial typing program on a computer by moving a cursor and selecting the intended letter. The experiment was performed using a subdural Resume II electrode from Medtronic. The patient was trained for 28 weeks after the implantation and was eventually able to type a letter every 52 seconds on average. Predictor autocorrection software decreased this time to 33 seconds. In another experiment, ECoG-based BMI allowed the patient to communicate via a speech synthesizer that is capable of decoding speech-related brain activity. In this experiment, Cortical neuronal signals were recorded using an ECoG microarray that was placed over the frontotemporal area. Additional ECoG arrays were implanted in the motor cortex to record signals associated with the movement of speech articulators. After proper training, it was possible to transfer recorded data into understandable speech acoustics, even when it was based on brain activity generated while the patients were reciting a sentence in a silent nonaudible manner. In Another experiment, ECoG-based BMI allowed a tetraplegic patient to control a 4-limb neuroprosthetic exoskeleton. The researchers used a wireless 64-channel ECoG recording implant developed for long-term clinical applications called WIMAGINE®. Although the system did not work as intended all the time, the patient was able to walk around and control a multi-jointed upper limb with 8 degrees of movement over 2 years [31].
Regardless of these encouraging results, the overall performance of noninvasive/ partially invasive BMI is restricted by a small number of commands. In this regard, invasive BMI with a high number of recording channels Significantly prevails [32].

Neuralink
Neuralink Corporation is a neurotechnology company that develops implantable BMI using invasive intracortical electrodes. The company was founded in 2016 by Elon Musk and a team of scientists and engineers. In 2019, Neural Links published a white paper to describe its first step toward a scalable high-bandwidth BMI system. Nuralink wants to overcome some of the big challenges in the field of BMI by developing its hardware, software, and techniques [33]. For example, Neuralink has developed an advanced robotic insertion approach that is capable of inserting a high number of threads (string structures that carry the electrodes) without damaging brain vasculature. The robot is driven by a system that links the insertion location to a specific coordinate related to a landmark on the skull. When combined with depth tracking and integrated custom software, this approach allows organized and accurate insertion of the threads. This feature along with the use of polyimide to fabricate the probe instead of the commonly used silicon probes boosts the biocompatibility and consequently the longevity of the system.
The use of a robot to insert the threads gives the Neuralink system an advantage over the Utah array where all electrodes are attached to a single base and have a fixed spacing in between. The robot has an auto-insertion mode that allows the insertion of six threads per minute (each thread carries 32 electrodes). Neuralink has also developed its electrodes based on flexible polymers. More than 20 various types of electrodes and threads were made. For example, in Linear Edge probes, the electrode contacts are arranged in line and spaced by 50 µm. In tree probes, the electrode contacts are branched from the central thread shaft and spaced by 75 µm. The threads themself are 4-6 µm thick, 5 µm to 50 µm wide and 20 mm long. Electrode contacts have a very small surface area and have been modified to lower the impedance and increase the effective charge-carrying capacity.
Each array in the Nuralink system consists of 48 or 96 threads, and each of them carries 32 gold-made electrodes. Continues recording from this sheer number of electrodes rises serious electronics and packaging challenges. For example, the signal amplifier and digitization mount need to be integrated with the array assembly to avoid the extortionate cable and connector requirements. On the other hand, this approach raises other problems about the size and energy requirements of the array.
To tackle these challenges, Neuralink developed an application-specific integrated circuit (ASIC) with built-in 256 programmable amplifiers (to process 256 channels), analog-to-digital converters (ADCs), and an electrical circuit to facilitate data output. The whole ASIC consumes around 6 mW. This ASIC forms the core building block for the Packaged sensor device that was implanted for research and development purposes as shown in the Nuralink white paper. The packaged sensor device is fitted with a USB-C connector for high-bandwidth data transfer. In their paper, Neuralink demonstrated two variants of the device, the one currently in use (variant A) is architected to be easy and fast in manufacturing while the first model of the device (variant B) was architected to carry the highest number of channels (as twice as much as the correct model).
the Neuralink ASIC was designed with the ability to deliver electrical stimulation to all attached channels, however, Neuralink did not provide any demonstration of this feature [33]. It is not known if the Neuralink system is capable of simultaneously delivering electrical impulses and recording neural activity without the induction of significant stimulus-induced artifacts. Currently, this is only possible via Optogenetics (a biological technique to monitor and control the activity of cells with light,

achieved via genetic engineering to express specifically light-sensitive ion channels or enzymes in the target cells.) [32]. This capability is critical to enable the interaction with neural activity in a continuous open–loop manner. The currently used Neuralink model is fitted with a 1536-channel recording system, meaning that it contains 6 ASICs. This model is 11 g in weight and has an overall power consumption of 550 mW. It has also a relatively small size (24.5 x 20 x 1.65 mm).
Using their own custom online spike-detection software, Neuralink researchers were able to simultaneously detect spikes from 1280 implanted electrodes in real-time in Long-Evans rats. The spiking yield of the channels was around 43.4%, with many spikes appearing on multiple neighboring channels, which is expected in such a high-density array. In another experiment using the first variant of the device (variant B), Neuralink reported that they were able to record from over 3000 electrodes simultaneously. This sheer number of electrodes along with the ability to implant multiple arrays in subjects highlights how extensible and scalable Neuralink BMI is [33]. Unfortunately, there is only one published paper by Neuralink and the vast majority of knowledge about the results and progress of their projects remains enclosed within the company, probably for commercial reasons. Hopefully, they will be able to publish details of what they have accomplished soon.

Neuropixels
Neuropixel probes are increasingly attracting attention in the field of BMI as a serious plausible competitor of Neuralink probes [34]. The Neuropixels platform was originally developed in 2017 using complementary metal-oxide semiconductor (CMOS) technology (a predominant fabrication process for manufacturing integrated circuits). It is designed to meet several vital requirements of BMI. The most eminent one is the high-density recording sites with narrow cross-sectional areas to minimize brain damage as much as possible. For example, a Neuropixels probe variant used in rodents had 960-1280 electrodes on a single, 10-mm long, shank with cross-section dimensions of 70 × 20 µm. It is also possible to add multiple shanks to increase electrode count and coverage. Shanks can be arranged in 12×12-µm sites in a staggered pattern with 4 columns and 20-µm pitch. This multi-chank implantation yields an electrode count of 5120. Another important feature of the Neuropixels system facilitated by CMOS technology is the presence of user-programmable switches, which allow the recording channels to simultaneously address 384 of the 960- 5120 total sites [35]. In addition, CMOS technology allows Voltage signals to be filtered, amplified, multiplexed, and digitized at the probe base. Thus, facilitating direct transmission of noise-free digital data [34].
Unlike Neuralink probe, Neuropixels is readily available for researchers and it has been used in many neuroscience laboratories. Due to its high spatial resolution, it has been shown that a single 384-channel Neuropixels probe can capture more neurons in the motor cortex, with features related to movement direction, than the Utah array, which is the current benchmark for BCIs that is available for the scientific community. Recently, Steinmetz and his colleague designed a miniature Neuropixels 2.0 probe that contains 5120 recording sites distributed over four shanks, with a single head-stage that is about 60% lighter (only 1.1 g) than the one used in Neuropixels 1.0, while maintaining 384 channels count per probe [36]. Since the probe has a dense and linearized geometry, Steinmetz and his colleague were able to implement post hoc computational motion correction using a custom-designed algorithm, to obtain a stable recording regardless of brain movement. This is a critical issue in BMI where the subject is expected to move freely in his environment doing all kinds of physical activities [36]. From a technical point of view, Neuropixels is probably the most promising currently available technology for the advent of BMI. Hopefully, it will be soon ready to be tested in human subjects to assess its clinical effectiveness in comparison to other BMI.

Challenges
Regardless of the exciting proof-of-concept demonstrations obtained so far, it is clear that we have been exposed only to a fraction of the full potential and capability of BMI. Extracting data from the brain is extremely challenging given the anatomical, histological, and physiological nature of the brain. Not to mention the apparent difficulty in the decoding of these data into useful information. In the next sections, we will discuss some of the main challenges that hinder the advancement of BMI.
One of the main objectives at the current stage is to increase the volume of the extracted brain data in a given brain area. Researchers experimented with higher channel counts per electrode and higher electrode counts to increase signal resolution. With the advance in technology, the number of electrodes has increased from 10s to 100s and 1000s [37]. As aforementioned, Neuropixels probes can have up to 1280 electrodes on one single shank this upscaling effort needs to take into consideration that channel count needs to be balanced with the percentage of electrodes that yield useable data (electrode yield). Otherwise, the extra number of channels and electrodes would be fruitless. The upscaling trend might also necessitate the presence of multiple devices tethered to the electrodes to maximize coverage [32].
Higher spatial resolution (bit depth) along with spike detection or sorting algorithms, ensures that the recorded action potentials represent the sum of a specific and a relatively smaller group of interconnected neurons [38]. Nonetheless, increasing channel count and data volume raises a problem with the ability to transfer these data to the external processing unit. Since the volume of the inside of the skull is fixed, an increase in intracranial mass would be translated into an increase in intracranial pressure. Therefore, increasing the number of wires from intracortical electrodes as well as the size of their intracranial implanted device might cause problems. Additionally, the transfer of large volumes of data to the outside of the skull might require thicker cables which is inconvenient for the participant. Wireless connection could be used to avoid this obstacle but it requires high bandwidth and Information transfer rate. Information transfer rate refers to the data flow in bits per second that is extracted from the neuronal population by the BMI system, given that the data is useful for that specific BMI system. Nonetheless, the

scalability of both wired and wireless connections is limited by available power that is either used to transmit data or even to perform some sort of initial data processing by intracranial implants [39]. On many occasions, researchers have to make a tradeoff between the delivered power and the quality/quantity of the extracted data. Even if the researchers manage to deliver high power, another challenge will arise due to the associated generated heat inside the brain. An increase in temperature as small as 0.5 C˚ can negatively affects adjacent brain tissue [37]. Therefore, researcher must consider thermal dissipation seriously upon increasing the power in BMI.

Other challenges are related to BMI biocompatibility and durability because there is a limited time for the neurons surrounding the electrodes before they degrade. This is occasionally referred to as implant lifetime. The longest implant lifetime achieved in vivo so far is a few years [40, 41]. The deterioration of viable cells around the electrodes could be attributed to implantation-induced microtrauma, which leads to chronic inflammation and fibrosis around the electrode [42]. This process could also be triggered with electrode micromotion relative to brain tissue as the electrodes are usually fixed and attached to the skull [39]. The micromotion could not only damage the surroundings cells it also alters the reordered spikes and makes them undetectable unless recalibration of BMI is performed. Even if micro-trauma and micro-movement problems were solved, brain tissue reaction to the electrodes is eminent. The human body is very sensitive and resistant to foreign bodies, and brain implants are no exception [43]. foreign body-induced reactions could also foster the degradation or deterioration of the electrodes over time.

Conclusion

The evolution of brain-machine interface (BMI) over the past decades represents an attractive convergence of medicine and technology, offering unprecedented promise in the field. The ability to decode speech, control robotic limbs, and predict handwriting movements illustrates BMI's potential innovative leaps in enhancing the quality of life for individuals with neurological disorders. Experiments involving invasive BMI means such as the Neuralink probe and Neuropixel probe demonstrated their superiority with regard to spatial and temporal resolution, emphasizing their significance in unlocking the full potential of BMI applications. Indeed, researchers need to resolve various challenges such as the analysis and transfer of large data volumes, energy consumption and heat dissipation, and the biocompatibility and reliability of BMI systems. Nonetheless, the progressive advance in the field of invasive BMI holds immense promise in improving healthcare and human well-being.

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References

1. Rus M, Matei R, Sandu ML, Delcea C, Siserman C. Emotional distress and coping strategies of health care workers during COVID-19 pandemic. Rom J Leg Med. 2020;28:442-50.
2. Delcea C, Siserman C. Validation and standardization of the questionnaire for evaluation of paraphilic disorders. Rom J Leg Med. 2020;28(1):14-20.
3. Rapeaux AB, Constandinou TG. Implantable brain machine interfaces: First-in-human studies, technology challenges and trends. Curr Opin Biotechnol. 2021;72:102-11.
4. National Center for Biotechnology Information. Annual average results number for a query with the key phrase “brain machine interface“ 2003-2012: PubMed; 2023. Available from: https://pubmed.ncbi.nlm.nih.gov/?term=brain+machine+interface&filter=years.2003-2012.
5. National Center for Biotechnology Information. Annual average results number for a query with the key phrase “brain machine interface“ 2013-2022: PubMed; 2023. Available from: https://pubmed.ncbi.nlm.nih.gov/?term=brain+machine+interface&filter=years.2013-2022.
6. Berger H. On the electroencephalogram of humans. Arch Psychiatry Nerv Dis. 1929;87(1):527-70.
7. Lotte F, Nam CS, Nijholt A. Introduction: Evolution of brain-computer interfaces. Taylor & Francis (CRC Press); 2018.
8. Kamiya J. Conscious control of brain waves. Psychology Today. 1968;1:56-60.
9. Evarts EV. Pyramidal tract activity associated with a conditioned hand movement in the monkey. J Neurophysiol. 1966;29(6):1011-27.
10. Davis KR. Brain-computer interfaces: The technology of our future. UC Merced Undergraduate Res J. 2022;14(1).
11. Fitzsimmons SM, van der Werf YD, van Campen AD, Arns M, Sack AT, Hoogendoorn AW, et al. Repetitive transcranial magnetic stimulation for obsessive-compulsive disorder: A systematic review and pairwise/network meta-analysis. J Affect Disord. 2022;302:302-12.

12. Fitzgerald PB. Targeting repetitive transcranial magnetic stimulation in depression: Do we really know what we are stimulating and how best to do it? Brain Stimul. 2021;14(3):730-6.
13. Research AM. Global brain computer interface market is expected to reach $ 1.46 Billion, by 2020 - Allied market research: Prnewswire; 2015. Available from: https://www.prnewswire.com/news-releases/global-brain-computer-interface-market-is-expected-to-reach--146-billion-by-2020---allied-market-research-500924201.html.
14. Research GV. Brain computer interface market size, share & trends analysis report by application (Healthcare, Communication & Control), By product (Invasive, Non-invasive), By end use (Medical, Military), and segment forecasts, 2023 - 2030: Grand View Research; 2020. Available from: https://www.grandviewresearch.com/industry-analysis/brain-computer-interfaces-market.
15. Silva GA. A new frontier: The convergence of nanotechnology, brain machine interfaces, and artificial intelligence. Front Neurosci. 2018;12:843.
16. Sousa AM, Meyer KA, Santpere G, Gulden FO, Sestan N. Evolution of the human nervous system function, structure, and development. Cell. 2017;170(2):226-47.
17. Spruston N. Pyramidal neurons: Dendritic structure and synaptic integration. Nat Rev Neurosci. 2008;9(3):206-21.
18. Rossant C, Kadir SN, Goodman DF, Schulman J, Hunter ML, Saleem AB, et al. Spike sorting for large, dense electrode arrays. Nat Neurosci. 2016;19(4):634-41.
19. Buzsáki G, Anastassiou CA, Koch C. The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. Nat Rev Neurosci. 2012;13(6):407-20.
20. Moioli RC, Nardelli PH, Barros MT, Saad W, Hekmatmanesh A, Silva PEG, et al. Neurosciences and wireless networks: The potential of brain-type communications and their applications. IEEE Commun Surv Tutor. 2021;23(3):1599-621.
21. Hochberg LR, Serruya MD, Friehs GM, Mukand JA, Saleh M, Caplan AH, et al. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature. 2006;442(7099):164-71.
22. Campbell PK, Jones KE, Huber RJ, Horch KW, Normann RA. A silicon-based, three-dimensional neural interface: Manufacturing processes for an intracortical electrode array. IEEE Trans Biomed Eng. 1991;38(8):758-68.
23. Wise KD, Najafi K. Microfabrication techniques for integrated sensors and microsystems. Science. 1991;254(5036):1335-42.
24. Normann RA, Fernandez E. Clinical applications of penetrating neural interfaces and Utah electrode array technologies. J Neural Eng. 2016;13(6):061003.
25. Wilson GH, Stavisky SD, Willett FR, Avansino DT, Kelemen JN, Hochberg LR, et al. Decoding spoken English from intracortical electrode arrays in dorsal precentral gyrus. J Neural Eng. 2020;17(6):066007.
26. Willett FR, Avansino DT, Hochberg LR, Henderson JM, Shenoy KV. High-performance brain-to-text communication via handwriting. Nature. 2021;593(7858):249-54.
27. Simeral JD, Hosman T, Saab J, Flesher SN, Vilela M, Franco B, et al. Home use of a percutaneous wireless intracortical brain-computer interface by individuals with tetraplegia. IEEE Trans Biomed Eng. 2021;68(7):2313-25.
28. Pochay P, Wise KD, Allard LF, Rutledge LT. A multichannel depth probe fabricated using electron-beam lithography. IEEE Trans Biomed Eng. 1979(4):199-206.
29. Choi JR, Kim SM, Ryu RH, Kim SP, Sohn JW. Implantable neural probes for brain-machine interfaces–Current developments and future prospects. Exp Neurobiol. 2018;27(6):453.
30. Krauss JK, Lipsman N, Aziz T, Boutet A, Brown P, Chang JW, et al. Technology of deep brain stimulation: Current status and future directions. Nat Rev Neurol. 2021;17(2):75-87.
31. Miller KJ, Hermes D, Staff NP. The current state of electrocorticography-based brain–computer interfaces. Neurosurg Focus. 2020;49(1):E2.
32. Pisarchik AN, Maksimenko VA, Hramov AE. From novel technology to novel applications: Comment on "An integrated brain-machine interface platform with thousands of channels" by Elon Musk and Neuralink. J Med Internet Res. 2019;21(10):e16356.
33. Musk E. An integrated brain-machine interface platform with thousands of channels. J Med Internet Res. 2019;21(10):e16194.
34. Jun JJ, Steinmetz NA, Siegle JH, Denman DJ, Bauza M, Barbarits B, et al. Fully integrated silicon probes for high-density recording of neural activity. Nature. 2017;551(7679):232-6.
35. Dutta B, Andrei A, Harris T, Lopez C, O'Callahan J, Putzeys J, et al., editors. The Neuropixels probe: A CMOS based integrated microsystems platform for neuroscience and brain-computer interfaces. 2019 IEEE International Electron Devices Meeting (IEDM); 2019: IEEE.
36. Steinmetz NA, Aydin C, Lebedeva A, Okun M, Pachitariu M, Bauza M, et al. Neuropixels 2.0: A miniaturized high-density probe for stable, long-term brain recordings. Science. 2021;372(6539):eabf4588.
37. Nurmikko A. Challenges for large-scale cortical interfaces. Neuron. 2020;108(2):259-69.
38. Even-Chen N, Muratore DG, Stavisky SD, Hochberg LR, Henderson JM, Murmann B, et al. Power-saving design opportunities for wireless intracortical brain–computer interfaces. Nat Biomed Eng. 2020;4(10):984-96.
39. Luan L, Robinson JT, Aazhang B, Chi T, Yang K, Li X, et al. Recent advances in electrical neural interface engineering: Minimal invasiveness, longevity, and scalability. Neuron. 2020;108(2):302-21.

40. Bullard AJ, Hutchison BC, Lee J, Chestek CA, Patil PG. Estimating risk for future intracranial, fully implanted, modular neuroprosthetic systems: A systematic review of hardware complications in clinical deep brain stimulation and experimental human intracortical arrays. Neuromodulation. 2020;23(4):411-26.
41. Colachis SC, Dunlap CF, Annetta NV, Tamrakar SM, Bockbrader MA, Friedenberg DA. Long-term intracortical microelectrode array performance in a human: A 5 year retrospective analysis. J Neural Eng. 2021;18(4):0460d7.
42. Salatino JW, Ludwig KA, Kozai TD, Purcell EK. Glial responses to implanted electrodes in the brain. Nat Biomed Eng. 2017;1(11):862-77.
43. Lecomte A, Descamps E, Bergaud C. A review on mechanical considerations for chronically-implanted neural probes. J Neural Eng. 2018;15(3):031001.