Brain-Machine Interface

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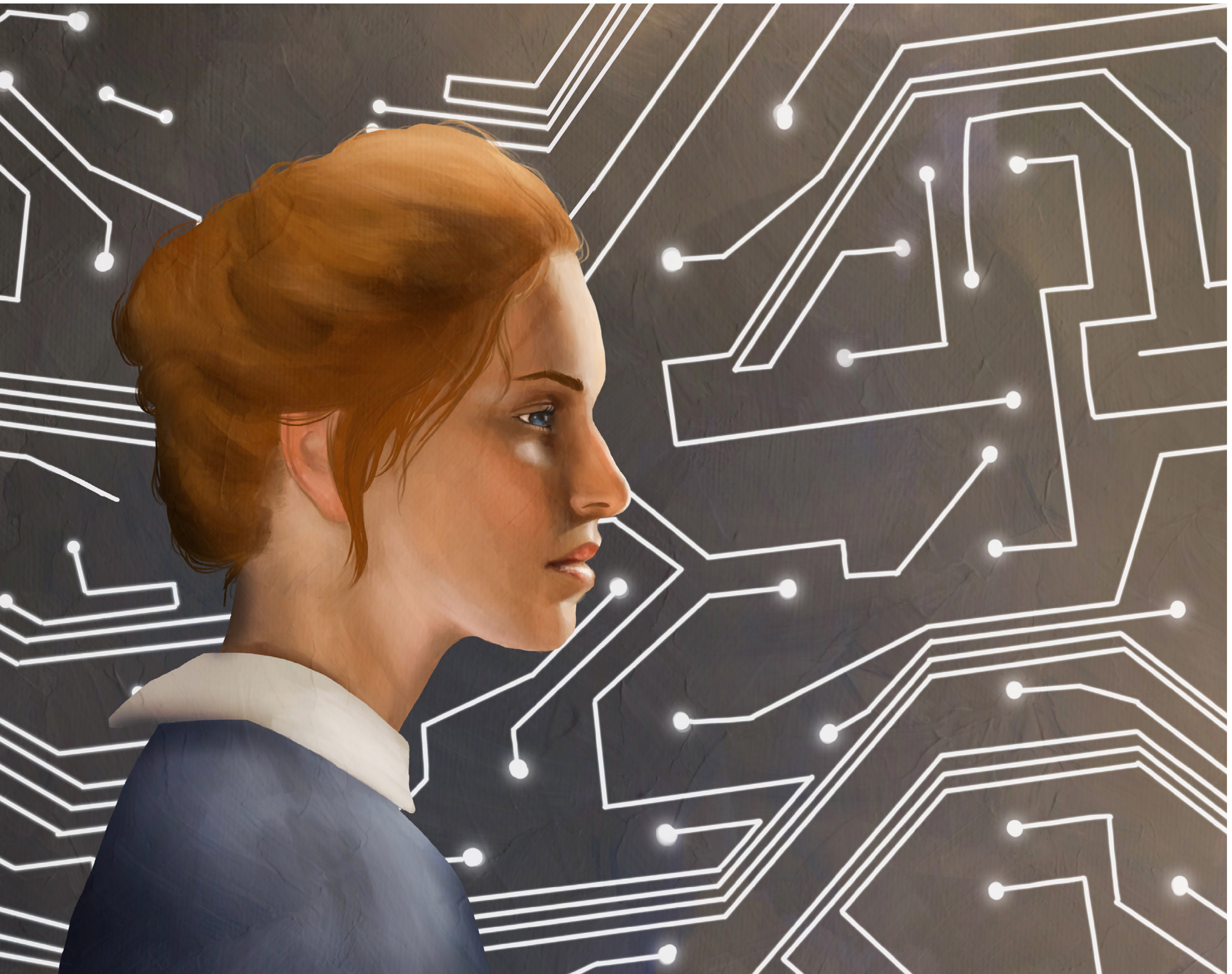

Requiring collaboration in the fields of neurobiology, electrophysiology, engineering, computer science, and biomedicine, Brain-Machine Interfaces (BMIs) are an emerging multidisciplinary technology with countless potential benefits. The ability to record and interpret neuronal activity at a higher resolution and specificity is one of the exciting promises of BMIs. The applications of this technology provide hope for a vast number of individuals who suffer from a wide range of neurological diseases and disorders. It can also be applied to artificial prostheses, to provide limb sensation for amputees. Although BMIs hold immense potential, questions within the realm of neuroethics have raised concern. In particular, the possible exploitation that could arise through medical practices with the advancement of technology [1]. Where humans may potentially be given capabilities that surpass the norm, changing the perception of what it means to be human [1]. It is important to take into account that there are BMIs currently in place that have provided relief for various conditions. To name a few, the use of deep brain stimulation in patients with Parkinson's, spinal cord stimulation for those with intractable pain, and the use of motor prosthesis for patients with epilepsy [1]. However, these methods oftentimes only provide temporary or mild relief and are not inerrant. The trajectory of the BMIs outlined herein aims toward finding an ideal invasive mechanism to solve these drawbacks of mild and temporary relief. There are a vast number of neurological disorders that continue to trouble humanity both emotionally and economically [1], that could substantially change through the use of BMIs.

RECORDING NEURAL ACTIVITY

Interfaces are used to measure and interpret neuronal activity and include two different approaches, invasive and non-invasive. Invasive interfaces require intracranial surgical procedures to implant electrodes. Software programmed in these electrodes records neuronal signals either from one or many cortical areas [2]. Non-invasive or non-surgical methods refer to the use of an electroencephalogram (EEG), where neurons readily generate sufficient electrical activity to be measured by an electrode cap through the skull. EEG is a commonly practiced application for interpreting neuronal electrical activity. Its use in BMIs can provide a basic level of communication for those with speech impairments, and has applications in computer operation via cursor control [2]. Non-invasive methods however pose bandwidth limitations. That is to say, they inefficiently record the activity of neurons due to the interference of the skull [2]. The human brain is composed of many cell types, including nearly 100 billion neurons. The sophistication and complexity with which these cells communicate contributes to the difficulty of interpreting neuronal electrical activity. Moreover, neurons form complex and circuitous communication networks which govern everyday motor activity, cognition, and autonomous bodily functions. The ability to accurately record the activity of these neuronal networks at a sufficiently high resolution has posed a challenge for scientists and researchers due to blood-brain barrier (BBB) disruption and biocompatibility.

Damage to neurovascular tissue at the site of implantation oftentimes causes the formation of scar tissue [3]. This disrupts the BBB leading to rejection of the electrodes or a decrease in resolution [3,4]. Additionally, biocompatibility is perhaps the main reason why advancement has been slow. For many BMI devices, researchers struggle to produce electrodes that are functional long-term in a living biological system. Many devices quickly begin to fail or lose resolution due to the sensitive nature of brain tissue [4]. Researchers and scientists are working toward finding a biocompatible polymer that integrates seamlessly with brain tissue in order to not offset the homeostatic nature of the BBB. Which serves as the underlying component in the long-term success of electrode performance in BMIs.

BLOOD-BRAIN BARRIER DISRUPTION & BIOCOMPATABILITY

The BBB is a dynamic complex of cellular and molecular components containing blood vessels that control neuronal homeostasis. Electrode function is largely influenced by this system since the imprint left behind from intracranial implantation can cause damage to the surrounding neurovascular tissue, leading to a disruption of the BBB [5]. Consequently, this triggers an influx of neurotoxins and pro-inflammatory cells, leading to rejection of the electrodes in the form of foreign body response [3,5]. The barrier acts as a selective gateway to what is able to gain entrance, where a minor intrusion of foreign bodies can impact the overall homeostasis of the mechanism. Endothelial cells account for the framework of blood vessels. However, in the BBB they are connected by a complex network of tight and adherens junctions, leading to the neuromuscular unit containing pericytes, astrocytes, microglia and neurons that maintain the selective regulation of the barrier [6]. For context, neurological disorders such as Alzheimer's disease is a result of a breach to the BBB. Furthermore, highlighting the importance of finding an invasive biocompatible method that minimizes BBB disruption. This has been done through the use of polymers, including poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS), poly(pyrrole) (PPy), polyimide, and Parylene-C [4]. To enhance the electrical characteristics and biocompatibility of these polymers, they must be used in combination with hydrogels [4]. As aforementioned, the potential of BMI resides in finding an effective polymer that is able to integrate with brain tissue [4], as it serves as the main component to produce longevity in the electrophysiology performance of the electrode itself. Although the possibilities of BMIs are equally exciting and promising, experimental applications are in their first stages and focused on resolving these challenges. There have been several innovations over the years to find biocompatible methods of introducing these foreign materials into the biological system.

DEVICES INTRODUCED OVER THE YEARS

In 1996, the Utah Intracortical Electrode Array (UIEA) was among the first BMIs introduced. Researchers implanted the device on the visual cortex of cats via craniotomy and recorded neuronal activity from cell clusters to convey activity in terms of large and small neuronal populations [7]. The array consisted of a 200µm thick silicon base with one hundred 1.2mm-long needles extending out of a 10x10 grid. This array was composed of polyimide to adhere to electrode impedance, filtering out only the necessary neuronal activity to be interpreted by the array, referred to as the signal-to-noise ratio (SNR) [4,7,9]. Although other BMIs exhibited functionality in the motor cortex, the UIEA was the first to apply this technology to the visual cortex. The main drawback with the UIEA was damage to neurovascular tissue; sixty percent of the needles from this array left evidence of hemorrhage, and edema was also commonly encountered within 24 hours of implantation [3].

NeuroRoots, introduced in the year 2018, is a more recent and promising iteration of BMI, with an array designed to mimic axonal bundles [8]. Each electrode is 7µm wide and 15µm thick, with a 100µm apparatus that records and interprets electrical signals on the terminal end [8]. Researchers evaluated two different designs based on the polymers parylene C and PEDOT:PSS to evaluate biocompatibility. The electrodes were implanted via stereotaxic surgery due to their soft mechanical design [8]. Guided by surface tension, capillary forces, and a 20µm microwire, the NeuroRoots were implanted in the CA1 region of rat hippocampi [8]. The researchers found several advantages to the self-guided approach described above, including minimal surgical footprint, low BBB disruption, and promising integration to neuronal tissue [8]. All of these are challenges which have thus far limited the use and application of BMI technology. A disadvantage with the array is the low channel count; each NeuroRoot was limited to a few dozen channels of electrodes.

Largely, this limitation is due to challenges finding effective connectors for the microwires in regards to the self-assembly approach [8]. However, future research may be able to solve this problem and promote recording from a larger area of the brain.

Another highly innovative BMI technology is Neuralink. First introduced in 2019, its large scale recording ability, surgical approach, and impressive compact size, sets it apart over the other technologies discussed. As mentioned previously, high channel count is an important characteristic for the success of BMIs, since a higher channel count allows for recording neuronal activity at a wider range. Neuralink introduced an automated neurosurgical robotic approach, where invasive techniques are performed by directly implanting electrodes into the brain of rats via ultra-fine flexible polymer probes [9]. About the size of a hair, these probes use a custom application-specific integrated circuit (ASIC) described in two configurations: System A has a 1536-channel recording capacity and System B a capacity of 3072 channels [9]. Incorporating these two customizable systems helps enhance the electrophysiological resolution of neuronal electrical activity. Each thread is 4-6µm thick and about 20mm long; thousands of threads and channels can be made available at one time [9]. To combat the length of the threads, a neurosurgical robotic approach is used with the polymers Parylene-C to aid in insertion, and PEDOT:SS as well as iridium oxide (IrOx) to sustain electrode impedance in two separate approaches [9]. A noteworthy characteristic that sets the neurosurgical robot apart is its integrated custom software. The software is able to detect and preselect the areas that are deemed best fit to avoid entanglement of the threads and damage to neurovascular tissue, while a trained surgeon retains full control and can intervene at any time should it be necessary [9]. Results from the rats implanted with each system indicated high yields, with System A recording 1344 of 1536 channels and System B recording all 3072 channels simultaneously [9]. There was also a succession rate of 90% in 40 of 44 attempted implantations with System A [9]. Although Neuralink has made vast advancements in the realm of BMIs, trials remain experimental.

CONCLUSION

Present applications for recording and interpreting neuronal activity have come a long way from non-invasive EEG practices [2]. However, BMIs still remain largely experimental, mostly due to the challenges in blood-brain barrier disruption, and biocompatibility. Each of these problems must be addressed before future human trials in order to enhance the clinical applications of this technology. The UIEA, NeuroRoots, and Neuralink have all contributed to the field of BMIs. With the growth of interest and innovation toward advancing this technology, it provides hope for individuals suffering from a range of neurological diseases and disorders, and advancements in artificial prosthesis in the near future.

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