PERSPECTIVE

The past and future depicted by neural electrode technology

Zhikai Yu,[1,3] Chen Liu,[2,3] Changming Wang,[1,*] and Guoguang Zhao[1,*]

[1]Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

[2]School of Microelectronics and the State Key Laboratory of Wide-Bandgap Semiconductor Devices and Integrated Technology, Xidian University, Xi'an 710071, China

[3]These authors contributed equally

*Correspondence: ggzhao@vip.sina.com (G.Z.); superwcm@163.com (C.W.)

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Neural electrode is the most direct part of brain computer interface technology to link the carbon based brain and silicon based computer. Here, we briefly reviewed the development history of neural electrode technology, and then presented our views on its prospects for the future. How to decipher the logic code of neural circuits and apply it to the electronic design is a most crucial biophysics topic for scientists in the long term, and ideas on two types of future neural electrode in the relatively short term are also delivered to our fellows around the world.

INTRODUCTION

Brain computer interface technology[1, 2] is a focal point of research in the disciplines of medical engineering and virtual reality. It enables the connection between silicon-based computers and carbon-based brains. By examining the information flow in the opposite direction—"from brain to computer" and "from computer to brain"—we can, practically speaking, develop brain-driven machine control technology or computer-driven closed-loop neural regulation technology. Our objective is to establish a therapeutics or aesthetic link between the virtual world and the human brain via electrical signals. Nevertheless, irrespective of one's standpoint, brain computer interface systems share a fundamental structure. In essence, a brain computer interface system comprises functional actuators, electrodes, and computers. The computers in question may be standard home computers, specialized servers, or bioelectronic devices that are implantable. A multitude of functional actuators exist, including but not limited to exoskeletons, typewriters, neural stimulators, and artificial neural network constructed world models. Furthermore, the neural electrode, which is the subject of this article, is a third, vital component in brain computer interface system's structural framework. They serve as the interface between the computer and the brain function or even human consciousness. By material composition, neural electrodes could be classified as glass electrodes (Figure 1a2, a3), metal electrodes (Figure 1a1, a4), or semiconductor electrodes, while by geometric distribution, they could be classified as traditional array electrodes (Figure 1b1), neuron like electrodes (Figure 1b2), intravascular electrodes (Figure 1b3). Besides, a type of transparent thin film electrode[3] that enables light recording via calcium imaging during electrical recording represents an endeavor to integrate the benefits of light imaging and electrical imaging (Figure 1b4). However, despite the fact that neural electrode technology is thriving and has a bright future, it is important to recognize that the progress made by humanity in this area represents a negligible limb on the tree of technology in an infinite time scale.

In this perspective paper, we would like to deliver several viewpoints from the scope of not only material science, but electronic science, computer science, life science, and imagination of ourselves. Indeed, within the realm of electronic communication, electronic devices utilizing any interface type —whether Type-C, Lightning, or USB —transform the trigger state, which is a representation of machine code, between one another in accordance with the protocols governing communication. Despite the increasing popularity of current neural electrode technology or brain computer interface technology, the functions they accomplish are still insignificant compared to the capabilities of computer to computer interfaces. The primary obstacles encountered by neural electrode technology and brain computer interface technology, according to our understandings, are not technological in nature but rather stem from the complexity of comprehending the communication protocols within the biological nervous system. In contrast, the configuration of neural electrodes within the brain remains a challenge due to the atypical and irregular growth and development of neurons in anatomical space, which makes it difficult to identify a standard interface comparable to that of an external computer interface. Besides, it will be challenging to establish communication protocol coupling between the brain and the computer, even if we one day gain a comprehensive understanding of the communication protocols within the brain. We enthusiastically endorse the involvement of further innovative scholars in the investigation and fabrication of neural electrodes. At the same time, we anticipate anecdotes similar to this: a cohort of genuine prodigies has deciphered neural communication protocols and integrated them with computing devices.

DISCUSSION

How to connect the human brain and computer

The telepathy system developed by the Musk team represents a magnum opus within the realm of brain-computer interfaces.[2] Reportedly, the initial recipient of a telepathy system implantation was capable of controlling electronic games with their thoughts, and their reaction time was considerably faster than that of average enthusiasts. The technical pathway by which computers are controlled by the human brain is, in fact, as follows: Signals are initially captured via neural electrodes before being transmitted via wired or wireless transmission systems. In the latest developments, whether it is the Telepathy system or the NEO system of Chinese team,[2] wireless signal and energy transmission have become an important feature of integrated brain computer interface systems. Upon reception of these signals, the computer employs an artificial neural network to decipher human intentions, thereby enabling the human brain to ultimately exert control over the computer. Conversely, the technological advancement of computer-assisted brain control typically pertains to closed-loop neural regulation technology. In response to neural signals, computers modify the parameters of functional electrical stimulation in an adaptive manner. At present, computer-based control of the human brain is restricted to straightforward therapeutic applications; furthermore, it is not feasible for humans to exert control over the intentions of other humans via computers. Undoubtedly, the eventual attainment of intention control will give rise to a multitude of ethical concerns.[4] Ethical issues require an ethical framework to regulate, which should be jointly discussed and developed by experts from all sectors of society. Of course, we are willing to be invited and participate in the development of this ethical framework.

How to decipher the operating system of the human brain

The subject matter of this paragraph is a highlighted scientific issue. The machine codes for the von Neumann architecture are known to be limited to the digits 0 and 1. All user-side programming languages, including C, Python, Matlab, and R, will have their values converted to machine side 0 and 1. The von Neumann architecture is predicated on a set of operation rules governing machine codes; therefore, some intriguing inquiries arise: what precisely are machine codes and what are the stipulations governing their operation within the logical architecture of the human brain? Moreover, the nature of consciousness represents a fundamental challenge for the human race, and the divide between subjectivity and objectivity seems to be impassable. Consequently, how does the human brain's machine code produce subjectivity? It is postulated that a distinct physical principle governs the relationship between subjectivity and objectivity, and that a unique neural component facilitates the transition from subjectivity to objectivity. Hence, we anticipate that neural electrodes will incorporate subjective codes of the nervous system in addition to current and potential measurements, in order to conform to the internal communication protocols of the nervous system.

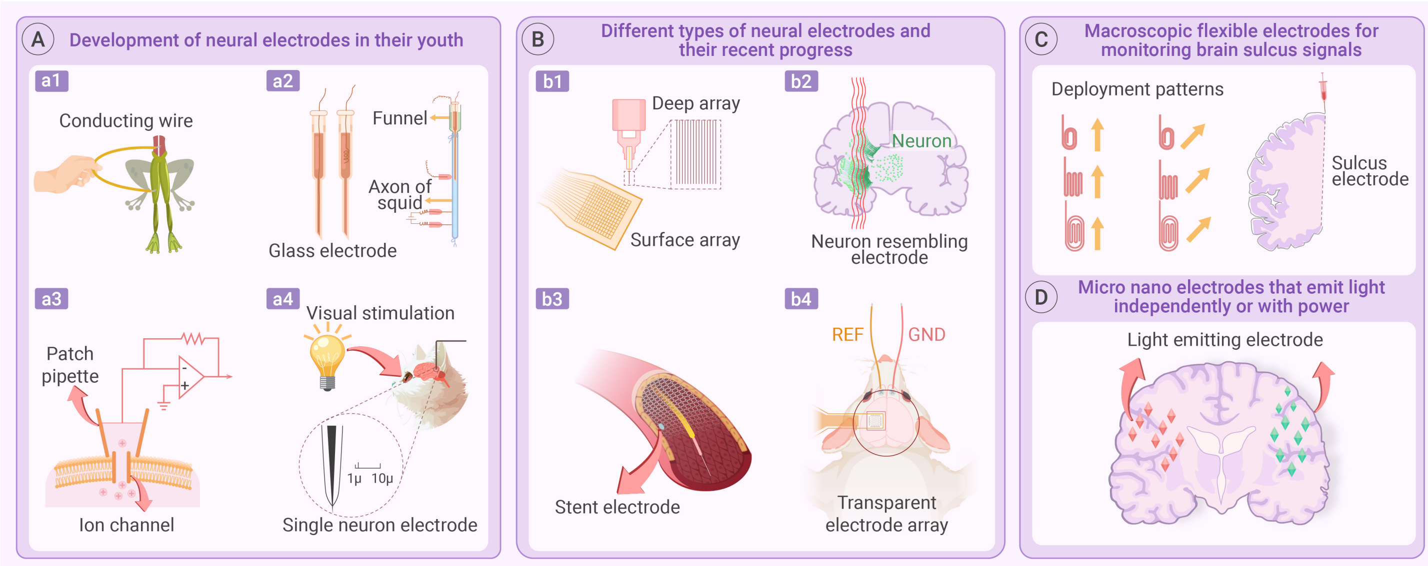

Figure 1. Historical proceeding of neural electrodes and two potential future ideas (A) Development of neural electrodes in their youth. a1) The metal wire used by Luigi Galvani. In 1786, Luigi Galvani discovered that touching the exposed nerves on a frog's leg with the tip of a knife could cause spasms in the frog's leg, originated from the animal's own electrical current. The simple electrodes he built with wires became the earliest neural electrodes. a2) The glass electrodes used by Hodgkin and Huxley. In 1939, 1945, and 1952, Hodgkin and Huxley demonstrated through a series of experiments that the essence of nerve impulses is the rapid reversal of cell membrane potential, which is only related to the cell membrane of nerve fibers. Their research was awarded the Nobel Prize in 1963. a3) Patch clamp invented by Neher and Sakmann. In 1976, Neher and Sakmann created patch clamp technology, which uses a miniature glass tube electrode to contact the cell membrane and form a micro area that is electrically isolated from the surrounding area, thereby monitoring the ion current in this area. Their research was awarded the Nobel Prize in 1991. a4) The Tungsten electrodes used by Hubel and Wiesel. In 1959, Hubel and Wiesel recorded the activity of individual neurons in the striatal cortex of cats using a type of tungsten electrode, and subsequently demonstrated the hierarchical structure and cortical plasticity of the visual system in information processing in a series of studies. Their research was awarded the Nobel Prize in 1981. The tungsten electrode they used itself was the earliest single neuron electrode in vivo. (B) Different types of neural electrodes and their recent progress. b1) Array electrodes with high surface density or linear density. The main development direction of array electrodes is flexibility and high density. On the one hand, flexible electrodes help reduce postoperative trauma and the possibility of glial cells forming scar like tissue. On the other hand, due to the extremely large number of neurons in brain tissue, high-density is the common pursuit of all different types of electrodes. Due to the sharp decrease in electrode surface area of ordinary passive electrodes, which leads to a sharp increase in resistance, various transistor electrodes have become a solution for electrode development towards ultra-high density. b2) Neuron like electrodes. Electrodes resembling neurons are highly flexible and can be entangled with neurons, thereby solving the problem of difficulty in recording neurons due to their uneven spatial distribution. b3) Intravascular electrodes. Stent electrode provides an intervention option for brain computer interface technology, which is a metal sheet attached to a vascular stent, implanted into the human body along with the intervention surgery of cerebral blood vessels. This implantation scheme greatly reduces the invasiveness of surgery while ensuring signal accuracy as much as possible. b4) A transparent thin film electrode that enables light recording. As the electrodes are transparent, experimental animals can wear an optical microscope while performing electrical recording, achieving simultaneous electrical and optical recording. (C) Macroscopic flexible electrodes for monitoring brain sulcus signals. This type of electrode utilizes the self unfolding strategy of the magnetic film to deliver the surface electrode to the bottom of the sulcus, thereby achieving a significant expansion of the recording range of the surface electrode in space, which is beneficial for us to understand the neural activity information at the bottom of the sulcus. Icons on the left show 6 patterns of deployment motion with magnetic membranes. (D) Micro nano electrodes that emit light independently or with power. A drawback of electrical recording is that the number of electrodes is limited, making it impossible to record large-scale continuous neural activity like light recording, and we are not sure if the actual placement of the electrodes is consistent with our expectations. The self luminous micro electrode can to some extent solve this defect, and this electrode also achieves the combination of electrical recording and optical recording. Meanwhile, this electrode also addresses an important drawback of light recording, as we do not need to inject toxic fluorescent indicators into the bodies of experimental animals or human subjects.

In this section, we endeavor to offer a more comprehensive explanation of this matter by employing the language of computer science and electronic science. The fundamental elements of electronic technology are transistors, and the combination of various transistors creates flip flops or bistable multivibrators, which are utilized to illustrate binary code in digital circuits. The integrated circuit as a carrier of machine language is composed of a variety of flip flops, and machine language is then translated into the operating system's language by a compiler. Neurons are analogous to transistors in neuroscience; however, the flip flop construction of nervous system remains obscure, as does the principle of compilation between action potentials and advanced brain functions. It is evident that the potential in the neural circuit is the only thing that can be collected in the current brain computer interface system, rather than the logic in the neural circuit. Neuroscientists with computer expertise are required to decipher the logic of neural circuits. Subsequently, researchers in the field of neural electrodes should integrate this knowledge to convert future neural electrodes into standardized logic interfaces. Although this scientific issue fall within the scope of biophysics, we might find inspirations from artificial neurons corresponding to artificial intelligence models, and such thought may enrich the application of artificial intelligence for life science and medicine.[5]

Two potential future ideas

Macroscopic flexible electrodes for monitoring brain sulcus signals. A macroscopic flexible electrode for monitoring brain sulcus signals is an original idea (Figure 1C). It is believed that most of the already known brain functions are executed via the protruding gyrus, according to the field of neuroscience; and at present, all ECoG electrodes are limited to covering its surface. However, it is common knowledge that the brain is a folded structure, and the sulcus, which is concealed beneath the overall contour, has an unidentified function and a larger surface area. In order to elucidate the function of the cerebral sulcus, one must initially observe the signals that correspond to it. How to reach, be adhered to, and cover the entire surface of brain sulcus is a main technological obstacle to be solved, so we here advise conducting array structure design utilizing a magnetic film technique that adhere along the tissue surface,[6] which is a type of membranes folded at first but could be deployed with magnetic control. By utilizing this technology, it is possible to organize the electrodes on the magnetic film's surface, allowing them to be delivered to the lower portion of the brain sulcus via the self-unfolding magnetic film.

Micro nano electrodes that emit light independently or with power. Another original idea pertains to micronano electrodes capable of emitting light either autonomously or in conjunction with power (Figure 1D). Electric recording and optical recording are the two most prevalent and significant techniques used to research brain function in the field of neurobiology, where optical recording typically pertains to the utilization of optogenetic imaging technology. Optical recording is considered more valuable in terms of spatial resolution when compared to electrical recording with following reasons. Electric recording must yield discontinuous spatial voxel information due to the discontinuity of the electrodes. Assessing the data generated by discontinuous voxels in space is akin to attempting to deduce the plot of a television series based on the intermittent movement of a few pixels across the screen. Consequently, the most significant benefit of optical recording is the uninterrupted imaging that occurs in space. Optical recording has also become capable of capturing the neural activity of deep nuclei since the advent of fiber optic sensors; furthermore, the capacity of single neuron recording through optical methods is significantly greater than that of microelectrode arrays at this time. Nevertheless, optical recording is not without its own set of challenges. The use of fluorescent indicators can result in biotoxicity, which is a significant concern. Consequently, optogenetic recording may never be applicable to human subjects. Therefore, what is the most effective method for assuring the advantages of optical recording while simultaneously avoiding its biological toxicity disadvantage? One potential remedy is to incorporate the fluorescent light source into the electrode's internal structure. The integration of electric and optical recording techniques can be achieved by allowing the nanoelectrodes to emit light and observing their continuous spatial images via an optical imaging system while simultaneously capturing electrical signals. Research teams engaged in the fabrication of nanoelectrodes could envision the technological pathway for this electrode, which consists of micro signal transmission devices, microelectrodes, micro wire conductors, and micro LEDs.[7]

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Z.Y. and C.L. arranged the previous investigations and wrote the manuscript together. Z.Y. proposed the conceptions and painted the original figures. C.W. and C.L. received the funding. C.W. and G.Z. reviewed the manuscript and will reply to the comments continuously.

DECLARATION OF INTERESTS

The authors declare no competing interests.

ETHICAL STATEMENT AND PATIENT CONSENT

Not applicable.

DATA AND CODE AVAILABILITY

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