

Advancements in Flexible Electrode Implantation for Invasive Brain-Computer Interfaces

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Abstract. In recent years, with the development of flexible electronic devices and advances in material science, flexible electrodes have played an important role in the field of invasive brain-computer interface (BCI). Compared with traditional rigid electrodes, flexible electrodes implanted in the brain cause less damage to brain tissue and are more biocompatible and stable. Most of the traditional invasive electrodes are made of glass or metal, which are prone to brain tissue damage, inflammation, and other problems, although they can avoid interference from the skull and skin and record neural signals accurately and with low noise. However, the main materials for flexible electrodes are polymers, hydrogels, graphene, etc., which can reduce immune rejection and prolong the service life of neural implants. This paper describes five main implantation methods for flexible electrodes in recent years: microneedle arrays, coiled implantation, minimally invasive injections, biodegradable electrodes, and stretchable electronics implantation. They can be used in the most appropriate way for electrodes of different structures to acquire neural signals with stable and reliable fidelity. Flexible electrodes have the potential for a wide range of applications in neuromonitoring providing a safer and more durable solution for invasive brain-computer interfaces. Then the authors will propose a new idea combining their respective advantages in the hope of bringing enlightenment.

Keywords: Intrusive brain-computer interface, flexible electrodes, electrode implantation.

1. Introduction

Invasive Brain-Computer Interface (IBCI) is a method of surgically implanting electrodes into the cerebral cortex. This means allows for higher resolution signals, clearer feedback and less noise interference than non-invasive brain-computer interfaces, as demonstrated in Fig. 1 [1]. These electrodes capture the brain's neuroelectric signals and convert them into data that can be applied to a computer, thus enabling the human brain to communicate with machines. Electrode implantation surgery requires high precision and carries the risk of infection, bleeding and causing damage to brain tissue. The procedure requires highly trained neurosurgeons and has a high cost. Besides, the implanted motors must be biocompatible and in contact with the brain for a long period of time without causing problems such as immune rejection or tissue damage.

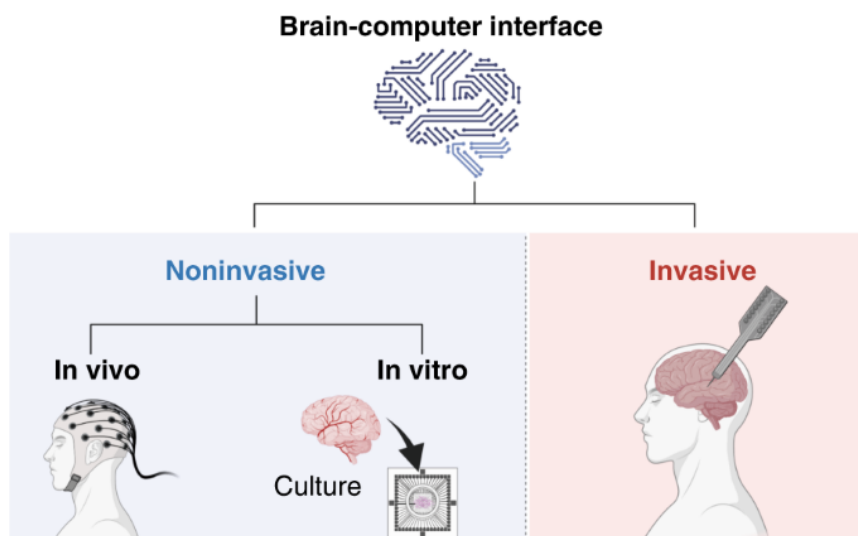


Fig. 1 Two different forms of brain-computer interfaces [1].

In addition, electrode materials for doing invasive brain-computer interfaces need to have biological characteristics such as high conductivity, low toxicity and good mechanical properties. There is still room for improvement in the biocompatibility and long-term stability of currently used materials. To improve signal acquisition accuracy and coverage, electrode arrays need more channels and smaller sizes. At the same time, miniaturization and multi-channel full-coverage design will lead to increased manufacturing difficulty and significant increase in manufacturing cost, while the implanted means have higher risks. In order to be compatible with different structures of flexible electrodes, this paper focuses on five typical corresponding implantation means and summarizes the types of electrode structures in the field today.

Conventional materials for rigid electrodes are often metal or glass, although their higher hardness, robust structure, ease of machining, and lack of deformation, as well as the possibility of high-precision recording of neural signals, such as Utah array electrodes. However, they are prone to causing brain tissue damage, triggering inflammatory reactions, and immune rejection during the implantation process or after use. Although invasive brain-computer interfaces are the potential of the future, these effects not only distort the signal, but also cause harm to the user.

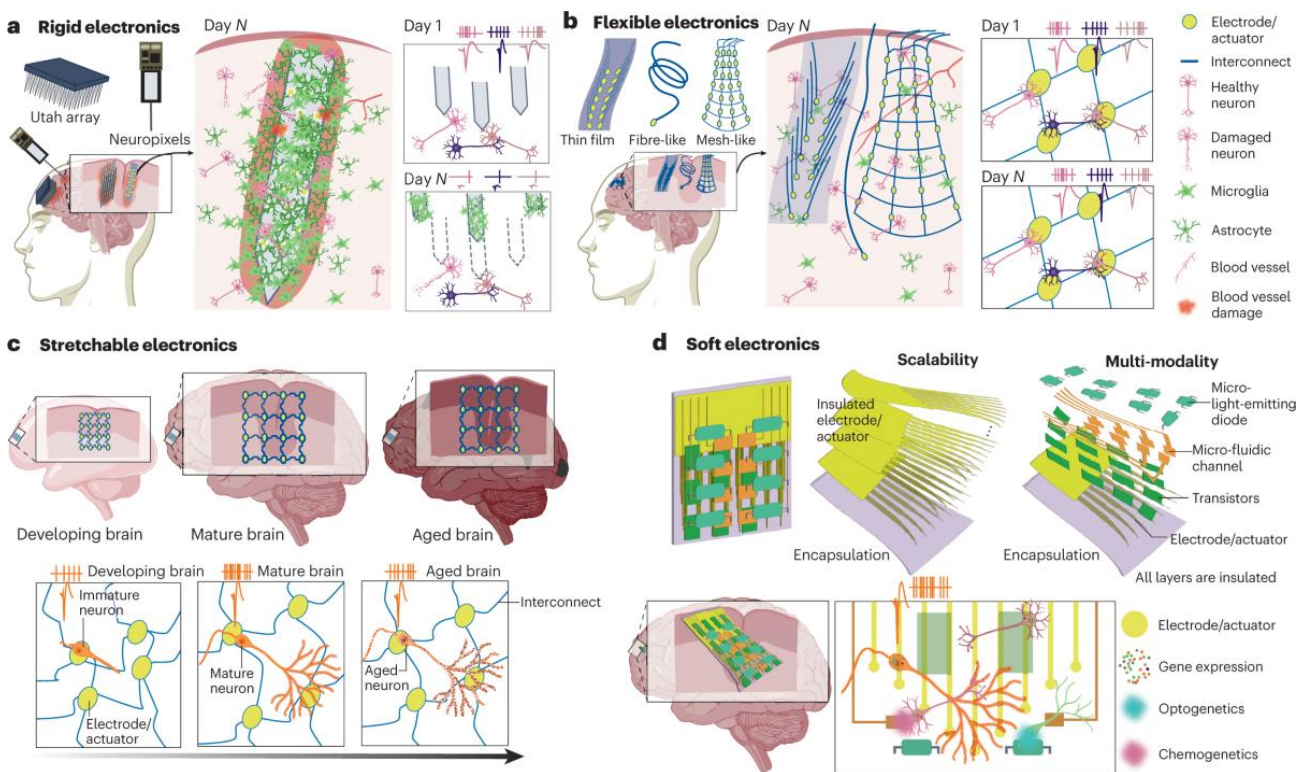


Fig. 2 Multiple brain-computer interface with flexible electrodes [2].

In contrast, flexible electrodes formed by combinations of e.g. polymers: polyimide (PI), polyethylene terephthalate (PET), polydimethylsiloxane (PDMS), polyvinyl alcohol resin (PVA), graphene, or conductive hydrogels are able to produce deformations that conform to the brain tissue reducing mechanical friction and disruption of the brain tissue, and higher biocompatibility results in better stability. Therefore, flexible electrodes are gradually being more widely used in future brain-computer interface technologies, especially in long-term neuromonitoring and feedback stimulation tasks in clinical medicine, developing many types of structures, as illustrated in Fig. 2 [2]. The five types of implantation methods that will be covered in the following section are all for flexible structures, and in the discussion the authors will also combine their advantages to propose a new vision of flexible structures, which will hopefully inspire related research.

2. Implantation Techniques for Flexible Brain-Computer Interfaces

2.1. Classification Basis for Flexible Brain-Computer Interface Implantation Modalities

Advances in material science have led to advances in flexible cortical electrode technology with better mechanical flexibility, adaptability, stability, and biocompatibility, which performs well in a variety of internal environments of the human body. As demonstrated in Fig. 3, it is now used in surgical manipulation of organs such as the heart, brain, and other organs of vital importance [3].

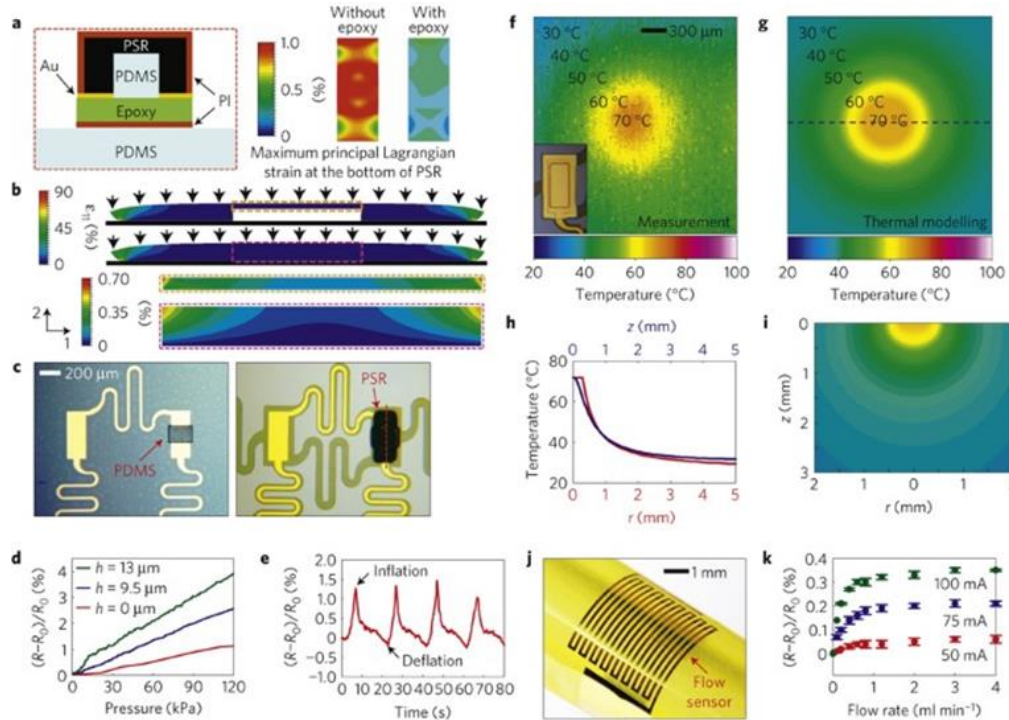


Fig. 3 Flexible cortical electrodes for applications in the heart and brain organs [3].

The means of implantation of flexible electrodes can be classified into the following five types according to the corresponding different electrode structures, which mainly include: microneedle array implantation, coiled implantation technique of minimally invasive injection implantation, temporary implantation of biodegradable electrodes, and implantation of stretchable electronic devices.

Microneedle array implantation refers to the use of high-density flexible microneedle arrays to achieve precise neural stimulation and recording, thereby reducing brain tissue damage, and is particularly suitable for local signal acquisition in deep brain regions [4, 5]. The coiled implantation technique coils or folds flexible electrodes, which are then implanted and unfolded to cover the surface of the brain through minimally invasive surgery. This allows for application in large-scale cortical mapping, as well as separation for multiple signal comparisons in different brain regions [6].

Minimally invasive injectable implantation reduces the extensive trauma of conventional surgery by implanting flexible electronic devices, especially filament electrodes and mesh electrodes, into the endothelial layer of the meninges or into multiple sites corresponding to the deeper layers of the brain by using a syringe and demonstrates a wide range of potential applications, especially in deep and precise implantation. Now Elon Musk's brain-computer interface company Neuralink basically relies on this approach for brain pathology studies of various diseases [7]. Temporarily implanted biodegradable electrodes are designed for short-term neuromonitoring or therapeutic tasks, and they gradually degrade and metabolise in the body after use, avoiding the secondary damage of surgical removal [8]. Stretchable electronics implants are able to maintain neural signal acquisition and transmission in complex dynamic environments through the use of elastic materials (e.g., conductive polymers and liquid metals) adapted to the natural deformation of brain tissue as summarized in Table 1 [9,10].

Table 1. Implantation methods and characteristics

Number	Method	Characteristic
1	Microneedle Arrays	Flexible basal microneedle electrodes for stabbing brain tissue
2	Coiled Implant Technology Minimally Invasive Injection Biodegradable Electrodes	Rolling or folding an implanted film to cover the brain surface
3		Flexible filament electrode injection implanted into brain tissue
4		Absorbs into the body and does not require surgical removal
5	Stretchable Electronic Devices	Elastic material extended to cover the brain surface

2.2. Microneedle Arrays

Microneedle electrodes on a flexible substrate made of biodegradable conductive polymers can be pierced into brain tissue to collect deep neural signals. The microneedles are fabricated by micro- and nanofabrication techniques and self-assembly or minimally invasive implantation techniques are used so that the electrode arrays are implanted within the brain tissue.

Existing flexible substrate materials based on traditional Utah electrode arrays, which are implanted by conventional surgery [4], can be combined with optogenetics to constitute miniature optoelectronic devices, thus enabling implantation by injection to explore the pathology of Alzheimer's disease from inside the brain [5], and in recent studies, can also be combined with stretchable deformable substrate materials as mentioned in the later section to make stretchable microneedle electrode arrays (SMNEAs), as illustrated in Fig. 4 [11]. This conventional method is able to use laser micromachining, replica moulding, transfer printing, spin-coating, etc., to achieve 60%-90% elongation, which also results in high flatness of the PI films. Chromium with a thickness of 10 nm and a conductive coating of gold at 150 nm were etched and deposited on them, thus connecting the conical polyimide microneedles (PI; PI-2610) with their overlaying parylene C insulating coatings (with a thickness of 3 μm) [11].

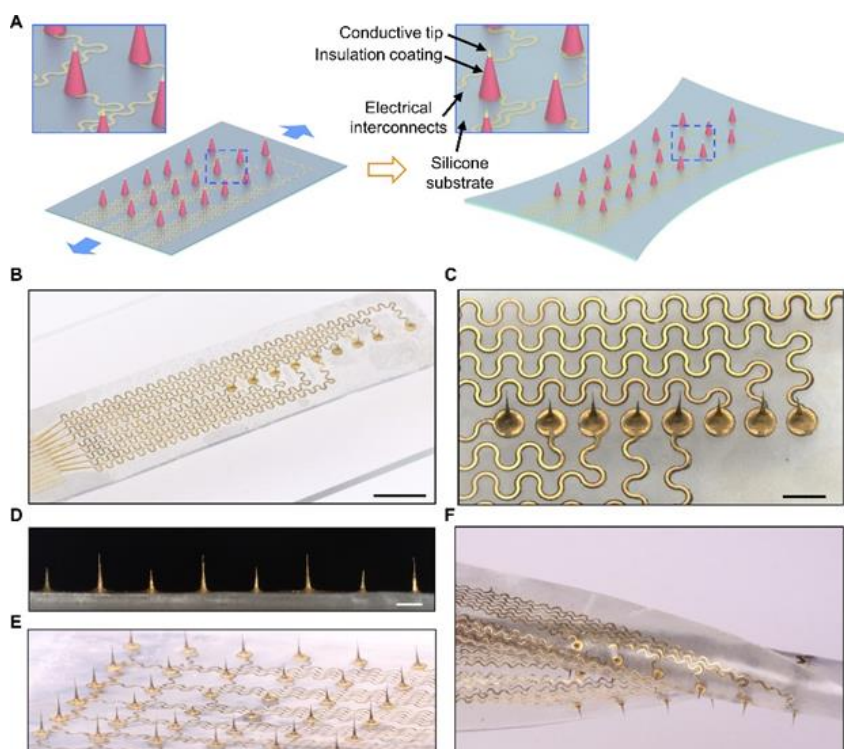


Fig. 4 Schematic structure of a flexible deformable microneedle array [11].

Flexible electrode arrays are suitable for high-resolution intracortical recording of neural signals or neural stimulation, especially in controlling neural prostheses or studying brain function, and the method is commonly used for high-density neural interfaces such as tactile prostheses controlled in conjunction with electromyographic signals or the study of deep brain function. Tissue damage induced by conventional rigid electrodes can be significantly reduced while maintaining the accuracy of the obtained Electroencephalography (EEG) signals.

2.3. Coiled Implant Technology

Metals such as gold and platinum are printed on the surface of ultrathin polymer films (e.g., PI, PDMS, or PET) to form conductive pathways that adapt to the minute movements of the brain tissue, thus providing long-term cortical neural recordings and stimulation, especially for epilepsy monitoring or chronic neurological diseases [6].

Flexible film electrodes are rolled or folded, unfolded and affixed to the surface of the brain by surgery or specialised equipment. The film electrodes are implanted with devices only from small wounds, thus covering the affixed brain surface or accessing the cerebral sulcus gyrus for multi-site and multi-threaded EEG signal extraction, and obtaining the ability to record neurological signals that are not readily available. The electrodes are also often fixed in place using biocompatible glue or light pressure to have long term reliable stability and also reduce cerebral cortical damage, post-operative complications and discomfort.

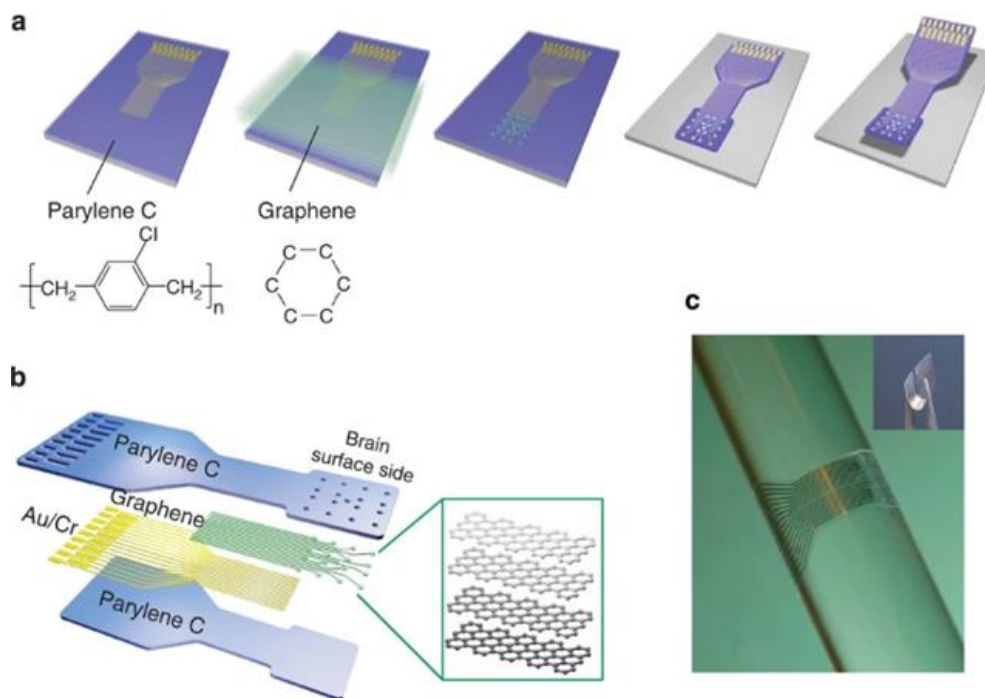


Fig. 5 Combination of graphene and flexible substrates for coiled implantation [12].

In addition, graphene is also a commonly used substrate material with very high electron mobility for precise conduction of neural signals. The structure is extremely light and thin enough to support structural loading for neuroimaging and optogenetics after unfolding, as shown in Fig. 5 [12]. Inspired by this prior combination of silicon-based microelectrodes and ultra-compliant thin film materials and mobilisation of van der Waals forces to achieve ohmic contact in a capillary structure [13], the biggest advancement to date has been the use of platinum nanoparticles by a US team to overcome the quantum capacitance limitations of graphene by embedding them in a thin, transparent, and pliable polymer, shrinking the diameter of the microelectrode down to 20 micrometres, allowing for an extremely small opening but a large transparent recording region without introducing any metal extensions, enabling high-density microelectrode arrays of up to 256 channels, as illustrated in Fig. 6 [14]. The polymer strip is coiled to be implanted in the brain and unfolded to fit snugly on the surface of the brain.

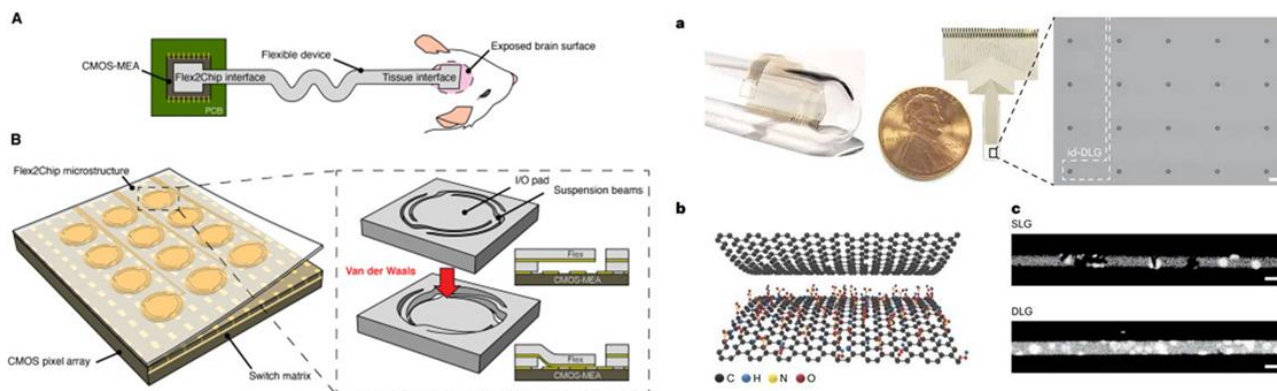


Fig. 6 Optical performance from the combination of silicon-based and graphene with coiled implantation [13, 14].

Exceptionally, because of the transparency and optics to be achieved, it was particularly ensured that a laser could be passed through, thus enabling two-photon microscopy to image calcium spikes in neurons located at a depth of 250 micrometres below the surface of the cortex. This groundbreaking means of replacing physical micro-needle damage to the brain with laser light, albeit with slightly less reliability, also allows observation of the mechanisms of inter-neuronal signalling, which is based on the means of placing flexible electrodes that can be folded or looped around to maintain the precision of the physical-optical features required to further maintain fidelity of the signal.

2.4. Minimally Invasive Injection

This type of approach refers to the implantation of flexible electrodes, especially filament electrodes and miniatures, into the brain tissue by means of injections, which minimises tissue damage and also allows for the precise localisation of the implantation site of the electrode. They are particularly suitable for the extraction of signals from deep brain areas that are difficult to access or for brain areas that require precise localisation, such as neural monitoring and stimulation of subcortical structures.

A 2015 study provided a new direction for this implantation field [7]. The team used filamentary electrodes that can be shrunk into a needle to connect into a mesh that is injected into the surface of the cerebral cortex for signal acquisition, and then removed directly from the original wound in the same way as it was used, with little to no impact on the normal structure of the brain, and the soft material avoids infections, immune rejection, and oedema. A similar structure can also be combined with graphene, similar to the previous method, but the structure is more subtle and precise, and can be shrunk into the needle to achieve multi-site injection, as displayed in Fig. 7 [15]. Almost all research projects of the American company NeuroLink are based on this type of technology, and with funding and talent, this type of interface must have a bright future and potential.

However, the softer the electrode the more complex the problem of fine micro-nano-machining it faces, and increasing the density of the implanted electrode is an effective way to hedge against the difficulty of machining. This type of implantation means inspired Chinese scientists to invent a brand-new means called ‘neural fringe’ [16]. This technique uses surface tension to polymerise the ‘tassels’ by immersing thousands of flexible nerve fiber electrodes close to the synaptic size of the neuron in a polyethylene glycol liquid, which are then automatically released after successful implantation and degradation of the metabolised polyethylene glycol. This method is also designed to increase the number of fiber electrodes in the brain by optimising the minimally invasive injection implantation method to achieve better signal acquisition.

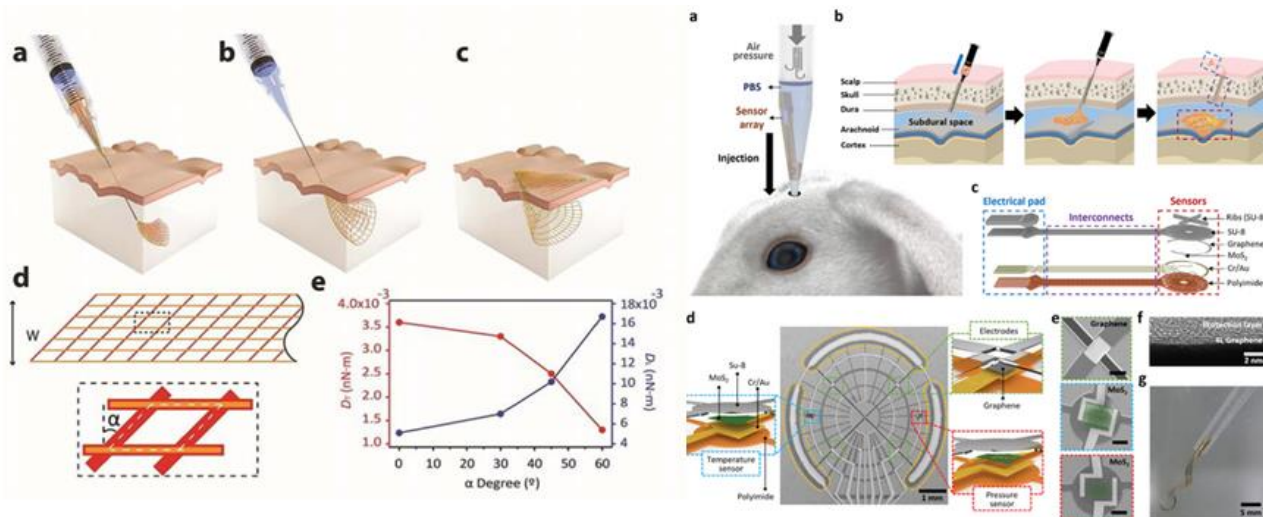


Fig. 7 Typical structure of minimally invasive injectable filament electrodes [7,15].

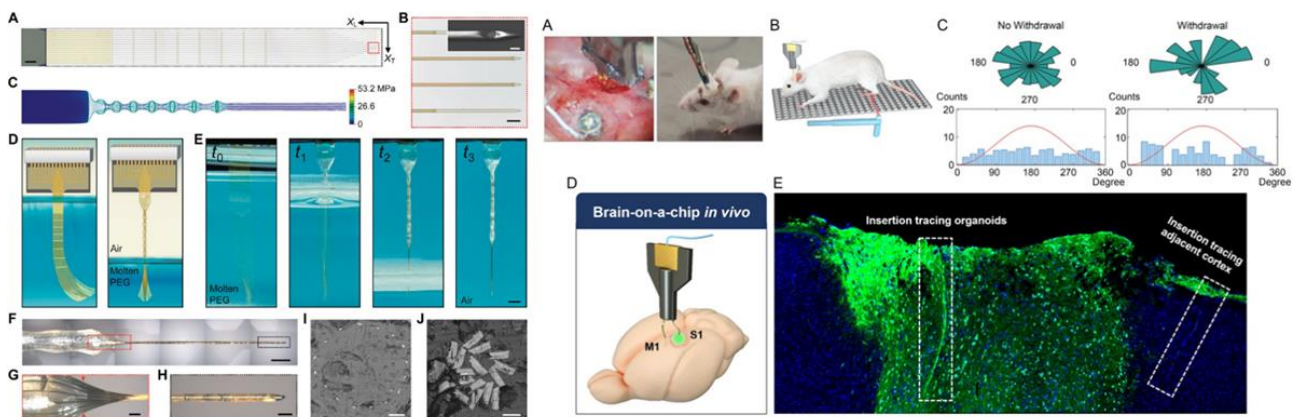


Fig. 8 Neurofringe technology and coupled implantation of on-chip brain-computer interfaces [16, 17].

In addition, minimally invasive injections are also useful for deep EEG signals. China's Haihe Lab team developed an on-chip brain-computer interface combined with low-intensity focused ultrasound technology, which takes minimally invasive injection of in vitro-cultured electrode chips and the brain coupled and then inserted into it, and verified that this method can promote the development and differentiation of brain tissue using immunofluorescence, single-cell Ribonucleic acid (RNA) sequencing, and cellular genealogical tracing, as demonstrated in Fig. 8 [17].

2.5. Biodegradable Electrodes

There is another technique related to biodegradation and metabolism, temporary biodegradable electrode implantation. The major difference from other methods is the use of biodegradable materials such as silk proteins, polylactic acid-hydroxyacetic acid copolymers (PLGA), etc [18]. These electrodes are able to naturally degrade in the organism within a few weeks or months after they have fulfilled their function without the need for a secondary surgical removal that would result in repetitive injuries, as demonstrated in Fig. 9 [8].

This technique is often used for short-term neuromonitoring or treatment, avoiding the inflammatory or rejection reactions associated with long-term implants. The disadvantages are also significant, as the use of special materials does not guarantee a stable and realistic signal, which is often interfered with by physico-chemical factors in the body. It is hoped that with future advances in biology and materials science, this implantation method will be the best way to integrate with the human body.

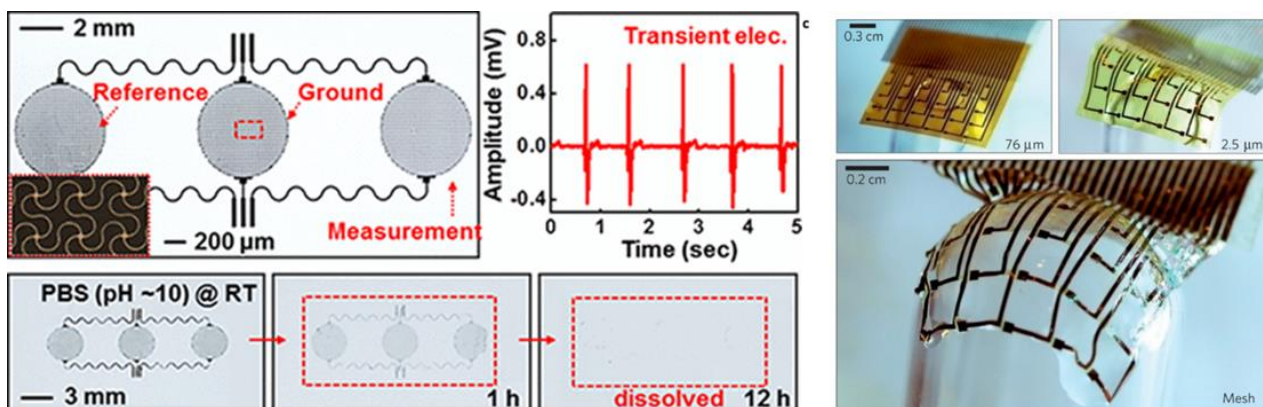


Fig. 9 Biodegradable elastomeric silicon nanomembranes [8,18].

2.6. Stretchable Electronic Devices

This type of implantation method has similarities to the means of the second coiled implantation technique, but focuses more on the stretching and elongation of the material itself. Examples include conductive polymers and liquid metals, such like rubber uniformly doping single-walled carbon nanotubes (SWNT) into a vinylidene fluoride-hexafluoropropylene copolymer matrix to form a composite film [19]. When electrode materials are implanted in the body, achieving the correct function is as important as having a biometric match to the brain. Interconnected physical and chemical electrodes are embedded in the silicone substrate, thereby withstanding multiple stretching and deformation, as well as electrochemical pulse stimulation with superior durability [9]. They fit into soft neural tissues, avoiding pathological interference caused by other hard implants, and are particularly useful at junctions such as the brainstem and spinal cord, where, together with the other four methods, they provide a full range of EEG signals. With the aid of the previous injections, new materials such as self-healing conductive hydrogels can also be synthesized to obtain wet electrodes that can be reshaped and re-injected as reusable, self-healing conductive hydrogel materials for flexible and stretchable neuroelectrodes, which are promising in brain-computer interface applications [20].

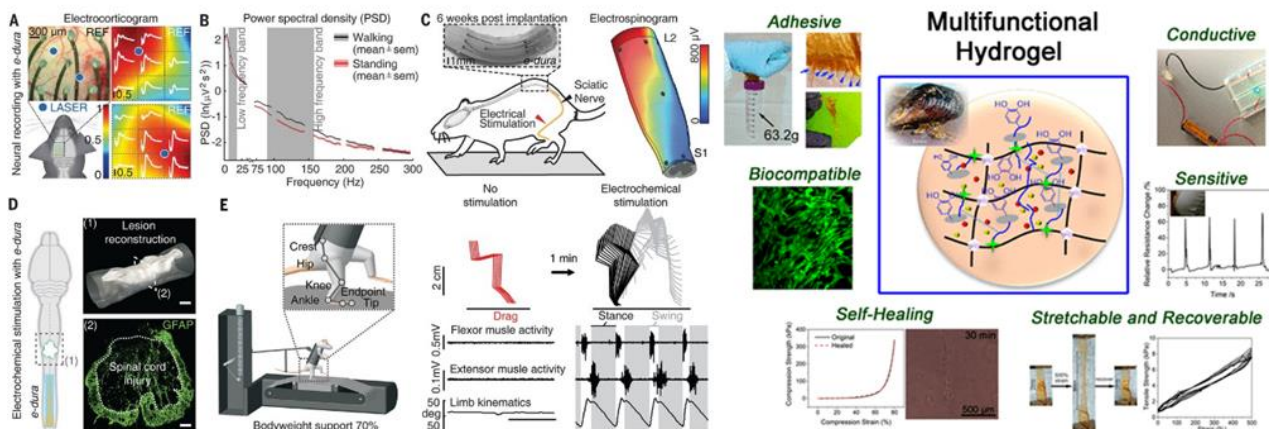


Fig. 10 Silicon-based ductile electrodes and new biomimetic materials inspired by shellfish [9,10].

In addition, this means of implantation is often associated with bionic biology. Inspired by the coat membranes of shellfish, a Chinese team doped polydopamine-coated talc (PDA-talc) nanoflakes into polyacrylamide (PAM) hydrogels to develop a self-healing hydrogel-dependent strain sensor, as demonstrated in Fig. 10 [10]. This novel electrode material is more than ten times malleable, has almost no plastic deformation after recovery, exhibits considerable biocompatibility and sensitivity, and is able to maintain neural signal acquisition and transmission in complex dynamic environments. This elastic electrode sensor can not only be surgically placed into the brain, but also has notable advantages in surface attachment to other organs in the human body.

3. Discussion

In neuroscience research and clinical applications, high-quality recordings of electrical activity in the cerebral cortex are essential for understanding brain function and developing therapeutic treatments. Conventional rigid electrodes exhibit many limitations in long-term implantation and dynamic environments due to their mechanical stiffness and poor biocompatibility. Existing flexible electrodes and injection methods suffer from the drawbacks of being thicker and less pliable, and can only be detected across the meninges, with more signal interference and insufficient accuracy. In addition, minimally invasive implantation, surgical craniotomy implantation, endoscopy-assisted implantation, and capsule injection methods have problems such as large wounds, susceptibility to infections, surgical difficulties, and easy movement of electrodes.

Most of the previous flexible electrodes used PDMS, which has better stability and biocompatibility, but the thickness of the support layer is 80 microns. In contrast, PIs have excellent thermal and oxidative stability, high toughness, chemical resistance and biocompatibility. Through sputtering preparation, gradient heat treatment and Krypton Fluoride (KrF) excimer laser scorching, PIs are able to achieve a thickness of 200 nm, resulting in an electrode thickness of no more than 600 nm. In addition, silver nanowires (AgNWs) will ensure a high electrical conductivity, which is transferred to the polyimide membrane through screen printing to complete the encapsulation. Collagen nanomembrane was wrapped around the outer side of the electrode to enhance biocompatibility. And the backside of the electrode is coated with chitosan, held in place by a kind of gelatin, polyvinyl alcohol resin (PVA) compression, and then placed in position determined by an in vitro imaging navigation system. In the presence of tissue fluid from the cerebral cortex, the gelatin gradually melts and is absorbed by the tissue, and the chitosan coating absorbs water and spontaneously adheres to the surface of the cerebral cortex. The electrode system contains multiple electrodes with probes. The probes will penetrate deep into the sulcus gyri and are made of a composite of polyurethane (PU) and carbon nanotubes (CNT) to meet the requirements of small diameter injections.

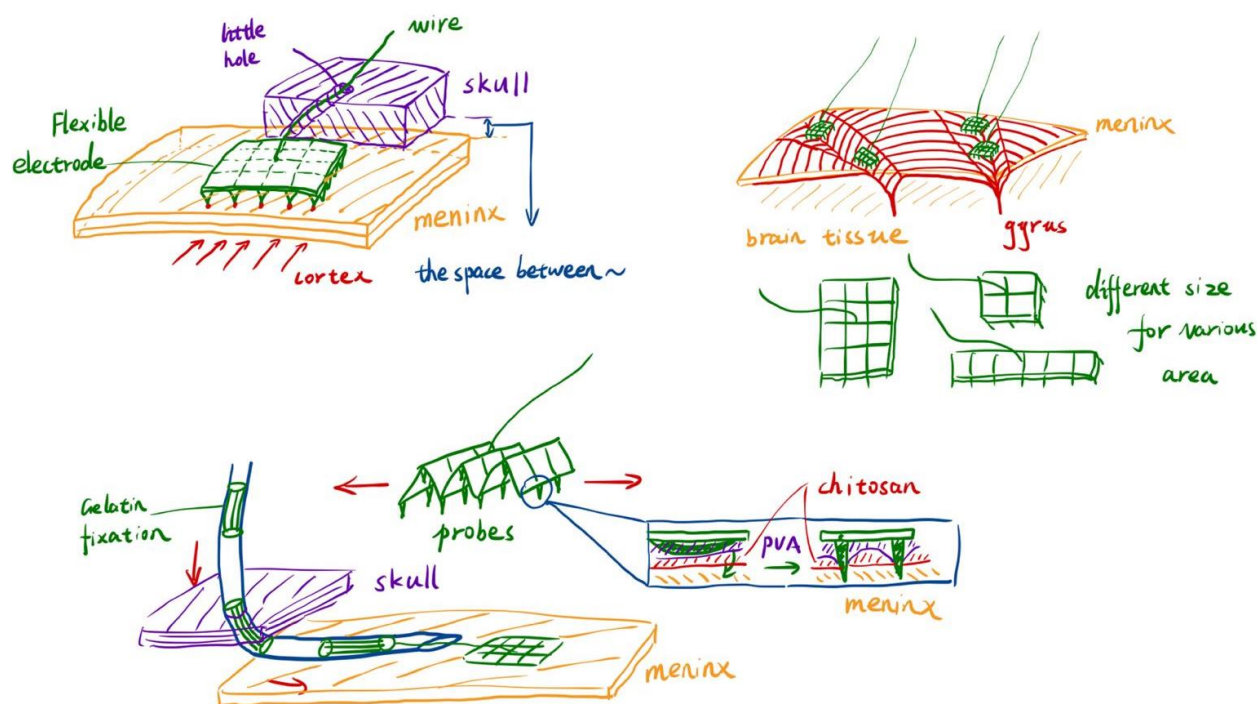


Fig. 11 Schematic diagram of the flexible electrode implantation method (Figure Credits: Original).

The new way of making PIs ensures that the thickness of the electrodes is low and it allows the electrodes to fit into the cerebral sulcus gyri with less noise and the signal will be clearer, as shown in Fig. 11. At the same time, the thinner flexible electrodes can be compressed into a smaller volume, appearing less invasive at the injection, reducing the risk of surgery and the probability of subsequent

infection. The probe can further enhance the clarity of the signal. Compared with existing cortical brain electrodes, the electrode array has advantages in terms of conformal mapping area, locus and signal quality. This method provides new opportunities for complete neural mapping of the entire cerebral cortex in multiple threads, offering new possibilities for diagnosis and treatment of neurological diseases and precise control.

4. Conclusion

The tremendous advances in flexible electrodes play a key role in safe, portable, reliable, and efficient invasive brain-computer interface applications. Although, exploring simple, cheap, and large-scale manufacturing methods to produce commercially available customized electrodes is a major dilemma for the brain-computer interface industry, and experimental constraints such as ethics have caused many of the subtle rays to be restricted to just animal experiments in the lab, making it difficult to move into everyday life. In addition, technologies such as neural fringes in China and neural particle electrodes in the U.S. hold great promise, but reliability and usability still need to be perfected and improved by subsequent scientists.

In this paper, from the implantation of flexible electrodes for invasive brain-computer interface, the author has sorted out the structure of five major types of electrodes, but no matter which one is used, the main goal is to accurately transmit EEG signals, to reduce the risk of surgery and damage to the brain, and to realize stable, reliable and long-lasting human-computer interaction hardware. In order to build a bridge between man and machine, in-depth understanding of the mechanism of the brain's work, and even the formation of memory and the source of learning ability, but also focus on Alzheimer's, Parkinson's and other pathologies of the attack, and ultimately not only to improve the quality of life of people with neurological dysfunctions, but also to help mankind to understand the structure of the brain and the principle of the brain that has been explored over the past 50 years. Flexible electrodes still need to be explored and developed in terms of materials, fabrication methods, and substrates. The authors propose an electrode that combines various advantages and hope to provide more exciting ideas and inspirations for future research to make flexible brain interface electrodes with more outstanding performance and great progress.

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