From the perspective of material science: a review of flexible electrodes for brain-computer interface

Guangwei He, Xufeng Dong* and Min Qi

Key Laboratory of Energy Materials and Devices (Liaoning Province), School of Materials Science and Engineering, Dalian University of Technology, Dalian 116024, People’s Republic of China

* Author to whom any correspondence should be addressed.

E-mail: dongxf@dlut.edu.cn and minqi@dlut.edu.cn

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Abstract

As an important branch of man-machine interaction, Brain-Computer Interface (BCI) has the potential to be widely used in various fields, such as health-care, physical efficiency, aerospace, intelligence traffic system, entertainment and so on. The flexible electrode is the crucial component of the BCI, and is the key for the development of the BCI technology. Recently, with the increasing demands on Brain-Computer Interface, plenty of flexible electrode materials and the structural design for applications in BCI technology have been developed. In this study, we review the development of the three kinds of flexible electrodes material selection and structural design in BCI, including non-intrusive electrodes, intrusive electrodes and semi-intrusive electrodes. The challenge and the problems that hinder the development of the flexible electrode are analyzed. Besides, from the perspective of material science, the future applications of the flexible electrode in the BCI field is prospected.

1. Introduction

Since the 1920s, when scientists first discovered the existence of electroencephalogram (EEG) signals, human beings have obtained a convenient way to research our brain. In the 21st century, the research on brain science has entered a brand-new phase. Many countries in the world have also put human brain engineering on the agenda, providing wisdom and solutions for urgent problems in the field of global human-computer interaction [1, 2].

Brain-Computer Interface (BCI) is the frontier of human brain engineering and a critical direction of human-computer interaction. It’s a disruptive technology that produced on the basis of intersection of electronic information, bio-medicine, materials science, mechanics and other disciplines [3]. Compared with other human-computer interaction systems, BCI doesn’t depend on the normal input and output ways of our brain. It’s a new non-muscle channel that established between the human brain and computers or other electronic devices. Thus, BCI can achieve direct information interaction and control of a real-time communication [4]. BCI is an alternative system built on artificial mechanisms and acts as a bridge between the brain and external devices. The aim of BCI is to convey human intentions to external devices by directly extracting brain signals. Eventually, the brain and computers would be highly integrated.

Brain diseases are a major potential hazard to human life, such as amyotrophic lateral sclerosis, epilepsy, dementia, tumors, stroke, cerebral palsy, etc [5]. The initial goal of BCI was the medical monitoring. There is abundant physiological and pathological information in the brain waves. BCI can monitor the neuron physiological activities of the brain by analyzing brain waves, providing important evidence for the diagnosis of brain diseases. As a new input and output manner, BCI also makes it possible for human brain signals to drive external devices directly. In 2014, at the opening ceremony of the Brazil World Cup, the paralyzed youth wore exoskeleton that was similar to the mechanical armor, kicking off the World Cup through BCI [6]. The emergence and development of BCI technology has not only brought the gospel of functional recovery to the disabled, but also provided opportunities of functional enhancement to healthy people. In recent years, the
application of BCI in non-medical fields has also become visible. Take the aerospace industry as an example, when astronauts perform complex missions in the space environment, they are likely to be restricted. The BCI can not only turn the astronaut’s thinking activities into operating instructions, but also monitor their neurological status, assisting them to complete the space mission [7]. In addition, the applications of BCI also involve intelligent transportation, identity verification, education and entertainment, among which the huge socioeconomic benefits and broad application prospects make BCI technology extremely competitive.

Electrodes are a crucial part of the brain–computer interface and the key to BCI technology. According to the electrode position and implantation method, the BCI can be divided into three ways, including non-intrusive electrodes, intrusive electrodes and semi-intrusive electrodes. Ensuring the quality of the collected EEG signals is an imperative prerequisite for BCI technology to obtain good comprehensive performance. The key of electrode lies in the choice of material and structural design. The inherent high elastic modulus, high density and weak bio-compatibility of traditional electrodes can’t meet the demands of EEG signal acquisition. Therefore, it’s particularly important to find flexible electrode materials with low elastic modulus, high porosity, wet softness and good bio-compatibility. Under the demands, the materials with high flexibility have become the most promising novel BCI materials, such as polymers, nanomaterials, carbon-based materials, bio-materials, hydrogels, etc [8]. With high flexibility, suitable mechanical compliance, good bio-compatibility and minimized structural, mechanical and topological differences, they have become the best candidates of BCI technology for brain electrical stimulation and signal acquisition. In this study, we will summarize the progress in brain–computer interface in terms of materials or structural selection and accurately design flexible electrodes of BCI according to the specific needs, which also provides new solutions for the next-generation BCI technology.

2. Non-intrusive flexible electrodes

Non-invasive, also known as wearable, doesn’t need to be implanted in the brain. This non-invasive method is less risky and can guarantee security. However, what is urgently needed is the issue of convenience. At present, the most mature application is electroencephalography (EEG), but the equipment is heavy and extremely inconvenient to use. The ideal wearable BCI electrodes should consider the stability of signal and the comfort of users, which brings new challenges and higher requirements for the design of materials and structures. Theoretically, non-intrusive BCI devices based on flexible electrodes can improve the precision, reliability and sensitivity, making them convenient to wear, complete in function and beautiful in appearance.

2.1. Materials considerations for engineering

The macroscopic flexibility of BCI devices is mainly determined by the electrode materials. At present, there are mainly two kinds of material design routes for flexible electrodes. One is adding conductive substance (metal, carbon-based material, etc) to the flexible matrix, and then forming flexible conductive mixture through physical mixing. For example, carbon-based materials are uniformly dispersed in the polydimethylsiloxane to make flexible electrodes [9]. The other is depositing or plating the conductive material on the flexible substrate, and then patterning it. Due to the stretch ability of flexible materials, flexible electrodes can increase contact area, reduce contact resistance and reduce motion artifacts.

The flexible substrate plays a role in buffering and damping. It’s an important part of the flexible electrode, and also a skeleton during the entire electrode preparation process. Generally, the aforementioned flexible materials mainly include polymers, carbon-based materials, nanomaterials, and the like. Polymers mainly include polyimide, polyurethane, parylene, polydimethylsiloxane, etc. The stiffness of these materials is two orders of magnitude lower than traditional materials (metal, inorganic silicon, etc) [10]. Carbon-based materials mainly include carbon nanotubes, graphene, carbon fibers, etc. Such materials have high flexibility, low density, good electrical and mechanical properties. It is the interconnected porous channels inside the materials that help to achieve the rapid migration of electron and ion, which greatly improves the electrochemical property [11]. As a typical nanomaterial for flexible electrode substrates, with abundant sources, low cost, high bio-compatibility, non-cytotoxicity, high mechanical strength, high degree of polymerization, high crystallinity and ultra-fine structure, nanocellulose is also an ideal material for the preparation of flexible electrodes [12]. Besides, the design of carbon nanofiber materials can also enhance flexibility by adjusting the micro structure, such as introducing pore structure, reducing fiber size, increasing the degree of graphitization, and so on.

2.2. Structured design of flexible electrodes

2.2.1. Wet electrodes

Compared with electrodes in other parts of the body, brain electrodes inevitably eliminate the interference caused by hair impedance. The cuticle is the top layer of the skin and has high impedance. In order to reduce the scalp resistance, traditional wet electrodes are usually adding the Ag/AgCl gel-like conductive medium between...
scalp and the electrode. And then the conductive gel would fill the pores between scalp and the electrode. The wet gel hydrates the stratum corneum, creating an ion path between the metal part of the electrode and the skin below the stratum corneum, making it easier to convert ion current into electronic current, and reducing the impedance between scalp and the electrode.

Currently, the almost research of Ag/AgCl is focused on manufacturing technology, preparation method and evaluation of electrode performance. However, the disadvantages of wet electrodes are also obvious. Although a good quality signal can be obtained in a short period of time, the gel is susceptible to loss water. Dehydration can cause signal distortion and affect sensitivity. Therefore, it’s suitable to make disposable electrodes and not suitable for long-term use. In addition, the test environment is limited. Weak sliding and offsetting can cause motion artifacts. The most maddening thing is that the operation process is complicated and the comfort experience is extremely poor. It may even trigger skin irritation and allergic reactions.

In order to solve the problem of hair resistance of traditional gel-based wet electrodes, Wu Hui’s research team developed a gel-free wet electrode (figure 1(a)) [13]. By using a flexible silver nanowire/polyvinyl polyether/melamine, this sponge electrode can prevent the electrode from thick hair without the hassle and complexity. Experimental results show that the newly modified wet electrode exhibits high electrical conductivity, good flexibility, excellent chemical and mechanical stability.

2.2.2. Dry flexible electrodes

The material and structure of electrode directly affect the quality, reliability and practicality of the EEG signal. How to make a suitable electrode for EEG acquisition is crucial, so that it can achieve a tight combination of the electrode and the skin, reduce motion artifacts and ensure the quality of the EEG signal while reducing the
limitation of the acquisition environment and exercise state. In order to solve the above problems of wet electrodes, a variety of dry electrodes emerged. The dry electrode doesn’t use any liquid conductive medium. It must directly contact the scalp across the hair. The thickness of the hair directly affects the state of contact with the scalp. Compared with wet electrodes, the contact resistance of dry electrodes is more stable. Meanwhile, dry electrodes also omit troublesome preparations and subsequent processes.

Sammy Krachunov et al used 3D printing technology to prepare micro-needle electrodes, and then coated the electrode surface with Ag/AgCl as a conductive substance (figure 1(b)) [14]. Cristian Grozea’s research group applied Ag particles to polymers by a conductive ink printing process (figure 1(c)) [15]. They prepared the brush electrode with dimensions of 12 mm × 12 mm × 10 mm. Alok Kumar Srivastava et al prepared a tapered micro-needle electrode based on a flexible polymer substrate (figure 1(d)), and then coated Au with a magnetron sputtering deposition process, which greatly reduced motion artifacts [16]. By coating the polyethylene dioxythiophene conductive polymer on the outer surface of nylon, Qiulin Tan’s group made a claw electrode, whose good elasticity ensures the comfort of users (figure 1(e)) [17].

Although the dry electrodes mentioned above overcome the shortcomings of wet electrodes to a certain extent, the coating is easy to peel off, resulting in an increase of electrode impedance. In addition, the number of pins, shape, gap size, length, etc are complicated from the structural design to the preparation process. So they still can’t satisfy the practical application. To overcome this limitation, Yu-Chun Chen’s team made a new type of spring electrode with an adaptive mechanical design (figure 1(f)) [18]. This structural design can maintain a good and stable skin-electrode contact state through spring compression and effectively reduce the impact of motion artifacts. Yongjun Lee et al designed an ultra-thin network structure based on graphene (figure 1(g)) [19]. Due to its stretch-ability, it can conformally contact the skin. Under stretching conditions, the relative resistance and voltage of the electrode can be controlled within 1%. Inspired by spiral vine plants, Yuanjin Zhao’s group used microfluidic spinning technology to encapsulate ionic liquids in hollow microspinnng wires and then embedded them in stretchable polydimethylsiloxane flexible films (figure 1(h)) [20]. The spiral structured electrode has excellent flexibility and elasticity, which makes it show good conductivity and reusability during the tensile test. To enhance the contact of electrode-skin, Shideh Kabiri Ameri et al developed a tattoo-like epidermal sensor system for recording the biopotential signals (figure 1(i)) [21]. This tattoo-like system consists of graphene-based electrodes. Its structure is designed as a stretchable mesh located on the silicone, which can adhere to the skin well and have a good contact.

2.2.3. Novel semi-dry flexible electrodes

In essence, the skin is a moist as well as soft material. Under the conditions of sports or hot, people will inevitably sweat, which may cause the short circuit. In response to this problem, scholars have proposed the concept of semi-dry electrodes on the basis of research on dry and wet electrodes. The principle is that the conductive liquid is continuously...
Table 1. The merits and demerits of three kinds of non-intrusive flexible electrodes.

| Classification          | Merits                                                                 | Demerits                                                                 |
|-------------------------|------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Wet electrodes          | 1. Reducing the impedance between scalp and the electrode.             | 1. The gel is susceptible to lose water, causing signal distortion and affecting sensitivity. |
|                         | 2. The manufacturing technology of Ag/AgCl layer and the preparation method of conductive gel are relatively mature. | 2. Due to weak sliding and offsetting, the test is susceptible to the motion artifacts. |
|                         | 3. A good quality signal can be obtained in a short period of time.    | 3. The operation process is complicated and the comfort experience is extremely poor. |
| Dry flexible electrodes | 1. Achieving tight combination of the electrode and skin, reducing motion artifacts while reducing the limitation of the acquisition environment and exercise state. | 1. The coating is easy to peel off, resulting in an increase of electrode impedance. |
|                         | 2. Omitting troublesome preparations and the subsequent processes.     | 2. The structural design and preparation process of pins, shape, gap size, length, etc are complicated. |
|                         | 3. Representative electrode structures: micro-needle electrode, brush electrode, tapered electrode, claw electrode, spring electrode, stretchable mesh electrode, spiral electrode, tattoo electrode. | 3. Need to use external tools to apply certain pressure to ensure the stable contact between the electrodes and skin. |
| Semi-dry flexible electrodes | 1. Avoiding the inconvenience of cleaning process of wet electrodes. | 1. Lacking of long-term stability. |
|                         | 2. Making up for the defects of the signal instability of dry electrodes. | 2. Causing skin discomfort during long-term monitoring. |
|                         | 3. Representative electrode structures: bionic humidity-sensitive electrode, textile electrode, sponge electrode, micro-osmotic electrode, foam electrode, multilayer foam electrode. | |
attracted widespread attention among researchers. Its application has begun to take shape and is showing a tendency to rapid development. At the Consumer Electronics Show in the US, Sonny company has developed a headband helmet that collects brain waves to prevent driving accidents. The Boston company has made the ‘electronic tattoos’ based on the nanomaterials, and is considered as the smallest brain-machine device in the world. It can stick directly to the skin, which is convenient and doesn’t affect aesthetics.

The merits and demerits of three kinds of non-intrusive flexible electrodes are summarized in table 1.

At present, non-invasive BCI devices have greatly improved in terms of bio-compatibility, wear-ability, and low energy consumption. And it’s developing more and more in the direction of flexibility, making it smaller, lighter, more comfortable and non-stressful to meet the needs of long-term wear. However, such electrodes also have many disadvantages in low space-time resolution, wake response sensitivity, poor stability, poor anti-interference ability and narrow sensing range.

- When electrodes undergo complex deformation such as bending, twisting, spiraling, kinking, etc, its contact resistance will change accordingly, introducing noise and causing the decrease of signal-to-noise ratio.
- Although some electrodes would increase the contact area by designing micro structures, most of them need to use external tools to apply certain pressure to ensure the stable contact between the electrodes and skin.
- It’s difficult to stably combine a conductive material with a flexible substrate. In particular, depositing a metal layer on the surface may easily cause it to crack or wrinkle, which would result in the failure of BCI device.
- Existing non-invasive BCI devices have less consideration of water permeability and air permeability, which makes it easy to cause skin discomfort during long-term monitoring. Due to the exfoliation of skin and the accumulation of sweat or oil, the signal quality would gradually decrease.

3. Intrusive flexible electrodes

Compared with non-invasive, electrodes implanted in the skull can provide better spatial resolution, higher signal-to-noise ratio and wider frequency range. It can be used for a long time and is less susceptible to motion artifacts and external noise, which makes it a unique advantage in practical applications of BCI.

3.1. Soft material strategies for improving overall properties

The human brain is very soft, while traditional electrode materials (silicon, titanium, platinum, iridium oxide, glassy carbon, stainless steel, etc) are generally more than four orders of magnitude harder than brain tissue. This mismatch in mechanical properties can easily cause brain damage [28]. It’s difficult for the substantially unrefomed, surface morphology of the rigid materials to adapt to the micro dynamics of the brain. So they lack the cell-compatible adhesion site. What’s more, the chemical inertness of rigid electrode materials would lead to chronic immune response, cause scar tissue or glial hyperglycemia, and wrap on the electrode surface, which seriously affects the conductive performance. In the micro-environment, metal electrode materials are prone to corrosion, which not only causes loss of electrical conductivity, but also releases toxic metal ions. The above disadvantages severely limit the application of traditional rigid electrode materials in the BCI field.

The proposal of flexible materials provides a new idea for solving the safety problem. Natural materials that have evolved over millions of years (alginate, chitosan, agarose, gelatin, collagen, silk fibroin, cellulose, etc) have excellent biological properties [29]. Their elastic modulus and shear modulus are similar to brain tissue, which makes them adapt to the curved topology of brain. The distance between the invasive electrode and the neuron significantly affects the strength and quality of the recorded signal. The ideal invasive electrode should be seamlessly integrated with the neural interface, blurring the boundary between human and machine. Most of the natural biological materials have the porous structure, which are ideal materials to produce the flexible and invasive electrodes. In addition, the low cost and richness of natural bio-materials also support the large-scale industrial manufacturing. Xingyu Jiang’s research team used the deposition technology to prepare multichannel electrode based on bacterial cellulose [30]. As the super soft nerve interface matrix, bacterial cellulose has more advantages in flexibility, stability and safety. In addition, with the advantages of excellent conductivity, bio-compatibility, optical transparency, flexibility, mechanical strength, and potential to induce cell differentiation, graphene stands out among various flexible materials, making its research attracting much attention [31]. Yichen Lu et al prepared a flexible neural electrode array based on three-dimensional porous graphene by the laser pyrolysis and deposition technology, which can be used for the micro stimulation and perception of cortical [32]. Experimental results reveal that it can show lower impedance characteristics. Rouhollah Jalili’s team fabricated Pt/graphene/fiber micro electrode arrays [33]. Compared with a single graphene electrode, the strong synergy exhibited by the composite material makes it have better performance, especially the stability and reliability.
As an intelligent material, the most important characteristic of shape memory polymers is that they can memorize their initial shapes during processing. And then they are given a temporary shape under the specific condition. Finally, it can restore the original shape under the condition of external stimulus (chemical, electrical, magnetic, optical, temperature, etc). Through external stimuli, shape memory materials can be driven to have shape memory effects and variable modulus, with large deformation, good process ability and strong shape recovery capability. It not only satisfies the requirements of BCI electrode materials, but also has the special properties of deformable structures [34]. Such materials can make the integration of material-structure-sensing-driving-function to achieve the purpose of ‘small stimulus and large response’, which provides an effective method to solve the problem of BCI flexible electrode considering both mechanics and function.

Except to the mature manufacturing processes (etching, spraying, microfluidics, photocuring, electrospinning, chemical vapor deposition, printing, etc), 4D printing is an emerging developed comprehensive technology based on deformable materials and 3D printing [35]. Compared with 3D printing, 4D printing increases the time dimension. Through the rapid prototyping of additive manufacturing technology, smart materials can change their shape with the stimulation of the environment (light, electricity, temperature, etc), which achieves the integration of material-structure-performance and the control of time or space dimensions. 4D printing has potential applications in improving aircraft wing performance, adjusting the flexibility of software robots and promoting the implantation of micro-biomedical devices.

3.2. Integration of structure and function

Early proposed invasive electrode structures can cause severe compression on nerves, such as Michigan probes and Utah arrays (figures 3(a), (b)). In order to solve the mechanical mismatch problem of the brain-computer interface, the thin metal layer (Cu, Au, Pt, etc) is usually deposited on a polyimide substrate to realize the preparation of flexible electrodes [36]. In order to make the electrode more stretchable, it is generally designed into a wave-like, strike-like (figure 3(c)) [37], cuff (figure 3(d)) [38], snake-like structure (figure 3(e)) [39] to offset deformation. Harbaljit S Sohal
et al designed a sinusoidal electrode using chemical vapor deposition and etching techniques (figure 3(f)) [40]. Compared with the micro-wire electrode, the sinusoidal probe reduces the mismatch between the electrode and the nerve, showing higher signal-to-noise ratio and more stable impedance. At the same time, it also prolongs the service life of electrodes. Sanghoon Lee et al developed a flexible open loop electrode that can be implanted in any desired location of the brain nerve [41]. This electrode can selectively stimulate and record the brain tissue, which has less compression and maintains good contact with nerves. Based on the ultra-low voltage characteristics of conductive hydrogels, professor Zhenan Bao’s group developed an ultra-thin stretchable electrode (figure 3(g)) [42]. Due to its excellent flexibility, the stretchable thin-film micro-electrodes can provide stable brain–computer interface, long-term bio-compatibility, and minor immune response.

Almost all of the above invasive flexible electrodes adopt a planar geometry. Such two-dimensional neural probes are limited to recording superficial brain regions, while brain tissue is usually a three-dimensional structure. In order to record different functional layers from deep and shallow positions of the brain, Zhuolin Xiang’s group prepared a three-dimensional micro-needle electrode based on the etching and sputtering processes (figure 3(h)) [43]. This electrode has both the stiffness of a micro-needle and the flexibility of a mesh substrate. Its base is completely conforming to the curved brain surface, and the micro-needles can penetrate into the tissue, greatly improving the quality of signal recording. However, it’s still challenging to completely mask the differences between the electrode and neural interface, and poor contact may lead to higher interface impedance. In order to design the ideal electrode structure perfectly, inspired by the climbing plant climbing, professor Xue Feng’s group developed a twined electrode based on the smart shape memory polymer of polyurethane (figure 3(i)) [44]. Driven by 37 °C physiological salines, the electrode changes from a temporary flat state to a 3D spiral state, forming a three-dimensional flexible neural interface. This highly flexible and stretchable wound electrode can adapt to the natural pulsation of the brain without causing excessive pressure on it, which provides a promising idea for the design of BCI invasive electrodes.

Figure 4. (a) Micro-wrinkled electrode (b) Micro-crack array (c) Nerve tassel electrode (d) Multichannel single cuff electrode (e) Self-closing cuff electrode (f) Flexible nerve clip electrode (g) Zipper self-locking electrode (h) U-shaped nanowire probe (i) Dynamic stimulus response electrode. Part (a) Reprinted from [46], Copyright (2019), with permission from Elsevier. Part (b) Reproduced from [47]. CC BY 4.0. Part (c) Reproduced from [48]. CC BY 4.0. Part (d) Reprinted from [49] by permission from Springer Nature. Part (e) © [2015] IEEE. Reprinted, with permission, from [50]. Part (f) Reproduced from [51]. CC BY 4.0. Part (g) Reproduced from [52]. © IOP Publishing Ltd. All rights reserved. Part (h) Reprinted from [53], Copyright (2020), with permission from Elsevier. Part (i) Reproduced with permission from [54]. Copyright: © Materials Research Society 2012.
Neurons in the brain are characterized by small size, high density, and large numbers. The greater the number of neurons recorded by the electrode, the more brain neural activity can be obtained. However, the brain space is limited, and the contact area between invading electrode and brain tissue is directly proportional to the compression on the nerve. Increasing the number of flexible nerve probe channels while minimizing their invasion area still remains a challenge. Therefore, on no account can we ignore the value of the high-density, ultra-small and multifunctional neural probes.

Generally, micro electrodes are manufactured on a flat substrate. However, limited by the inherent contact area, increasing the contact area would cause severe compression on nerves. The transition from two to three-dimensional surface morphology can provide a solution to this problem, such as improving the effective surface area of the electrode to roughen the surface [45]. Jingquan Liu’s team prepared a micro-wrinkled structure by depositing Au onto polydimethylsiloxane (figure 4(a)) [46]. Compared with flat structures, tests show that micro electrodes with the wrinkled structure exhibit better electrochemical performance, which also highlights the importance of micro-structures in the flexible electrode design. Francesco Decataldo et al developed a highly stretchable and low resistance micro-cracked electrode based on Au and the conductive polymer of polyethylene dioxythiophene (figure 4(b)) [47]. Ying Fang’s research team reported a polyimide-based nerve tassel electrode (figure 4(c)) [48]. It adopts the micro-nano processing technology and consists of a series of flexible and high aspect ratio micro-electrode wires. The nerve tassel electrode has ultra-small size, high flexibility and expandability. In addition, its transitional mechanical properties ensure the stability of flexible nerve tassel and form the high-density integration of flexible nerve electrodes, which provides a new method for stable recording and nerve repair. The team of Dosik Hwang and Inchan Youn prepared the single multichannel cuff electrode based on Au/polyimide (figure 4(d)) [49]. The polyimide substrate will self-bias into a roll with a certain inner diameter. Subsequently, this electrode will self-bias into a roll with a certain inner diameter. This method shows that the multiple channel records can be acquired simultaneously and the electrical stimulation is induced at the nerve. Such compact BCI flexible electrodes have been proven to overcome space constraints and meet the demand of multiple intrusive electrodes.

Designing a flexible electrode structure interface for a brain–computer interface also defines the nature of BCI. Once the neural probe enters the brain, it must adapt to the micro-dynamics of the brain. Although the cuff or strip electrodes can release some pressure from the nerves, they may lead to severe damage because of the friction during exercise. What’s more, poor contact also results in higher interface impedance. In order to completely adapt to the natural pulsation of the brain, the BCI device needs to have the flexibility and compliance consistent with the neuron motor organs of the brain, which poses a huge challenge to the flexibility of the electrode structure design. In response to this problem, professor Chunsheng Yang’s team developed a micro-cuff electrode with the self-closing structure based on a thin and soft parylene material (figure 4(e)), which can minimize the mechanical damage to the brain nerve and surrounding tissues [50]. Compared with conventional cuff electrodes, this self-closing structure without any additional mechanical locking can minimize the mechanical differences of the brain–computer interface. Shih-Cheng Yen and Chengkouo Lee’s research team designed a flexible nerve clip electrode based on Au/polyimide, intending to be mechanically clamped on the brain nerve after implantation (figure 4(f)) [51]. The interface can be conformally and easily attached to brain tissue without causing nerve damage. Timothy J Gardner et al designed a flexible electrode with an interlocking effect similar to a zipper (figure 4(g)), which can permanently fix the electrode around the brain nerve tissue without lashing [52]. This novel structure enables the BCI flexible electrode to withstand motion without detaching from its nerve location.

Although a large number of studies on stretchable neural devices have shown their good biocompatibility and seamless connection between the peripheral nervous system and central nervous system, their adaptability in tissue development and growth still faces many challenges. That is, the fixed size of the implantable device can’t accommodate the rapid growth of tissue and may impair development. For this challenge, Prof Bao Zhenan and Prof Paul M George from Stanford University solved this limitation through the research of deformable bio-electronic components [53]. They designed multi-layer implantable and deformable bioelectronic devices that composed of viscoplastic electrodes and strain sensors. With the self-healing ability, it can eliminate the interface stress between the electronic device and the growing tissue. Deformable electronic devices can adapt to the growth of neural tissue with minimal mechanical constraints, which provides a promising idea for the flexible design of BCI implantable devices.

Because nanometer size is comparable to the cellular level of brain tissue, compared with other structures, nanostructures have the potential to improve sensitivity and spatial resolution [54]. In order to achieve intracellular recording of complex brain neural networks, professor Charles M Lieber reported the U-shaped nanowire probe (figure 4(h)) [55] and the nano-dot detector [56], which promotes the development of BCI technology with unprecedented resolution and accuracy.
### Table 2. The merits and demerits of intrusive flexible electrodes.

| Classification                  | Merits                                                                                                                                                                                                 | Demerits                                                                                                                                                                                                 |
|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Two-dimensional electrodes      | 1. Reducing the mechanical mismatch problem of the brain-computer interface.  
2. Designing structure to offset deformation, which makes the electrode more stretchable.  
3. Bring less compression and maintaining good contact with nerves.  
4. Representative electrode structures: wave-like, strike-like, cuff, snake-like structure, sinusoidal electrode, loop electrode, ultra-thin stretchable electrode. | 1. Such two-dimensional neural probes are limited to recording superficial brain regions, while brain tissue is usually a three-dimensional structure.  
2. Can’t record different functional layers from deep and shallow positions of the brain. |
| Three-dimensional electrodes    | 1. Forming a three-dimensional flexible neural interface, which can record signals from different functional areas of the brain.  
2. Adapting to the natural pulsation of the brain without causing excessive pressure on it.  
3. Representative electrode structures: three-dimensional micro-needle electrode, twined electrode. | 1. It’s still challenging to completely mask the differences between the electrode and neural interface.  
2. Poor contact may lead to higher interface impedance. |
| Highly integrated & ultra-small neural probe | 1. Such neural probes can roughen the surface, improving the effective surface area of the electrode.  
2. Ultra-small size, high flexibility and expandability.  
3. Representative electrode structures: micro-wrinkled structure, micro-cracked electrode, nerve tassel electrode. | 1. Due to the rough surface, they may lead to severe damage during the frictional motion.  
2. Poor contact also results in higher interface impedance. |
| Self-closing structure electrodes | 1. The flexibility of electrode structures design has flexibility and compliance consistent with the neuron motor organs.  
2. Self-closing structure without any additional mechanical locking can minimize the mechanical differences.  
3. Enabling withstand motion without detaching nerve location.  
4. Representative electrode structures: micro-cuff electrode, flexible nerve clip electrode, zipper structure electrode. | 1. Poor stability.  
2. Vulnerability. |
| Nanoprobe                       | 1. Nanometer size is comparable to the cellular level of brain tissue, improving sensitivity and spatial resolution.  
2. Improving the accuracy of the recorded signal.  
3. Representative electrode structures: U-shaped nanowire probe, nano-dot detector. | The coverage of the brain area is limited, which restricts the monitoring range of EEG signals. |
| Variable stiffness electrodes    | 1. Adjusting the modulus of the flexible electrode at the neural interface to match the mechanical properties of the brain.  
2. It has a controllable stiffness. It is rigid enough to be easily implanted in the brain while it can | Slow response rate. |
In future research, the stability and reliability of invasive electrodes should be maximized, and the electrode size design, interface impedance and immune response.

3.4. Current challenges and future outlook

The merits and demerits of intrusive flexible electrodes are summarized in table 2.

At present, the basic theory, preparation technology, performance modification and other aspects of invasive electrodes have been further studied all over the world. However, there are still some challenges in electrode life, size design, interface impedance and immune response.

- In future research, the stability and reliability of invasive electrodes should be maximized, and the electrode life should be improved.
• The size of the electrodes should be optimized. If the size of the electrode is too large, it could compress the nerve. While reducing the electrode surface area would lead to extremely high impedance.

• The research of the integration design between materials and structures should be carried out, which can avoid acute or chronic immune response after implantation.

 Anyway, whether the risk of surgical infections or the expensive and cumbersome procedures, security is still a major problem of BCI invasive techniques.

4. Semi-invasive flexible electrodes

Although the non-intrusive BCI has the performance of security, the quality of the collected signal is poor and unstable. The invasive BCI guarantees the strength and quality of the EEG signal but sacrifices security. In terms of the shortcomings of the above two types of BCI, scholars have proposed the concept of semi-invasive technology. Semi-invasive, also known as injectable, combines the advantages of non-invasive and invasive, that is, injecting through a syringe can accurately target and locate in specific brain regions, which not only ensures safety but also improves the strength and quality of EEG signals. This minimally invasive procedure reduces the pain of patients, avoids the acute immune response during implantation and minimizes damage to the neural circuit [66]. Further, from the perspective of medical transplants, the damaged parts of brain tissue are usually irregular. Compared with the pre-molded invasive BCI device, this injectable type can achieve the effect of tight filling.

Semi-invasive BCI electrodes can be subdivided into extraneural and intraneural electrodes [67]. The so-called external electrodes are in conformal contact with the surface of the brain tissue while the internal electrodes are the type of soft penetration. The external electrodes abandon the idea of chip-based, connect electronic devices with the internal structure of nerves, further blur the brain-computer interface, and truly realize the natural relationship between electrodes and biological tissues. Technically, flexible electrodes have gradually transformed from neural probes to bionic chips. The aim of non-invasive electrodes is low elastic modulus, low electrode impedance and compliant mechanical structure to adapt to the dynamic deformation of the brain, making it rely on the natural adhesion to achieve conformal integration, embedded interconnection and three-dimensional interpenetration.

4.1. Bio-mimetic material: hydrogels

On the basis of the choice of invasive BCI electrode materials, the semi-invasive type also requires unique rheological properties. In particular, hydrogels are one of the few materials that can be designed to have the feature of injectable. It has both solid-liquid properties and swells in water without dissolving [68]. The stable three-dimensional porous network structure not only provides good permeability to exchange nutrients, but also provides surface area for cell adhesion and interaction. Its hydration environment is similar to the extracellular matrix, which can induce neurons and their synapses to grow to electrode sites to achieve tight binding. The injectable mechanism of hydrogel materials is as follows: under the external stimulus (such as temperature, pH, pressure, light, shear, etc.), the material undergoes changes in state and molecular conformation under the condition of physiological. Subsequently, it undergoes a transition from a sol state to a gel state, or the gel state undergoes shear thinning and then returns to a gel state [69]. Recent studies have shown that hydrogels can promote the formation of neural tissue even without the growth factors [70].

Agarose is a good brain tissue mimic because its Young’s modulus is similar to that of brain tissue [71]. Its porous property is suitable for preparing templates of flexible electrodes. Agarose is insoluble in water at room temperature. Above 90 °C, it can completely dissolve and form a uniform and transparent aqueous solution. When the temperature drops to 37 °C , the human body temperature, it can form a stable hydrogel structure, which can be used as a temperature-sensitive hydrogel. In addition, the typical temperature-sensitive hydrogel materials include N-isopropylacrylamide, chitosan, gelatin, nanocellulose, etc [72].

4.2. Bionic structure electrode: embedded interconnect and 3D interpenetrating

Inspired by biology or simulating biological concepts, designing new materials and structures is a strategy for developing innovative semi-invasive BCI flexible electrodes [73]. The bionic flexible electrode is not only reflected in mechanical properties, but is also a significant part of simulating the topology of the brain. Our brain is a three-dimensional network that consists of a large number of interconnected neurons. Although too much research has focused on minimizing brain-computer differences by optimizing structural designs or developing more flexible materials, in terms of structure, the existing probes are still foreign to the brain in nature. The ideal semi-invasive BCI flexible electrode should be able to combine living cells with the electrode and gradually penetrate into the electrode to grow. Therefore, it’s also called ‘living electrode’ [74].
Charles M Lieber’s team invented a super-flexible open mesh structure (figure 5(a)) [75]. The compressed mesh electrode is injected into the skull through a syringe, and the mesh will stretch itself. It can fit to the brain tissue very softly and achieve the collection and recording of EEG signals in a wide range. They used automatic conductive ink printing technology to embed mesh-like electronic devices in agarose hydrogels, and then injected them into the brain through a needle using a micro-sensor to achieve target delivery with a spatial accuracy of 20 μm [76]. Their team continued to develop the epoxy-based macroporous nano-mesh probe with porosity as high as 99% [77]. The experimental results revealed that the mesh probe was able to record neural activities with high temporal and spatial resolution from deep and shallow brain regions. Within two weeks to one year of injection, neurons were successfully induced to penetrate into the interior of the mesh probe. The distribution of neuronal cell bodies and axons at the interface of the mesh probe is almost same as natural tissues, which proves the formation of a seamless neural interface.

In addition, Charles M Lieber’s team also compared flexible thin-film probes with networked electronic structures (figure 5(b)) [78, 79]. The results showed that the mesh structure caused less inflammatory response and scar tissue, and the acquired signals had higher resolution. Flexible mesh electrodes are closer to the neural network structure of the brain because they can cover multiple cortical regions of the brain. However, due to the extremely low bending rigidity, potential folds and entanglement of the mesh structure electrode during injection may cause a gap between the electrode recording and the expected effect, so the mesh structure needs to be further optimized. Based on this, this research group developed a neuron-like electrode based on the structure and morphology of brain tissue [80]. The implanted BCI device further simulated the subcellular structural characteristics and the mechanical properties of neurons, highlighting the structural indistinguishability and tight interpenetration between the flexible electrodes and neurons.

The injectability avoids the invasiveness, complexity and high cost during the implantation process. Kip A Ludwig and Andrew J Shoffstall’s team injected a flowing composite of Ag/polydimethylsiloxane into the desired brain tissue to form highly compliant nerve electrodes [81]. Consistent with the target structure, the hardness of this conductive interface is also several orders of magnitude smaller than that of conventional nerve electrodes. Kevin J Otto’s research group injected a polyethylene dioxythiophene-based conductive compound into peripheral nerves (figure 5(c)) [82]. And then an in situ electrochemical polymerization reaction occurred, which formed a soft, precisely positioned, injectable BCI flexible electrode.
Hydrogels, a nanocomposite material that can stimulate nerve growth, are increasingly favored by academics [83]. For example, G Ciardelli’s team made an injectable composite hydrogel flexible electrode based on agarose/gelatin [84]. The team of Ryan J Gilbert first injected the collagen fiber hydrogel solution, and then used magnetic orientation to promote the in situ alignment of the brain nerve-electrodes, thereby the fibers were aligned along the magnetic direction, and finally induced the directional growth of brain nerve cells (figure 5(d)) [85]. It was proved that the cells can penetrate into the flexible electrode and complete their combination.

4.3. Challenges

The merits and demerits of semi-intrusive flexible electrodes are summarized in table 3.

| Classification       | Merits                                                                 | Demerits                                                                 |
|----------------------|------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Mesh structure       | 1. Causing less inflammatory response and scar tissue, and the acquired signals have higher resolution. | 1. Potential wrinkles and tangles during injection may affect accuracy.   |
|                      | 2. Flexible mesh electrodes are closer to the neural network structure of the brain because they can cover multiple cortical regions of the brain. | 2. The stacking phenomenon after injection will restrict the detection range of the brain area. |
| Neuron-like electrode| 1. Further simulating the subcellular structural characteristics and the mechanical properties of neurons. | Local burst during injection.                                             |
|                      | 2. Highlighting the structural indistinguishability and tight interpenetration between electrodes and neurons. |                                                                          |

Hydrogels, a nanocomposite material that can stimulate nerve growth, are increasingly favored by academics [83]. For example, G Ciardelli’s team made an injectable composite hydrogel flexible electrode based on agarose/gelatin [84]. The team of Ryan J Gilbert first injected the collagen fiber hydrogel solution, and then used magnetic orientation to promote the in situ alignment of the brain nerve-electrodes, thereby the fibers were aligned along the magnetic direction, and finally induced the directional growth of brain nerve cells (figure 5(d)) [85]. It was proved that the cells can penetrate into the flexible electrode and complete their combination.

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Semi-invasive electrodes have attracted widespread attention in the academic world due to their unique advantages such as low material cost, simple and efficient preparation, no irritation or sensitization and so on. However, there are great challenges in functional design of materials, smooth injection, and intelligent controlled release. It is worth mentioning that the Neuralink company founded by Elon Musk released the latest BCI products in July 2019. They claimed to have implanted a flexible electrode with a diameter of 4–6 microns into the monkey brain and completed the preliminary testing and evaluation [86].

- The function of a single material is limited when used, while the introduction of other ingredients could lead to sensitivity issues.
- Whether the material can move smoothly in the needle tube and the potential for fold or tangle all need to be further improved.
- It’s high time that needle diameter, volume of fluid injected and local burst during injection should be considered.

In a nutshell, the research on semi-invasive flexible electrodes in various countries is still in its infancy and there are relatively few related reports. However, with the increasing demands of BCI around the world, the development of such electrodes will make breakthrough progress.

5. Summary: challenges, opportunities and prospect

Nowadays, the research bandwagon of BCI has surged. Advantages always be side with risks, and opportunities live with challenges. Scholars have achieved some basic research works with academic value and potential applications in the field of BCI flexible electrodes. What’s more, its application in the field of medical rehabilitation and entertainment is also emerging. The materials, performance profiles and application classifications of brain-computer interface flexible electrodes that have been studied are summarized in table 4. The merits and demerits of three kinds of BCI flexible electrodes are summarized in table 5.

At present, certain research progress has been made in the three kinds of BCI electrode materials or structures. From the materials design to the optimization and upgrading of structural processes, the application of BCI can be expected in the future. However, existing brain-computer interface materials still fail to provide sufficient spatial and temporal resolution to monitor more brain regions, nor can they guarantee the reliability and stability of long-term recordings. The further improvement of electrode materials performance, the continuous optimization of structural design and the uninterrupted improvement of processing technology are the only way for BCI technology to continuously strengthen and achieve large-scale production.
| Material                  | Property                                                                 | Application classification                  | References        |
|---------------------------|--------------------------------------------------------------------------|---------------------------------------------|-------------------|
| Polyimide                 | It’s generally used as the substrate material and has been increasingly used in the BCI field in recent years. It has a small inflammatory response and good bio-compatibility, making it the most widely used polymer. | Non-intrusive and Intrusive Electrodes      | [48–51, 87–89]   |
| Polyurethane              | Excellent flexibility, high adhesion, outstanding comprehensive mechanical properties and good processability. | Non-intrusive and Intrusive Electrodes      | [23, 26, 44, 90]  |
| Parylene                  | It has low Young’s modulus, high bio-compatibility, and excellent mechanical properties. However, it has poor adhesion to many materials in a humid micro environment, which limits the applications. | Non-intrusive and Intrusive Electrodes      | [52, 91–93]      |
| Polydimethylsiloxane      | With high flexibility, viscoelasticity, permeability, low dielectric constant, low Young’s modulus and easy processing, it is an ideal material for preparing BCI electrode flexible substrates. | Non-intrusive, Intrusive and Semi-intrusive Electrodes | [9, 20, 27, 46, 82] |
| Polyethylene dioxythiophene| As a new conductive polymer material, it has high conductivity, good environmental stability, and excellent mechanical strength, making it often used in artificial nerves. | Non-intrusive, Intrusive and Semi-intrusive Electrodes | [17, 47, 59, 83]  |
| Epoxy Resin               | High mechanical properties, strong adhesion, good electrochemical stability and excellent process performance. | Non-intrusive, Intrusive and Semi-intrusive Electrodes | [60, 78, 94, 95]  |
| Carbon Nanotubes          | With low impedance, high specific surface area and excellent mechanical strength, compared with other flexible materials, CNT has disadvantages such as difficult preparation process, high cost, biological toxicity and so on. | Non-intrusive and Intrusive Electrodes      | [96–98]          |
| Graphene                  | Due to the excellent electrical conductivity, bio-compatibility, optical transparency, high flexibility, mechanical strength as well as good bio-compatibility, GNS can adsorb proteins and small molecular substances and induce cell differentiation. | Non-intrusive and Intrusive Electrodes      | [21, 22, 32, 33, 61] |
| Alginate                  | It has a shape memory effect, good bio-compatibility and low toxicity, which promotes cell adhesion and migration. | Non-intrusive, Intrusive and Semi-intrusive Electrodes | [66, 99–101]     |
| Chitosan                  | It has high bio-compatibility, bio-adhesion and excellent antibacterial properties, making it an ideal choice for preparing neural interface nanocomposites. | Non-intrusive, Intrusive and Semi-intrusive Electrodes | [102–105]        |
| Agarose                   | It’s a good brain tissue mimic. It’s because its Young’s modulus and shear modulus are similar to brain tissue. Besides, the porous nature can be used as a template for preparing nanocomposites. It is obviously that its bio-compatibility can be used as a flexible electrode material. | Intrusive and Semi-intrusive Electrodes      | [77, 85, 106–108] |
| Silk fibroin              | It has high mechanical flexibility to adapt to curved and dynamic brain tissue. Moreover, bio-compatible, non-toxic and harmless properties can achieve seamless integration at the interface between invasive electrodes and biological tissues, which avoids allergic and inflammatory reactions. | Non-intrusive and Intrusive Electrodes      | [29, 109–111]    |
| Cellulose                 | With widely sourced, high bio-compatibility, mechanical strength, degree of polymerization, crystallinity, hydrophilicity as well as ultra-fine structure. Its diameter is of the same order of magnitude as the element size in the extracellular matrix, which is ideal for preparing ultra-soft nerve interface matrix. | Non-intrusive and Intrusive Electrodes      | [24, 30, 64, 112–114] |
In terms of non-invasive electrodes, it’s necessary to focus on the accuracy issues such as sensitivity and stability. We also need to further develop the sensing sites based on soft materials to provide more functionality of the device. On no account can we ignore the value of optimizing the geometric properties, such as size, volume, shape, surface morphology, etc. Besides, there are few experimental tests in harsh environments, such as humid, cold and space environments.

When it comes to invasive electrodes, it’s urgent to address the issues of implantability and implant safety. In terms of electrical characteristics, low impedance and high electrical conductivity need to be further improved to enhance the quality of signal recording and suppress tissue damage during nerve stimulation. In terms of mechanical properties, the strength and flexibility can be designed to minimize the mechanical trauma of electrode implantation and brain micro-motion. In terms of physicochemical properties, chemical stability should be further enhanced to promote bio-compatibility at the electrode-brain tissue interface.

Concerning the semi-invasive electrodes, we need continue to explore the problems of precise positioning, smooth injection and intelligent controlled release. Furthermore, the communication mechanism at the interface (such as the mutual conversion of ionic, biological, chemical, and electrical signals) is not yet complete, and there is no unified theoretical explanation. Actually, a single material is limited to improve the overall performance of the electrodes. So the interdependence of design variables should be weighed to maximize the benefits.

**ORCID iDs**

Xufeng Dong [https://orcid.org/0000-0001-5556-280X](https://orcid.org/0000-0001-5556-280X)

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Table 5. The merits and demerits of three kinds of BCI flexible electrodes.

| Classification                  | Merits                                                                 | Demerits                                                                 |
|--------------------------------|------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Non-intrusive flexible electrodes | 1. Less risky and guaranteeing security.                                | 1. Low space-time resolution, wake response sensitivity, poor stability, poor anti-interference ability and narrow sensing range. |
|                                | 2. Bio-compatibility, wear-ability, low energy consumption.            | 2. The quality of the collected signal is poor and unstable.              |
|                                | 3. It’s developing more and more in the direction of flexibility, making it smaller, lighter, more comfortable. | 3. The issue of convenience.                                              |
| Intrusive flexible electrodes                     | 1. Guaranteeing the strength and quality of the EEG signal.            | 1. The risk of surgical infections.                                      |
|                                | 2. Providing better spatial resolution, higher signal-to-noise ratio and wider frequency range. | 2. The expensive and cumbersome procedures.                              |
|                                | 3. It can be used for a long time and is less susceptible to motion artifacts and external noise. | 3. Security is still a major problem of BCI invasive techniques.          |
| Semi-intrusive flexible electrodes                     | 1. Reducing the pain of patients, avoiding the acute immune response during implantation and minimizing damage to the neural circuit. | 1. The material can’t move smoothly in the needle tube and cause the problem of fold or tangle. |
|                                | 2. Ensuring safety.                                                   | 2. Local burst during injection.                                         |
|                                | 3. Improving the strength and quality of EEG signals.                 |                                                                          |
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