Emerging peripheral nerve injuries recovery: advanced nerve-cuff electrode model interface for implantable devices

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***Abstract*—Peripheral nerve injuries (PNIs) present significant clinical challenges due to their potential to cause chronic disability and substantial healthcare costs. Traditional treatments often fail due to inconsistent outcomes and long recovery times. In this paper, we present a comprehensive review that summarizes current advancements in PNI treatment and outlines a framework for overcoming existing barriers and improving patient outcomes through innovative therapies. Unlike reviews that focus solely on the limitations of existing treatments, our approach provides a detailed analysis of future challenges and integration strategies. Innovations in neurostimulation, materials science, and miniaturization are driving the development of next-generation neural interfaces aimed at restoring sensory and motor functions. Understanding the detailed electrical model of the device-tissue interface is crucial for optimizing electrode design for improved neural recording and stimulation. Continuous research and development are essential for overcoming existing challenges and providing widespread access to these treatments. We highlight the importance of a multidisciplinary approach to achieve more effective and personalized therapies for PNI, contributing valuable insights to the field and setting the stage for future advancements.**

Keywords— Cuff Electrode, Implantable Device, Neural interface, Peripheral Nerve Injury.

I. INTRODUCTION

Peripheral nerves play a crucial role in somatic and autonomic functions. They receive various sensory inputs and integrate them from the whole body into the brain, which generates appropriate responses. As these are some of the most delicate and fragile structures in the body, they are highly susceptible to damage from crushing, compression, or trauma, resulting in disruptions in the brain's communication with target organs, Fig. 1a. These injuries are called peripheral nerve injuries (PNI) and represent a significant clinical challenge due to their potential to cause chronic disability and impose substantial healthcare costs. They can result from different types of traumas, causing disruptions in the brain's communication with target organs. When a peripheral nerve axon is destroyed at any point in its course away from the cell body, it undergoes a degeneration process called Wallerian degeneration, Fig. 1b [1]. This degeneration leads to the interruption of the communication between the brain and the target organs.

To guarantee the correct functionality of the affected district, it is essential to intervene to restore the connection. The future of PNI treatment depends on its effectiveness in restoring sensory and motor functions after nerve injury. The development of advanced devices seems promising for the treatment of PNI [2]. However, such devices face several challenges in integrating modern technologies into clinical practice. To introduce a device on the market, it is necessary to guarantee biocompatibility, hermeticity, structural design, power management, wireless communication, data security, regulatory compliance, and ethical considerations [3]. Furthermore, it must be considered that not all lesions have the same level of severity, and the most appropriate therapy must be performed based on the level identified. About this, Herbert Seddon's classification allows peripheral nerve injuries to be divided based on the extent of damage to the nerve and its ability to recover [4].

Aim of the work: Within this paper, we present a comprehensive review that summarizes current advancements in PNI treatment and outlines a framework for overcoming existing barriers and improving patient outcomes through innovative therapies. Unlike reviews such as [3], which primarily explore future perspectives in neuromodulation, or [5], which discusses current concepts and emerging techniques but lacks an in-depth analysis of future integration, our approach offers a comprehensive evaluation of the currently available solutions as alternatives to traditional methods. We examine their advantages and challenges, while also providing insights into future research directions in this field. By integrating both present and future aspects within a single review, our work aims to bridge the gap between existing technologies and their potential future developments. Additionally, compared to the other works, our approach emphasizes the importance of multidisciplinary

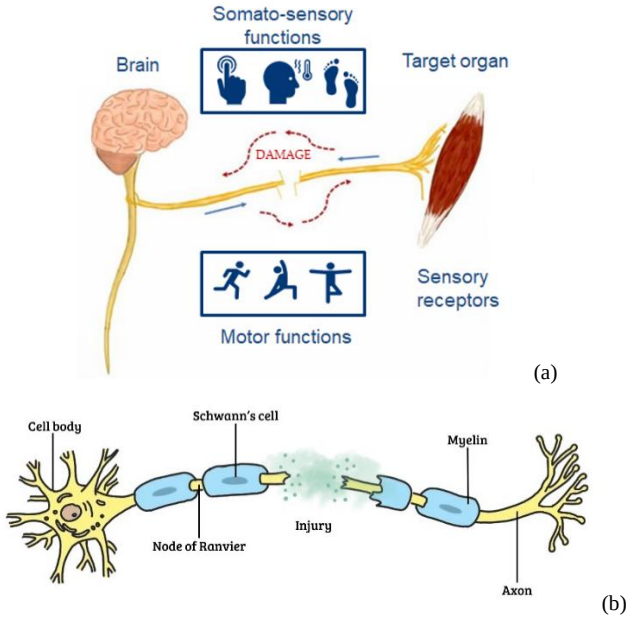

Figure 1: Representation of (a) nerve injury and related issue [2] and (b) nerve degeneration.

advances to achieve more effective and personalized therapies for PNI.

II. PNI OCCURRENCE

Within this paragraph, a detailed clinical overview of PNI will be presented. A study reported in [6] shows that the majority of the population affected by PNI was men (74%), with an average age of 32.4 years. Isolated PNIs accounted for 83% of cases, with combined lesions often involving the ulnar and median nerves. Upper extremity PNIs were the most common, occurring in 73.5% of cases, with the ulnar nerve being the most frequently damaged, alone or in combination with other nerves. The leading cause of injuries was traffic accidents (especially motorcycle accidents), affecting various nerves, including the brachial plexus, radial, sciatic, facial, and peroneal nerves. A secondary cause of the lesion is the penetrating trauma. Those mainly damaged the ulnar and median nerves. Additionally, falls and gunshot wounds commonly cause injuries to the ulnar, radial, and median nerves. Sports injuries primarily impact the peroneal and tibial nerves, particularly in football. In all these cases, complete denervation was observed most frequently in the peroneal nerves (65%), followed by the brachial plexus (51%), suprascapular (50%), sciatic (49%), facial (48%), and posterior interosseous nerves. (47%). Regarding the severity level, the study found that neurotmesis occurred in 41% of cases, axonotmesis in 45%, and neurapraxia in 14%. The individual levels will be analyzed in detail to learn more about the severity of these injuries.

Neurapraxia [7] corresponds to grade 1 in the Seddon classification. It is characterized by a temporary block of nerve conduction in the injured area without interruption of the structural components of the nerve. The etiology of neurapraxia includes bone fractures, improper positioning during anesthesia, and high-impact sports. Specific data include a 6-19% incidence of supracondylar humerus fractures affecting the median and ulnar nerves, 20.9% incidence of nerve injury in shoulder joint replacements, and 50-65% incidence in football players due to brachial plexus injuries. The prognosis for neurapraxia is generally excellent, with recovery expected within 2 to 3 months. Treatment typically involves conservative measures, and surgery is considered if there is no improvement within 3 to 6 months. Complications can include neuropathic pain and muscle atrophy if incorrectly diagnosed.

Regarding *axonotmesis* [8], this type of injury is commonly caused by crushing and stretching injuries, leading to distal Wallerian degeneration of the lesion [1]. The incidence of PNI following extremity trauma ranges from 1.64% to 3.4%, with upper extremity injuries more common than lower extremity injuries. Specific data show an annual incidence of 43.8 cases per 1 million individuals for upper extremity PNI and 13.3 cases per 1 million for lower extremity PNI. Treatment may involve conservative observation or surgery, depending on the injury's severity and recovery progress. Nerve regeneration occurs at a rate of 1-2 mm/day, with distal lesions having a better prognosis. Surgical options include primary repair, neurolysis, nerve grafts, and nerve transfers. Without intervention, complications such as neuroma formation and persistent neuropathic pain can occur.

Finally, *neurotmesis* [9] is present at the most severe level. This injury causes total loss of sensory and motor functions in the affected area, with minimal spontaneous recovery without surgery. High-velocity trauma, lacerations, and severe crush injuries often cause neurotmesis. In wartime, neurotmesis accounted for 20% of nerve injuries, while in peacetime, automobile accidents are the most common cause. The incidence of traumatic nerve injuries is approximately 350,000 per year, with young adults between the ages of 32 and 39 being the most affected. Surgical repair is critical, with primary repair ideally performed within 72 hours. Blunt transactions may require delayed repair. Return of function is best in patients under 25 years of age, with pediatric patients showing a recovery rate of 95.4%. Complications may include failure to regenerate, muscle atrophy, and neuropathic pain. An interprofessional approach involving different specialists is essential for optimal management and recovery of patients with neurotmesis.

III. PNI TREATMENT

There are different approaches that can be used to treat PNI. These are generally divided into traditional and advanced techniques. Traditional treatments for neuropathies include pharmacological treatment, physiotherapy, transcutaneous stimulation, acupuncture, and surgical interventions. Advanced techniques include surgery

A. Traditional treatment

Pharmacological treatment includes the use of analgesics, opioids, and atypical pain-relieving drugs such as antiepileptics, antidepressants, and benzodiazepines [10]. However, these treatments present several challenges, including common adverse effects such as sedation, dizziness, and gastrointestinal disturbances [11]. Furthermore, efficacy varies significantly between individuals, and long-term use of opioids can lead to tolerance and dependence [11]. The cost of some effective medications for neuropathic pain can be prohibitive [11]. Regular physical activity, such as stretching and sports, improves blood circulation and oxygen flow to nerve tissues, which are crucial for nerve health. However, physiotherapy

interventions often lead to only modest improvements, with benefits that may be reduced without continuous therapy and constant monitoring [12]. Transcutaneous electrical nerve stimulation uses low-voltage electrical currents to reduce pain by interrupting pain signals. This non-invasive method is helpful for some patients with neuropathic pain [13]. However, it may cause skin irritation at the electrode placement site [14]. Neural mobilization is a movement-based therapy that seeks to reduce neuropathic symptoms through mechanical or neurophysiological mechanisms [15]. However, limited evidence supports the effectiveness of the technique for some pathological conditions, and repetitive applications may damage the nerve. An accurate assessment of the patient's response is necessary [16]. Acupuncture, a traditional Chinese medicine technique, relieves neuropathic pain by stimulating the nervous system via fine needles inserted into specific points of the body [17]. The beneficial effects of acupuncture are often short-term, with limited long-term impact and pain at insertion sites [17]. Surgical interventions for neuropathy, with or without autograft (tissue transplanted from one part of the patient itself) or allograft (from a donor), have mixed outcomes due to variability in pain characteristics, injury severity, and time from injury to surgery [18]. The best results are observed with early surgical interventions, as delays exceeding six months significantly reduce the chances of recovery [19]. Management of neurogenic muscle atrophy is critical, with timely interventions needed to prevent severe muscle loss and improve functional recovery [20].

B. Advanced techniques

Regarding advanced techniques, in recent decades, research has focused on the development of novel devices for the treatment of peripheral nerve injuries, Fig. 2. These devices, generally implanted, aim for more effective and minimally invasive solutions, promising to improve patients' quality of life significantly. Thanks to technological development, advances in neuroanatomical understanding, stimulation mechanisms, materials science, miniaturization, and energy storage and delivery are leading to the evolution of these devices [3]. Neuromodulation approaches are evolving, offering flexible treatments and continuous stimulation. The use of electrical stimulation devices has expanded in various medical fields, such as the management of Parkinson's disease, dystonia, tremor, obsessive-compulsive disorder, epilepsy, and deafness [3]. Cardiac devices, including pacemakers and defibrillators, are essential for treating arrhythmias [3], while devices for the peripheral nervous system currently treat conditions such as incontinence, chronic pain, and sleep apnea [3]. A key area for future implementation is the integration of closed-loop systems. These adjust stimulation in response to physiological signals, improving precision and effectiveness. Some non-invasive techniques, such as focused ultrasound and optogenetics, offer new avenues for neuromodulation, although they are still in the experimental phase [3]. Emerging techniques in the regeneration of peripheral nerve lesions, such as cellularized nerve allografts, have shown great potential [5]. These approaches promise more precise, effective, and personalized interventions, improving patient outcomes and quality of life. Among the various innovations, thin-film devices powered wirelessly by traditional rigid electronics stand out. These devices, which integrate electronics on thin films, reduce volume and improve energy availability, offering precise and programmable electrical

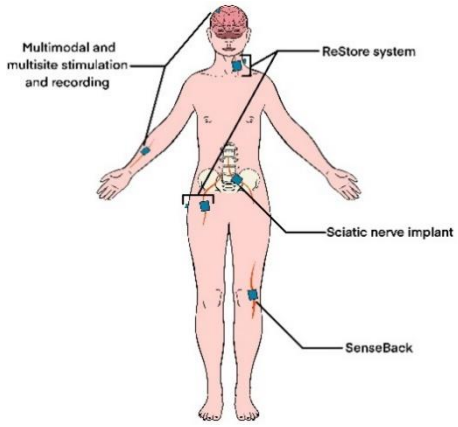

Figure 1: Examples of clinical applications with electrical stimulation devices.

stimulation. One example is a miniature device capable of wireless electrical stimulation of peripheral nerves, operating up to 10.5 cm inside a tissue phantom [21]. This method improves the depth-to-volume ratio compared to existing IC-based neural stimulators, although further *in vivo* experiments and biocompatible packaging research are needed. The ReStore system represents a significant advance in peripheral nerve stimulation technology, overcoming the limitations of traditional implantable pulse generators [22]. The system includes an IPG, an external relay module for inductive power, and a Bluetooth-controlled programming module. Recent developments include fully wireless implantable devices, using near-field resonant power transfer for high energy availability and seamless integration with neural tissues [23]. These devices, featuring soft polymer encapsulations and polyimide substrates, offer advanced capabilities for multimodal and multisite stimulation and recording, crucial for understanding neural dynamics and developing therapeutic interventions. These systems promise applications in both the central and peripheral nervous systems, supporting techniques such as optogenetic and electrochemical stimulation for comprehensive chronic studies and new therapeutic applications. These studies, along with others available in the literature, demonstrate the growing interest in research into the development of innovative implantable devices for peripheral nerve injuries, which is advancing rapidly. In [3], they expect that by 2035, neurologists will have access to cutting-edge neuromodulation devices that will allow them to provide precise, customized, and adaptable neuromodulation treatments. Current neuromodulation treatments already show benefits, with many more expected to demonstrate efficacy soon. These advancements will enhance the treatment and management of peripheral nerve injuries.

IV. FUTURE PROBLEMS

The development of implantable medical devices is a complex field that requires addressing a multitude of challenges to ensure safety, efficacy, and longevity. The engineering and medical communities face significant obstacles with the increasing demand for these devices in a super-aging society. One of the primary considerations is biocompatibility, which is critical to prevent adverse immune responses. Implantable materials must undergo rigorous testing to confirm that they do not cause inflammation or rejection [24][3]. Surface modification techniques, such as

coating with biocompatible polymers or applying bioactive materials, are being explored to improve the integration of devices with biological tissues. These modifications can help minimize fibrotic encapsulation and improve the long-term functionality of implants [24].

Another critical aspect is the packaging and hermetic sealing of devices designed to protect internal components from bodily fluids, preventing corrosion and short circuits. Ensuring airtightness is vital to maintaining device functionality and longevity. Biocompatible materials such as ceramics, metals, and specialized polymers are commonly used to achieve airtightness [24][3]; however, they are expensive to produce. Recent advances in materials science and nanotechnology are paving the way for the development of new materials with improved properties and low cost [24][3]. An affordable approach would make these devices more accessible to poorer populations.

The structural design and size of implantable devices must be carefully considered to fit the anatomy of the human body without compromising functionality. This challenge requires the use of advanced technologies such as microelectromechanical systems (MEMS), which enable miniaturization of devices while maintaining performance [24][3]. MEMS technology is particularly advantageous in creating smaller, more efficient devices that can be implanted with minimal invasiveness. Additionally, researchers are investigating flexible and stretchable electronics that can adapt to the dynamic environment of the human body. This would allow implants to adapt to physiological changes in the human body, such as body movement or aging [3].

Power management is another critical area for implantable devices, which have traditionally relied on disposable or rechargeable batteries. The longevity and reliability of these power sources are crucial, as surgical replacement carries risks and costs. Recent research focuses on energy harvesting technologies, such as using body heat, motion, or biochemical processes to generate power. Although these technologies are promising, they currently produce low energy output, limiting their application in high-power devices [24]. The development of more efficient energy harvesting systems, such as biofuel cells and piezoelectric generators, could significantly improve the autonomy of these devices, reducing the frequency of battery replacements and improving patients' quality of life [24][3].

Wireless communication is essential for monitoring implantable devices. However, it presents significant challenges due to variations in data transfer efficiency through body fluids. The 402-405 MHz band, designated for implantable devices, aims to improve wireless communication by minimizing interference and optimizing signal penetration through tissue [24]. Researchers are exploring alternative communication methods, such as optical and ultrasonic transmission, to overcome the limitations of current radio frequency technologies. These innovations could lead to more reliable and efficient communication systems, enabling real-time data transmission and remote patient health monitoring [24][3]. Integrating these technologies into existing device architectures can improve connectivity and reliability, paving the way for more intelligent and responsive medical implants [3].

Data security and privacy are critical as implantable devices increasingly collect and transmit sensitive health information. Protecting this data from unauthorized access is essential to maintaining patient trust and complying with legal regulations. Advanced encryption and secure storage solutions are needed to safeguard patient data, especially as these devices become more interconnected with other healthcare systems and the Internet [3]. Developing robust cybersecurity measures and establishing clear data management protocols are essential to ensure these devices can be trusted to securely handle sensitive health information [3].

Regulatory challenges play a crucial role in the development of implantable devices. These devices must meet rigorous safety, efficacy, and reliability standards established by regulatory authorities. Compliance involves comprehensive clinical studies, detailed documentation, and post-market surveillance, all of which require significant investments of time and resources [25][26]. As technology advances, regulatory frameworks must evolve to accommodate new device types and functionalities while ensuring patient safety. This includes addressing the unique challenges posed by novel materials and technologies, such as 3D-printed implants and smart devices, which may require new testing and approval pathways [3].

Finally, ethical considerations surrounding implantable medical devices, particularly neurotechnologies, raise important questions about their impact on identity and autonomy. Ethical guidelines are essential to ensure that technological advances are aligned with societal values and to prevent misuse or unintended consequences of new technologies. The potential of devices to influence cognitive functions or behavior introduces complex ethical dilemmas, which require careful consideration and ongoing dialogue between stakeholders: patients, healthcare professionals, engineers, ethicists, and policymakers [3]. As implantable devices become more sophisticated and pervasive, it is critical to address these ethical challenges to ensure that innovations benefit society as a whole and do not exacerbate existing inequalities or create new forms of discrimination [3].

V. Acquisition systems

Nerve bundles are complex structures that contain a multitude of fibers, each with distinct functions and unique thresholds for activation, all densely packed within a confined space. Acquisition systems for peripheral nerves implantable devices are designed to monitor and modulate neural activity, providing real-time feedback and improving the efficacy of neuroprosthetic therapies. Technological innovation in this field aims to develop increasingly miniaturized, biocompatible, and energy-efficient devices capable of seamlessly integrating with nervous tissue for long-term operation [27]. These advancements are essential for the evolution of targeted and personalized therapies in the field of clinical neuroscience and neural prosthetics [27]. Acquisition systems for the treatment of those pathologies are divided into two main classes: extra-fascicular and inter-fascicular. An example is reported in Fig. 3.

Inter-fascicular electrodes are placed within a fascicle in the nerve and have direct contact with the targeted fibers. Hence, despite being more invasive than extra neural

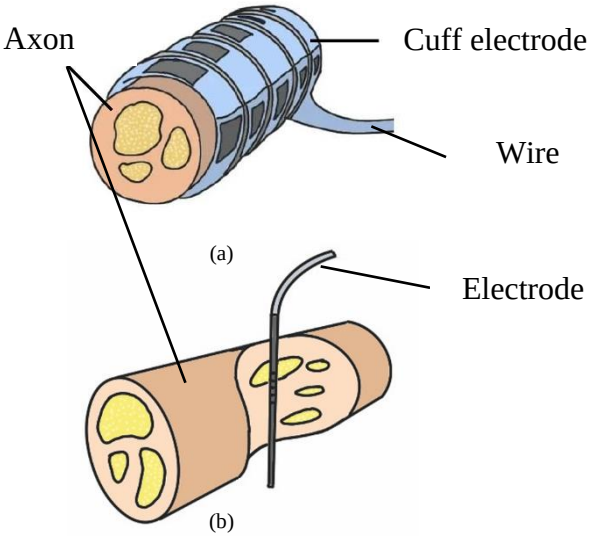

Figure 3: (a) extraneural and (b) intraneural PNI interface representation.

electrodes, they provide an enhanced signal-to-noise ratio and the opportunity to monitor single-unit action potentials [28]. Penetrating electrodes of various geometry were developed to be placed inside the epineurium, including Longitudinal intra-fascicular electrode (LIFE), which are implanted longitudinally within individual nerve fascicles, and Transverse interfascicular multichannel electrode (TIME), inserted transversely through nerve fascicles [29].

Extra-fascicular acquisition systems are placed on the surface of the nerve, resulting in lower invasiveness. This class includes systems such as the epineural electrode, the helical electrode, the book electrode, and the cuff electrode [30]. Epineural electrodes are composed of a layer of insulation material, which contains one or more electrical contacts and are sutured onto the epineurium [30]. Helical electrodes are designed to wrap around the nerve, interfacing with one or multiple electrical contacts [30]. Book electrodes are well-known for their extensive use in sacral anterior root stimulation for bladder control. Each book electrode has three or five thin silicone rubber "pages", and each spinal nerve root is inserted into one of two or four slots between these pages, although other configurations have been proposed as well [30]. Cuff electrodes are the most widely used peripheral nerve interfaces, Fig. 3. They are fabricated with various designs and continue to be developed in advanced forms [31]. Cuff electrodes have a cylindrical or tubular shape, allowing them to wrap around a nerve like a sleeve or cuff. The electrodes contain multiple contacts with the nerve that can be arranged circumferentially around it. This configuration allows for differential stimulation or recording from different parts of the nerve [31]. They are typically made from flexible and biocompatible materials such as silicone or polyurethane, which can be embedded with conductive elements like platinum or stainless steel to form electrode contacts [31]. Despite their advantages of simplicity of handling and the ability to stimulate and record general activity from the outer parts of the nerve, they still have many disadvantages to consider. First, their selectivity is limited to subgroups and superficial fibers in the nerve. Secondly, the nerve can be damaged due to micromotion of the electrode array, especially in peripheral nerves of the limbs [27]. Finally, the phantom sensations they generate are unstable due to the limited contact area between the active sites of the electrode and the nerve tissue [32]. An example of an advanced form of cuff electrode is the flat-interface nerve electrode (FINE), designed to achieve better selectivity [33]. It transforms the nerve from an elliptical shape into a flatter ribbon-like shape, giving access to deeper fascicles. However, since this reshaping requires the slow application of a relatively high force, only moderate flattening of the nerve is possible without inducing nerve damage [33].

In addition, Microelectrode Arrays (MEAs) are acquisition systems for peripheral nerve devices that are widely used. They consist of multiple, small-scale electrodes arranged in a grid-like pattern and can be both extra-fascicular and inter-fascicular [28].

In literature, there are advancements not only regarding the design of acquisition systems, but also regarding materials and working principles of the interface between the electrode and the nerve. Examples are organic semiconducting electrodes, which typically provide softer and more flexible interfaces with tissue with excellent biocompatibility, and inorganic semiconducting electrodes, commonly used in their crystalline forms, resulting in higher electron mobility and lower operating voltages of devices [34].

VI. Electrical Models

Electrical models are essential for understanding and optimizing the interaction between cuff electrodes and nerve fibers. These models facilitate the prediction of neural responses to electrical stimulation, the design of effective neural prosthetics, and the improvement of neural recording and stimulation techniques. They are crucial for developing implantable devices aimed at treating PNI. Several models can be designed to improve our understanding of stimulation detection systems. The primary models in this field include neuron action potential generation models, which focus on the activity of a single axon at a specific moment. Following these, axon propagation models illustrate how this single activity propagates along the axon over time. Finally, the probe/tissue interface models explain how multiple axons interact to create a composite signal. Together, these models provide a comprehensive understanding of the mechanisms underlying stimulation detection systems.

A. Neuron Action Potential Generation Models

Among the most valuable models in the literature for neuron action potential generation are the Integrate-and-Fire (IF) model and its variant, the Leaky Integrate-and-Fire (LIF) model [35]. The IF model simplifies AP generation using a capacitor to represent the membrane potential, which resets when a threshold is exceeded, mimicking AP generation without detailing ion channel dynamics. The LIF model enhances this by incorporating a parallel resistor, allowing for membrane potential decay over time.

In contrast, the Hodgkin-Huxley (HH) model [36] offers a more detailed and quantitative description of membrane currents based on the study of the squid giant axon. This model incorporates specific ion channels and their dynamics, represented through differential equations, providing a comprehensive understanding of neuronal behavior despite its higher computational demands.

The Izhikevich model [37] strikes a balance between the IF model's simplicity and the HH model's detailed nature. It

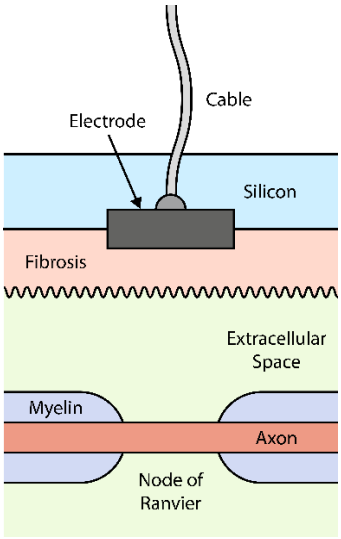

Figure 4: electrode-tissue interface.

can replicate a variety of neuronal behaviors observed in the central nervous system with a relatively low computational cost, making it suitable for large-scale network simulations.

B. Axon Models

Axon models are crucial for simulating the propagation of electrical signals along nerve fibers. McNeal's model [38] is pioneering in this domain, representing axons as compartments connected by conductances, primarily focusing on the nodes of Ranvier while assuming the myelin sheath to be a perfect insulator. This model, however, simplifies the complexity of myelinated nerve fibers.

The Chiu-Ritchie-Rogart-Stagg-Sweeney (CRRSS) model [39] builds upon McNeal's work by incorporating conductance and capacitance of the myelin sheath, thus providing a more realistic representation of mammalian axons. This model alternates between nodal and internodal compartments, each with distinct electrical properties.

A significant advancement is the McIntyre-Richardson-Grill (MRG) model [40], which introduces a double-cable structure accounting for both the axonal and periaxonal spaces. This model emphasizes the role of the myelin attachment segment in generating depolarizing afterpotentials (DAP), which is crucial for understanding nerve excitability and accurately predicting stimulation thresholds. The MRG model's detailed segmentation, including the paranodal and internodal regions, offers a sophisticated framework for simulating the electrical behavior of myelinated nerve fibers.

C. Probe/Tissue Interface Models

Understanding the probe/tissue interface [41] is crucial for optimizing neural recording and stimulation devices. This interface is often modeled as an equivalent circuit with several key components. First, the voltage source represents the bioelectric potential generated by neuronal activity. The extracellular space impedance, affected by the geometry and conductive properties of the surrounding tissue, influences signal transduction efficiency. The electrode leakage resistance is another critical component; higher resistance minimizes unwanted current paths, reducing signal degradation. Additionally, the electrode-tissue capacitance, determined by the double-layer capacitance at the interface, is vital for signal transduction. This capacitance value impacts the frequency response and the overall fidelity of the recorded neural signals.

This model is essential for optimizing electrode design, improving signal fidelity, and enhancing the biointegration of implantable devices. Correctly modeling these components allows for accurate simulation and effective functioning of neural interfaces. The detailed insights provided by these models support the development of more effective and reliable neural prosthetics and stimulation devices, which are crucial for advancing treatments for peripheral nervous system damage.

VII. Conclusions

In this paper, we have explored the significant advancements and ongoing challenges in the treatment of PNIs, which pose a significant clinical challenge, leading to chronic disability and high healthcare costs. Our review highlights the promising potential of next-generation neural interfaces. These technologies demonstrate the capability to restore sensory and motor functions, offering a substantial improvement over traditional therapeutic approach. However, their successful integration into clinical practice requires overcoming substantial challenges, including biocompatibility, structural design, power management, wireless communication, data security, and regulatory compliance. Future research should focus on overcoming the current limitations of these technologies, particularly in the areas of energy efficiency, long-term biocompatibility, and the development of fully autonomous systems. Innovations in biocompatible materials and wireless technologies are crucial for the development of next-generation neural interfaces. Continuous research and development are essential to fully realize the potential of these advanced PNI treatments, which promise to improve the quality of life for patients significantly. As we move forward, several critical questions remain: How can we ensure that these innovations are accessible to all patients, regardless of socioeconomic status? What ethical considerations must be addressed to prevent misuse of these technologies? How can regulatory frameworks evolve to keep pace with rapid technological advancements while ensuring patient safety? Addressing these questions will be key to realizing the full potential of advanced treatments for PNIs.

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