Peripheral Nerve Interfaces

Bioelectronics and Biomedical Microelectronics

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***Abstract*—Peripheral Nerve Interfaces (PNIs) enable communication between electronic systems and the peripheral nervous system (PNS), with applications in prosthetics, neuromodulation, sensory restoration, and functional rehabilitation for individuals with neurological disorders or injuries. This paper reviews PNI technologies, focusing on the challenges of achieving high specificity, long-term stability, and improved signal-to-noise ratios, which are essential for reliable stimulation and recording. Various PNI types, from non-invasive surface electrodes to invasive intrafascicular and penetrating designs, are evaluated with respect to their advantages and limitations. The paper also examines current clinical applications, including neural decoding, motor control in prosthetics, chronic pain management, and sensory feedback restoration, and explores future advancements to address existing challenges and enhance the functionality and reliability of PNIs.**

I. Introduction

Peripheral Nerve Interfaces (PNI) are devices or systems designed to establish a connection between electronic systems and peripheral nervous system (PNS). They can record neural signals (afferent information), stimulate nerves (efferent commands), or both [1]. The PNS encompasses all neural elements outside the brain and spinal cord, connecting the central nervous system (CNS) and the rest of the body. It is divided into the somatic nervous system, which governs voluntary movements and transmits sensory information, and the autonomic nervous system, responsible for involuntary functions such as heart rate and digestion. PNIs have a wide range of applications, including prosthetics, neuromodulation, and restoration of function. The development of PNIs is driven by the need to improve the quality of life for individuals with neurological disorders or injuries. This paper provides an overview of the challenges in PNI development, the types of PNIs, and their applications.[2]

II. Challenges in PNI Development

A. Technical challenges

1) Specificity: Specificity refers to the ability of a peripheral nerve interface (PNI) to distinguish and interact with signals from specific nerve fibers or fascicles. High specificity is critical for accurate stimulation and recording, which ensures that only the intended fibers are targeted without activating or recording from the unintended ones. Achieving high specificity is however challenging in PNIs since the nerves consist of tightly packed fascicles surrounded by connective tissue. Electrodes must achieve precise alignment with the target fibers to minimize signal crosstalk and unintentional activation, however the tissue encapsulation, micromotion, scar formation, and variability in nerve structure can disrupt electrode alignment and degrade performance over time.

2) Stability: Stability refers to the ability of the PNI to maintain consistent performance over time. High stability is essential for reliable stimulation and recording, as any variation can compromise the functionality, degrade signal quality or lead to unintended nerve activation. The primary challenges to stability stem from hardware, mechanical and biological factors. In terms of harware electrode degradation can lead to signal drift. Mechanically, repeated nerve movement and micromotion can cause electrode displacement or damage, leading or signal drift or loss of functionality. Biologically, chronic implantation can trigger foreign body responses, including inflammation and scar tissue formation, which can alter the electrode-tissue interface. These responses can increase impedance, reduce signal quality and even result in the failure of the interface.

3) Signal-to-noise ratio: Signal-to-noise ratio (SNR) is a critical parameter in PNIs. A high SNR is essential for accurate neural recording, enabling precise decoding of nerve acitvity. The challenges in maintaining a high SNR arise from multiple sources. Neural signals are often weak and must go through multiple interfaces, which each introduces potential noise. Biological factors, such as muscle activity, tissue impedance and motion artifacts, also contribute to interference, particularly in non-invasive or minimally invasive systems. Invasive PNIs face other issues such as scar tissue formation or electrode degradation which can increase noise over time.

B. Biological challenges

1) Foreign body response: When a PNI is implanted, the body reacts by initiating a foreign body response. This begins with acute inflammation, followed by the formation of fibrous scar tissue around the impant. This encapsulation increases impedance at the electrode-tissue interface, degrading the device's ability to record or stimulate neural signals.

2) Nerve damage: PNIs can cause mechanical and biological damage to nerves during implantation or over time. Mechanical trauma from penetrating electrodes can sever nerve fibers, while cuff electrodes may compress or irritate the nerve, leading to ischemia and demyelination. Chronic micromotion between the electrode and nerve tissue can exacerbate these issues.

III. Types of Peripheral Nerve Interfaces

In this section, different forms of peripheral nerve interfaces are presented along with their benefits and drawbacks in light of the issues outlined above.

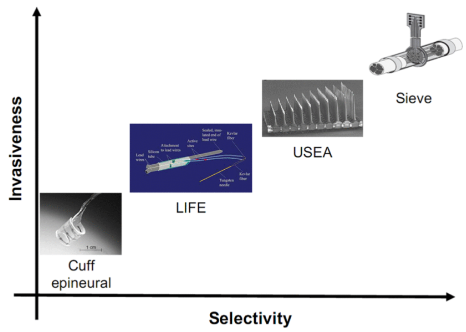

Fig. 1. Types of peripheral nerve interfaces [3]

A. Non-invasive Interfaces

1) Surface Electrodes: Surface electrodes, placed on the skin above the target peripheral nerve are commonly used for electrical stimulation or activity recording. However, recording neural signals directly with these electrodes is nearly impossible due to weak signals and interference form muscle activity and skin impedance. Therefore muscle signals are often used as an indirect "magnifier" of nerve activity, where applicable. While simple, affordable, and non-invasive, surface electrodes have low selectivity often affects multiple nerve branches and surrounding tissues. Stability is also influenced by skin condition, placement, and movement. These limitations make invasive interfaces necessary for more accurate stimulation and recording.

B. Minimally Invasive Interfaces

1) Cuff electrodes: Cuff electrodes are minimally invasive and designed to encircle peripheral nerves without penetrating them. Their design allows the to stimulate and record from nerve trunks while minimizing the risk of nerve damage and inflammation. Hybrid polyimide cuff electrodes embedded in silicone guidance channels have been fabricated for functional electrical stimulation of peripheral nerves [4]. Among the advancements in cuff electrode technology is the Flat Interface Nerve Electrode (FINE), which enhances selectivity by reshaping the nerve and optimizing electrode placement [5].

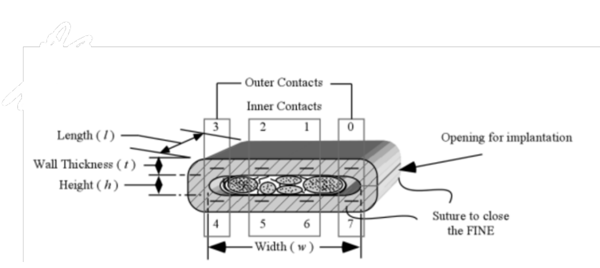

Fig. 2. FINE electrode [5]

2) Flat Interface Nerve Electrodes (FINE): The Flat Interface Nerve Electrode is a specialized cuff electrode designed to increase contact with individual nerve fascicles within a peripheral nerve. Unlike standard cuff electrodes the FINE reshapes the cylindrical cross-section of the nerve into a flatter profile. This increases the surface area of the nerve exposed to the electrodes, improving access to individual fascicles and allowing for more selective stimulation and recording, thus increasing the selectivity. The suture-based closure mechanism and the consistent contact between the electrode and the reshaped nerve also leads to improved stability. While the reshaping introduces some mechanical stress to the nerve, the flexibility of the FINE cuff mitigates long-term damage, making it viable for chronic use. [5]

C. Invasive Interfaces

1) Intrafascicular Electrodes: These electrodes are inserted within a nerve fascicle, providing selective access to individual nerve fibers. Popular designs are LIFE and TIME electrodes. These provide remarkable specificity and SNR for neural interfacing. LIFEs have a moderate specificity but higher stability as compared to TIMEs. Meaning that LIFEs are applicable to broad stimulation/recording tasks, but for high-precision, multi-channel neural interfacing TIMEs are preferable. [6]

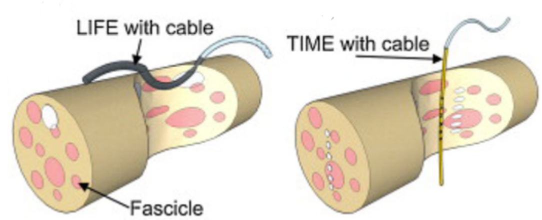

Fig. 3. Intrafascicular electrodes LIFE and TIME [6]

a) Longitudinal Intrafascicular Electrodes (LIFEs): A LIFE is a thin, flexible electrode implanted within a nerve fascicle to enable precise electrical stimulation and recording of individual nerve fibers. It's longitudinal alignment enables precise electrical interfacing with specific nerve fibers, which reduces cross-talk between signals and ensures high signal to noise ratio. However, some noise can arise from the electrode's limited isolation. [6]

b) Thin-Film Longitudinal Intrafasicular Electrodes (tfLIFEs): An advanced version of LIFEs, tfLIFEs, use thin-film technology to improve electrode properties. This enhances the spatial selectivity due to the miniaturization of the recording sites and the SNR due to the improved electrode-tissue interface provided by the leads. The thin-film design also reduces mechanical stress on tissues, leading to reduced inflammation. [7]

c) Transverse Intrafascicular Multichannel Electrodes (TIME): Designed to penetrate transversally across a nerve fascicle, TIMEs create multiple recording and stimulation sites. The multichannel configuration of TIMEs increases the ability to record and stimulate distinct population of nerve fibers, which enables multiplexed neural interfacing. However it might lead to increased mechanical stress and tissue damage as compared to LIFEs, which can potentially affect long-term stability. The proximity of multiple recording sites within the fascicle also boosts the SNR by capturing stronger signals from adjacent fibers while maintaining high spatial resolution. [6]

2) Penetrating Electrodes:

a) Microwire: Made from insulated microwires these electrodes can be used for long-lasting single neuron recordings. Their advantage is that they can be used to access deep brain structures. It is also possible to do multi-neuronal recordings using arrays of microwires for simultaneous recording at the level of neuronal populations as well as at the single neuron level. Specifically using a microwire tetrode, extracellular recording of pyramidal cells. [4]

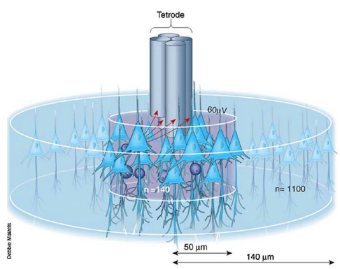

Fig. 4. Microwire tetrode bundle [4]

These microwire bundles are widely used, however the precise location of the electrode tips relative to each other cannot be controlled since the wires bend during implantation. This leads to poor specificity since the desired neural population may not be effectively targeted. The stability is also poor since the tips may move apart after chronic implantation. [4]

b) Silicon-based electrodes: Silicon multifabrication using standard planar photolithographic CMOS-compatible techniques on silicon wafers enables precise, planar or three-dimension electrode arrays [4]. For peripheral nerves the Utah array is the most applicable since it has a 3D configuration that allows it to access multiple fascicles simultaneously.

The Utah electrode array is a three-dimensional electrode array which consists of 100 conductive, sharpened silicon needles, each of which is electrically isolated from its neighbors. Each needle acts as an independent electrode, allowing simultaneous interaction with multiple neural sites across a 3D volume of the peripheral nerve. This provides a higher density of sensors while reducing the displaced tissue and increasing the reproducibility and spatial resolution when compared to a microwire bundle [4]. However because of its rigidity it can cause inflammation in the surrounding tissue, this is though not as large of a concern as in brain tissue since the tissue in peripheral nerves is tougher and more resistant to micromotion.

3) Sieve electrodes: Sieve electrodes are thin, perforated planar structures designed to interface with severed peripheral nerves. These electrodes are positioned between the cut ends of a nerve, allowing regenerating sensory and motor fibers to grow through the holes in the sieve, thereby re-establishing functional connections. Polyimide-based sieve electrodes have been further enhanced with neuronal growth factors applied near the recording sites to promote targeted neurite growth, improving the selectivity and performance of the interface. This approach enables precise stimulation and recording while leveraging the body's natural regenerative capacity. [4]

IV. System Architecture

PNIs consist of the following main parts: the electrode, amplifier circuits, a Digital-to-Analog Converters (DAC), in the case of stimulation, and Analog-to-Digital Converters (ADC), for recording the nerve signals, following various filter stages, before they are sent to or from a respective recording or stimulation device. Recently these devices are fully implantable and either send or receive the recording or stimulation signals wirelessly, therefore they require circuitry for battery power management (PM) and telemetry. [2]

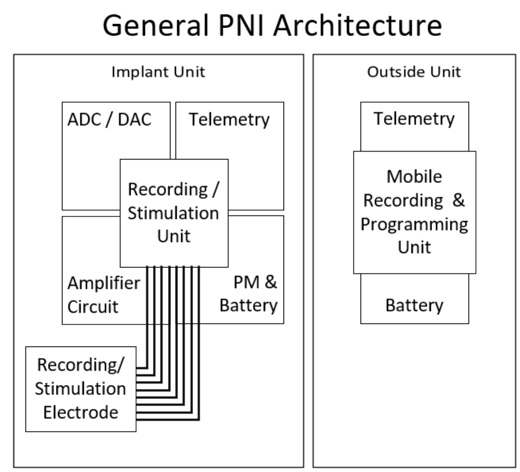

Fig. 5. PNI Architecture

V. Applications of Peripheral Nerve Interfaces

A. Decoding Neural Signals

1) Electroneurography (ENG): PNIs enable the recording of neural activity from peripheral nerves through electroneurography, crucial for diagnosing and monitoring neurological disorders, providing insights into nerve function and aiding in clinical assessments [2].

2) Electromyography (EMG): EMG is an application of PNIs, involving the recording of muscle activity through electrodes placed on the skin. This technique is used to assess muscle function, and guide rehabilitation programs. [2].

B. Neuromodulation & Sensory Restoration

1) Chronic Pain Management & Epilepsy: Peripheral nerve interfaces (PNIs) have been employed in neuromodulation therapies to manage chronic pain and epilepsy. Electrical stimulation of peripheral nerves can modulate neural activity, providing therapeutic benefits for these conditions. For instance, PNIs have been used to alleviate chronic pain by targeting specific nerves involved in pain pathways, like the dorsal root ganglion, offering an alternative to pharmacological treatments. Similarly, vagus nerve stimulation has been utilized to treat epilepsy by delivering electrical impulses to the vagus nerve, thereby reducing seizure frequency.[8], [9].

2) Artificial Sensory Feedback: PNIs facilitate the restoration of sensory feedback in individuals with sensory deficits. By interfacing with sensory nerves, these devices can provide artificial sensations, enhancing the functionality of prosthetic limbs. This approach enables users to experience a sense of touch, improving the control and perception of prosthetic devices [10].

C. Prosthetics

1) Motor Function Restoration: In cases of loss of motor function due to injury or disease, PNIs can bridge damaged neural pathways, enabling the restoration of voluntary muscle control. Techniques such as regenerative peripheral nerve interfaces (RPNIs) using Sieve electrodes have shown promise in reestablishing motor functions by connecting residual nerves to muscle grafts, facilitating neural signal transmission to prosthetic limbs [10], [2], [11].

2) Control of Prosthetic Hands & Upper Limbs: The control of prosthetic hands and upper limbs has been significantly enhanced by the use of advanced PNIs that enable high precision and dexterity. Electrodes such as LIFEs and tfLIFE are usually used to interface with residual nerves, providing access to neural signals associated with fine motor control. By interpreting decoding efferent neural activity from residual upper limbs, these electrodes allow for the precise manipulation of individual fingers, enabling tasks such as grasping and manipulating objects. Closed loop systems with sensory feedback further improve user experience by restoring a sense of touch, which enhances natural feel and precision of prosthetic use [10], [11], [12].

3) Control of Prosthetic Lower Limbs: For lower limp prosthetics, PNIs such as TIMEs have shown promising results in decoding neural signals for seamless control. These interfaces capture efferent activity from residual nerves to enable movements like walking, climbing stairs, and maintaining balance. [10], [12].

D. Restoration of Function

1) Respiratory Pacing: For patients suffering from spinal cord injuries or sleep apnea PNIs using FES to stimulate the phrenic nerve can provide an alternative solution to traditional ventilation. Phrenic nerve stimulation restores diaphragm movement through inducing rhythmic contractions, enabling natural breathing [2]

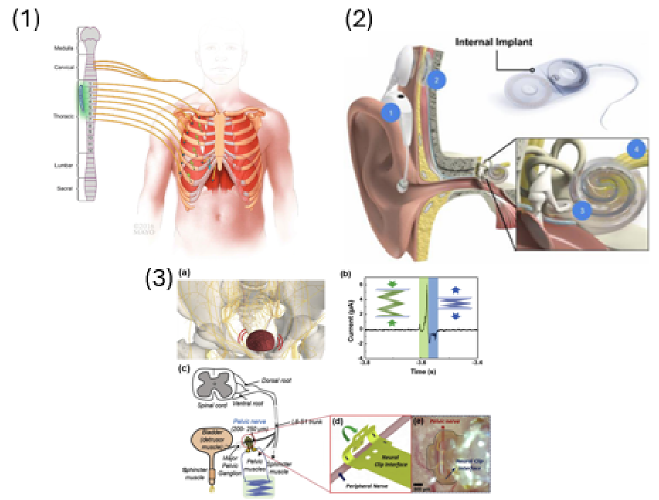

Fig. 6. (1) Respiratory Pacing, (2) Cochlear Implant, (3) Bladder Control [2], [13], [14]

2) Auditory Function Restoration with Cochlear Implants: Cochlear implants are medical devices designed to restore hearing in individuals with severe to profound sensorineural hearing loss. They bypass damaged hair cells in the cochlea by directly stimulating the auditory nerve fibers. The implant consists of an external processor and an internal electrode array surgically inserted into the cochlea. [13]

3) Control of Bladder or Bowel Functions in Paraplegic Individuals: For individuals with paraplegia, PNIs can assist in managing autonomic functions like bladder and bowel control. Electrical stimulation of specific peripheral nerves can restore these functions, significantly improving quality of life [14].

VI. Discussion

A. Conclusion

Peripheral nerve interfaces (PNIs) represent a transformative technology for bridging electronic systems with the peripheral nervous system, offering applications in prosthetics, neuromodulation, and functional restoration. However, challenges such as low specificity, stability issues, and poor signal-to-noise ratio (SNR) hinder their long-term performance. Due to constraints in the assignment we did not go into details of bioelectrical circuits of PNIs, as well as advanced materials, that are being explored to mitigate inflammation and improve electrode-tissue interfaces.

B. Future Directions

Future directions include wireless and energy-harvesting technologies that could reduce device bulk and increase usability. Integrating PNIs into bioelectronic medicine could treat systemic conditions like chronic pain and inflammation, and the development of regenerative interfaces could ensure long-term compatibility with healing nerves. With machine learning algorithms used to enhance neural decoding in noisy environments and further connectivity, individual treatment could be further improved. [15]

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