Bioelectric Interfaces for the Peripheral Nervous System

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***Abstract*— The peripheral nervous system (PNS) is an attractive target for those developing neural interfaces as an access point to the information flow coursing within our bodies. A successful neural interface could not only offer the means to understand basic neurophysiological mechanisms, such as how the body accomplishes complex coordinated control of multi degree of freedom body segments, but also could serve as the means of delivering treatment or therapies to restore physiological functions lost due to injury or disease. Our work in the development of such a neural interface focuses upon multi-microelectrode devices that are placed within the body of the nerve fascicle; mulit-channel intra-fascicular devices called the thin-film Longitudinal Intra-Fascicular Electrode (tfLIFE) and the Transversely Implanted Multi-Electrode (TIME). These structures provide high resolution access to the PNS and have demonstrated promise in animal work as well as in preliminary sub-acute work in human volunteers. However, work remains to improve upon their longevity and biocompatibility before full translation to clinical work can occur.** ρ

I. INTRODUCTION

All that we are, our thoughts, our dreams, our memories, involve the sum of all our experiences, experiences and interactions between the brain, our bodies and the outside world. Almost all of these interactions involve information generated, conveyed, and relayed through neural pathways that link the brain to sensors and actuators embedded throughout our bodies. They are linked through the body's internal neural wiring, the peripheral nervous system (PNS). If a neural interfacing method to intercept the information from, or artificially place information into the nervous system can be perfected, it would revolutionize the way the brain interacts with the body and the environment. Moreover, the method could provide treatment modalities to those who have lost function or suffer from pathological function in their bodies, due to traumatic injury or disease that is currently non-existent.

The peripheral nervous system is the portion of the nervous system that lies outside the protective environment of the skull and vertebral column. It is an attractive site to place a neuroprosthetic since it can easily be surgically accessed through soft-tissue without breaching any bony structures. It defines the pathway that conveys information to and from the central nervous system (brain and spinal cord) and the natural sensors and actuators embedded and distributed throughout the body. Thus, a device that can adequately tap into this information stream could provide a convenient access point to glimpse into the neural information flow or to add/substitute/modify that information flow to alter pathological functions.

II. PERIPHERAL NERVE INTERFACES

Various neural prostheses for the PNS have been proposed by various groups over the years. They differ in their placement and in the quality of the interface to the neural information stream. As summarized by Fig.1, devices can be placed: 1) outside the nerve fascicle or extrafascicularly as in the case of the nerve cuff electrode [1]–[4] or FINE [5], 2) between the nerve fascicles or interfascicularly [5], [6], or 3) within the nerve fascicle, intrafascicularly as in the case of the USA [7]–[9], LIFE [10]–[13], polyLIFE [14], [15] and sieve electrodes.

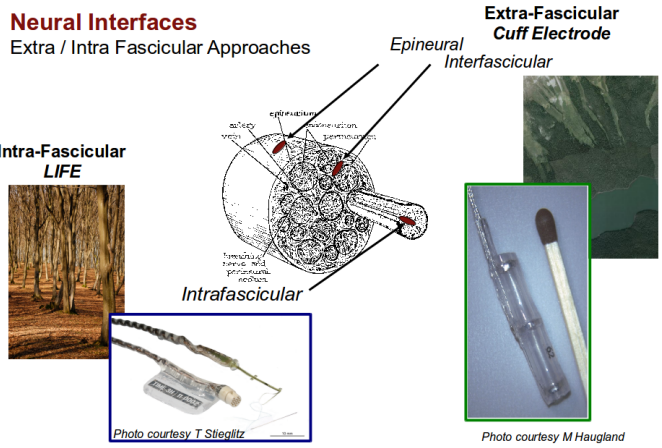

Fig. 1. Neural interfaces in the peripheral nerve can be placed outside the nerve fascicle or extra-fascicularly, between nerve fascicles or inter-fascicularly, or within the nerve fascicle or intra-fascicularly. An example of a spiral cuff designed to wrap around the nerve trunk is shown right, while an example of an intra-fascicular (TIME) device is shown left. The interface achieved by these two structures are at different granularities. Intrafascicular approaches are akin to resolving the trees in the forest or small groups of units, while large extrafascicular devices are akin to visualizing the forest or population.

A. The Intrafascicular Approach

The direction we have taken has been the intrafascicular approach. Our structures aim to place multiple microelectrode contacts within the fascicle of the peripheral nerve, in the intrafascicular space in intimate contact with the nerve fiber. In order to understand the rational of our approach,

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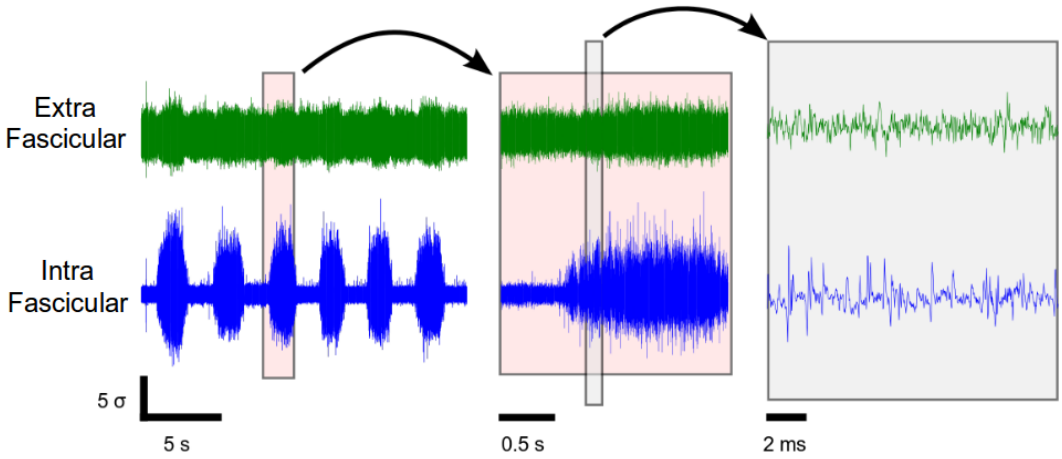

Fig. 2. Simultaneous recordings from an extrafascicular (circumferential cuff electrode) placed around the sciatic nerve and an intrafascicular (tfLIFE) implanted in the tibial nerve of a rabbit. The neural activity is in response to stretching of the triceps surae muscle, which activates the proprioceptors in the muscle. The magnitudes are autoscaled to the standard deviation of the baseline noise to enable comparison between the two electrode types. The figure demonstrates the difference in the signal to noise of the recording by placing the contacts of the neural interface within the nerve fascicle. The measurement from the tfLIFE channel can further be zoomed in to reveal the mixed multi-unit activity of the active nerve fibers in the vicinity of the electrode. Each fiber has an unique spatial relationship to the electrode, and thus manifests an extracellular action potential shape detected by the electrode whose shape is unique.

it is important to understand the nature of how information is transmitted in the PNS, and how this information can be transduced. Data are conveyed along the myriads of nerve fibers, or axons, within the nerve trunks. Each axon transmits a single channel of information from one end of the fiber to the other using a propagating bioelectric waveform called the action potential. Current neural interfaces act upon the action potential and the underlying bioelectric phenomenon through the use of electrodes placed in the vicinity of the active nerve fiber. The sensitivity of the electrode is largest at the electrode and decays generally as a function inversely proportional to the distance from the electrode. Second, the larger the electrode, the flatter and broader the electrode sensitivity function becomes. The smaller the electrode, the sharper the electrode sensitivity function. Thus, the placement, geometry and configuration of the electrode and its relationship to the PNS nerve fibers plays a major role in the quality of the interface.

Proximity to the nerve fiber and small site size results in an extremely high interfacial selectivity, while the multiplicity of sites aims to reach fibers in different parts of the nerve. This has led to the development of flexible, microfabricated, linear arrays of high selectivity microelectrode sites that are designed to be implanted within the body of the peripheral nerve; the thin-film Longitudinal Intra-Fascicular Electrode (tfLIFE) [16], [17] and TIME devices [18]–[22].

Focusing upon the recording aspect of our neural interfaces, we have found in acute animal work that the electrodes provide relatively high signal to noise recordings of nerve activity. These records show multiunit activity that propagates and modulates with driven natural sensors. Moreover, the recording selectivity is sufficient to resolve single fiber, even at high levels of population activity Fig.2. More recent work we have been pursuing has been to determine methods to optimally separate the activity of single fibers given the multi-unit records generated by the tfLIFE and TIME structures. Like intracortical recordings, the general method used is basis of separation is on shape differences in the extracellular action potentials from different nerve fibers. Unlike intracortical recordings where the volume conductor is large and unrestricted, and the most of the signal is sourced from the soma of the neuron, the peripheral nerve space is constricted, and the sources are similar. Thus, the feature differences between the shapes are much smaller. As such, we have explored methods to retain shape differences as much as possible through the hardware [23] and software processing chain [24] (see Fig.3).

Furthermore, we have explored methods to extract information about the nerve fiber and it's relative position to the electrode site through analysis of the single fiber action potential waveform [25], [26].

Colleagues working with our electrodes are currently translating them from development and validation in the animal model to application in sub-chronic human implants to treat phantom limb pain and as a putative human machine interface to control advanced prosthetics [27].

III. REMAINING CHALLENGES

The tfLIFE and TIME devices that we have developed have performed remarkably well in acute trials and applications, showing relatively high stimulation and recording selectivity. Moreover, like other well tolerated biocompatible devices, they undergo encapsulation. However, the encapsulation and gliotic scar form between the electrode structure and the nerve fibers. This increases the all important distance between fiber and electrode, degrading performance of the implant. We hypothesized that mechanical mismatch between the nerve stiffness and elasticity relative to that of the

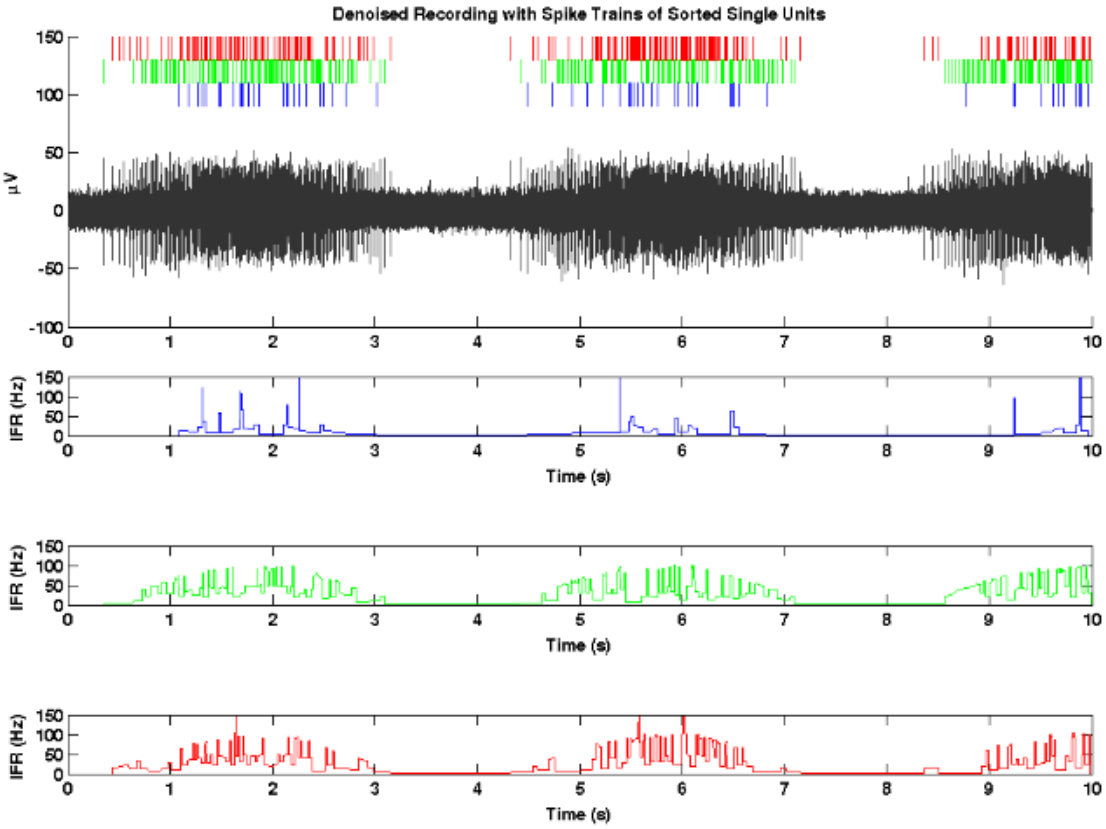

Fig. 3. Specific information from a single nerve fiber can only be extracted from the raw neural interface recording if the mixed neural activity picked up by the electrode can be unmixed to reveal the rate code of information on each neural unit. The upper panel of the figure shows the optimally filtered neural recording (black) and the unmixed activity of three nerve fibers extracted from the recording whose instantaneous firing is denoted as the red, green and blue hash marks above the electroneurogram. The firing instances were determined by identifying the unique shapes of the three units in the electroneurogram to create a template waveform, and extracting the instance where the recording matches the template waveform. Once the firing instances of the three units are determined, the instantaneous firing rate (the three lower traces) can be determined to estimate the rate code carried by each of the three units.

electrode was the major contributor to the thickness of the glial scar. Even with the micropatterend polymer structures we have developed, the mechanical stiffness of the devices remain well over 5 orders of magnitude stiffer than the living nerve tissue. Moreover, peripheral nerve can sustain up to 10% strain during the course of normal movement , a degree of strain that is not possible with even polyimide based structure. The advent of new materials could finally address these remaining issues. Materials that can sustain the relatively high temperatures needed for micro fabrication patterning and processing such as graphene [28], shape memory polymers [29], [30], ultra-elastic conductive and insulating polymers could be used to implement tfLIFE or TIME like structures to make a robust neural interface with mechanical properties that approach that of the nerve and whose performance does not degrade with time.

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