Towards a full-stack peripheral nerve recording interface: Challenges on integration and possible solutions

Towards a Full-Stack Peripheral Nerve Recording Interface: Challenges on Integration and Possible Solutions

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***Abstract*— Peripheral nerve recording interfaces are a new frontier in neuroprosthetic applications. Nevertheless, an integrated medical device offering both electroneurographic (ENG) signal sensing and decoding is still missing.**

This paper aims to summarize the process of integrating existing technologies into a full-stack recording device. To this end, the system requirements are provided, together with a description of the building blocks that compose a recording interface: electrode, acquisition system, classification algorithm, power and communication units. The core of our contribution is a detailed analysis of the unsolved conflicts which arise during the assembling process, followed by the proposal of a few compromise solutions.

***Index Terms*— PNI, Recording Interface, ENG Sensing, ENG Decoding, Integration**

I. Introduction

Peripheral Nerve Interfaces (PNIs) are implantable devices in direct contact with the Peripheral Nervous System (PNS). Most common clinical PNIs aim at modulating the nerve activity through nerve stimulation [1]. However, an emerging field of research is trying to stabilize these stimulating interfaces with recording systems which detect a specific signal, indicative of the stimulation outputs, so as to close the feedback loop [2]. In particular, some studies have proposed the detection of the ENG itself for feedback, thus shifting the focus to the development of an effective peripheral nerve recording interface [3]. In this direction, a device capable of both sensing and decoding a peripheral nerve signal could potentially offer numerous other opportunities. In peripheral mononeuropathies, for instance, a recording interface would possibly support or replace the PNS in the transmission of signals, acting as a bypass device that is able to extract the electrical activity above the damaged portion of the nerve and forward the information across the injury.

The high-level architecture of this recording interface includes the following fundamental building blocks and functionalities (Fig. 1). Firstly, the local potentials at the point of interest are recorded by a transducer made of sensing electrodes placed inside or around the nerve. The collected signal is then elaborated by a circuit that performs a cascade of pre-processing operations. Finally, data are fed to a classification algorithm that reconstructs information about the activity that triggered the detected signal, such as the category of the stimulus or its intensity. The functioning of these three fundamental blocks must be ensured by the presence of auxiliary components, such as a power supply module and, possibly, a communication unit. The latter is needed either when the classification is performed externally or when the interface is coupled with an external actuator.

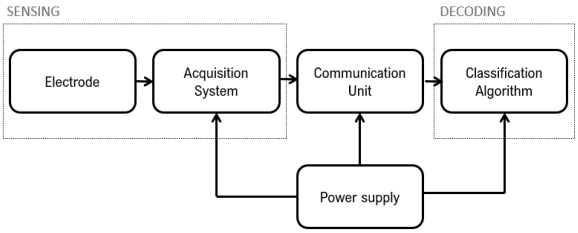

Fig. 1: Block diagram of a full-stack peripheral nerve recording interface.

Several studies have focused on every single component of the recording system. However, very few of them have addressed the challenges that arise during the integration of all parts into a full-stack recording device [4]. For this reason, this paper aims to outline some of the principal hurdles that we think remain to be tackled towards the combination of the existing technologies into an integrated device.

The rest of the article is organized as follows. Section II delineates the basic functional requirements and design constraints we have identified for a fully-implantable peripheral nerve recording system. Section III reviews the main families of approaches found in the literature for the individual building blocks of the system, highlighting some critical aspects from which problems could arise during integration. Specifically, section IV investigates and analyzes technical challenges that, in our opinion, still remain to be faced for effective integration of the components. Lastly, section V summarizes the main findings, suggesting two examples of trade-off solutions realizable with the existing technologies.

II. Analysis of the Requirements

Important technical requirements that need to be satisfied by peripheral nerve recording interfaces are biocompatibility, accuracy, real-time functioning, and durability.

Biocompatibility can be inspected from a biological or anatomic point of view. Biological biocompatibility requires the device materials and structural composition to be such that no local or systemic unwanted effect is triggered in the host organism's tissues. One notable example of such undesirable effect is overheating [5]. On the other hand,

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anatomic biocompatibility imposes constraints on the shape, size, weight, and other geometrical and physical properties of the device, which must be compatible with those of the implant location. The risk for biocompatibility issues is particularly prominent during implant surgery, which should be made as quick and straightforward as possible.

Accuracy demands that the device be able to correctly interpret the recorded signals, which means recognize the endogenous and exogenous sources that have triggered the detected nerve activity. This implies that the classification must be robust against noise and able to extract meaningful information from the recorded signal.

Real-time functioning implies that the decision-motion and stimulus-perception time intervals must be comparable with the physiological ones. Indeed, a slow response could jeopardize all the effort put to have an accurate classifier.

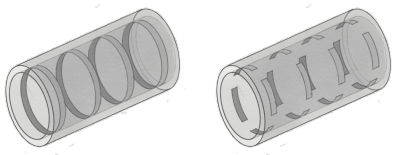
Durability is intended as the capability of remaining functioning in the long-term, both in terms of continuous power supply and classification accuracy. To fulfill this last requirement, the classification stage will most likely need periodic re-calibration: the device must be made adaptable to the physiological or pathological modifications that might happen throughout the duration of the implant.

III. Building blocks

The technologies that have been proposed for each component of a fully-implantable system for peripheral nerve recording are summarized in the following.

A. Electrode

Electrodes are classified according to the degree to which they penetrate the fascicular nerve structure [6]: *intraneural* electrodes pierce the epineurium and are further divided into regenerative, intrafascicular and interfascicular; *extraneural* electrodes, such as nerve cuff electrodes, leave the epineurium intact reducing the nerve damage and increasing durability. Importantly, the degree of invasiveness is closely related to the electrode selectivity: to obtain high selectivity one should place the electrode as close as possible to the signal source, with the risk of causing a stronger inflammatory response [7]. Although a few works on intraneural electrodes have been published with promising results [8], the extraneural electrode remains nowadays the most commonly accepted design, with numerous clinical applications for nerve stimulation [9]. Cuff electrodes, in particular, offer an easier implantation procedure than their intraneural counterparts and are shown to remain physically and functionally stable over 10 years [10].



(a) (b)

Fig. 2: Different types of cuff electrode arrangements: (a) multi-ring electrode, (b) multi-contact electrode.

In terms of materials, the market has established a common norm of using silicone or polyimide host substrates and platinum contacts, leaving the end users to select their electrodes based on the channel count and the design of the cuffs [6]. On that regard, different arrangements have been proposed: single-channel, multi-ring, or multi-contact cuff electrode configuration (Fig. 2).

B. Acquisition system

The pre-processing chain is traditionally composed of amplifiers, an Analog-to-Digital Converter (ADC) and filtering blocks. First-stage amplifiers can be arranged into configurations such as bipolar, tripolar, and screened tripolar, which provide initial noise rejection [1]. The ADC can be placed before or after the filtering stage.

Independently of the modules sequence, signal acquisition can be performed either in continuous or discontinuous mode, the latter being more efficient in terms of power consumption and data transmission rate. In this regard, it is worth stressing that the circuit operates on signals with a power peak of around 2 kHz [11]. This requires a sampling frequency higher than the one usually needed for other biopotentials like electrocardiogram or electromyogram. The major consequence is that also the dynamic power consumption and data rate increase with respect to other recording systems.

C. Classification algorithm

The aim of the classifier is to identify which stimulus has triggered the recorded neural activity. To this end, the algorithm tries to extract meaningful information from the recordings (e.g. waveform, propagation velocity) and use it to distinguish one stimulus from another. The crucial point here is that different kinds of information can be extracted depending on the type of electrode configuration used. Specifically, speaking about nerve cuff electrodes, single-channel configurations output only one signal, while multi-ring and multi-contact electrodes allow exploiting the joint information from multiple channels. The presence of multiple contacts placed longitudinally allows for inference of the conduction velocity, from which the fiber type can be estimated [12]. On the other hand, contacts distributed around the nerve circumference allow, at least in principle, to extract information about where the signal source is located in the nerve cross-section [13].

Another important design choice concerns whether to implement the classifier subcutaneously on the implanted circuit or rather on an external module, for instance, carried by the patient on a chest strap. An external classifier is less constrained in terms of size and more easily accessible for maintenance. On the other hand, the implanted version has the advantage of being unobtrusive and bringing elaboration and classification all in one location.

D. Communication and power supply

Wired trans-cutaneous connections allow both communication and power supply in a single system with maximum

efficiency. However, this comes with a high risk of infection due to the presence of an access between exterior and interior. Since the benefits of this non-life support system do not outweigh the risks, this approach is not applicable in a clinical setting.

With respect to powering, implantable non-refillable batteries for Active Implantable Medical Devices (AIMDs) are unlikely to guarantee years-long durability in a device with a power consumption of the order of $10 - 100\ mW$ [14]. Two alternatives have been proposed: the first includes the use of external batteries continuously feeding power to the implanted circuit via wireless transmission, the second involves implantable batteries rechargeable from the outside [15]. Wireless power transfer technologies are required either with external batteries or implanted rechargeable ones. Wireless approaches include mainly inductive coupling and ultrasounds. The first has the advantage of being suitable also for communication in an all-in-one module. However, the attenuation effect on electromagnetic fields by tissues implies this solution to work just in a short-range [16]. Ultrasounds, instead, have the potential to penetrate deeper into the tissues but only if continuity of the propagation medium, in terms of acoustic impedance, is guaranteed [16]. Having to interpose gel between the external transducer and the patient's skin to assure this continuity, ultrasounds are practically inadequate for a continuous power transfer to the device and can be considered just for recharging internally implanted batteries.

Communication, on the other hand, can be implemented by introducing modulation within the inductive system or using antennas. In both cases, the use of a high transmission frequency to reach high bit rates implies a higher tissue attenuation, increasing in turn the power demand of the communication system.

IV. Technical challenges towards integration

In addition to the technical challenges that can emerge during the development of every single component of a recording interface, some new conflicts come about when trying to perform the integration of them, and others derive from the strict regulations in the field of medical devices.

A. Electrode selectivity

The combination of long-term biocompatibility with effective ENG decoding still represents an unsolved challenge. Indeed, the choice of a cuff electrode, still preferable for chronic application [10], comes at the cost of a number of severe consequences. First of all, when recording the activity on the surface of the epineurium, the signal is affected by the contribution of all the fibers present inside the nerve making it difficult to discriminate which specific fibers were activated. Moreover, the amplitude of the recorded activity is typically of the order of $10\ \mu V$ [11], requiring greater amplification and thus greater power consumption. Lastly, cuff electrodes are also more affected by the presence of external noise sources (primarily EMG) that complicates signal processing and interpretation, increasing the required filtering effort [1].

B. Overheating

The second unsolved technical challenge is ensuring biocompatibility limiting tissue overheating, while supplying power and transmitting data. In fact, thermal energy absorbed by tissues surrounding the device must not be such as to cause cellular suffering, inflammation or burns. To contain such risks, the CEI EN 45502-1 norm for AIMDs establishes a maximum increase in temperature of $2°\text{C}$.

Overheating can arise from mainly two sources: the components of the circuit, and the powering module. Circuits components cause an increment in temperature due to the power consumption linked with their functioning. To tackle this issue, low-consumption active components could be considered to reduce the demand in terms of power supply and thereby the energy absorbed by the circuit. However, it is worth mentioning that other technical issues arise when low-power components are used (e.g. lower performances in terms of bandwidth, output drive, and noise level). Likewise, when fixing an upper bound on power consumption, the reachable operating frequencies of the digital components may not fit the system requirements for sampling and data transmission. Concerning powering modules, instead, the principal source of overheating is the wireless power transfer across tissue, present with both external batteries continuously feeding power to the implanted circuit, and implantable batteries rechargeable from the outside. Inductive coupling, for instance, despite being the most popular technology for AIMDs, still suffers from low transmission efficiency which often causes overheating around the coils [14]. Of note, when implantable batteries are used, their heating during recharge causes an additional temperature increment. To address these limitations, more efficient wireless powering technologies and a trade-off between overheating and charging time for rechargeable batteries must be identified.

C. Number of recording channels

Another major challenge that remains to be addressed regards the management of a high number of recording channels. Indeed, several studies over the last few years have shown that cuff electrodes with a high number of channels offer the best classification performance with respect to other configurations [13]. However, the presence of a high number of channels, typically from 10 to 60, implies 10 to 60 tracks to be processed and, possibly, transmitted. This means that, as the number of channels to be processed subcutaneously raises, the size and power consumption for the implanted circuit increase as well. The same happens to the bit rate required to transmit data, in cases where signals are digitized and then transmitted to an external classifier to perform post-processing in real-time. The main consequence is that the acquisition of such a large number of input channels might be unfeasible, especially given the high sampling frequency required for ENG signals.

D. Classifier re-training

Classifier re-training, aimed at fulfilling the durability requirement, represents another important technical challenge.

As mentioned in the requirement analysis, the classifier must be able to respond adequately to any physiological change in the nerve during the implant lifetime. To meet this end, the most common technique is to re-train the classifier after a certain period. This process is relatively simple for an external classifier because the classifier parameters are easy to access and update. On the contrary, if classification is performed directly on an implanted integrated circuit, re-training becomes a non-trivial task. A solution might be to equip the device with a feedback system for periodic self re-calibrations. Such system has not, to the best of our knowledge, been developed for ENG signals, although successful examples exist e.g. for prosthetic control through EMG signal classification [17].

V. Trade-off solutions

The discussion above highlights that, even when there are standards for individual elements of the system, their integration is not straightforward. To give an example, even though multi-contact cuffs seem to be a valuable option for the electrode interface, no unique solution has been identified for the transmission of such a large amount of data. Likewise, although an inductive unit for both power supply and data transmission remains nowadays the most common approach for AIMDs, a standardized strategy to limit overheating has yet to be defined. In other words, what remains to be really investigated are innovative solutions to embed these technologies into a full-stack device.

To address the transmission of a high number of channels, for instance, we propose two different trade-off solutions. A clever subcutaneous pre-processing of recorded signals may be used to reduce the amount of data to be transmitted, imposing a milder constraint on the bit rate. This approach may provide a promising opportunity to reduce the transmission load, without massive loss of information. For example, a stage can be added to the analog amplification chain that averages together groups of tracks, taking advantage of the redundancy inherently present in multi-channel recordings. Alternatively, the classifier could be integrated with the implanted circuit, so that only the classification outputs need to be transmitted externally. This approach optimizes the converter efficiency, increasing the battery life and decreasing the human tissue absorption. On the other hand, it would require a self-retraining classifier, raising the complexity of the integrated circuit, already typically highly resource-demanding due to the widespread use of deep learning algorithms in biosignal classification [18].

VI. Conclusion

Research in the field of PNIs is optimizing individual components with promising results. However, no full-stack recording interface is currently available. To speed up its realization, trade-off solutions obtained by embedding existing technologies can already be investigated. The examples proposed in this paper show that these compromise solutions can be identified by means of an interdisciplinary approach that considers the integration of all individual components from the beginning of the design process.

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