Restoring upper limb and hand/fingers function after a spinal cord injury

Technical report

Team 11

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1 Introduction

Spinal cord injury (SCI) remains a significant global health challenge, with estimates suggesting that approximately 15.4 million people were living with SCI in 2021, a number that continues to rise annually [1]. Among the various injury sites, SCI at the neck level is notably prevalent and has a higher incidence, often leading to severe disabilities, including upper limb paralysis. Consequently, the development of effective measures to prevent and manage SCI is critical to address the increasing population of patients affected by this condition.

Understanding the origin and impact of SCI is essential for its management and potential healing. SCI involves a partial or complete injury to the spinal cord, disrupting the transmission of signals from the brain to the muscles. Despite the brain and peripheral nerves remaining intact, this injury severs the communication pathway between them. Normally, the primary motor cortex sends motor signals of the hand, wrist and elbow to the brachial plexus located between C5 and T1 spinal roots — a network of nerves that controls the muscles of the shoulder, arm, forearm, and hand. From there, three main nerves—ulnar, radial, and median—emerge from the brachial plexus, each responsible for different aspects of upper limb motor functions.

Previous studies, such as Epidural Electrical Stimulation (EES)[2] and Functional Electrical Stimulation (FES) [3], have demonstrated the potential to restore basic functions like reaching and grasping in individuals with SCI but there are still limited in term of selectivity and performance. Indeed, FES, which consist of numerous electrodes implanted in the arm and placed on the muscles, has been tested clinically and can restore reaching and grasping, but causes a lot of muscle fatigue and is surgically difficult and risky. EES, which consist of the placement of electrodes on the cervical spinal cord, has also been tested clinically and is a treatment for chronic pain, but it has limited performance as it can only restore coarse movements. That is why, the focus of this research is on restoring more degrees of freedom and distal hand functions with the use of intrafascicular recording.

Distal hand function, which involve fine motor skills of the fingers and wrist, is regulated primarily by the median and ulnar nerves and is crucial for daily activities requiring dexterity and precision. The median nerve, in particular, plays a vital role in enabling tasks such as buttoning a shirt, typing on a computer, and brushing teeth. Restoration of these functions is essential for fostering independence and competence in everyday activities.

Our approach involves developing a neuroprosthesis designed to restore upper limb and hand/finger movements following spinal cord injury. This system integrates two key technologies: intrafascicular stimulation and intracortical recording. Rather than aiming to create a final product immediately, our strategy focuses on optimizing each component individually, selecting the best approach based on current advancements.

We then provide a comprehensive overview of how these components could function together in a closed-loop system, simulating real-life applications. This integrated view includes an assessment of the potential limitations and identifies areas for future improvement, ensuring a practical and effective solution for restoring motor functions in individuals with SCI.

2 Recording electrodes

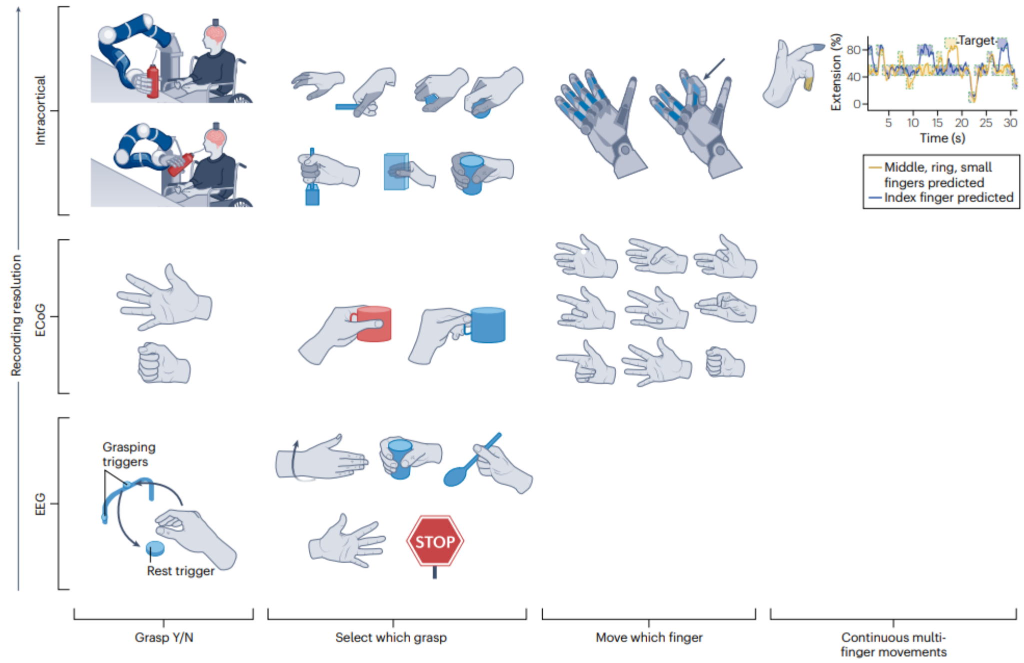

Figure 1: Interfaces and strategies to decode hand movements from brain activity [3]

Restoring upper limb movement in individuals with paralysis or severe motor impairments is a complex challenge that involves interpreting neural signals accurately and translating them into actionable commands for assistive devices or direct muscle stimulation. Recording electrodes play a pivotal role in capturing brain signals crucial for decoding the intention of movement following spinal cord injury (SCI). It exist different recording technologies, ranging from non-invasive methods such as electroencephalography (EEG) and electrocorticography (ECoG) to more invasive techniques like intracortical micro-electrode arrays. EEG offers a non-invasive means to capture neural activity by recording electrical signals generated by the brain's cortical neurons. While EEG provides valuable insights, its spatial resolution is limited and cannot record precise information to restore upper limb and hand movement. ECoG, on the other hand, involves placing electrodes directly on the surface of the brain, offering higher spatial resolution compared to EEG. However, both EEG and ECoG are constrained by their inability to access deep brain structures. In contrast, intracortical micro-electrode arrays penetrate the brain's cortex, enabling precise recording from individual neurons. This invasive approach provides unparalleled spatial and temporal resolution, essential for decoding neural signals associated with specific motor intentions. By using the capabilities of intracortical electrodes, we aim to decode neural activity, establish brain-computer interfaces, and ultimately restore upper limb and hand function in individuals with SCI.

2.1 Why choosing Intracortical Electrodes?

Choosing intracortical electrodes, such as microelectrode arrays (MEAs), for recording neural activity to restore upper limb movement offers significant advantages, particularly due to their high spatial and temporal resolution. Intracortical electrodes penetrate the brain tissue, enabling the recording of neural activity at the level of individual neurons or small groups of neurons within the motor cortex. This fine spatial resolution allows precise localization of neural signals related to specific movements [4]. Additionally, intracortical electrodes provide excellent temporal resolution, capturing rapid changes in neural firing. This capability is crucial for real-time interpretation of motor commands support continuous multi-finger movements, which are crucial for restoring functional hand use.

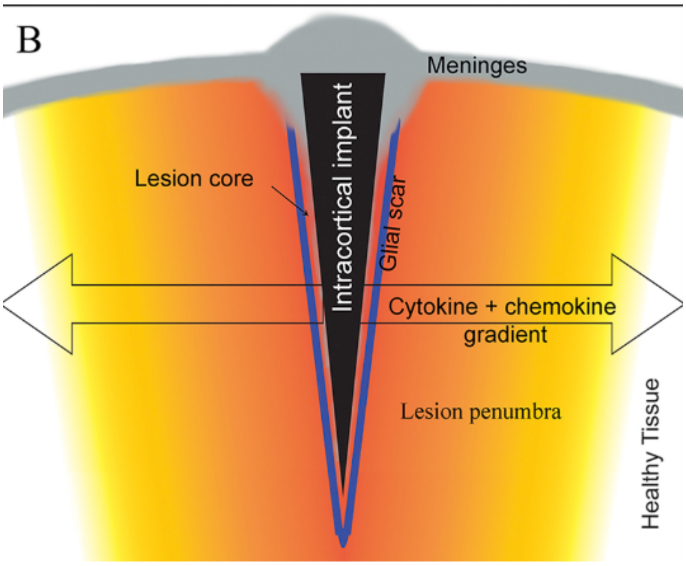

Figure 2: Cross-sectional schematic representations of a CNS lesion with an intracortical implant [5]

Additionally, intracortical electrodes have already been shown to restore at least seven degrees of freedom in the hand and arm, with potential improvements reaching up to ten DoFs, which aligns with the level of precision we aim to achieve. However, the invasive nature of intracortical electrodes poses significant challenges, particularly concerning potential tissue damage and long-term biocompatibility issues. When electrodes are implanted directly into the brain tissue, they can cause inflammation, scarring, and neuronal loss over time (figure 2).These reactions impair the functionality of the electrodes and pose risks to the patient's health.

2.2 Subcellular Carbon Fiber Electrodes

To address these challenges, we will use advanced electrode technology designed to minimize tissue response and enhance long-term stability. Our electrodes are coated with biocompatible materials that reduce inflammatory reactions and are designed to be flexible, which reduces mechanical strain on the surrounding brain tissue. Additionally, we are exploring the use of novel materials and surface modifications to improve the integration of the electrodes with neural tissue, promoting more stable and reliable long-term recordings. Through these innovations, we aim to create a more sustainable and less invasive solution for neural interfacing, improving the overall safety and efficacy of upper limb movement restoration technologies.

Our solution leverages subcellular-scale carbon fiber electrodes (figure 3) to create a highly effective and minimally invasive neural interface for brain-machine interfaces (BMIs). These electrodes utilize carbon fiber with cross-sectional areas of 6.8 μm to minimize tissue damage and scarring. Made from soft materials like carbon fiber, they can achieve higher long-term neuronal yields compared to traditional silicon arrays. This also allow to maintain high neuron densities after chronic implantation [6].

Additionally, we coat the implanted electrodes with a neuroadhesive protein coating, specifically 800 nm of Parylene C, to minimize the foreign body response and improve biocompatibility [7]. This coating enhances long-term stability and neuronal yield, making our subcellular carbon fiber electrodes a novel and promising solution for recording neural activity and restoring motor functions in individuals with SCI. Combining existing technologies and emerging advancements, our approach aims to achieve high stability, biocompatibility, and effective wire transmission, paving the way for advanced BMIs in the coming decades. This solution has been tested on rats, in the layer 5 of the motor cortex and has been shown promising results. Our goal now is to translate to human.

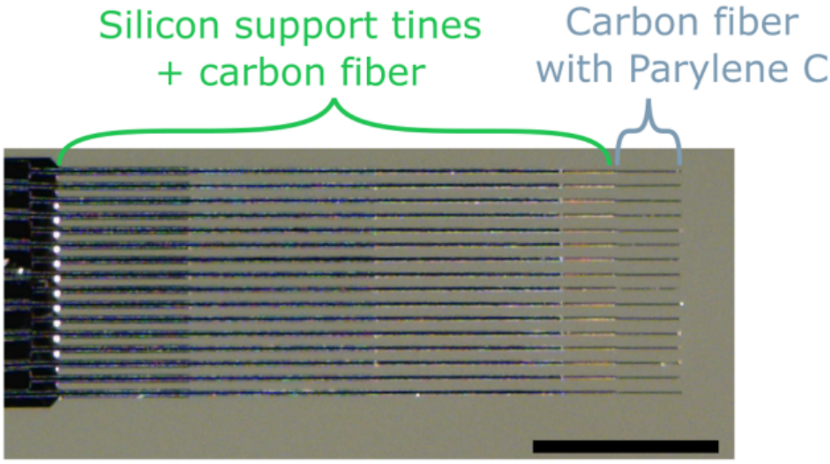

Figure 3: Subcellular High Density Carbon Fibers Electrode Array

3 Decoding algorithm

Before stimulating the upper limb with lost function, the device needs to interpret and decode the recorded signals. The decoding algorithm has to meet several requirements that are considered most important for patients. It must provide accurate output signals, be consistent over a long period of time and also have an effective response time. Another aspect of the recorded signals can be addressed by the decoding algorithm. Typical intracortical electrodes suffer from signal degradation over time due to small displacements caused by natural cortical movements. This forces patients to return to the clinic regularly to recalibrate the recorded signals. Although the subcellular carbon fibre electrodes aim to address this problem, we can fine-tune it by implementing automatic signal recalibration in the decoding algorithm.
The algorithm would need to process a large number of features to restore seven degrees of freedom. For practical reasons for the patient, the algorithm would also need to restore continuous movements to recreate more realistic movements, and should have independent control over both arms.

There are several different models in machine learning that could meet these requirements. However, deep neural networks have the ability to handle high feature dimensionality, capture the complex patterns needed to restore the seven degrees of freedom and allow multiple simultaneous movements of the upper limb with high accuracy [8].

Among the variety of different machine learning models, the use of recurrent neural networks (RNNs) is particularly well suited to the simultaneous control of bimanual movements. RNNs is designed for capturing the temporal dependencies of input signal characteristics, which is crucial given the non-linear structure of the neural code associated with time dependent movement kinematics. The study of Darrel R. Deo et al. published in 2024 [9] shows that RNNs can exploit a neural dimension of laterality to discriminate between left and right hand movements. This laterality dimension encodes information about which side of the body the movement is occurring on, independent of the direction of the movement. By altering the temporal structure of the training data by stretching and compressing it in time and reordering it, the study showed that RNNs could successfully generalise to online environments, allowing a paralysed person to control two computer cursors simultaneously.

Compared to linear regression models, RNNs offer superior performance in decoding complex, non-linear neural signals. The study was able to compute the firing rate vector within 300-700 ms after the go cue (time between start and execution), demonstrating that RNNs can achieve real-time decoding performance. Although the acquisition time (time taken for the neural signals to be recorded, processed, and transmitted) for linear regression models ranges from 4 to 10 seconds, RNNs trained with time-varying data showed improved control, resulting in faster and more accurate target acquisition. This improved performance highlights the potential of RNNs to facilitate high-quality bimanual control in brain-computer interfaces.

Another study published by Xuan Ma et al. in 2023 [10] demonstrated increased decoder stability using a variant of a Generative Adversarial Network (GAN), called a Cycle-Consistent Adversarial Network (Cycle-GAN), to counteract the signal decay caused by the turnover of recorded neurons. A GAN is a model that uses two networks: a generator trained to transform a source distribution into a target distribution, and a discriminator trained to determine whether a distribution is real or synthesised by the generator. Cycle-GAN introduces a mechanism called cycle consistency, which helps to regularise model performance by enforcing that the transformation between the source and target domains is invertible.

The study found that Cycle-GAN effectively aligns the distributions of neural recordings over time, maintaining the stability of intracortical brain-computer interfaces (iBCIs). Model analysis showed an inference time of less than 1 ms per 50 ms sample (1ms to process 50 ms each segment of neural data) for continuously recorded data, demonstrating its suitability for real-time applications. Furthermore, Cycle-GAN outperformed other alignment methods, such as Adversarial Domain Adaptation Network (ADAN) and Procrustes Alignment of Factors (PAF), in terms of robustness to hyperparameter settings and overall performance. These results highlight the potential of Cycle-GAN to significantly improve the long-term stability and accuracy of iBCI systems.

Considering these two promising solutions, the decoding module would contain two submodules, with first a pretrained cycle GAN model, which would perform an automatic signal recalibration of the recorded neuron signals, and passing these signals to the pretrained RNN, which calculates the input motor signals.

4 Stimulation device

The purpose of the proposed stimulation device is to attain sufficient selectivity to effectively restore at least five degrees of freedom, thereby facilitating the rehabilitation of upper limb and precise hand functions following a spinal cord injury. Restoration of hand movements can be achieved through the application of electrical stimulation at various points along the neuromaterial pathway, from the distal to the proximal ends, utilizing interfaces that vary in their degree of invasiveness. This exploration encompasses several techniques, each evaluated based on three pivotal criteria: the dexterity restored, the level of invasiveness, and the comfort during use. The following description of the strategies available for restoring limb movements is partially derived from the work of Losanno et al. [3].

A notable example is Surface Functional Electrical Stimulation (FES), which involves positioning large electrodes on the skin over the targeted muscles. This method allows for direct muscle stimulation from the surface, rendering it non-invasive, cost-effective, and straightforward to deploy. However, the dexterity achievable with Surface FES is somewhat limited, enabling only two types of grasps: lateral and palmar. Moreover, muscles are not ideally suited for direct electrode stimulation, which leads to rapid fatigue and diminished comfort during use. In contrast, Implanted FES addresses the issues of fatigue and limited mobility restoration by surgically inserting electrodes intramuscularly or onto the muscle epimysium. By targeting smaller, deeper muscles individually, this method enhances muscular selectivity and reduces fatigue. Nevertheless, its high invasiveness and the extensive, costly surgical procedures required for electrode implementation make it less favorable for widespread use.

Another promising technique is Spinal Cord Stimulation (SCS), which involves electrically stimulating the spinal cord at the cervical level using various electrode types such as transcutaneous, epidural, or intraspinal. This approach activates motor-neurons by engaging the primary sensory afferents within the dorsal columns and root, and has demonstrated significant success in restoring hand functions in non-human primates (NHPs) and tetraplegic patients. Like Surface FES, SCS suffers from relatively low selectivity, capable of restoring only a few types of grasps. However, it offers greater resistance to fatigue and a higher comfort level, with the potential for broader application given the non-invasive nature of transcutaneous SCS and the well-established surgical techniques for epidural SCS.

A final alternative, Peripheral Nerve Stimulation (PNS), directly stimulates nerves above their bifurcations. Due to the somatotopy of the nervous system, a single nerve electrode can trigger multiple muscles by individually accessing motoneuron populations. This results in extremely high selectivity in muscle recruitment, thus restoring a wide range of hand and finger movements and achieving the desired degrees of freedom. The comfort level of PNS is notably high. Specifically, intrafascicular PNS provides similar dexterity to implanted FES but with a higher deployment potential, as it requires fewer electrodes. The procedure is less costly, and the simplified cabling due to fewer electrodes adds to its appeal.

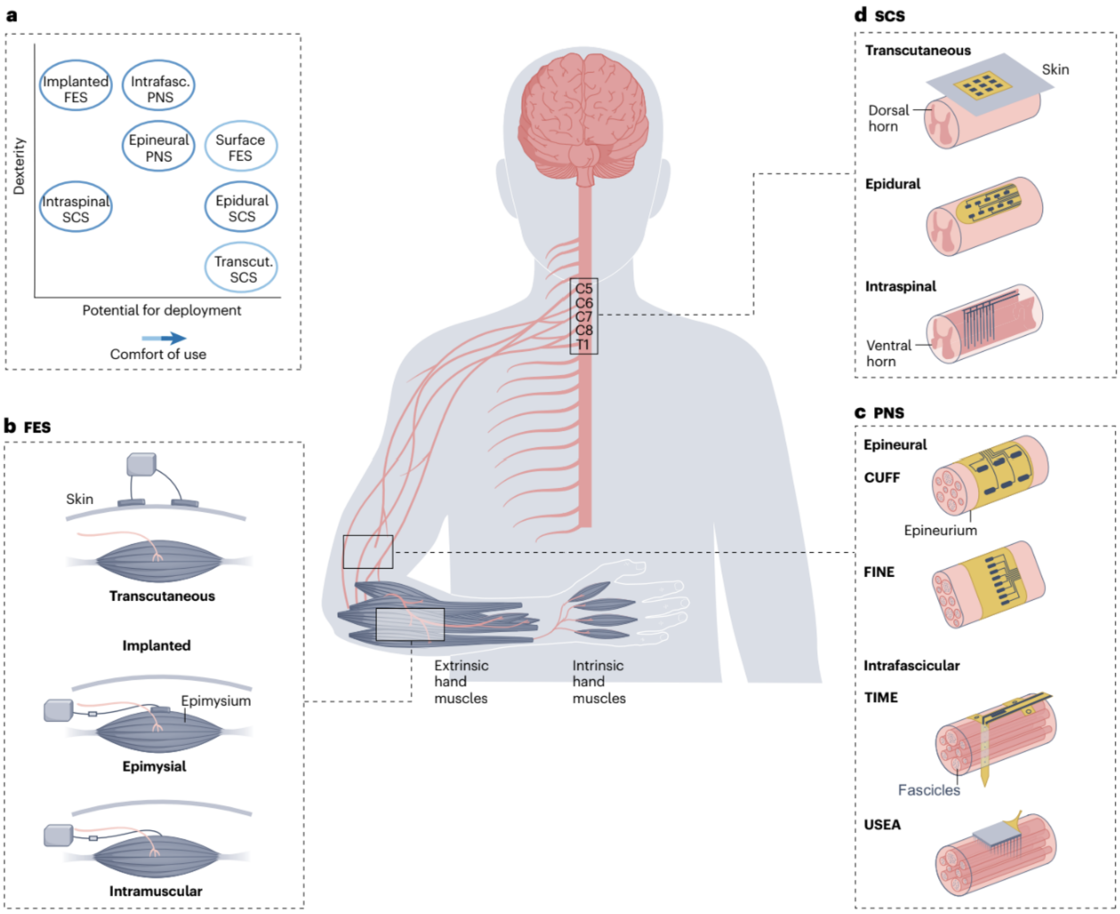

Figure 4: Neurotechnologies to restore hand functions

Studies in NHPs have shown that intrafascicular TIMES (Transcutaneous Implantable Muscle Electrode) electrodes positioned two centimeters above the elbow lead to optimal muscle recruitment, selectively activating more muscles than other techniques such as epidural CUFF and FINE electrodes [11]. Implanting the electrodes at this specific location results in the most selective muscle activation, without additional gains from altering the position slightly up or down the limb. Given the consistency in anatomical features between monkeys, these findings are likely applicable to humans as well. Therefore, for this project, we will adopt intrafascicular TIMES electrodes, implementing them two centimeters above the elbow of the patient to maximize selective muscle recruitment and enhance functional recovery.

To achieve a considerable range of motion and the highest possible selectivity in muscle recruitment, we have employed the STIMEP wearable neural stimulator system [12]. This innovative device was developed by the CAMIN team at the University of Montpellier, in collaboration with Axonic company. The system includes a central controller (SOC device) that orchestrates the operation of four distributed stimulation units (DSUs). These units are capable of independently driving up to four TIME devices simultaneously, enhancing spatial selectivity in motor fiber recruitment and consequently improving arm mobility. For configuring and operating the STIMEP controller, we utilize the SYNERGY software. This software enables the creation of complex stimulation patterns through precise adjustments of stimulation parameters and waveforms across multiple independent channels. The decoding algorithm, detailed in the Decoding Algorithm section, processes neural signals and transmits relevant control signals to the SYNERGY software. This setup allows the software to effectively manage the STIMEP controller, which in turn controls the TIMES electrodes to restore upper limb mobility. Tests on rodents have demonstrated promising outcomes with the STIMEP controller. By reducing the pulse duration to 20 microseconds, the selectivity of stimulation is significantly enhanced, allowing for more precise muscle activation. Furthermore, using biphasic pulses with short pulse widths (approximately 20 microseconds) and a 100-microsecond interphase delay provides the optimal modulation of muscle activity, thereby improving the selectivity and effectiveness of the stimulation. This methodological refinement contributes to the overall success of the system in achieving fine motor control.

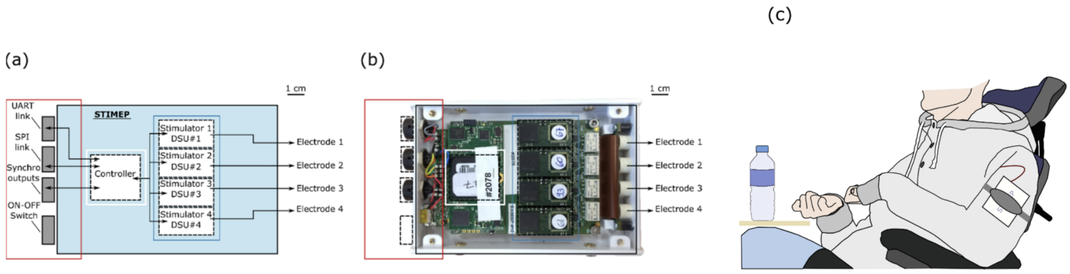

Figure 5: (a) Diagram of STIMEP hardware and (b) picture of the corresponding device at the same scale. (c) Restoration of upper limb movements in individuals with spinal cord injury using TIMES electrodes and STIMEP neurostimulator

5 Sensory restoration

5.1 Sensory Restoration: Motivations and Objectives

The restoration of sensory function, particularly tactile sensation and proprioception, is a crucial aspect of rehabilitation for individuals with spinal cord injuries (SCI). Sensory feedback is essential for enhancing motor control, improving the safety and efficiency of movement, and ultimately, for restoring a sense of normalcy in daily activities.

5.1.1 Motivations

One of the primary motivations for sensory restoration is the improvement of movement planning and control. Tactile sensations and proprioception provide critical feedback that helps individuals coordinate their movements more effectively allowing for more precise adjustments during tasks, reducing the likelihood of errors and enhancing the fluidity of motion. As highlighted in Flesher et al. (2021), incorporating tactile feedback into brain-computer interface (BCI) systems significantly improved the performance of a person with tetraplegia in manipulating objects with a robotic limb: reuslts in the study demonstrated that trial times on a clinical upper-limb assessment were reduced by half, from a median time of 20.9 seconds to 10.2 seconds, with a significant improvement in time spent attempting to grasp objects [13].

Additionally, sensory restoration is vital for ensuring safety during interactions with the environment. Nociception, or the ability to perceive pain, is necessary to prevent accidents and avoid limb damage. Without sensory feedback, individuals are at a higher risk of unknowingly causing injury to themselves, as they cannot feel and react quickly to potentially harmful stimuli such as temperature or sharp objects.

5.1.2 Objectives

The objectives of sensory restoration in the context of SCI are twofold. First, it aims to evoke tactile sensations with magnitudes sufficient for everyday object manipulations. Specifically, this involves generating tactile feedback that can be perceived with enough intensity and clarity to aid in performing daily tasks, such as holding utensils or handling fragile items. As already mentioned it has been shown that the artificial tactile feedback, created through intracortical microstimulation (ICMS) of the somatosensory cortex, enabled the participant to perform functional tasks at speeds comparable to able-bodied individuals. The presence of these tactile sensations allowed for more confident and accurate movements, significantly enhancing task performance [13] and, in the context of our project, improving the quality of life of our patients.

Second, the objective is to achieve sufficient discriminable levels of force to enable precise control. Research indicates that healthy individuals can distinguish approximately 50 levels of force applied by their fingers, a critical aspect for precise motor tasks [14]. Moreover, it is essential to evoke tactile sensations with forces on the order of newtons to facilitate everyday object manipulations [14] and enable tasks that require delicate handling and precise force application, such as typing or using tools.

5.2 Sensory Restoration: Challenges

Several options were considered for achieving sensory restoration, including Peripheral Nerve Stimulation (PNS), transcutaneous Spinal Cord Stimulation (tSCS), and Sensory Cortex Stimulation (SCS). Ultimately, Sensory Cortex Stimulation (SCS) was chosen as the most viable method.

Based on our review of the available research, particularly from Letner et. Al (2023) [6], we found that the results for tSCS were not satisfactory in providing consistent and effective sensory feedback due to significant limitations in the efficacy and reliability of tSCS for sensory restoration in SCI patients with little to no functionality remaining.

Furthermore, Peripheral Nerve Stimulation (PNS) was deemed unfeasible because the sensory signals from the Peripheral Nervous System could not effectively reach the brain due to the disruption caused by the spinal cord injury, making PNS an impractical solution for our objectives.

In contrast, Sensory Cortex Stimulation demonstrated more promising results. SCS directly targets the sensory cortex, bypassing the damaged spinal pathways and providing a more direct method of restoring sensory feedback. This approach has shown great potential in animal and pre-clinical studies for re-establishing sensory perception for individuals with SCI [14], [15] but remains non-ideal as several concerns, chief among them the invasiveness of the method, need to be addressed in order to propose an effective and feasible solution.

5.2.1 Stability

One of the primary challenges is the stability of intracortical microstimulation (ICMS) devices over time. Current IC microstimulators often exhibit issues with consistency, as their performance can degrade, leading to unreliable sensory feedback. This instability is primarily due to the biological responses to the implanted devices, such as tissue encapsulation and electrode degradation, which can alter the electrical properties and reduce the effectiveness of stimulation over time [16]. Research by Armenta Salas et al. (2018) demonstrated that maintaining a stable tissue-electrode interface is critical for the long-term functionality of these devices, with more flexible electrodes able to integrate more seamlessly with neural tissue, significantly improves their chronic stability and performance [16].

5.2.2 Selectivity

Another critical challenge is the selectivity of stimulation. Precisely targeting specific neurons to evoke distinct sensations without causing overlap or unintended stimulation of adjacent areas is difficult. The somatosensory cortex is highly organized, and the ability to selectively stimulate neurons within this complex structure is paramount. Studies have shown that spatial selectivity can be influenced by the current amplitude and the physical spacing of electrodes: For instance, at lower currents, spatial selectivity is higher, allowing for more precise targeting of neural populations. However, as the current increases, selectivity decreases, which can lead to the activation of unintended neurons [16]. Achieving greater selectivity is essential for differentiating between various sensory modalities and ensuring that sensations are spatially accurate and naturalistic [16].

5.2.3 Invasiveness

The invasiveness of ICMS devices poses another significant challenge. The process of implanting these devices can lead to scarring and infection, which not only affects the health of the patient but also impacts the performance of the device. Inflammation and glial scarring can insulate the electrodes from the surrounding neural tissue, thereby increasing the stimulation thresholds and reducing the effectiveness of the sensory feedback [16]. Advances in the design of electrodes, such as the use of ultraflexible materials that minimize tissue damage and promote better integration with neural tissue, have shown promise in mitigating these issues. Studies have indicated that reducing the mechanical mismatch between the electrode and the brain tissue can significantly decrease the adverse biological responses, leading to improved long-term stability and functionality [16].

5.2.4 Responses Evoked in the Motor Cortex by Stimulation in the Sensory Cortex

Stimulation of the somatosensory cortex (S1) can evoke responses in the motor cortex (M1), highlighting the intricate connectivity between these regions. Intracortical microstimulation (ICMS) in S1 has been shown to modulate the activity of M1 neurons. For example, ICMS pulse trains delivered through individual electrodes in S1 can lead to both increases and decreases in the activity of M1 channels, depending on the stimulation channel used [17]. This modulation varies significantly across different participants, with some showing primarily excitatory responses and others a mix of excitatory and inhibitory responses.

The temporal characteristics of these responses suggest that some of the ICMS-evoked activation in M1 is directly linked to S1 stimulation, with short latencies consistent with monosynaptic connections. Specifically, responses in M1 can occur between 2 to 6 milliseconds after the onset of the stimulation pulse, indicating a direct, possibly monosynaptic, input from S1 [17]. However, most of the ICMS-evoked activity in M1 reflects more complex, indirect effects, likely involving polysynaptic pathways.

Spatially, the patterns of M1 activation evoked by S1 stimulation vary systematically depending on the location of the stimulating electrodes. Neighboring electrodes in S1 tend to produce more similar patterns of M1 activation compared to distant electrodes, which can produce entirely non-overlapping patterns. This spatial organization suggests a somatotopic relationship between S1 and M1, where stimulation of specific areas in S1 preferentially activates corresponding regions in M1 [17].

Moreover, the evoked responses in M1 are task-dependent. The magnitude and even the sign of the ICMS-induced modulation can vary depending on the task being performed, highlighting the context-dependent nature of sensorimotor integration. For instance, during different motor tasks, the patterns of M1 activation induced by S1 stimulation can change, reflecting the dynamic interplay between sensory inputs and motor outputs [17].

5.3 Our Solutions

The development and deployment of sensory restoration technologies face significant challenges, including stability, selectivity, and invasiveness: Addressing these issues is essential for achieving reliable and effective sensory feedback systems. Advances in flexible microelectrodes and biomimetic stimulation offer promising solutions.

5.3.1 Flexible Microelectrodes

One of the primary challenges in intracortical microstimulation (ICMS) devices is maintaining long-term stability. Flexible microelectrodes, such as the ultraflexible StimNETs [15], have shown significant promise in improving the stability of the tissue-electrode interface. The design of these electrodes minimizes the bending stiffness, providing tight integration with neural tissue. This close integration reduces the immune response, minimizing scarring and maintaining functionality over extended periods.

A study by Lycke et al. (2023) demonstrated that StimNETs, with a thickness of 1 micrometer and a cap ring thickness of 0.3 micrometers, remain seamlessly integrated with the nervous tissue throughout chronic stimulation periods. These electrodes exhibited stable, focal neuronal activation at low currents of 2 μA and maintained stable behavioral responses for over eight months at a low charge injection of 0.25 nC/phase. Histological analyses confirmed that chronic ICMS using StimNETs did not induce neuronal degeneration or glial scarring, highlighting the importance of tight tissue-electrode integration for long-lasting, high-resolution neuromodulation [15].

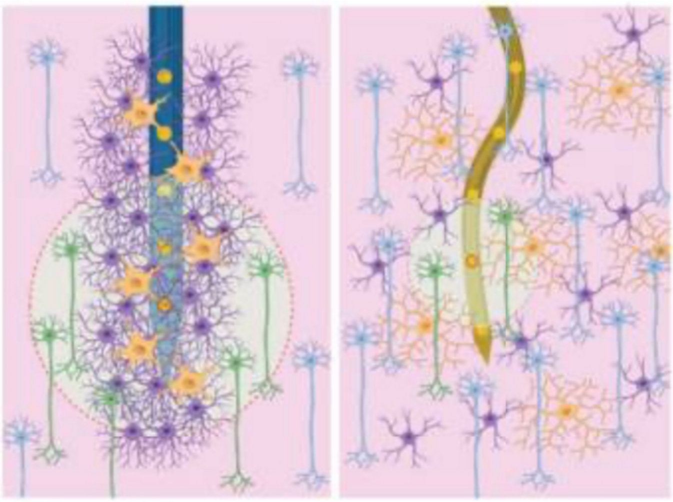

Figure 6: Demonstration of function of ultrathin StimNet electrodes: notice the reduced glial scarring and infection close to the insertion site.[15]

Additionally, the electrodes' ultraflexible nature allows them to closely interface with neural tissue, reducing the current spread and enabling more precise targeting of neurons. In the study by Lycke et al., simulations showed that reducing glial scar thickness around the electrodes significantly lowered the activation threshold, decreased the number of activated neurons at threshold, and improved the focality of neuronal activation. This improvement in selectivity was observed with thinner scars, demonstrating that closely spaced stimulation sites without scar encapsulation provided the most spatially distinct tissue activation compared to those with thicker scars [15].

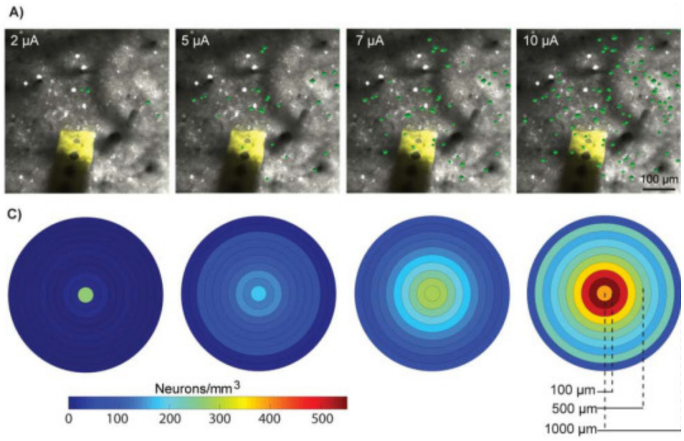

Figure 7: Spatial Selectivity achieved with ultraflexible microelectrodes StimNet [15]

5.3.2 Biomimetic Stimulation

Biomimetic stimulation involves creating sensory feedback that mimics natural touch patterns by augmenting stimulation during initial contact and object release phases, while reducing it during sustained contact. By replicating the dynamic nature of tactile interactions, biomimetic stimulation aims to provide a more naturalistic and intuitive sensory experience for the user while improving atthe same time the perceptual discrimination of force overall sensitivity.

A key aspect of biomimetic stimulation is its ability to reproduce the transient phases of object contact, such as the onset and offset of touch. This is crucial for accurately conveying the texture, shape, and firmness of objects, which are essential for performing delicate tasks that require fine motor skills. The study by Hughes et al. (2023) demonstrated that using biomimetic ICMS-based feedback significantly improved task performance by providing more precise and varied sensory inputs. This improvement was particularly evident in tasks requiring precise force modulation and dexterity, such as manipulating small objects or using tools.

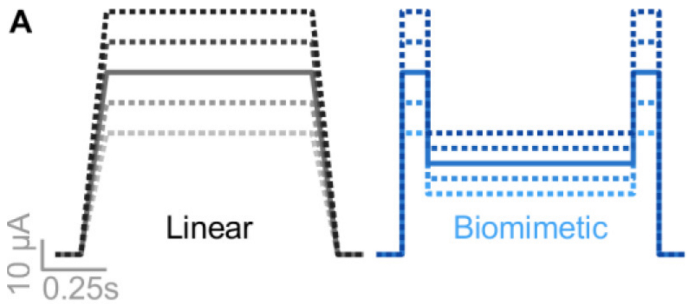

Figure 8: Biomimetic Stimulationn protocols: notice the increased stimulation amplitude (in μA) delivered at onset and end of touch

In addition to enhancing initial contact phases, biomimetic stimulation also reduces the need for sustained stimulation which can lead to sensory adaptation and fatigue, reducing over timethe effectiveness of sensory feedback. By emphasizing transient stimulation, biomimetic approaches help maintain high sensitivity and responsiveness, critical for continuous, real-time interaction with the environment.

Additionally, by utilizing multiple stimulation electrodes at the same time, biomimetic approaches can create more complex and varied tactile sensations, further enhancing the user's ability to discriminate between different textures and forces. This multi-channel approach is particularly beneficial for tasks that involve complex hand movements and require high levels of tactile acuity, as it allows us to restore as much as 40 out of 50 discriminable levels of force and to elicit sensations corresponding to the order of magnitude of Newtons [14], restoring a significant portion of healty daily functionalities in patients with SCI

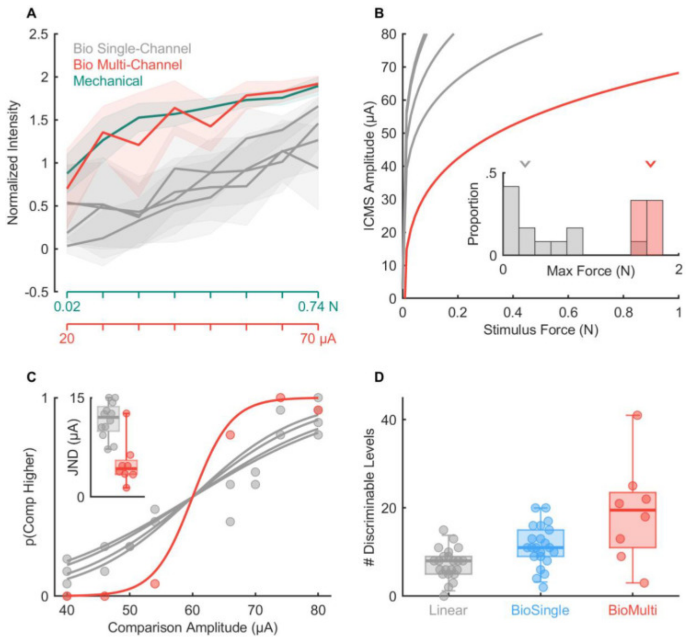

Figure 9: Restored Discriminable levels of force and Force magnitude through multichannel biomimetic stimulation, as shown in [14]

In conclusion, the combination of ultraflexible microelectrodes and biomimetic stimulation provides a promising approach to addressing the challenges of stability, selectivity, and invasiveness in sensory restoration technologies. Despite these solutions being still requiring extensive research (as we will mention in the following sections) biomimetic stimulation principles and ultraflexible electrodes represent the best way forward for developing prosthetic devices that offer more natural and effective interactions, bringing us closer to helping patients regain greater independence and functionality in their daily lives.

6 Power consumption and Battery Capacity

Our neuroprosthesis system aims to restore upper limb and hand/finger movements following spinal cord injury by integrating different modules and linking them together :
First, the recording module integrates intracortical implants on the primary motor area for motor recording. Then the decoding module [18] is integrated in a lightweight backpack providing the necessary computational power and autonomy for real-life applications. And finally, the stimulation module [12] integrates a controller and intrafascicular electrodes ensuring safe, comfortable, and selective motor restoration.

Following that, we did some power consumption and battery size and duration estimation to justify the linking between each module and the choice of the backpack. To do so, we used the following formula :

$$\text{Battery Capacity (mAh)} = \frac{P_{\text{total}} \times \text{Operating Time (hours)} \times 1000}{\text{Voltage (V)}} \tag{1}$$

In terms of power consumption, the recording module, which includes sub-cellular electrodes, a microcontroller, signal preconditioning, ADC, and amplifiers [19], consumes around 0.67W. Based on that value we chose the battery by considering the best operating time and battery size ratio. As this module is attached on the head, it should not be too big, that is why we chose the LiPo Battery which size is 2cm*3cm*4mm and offers approximately 3 hours of operation without a computer. The decoding module, featuring a deep neural network (DNN), consumes around 1W and should be able to last a long time without recharging, that is why we chose a 2162 mAh lithium polymer laptop battery which size is 15cm*7.7cm and provides around 8 hours of operation. Finally, the PNS module, comprising a STIMEP controller, stimulation units, and UART, consumes around 0.918W and operates on a 2000 mAh lithium-ion battery, also supporting 8 hours of use.

Despite these advancements, the system has certain limitations. First, the operating time of the recording module is relatively short, that is why we didn't choose a wireless solution for the communication between the recording module and the decoding module, but rather chose a solution with a cable that links the two module and help for the communication and battery lifetime performance.
Additionally, the computational power needed for real-time processing lead to the need of a large battery that integrated into a computer. The bulkiness of this component may impact seamless integration into everyday activities.

Following those limitations, potential improvements should include the optimization of power consumption across all modules for power saving and extending battery life. But also, miniaturizing the components and using flexible electronics could reduce the overall size and weight of the system. Finally, developing more efficient algorithms for real-time neural signal processing could reduce computational demands, thereby lowering power consumption and improving response times.
Addressing these limitations will be crucial for enhancing the functionality, comfort, and usability of the neuroprosthesis in real-world scenarios.

7 Translation into a Feasible Device for Clinical Testing

To translate our proposed solutions into a clinically testable device, we need to integrate the key components—recording electrodes, decoding algorithms, and stimulation devices—into a cohesive and practical system. This system must address several clinical challenges to ensure its feasibility, safety, and efficacy.

7.1 Recording Electrodes

In the future, wireless transmission could be considered to eliminate the need for cables within the brain to transmit information, thereby reducing the inflammatory response. Despite the invasiveness of the subcellular carbon fiber electrodes, the damage to the brain is quit limited compare to classical intracortical electrodes and have shown promising results. Furthermore, this approach has been successfully tested in rats and needs to be adapted for use in humans.

To assess the feasibility and effectiveness of wireless transmission for intracortical communication, we could propose a two-phase experimental study. A first phase would evaluate the performance and biocompatibility of wireless subcellular carbon fibre electrodes in a rat model. It would consist of implanting the electrodes in the motor cortex, establishing a wireless transmission protocol and monitoring neural activity, signal quality and transmission latency. The inflammatory response and tissue damage between wireless and traditional wired implants, long-term stability and motor control task performance would be assessed. The second phase would adapt this technology for preliminary human testing. This phase would involve designing human compatible electrodes, implanting them in volunteer participants and establishing a wireless communication protocol. Inflammatory responses, electrode stability, signal integrity and practicality in daily activities would be measured.

7.2 Decoding Algorithms

We propose a two-layer approach using a Cycle GAN for automatic signal recalibration and a Recurrent Neural Network (RNN) for decoding motor commands. To ensure real-time processing, the system needs to be optimised for computational efficiency. Despite promising preliminary results, the RNN acquisition time remains prohibitively long for practical implementation in patients' daily lives. However, with the rapid advances in low-power, high-performance embedded processors capable of running machine learning models in real time, this approach warrants further in-depth research to optimise accuracy and transmission time.

Although the Cycle-GAN has shown encouraging results in counteracting signal decay in monkeys, the RNN implementation in the referenced study remains preliminary. Further trials and research are needed to restore complex, continuous, simultaneous movements, as performance was assessed on the basis of patients controlling 2-D cursors on a screen.

To evaluate these solutions, an experiment could be conducted in which mechanical arms are simulated and controlled by the patient via the recorder/decoder unit. The aim would be to improve accuracy while reducing computational cost, and to optimise the model accordingly.

7.3 Stimulation Device

The primary challenge in translating our sensory restoration solutions into a clinically testable device lies in the extensive testing required on human subjects. For instance, Peripheral Nerve Stimulation (PNS) has only been tested on macaques so far, necessitating further validation through human trials. Similarly, the STIMEP device has been tested on rodents, but additional testing on both monkeys and humans will be required, demanding significant time and financial investment.

Despite these challenges, the results of PNS on monkeys have been highly promising, demonstrating high selectivity, low muscle fatigue, excellent comfort, and practicality. These attributes suggest that PNS could be highly effective in restoring upper limb movements in humans. However, the technique's invasiveness poses a significant concern, as it involves causing some nerve damage to implant the TIME electrode. This invasiveness is a trade-off necessary to achieve the high selectivity required for effective muscle control.

The integration of the decoding output from the wireless subcellular carbon fibre electrodes with the STIMEP device would need to be evaluated to ensure that a fully integrated system for sensory restoration is created. An experiment, first in macaques and then in humans, could be designed to assess the accuracy of the induced movements produced by the STIMEP device, given the decoder outputs for the hand, distal upper limb and full upper limb.

7.4 Sensory Restoration

The combination of ultraflexible microelectrodes and biomimetic stimulation provides a promising approach to address the challenges of stability, selectivity, and invasiveness in sensory restoration technologies.

The primary challenge in translating our sensory restoration solutions into a clinical device lies in the extensive testing required on human subjects. Initial trials with macaques and rodents, as descibed in [14] and [15], have shown promising results but further validation through human trials is necessary. This process demands significant time and financial investment, yet it is crucial for ensuring the safety and efficacy of these devices in a clinical setting.

The integration of decoding outputs from wireless subcellular carbon fiber electrodes with the sensory restoration device will also need to be assessed. Ensuring a fully integrated system that provides reliable sensory feedback is essential. An experiment, first conducted with macaques and then extended to humans, could be designed to assess the accuracy of induced sensations and movements facilitated by the device, focusing on the hand, distal upper limb, and full upper limb.

Of particular concern is the need to better quantify and clarify the relationship between the stimulation of the somatosensory cortex and the motor cortex. Future studies should focus on characterizing the specific parameters of ICMS-evoked responses in the motor cortex, including latency, amplitude, and spatial distribution. Investigating the underlying mechanisms of sensorimotor integration can help elucidate how sensory input is processed and translated into motor commands.

Developing adaptive algorithms that can modulate stimulation parameters in real-time based on feedback from motor cortex activity could enhance the precision and effectiveness of sensory feedback systems. Long-term studies to assess the stability and consistency of ICMS-evoked responses over extended periods are crucial for understanding how chronic use of these systems impacts neural plasticity and overall functionality.

7.5 General Overview and Limitations

As explained earlier, the device is not a finished product, but a collection of modular solutions that show promising results independently. Each module needs to be improved and tested before the fully integrated device can be tested. The final translation of the devices would need to be miniaturised, biocompatible, efficient and long lasting so that patients do not need to return to the clinic on a regular basis. The practicality of this solution is limited by the need to carry a backpack containing the computing unit and batteries. However, the modular design also allows the decoding, stimulation, sensory restoration and battery unit to be efficiently changed as better solutions or algorithms are found.

Each module would be a Class III risk under the European Medical Devices Regulation [20] because it contains invasive devices and softwares that can affect the central nervous system, active devices and software that can affect the central nervous system or are designed to be long-term active implants that can be dangerous to patients. Therefore, the translation of the devices would also need to include a quality management system along with the improvements made during the research and development to be able to obtain the approval of the regulatory authorities to start the clinical trials of the final product.

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