PRINCIPAL ACADEMIC TUTOR
Maurizio Magarini, DEIB, Politecnico di Milano

ACADEMIC TUTOR
Danilo Demarchi, DET, Politecnico di Torino

OTHER ACADEMIC TUTORS
Antonio Coviello, DEIB, Politecnico di MILANO
Paolo Motto Ros, DET, Politecnico di Torino

EXTERNAL INSTITUTIONS
Teoresi S.p.A.
San Gerardo Hospital (Monza)
University of Milano Bicocca
Imperial College London

EXTERNAL TUTOR
Marco Bazzani, Teoresi S.p.A.

TEAM MEMBERS

Federica Burinato
Biomedical Engineering, Politecnico di MILANO

Chiara Cavigliano
Biomedical Engineering, Politecnico di MILANO

Andrea Cerutti
Computer Science and Engineering, Politecnico di MILANO

Giulio Franceschini
Aeronautical Engineering, Politecnico di MILANO

Yeshua Giacalone
Mathematical Engineering, Politecnico di MILANO

Anna Simeone
Biomedical Engineering, Politecnico di MILANO

Virginia Tasso
Biomedical Engineering, Politecnico di MILANO

PNRelay

Executive summary

Peripheral nerve injuries (PNIs) interrupt the transmission of motor and sensory signals between the brain and body, causing both physical disability and severe psychological consequences. Patients with PNIs are eight times more likely to develop anxiety and depression, while the healthcare burden, including surgery, rehabilitation, and disability support, can exceed two million dollars per case. With incidence expected to rise due to aging populations and the growing prevalence of hypertension and diabetes, new therapeutic approaches are urgently needed.

Current treatments, such as autografting, restore function in only half of patients and are associated with significant complications, including infection, neuroma formation, and donor-site morbidity. Progress in clinical outcomes has been minimal over the last twenty-five years, underscoring the need for transformative solutions.

The PNRelay project proposes an innovative alternative: an implantable neural bypass designed to re-establish communication across the site of injury without harvesting healthy nerves. The device records neural activity proximal to the lesion, transmits the signals externally for real-time classification, and reinjects the appropriate stimulus distally, restoring purposeful movement and sensation. The project pipeline encompasses research, prototype development, animal testing, human trials, and eventual commercialization. During the first two phases, the team has already developed a proof-of-concept prototype, designed and optimized wireless powering systems, refined algorithms for real-time signal processing, and advanced mathematical models for axon-level simulations. This work has been accompanied by a thorough review of the state of the art, resulting in two publications. Collaborations with the University of Pavia are enabling the transition to in vivo validation, while future work will focus on the design of a human-suitable prototype and the expansion of the project into a start-up ecosystem.

If successful, PNRelay will offer a safe, effective, and scalable therapy for peripheral nerve injuries, restoring independence to millions of patients and reducing healthcare costs. It represents not only a technological innovation but also a concrete step toward the mission of Politecnico di Milano: advancing technology for humanity.

Key Words
Peripheral Nerve Injuries, Neural bypass, Electroneurographic signal classification, Implantable device

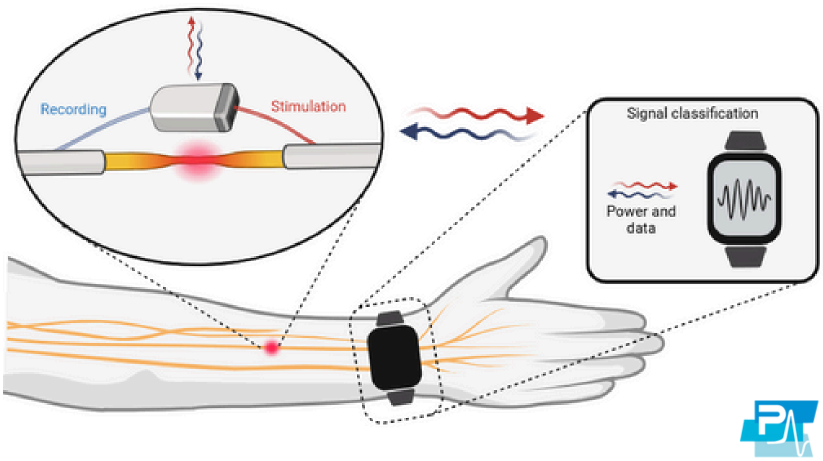

Fig. 1: Concept of the PNRelay system

The device bypasses the injury by recording, processing, and restoring nerve signals

Project description written by the Principal Academic Tutor

Peripheral neuropathies affect 2%–3% of the world population and seriously interfere with the quality of life. Among these, mechanical nerve injuries are frequent, occurring in about 2.8% of trauma patients. The nerve regeneration is usually unsatisfactory, especially after severe injuries.

So far, there is no technique to guarantee the total recovery and normalization of the nerve function, despite several possible procedures used, ranging from surgical (e.g., nerve grafting and conduit) to non-surgical interventions (e.g., medications, physiotherapy). New therapies are therefore mandatory based on new technologies that are able to (i) restore the nerve function; (ii) preserve the distal stump of the nerve; (iii) keep the denervated muscles functionally active; (iv) promote nerve regeneration.

Peripheral Nerve Interfaces (PNIs) are implantable devices used to monitor and modulate peripheral nerve (PN) activity. Most of the existing PNIs focus on the stimulation of the nerve to restore sensory feedback in assistive devices. Nowadays, PNIs integrating both stimulation and recording capabilities are not available due to the complexity of nerve injury physiology. By leveraging on multidisciplinary competencies, the "Peripheral Nerve Bypass Nanotechnology for Neuroprosthetic Applications" project has focused on the design of a fully implantable and highly compact neural interface to sense PN activity.

The main goal is that of developing a device implanted on an interrupted nerve to electrically connect and stimulate the proximal and distal portions via bidirectional (internal-external) communication with other sub systems. This device will prevent distal nerve stump degeneration and provide functional recovery. The main results achieved during the project are:

1. Development of machine learning-based classification algorithms to recover the information encoded in PN signals and translate them into actuation signals for neuroprostheses [1].
2. Definition of the experimental protocol to encapsulate an electronic implantable device with a biocompatible material.
3. Analysis and design of wireless/wired technologies to power the PNI.

The development of the implantable neural interface device has benefitted from the competencies of external institutions that are at the forefront in the creation of innovative neuro-technologies to enable the communication between the nervous system and electronic devices for research tools and medical devices and from Neurologist/Neurophysiologist to support an approach suitable to be transferred to a translational research setting, thus allowing for a quick clinical application.

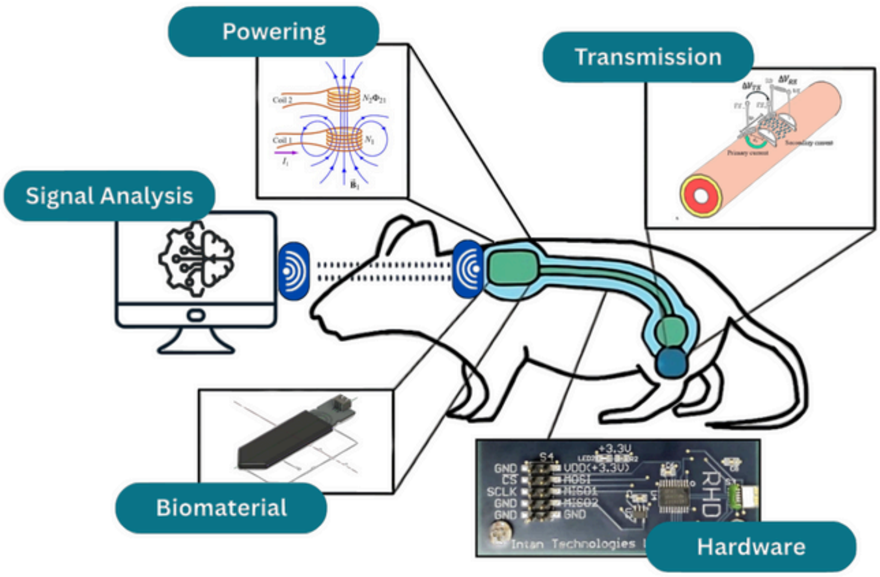

Fig. 2: Core areas of the PNRelay system

Overview of the key areas of the PNRelay system, illustrating the overall structure and main functional components.

Team description by skill

The PN Relay team is composed of 7 engineering students:
Federica Burinato is a Biomedical Engineering student at Politecnico di Milano. Her contribution to the project revolved around developing the power system for the device.
Chiara Cavigliano is a Biomedical Engineering student at Politecnico di Milano. She focused on simulating intrabody communication.
Andrea Cerutti is a Computer Science and Engineering student at Politecnico di Milano. He worked on the signal analysis pipeline for characterizing neural activity.
Giulio Franceschini is an Aeronautical Engineering student at Politecnico di Milano. He was responsible for developing the hardware for the device.
Yeshua Giacalone is a Mathematical Engineering student at Politecnico di Milano. His work involved mathematical simulations to model the nerve structure.
Anna Simeone is a Biomedical Engineering student at Politecnico di Milano. She focused on selecting suitable biomaterials for encapsulating the device.
Virginia Tasso is a Biomedical Engineering student at Politecnico di Milano. Her work centered around the signal analysis pipeline for characterizing neural activity.

Fig. 3: PNRelay team
The PNRelay team at Bardonecchia (TO)

The PNRelay project therefore, addresses the main technical challenges that limit current solutions and must be overcome to enable a functional neural bypass:

- **Biocompatibility and encapsulation**. The implant must remain safe and stable inside the body for extended periods. Encapsulation materials and geometries must minimize inflammatory reactions, prevent fluid infiltration, and protect sensitive electronics, while maintaining patient comfort.
- **Reliable powering**. The device requires a continuous energy supply that is both efficient and safe. Wireless powering avoids the drawbacks of wired connections but risks overheating surrounding tissue. Optimizing transfer efficiency through COMSOL simulations and wireless prototypes was essential to balance reliability with thermal safety.
- **Signal acquisition and processing**. Electroneurographic signals are extremely weak and easily corrupted by biological and instrumental noise. Robust preprocessing is necessary to preserve relevant features, while machine learning algorithms must achieve real-time decoding of intended movements with both speed and accuracy.
- **Electrode design and selectivity**. Electrodes must be minimally invasive yet capable of capturing meaningful neural information. Extraneural cuffs reduce surgical risks but offer poor resolution if not carefully optimized. Computational modeling guides the choice of materials, array geometry, and placement to maximize sensitivity and selectivity.

These challenges highlight the limitations of existing therapies and define the engineering hurdles PNRelay must overcome to deliver a safe and effective neural bypass.

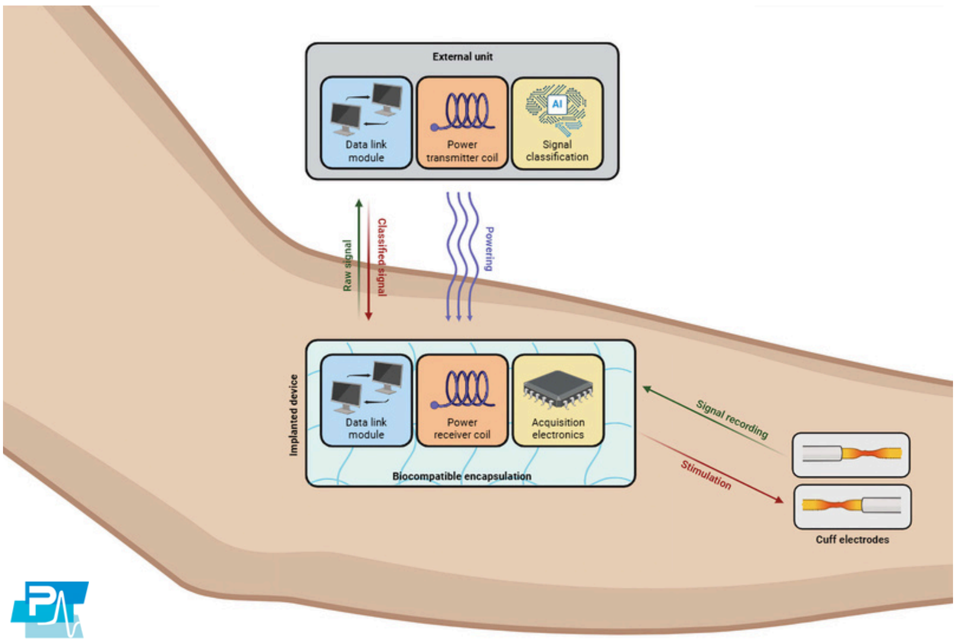

Fig. 4: Architecture of the PNRelay system
The implant records neural signals and receives wireless power, while the external unit classifies the data and sends back commands for stimulation.

Exploring the opportunities

To address the identified challenges, several technological alternatives were analyzed and compared. Each subsystem of the PNRelay device required balancing feasibility, performance, and long-term potential.

Electrodes. Extraneural cuffs were selected as the safest option in terms of invasiveness, but they present limited selectivity. Spiral and multi-contact geometries can improve resolution, at the cost of higher design complexity and manufacturing effort. Computational models were used to evaluate these trade-offs before physical prototyping.

Encapsulation. Literature points to silicone-based solutions. Commercial housings are robust and easy to use, but custom silicone cases provide better adaptability to anatomy. The main trade-off lies between reliability and flexibility.

Power transfer. Battery-powered and transcutaneous systems face challenges related to battery life and infections. Therefore, the most promising solution is wireless power transfer, particularly inductive coupling, which avoids the complications of wires and enhances patient comfort [4]. It's very efficient for short distances and safe for tissues; however, challenges remain in terms of tissue heating and data transfer rates.

Signal processing. Raw electroneurographic signals are noisy and require robust preprocessing [VIRGI]. Classical filtering approaches are simpler but risk losing relevant features. Machine learning classifiers, such as support vector machines and artificial neural networks, increase accuracy and speed but demand higher computational resources and careful optimization to be transferable across tasks and individuals.

System-level modelling. Full physiological simulations are accurate but computationally expensive. Mathematical models of axonal dynamics, though less detailed, allow faster exploration of design options and accelerate the iteration process.

Generating a solution

Our final solution was conceived as a functional neural bypass, designed to bridge the interruption caused by peripheral nerve injury and restore the flow of information between the central nervous system and peripheral effectors. The system is built around two complementary components: an implantable unit that directly interfaces with the nerve, and an external processor that provides advanced computation and flexible power management.

Neural activity is recorded upstream of the lesion through cuff electrodes connected to a custom acquisition chain. The signals, which are in the order of tens of microvolts and highly susceptible to interference, undergo amplification, digitization, and transfer to an external processor. Special attention was given to optimizing hardware filters and transmission protocols, ensuring that stable and reproducible recordings could be obtained even in challenging experimental conditions.

The external processor decodes neural patterns using a tailored machine learning and deep learning pipeline. Preprocessing includes noise reduction, outlier removal, and feature extraction, allowing classifiers to discriminate between multiple motor and sensory tasks with accuracy exceeding 90% in preliminary tests. Computational efficiency was also prioritized: algorithmic refinements yielded a significant reduction in latency, a key step toward achieving closed-loop control with end-to-end delays below 300 ms.

Safety and durability were addressed by focusing on encapsulation. Inspired by implantable clinical devices, we developed silicone-based coatings with controlled thickness and smooth geometry to minimize tissue irritation and fibrotic response. Candidate formulations were screened for permeability, mechanical compliance, and ease of processing, and mold-casting protocols were validated to guarantee uniform coverage and reproducibility.

Powering the implant posed another critical challenge. While wireless inductive coupling represents the long-term goal, simulations revealed limitations in efficiency and tissue heating for continuous operation. For preclinical validation, we focused on developing and testing a wireless cage prototype with multi-coil transmission. This approach ensured reliable operation during animal trials and provided a clear path toward clinical-grade wireless systems.

Electrode design was also optimized. Computational models confirmed that reducing electrode–nerve distance improves selectivity and sensitivity, whereas oversizing electrodes leads to loss of discriminative information. Multi-contact geometries emerged as the most promising solution to balance minimal invasiveness with rich spatial information.

Finally, mathematical modeling of axonal behavior supported experimental design, enabling the simulation of ionic currents and signal propagation at reduced computational cost. This modeling framework provides predictive insights and accelerates iteration cycles, complementing laboratory validation.
By integrating advances in bioelectronics, biomaterials, signal processing, power transfer, and computational modeling, PNRelay demonstrates a modular and realistic solution. The system not only records and analyzes neural activity but also establishes the foundation for restoring communication across damaged nerves. This constitutes a significant step toward preclinical trials and, ultimately, toward human translation.

Main bibliographic references

[1] Brunton, Emma, Christoph W. Blau, and Kianoush Nazarpour. "Separability of neural responses to standardised mechanical stimulation of limbs." Scientific reports 7.1 (2017): 11138.

[2] Coviello, Antonio, et al. "Emerging peripheral nerve injuries recovery: advanced nerve-cuff electrode model interface for implantable devices." 2024 Global Conference on Wireless and Optical Technologies (GCWOT). IEEE, 2024.

[3] Burinato, Federica, et al. "Advanced Implantable Devices and Data Analysis Techniques for Peripheral Nerve Injury Treatment: Challenges and Innovations." EAI BODYNETS 2024 (2024): 1-16.

[4] E. Marini, A. Coviello, and M. Magarini. Optimizing inductive link design for wireless power transfer to implanted medical devices in preclinical studies with comsol. In 2025 International Symposium on Medical Information and Communication Technology (ISMICT). IEEE, 2025.