



SpineRepair

HYBRID CMOS-POLYMER NEURAL INTERFACES FOR RESTORATION
OF SENSORIMOTOR FUNCTIONS AFTER SPINAL CORD INJURY



Prof. Stéphanie Lacour, EPFL



Prof. Grégoire Courtine,
EPFL



Prof. Andreas Hierle-
mann, ETHZ



Prof. Silvestro Micera,
EPFL



Dr. Alain-Serge Porret,
CSEM



Prof. Janos Vörös,
ETHZ

What it's about...

Developing a novel spinal cord (SC) neuroprosthesis by integrating soft tissue-like materials, implantable customized electronic hardware and SC stimulation protocols with robotic rehabilitation training to facilitate functional recovery after spinal cord injury.

Context and project goals

This project proposes to optimise, manufacture, assemble and validate a fundamentally different technology to produce an electrical stimulation neuroprosthetic system based on ultra-compliant microelectrode arrays, embedded low-power analog electronics and efficient telemetry unit.

We focus on a cutting-edge spinal cord neuroprosthesis designed to facilitate motor control and functional recovery in rats paralyzed after spinal cord injury. The spinal neuroprosthesis builds upon pioneering work from our group using a combination of robotic training, epidural electrical stimulation and monoamine agonists in rats to restore impressive locomotor capacities, provided the spinal cord injury spared a few cortical axonal projections.

Based on these exciting results, we propose to integrate an autonomous spinal neuroprosthesis with a high density of surface electrodes and embedded electronics that will allow for the definition and evaluation of unique electrical stimulation patterns thereby providing guidelines for adaptive stimulation strategies to restore, efficiently and durably, locomotion after spinal cord injury.

How it differentiates from similar projects in the field

The team is multidisciplinary, and has developed a solid and truly collaborative framework to engineer the spinal neuroprosthetic system.

The project gathers experts in neurotechnology, electronic hardware and telemetry, neural engineering and repair following spinal cord injury, all groups are at the forefront of their fields.

Quick summary of the project status and key results

The team has demonstrated the first biointegrated spinal implant capable of concurrent delivery of biochemical and electrical stimulation of the spinal cord, and so without damaging the underlying delicate tissue of the spinal cord. The implant, called electronic dura mater, matches mechanically the response of the native dura mater, the protective skin of the spinal and cord and the brain. The implant is so compliant that it was surgically positioned below the natural dura mater and enabled efficient neurostimulation of the spinal cord after weeks of implantation. Using e-dura, the SpineRepair team was able to restore leg motor control in paralyzed rats.

In view of the final spinal neuroprosthetic system, the team has also designed and tested the first generation of a customized CMOS chip to transmit, adjust and control precise stimulation patterns to the spinal implant electrodes. The new chip was also integrated with a telemetry unit. Upcoming experiments will aim at integrating the electronic hardware with the spinal electrode arrays.

Success stories

SpineRepair is an engineering project with a focused application to restore motor functions after spinal cord injury. The success of the project as a whole relies on the integration and communication of the team, which gathers material scientists, electrical engineers, bioengineers and neuroscientists.

A common vision and language has been established throughout the consortium, which will surely help to reach the ultimate goal: to implement and validate a wireless spinal cord neuroprosthesis in SC animal models.

Results from the SpineRepair team were presented in several conferences in talk or poster-formats, throughout the year.

Presence in the media

TEDGlobal, Edinburgh, June 2013

Le Monde, August 2013

CQFD, Radio-Télévision Suisse, March 2014

The “e-dura” paper was published in Science in January 2015. The publication demonstrated the empirical assumption that the biomechanical coupling between implants and host tissue is critical to achieve long-term bio-integration and reported on the restoration of locomotion in a paralyzed rat with our soft implant. The paper has received worldwide press coverage, both in the scientific community and general public. In particular, it has been featured in Nature Materials, Science, IEEE Spectrum, MRS Bulletin, NeuroNews, Spin Magazine, C&EN, RTS émission CQFD, Le Monde, Le Temps, BBC Worldnews and multiple radio interviews worldwide:

Nature Materials, 14, 267 (2015) doi:10.1038/nmat4235,
Bioelectronics: Soft implants for long-term use. Luigi Martiradonna

American Association for the Advancement of Science (AAAS),
Soft, Durable Implant Restores Movement in Paralyzed Rats, Jan. 2015.

Science, 347 (6218): 114 (2015), DOI:10.1126/science.347.6218.114
Bioelectronics: A soft approach kick-starts cybernetic implants.
Robert Service

Patents

- **Patent 1 by G. Courtine** (patent filed to EPO, MBP13367-EP)
“System to deliver adaptive electrical spinal cord stimulation to facilitate and restore locomotion after a neuromotor impairment”. The patent covers the description and therapeutic use of a closed-loop system for real-time control of epidural electrical stimulation after neuromotor disorders. The system spans the inter-connected devices required for online monitoring of motor performance, and the algorithms for adapting stimulation parameters in order to improve rehabilitation.
- **Patent 2 by SP Lacour, IR Minev** (patent filed to EPO in May 2014)
“Dry encapsulation method for electrode arrays”. The method enables the electrical passivation of electrode arrays with elastomeric dielectric films of arbitrary thickness. The passivation layer may contain circular (or any shape) openings at arbitrary locations for the purpose of creating vias or exposing active electrode sites.
- **Patent 3**
EPFL : Raspopovic Stanisa, Petrini Francesco Maria, Capogrosso Marco, Bonizzato Marco, Micera Silvestro
“Bidirectional limb neuro-prosthesis” P2670PCOP / 13-280 ar/ab
- **Patent 4**
I.R. Minev, A. Hirsch, P. Musienko, G. Courtine, S.P. Lacour.
Electronic Dural Mater for Recording and Modulation of Physiological Activities, filed 01.2015

Main publications

Capogrosso M, Wenger N, Raspopovic S, Musienko P, Beauparlant J, Bassi Luciani L, Courtine G and Micera S, A Computational Model for Epidural Electrical Stimulation of Spinal Sensorimotor Circuits, The Journal of Neuroscience, December 4, 2013 33(49): 19326-19340.

Wenger N*, Martin Moraud E*, Raspopovic S, Bonizzato M, DiGiovanna J, Musienko P, Morari M, Micera S* and Courtine G*, Closed-loop neuromodulation of spinal sensorimotor circuits controls refined locomotion after complete spinal cord injury., Science Translational Medicine, in press.

David Borton, Marco Bonizzato, Janine Beauparlant, Jack DiGiovanna, Eduardo M. Moraud, Nikolaus Wenger, Pavel Musienko, Ivan R. Minev, Stéphanie P. Lacour, José del R. Millán, Silvestro Micera, Grégoire Courtine, Corticospinal neuroprostheses to restore locomotion after spinal cord injury, Neuroscience Research, 2014, 78, 21-29.

Minev IR; Musienko P; Hirsch A; Barraud Q; Wenger N; Moraud EM; Gandar J; Capogrosso M; Milekovic T; Asboth L; Torres RF; Vachicouras N; Liu Q; Pavlova N; Duis S; Larmagnac A; Vörös J; Micera S; Suo Z; Courtine G; Lacour SP, Biomaterials. Electronic dura mater for long-term multimodal neural interfaces., Science. 2015 Jan 9;347(6218):159-63. doi: 10.1126/science.1260318..

Y. Tao, Y. Lian, A. Hierlemann, A Frequency-Domain Analysis of Latch Comparator Offset due to Load Capacitor Mismatch, IEEE Transactions on Circuits and Systems II: Express Briefs, June 2015 62(6), 527-532..

Flurin Stauffer, Vincent Martinez, Mohammed O. Adagunodo, Csaba Forro, Janos Vörös, Alexandre Larmagnac, Stretchable Silver Nanowire–Elastomer Composite Microelectrodes with Tailored Electrical Properties, ACS Applied Materials & Interfaces, 2015, 7, 13467-13475..

Minev IR; Wenger N; Courtine G; Lacour SP, Platinum-elastomer mesocomposite as neural electrode coating, Applied Physics Letters Materials 3, 014701 (2015); doi: 10.1063/1.4906502.

“High-performance spinal cord neuroprosthesis
for restoration of locomotion after spinal cord injury”