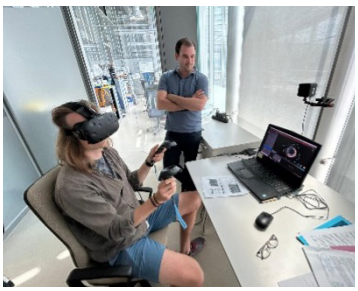
ReWIRE Newsletter

Welcome to the fourth edition of the ReWIRE Newsletter!

The ReWIRE Suisse Workshop and Network Meeting took place from July 2–5, 2024, hosted by our partners at EPFL and CHUV. The three-day workshop featured inspiring talks and activities centered around electrical stimulation and rehabilitation, aiming to establish new neuronal circuits essential for functional recovery. The first two days were packed with engaging presentations by leading experts: Nako Nakatsuka: Insights into biosensors, Nicholas James: Neuroprosthetics for restoring upper limb function, Mark Anderson: Regenerative therapies, Stephanie Lacour: Soft biotechnological interfaces. The sessions also featured an engaging discussion led by Nico Vachicouras, exploring the challenges and opportunities of launching a startup. In addition to the talks, participants experienced lab tours and hands-on activities organized by Vi Anh and her team, learning about tissue clearing methods, imaging, and data analysis. After the busy schedules, participants took the opportunity to relax and enjoy the Swiss sun and lakeside.

On the third day, the DCs and PIs gathered at CHUV for their Network Meeting, where members presented project updates. This exchange of ideas and knowledge fostered collaboration and innovation. Additionally, the DCs participated in an online meeting with Mattia Zilli, the REA Project Officer, to discuss current challenges and unresolved questions. The final day began with a visit to the .NeuroRestore Clinical Division, offering participants valuable insights into the clinical experiences of SCI patients. Later, interactive demos were hosted by Bianca and her team, focusing on brain decoding, stimulation technologies, lower and upper limb rehabilitation. The DCs expressed their heartfelt gratitude to the organizers for creating such an enriching and enjoyable experience in Switzerland.



Let's find out how the individual projects are progressing!

Jace Vu managed to form interlinked-microgels scaffolds under certain conditions. The PEG-VS and PEG-SH microgels made via microfluidics could now form a semi-stable structure in the presence of the activated Factor XIII, however, challenges remain as alignment was not seen as noticeably with these microgels. Preliminary cell studies on the IKVAV-functionalized scaffold show both the fibroblasts and DRGs did not spread on these microgels. His future research will focus on increasing the aligning ability of these microgels and the biocompatibility of the scaffold with other cell-adhesive peptide sequences. **Elif Onsoz** conducted in vitro studies to evaluate the PMMA and biodegradable variants of the mechanical microconnector system (mMS+). Results show epithelial stem cells successfully migrate through the mMS structure and proliferate beneath it, demonstrating that both materials are biocompatible and support cell viability without eliciting cytotoxic responses. She scheduled a mock surgical procedure to assess the mechanical and structural compatibility of the mMS for implantation in the rat spinal cord, serving as a preparatory step toward in vivo experimentation. **Catarina Tavares** has synthesized Poly (N -acryloyl glycinamide) microgels using microfluidics and in-tube free-radical polymerization techniques while incorporating various co-monomers, such as methyl methacrylate, and adjusting monomer ratios to fine-tune their thermoresponsive behavior. These microgels were then characterized at different temperatures to evaluate their swelling capacity in PBS. Additionally, other stimuli-responsive strategies for on-demand cargo delivery are under investigation, including the development of hollow microgel systems produced via microfluidics with an optimized polymer shell designed for degradation via lipase-sensitive thiol-ene chemistry. **Alessandro Ippoliti** improved the fabrication procedure for the molded mMS by integrating an SLE rapid prototyping technology in the existing setup. This technique is used to fabricate the initial pre-master, previously made through more-time consuming silicon microfabrication techniques, thereby facilitating the future optimization of mMS design. Finally, he delivered the first batch of mMS samples to DWI for compatibility testing.

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Simay Geniscan attended the International Spinal Cord Injury School in Zurich in July, where she connected with pioneers in the field and introduced the ReWIRE program. She conducted in vitro studies with Cerebral Granule Neuron cultures to establish a mitochondrial dysfunction model. This work is enhancing her understanding of the intrinsic mechanisms that impact successful neural regeneration. **Vi Anh Nguyen** extended her study by collaborating with an additional neurorehabilitation group to validate and complete their findings. They replicated the Vsx2 experiments, this time targeting PV, Vglut2, and Vgat neuron populations, with promising results indicating differential involvement in micturition reflexes. She initiated a similar protocol for Chat neurons, with these experiments currently in progress. This multi-population approach aims to further clarify the local neural circuitry underpinning EES-mediated bladder function restoration after spinal cord injury. **Firman Isma Serdana** is starting his first first-in-human clinical trial aimed at validating Intrafascicular Peripheral Stimulation (IS) with Thin-film Intrafascicular Multielectrode Arrays (TIMEs) in the median and radial nerves of tetraplegic patients. This study seeks to restore fine hand manipulation through low-dimensional voluntary control. To complement IS with naturalistic control, they are also benchmarking and optimizing decoding strategies for hand kinematics from intracortical signals using non-human primate data. He presented his preliminary results at Neuroscience 2024 in Chicago, IL, USA, in a nanosymposium, with a follow-up article in preparation for publication. Clinical trials were conducted to identify real-time hand kinematics intentions in incomplete tetraplegics using residual electromyography (EMG). They employed both cost-effective, non-invasive bipolar EMG and a Medium Density-EMG sleeve. **Carlo Carraro** has been developing an innovative patient-controlled device to enhance Epidural Electrical Stimulation (EES)-supported mobility. This device will empower patients with finer, more precise control over EES and features a novel method for modulating stimulation amplitude, encouraging more natural and physiological movements. His work also focuses on clonus, a neurological condition linked to spinal cord injuries that causes involuntary, rhythmic muscle contractions. He is investigating how EES combined with orthotic devices can be used to alleviate this challenging condition. **Bianca Yu** has begun work on transcutaneous spinal cord stimulation (TSCS). She will soon conduct a study in healthy participants to better understand the TSCS stimulation parameters that yield the highest recruitment selectivity of the upper-limb muscles. She also presented at the International Conference of NeuroRehabilitation in Segovia, Spain on her previous work involving computer modeling and simulation of electrode leads for optimization of recruitment selectivity with EES. She will incorporate this computational pipeline into her upcoming TSCS study to further investigate the relationship between stimulation parameters and resultant muscle activity. **Scott Andrew Erickson** focused his work on promoting axon extension and controlling cell migration through the use of surface treatments and inhibitors, in order to help generate a spinal cord injury model. Additionally, he evaluates the electrophysiological via microelectrode array recordings and calcium imaging. **Navami Prabhakar Koyande** has used the previously established CLIPSTM cyclization process on solid phase to examine peptide libraries with different peptide sequences, isomers, and protecting groups. Optimization of the protocol for high-throughput CLIPS cyclisation is currently ongoing. She completed a quick training of the phage display. Next, she is planning to utilize phage display to find laminin and IL-6 mimics that attach to integrin and IL-6 receptors. The ability of these peptides to bind to their particular receptors will then be examined in vitro. Further with GCI technology, the affinity strength binding will be studied. Lastly, they will be combined with biomaterials in order to assess their efficacy in both in vitro and in vivo spinal cord regeneration. **Paula Holban** has conducted cellular studies on different UPy-peptide systems that she previously synthesized. For this purpose, she used two different types of cells, SH-SY5Y and Neural Stem Cells (NSCs) that she derived from iPSCs, that she seeded on UPy-peptide based coatings. In order to quantify the neuronal differentiation of these cells treated with different bioactive moieties, she used flow cytometry and confocal microscopy. She studied the assembly of these molecules in solution, using circular dichroism (CD) and as a dried coating using atomic force microscopy (AFM). She presented her work at the Macromolecular Chemistry and Soft Matter Connects Symposium at DWI and at the NBTE Conference. Also, she pitched her research and introduced the ReWIRE project at the Great Small Talk organized at TU/e by the Smart Biomaterials Consortium. **Miklovana Tuci** is currently working on an in silico evaluation of identified historic controls within the NISCI trial scenario, demonstrating this concept for practical application in clinical trials. Additionally, she is developing algorithms that integrate different data modalities, such as ISNCSCI assessment, electrophysiology, etc, to provide a more comprehensive characterization of SCI severity and recovery prediction. **Rui Chen** has developed a prototype of a novel soft pneumatic actuator, which has been applied to a soft elbow flexion exoskeleton (exosuit). Preliminary experimental results demonstrate that the exosuit can effectively reduce muscle activation for users, indicating its potential in assistive and rehabilitation applications. The next phase of research will involve further testing of the exosuit and the development of a soft glove designed to assist patients in flexing and extending their fingers.

Looking ahead: Midterm Meeting and Workshop in January 2025

We are excited to announce that the next Midterm Meeting and Workshop is scheduled for January 2025 and will be hosted by Biosynth in Lelystad, the Netherlands. The DCs will provide detailed updates on their projects and results. The REA Project Officer will be present and an external expert from GOLIN Science Management will conduct a specialized training session.

Stay tuned for more updates!

Written by Paula Holban

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