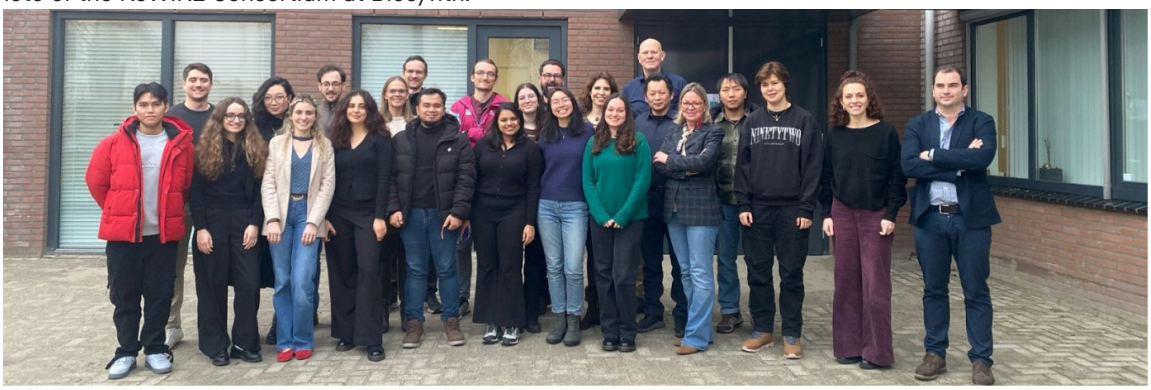
ReWIRE Newsletter

Welcome to the fifth edition of the ReWIRE Newsletter!

The ReWIRE Workshop and MidTerm Meeting took place from January 21-23, 2025, hosted by our partner Biosynth in Lelystad, the Netherlands. The two-day workshop was centered around communication and presentation skills in the academic context and it was held by Amanda Habbershaw from Golin Science Management. During this training, the Doctoral candidates (DCs) learnt the basics of effective communication and presentation, audience orientation, and how to deal with challenging situations. One engaging activity they undertook was learning how to communicate and tailor their scientific message for a different target audience. They also learned 12 fundamentals that lead to a successful presentation, covering tricks on how to attract attention with an introduction and how to communicate with the body. They ended the workshop with a nice dinner between DCs and PIs.

The Midterm Meeting was a great opportunity for the DCs to discuss their experiences within the network with the assigned project officer accompanied by a scientific expert. They addressed important topics including training foreseen, supervision arrangements, progress and secondments. They also presented a short research update implementing the skills they learned earlier in the workshop. The DCs expressed their gratitude to the organizers for creating such an informative and enjoyable experience in the Netherlands.

Here is a photo of the ReWIRE Consortium at Biosynth:



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

Simay Geniscan published her first-author paper titled "Enhancing neural stem cell integration in the injured spinal cord through targeted PTEN modulation", marking a significant milestone in her research journey. She visited the Joost Verhaagen lab at the Netherlands Institute for Neuroscience and gained hands-on experience in the production of AAV and lentiviral vectors. She presented her project and introduced the ReWIRE program to the team, fostering valuable scientific exchange. She is actively involved in communication activities, sharing updates about her research through presentations and networking at King's College London. Excitingly, her current project is advancing well, with promising preliminary data emerging from tests on two newly developed viral vectors and drugs that were screened in vitro. **Catarina Tavares'** work continued with the optimization of thermoresponsive poly(N-acryloyl glycinamide) (PNAGA) microgel's network (diameter 50-70 µm) by adjusting the concentration of NAGA monomers and crosslinker. Size-selective encapsulation was possible, enabling the microgels to carry a range of therapeutic agents depending on their molecular size. The swelling of the microgels and the diffusion of different-sized FITC-Dextran molecules into them, used to simulate potential therapeutic molecules, were tested at both room temperature (20°C) and body temperature (37°C). This helped identify conditions suitable for encapsulation at room temperature and release of the microgel's contents once inside the body. As part of another research project, the production of PEG capsules and shell porosity was optimized for future works where the core of the capsules would encapsulate FGF2 and RNA with a FGF2 binding sequence. **Rui Chen** has been focusing on the research of a rehabilitation glove and has developed a prototype of a customized, lightweight, and flexible soft glove. Preliminary experiments on healthy subjects have demonstrated the glove can effectively reduce muscle activity during flexion. This work has been accepted by the IEEE International Conference on Rehabilitation Robotics (ICORR) 2025 and was presented as a poster. **Scott Erickson** has been focusing on controlling axonal outgrowth by using different biomaterials and coating strategies, including the use of a bioprinter. Additionally, he has been working on optimizing electrical stimulation parameters to modulate neuron activity on the device. He recently presented his progress at the Tissue Engineering and Regenerative Medicine (TERMIS) conference in Freiburg, Germany. **Carlo Carraro** has developed an innovative, patient-controlled device designed to enhance mobility supported by Epidural Electrical Stimulation (EES). These devices were co-designed in close collaboration with participants to address specific user needs and have already been successfully tested with participants. They are now ready for inclusion in upcoming clinical trials. Carlo has been working on the development of a neuromuscular model to investigate clonus in individuals with SCI and to explore how EES can be used to suppress it. He has designed an orthotic assistive device to collect valuable anatomical data and help patients to improve their balance that has been successfully tested with a subject. **Alessandro Ippoliti** explored the use of a new bioresorbable PCL-based resin for the two-photon polymerization (2PP) of the mMS, and prototypes are currently being printed. After he reviewed the literature, a silk fibroin composite with tungsten nanoparticles as conductive fillers has been

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identified as a promising composite for electrode integration through Direct Ink Writing (DIW). **Bianca Yu** is running two studies focused on cervical spinal cord stimulation for upper-limb muscle recruitment. First, she is working with the current patient with tetraplegia in the UP2 clinical trial for brain-controlled epidural electrical stimulation (EES) used during rehab. So far, the patient has recovered strength in the muscles of the right arm and has learned to use the system for effective rehab. Second, she has recruited 5 participants for a study investigating transcutaneous spinal cord stimulation (TSCS) in healthy participants. Each stimulation session tests a variety of protocols in order to map stimulation parameters to muscle recruitment. She is excited to share that patients in the UP2 clinical trial were recently featured in a segment on the television show 60 Minutes. The feature discusses the lab's progress on using brain-controlled EES for restoration of voluntary movement after paralysis due to SCI. **Firman Serdana** initiated his first first-in-human clinical trial aimed at validating Peripheral Nerve Stimulation (PNS) with Transverse Intrafascicular Multichannel Electrodes (TIMEs) in the median and radial nerves of tetraplegic patients. This study seeks to restore fine hand manipulation through low-dimensional voluntary control based on residual body movements. The results on the first clinical trial are to be published with the next clinical trial to be conducted this year (1). To complement PNS with naturalistic control, they are also benchmarking and optimizing decoding strategies for hand kinematics from intracortical signals using non-human primate (NHP) data. Preliminary results were presented in a nanosymposium at the Society for Neuroscience (SfN) Meeting 2024 in Chicago (IL, USA), and a follow-up article is in preparation for publication (2). In parallel, clinical experiments were conducted to decode hand motor intentions in incomplete tetraplegics using residual forearm electromyography (EMG). Initial results were showcased in poster form at the FENS Forum 2024 in Vienna and at the SfN Meeting 2024 in Chicago, USA. **Elif Onsoz** extended in vitro testing of the mechanical microconnector system (mMS+) to dissociated dorsal root ganglion (DRG) neurons. Both PMMA and biodegradable versions supported successful neuronal migration through the structure and proliferation beneath it. The biodegradable mMS+ was further modified with IKVAV coating, which significantly improved neuronal attachment and also accelerated material degradation due to enhanced cell interaction. Concurrently, she is working on loading exosomes with miR-21 for PTEN silencing, aiming to boost neuronal regeneration. Mock surgical procedures in rats continue to evaluate the mechanical and structural compatibility of mMS+ for spinal cord implantation. Her Master's thesis, titled "Possible Regenerative Effect of Bone Marrow Mesenchymal Stem Cell-Derived Exosomes in Oleic Acid-Induced Lung Injury in Rats," has been successfully published. **Vi Anh Nguyen** initiated RNA sequencing to identify neuronal populations most affected by SCI in the context of bladder dysfunction, as well as those most responsive to epidural stimulation aimed at restoring bladder function. To complement these molecular findings, she conducted functional studies assessing cFos expression as a marker of neuronal activation within the pontine micturition center. These studies were carried out across multiple conditions, including uninjured, contused, transected, and contused with stimulation, to characterize injury-induced changes in neural activity and identify stimulation-responsive circuits. **Paula Holban** identified a new biomaterial platform that might be suitable for the neurite extension of different cell platforms. So far, the fabrication of the so-called supramolecular tactoids on a string was optimized by incorporating different bioactive epitopes. First cell experiments studies showed successful biomaterial-cells interaction, on iPSCs and SH-SY5Y lines. Next step is to conduct extensive studies on DRGs and possible neurite extension during her secondment in Aachen at DWI. In the meantime she also works on some previous established projects and tends to go to different conferences (SupraLife, Dutch Peptide Symposium, NBTE) and present her work and the ReWIRE network at colloquiums at TU/e. **Navami Koyande** employed phage disply to identify IL-6 mimetic peptides capable of binding to the IL-6 receptor. After three rounds of selection, the enriched phage pools were sent for next-generation sequencing (NGS) to determine the peptide sequences. The identified sequences were analyzed and shortlisted for crude peptide synthesis. These peptides were then CLIPS™-cyclized and initially screened for IL-6 receptor binding using ELISA. The best-performing binders from the ELISA were further evaluated using Grating-Coupled Interferometry (GCI) to study their binding affinity and kinetics. The top binders identified from GCI analysis are now being synthesized in pure, cyclized, and purified form. These will be retested via GCI to validate their binding characteristics. The most promising candidates will then be synthesized on a larger scale for subsequent in vitro and in vivo evaluations. **Miklovana Tuci** recently had the opportunity to present her work on historical controls at the 2024 International Conference on Neurorehabilitation in La Granja. She was an invited speaker at the Data Science Pre-Course of the 2025 ASIA Annual Scientific Meeting, where she discussed work on improving clinical trial design using historical data. She presented a poster on review work on the current status of recovery prediction in SCI. She hosted the EMSCI Data Science Meeting in Zurich and presented some of the projects they developed using the EMSCI dataset. Finally, she will soon begin working on a federated approach to recovery prediction.

Looking ahead: Next ReWIRE Meeting and Summer School in July 2025

We are excited to announce the fifth ReWIRE Meeting and the Summer School taking place in beautiful Pisa, Italy. The DCs will have the unique opportunity to visit the WR-Machine Intelligence Institute and the BioRobotics Institute in Pontedera. Most importantly, they will get to meet and have fruitful scientific discussions with Prof. Wolfram Tetzlaff, a well-known expert in the field of CNS injury and repair and the director of the renowned ICORD institute for more than a decade. **Stay tuned for more updates!**

Written and coordinated by Paula Holban

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