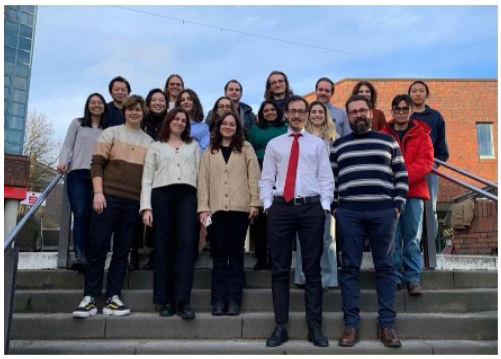
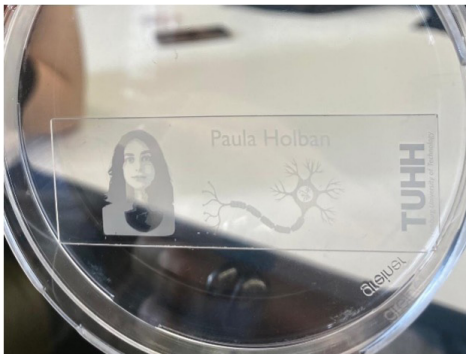
ReWIRE Newsletter

Welcome to the third edition of the ReWIRE Newsletter!

The 1st Workshop, organized by Prof. Elizabeth Bradbury's team at the Sensory, Pain and Regeneration Centre, King's College, London, took place from the 20th-21st of November and involved a wide range of lectures, interactive discussions, practical lab tours, and dedicated networking sessions. External speakers (Prof James Fawcett, Prof. Peter Timmerman, Dr. Fred de Winter, Prof. Laura De Laporte) and internal speakers (Prof. Elizabeth Bradbury, Prof. Robin Ali, Dr. Richard Eva, Dr. Aminul Ahmed), discussed "Drug Delivery Systems" from different perspectives - experimental, therapeutic, and clinical. Topics spanned regeneration research, spinal cord neurobiology, advanced therapeutics, biomaterials, peptides, gene therapy, and clinical research. Interactive talks and workshops initiated great discussion, with multidisciplinary viewpoints. The workshop received excellent feedback.

The 3rd ReWIRE Workshop hosted by the team of Prof. Hoc Khiem Trieu at Hamburg University of Technology took place from the 20th until the 23rd of February 2024. The workshop focused on learning more about Micro-electromechanical systems for medical engineering. Excellent speakers (Prof. Hoc Khiem Trieu, Dr. Daybith Venegas-Rojas) provided more insights into 3D microfabrication with femtosecond laser and multiphoton process and development of novel microfluidic bypass. Additionally, Dr. Veronica Estrada delved into the existing experimental therapies for spinal cord injury. The DCs enjoyed a campus tour and visited the lab facilities, where they were introduced to some primary data by the researchers (Sven Bohne and Konstanze Schober). Alessandro Ippoliti and Lukas Rennpferdt were in charge of the microfabrication workshop on the 21st of February, during which they could explain to the ReWIRE DCs the technology behind the LightFab machine, which uses a 515 nm femtosecond pulsed laser at 10kHz-10MHz repetition rate to perform both Selective Laser Etching (SLE) and Two-Photon Polymerization (2PP). Moreover, they designed a particular and personalized gift for all the DCs (pictured on the right below) using femtosecond laser glass surface micromachining.





During the second Network and Supervisory Meeting the DCs had the chance to talk in more details about their planned secondments during the PhD, and to elect their first DC President. The results of the voting revealed Maria Justino as President and Alessandro Ippoliti as Vice President!

After these exciting ReWIRE events, we are already looking forward to the DC presentations and to further updates and discussions at the next Network Meeting! We are happy to announce the next ReWIRE events (4th Workshop, and 3rd Network and Supervisory Meetings) in July 2024, in Switzerland, hosted by our Swiss partners at EPFL and the CHUV. During the Network Meeting, the students will have their first official Midterm, where they will present their project updates and progress. Stay tuned!

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

Jace Vu's attempt to interlink the microfluidics-generated microgels of 50x50x250 µm was proven succesful at high concentration of anchoring K/Q peptides and catalytic FXIIIa enzyme. The resulting annealed microgels scaffold was proven stable at basic pH. Currently, he is optimizing the system in order to minimize the use of peptides and enzymes. Next, he will focus on studying the magnetic alignment and DRG interactions. **Simay Geniscan** started her first in vivo spinal cord injury study by testing three versions of AAV-ChABC vectors from our collaborators. Using a contused T9 spinal cord model and a horizontal impactor, she administered the vectors both above and below the injury site. Additionally, she have begun histology analysis to compare tissue preservation, CSPG digestion, and immune response differences among the experimental groups. She is enjoying the good weather in London and looks forward to visiting Switzerland soon for the next workshop. **Catarina Tavares** produced P[NAGA] microgels with different polymer weight percentages, cross linker/monomer ratios, different sized iron oxide nanoparticles (Spions) and Gold nanoparticles, using microfluidics and in-tube free-radical polymerization techniques. The swelling response of the microgels with particles was observed with the presence of an alternating magnetic field, in the case of Spions, and with the presence of Infra-red light for the Gold nanoparticle microgels. Currently she is working on optimizing the microfluidic production of hollow microgel systems with this thermoresponsive polymer. **Elif Onsoz'**s project focuses on four main phases: isolating and characterizing bone marrow stem cell exosomes, conducting in vitro and in vivo biodegradability studies of mMS+ in neuronal cells and rats, placing mMS+ in the spinal cords of rats with both acute and chronic injuries,

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and performing molecular biology experiments on the treated animals. Thus far, she has focused on developing a method for silencing PTEN in exosomes and obtaining lab animal certification. She plans to learn the PRINT technique to create 3D hydrogel structures essential for mMS+ fabrication. **Bianca Yu** has been working on computer simulations to compare the potential efficacy of 3 candidate implantable electrode lead designs for the cervical spinal cord. Computing a selectivity index allows for characterization of each lead's ability to selectively activate specific groups of neurons (rootlets) in the cervical dorsal roots while minimizing activation of non-targeted rootlets. Through these simulations, she identified a preferred electrode lead, quantified differences in selectivity due to implant placement and anatomical variation, and determined optimal electrode configurations for targeted electrical stimulation at the rootlet level. **Paula Holban** focused on purifying the UPy-peptide library she synthesized previously. A first trial to differentiate iPSCs to neuro progenitor cells (NPCs) was performed on a defined coating (vitronectin) and on a synthetic coating made by combining UPy-Lysine with bioactive additives in different concentrations. The differentiation performed on UPy-Lys + Upy-cRGD was successful and showed similar behavior when compared to Vitronectin. The embryoid bodies attached to the coating and spread out into neural rosettes. At day 16th of differentiation, she performed a first flow cytometry experiment and data analysis displayed expression of the neuronal marker Beta-tubulin III. **Alessandro Ippoliti** has fabricated different versions of the necessary glass pre-master and silicone master molds through SLE for the hot-embossing process. He used the medical-grade silicone material "Aquasil" for the creation of the master molds and identified two biodegradable materials that possess suitable mechanical and biodegradation properties for the creation of the mMS+., a PLGA blend and a PEG-PLA blend. He will now focus on performing his initial tests for creating a fully bioresorbable 2-photon polymerized mMS+. **Scott Erickson**'s work has continued with the microelectrode array platforms for organoid culture and electrophysiology. He successfully cultured organoids for more than three months and periodically recorded the activity. His focus is on evaluating the effects of standard surface coatings on organoid growth and analyzing electrophysiology data. **Vi Anh Nguyen'**s work focused on investigating the impact of epidural electrical stimulation (EES) on bladder control using a chronic rat model. Rats received contusions at the T9 spinal segment and were implanted with e-dura soft neuroprostheses (six electrodes each) at L6-S1 of the spinal cord. Continuous monitoring and urodynamic assessments showed improved micturition reflexes in all implanted rats, post-rehabilitation. To further explore the mechanisms behind EES-mediated restoration of bladder function, she utilized Vsx2-Cre mice injected with a DTR Cre-dependent virus at the sacral spinal cord (L6-S1) and subjected them to T9 contusions. **Firman Isma Serdana** is engaged in three concurrent research projects to restore hand functionality in SCI patients. To enhance Intrafascicular Peripheral Stimulation (IS) natural control, he optimized strategies to decode hand kinematics from intracortical signals, based on preclinical non-human primate data. He is conducting clinical trials to decode real-time hand kinematics intentions from residual hand electromyographic (EMG) signals in incomplete tetraplegics, utilizing a cost-effective, non-invasive bipolar EMGs and state of the art Medium Density-EMG sleeve developed by EPFL TNE. **Rui Chen** has developed a new type of soft pneumatic actuator. To evaluate the performance of the actuator , a mechanical test platform has been developed. In preliminary tests, the soft actuators demonstrated light weight, high force, and good strain properties. Now, he is developing a soft elbow exoskeleton with a serial of designed soft pneumatic actuators, and he is going to explore more experiments with the exoskeleton. **Navami Prabhakar Koyande** has successfully learned the laboratory techniques for cyclizing peptides with the CLIPS™ molecule in solution. She established and standardized a protocol for performing CLIPS™ reactions on solid phase and is currently testing this on peptide libraries that include multiple peptide sequences, peptide isomers, and protective groups. She received training in ELISA and future plans include further training on the phage display platform. **Maria Justino'**s work involved studying various methods to compensate for the variability of neural patterns over time, with the creation of more autonomous and accessible home-use systems for SCI patients in mind. The first few implementations of these methods have been carried out with promising results. **Miklovana Tuci'**s systematic review identified 65 studies on data-driven models for predicting SCI recovery, highlighting an increasing interest in this approach over time. Standard regression models and tree-based ML architectures were the most commonly used, with routinely acquired data like ISNCSCI scores and demographics. She remarked that clinical significance scores were consistently high, but reproducibility was hindered by a lack of accessible code and detailed methodology. There was significant variability in generalizability, ML quality, and performance, indicating areas needing improvement in terms of robustness and reporting standards.

Introducing a new PhD student!

Carlo Carraro is from Italy and recently completed his Master's degree in Bioengineering at Politecnico di Milano, where he specialized in electronics and wearable device technologies. Currently, he is pursuing a PhD under the guidance of Prof. Dr.-Ing. Vallery Heike (Institute of Automatic Control, RWTH Aachen University) and Dr. Joachim von Zitzewitz (ONWARD Medical). His research focuses on developing personalized orthosis and sensor/control platforms for movement intention recognition, both with the goal to improve EES-supported (Epidural Electrical Stimulation) locomotion for people with spinal cord injury.

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