European School of Molecular Medicine

RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname: Philipp S Erdmann

* Affiliation HT

PHD PROJECT DETAILS

* Title of the proposed project

A High-Resolution Approach to Reconstituting Excitatory Synapses

* Short description of the project (up to 300 words)

Synapses—the connections between neurons—are essential for brain function, but their intricate structure makes them challenging to study. While we know that specific proteins (like for example neurexins) help trigger synapse formation, the fine details of how these molecules assemble into functional units remain unclear.
In this project, we aim to simplify this complexity by reconstructing synapses step-by-step in controlled systems, allowing us to observe their nanoscale organization with cutting-edge microscopy techniques. By comparing these reconstituted synapses to natural ones, we hope to uncover fundamental principles governing their formation.
In later phases, we will explore whether disruptions in this process contribute to neurodevelopmental conditions, such as autism spectrum disorder, where synaptic proteins are often altered. By analyzing differences between healthy and patient-derived neurons, we aim to identify potential structural biomarkers of disease.
This work could not only deepen our understanding of how synapses form but also provide a platform for studying neurological disorders in unprecedented detail.

* Indicate the main research area for the project described above Structural Biology

If needed indicate a second research area for the project described above -

* Provide up to 3 key words for project:

synapse, neurotransmission

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

Cryo-electron tomography, cryo-electron microscopy, membrane-less organelles, phase separation, neuro

* Short description of the lab activity (up to 500 words)

In short, our goal is to enable "A Biopsy at the Nanoscale". This means making medically relevant samples accessible to high-resolution cryo-electron tomography (cryo-ET). For this goal, we develop pipelines and new sample preparation strategies for cryo-electron microscopy (cryo-EM). By enabling cryo-ET in organoids and tissue, we can follow cellular processes as they happen at high resolution — one day ideally without the need of model systems directly in patient-derived samples.

Biologically, we are interested in phenomena related to liquid phase separation (LLPS) or biomolecular condensation in the setting of human diseases.

Here, we seek to answer both basic questions, i.e., how they form and what are their biomechanical properties, but also how biomolecular condensates (BMCs) interact with their surroundings and shape cellular pathways. As these liquid-like compartments are involved in many normal but also disease-related cellular processes, understanding their composition and internal organization may be critical to revealing primary cellular function as well as developing new treatment strategies.

With a goal of gaining molecular-level insights from organoids and tissue, our work at HT has so far been focused on creating robust workflows for making large samples such as organoids and tissue compatible with high-pressure freezing (HPF) and in situ cryo-ET. For this, we recently developed Serialized On-grid Lift-In Sectioning for Tomography (SOLIST), significantly improving stability and throughput of cryo-lift out. We will continue developing techniques to address technological needs of the "biopsy at the nanoscale", such as markers or a "GFP" for cryo-EM.

BMCs have a prominent role for my group since they are involved in many human diseases, including cancer and neurological disorders. At HT there are ample opportunities to dive deeply into these topics thanks to the organoids facility (ASCOF) and other research groups. And we think that understanding the molecular mechanisms that govern formation of BMCs with a unique, high-resolution perspective, can only be provided by cryo-ET. With this, we hope to give a unique "spin" to this field of research, collaborating with groups and facilities at HT, integrating also other cutting-edge methods such expansion microscopy (ExM) and cross-linking mass spectrometry (MS).

* Recent bibliography (max 5 references)

5 Most Recent Publications:

Beyond Dimerization: Harnessing Tetrameric Coiled-Coils for Nanostructure Assembly 2025
R Jerala, S Vidmar, T Šmidlehner, J Aupič, Ž Strmšek, A Ljubetič, F Xiao, ...
Angewandte Chemie International Edition

TOMOMAN: a software package for large-scale cryo-electron tomography data preprocessing, community data sharing and collaborative computing 8 2024
S Khavnekar, PS Erdmann, W Wan
Applied Crystallography 57 (6)

Serialized on-grid lift-in sectioning for tomography (SOLIST) enables a biopsy at the nanoscale 9 2024
HTD Nguyen, G Perone, N Klena, R Vazzana, F Kaluthantrige Don, ...
Nature Methods 21 (9), 1693-1701

In Situ Cryo-Electron Tomography and Advanced Micromanipulator Techniques 2024
S Klumpe, PS Erdmann
Cryo-Electron Tomography: Structural Biology in situ, 151-165

Beyond Dimerization: Harnessing Tetrameric Coiled-Coils for Nanostructure Assembly 2024
S Vidmar, T Šmidlehner, J Aupič, Ž Strmšek, A Ljubetič, F Xiao, G Hu, ...
Angewandte Chemie International Edition, e202422075

Full Bibliography:

https://scholar.google.com/citations?hl=de&user=pCHFZzQAAAAJ&view_op=list_works&sortby=pubdate

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

4 x PhD, 1 x Postdoc, 1x technician, 2 x undergrad (current state March 2025; 2 PhD will be replaced this year)

Institutional page link

https://humantechnopole.it/en/

Lab website link, if any

https://humantechnopole.it/en/research-groups/erdmann-group/

Social media links, if any

https://x.com/3P1L

If you prepare a video to promote your lab/project, please include the link below