University of Zurich[UZH]

URPP Adaptive Brain Circuits in Development and Learning (AdaBD)

Progress Report University Research Priority Program (URPP)

Adaptive Brain Circuits in Development and Learning (AdaBD)

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Scientific Report of the URPP AdaBD

1 Management Summary

The University Research Priority Program (URPP) „Adaptive Brain Circuits in Development and Learning" (AdaBD) wants to understand behavioral changes during development and learning in terms of the underlying adaptations of brain circuits. Besides revealing physiological processes, we aim to establish causal links between learning deficits or developmental delay and impaired mechanisms of brain circuit adaptation. We aim to uncover molecular mechanisms underlying brain circuit development and to identify mutations affecting circuit formation and multi-sensory processing. Finally, we aim to translate new insights from our research to the clinic and to develop new diagnostic tools as well as innovative treatment strategies.

The URPP AdaBD started 2021 in its first four-year-period (2021 – 2024). During the second year of existence, we successfully continued our research projects and started new ones. Our projects are truly cooperative and must be led by at least two AdaBD members. Within our research projects, we have created 17 positions for PhD Students (as of March 2023). Additional students are collaborating while being paid by other sources. Some first research results have been published this year.

Our four PLATFORMS and PLATFORM SEEDS are running and successfully support URPP researchers in high-resolution microscopy, high-dimensional data analysis, induced pluripotent stem cell (iPSC)-based models for neuroscience, and in identifying subtypes of developmental deficits as well as in recruiting study participants.

A major goal in the first two years was to improve and establish innovative methodologies supporting collaborative research projects. We have purchased several equipment items that allow us to improve the quality of our images and measurements of brain structure and function.

Despite obvious difficulties due to the pandemic, we organized an online Symposium in January 2022 and continued our online research seminar series. As soon as the epidemiological situation allowed, we started meeting in person. During Spring 2022, we launched a series of informal lab visits to promote networking within the AdaBD community: During a two-hour tour, the host institutes presented their workspaces, working techniques and research projects. Each lab visit was followed by a get-together with Apéro. The lab visits have been very well appreciated and helped us to establish contacts. In addition, we organized an in-person Symposium for the entire consortium in July 2022. We discussed all AdaBD research projects either in short talks or during a poster session.

The URPP AdaBD wants to promote dialogue within the science community and between science and society. In 2022, we created our own newsletter, which was launched in January 2023. Furthermore, we organized a "day of continuing education" for secondary school teachers from Winterthur and were strongly involved in the organization of the BrainFair 2023. Several AdaBD members participated in outreach events, which are listed in Chapter 4.2.

The URPP AdaBD webpage contains news and information about our network and our events. We have expanded it with more information about our research projects. More content will be added in the near future. We run a Twitter account to act as a link between the URPP and other networks in our fields, as well as between the interested society and us.

2 Objectives

2.1 Scientific, structural and organizational objectives

In 2022, we consolidated our joint research efforts and we started new collaborative projects. We expanded the possibilities and the applicability of the mesoSPIM platform. Finally, we bought several pieces of equipment that will facilitate our research projects.

2.1.1 Scientific objectives

We aimed to continue and strengthen the research projects that started in 2021. For 2022, we had the following additional specific scientific objectives:

PATH1: From molecules to behavior

- Start a new project using modern microscopy methods to elucidate how gene variants causing neurodevelopmental disorders affect neural circuit architecture *(collaboration Müller, Stoeckli, Rauch)*

PATH2: From behavior to molecules

- Start a research project exploiting recent advances in artificial intelligence to build more powerful and better interpretable models of brain function in health and disease *(collaboration Mante, Helmchen)*
- Start a research project investigating integration of multisensory inputs in dendrites of neocortical pyramidal neurons during learning *(collaboration Helmchen, Ruff, Brem, Mante)*

PATH3: From humans to animals and back

- Start a research project employing a combination of novel experimental tasks, behavioral modelling and fMRI to investigate disrupted brain mechanisms in dyscalculia and how they affect risk-taking behavior in financial decisions *(collaboration Ruff, Kucian, Brem)*

2.1.2 Structural and organizational objectives

- Hiring of additional personnel (coordinating office, PhD and Postdoc positions).
- Establishing an assistant professorship in the research area of "Modeling Brain Diseases with Stem Cell Technology" in collaboration with the ZNZ, with links to the AdaBD iPSC Platform SEED
- Supporting the establishment of an ad personam professorship for Prof. Dr. Ruxandra Bachmann
- Continuing regular workshops and seminars. In addition, establishing a series of lab visits to increase networking within the AdaBD community

2.1.3 Communication and outreach

- Expanding our webpage with more information especially on the research projects
- Launching the AdaBD Newsletter containing announcements, information and research activities
- Continuing partnerships with McGill and Queensland Universities in collaboration with the ZNZ
- Continuing and expanding our activities on Twitter
- Continuing the collaboration with the communication office of the University

– Establishing contact with schools and patient organizations to promote the visibility of our research. Towards this end, we planned to create a brochure describing our research.

2.2 Which objectives and milestones were achieved? Which not?

2.2.1 Scientific objectives

– We successfully started the planned new research projects and continued the ongoing ones. We also planned and started additional projects that had not been listed in the objectives. The specific goals and first insights are described in Chapter 3.
– We could reach important milestones for further development of our imaging systems. The Benchtop mesoSPIM system has been equipped with a new laser combiner and new objectives. For improvement of our MRI measurements, we purchased a new camera for motion correction and integrated it in our system. Further, we bought standardized MR phantoms for quality measurements to guarantee that the images can be compared across sites.

2.2.2 Structural and organizational objectives

– The URPP was very successful in hiring additional personnel. *Laura Zanetti* started on June 1st as scientific coordinator (40%) in the coordinating office. She is a biologist and primary school teacher and is especially supporting our public outreach efforts towards schools and families. In addition, the URPP hired 4 PhD Students in 2022 and 3 PostDocs (as of December 31, 2022). Additional researchers working on the projects were paid by other funds.
– The scientific advisory board has been completed with *Prof. Marie Schaer*, University of Geneva, who is covering clinical research. Mark Robinson stepped back as Open Science Delegate since he is not anymore covering this role at the University of Zurich. His successor at the University of Zurich as well as in our Advisory Board is *Prof. Leonhard Held*.
– We are supporting an ad personam professorship for Prof. Dr. Ruxandra Bachmann starting in summer 2023. However, negotiations with the University of Zurich are still ongoing.
– Since October 2022, we are supporting the assistant professorship at the Medical Faculty of András Jakab by financing 10% of his salary. He was able to secure third-party funding for 80% of his salary. The Children's Hospital covers 10% of his salary, due to his clinical work in the hospital.
– Finally, we are working in close collaboration with the Neuroscience Center Zurich (ZNZ) on creating an assistant professorship tenure-track for "Modeling Brain Diseases with Stem Cell Technology" at the Science Faculty (double professorship with the Medical Faculty). The URPP AdaBD has committed financial support for this assistant professorship, supplementing a generous donation from the private bank Rahn & Bodmer.
– We opened an additional common network drive hosted by the UZH for storage of big data files that need to be analyzed by groups of the URPP network belonging to different institutes.
– We continued a biweekly online seminar series with the goal to present progress of the research projects. Further, we organized one online Symposium in January and one in-person Symposium for all AdaBD research groups in July. In addition, we organized a series of lab visits with the goal to learn more about the work of the different research groups and to increase networking.

2.2.3 Communication and outreach

- The webpage of the URPP (www.adabd.uzh.ch) has been expanded with more information on our research. Further, we continued our activities on Twitter.
- The AdaBD Newsletter containing announcements and information has been launched January 2023.
- The URPP participates in partnerships with the *McGill University* and the *University of Queensland*, by organizing workshops and seminars (both online and in-person), partially together with the Neuroscience Center Zurich (ZNZ). This year, we organized seminars in collaboration with the University of Queensland (see Chapter 4).
- The communication office of the University published an edition of the *UZH Magazin* on the topic "Lernen". They included a long interview with AdaBD Director Fritjof Helmchen and an article on lifelong learning with inputs from AdaBD member Nora Raschle.
- We established contacts with secondary school teachers from Winterthur and organized a "day of continuing education" for them (see Chapter 4.3). In addition, we established contacts to primary school and Kindergarten classes in Zürich and Staufen AG, who participated in pilot studies within our research project ChildBrainCircuits. Contacts with patient organizations have been maintained by some URPP members (see Chapter 4.2), but we did not establish direct contacts as URPP, yet.
- We were working on a brochure describing our research, which has been printed in March 2023.
- Some URPP members participated to further outreach events (see Chapter 4.2).

2.3 Updated project planning

2.3.1 Scientific objectives

- All research projects will be continued. We expect to publish some additional results within the next year.
- We start the following new projects:

  PATH1
  - Brain circuit rewiring and its consequences on learning and memory *(collaboration Földy, Helmchen, mesoSPIM Platform)*

  PATH3
  - Development and evaluation of an intervention for adolescents and adults with dyscalculia *(collaboration Kucian, Ruff, Brem and external collaboration with E. Moser-Opitz from the Developmental Science Network Zurich (DSN-ZH))*
  - A 3D mesoscale atlas of intrathalamic inhibitory interneurons in the human brain *(collaboration Jakab, Helmchen, Karayannis, HDDA Platform)*
- The imaging technologies will be further developed.
- URPP consortia will explore opportunities to jointly apply for external funding for AdaBD research projects.

2.3.2 Structural and organizational objectives

- Hiring of additional personnel (PhD positions).

- Establishing an assistant professorship in the research area of "Modeling Brain Diseases with Stem Cell Technology" in collaboration with the ZNZ by 2024, with links to the AdaBD iPSC Platform SEED.
- Supporting the establishment of an ad personam professorship for Prof. Dr. Ruxandra Bachmann by summer 2023
- Continuing regular workshops, seminars and informal events
- Organizing a two-day scientific retreat for URPP researchers. The main goals of the retreat are networking and brainstorming on the future development of the URPP. The Advisory Board will be invited.
- Organizing educational workshops for PhD Students and other researchers of the network on the topics Open Science and science communication

2.3.3 Communication and outreach

- Establishing a regular *AdaBD Newsletter* containing announcements, information and research activities
- Continuing *partnerships with McGill and Queensland Universities* in collaboration with the ZNZ
- Increasing collaboration with other research institutions in Zurich, such as *other URPPs* or the *DSN-ZH*, e.g. by organizing common networking events.
- Continuing and expanding our activities on *Twitter*
- Continuing the collaboration with the *communication office* of the University
- Establishing further contact with schools, patient organizations and the interested public to promote the visibility of our research. Towards this end, we co-organize the *BrainFair 2023* and plan to participate in the *Scientifica 2023*. A *brochure* describing our research has been printed in March 2023.
- Expanding our *webpage* with more information for laypersons and schools.

3 Research

During the second year, we further built up our PLATFORMS and PLATFORMS SEEDS (for simplicity called Platforms in the following text). We continued our research projects and started some new ones in the context of the three major PATHs. We pursued our strategy to assign research funds based on regular internal calls for proposals. We are convinced that this procedure allows us to plan in a flexible way new collaborations based on first insights from running projects. Our strategy makes budgeting and controlling challenging but we are confident that we will spend all funds by the end of 2024. In addition to the cooperative projects and the platforms, we funded the purchase of equipment that is required for URPP projects and provides added value for the network, e.g. by providing new technologies (again through internal calls).

3.1 URPP PLATFORMS

3.1.1 Light-sheet microscopy PLATFORM (mesoSPIM PLATFORM)

The mesoSPIM microscopy platform offers three custom-built light-sheet microscopes that allow imaging of cleared samples that are too large for traditional microscopes, such as entire mouse brains or post-mortem human tissues. We offer user training, consulting, customization of software and hardware, and carry out our own R&D in light-sheet microscopy. We develop our microscopes as an

open-source project (www.mesospim.org), including video tutorials (https://www.youtube.com/@mesoSPIM) and user meetings. Further, the project was presented at several conferences.
Eight AdaBD groups are actively using the mesoSPIM platform. During 2022, the new (Benchtop) mesoSPIM system was improved with increased magnification range, resolution, throughput and decreased costs compared with older systems. Advanced image processing remains challenging for many users. We are currently working on this problem in close collaboration with HDDA Platform, which now offers some tools as part of the dspace toolbox.
The mesoSPIM was also used in combination with the new mirror-based Schmidt objective developed in the *Helmchen* group (published 2023).

3.1.2 Developmental Delay Database PLATFORM (DD DB)

In the canton of Zurich, the two units of special needs education (USNE) determine remedial therapy and speech therapy needs in all referred pre-school children in a centralised and standardised procedure. For this purpose, the USNE collect and store in a joint database (Developmental Delay Database -DD DB) detailed information about personal data, children's development and the therapy measures recommended in each case. The DD DB can be used to specifically target potential study participants for recruitment, to provide broad data on enrolled participants, and to analyze anonymized data for scientific purposes in the framework of the URPP AdaBD. During 2022, the Platform mainly collaborated with the AdaBD Project ChildBrainCircuits by screening the database for potential study participants. Around 600 families have been selected and will be contacted soon. Additional collaborations with research groups and with the HDDA Platform are in the planning stage.

3.1.3 The iPSC PLATFORM SEED

The iPSC **PLATFORM** is a resource that provides iPSC-derived material, expertise and support. Current focus is on neuronal differentiations (cortical, dopaminergic, commissural, cerebellum) and microglia. iPSC differentiation protocols have been successfully set up. Collaborations with *Martin Müller* (for visualization of synapses), *Esther Stoeckli* (for transplantation of iPSC-derived commissural neurons to chicken embryos) and *Ruxandra Bachmann* (for analysis of primary cilia in neural progenitors and different matured neurons) are ongoing and showing promising results. In addition, the scientist leading the platform, *Walther Hänseler*, is following up on his own projects on topics relevant for circuit formation.

3.1.4 The High-Dimensional Data Analysis (HDDA) PLATFORM SEED

The HDDA data-science platform is based on the software "dataspace" (dspace), which has been created and developed by *Sepp Kollmorgen*. *Dspace* is based on the assumption that a substantial part of data analysis tasks can be broken down to a few primitives. These primitives are made available to combine in a Lego-like setting within a graphical user interface (GUI). All actions performed are automatically logged and expressed as programming code. Code-based workflows and GUI-based workflows can merge seamlessly, enabling analyses without coding but also integration with users' existing code and analysis pipelines. Data and expansions of dspace can be easily shared. Dspace and dspace documentation is available to URPP members for download. During the last year, structure and design of the platform have been significantly improved. Projects supported by dspace are ongoing with eight URPP AdaBD research groups as well as with some UZH research groups not belonging to

the URPP. Dspace expansions enabling the analysis and exploration of light-sheet microscopy data (in particular data produced by the mesoSPIM platform) and of analysis of unimodal and multimodal time series data (e.g. analysis of behavior and neural activity) have been improved and are currently being refined and tested. A dspace expansion enabling the analysis and exploration of data held in the datajoint format is currently being developed and tested.

3.2 Research projects

3.2.1 PATH 1: From molecules to behavior

Workpackage leaders: Esther Stoeckli and Martin Müller
The general objectives are to discover new molecular mechanisms underlying neural circuit development under physiological conditions and to investigate how newly identified pathogenic gene mutations that cause neurodevelopmental phenotypes affect neural circuit formation and multi-sensory processing. During the last two years, we started several projects and collected first research results (see below). We are analyzing the organization of specific cell types during brain development and are studying the contribution for circuit formation of genes associated with developmental delay. Further, we are improving technologies to study neural circuit architecture across spatial scales from the subsynaptic to the circuit level. In another project, we are studying how the capacity of neuronal wiring can be reactivated and controlled in adult neurons. This may be a prerequisite for an eventual cure of intellectual disabilities. Last but not least, we are developing hippocampal organoids to study human brain development.

3.2.1.1 Revealing the cortical distribution of human Cajal-Retzius cells in a joint MRI + mesoSPIM reference space

Research Groups: Theo Karayannis, Andras Jakab. PhD Student: Maria Karatsoli
There is evidence that Cajal-Retzius (CR) cells are crucial building blocks of the brain's neuronal circuitry responsible for complex cognition, but we still lack a map of how they are organized in the developing human brain. Our project aims to establish novel 3D microscopic techniques as well as high-field MRI and apply them to study this specific cell population in the brain. We performed preliminary DT-MRI (9.4T) tractography on adult mouse line followed by mesoSPIM imaging, with additional MRI scanning. The combined MRI and mesoSPIM preliminary data is being analyzed using the software dspace (HDDA Platform). Further, we successfully cleared mid-gestational human fetal brain for imaging with the mesoSPIM. The new knowledge and methods generated will allow the URPP AdaBD network to target different neuronal populations and candidate genes that are relevant for studying neuronal circuits during development and learning.

3.2.1.2 Molecular Mechanisms of Cerebellar Circuit Formation - Contribution of Genes Associated with Joubert Syndrome

Research Groups: Ruxandra Bachmann, Esther Stoeckli. PhD Students: Alexandra Noble, Elkhan Yusifov
Collaborating lab members: Alexander Dumoulin, Martina Schaettin
Axon growth and pathfinding to reach the correct target depend on signaling pathways. The primary cilium, a ubiquitous organelle that serves as the antenna of cells, regulates the transmission of these pathways. We aim to elucidate the role of primary cilia in the establishment of neuronal circuits, with a special focus on cerebellar circuits in the zebrafish and in the chick embryo. We have found that

cerebellar neurons of zebrafish mutants for the ciliopathy genes *cc2d2a* and *talpid3* have fewer primary cilia positive for the ciliary GTPase Arl13b compared to wild type controls. However, this does not result in alterations to cerebellar morphology at larval stages in both mutants, or at adult stages in *cc2d2a* mutants. A more detailed analysis of cerebellar axon tract morphology is ongoing. Nevertheless, transcriptomic analyses of *cc2d2a* mutant larvae show dysregulated expression of voltage-gated ion channels, which are important for neuronal function. As this implies that this mutant may exhibit a more subtle neurological defect rather than a gross morphological defect, we are now using transgenic zebrafish lines expressing neuron-specific genetically encoded calcium indicators in combination with behavioural assays to analyse neuronal function in *cc2d2a* mutants.

3.2.1.3 Expanding the dynamic range of light microscopy-based analysis of physiological and aberrant neural circuit development (EXPAND)

Research Groups: Martin Müller, Esther Stoeckli, Anita Rauch. PhD Students: Marta Brasili, Hanna Yeliseyeva, Collaborating lab members: Gonzalo Saiz Castro, Paola Muttathukunnel, Gabriele Siegel
We combine Expansion Microscopy, a method that expands biological samples and allows imaging at the subsynaptic level, with super-resolution microscopy and mesoSPIM light-sheet microscopy. This allows us to elucidate how gene variants causing neurodevelopmental disorders affect neural circuit architecture across spatial scales. We established protocols in the Drosophila neuromuscular junction, human iPSC-derived neuronal cultures, and chicken cerebellum. We started analyzing the role of FoxP family genes – which have been associated with autism spectrum disorders – in axon guidance. High-resolution imaging across scales allows bridging the gap between the subsynaptic and the neuronal circuit level for characterization of candidate disease genes identified in patients.

3.2.1.4 Molecular mechanisms of circuit wiring in the developing and adult brain

Research Groups: Csaba Földy, Sebastian Jessberger. PhD Student: Matteo Egger
Collaborating Postdoc: Wenshu Luo
During development, improper neuronal wiring can lead to formation of persistently altered brain circuits and onset of intellectual disabilities. In this project, we investigate how the capacity of wiring can be reactivated and controlled in adult hippocampal neurons, which are critically involved in certain forms of learning and memory. Reactivating wiring in adult neurons may be a prerequisite for an eventual cure of intellectual disabilities. Our recent results include:
(1) The identification of a synaptic cell surface/adhesion molecule, Pcdh11x, which is important for the target specification of the so-called mossy fiber sprouting (Luo et al., 2022, Front Neurosci).
(2) The identification of a rapid and pronounced form of wiring between the two brain hemispheres in adults (Egger at al., 2023, PNAS Nexus, in press)
(3) The characterization of a transcription factor, whose genetic activation can induce further wiring in different types of adult neurons (to be submitted later this year).

3.2.1.5 Using hippocampal organoids to study human brain development

Research Groups: Sebastian Jessberger, Csaba Földy, Fritjof Helmchen. PhD Student: Daniel Gonzalez
Human pluripotent stem cells can be guided to form neural organoids (so called mini-brains), self-organizing structures that mimic the morphology and molecular composition of early embryonic brains. We made substantial progress in developing organoids that differentiate into 3-dimensional structures that contain cells with a hippocampal neuronal phenotype (e.g., granule cells). Indeed, we observed

significant co-clustering of RNA expression signatures between hippocampus-like organoids and the developing human hippocampus. Additional molecular and functional phenotyping is ongoing.

3.2.2 PATH 2: From behavior to molecules

Workpackage leaders: Fritjof Helmchen and Anita Rauch
The general objectives are to investigate multi-sensory learning and decision-making behavior and to reveal the underlying circuit mechanisms and signal flow changes. Further, we want to relate circuit dysfunctions to learning deficits. During the last two years, we started several projects and collected first research results (see below). We could track dendritic activity during learning in mice and have shown that the signals were relevant for learning. We are now further developing the tasks for quantification of multi-sensory learning in mice and for comparison with measurements in humans (see Chapter 3.2.3). Further, we are studying the development of the prefrontal cortex in mice and the effect of perturbing environmental factors on its maturation and on multi-sensory learning. In a further side-project, we investigate how death of a specific cell type after birth is key for development of somatosensory processing in mice. Finally, we are improving computational models of brain development that may help simplifying comparison between species.

3.2.2.1 Dendritic adaptations during learning

Research Groups: Fritjof Helmchen, Valerio Mante. PhD Student: Gwendolin Schönfeld
Goal-related learning requires changes of synaptic integration in the dendrites of individual neurons, but it remains elusive how dendritic responses adapt during learning. In this project, we tracked dendritic activity in mouse barrel cortex during texture discrimination learning. In addition, we applied optogenetic inhibition to test whether the observed signals are relevant for learning. We identified two distinct classes of dendritic responses that differed in their task- and learning-related dynamics representing either contextual/sensory information or reward information. When we blocked the reward representation in naïve animals using optogenetics, mice failed to learn until we released the block. A preprint of this study is currently under revision.

3.2.2.2 Dendritic Integration in Neocortical Pyramidal Neurons as Basis for Multisensory Learning

Groups: Fritjof Helmchen, Christian Ruff, Silvia Brem, Valerio Mante. PhD Student: Johanna Nieweler
In many cortical areas, information from different sensory modalities (visual, auditory, tactile) converge onto the superficial dendritic tufts of pyramidal neurons. In this project, we use and expand the tools developed in the project Dendritic adaptation during learning, with the goal to reveal in how far multi-sensory learning depends on dendritic integration of distinct converging projections. We aim to develop a behavioral paradigm for quantification of multi-sensory learning in mice in collaboration with the research projects FuncMechanisms and ChildBrainCircuits, who apply similar tasks in human experiments. We aim to measure dendritic activity and its learning-related changes using chronic two-photon calcium imaging during stimulus presentation and during reward-based learning. In addition, by interfering with dendritic integration using optogenetic or chemogenetic tools, we will verify the relevance of such changes for successful adaptation of behavior. Our work will help to understand the activity patterns and functional connectivity changes during multi-sensory learning observed on the systems level in adults and children.

3.2.2.3 The development of prefrontal cortex and executive functions in mice

Research Groups: Christopher Pryce, Theo Karayannis, Benjamin Grewe. PhD Student: Sarah Wicki, Roy Missall

The prefrontal cortex of the mammalian brain is essential for the regulation of psychological processes such as attention, multi-sensory learning, and impulsivity - so-called executive functions. Its maturation is completed in late adolescence and is susceptible to environmental challenges during development that can lead to neuropsychiatric disorders. We want to better understand these processes in animal and modelling studies. In mice, we are establishing the age at development of adult levels of multi-sensory learning in the visual and somatosensory domains. The applied task is working and 75% of the data have been collected. Further, we want to identify some changes in specific populations of neurons in the prefrontal cortex by immunohistochemical assessment. Then, we will study the effects of reduced socialization during adolescence on prefrontal cortex maturation and multi-sensory learning. Computational modelling with the generated data will further allow for improved understanding of the inter-dependence between development, prefrontal cortex, and multi-sensory learning.

3.2.2.4 The impact of Cajal-Retzius cell death on the development of the cortical circuit

Groups: Theofanis Karayannis, Fritjof Helmchen. PhD Student: Angeliki Damilou

Cajal Retzius cells (CRs) located in the developing cortical layer 1 are synaptically integrated in the local circuit and have been shown to mainly receive inputs from GABAergic interneurons. Over the course of the first two postnatal weeks the number of CRs decreases. In this project, we use anatomical, functional and behavioral approaches and show that CRs death contributes to the formation of the mature neocortical somatosensory circuit and is key for the development of somatosensory processing. We expect this project to be finalized within the next months.

3.2.2.5 Linking brain-wide connectivity, function and dynamics with artificial neural networks

Groups: Valerio Mante, Fritjof Helmchen. PhD Student: Lucas Pompe

Computational models play a key role in explaining how brain activity emerges from the underlying neural networks, and how this activity ultimately leads to thoughts and behaviors. Such models can help in identifying the critical differences in the function of healthy and diseased brains. We have developed a novel machine learning approach for fitting artificial, recurrent neural networks to large-scale neural activity. We extensively validated this approach on synthetic, simulated neural activity, and applied it to explain brain-wide neural activity measured with calcium imaging in mice engaged in a decision-making task. Unlike past modeling approaches, the fitted networks capture not just the average activity over many task trials, but also the prominent variability apparent in individual trials. The framework developed in this project will easily generalize to other tasks and recordings and could be applied in mice and in humans, potentially simplifying comparisons between species.

3.2.3 PATH 3: From humans to animals and back

Workpackage leaders: Christian Ruff and Bea Latal

The general objectives are to relate animal to human learning and to translate mechanistic insights from basic research to the clinics. Eventually, we want to improve developmental delay diagnosis and treatment strategies. During the last two years, we started several projects and collected first research

results (see below). We developed tasks to assess multi-sensory learning in humans and combined them with fMRI measurements in healthy adults and children as well as in patients affected by learning disorders. We want to identify brain areas involved in learning of multi-sensory associations. Further, we are studying the neural origins of disrupted magnitude processing in dyscalculia. We are establishing techniques to reveal human brain connectome features that may differ in patients with developmental delay. Also, we are testing the effect of clinical risk and environmental factors incl. trauma on brain connectivity and learning. Finally, we identified genetic variants in a cohort of patients with congenital heart disease and developmental delay. In future projects, we will test the functional significance of these variants in animal models.

3.2.3.1 Functional brain network mechanisms underlying multisensory learning (FuncMechanisms)

Research Groups: Christian Ruff, Fritjof Helmchen, Silvia Brem. PhD Students: Ella Casimiro, Saurabh Bedi
Collaborating Postdoc: Gilles de Hollander
In order to identify functional brain network mechanisms underlying multi-sensory learning, we have successfully developed a task to assess both reward-based and statistical multisensory learning in healthy adults. Variants of this task will also be employed in AdaBD projects in mice and children with learning disorders. We already combined this task with fMRI in a first set of neurotypical adults to identify brain areas where neural activity tracks the learning of multi-sensory associations. The focus of the ongoing analyses will not only be on local activity but also on functional connectivity between these areas. We will then employ non-invasive brain stimulation methods (TMS) to test whether activity disruptions in the identified cortical areas lead to problems with either reward-based or statistical multisensory learning, or both.

3.2.3.2 Neural basis of multisensory learning and processing during child development (ChildBrainCircuits)

Research Groups: Silvia Brem, Nora Raschle, Anita Rauch, Christian Ruff, Michael von Rhein. PhD Students: Nina Raduner, Nico Ehrhardt, Sarah Di Pietro. Assistant: Sarah Ismail
Collaborating lab members: Plamina Dimanova, Réka Borbás, Iliana Karipidis, Maya Schneebeli, several master students
Efficient integration and processing of multisensory information is fundamental for perception, cognition, learning, and language development. Our project aims to provide novel insights into how brain regions adapt in terms of activation and connectivity during multi-sensory learning across early and middle childhood, both in healthy children and patients with developmental language disorders. After receiving ethical approval to start the project, we adapted the audiovisual and visuotactile learning and processing tasks that were originally developed for healthy adults and started testing them in kindergarten and primary school classes. The analyses of these data have indicated that further adjustments for young children are necessary. Furthermore, we are developing a multi-sensory naturalistic movie task that allows for the investigation of conceptual and auditory language processing in young children and adults alike. In the meantime, we have screened the DD-DB for potential study participants and selected more than 600 families who fulfill our criteria and who will be contacted in the next few months.
In addition, we have analyzed previously collected fMRI datasets in primary school children to examine the network connectivity and trajectories of functional activation during visual and auditory letter processing in development. We have published results that suggest divergent development of

connectivity between attentional regions and the occipitotemporal visual word form processing region in affected children.

3.2.3.3 Neural origins of disrupted magnitude processing and risk taking in dyscalculia (NumRisk)

Research Groups: Christian Ruff, Karin Kucian, Silvia Brem. PhD Student: Maike Renkert
Collaborating Postdoc: Gilles de Hollander
Dyscalculia is a common neurodevelopmental disorder that majorly affects numerical competence. In this project, we investigate the precision with which the brains of adolescents diagnosed with dyscalculia represent abstract magnitude information, and how this affects their risk taking behavior in financial decisions with real-life consequences. Towards this aim, we developed a novel computerized task battery, planned fMRI protocols, questionnaire and psychometric measures. We already piloted them in control participants and we are currently starting data collection in the dyscalculic adolescents. Our project will directly pave the way for novel diagnostic and therapeutic measures.

3.2.3.4 Structural basis of mild developmental delay in the developing human brain connectome

Research Groups: Andras Jakab, Bea Latal, Michael von Rhein, Valerio Mante. PhD Student: Anna Speckert
Collaborating PhD Student: Hui Ji
Many reasons exist why a child may show a developmental delay and we do not know yet if they share neural conditions such as similar deficits in neural circuits. This project aims to characterize the macroscale neuronal circuit structure in children who present mild to moderate development delay with mixed reasons. We analyze existing structural neuronal network (connectome) data from fetal to adolescent ages. The results will be associated with cognitive outcomes. We started analyzing the data with the software dspace (HDDA Platform) and are implementing techniques in order to be able to reveal connectome features that might separate groups (normal vs. pathological). Once established, the analysis could be applied to additional datasets, such as cases from the DD DB, as well as for cross-species comparisons.

3.2.3.5 The impact of clinical risk and environmental resilience factors on brain circuits & learning: A network connectivity analysis in adolescents with congenital heart disease

Research Groups: Bea Latal, Andras Jakab. PostDoc: Melanie Ehrler
To enable adaptive learning, executive functions (EF), a set of cognitive skills such as working memory or attentional control, are essential. Investigating the underlying brain circuits of EF will help to better understand and predict learning impairments. We determined alterations in brain circuits in patients with congenital heart disease by processing diffusion MRI data and estimating their brain connectomes. Further, we calculated a cumulative clinical risk score and found an association with executive function performance. In a next step, we will test whether brain connectome strength is associated with the clinical risk score and with executive function performance. We will also investigate the influence of environmental resilience factors on these associations. We are expecting to publish our data next year, advancing our understanding of the brain behavior connections and of associated risk and resilience factors.

3.2.3.6 The effect of early childhood and in-utero trauma on brain development, educational outcomes and professional attainment: Large-scale evidence from the UK Biobank

Research Groups: Christian Ruff, Valerio Mante, HDDA Platform. PostDoc: Gökhan Aydogan
In this project, we aim to identify mechanistic links between Early Childhood Trauma (ECT), neural development, and long-term educational and professional attainment. In collaboration with the HDDA Platform, we analyzed genetic, neural and behavioral data obtained in a prospective epidemiological study of 500,000 individuals (UKBiobank). Our analysis indicates a reduction in grey matter substance across the whole brain and a significantly lower IQ after ECT. Further, we found that air-raids within 1km radius of self-reported birth location within the last trimester of pregnancy exhibit a significant impact on grey matter volume mostly in frontal brain areas and cerebellar structures. We plan to publish these results soon.

3.2.3.7 The genetic contribution to mild neurodevelopmental impairments in congenital heart disease: direct or indirect effect

Research Groups: Bea Latal, Anita Rauch. Assistant: Nils Braun
Children with congenital heart defect have an increased risk of developmental disabilities. So far, it is largely unknown whether this is a secondary result of decreased blood flow due to the heart defect or if it is a primary genetic problem that may be linked to the etiology of the heart defect. At the University Children's Hospital, Bea Latal established a longitudinal cohort of patients with congenital heart defects who underwent neurodevelopmental and behavioral assessments. Within the AdaBD project, we aim to identify potentially causative genetic variants in the cohort and to correlate them with the clinical data. We identified 68 de novo and 75 homozygous rare variants. Additionally, we identified compound heterozygosity in 420 unique genes. Literature research and preliminary bioinformatic analysis indicate that many of these variants are promising candidates for future investigation. Currently, we are analyzing data from a control cohort, which will make more complex statistical analyses possible. Our results will allow other members of the URPP AdaBD to develop animal models to test for the functional significance and affected pathways in these genetic alterations.

4 Scientific Activities and Outreach

4.1 Scientific activities

Due to the COVID-19 pandemic, regular in-person meetings have not been possible during winter 2022. Nevertheless, we organized an online **AdaBD Symposium** on January 21th, which was open to all members of the AdaBD research groups. We first listened to a lecture by *Karin Kucian*, MR-Center, Children's Hospital Zurich, who had recently joined the URPP AdaBD as a new PI. Afterwards, we had three parallel workshops on the topic "How to reach our goals": One workshop on "Analysis of high dimensional microscopy data" was led by the managers of the mesoSPIM and of the HDDA Platforms *Nikita Vladimirov* and *Sepp Kollmorgen*. A second workshop on "Working with the Development Delay Database" was led by *Marion Wenger* and *Michael von Rhein*. A third workshop on "Scientific events, measures to promote young scientists and Public outreach" was led by the general manager *Sabina Huber*. Take-home messages from the three workshops have been discussed in a plenary session at the end of the Symposium.

An **in-person AdaBD Symposium** again open to all members of the AdaBD research groups took place on July 4th. A keynote lecture was given by *Prof. Dr. Denis Jabaudon*, Department of Basic Neuroscience, University of Geneva, and member of the URPP AdaBD Advisory Board. *(Fate and freedom in developing neocortical circuits)*. A second keynote lecture was given by *Prof. Dr. Samantha Johnson*, Department of Health Sciences, University of Leicester, UK (*Improving educational support for children born preterm: From evidence to intervention)*. In addition, the AdaBD research projects have been presented either during short oral presentations (three presentations by *Gwendolin Schönfeld*, *Daniel Gonzalez* and *Melanie Ehrler)* or during a poster session. The Symposium was followed by an apéro riche, a great opportunity to get to know each other and network.

The URPP AdaBD organized one parallel **workshop at the ZNZ Symposium** on September 17th. The title of the 1.5h-workshop was *"Structural and functional adaptations of brain networks"*. The workshop was moderated by AdaBD directors *Esther Stoeckli* and *Fritjof Helmchen* and included short presentations by AdaBD members *Silvia Brem* and *Csaba Földy* as well as by external speakers (*Peter Scheiffele*, Universität Basel; *Tina Notter* Institute of Pharmacology and Toxicology, UZH; *Yaroslav Sych*, Institute of Cellular and Integrative Neurosciences, University of Strasbourg and CNRS). For a detailed description of the workshop, see program on the website of the Neuroscience Center.

We continued the well-established **biweekly online seminar series**, with the goal to present the AdaBD research groups and their contribution to the URPP. A short general introduction by the PI (around 10 minutes) is followed by a progress report by the PhD Student(s) involved in the URPP research project and by a discussion with the attendees. The seminars are of outstanding importance not only as progress reports but also to generate new ideas for follow-up projects within the network. We decided to stick to online seminars to allow a large amount of AdaBD researchers to participate despite being located at different places in the city. We often have more than 50 participants.
The program of the online seminar series can be found on our website.

We established a round of **lab visits** with the goal to learn more about the work of the different research groups, to see the specialized experimental setups, and to increase networking. The host institutes presented their working spaces, working techniques and research projects during a two-hours guided tour. Each lab visit was followed by a get-together with apéro. The lab visits have been very well appreciated and will be repeated in the future.

Three **Special Seminars** have been organized. *Prof. Jason B. Mattingley*, Queensland Brain Institute & School of Psychology, The University of Queensland, Brisbane, Australia, presented on September 7th *(Understanding the role of prediction in sensory encoding)*, *Dr. Dragan Rangelov*, Queensland Brain Institute, The University of Queensland, Brisbane, Australia on September 6th *(Cognitive and neural mechanisms of integrative perceptual decisions),* and *Prof. Marie Schaer*, Faculty of Medicine, University of Geneva Hospitals, Department of Psychiatry on December 16th (*What neuroscience can teach us to better support the development of children with autism).*

Some **Platforms organized workshops and attended meetings** to promote their services and to train users:
Developmental Delay Database:

- Presentation of the database at outreach events for the science community:
  - **Meeting of Registry Managers**, 22.09.2022, Children's Research Center Zurich
  - **SwissPedNet**, 26.10.2022, University of Berne

mesoSPIM Platform:

- Organization of the first **mesoSPIM User Meeting**, 10.03.2022, Online, 209 registered participants from all over the world. The talks are now posted on mesoSPIM YouTube channel. Some talks are edited or omitted at the speaker's request due to confidential information (a no-publish request).
- Participation at **several conferences and courses** in Switzerland and abroad with demos, talks and tutorials (e.g., Cajal School **Neural circuit basis of computation and behaviour**, May 2022, Bordeaux).

iPSC:

- Presentation of the platform seed at the iPSZürich Symposium, 20.04.2022.

Several AdaBD members **(co)-organized** congresses and seminars directly related to the URPP:

Silvia Brem:

- **Co_Air Webinar series**, 09.2020 – 02.2022, online webinar four times a year, International forum on the current opinion on audiovisual integration and reading
- **Research Seminar with Prof. Sendy Cafarra**, 28.09.2022, University of Zurch ("*Development of visual white matter pathways is linked to electrophysiological response*"). Topic: Brain development, developmental dyslexia, reading

Fritjof Helmchen:

- **Conference on Neuronal Circuits**, 16.-19-3.2022, Cold Spring Harbor Laboratory, NY. *Co-Organizer.* Topic: Structure and function of neuronal circuits.
- **Cajal School on Neural circuit basis of computation and behaviour**, 2.-22.5.2022, Bordeaux. *Course Director*. Topic: Advanced Neuroscience Training, concepts and techniques to study neural circuit adaptations. Participation of *Gwendolin Schoenfeld* (AdaBD PhD student) as course assistant and *Nikita Vladimirov* (head of mesoSPIM platform) as course instructor.
- **Conference on Barrel Cortex**, EPFL Neuro Symposium, 6.-8.7.2022, Co-Organizer. Topic: Neural circuits and plasticity in rodent somatosensory cortex.
- **Annual Symposium of the Clinical Neuroscience Center Zurich** (KNZ), 30.11.2022, Neurology Department, University Hospital Zurich, *Co-Organizer*. Topic: „Neuroplasticity: novel insights from basic to clinical science".

Sebastian Jessberger:

- **Conference on Neurogenesis from development to adulthood in health and disease**, 20-23.03.2022, Ascona. Co-Organizer together with *Denis Jabaudon (Member of the AdaBD Advisory Board), Marlen Knobloch und Fiona Doetsch.* Topic: Developmental Neurobiology using model organisms and human tissues

Bea Latal:

- **3rd and 4th Transatlantic Research Meetings** on brain development in patients with congenital heart disease, 12.01.2022 and 06.12.2022, online

Nora Raschle:

– **FLUX Congress 2022**, 07-09.09.2022, Sorbonne, Paris. *Member of the Scientific Program Committee. International Society and Conference on cognitive developmental neuroscience. With the participation of several PIs and students of the URPP AdaBD.*

Christian Ruff:

– **5th Annual Marlene Porsche Graduate School of Neuroeconomics Symposium**, 09.12.2022, Zurich. *Co-Organizer,* Presentation of URPP work on multisensory learning

Activities related to open science are listed in chapter 6.2.

Several AdaBD members *(S. Brem, F. Helmchen, S. Jessberger, M. Müller, Ch. Pryce, Ch. Ruff, E. Stoeckli)* are involved in the new **Strategic Partnership of UZH and *University of Queensland*** within the Neuroscience Cluster. An online workshop took place on March 29, 2022. Der UFSP AdaBD organized two **Special Seminars** with researchers of the University of Queensland (see above).

4.2 Outreach activities

4.2.1 Outreach in the science community

Some AdaBD members presented research projects of the URPP AdaBD at congresses and seminars:
Silvia Brem:

– **Invited talk at the Katholieke Universiteit Leuven**, 04.10.2022, *Presentation of data of the AdaBD project ChildBrainCircuits*
– **Tagung Verband Dyslexie Schweiz,** 12.11.2022, University of Zurich, *Booth on brain and speech development and neuroimaging, incl. a poster on the AdaBD project ChildBrainCircuits*

Fritjof Helmchen:

– **Invited talk at the Homburg SFB894 Symposium** "Cutting edge concepts in calcium signaling"**,** 15.-18.6.2022, *Presentation of data of the AdaBD project "Dendritic Adaptations During Learning"*.
– **Invited talk at the Göttingen SFB889 Symposium** "Cellular Mechanisms of Sensory Processing", 1.-2.11.2022, *Presentation of data of the AdaBD project Dendritic Adaptations During Learning*.

Karin Kucian gave several invited talks related to the AdaBD project NumRisk (Institute of Education UZH, Swiss Psychological Society, Cuban Neuroscience Center, Mathematical Cognition and Learning Society, Fachtagung LVL-Bayern)
Martin Müller gave a talk connected to the AdaBD project EXPAND at Marine Biological Laboratory, Woods Hole, MS, USA.
Christian Ruff gave invited online talks at the **Hong Kong Polytechnic University** and within the **Bonn-Melbourne Seminar Series in Decision Making**

4.2.2 Public Outreach

The URPP AdaBD organized a **"continuing education day"** on October 5, 2022 for 30 teachers of the secondary school Mattenbach, Winterthur. *Fritjof Helmchen* and *Martin Müller* organized visits in their labs, and *Fritjof Helmchen* introduced the URPP AdaBD. *Silvia Brem* and *Iliana Karapidis* organized a lab visit at the MR Center of the psychiatric clinic and presented the AdaBD research Project ChildBrainCircuits.

URPP member *Silvia Brem* organized the "**"Tagung Verband Dyslexie Schweiz"** and participated to information events on dyslexia for affected persons and laypersons (Kosmos Kind, Dybuster Geburtstagssymposium ETH).
URPP member *Fritjof Helmchen* held the **public lecture** "**Licht im Dickicht des Gehirns: Lernvorgänge sichtbar machen**" within the Ringvorlesungen "Wege zur Erforschung des Gehirns", Bernstein Zentrum Freiburg (via Zoom).
URPP member *Karin Kucian* taught on dyscalculia at the "Kirchliche Pädagogische Hochschule Stamd, Tirol, Austria (2-day workshop for aspiring primary school teachers) and gave a workshop for the Verband Dyslexie Schweiz. Further, she gave an interview for a Wissenspodcast.
URPP member *Nora Raschle* participated to several outreach events. A list of all events can be found here . She also received a **Cogito Research Grant** for a science outreach and communication project including the development of science dialogue, workshops and school events around the topic of human brain and behavioral development.
URPP member *Anita Rauch* participated to the "Zukunftstag der Stiftung Bühl" on 10.06.2022 and gave a talk with the title «Wie werden genetische Erkenntnisse über geistige Behinderung die Zukunft beeinflussen?»
URPP member *Christian Ruff* participated to the **"Zukunftstag"** on 10.11.2022 and presented his work and research environment to interested youth.

In March 2021 we opened a **Twitter account** (https://twitter.com/UZH_AdaBD) with the aim to present the highlights of our research both to the scientific community and to the interested general public. We are using the account to advertise activities that may be interesting for the science community outside UZH and/or for the general public. Due to time constraints, we are not able to actively participate to exchanges within the science community as we would wish.

Our **webpage** has been expanded with more information about our research. We will add soon more information about each research project.

We planned an own **newsletter** for the science community and the interested general public. The first issue was published in January 2023.

We have been working on a **brochure** that explains our work in simple words. We printed a first version of it in March 2023.

5 Academic Career Development

5.1 Academic career development

As of today, the URPP AdaBD (in some cases partially) financed a total of **20 PhD Students**. Additional students are working on URPP research projects while being financed with third-party funds of their supervisors. The URPP offers students a scientific environment that combines basic and clinical research and gives them a chance to work on a truly collaborative and interdisciplinary research project. All PhD Students are supervised by at least two URPP PIs. They are enrolled in the Neuroscience PhD Program run by the Neuroscience Center Zurich (ZNZ) and have access to courses, retreats and career development events.

We are complementing this offer with courses and events tailored to the needs of our students. They are actively involved in the planning. One of them, *Anna Speckert*, is an active member of the Steering Committee as a PhD student representative. Together with *Sepp Kollmorgen*, she organized an informal networking event for PhD Students on July 19. The students had the opportunity to get to know each other in person in a casual environment and to discuss their research projects, their problems and needs, as well as ideas for future events. As a result of this exchange, for example, we now rent more shared storage space for data exchange among AdaBD research groups. In addition, *Anna Speckert* is a member of the Organizing Committee of the BrainFair 2023. Her goal is to help adding content that may be of interest for young scientists.

Young academics in our research groups can profit from an interdisciplinary environment, symposia, online seminars and support from the database managers on specific topics related to the URPP, such as data analysis, imaging, cell culture or participant recruitment for human studies.

Several URPP members are young **group leaders and assistant professors** *(Ruxandra Bachmann, Silvia Brem, Andras Jakab, Karin Kucian, Theo Karayannis, Nora Raschle,)* who have the opportunity to work in an inspiring interdisciplinary network and to increase their scientific output. *Silvia Brem* has been appointed as Associate Professor of Childhood and Adolescent Cognitive Neuroscience in October 2022 and took up her post on February 1, 2023.
We are supporting an *ad personam* professorship for Ruxandra Bachmann as well as the establishment of a new assistant professorship in the field of "Modeling Brain Diseases with Stem Cell technology" in collaboration with the ZNZ.
We supported the establishment of an assistant professorship for András Jakab at the Childrens' Hospital, and are financially supporting him with 10% of the salary. This because he is working 90% in research instead of the usual 80%.

The positions as **PLATFORM managers** are a great opportunity to develop careers from postdoctoral positions towards more independence and service orientation.

The **coordinating office** covers tasks that are ideal for development of a career in the Third Space.

5.2 Gender equality development

The URPP AdaBD commits to a favorable gender balance and has the goal to provide family friendly working conditions. As one measure, the AdaBD general manager *Sabina Huber-Reggi* acts as **representative for gender equality** in the steering committee. We mention our equal opportunity efforts in job advertisements. Further, when planning seminars and symposia, we always ensure gender balance.

Among the **PIs**, the proportion of women is 42%. Within the **Steering committee**, the proportion of women is 56% and within the **Advisory Board** 40%.

As of today, 75% of the **PhD Students** and 75% of the **PostDocs** financed by the URPP are women. One platform manager out of four is a woman and works part-time (80%). Two PIs are working part-time due to family commitments. The Coordinating Office is run with family friendly part-time positions, which are ideal for parents looking for part-time careers in the Third Space.

6 Publications

6.1 List of publications

Within the second year of existence, URPP-funded initiatives already gave rise to some publications.

The list contains only publications in which the URPP is mentioned in the acknowledgements. URPP researchers are underlined.

Peer-reviewed publications

*Baeriswyl T, Schaettin M, Leoni S, Dumoulin A, Stoeckli ET. Endoglycan Regulates Purkinje Cell Migration by Balancing Cell-Cell Adhesion. *Front Neurosci*. 16, 894962 (2022). https://doi: 10.3389/fnins.2022.894962 .

De Silvestro AA, Krueger B, Steger C, Feldmann M, Payette K, Krueger J, Kottke R, Hagmann C, Bosshart M, Bürki C, Dave H, Tuura R, Latal B, Jakab A, Knirsch W, Cerebral desaturation during neonatal congenital heart surgery is associated with perioperative brain structure alterations but not with neurodevelopmental outcome at 1 year. *Eur J Cardiothorac Surg* **62**(5) (2022) https://doi.org/10.1093/ejcts/ezac138

*Denoth-Lippuner A, Royall LN, Gonzalez-Bohorquez D, Machado D, Jessberger S, Injection and electroporation of plasmid DNA into human cortical organoids. *STAR Protocols* **3**:101129 (2022). https://doi.org/10.1016/j.xpro.2022.101129

Diederich, B, Müllenbroich, C, Vladimirov, N, Bowman R, Stirling J, Reynaud EG, CAD we share? Publishing reproducible microscope hardware. *Nat Methods* **19**, 1026–1030 (2022). https://doi.org/10.1038/s41592-022-01484-5

*Fraga-González G, Di Pietro SV, Pleisch G, Walitza S, Brandeis D, Karipidis II, Brem S, Visual Occipito-Temporal N1 Sensitivity to Digits Across Elementary School. *Frontiers in Human Neuroscience* **16**:887413 (2022). https://doi.org/10.3389/fnhum.2022.887413

*Gonzalez-Bohorquez D, Gallego Lopez IM, Jaeger BN, Pfammatter S, Bowers M, Semenkovich CF, Jessberger S, FASN-dependent de novo lipogenesis is required for brain development. *Proceedings of the National Academy of Sciences of the United States of America* **119** (2022). https://doi.org/10.1073/pnas.2112040119

*Kebiri H, Canales-Rodríguez EJ, Lajous H, de Dumast P, Girard G, Alemán-Gómez Y, Koob M, Jakab A, Bach Cuadra M, Through-Plane Super-Resolution With Autoencoders in Diffusion Magnetic Resonance Imaging of the Developing Human Brain. *Front Neurol.* **13**:827816 (2022). https://doi.org/10.3389/fneur.2022.827816

*Luo W, Cruz-Ochoa NA, Seng C, Egger M, Lukacsovich D, Lukacsovich T, Földy C, *Pcdh11x* controls target specification of mossy fiber sprouting. *Front Neurosci.* **16**:888362 (2022). https://doi.org/10.3389/fnins.2022.888362

*Muttathukunnel P, Frei P, Perry S, Dickman D, Müller M, Rapid homeostatic modulation of transsynaptic nanocolumn rings. *Proceedings of the National Academy of Sciences of the United States of America* **119**. (2022)
https://doi.org/10.1073/pnas.2119044119

* *Open Access*

6.2 Activities to promote open science

Open Access publishing
Peer-reviewed publications marked with a * have been published open access (see Chapter 6.1).

Open research data
Some datasets from URPP research projects have been deposited last year on public repositories (see Scientific Report 2021). During 2022, we did not deposit any datasets but we are planning to do so in the near future.

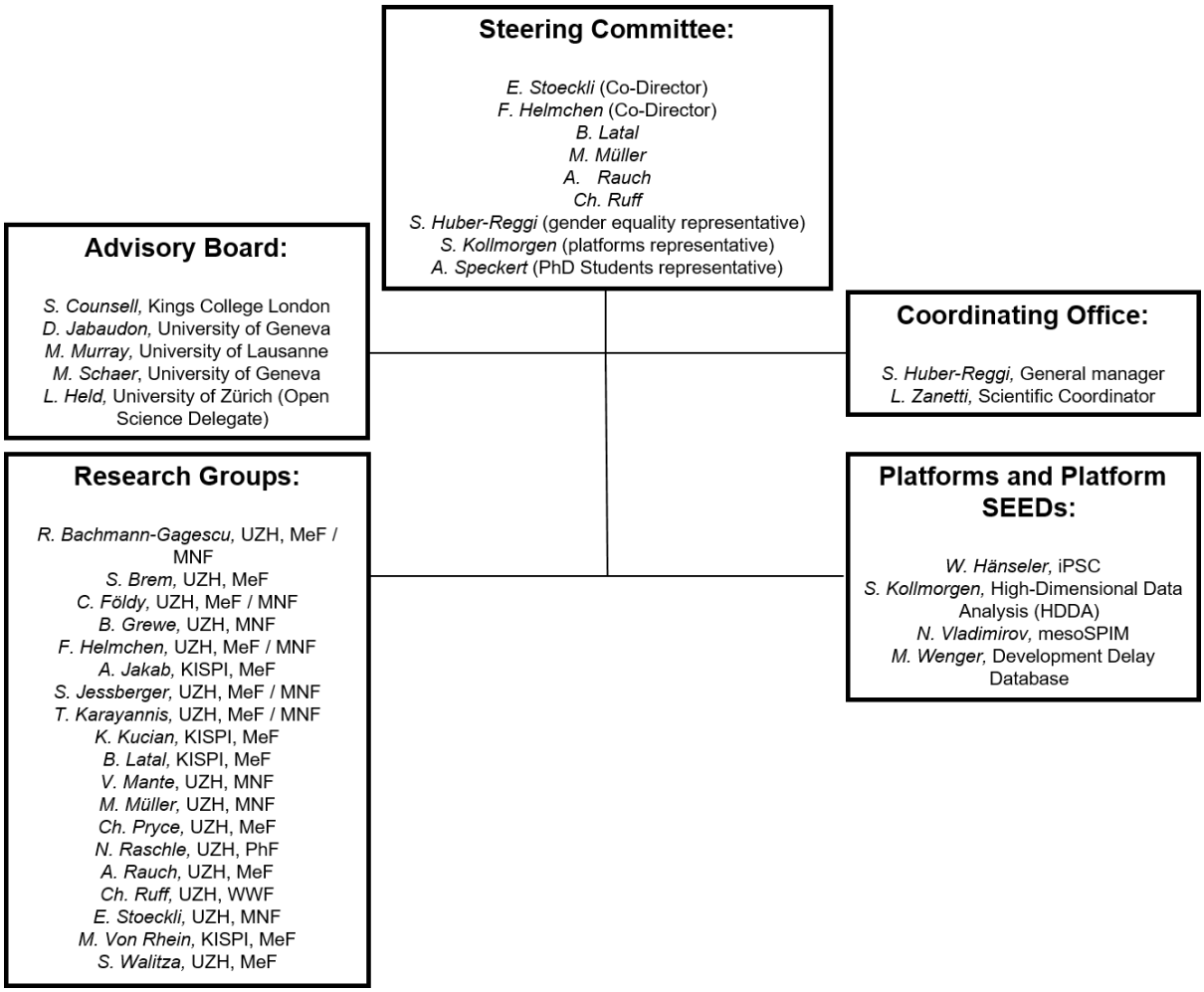
Further Open Science measures

The mesoSPIM PLATFORM sustains and expands the mesoSPIM initiative, which was launched 2019 as an open source project (mesospim.org). Following open science measures could be achieved 2022:

- Three new mesoSPIM v1.5 setups were built around the world (Shanghai; Cambridge, USA; Hong Kong, see http://mesospim.org/setups/) and we remotely assisted some of them.
- One new video tutorial was created for user training on microscope operation (https://www.youtube.com/@mesoSPIM).
- One release of mesoSPIM open-source software was made in November, with improved functionality for the users.
- The mesoSPIM hardware wiki (https://github.com/mesoSPIM/mesoSPIM-hardware-documentation/wiki) was updated with new documentation on sample mounting methods.
- The Benchtop mesoSPIM 2.0 github repository (https://github.com/mesoSPIM/benchtop-hardware, currently private) was open for early access to six collaborators who may build their own Benchtops. The Wiki is currently being actively updated and prepared for official release and publication.

Open Science awareness
The Steering Committee and the Advisory Board of the URPP AdaBD met online on November 18, 2022. One main topic was planning of Open Science measures. Some workshops are planned for 2023 with the goal to define a common strategy for AdaBD projects.

7 Structures



31.12.2022