Annual Report 2024

of the
Collaborative Research Center CRC 1540

Exploring Brain Mechanics (EBM)

Understanding, engineering and exploiting mechanical properties and signals in central nervous system development, physiology and pathology

Friedrich-Alexander-Universität
Erlangen-Nürnberg

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Understanding, engineering, and exploiting mechanical properties and signals in central nervous system development, physiology and pathology

at the

Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU)

Prof. Dr.-Ing. Paul Steinmann (spokesperson)

Prof. Dr.-Ing. Silvia Budday (co-spokesperson)

2024

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Preface

The second year of EBM was marked by consolidation and significant progress across all areas. Building on the solid foundation established in the first year, we further developed our structures and intensified interdisciplinary collaboration. These efforts have resulted not only in remarkable scientific achievements but also in a deeper understanding of brain mechanics and the fact that we grew even closer together.

A key research highlight of the past year was the EBM Update Meeting held in February 2024. This event provided researchers with a valuable platform to present advancements in the three core research areas – brain mechanics, spinal cord mechanics, and cellular mechanics – as well as in the cross-sectional projects. The vibrant exchange of ideas and intensive discussions strengthened collaboration and fostered the development of new initiatives. Another major research highlight was the second EBM Retreat, hosted in picturesque Franconian Switzerland in October 2024. This event continued the dynamic momentum from the Update Meeting, featuring insightful presentations by our (post)doctoral researchers, lively discussions, and guest lectures offering fresh, inspiring perspectives.

In addition to our scientific activities, we made significant contributions to public outreach. One outstanding example was the event “Das Gehirn – Musikalische Erkundungen” in September 2024 at the Matthäuskirche in Erlangen. In close cooperation with church music director Susanne Hartwich-Düfel and the media studios of the Institute for Theater and Media Studies (FAU), science and art were combined into an impressive audiovisual experience. Such initiatives underscore our commitment to making science accessible to a broader audience and exploring innovative approaches to disseminating knowledge.

Our network continues to grow steadily, with new associated principal investigators, doctoral researchers, and, for the first time, master’s students joining our efforts. Supporting early-career researchers remains a central priority. Our tailored qualification program provides a dynamic environment for young scientists to develop their skills, collaborate internationally, and make substantial contributions to our research goals.

This report highlights the dedicated efforts of all those involved and documents the progress we have achieved in advancing brain mechanics research through our interdisciplinary approach. Looking ahead, we are confident that our work will continue to drive breakthroughs that enrich both fundamental research and its medical applications. We extend our heartfelt thanks to every member of our team for their dedication, passion, and hard work, and we eagerly anticipate another year filled with discovery and collaboration.

Erlangen, December 2024

Paul Steinmann and *Silvia Budday*

CONTENT

Figure 1: Group photo at the 2nd EBM Retreat in Waischenfeld on October 10, 2024. (Image: L. Wißmeier)

1 RESEARCH PROGRAM

The CRC1540 EBM focuses on unraveling the mechanical aspects influencing the central nervous system (CNS). Despite advancements in understanding biochemical and genetic regulations, many CNS processes and diseases remain elusive. The program addresses challenges such as unpredictable axon growth, imprecise diagnosis of CNS-related diseases, and the promotion of neuronal regeneration post-spinal cord injuries.

Researchers associated with EBM, and a few other groups worldwide, have recently identified the significant impact of mechanical signals on CNS cell function. Examples include the influence of brain tissue mechanics on axon growth, the role of mechanical forces in cortical folding, and the link between brain stiffness and age-related remyelination issues. These insights suggest that mechanics plays a vital role in diverse CNS functions, interacting intensely with chemical signals at cellular and tissue levels.

EBM brings together a multidisciplinary team of engineers, physicists, biologists, medical researchers, and clinicians in Erlangen. Leveraging advanced techniques across various time and length scales, the team aims to understand how mechanical forces and properties like stiffness affect CNS function, with a specific focus on cerebral, spinal, and cellular mechanics.

In vivo and *in vitro* studies provide fundamental insights and identify key mechano-chemical factors. *In silico* models enable hypothesis testing without extensive experiments, facilitate data transfer across species and scales, and optimize parameters for the development of *in vitro* brain tissue-like matrices. Ultimately, EBM seeks to exploit mechanics-based approaches to enhance our understanding of CNS function, laying the groundwork for improved diagnosis and treatment of neurological disorders.

1.1 RESEARCH PROJECTS

EBM is structured into three focal research areas (FRA) focusing on cerebral (**A**), spinal (**B**), and cellular mechanics (**C**), and an overarching cross-sectional research area (**X**RA).

FRA A – Cerebral Mechanics:

FRA **A** focuses on brain development with special emphasis on brain malformations associated with neurological disorders such as epilepsy. Computational modeling in **A01** will help systematically understand physical mechanisms underlying brain malformations and benefits from quantitative characterization of human brain malformations in **A02** and the *in vitro* and *in vivo* insights gained for brain development in *Xenopus* (**A03**/**A05**) and organoids (**A03**/**A04**) based on engineered brain tissue-like matrices.

FRA B – Spinal Mechanics:

FRA **B** focuses on spinal cord injury and disease with special emphasis on mechanically stimulated regeneration of CNS function. Computational modeling of spinal cord injury, disease and regeneration in **B01** assists and builds on unraveling regeneration/disease-promoting/limiting characteristics and determinants of its mechanical landscape in **B02**, **B03**, **B04**, and exploration of *in vivo* mechanical manipulation in **B05**.

FRA C – Cellular Mechanics:

FRA **C** focuses on the role of mechanics in cell-matrix interactions. Computational modeling of cell-matrix-interactions in **C01** targets the role of mechanics for neuronal “plasticity”, seizure-like hyperactivity and cellular differentiation investigated in **C02**, **C03** and **C04**, all informed by the versatile experimental platform established in **C05** and corresponding insights into mechanosensing and -transduction.

XRA – Cross-Sectional Projects:

The overarching cross-sectional projects in **X**RA will focus on the standardization and integration of *in vivo* and *ex vivo* testing data across scales (**X01**), the transferability of data from different species and experimental methods through advanced machine learning techniques (**X02**), and the design of engineered substitute materials for brain tissue (**X03**)

Table 1 subsumes EBM's projects:

Table 1: EBM projects

FOCAL RESEARCH AREA A: CEREBRAL MECHANICS		
A01	*In silico* modeling of brain malformations	S. Budday
A02	Quantitative characterization of brain malformations	I. Blümcke, A. Dörfler, F. Paulsen
A03	*In vitro* model for the mechanics of early brain development	A. Schambony
A04	The role of mechanics in orchestrating neural lineage decisions	M. Karow, S. Falk
A05	*In vivo* model for the mechanics of brain development	K. Franze
FOCAL RESEARCH AREA B: SPINAL MECHANICS		
B01	*In silico* modeling of spinal cord regeneration	P. Steinmann, S. Budday
B02	Pre and post-metamorphosis spinal cord regeneration in frogs	K. Franze
B03	The determinants of spinal cord mechanics in homeostasis	J. Guck, S. Möllmert
B04	Spinal cord mechanics in a mouse model of multiple sclerosis	S. Kürten
B05	*In vivo* mechanical manipulation of spinal cord regeneration	D. Wehner
FOCAL RESEARCH AREA C: CELLULAR MECHANICS		
C01	*In silico* modeling of mechanical cell-matrix interactions	V. Zaburdaev, P. Steinmann
C02	The role of mechanics for neuronal "plasticity"	R. Frischknecht
C03	The role of matrix mechanics in synchronized neuronal activity	K. Kobow
C04	Cellular differentiation in brain tissue-like matrices	A. Bosserhoff
C05	Molecular mechanisms of neuronal mechanotransduction	B. Fabry
CROSS-SECTIONAL RESEARCH AREA X: CROSS-SECTIONAL PROJECTS		
X01	Model-based reconciliation of *ex vivo* and *in vivo* test data	J. Guo, I. Sack, P. Steinmann, K. Willner
X02	Data analysis and machine learning for heterogeneous, cross-species data	A. Maier, K. Breininger
X03	Engineering brain tissue-like matrices	A.R. Boccaccini
Y	Establishing magnetic resonance elastography at FAU	A. Dörfler, F. Laun, J. Guo, I. Sack

1.2 PROJECT REPORTS

A01 Inverse mechanical characterization of human brain tissue

Jan Hinrichsen, Silvia Budday

Inverse mechanical characterization and structural analysis of human brain tissue from body donors and resected tissue

The overall goal of project **A01** is the implementation of a computational model to predict cortical malformations. An important preliminary step is the mechanical characterization of healthy and diseased human brain tissue. The close collaboration with **A02** has enabled us to obtain data from whole human brains of body donors as well as from tissue from epilepsy and tumor patients that is tested shortly after its surgical resection. These data allow us to calibrate mechanical models for simulations modeling the human brain, as shown in Figure 2, and to investigate the influence of cell-level structural parameters as well as pathologies on mechanical properties. We have successfully established a pipeline, where the mechanically tested specimens are subsequently stained and labeled with pathologies associated with brain malformations by project **A02**. The shear moduli of the specimens in Figure 3 characterize the tissue stiffness and show similar values for different epilepsy diagnoses while they lie in a lower range than those obtained from body donors. A further collaboration with project **X02** enables the automatic detection of cells in stained images using machine learning tools and the subsequent extraction of structural parameters, such as cell density. This is especially facilitated by the Exact platform [1], which is maintained by **X02** and allows for collaborative work on stained image datasets.

Besides the generation of these datasets, we have also investigated approaches to speed up the computationally intensive inverse parameter identification using machine learning techniques and have published our results in this area [2].

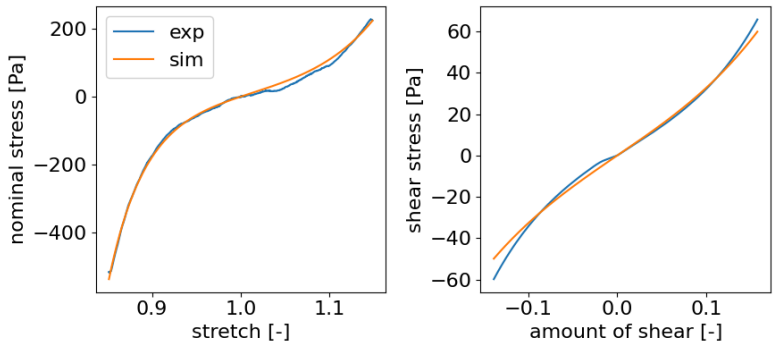

Figure 2: A modified two term Ogden model is fitted to experimental data from human brain tissue.

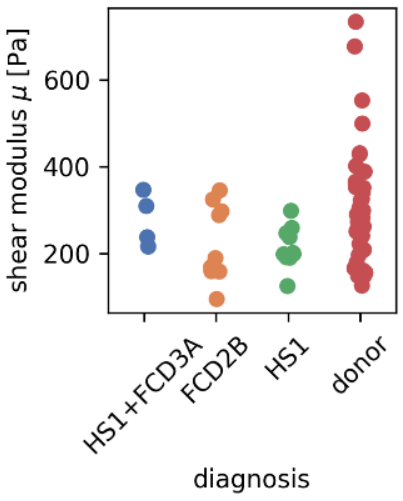

Figure 3: The shear moduli of specimens from resected tissue with different epilepsy diagnoses as well as body donors.

References

[1] Marzahl, C., Aubreville, M., Bertram, C. A., Maier, J., Bergler, C., Kröger, C., Voigt, J., **Breininger, K.**, Klopfleisch, R., & **Maier, A.** (2021). EXACT: A collaboration toolset for algorithm-aided annotation of images with annotation version control. *Scientific Reports, 11*(1), 4343. https://doi.org/10.1038/s41598-021-83827-4

[2] **Hinrichsen, J.**, Ferlay, C., **Reiter, N.**, & **Budday, S.** (2024). Using dropout-based active learning and surrogate models in the inverse viscoelastic parameter identification of human brain tissue. *Frontiers in Physiology, 15*. https://doi.org/10.3389/fphys.2024.1321298

A02 Quantitative characterization of brain malformations

Sophia Auer, Erica Cecchini, Stefan Rampp, Lucas Hoffmann, Ingmar Blümcke, Arnd Dörfler, Friedrich Paulsen

WP1: The generation of normal/healthy human brain datasets commonly usable for EBM members

We continued to create comprehensive brain datasets using healthy human brain samples (from 4 additional body donors). All brains were scanned *ex vivo* by 3T as well as 7T MRT (see below WP 2.2.2). Selected anatomical regions were dissected and mechanically tested by our EBM partners from **A01** (see report therein). All tissues were fixed in formalin, embedded into paraffin and serially sectioned into 4µm thin sections (WP3). This tissue collection effort will continue in the upcoming years to further enrich our common dataset of healthy human brain tissue and serve as an essential reference for understanding mechanical abnormalities in the epileptogenic brain. We also shared 22 surgical tissue samples from patients submitted to epilepsy surgery, including hippocampal sclerosis and Focal Cortical Malformations. The same pipeline of presurgical MRI scanning at 3T (WP2), mechanical testing *ex vivo* by **A01** and histopathology analysis of all available tissue samples was implemented (WP3).

WP2: (Ultra-) High-field imaging of human brain malformations

In 2024, we scanned four more brains from body donors at 3T and 7T. For this purpose, we improved the procedures by 3D-printing a brain holder device according to the study by Kim et al., 2021. This device suspends the specimen in liquid (artificial CSF) to minimize susceptibility artifacts. However, this characteristic complicates MR elastography acquisitions, as the liquid significantly dampens the vibrations used for MRE. Therefore, we have developed an alternative device that allows close contact over larger parts of the brain (Figure 4**a**). After several iterations and tests, the design was finalized and printed. As a result of implementation advances, a first body donor brain was scanned with MRE in addition to the structural 3T and 7T scans.

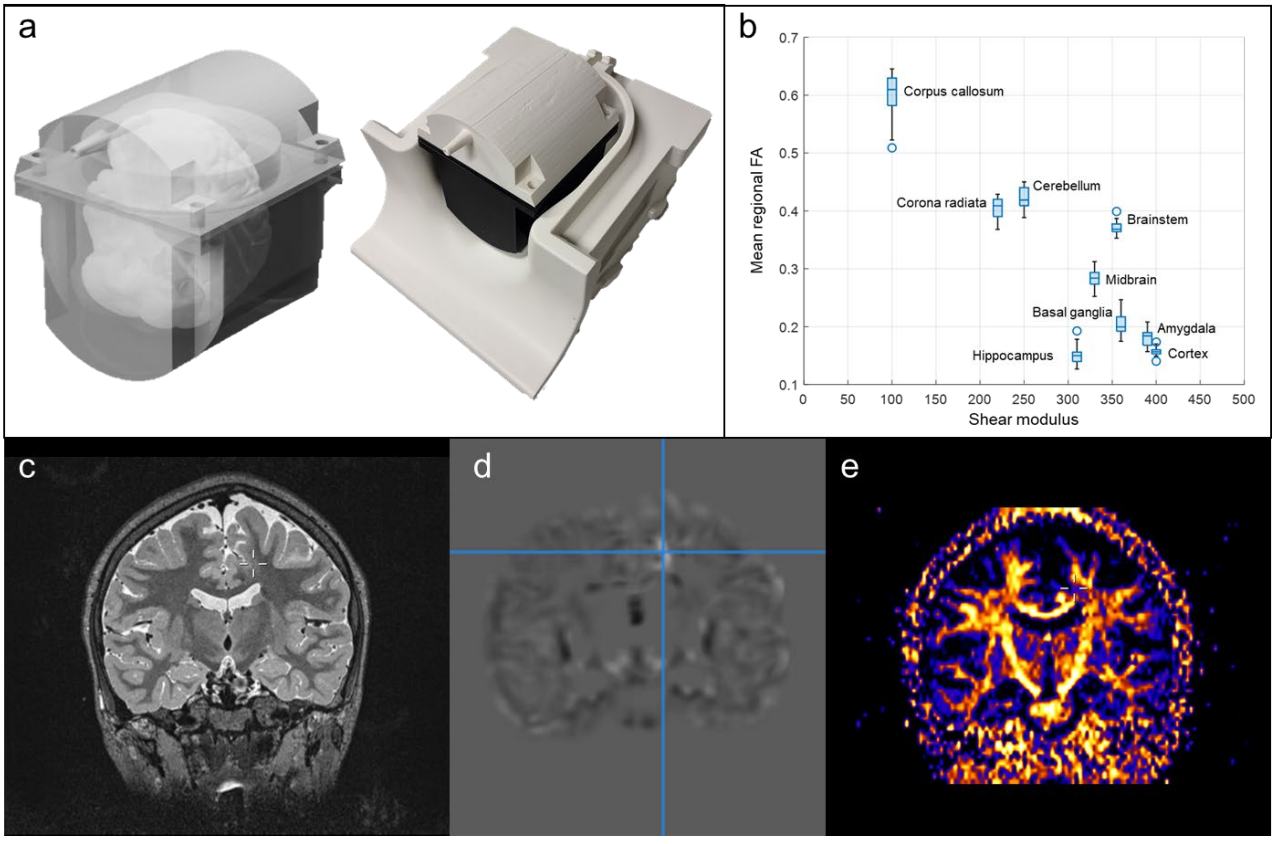

Figure 4: a. 3D-rendering and printed prototype of the brain holder device. b. Correlation between DWI-FA in 26 healthy individuals and shear modulus determined from body donor brains (Hinrichsen et al., 2023). c. Example of FLAIR images of a patient with fronto-mesial FCD (marked). d. FLAT1 MRI-postprocessing analysis. e. FA image with reduction of FA values at the location of the lesion.

We continued to explore quantitative MRI, MRI post-processing, segmentation and registration to evaluate patients with brain malformations (Kasper et al., 2024; Rampp et al., 2021) based on existing datasets as well as newly acquired images from healthy controls and patients with focal epilepsy. Especially in patients with subtle lesions, such techniques could have considerable clinical value (see recent review in Kreidenhuber et al., 2024). In addition to the established voxel-based morphometry method “MAP”, we made the FLAT1 method available, which combines the analysis of both T1 and FLAIR images. Furthermore, the analysis of radiomics feature maps was initiated for the existing and new datasets.

As a main finding, we could demonstrate that fractional anisotropy (FA) of diffusion-weighted imaging (DWI) is strongly correlated to the shear modulus of the Ogden hyperelastic material model determined from (separate) body donor brains (Figure 4**b**). First evaluated in data from a healthy volunteer, we have confirmed this finding in a public dataset including data from 26 healthy individuals across a broad age range. We now extend this line of research to compare mechanical properties determined by **A01** and FA in the same body donor brains. Furthermore, this finding allows the construction of whole-brain models with voxel-wise definition of the shear modulus from FA (**A01**, **X01**). FA analysis may also be helpful to detect subtle lesions (Figure 4**c-e**).

WP3: Deep histopathology phenotyping of genetically characterized human MCD

Over the past year, we advanced our study of MOGHE brain tissue samples, focusing on cases carrying somatic variants in the SLC35A2 gene. We refined our approach by subdividing the patients into three groups: individuals with MOGHE with no SLC35A2 variants, MOGHE individuals with nonsense variants, and MOGHE individuals carrying missense variants. This distinction is relevant as these variant types have distinct impacts on protein transcription and translation. Our cohort included 59 individuals with MOGHE: 31 cases with no variants within SLC35A2, 13 cases with missense variants, and 15 cases with nonsense variants. We demonstrated protein loss in MOGHE cases carrying nonsense variants, which highlights the pathological significance of these mutations, and we are currently in the process of publishing our results

Spatial Transcriptomics: Pipeline Development and Initial Experiments

Parallel to these investigations, we initiated experiments to establish a pipeline for using 10x Genomics Visium Spatial Gene Expression technology. This cutting-edge approach enables spatially

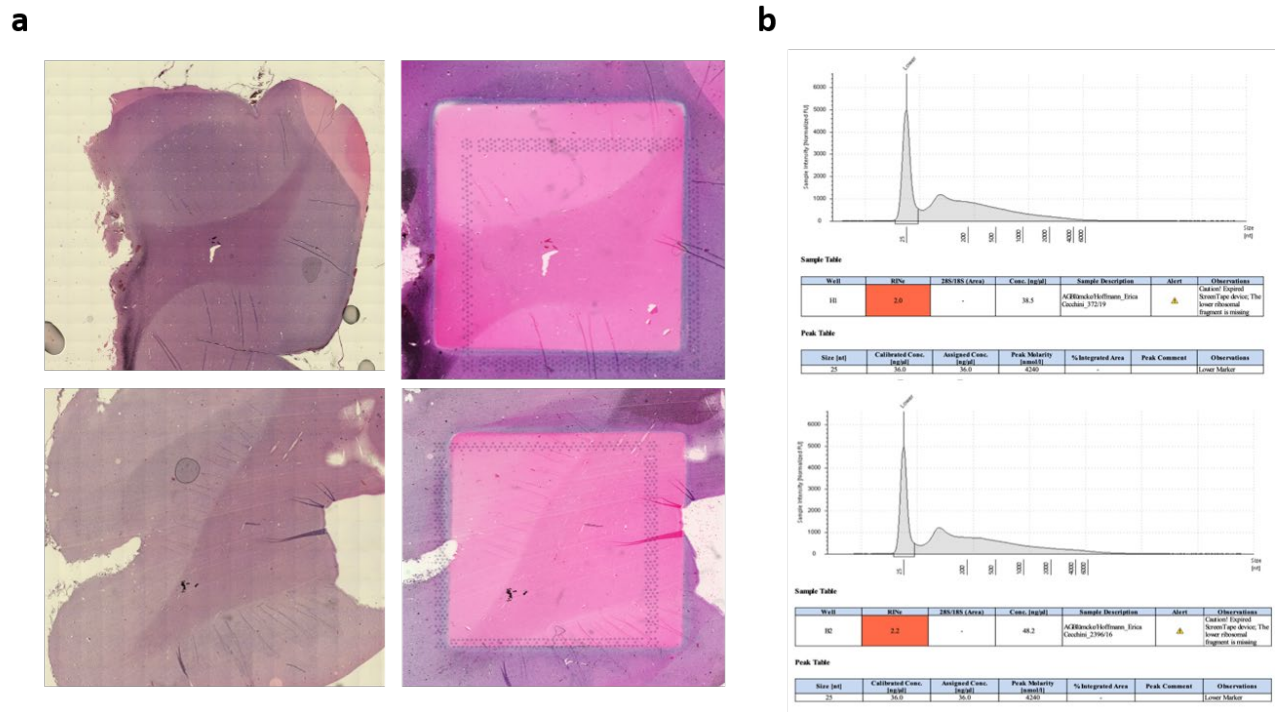

*Figure 5: **a**. Snapshots of H&E FFPE brain tissue acquired in the initial stage of sample preparation and imaging, and relative high magnification brain area assayed in the 6.5x6.5mm barcoded areas. **b**. RNA quality plots of the relative samples shown in a reveal a quality level in need of further improvement to obtain results of high confidence.*

resolved molecular profiling, a necessary tool for advancing our understanding of MOGHE at the cellular level.

RNA Integrity Analysis

Our first step involved assessing RNA quality in 19 human surgical brain samples diagnosed with MOGHE. These samples were collected from surgeries performed between 2012 and 2019. Regions of interest were selected based on their characteristic histopathological features, such as increased oligodendrocyte density, presence of heterotopic neurons, and evidence of hypomyelination. These areas were chosen as they represent key regions of disrupted signaling and extracellular matrix maintenance.

Preliminary Trials with Visium Spatial Gene Expression Tool

Among the 19 samples, four with the highest RNA quality were selected for an initial trial using Visium Spatial Gene Expression. Each trial run included two samples, utilizing the CytAssist Spatial Gene Expression slides v2 (6.5mm) and Visium CytAssist. In the first run, the suboptimal RNA quality limited the generation of a cDNA library and impacted assay success. The second run showed a slight improvement in RNA quality, though results were not yet optimal for high-confidence data.

Despite encountering challenges with RNA integrity, particularly during the first run, the trial provided insights for planning the upcoming tests.

Challenges and Optimization Efforts

A major obstacle in this work is the inherent vulnerability of RNA to degradation, particularly in formalin-fixed paraffin-embedded (FFPE) tissue, which constitutes much of our archival material. To address these issues, we focused on optimizing RNA extraction protocols to preserve RNA integrity and enhancing sample preparation procedures to minimize RNA degradation and fragmentation, aiming for longer RNA reads and improved quality. These trials are ongoing, and our preliminary results have provided valuable results for refining the protocol (see Figure 6).

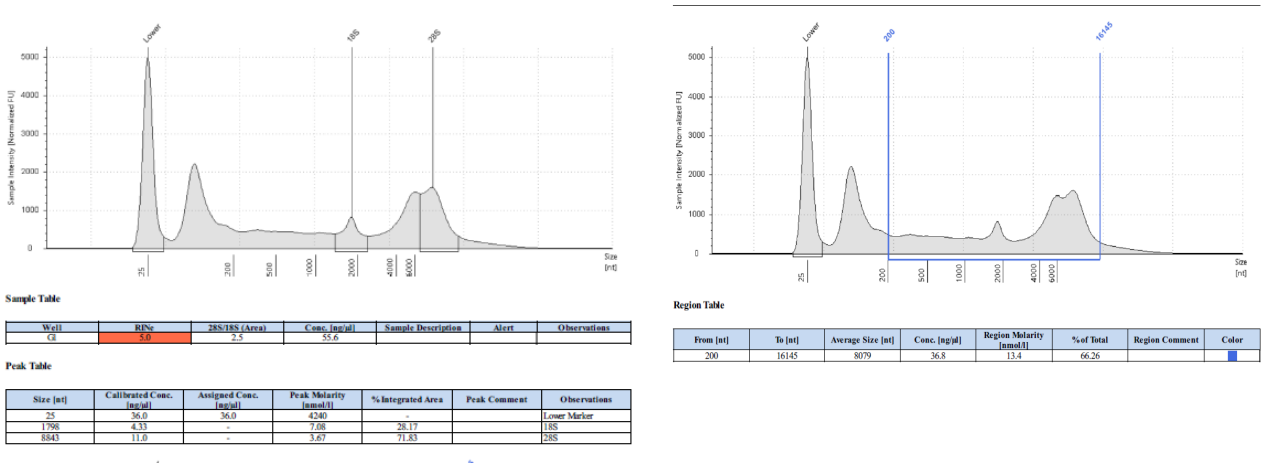

Figure 6: The RNA quality plot illustrates the distribution of detected RNA read lengths, measured in nucleotides (nt) along the horizontal axis. According to 10x Genomics®, the optimal RNA read length begins at 200 base pairs (bp). In our most recent trials, we achieved an area under the curve representing RNA reads ranging from 200 to 16,145 nt, accounting for 66.26% of the total RNA content, as shown in the right image.

Future Directions

In the coming year, we will continue to optimize RNA extraction and tissue preparation processes to improve sample quality for spatial transcriptomics. Additionally, we will expand our sample cohort and aim to establish a robust workflow for generating high-quality spatial RNA expression data. These advancements will enhance our ability to interrogate MOGHE-associated molecular pathologies.

Reference

[1] **Cecchini, E.**, Coras, R., Katoch, M., **Kobow, K.,** Hartlieb, T., Bien, C. G., **Blümcke, I.**, & **Hoffmann, L.** (2024). Brain somatic mosaicism of sex chromosomes defines MOGHE. *Epilepsia*, *65*(S1), 50-51 (abstract 1297). https://doi.org/https://doi.org/10.1111/epi.18151

WP4: Deep extracellular matrix (ECM) quantification and phenotyping in healthy human brain and cortical malformations

In WP4, our primary aim is to investigate proteomic changes within the extracellular matrix (ECM) in epileptic brain pathologies, focusing on malformations of cortical development (MCD) and temporal lobe epilepsy (TLE). As part of this objective, we conducted a comprehensive proteomic analysis of tissue samples from MCDs, including MOGHE (mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy), and FCD (focal cortical dysplasia), as well as TLE (temporal lobe epilepsy). This analysis revealed significant differences in the proteome across these pathologies, with particular emphasis on proteins involved in the ECM and synaptic system (poster: E*xtracellular Matrix and Synaptic Alterations in Epileptic Brain Pathologies: A Proteomic Analysis of MOGHE*; Sophia Auer, Lucas Hoffmann, Martin Schicht, Ingmar Blümcke, and Friedrich Paulsen; 118th Annual Meeting of the Anatomische Gesellschaft, Tripartite Meeting, Graz 2024). In MOGHE, we identified alterations within key components of the ECM and in the synaptic system (Figure 7). These alterations within the proteome may highlight potential mechanisms underlying the pathogenesis and epileptogenesis of this condition. To strengthen these findings, additional MOGHE samples will be analyzed in a follow-up proteomic study early next year. This expanded analysis will allow us to validate the results and to potentially identify novel biomarkers or therapeutic targets specific to MOGHE.

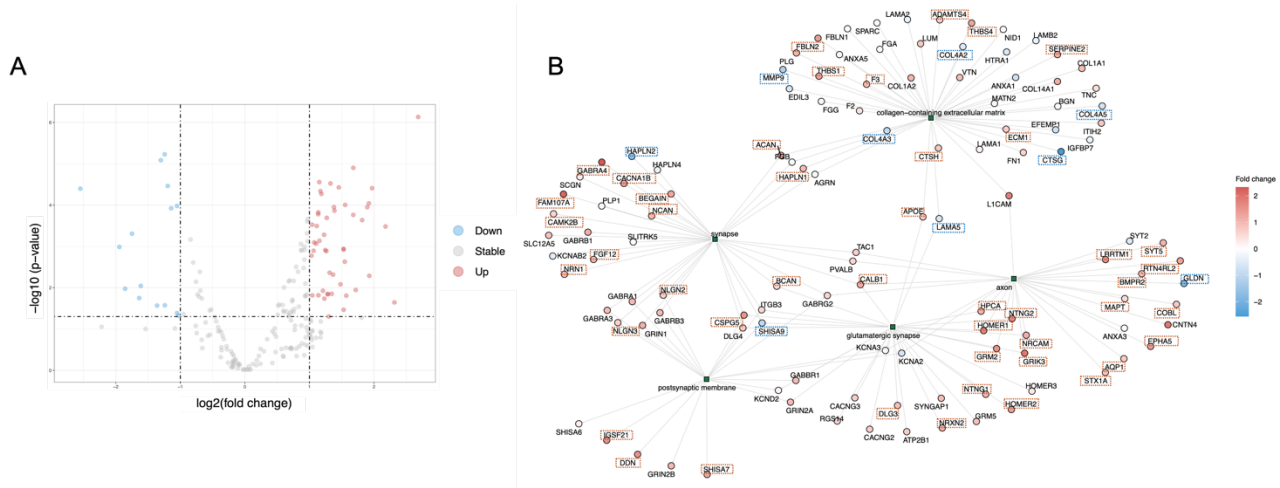

Figure 7: A – Volcano Plot illustrating significantly differentially expressed proteins in MOGHE. X-axis shows the log2 fold change and y-axis denotated the p-value log10. Red dots represent significantly upregulated proteins, whereas blue dots mark significantly downregulated proteins. Horizontal dashed line depicts the p-value threshold of 0.05. The vertical dashed line marks the threshold for a log2 fold change ≥1. B – Over representation analysis (ORA) of proteins altered in GO-annotated cellular components in MOGHE. The network plot shows the top 5 enriched cellular components (green squares) and each altered protein (colored dots). It gives information on upregulation and downregulation of proteins in the annotated cellular components through the log2 fold change. The color scale represents the log2 fold change with blue indicating downregulation and red upregulation. Highlighted proteins (dotted lines in blue or orange) display a significant regulation (p ≤ 0.05).

Another key focus of WP4 is the characterization and quantification of perineuronal nets (PNNs), specialized ECM structures essential for synaptic stability and function. Over the past year, we examined PNNs in cortical and subcortical regions of MCDs and observed distinct age-dependent trends. In the cortical regions, PNN density, as assessed by Aggrecan antibody staining and pixel classifier, exhibited an age-dependent increase in both MOGHE and control samples. Conversely, in the subcortical white matter, an age-dependent decrease in Aggrecan staining intensity was identified (Figure 8). Building of these results, we aim to further investigate the functional implications of the observed age-dependent changes, particularly the reduction of Aggrecan levels in the white matter.

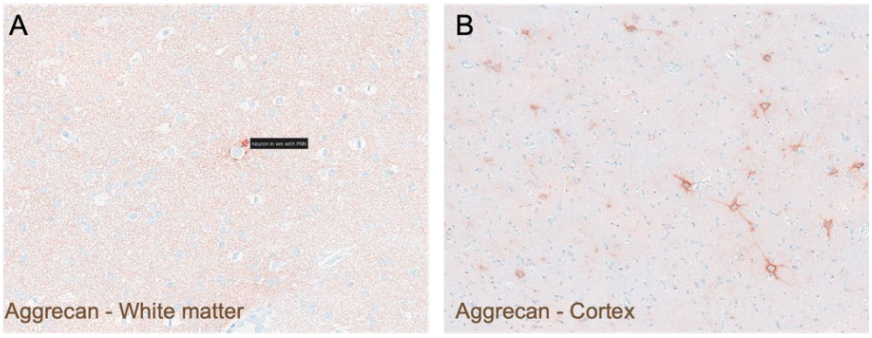

Figure 8: ***Representative images showing Aggrecan immunohistochemical staining in (A) subcortical white matter and (B) cortical regions. A*** *– Staining of white matter tissue from a young MOGHE patient (3 years old) reveals diffuse Aggrecan labeling throughout the white matter region.* ***B*** *– In cortical tissue from an older MOGHE patient (43 years old), Aggrecan staining highlights PNNs as distinct, dense brown staining surrounding neurons in the cortical area.*

Successful application in the large-scale research equipment program in accordance with Art. 91b GG

With the support of several PIs within the CRC1540, we were also able to acquire a digital slide scanner (Hamamatsu, NanoZoomer S360 Ruo, Figure 9) via a large-scale equipment application to the German Research Foundation (DFG), which now can be used to create digital images of tissue sections in the best quality and highest level of detail. The device, which has already been put into operation, can scan extensive serial sections of tissue blocks in a short time, which can then be reconstructed in 3D using a software solution from Chimaera company (Erlangen, Tennenlohe). The slide scanner digitizes complete slides in bright field at high speed. Thanks to relatively intuitive software, it is easy to operate and offers flexibility to meet all necessary requirements. From the beginning of 2025, we will be able to scan around 42,000 sections per year. The extensive digital image files are stored separately on the servers of FAU's Erlangen Regional Computing Center (RRZE) for each CRC1540 working group that wants to use the slide scanner for 3D visualization purposes.

Figure 9: Hamamatsu, NanoZoomer S360 Ruo.

A03 *In vitro* model for the mechanics of early brain development

Clara Froidevaux, Miriam Mager, Alexandra Schambony

The brain develops from a flat sheet of dorsal ectoderm, the neural plate, which undergoes extensive morphogenesis and shape changes to form the three primary ventricles of the brain and the spinal cord. We are developing and characterizing an organoid model system derived from *Xenopus laevis* neural plate tissue to investigate the interplay between mechanics and biochemical signaling in early brain morphogenesis.

WP1.1: Mapping the mechanical landscape of neural plate organoids

The mechanical properties of early neural plate tissue have been analyzed using AFM and Brillouin microscopy [1]. The feasibility of Brillouin measurements for *Xenopus laevis* neural plate organoids needed to be evaluated since this tissue is not transparent due to the high yolk content in the cells. Notably, we have been able to establish Brillouin microscopy on *Xenopus* neural plate organoids in collaboration with Stephanie Möllmert and Jana Bachir.

Comparative analysis of tissue mechanical properties using Brillouin microscopy and AFM microscopy was done on a series of organoids covering the phase from the earliest open neural plate stage to advanced neurulation stages. Although the extracted values of tissue stiffness and elasticity parameters are not directly convertible, both methods revealed highly dynamic changes in tissue mechanics in the early phase of neural plate development. More specifically, the organoids show dynamic changes particularly in the first 2-3 hours of neural development with a softening of the tissue between the specification of the neural plate and the onset of neurulation, i.e. morphogenesis of the neural tube, followed by re-stiffening during neurulation. In the next months, we will repeat and complete these analyses.

WP2: Analyzing the influence of global mechanical cues on brain morphogenesis and tissue mechanics.

In the first months of the project, we observed that organoids cultured on 1.5% Alginate for 48h developed eyes with pigmented retinae (annual report 2023), which is remarkable since the retina is a derivative of the brain. In addition, we have detected *neurogenin 1* - positive neuronal precursor cells in such organoids, indicating neural and brain-specific differentiation in the organoids. Further, fibronectin functionalization of the Alginate hydrogel promotes the migration of neural crest cells and epidermal cells from the organoid to the hydrogel. Together, these results indicate that neural plate organoids develop and differentiate normally on Alginate hydrogels. We have followed up on these results by optimizing culture conditions on Alginate substrates and testing different substrate stiffnesses.

The hydrogel substrates were subjected to a degradation study, which demonstrated that the substrates are stable with constant stiffness for at least 48 hours. Notably, we could confirm that eye structures only formed on the stiffest substrate tested, which was 1.5% Alginate with an average Young's modulus of 41.7 kPa. The experiments have also been carried out on softer substrates, specifically 0.75% and 0.375 % Alginate with average Young's moduli of 12.4 kPa and 3.3 kPa, respectively. Organoids did not develop eye structures but still elongated similarly on 0.75% and 0.375% Alginate hydrogels.

In addition, we investigated, which effect embedding of the organoids in a 3D agarose gel might have. Interestingly, preliminary results suggest that although neural plate and neural tube morphogenesis are strongly affected, neural differentiation might still take place to some extent. We will continue along this line of experiments to address this issue in more detail.

Reference

[1] Kabakova, I., Zhang, J., Xiang, Y., & others. (2024). Brillouin microscopy. *Nature Reviews Methods Primers, 4*(8). https://doi.org/10.1038/s43586-023-00286-z

A04 The role of mechanics in orchestrating neural lineage decisions

Michael Tranchina, Matthias Görtz-Lizarraga, Marisa Karow, Sven Falk

Objectives

The overall goal of **A04** is to understand how mechanical manipulations impact on human neural stem cell lineage decisions and to elucidate the molecular counterparts relaying this information. We are using human induced pluripotent stem cell (hiPSC) - derived brain organoids and neural cells derived thereof to address this question. Ultimately, we aim to chart the molecular landscape modulated in neural stem cells by the mechanical environment to determine molecular key nodes responsible for orchestrating neural stem cell lineage decisions.

Main achievements and conclusions

We have shown that an acute mechanical impact on human brain organoids as applied through a rheometer, not only results in an increase in the number of neural stem cells but also increases protein levels of the neural stem cell factor SOX2 directly correlating with the strength of the physical force acting on the respective organoid. Leveraging the bulk- and scRNA-seq data of compressed organoids, we found that upon an acute mechanical impact, organoid resident cells reduce their metabolic reliance on oxidative phosphorylation, which is used primarily by neurons for their energy production, and they instead, shift towards lipid metabolism (Figure 10A, Figure 10B).

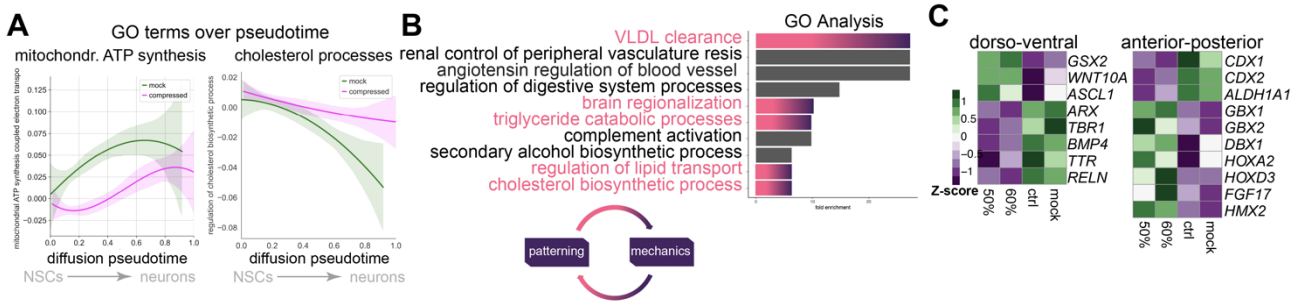

Figure 10: A) GO terms along pseudotime revealing the metabolic changes upon compression. B) GO terms associated with patterning processes impacted in cells of compressed human brain organoids. C) Heatmap showing deregulation of patterning associated genes.

Since mitochondria play a role in both these processes, this suggests that mechanical forces significantly impact mitochondrial function in general. Additionally, we identified compression-induced alterations in genes associated with patterning (Figure 10C) indicating a crosstalk between mechanical forces and the acquisition of brain regional identity.

Furthermore, we derived new data on brain organoids embedded in hydrogels with defined physical properties allowing us to assess how a persistent change in the mechanical environment impacts on neural stem cell lineage decisions in brain organoids. Interestingly, those experiments also revealed that the fraction of SOX2-expressing cells is increased depending on the hydrogels used (Figure 11).

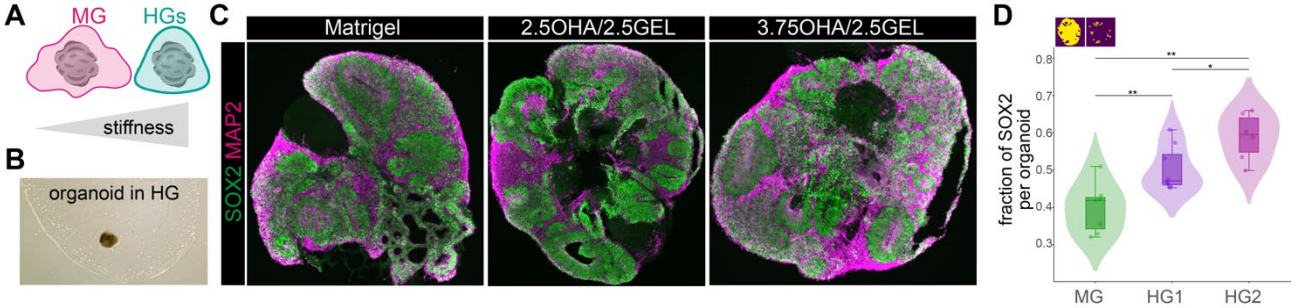

Figure 11: A) Scheme showing difference in stiffness between MG (matrigel) and HG (hydrogel). B) Organoid embedded in hydrogel. C) Images showing SOX2 and MAP2 in organoid slices grown in different hydrogels. D) Quantification of the fraction of SOX2 per organoid sections showing increase in hydrogel conditions compared to SOX2 in organoids embedded in MG.

Outlook

In the next steps, we want to assess the molecular profile of brain organoids embedded in hydrogels of defined physical properties. These transcriptome data will then be compared with the bulk and scRNA-seq data of compressed organoids to identify putative shared molecular nexuses relaying the effects of mechanical manipulations.

In collaboration with Kristian Franze´s lab, we will use AFM (atomic force microscopy) to determine the mechanical properties in slices derived from human brain organoids embedded in hydrogels with different mechanical properties.

Furthermore, we refine the analyses of the acute rheometer-mediated mechanical manipulation by labeling the compression axis allowing us to extract how the geometric and spatial organization of the neural tissue influences the cellular response to mechanical stimuli.

A05 *In vivo* model for the mechanics of brain development

Sebastián Vásquez-Sepúlveda, Kristian Franze

Objectives

1. Characterize brain viscoelasticity *in vivo*.
2. Determine mechanics and morphology of brains with gene mutations leading to malformations.
3. Rescue brain mechanics and test the effect on brain morphology and malformations.

In 2024, our work aimed to learn how to measure tissue stiffness using the atomic force microscopy setup. Specifically for objective 1, the first assays for *in vivo* stiffness mapping were obtained and can be seen in Figure 12.

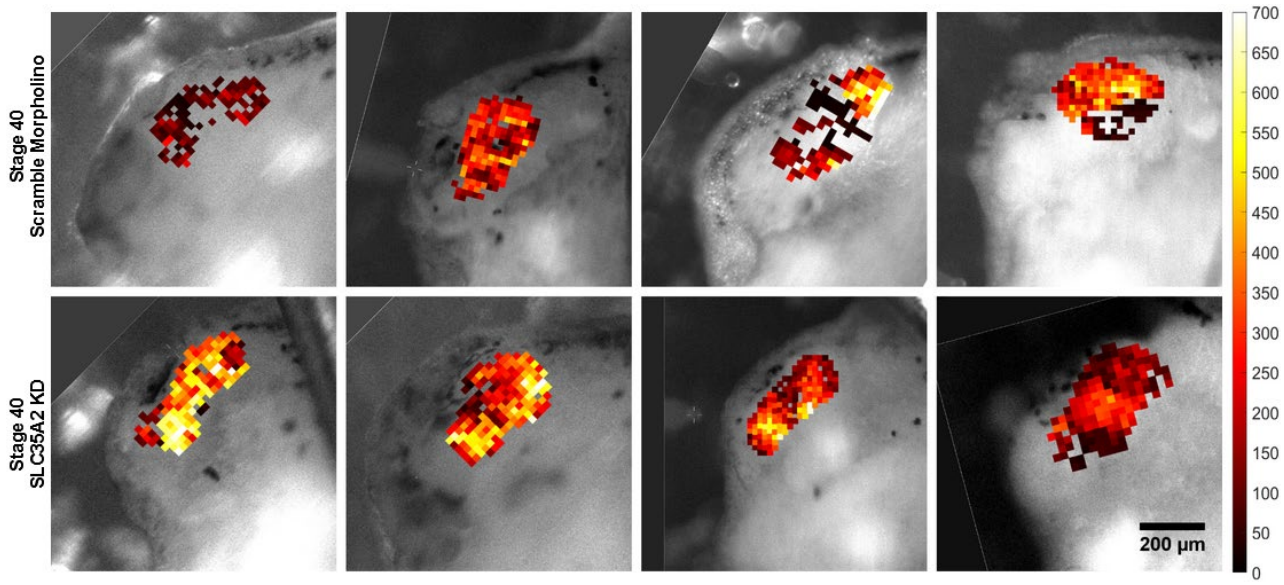

*Figure 12: **Result of stiffness mapping on live Xenopus laevis embryos at stage 40**. Stiffness maps of the dienceph-alon and mesencephalon of 4 wild-type embryos (top row) and 4 SLC35A2 KD embryos (bottom row). The scale bar of the stiffness values is measured in Pascal (Pa).*

For objective 2, the focus was on obtaining viable knockdowns of SLC35A2 in Xenopus embryos, for which a morpholino was designed and evaluated by Western blot as shown in Figure 13.

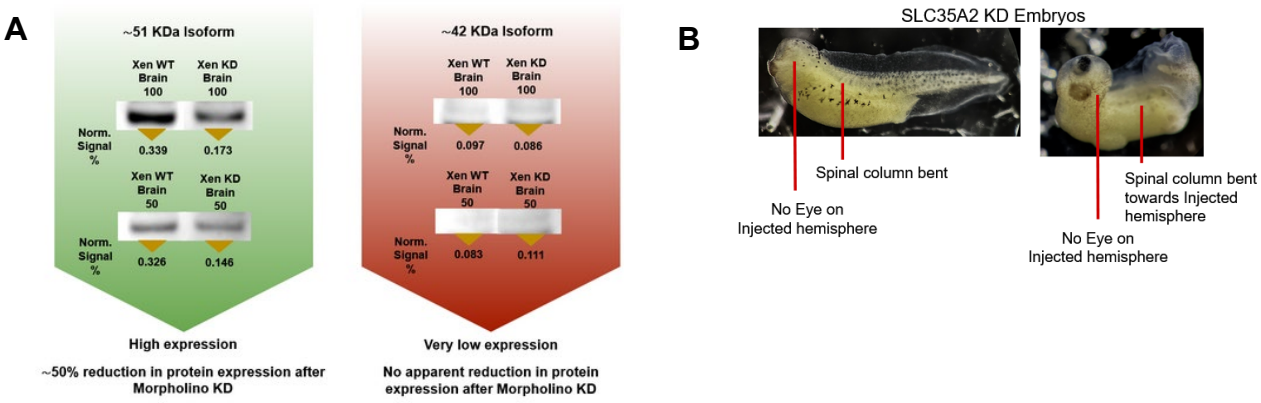

*Figure 13: **Results of SLC35A2 Knockdown in Xenopus laevis embryos**. A) Western blot showing the de-crease of Slc35a2 protein expression after the injection of an "slc35a2.S" morpholino at the 4-cell stage into both dorsal blastomeres. B) Effect on morphology after the injection of "slc35a2.S" morpholino at the 4-cell stage into one of the dorsal blastomeres.*

As of November 2024, this work has been presented at the 1st EBM annual Update meeting on February 9, 2024, and at the "Forces across scales I3S" conference in Porto, Portugal, March 6-9, 2024.

The techniques learned during this period are key to the progress of project **A05**. The establishment of a viable morpholino knockdown enables us to directly observe and measure the effects of this phenotype on brain mechanics. The proper training in the use of AFM allows us to obtain reliable measurements on brain tissue *in vivo*, and collaborate with other members of the consortium to measure other types of materials, such as hydrogels, organoids, or single cells.

References

[1] Thompson, A. J., Pillai, E. K., Foster, S. K., Holt, C. E., & **Franze, K.** (2019). Rapid changes in tissue mechanics regulate cell behaviour in the developing embryonic brain. *eLife, 8*, e39356. https://doi.org/10.7554/eLife.39356

[2] D'Gama, A. M., Woodworth, M. B., Hossain, A. A., Bizzotto, S., Hatem, N. E., LaCoursiere, C. M., Najm, I., Ying, Z., Yang, E., Barkovich, A. J., Kwiatkowski, D. J., Vinters, H. V., Madsen, J. R., Mathern, G. W., **Blümcke, I.**, Poduri, A., & Walsh, C. A. (2017). Somatic mutations activating the mTOR pathway in dorsal telencephalic progenitors cause a continuum of cortical dysplasias. *Cell Reports, 21*(13), 3754–3766. https://doi.org/10.1016/j.celrep.2017.11.106

[3] Bonduelle, T., Hartlieb, T., Baldassari, S., et al. (2021). Frequent SLC35A2 brain mosaicism in mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy (MOGHE). *Acta Neuropathologica Communications, 9*, 3. https://doi.org/10.1186/s40478-020-01085-3

[4] Koser, D. E., Thompson, A. J., Foster, S. K., Dwivedy, A., Pillai, E. K., Sheridan, G. K., Svoboda, H., Viana, M., Costa, L. D., **Guck, J.**, Holt, C. E., & **Franze, K.** (2016). Mechanosensing is critical for axon growth in the developing brain. *Nature Neuroscience, 19*(12), 1592–1598. https://doi.org/10.1038/nn.4394

aA05 Mechanical interactions between neural stem cells and their niche

Kathrin Welsch, Sebastián Vásquez-Sepúlveda, Kristian Franze

We are investigating the mechanical properties of the dentate gyrus within the adult, murine hippocampus specifically in animals with a knockout of the transcription factors FoxO1,3 and 4. This project presents itself in three work packages, which progressed as follows over the last year:

One of our aims is to **characterize the morphology and mechanical properties of neural stem/progenitor cells (NSPCs) extracted from adult mouse hippocampi *in vitro***. I have tested several protocols for isolation and culture of murine NSPCs with varying success. Currently I am being trained in working with these cells by the group of Prof. Tomohisa Toda, who has done so successfully for many years now. I am planning on performing first experiments in January 2025. These will include the evaluation of proliferation rates, morphology and differentiation of NSPCs grown on hydrogels of different stiffnesses.

Our *in vivo* approach relies on **atomic force microscopy (AFM) in order to determine the stiffness of wild-type versus knock-out tissue**. For this purpose, Dr. Julia Becker in Cambridge has trained me in isolating the tissue, generating sections on a vibratome, performing measurements and creating stiffness maps out of the obtained data. At the moment we are setting up this pipeline at our lab at the MPZPM and anticipate first measurements early in 2025.

In order to determine the influence of the extracellular matrix (ECM) on the overall tissue mechanics, we will perform **experiments on decellularized hippocampal tissue**. I learned about decellularization methods at the lab of Prof. Magdalena Götz in Munich who shared their knowledge on the topic with me. There I tested two published protocols and successfully removed cells from brain sections while maintaining the anatomical structures within the hippocampus. We plan on testing these protocols in Erlangen in the upcoming spring and performing AFM measurements on decellularized sections. In addition, we will grow and evaluate wild-type NSPCs on knock-out ECM and vice versa.

B01 *In silico* modeling of spinal cord regeneration

Rahul Gopalan Ramachandran, Oskar Neumann, Silvia Budday, Paul Steinmann

Current scientific efforts within the **B01** project are focused on understanding the complex mechanical nature of spinal cord tissue under different types of loading. In addition, a first continuum mechanical model for the process of spinal cord regeneration has been developed and simulated.

To study the mechanical properties of spinal cord tissue, project **B01** extensively performed indentation experiments (spherical indenter with a diameter of 200 µm) [1]. We measured consistent tissue mechanics when using different indenter tip diameter sizes on the mesoscale (diameter: 100 to 400 µm). The faster the loading rate, the stiffer is the material response; the higher the temperature, the softer is the material response (with an approximately linear relation for a range from room to body temperature). Stress relaxation equilibrated after approximately 300 seconds. Preconditioning by cyclic spherical indentation loadings led to a reduction in stiffness by up to 20 % after 5 cycles. Spinal cord white matter is softer than spinal cord gray matter tissue. It shows lower storage moduli and similar loss moduli as gray matter tissue in a dynamic mechanical analysis.

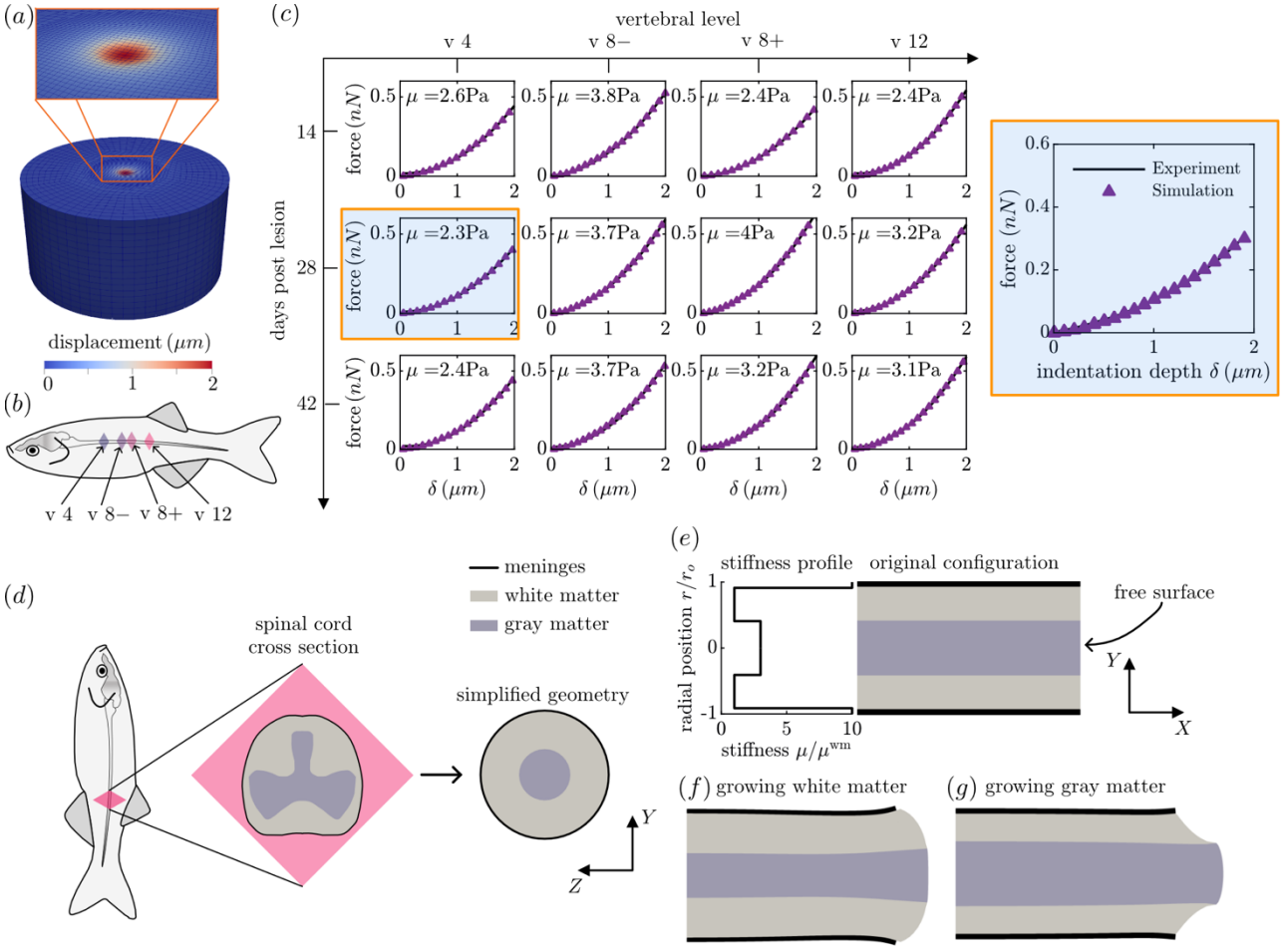

Figure 14: Data evaluation and overview for spinal cord regeneration model: (a) Exemplary FEM simulation of indentation experiment. (b) Vertebral levels in a zebrafish indicated with colored planes (c) Overview of evaluated mechanical data for adult zebrafish spinal cord regeneration. Regrowth simulation of spinal cord tissue. (d) Illustration of Central Nervous System (CNS) and spinal cord cross-section with the simplification of the cross-section geometry into concentric circles. (e) The simulation geometry in the original configuration with a plot of normalized radial stiffness distribution against normalized radial position. (f) Deformed configuration of regrowth simulation with growing white matter. (g) Deformed configuration of the regrowth simulation with growing gray matter.

In a first experimental pipeline, we successively analyzed the same spinal cord sample with Brillouin microscopy (with the support of project **B03**), atomic force microscopy (together with **B02** and **B03**), indentation and large-strain cyclic loading using a rheometer (guided by **A01**). In another multi-modality pipeline, we tested the same sample with table-top magnetic resonance elastography (in collaboration with project **X01**), indentation, and the rheometer. These initial trials have demonstrated the general feasibility, but also the challenges associated with multi-modality testing. In the future,

the setups and overall protocol will be improved and further developed to systematically investigate the mechanical properties of spinal cord tissue on various temporal (quasi-static to GHz) and spatial scales (µm to cm).

Based on these experimental insights into the mechanics of spinal cord tissue and the available data within the consortium of EBM, we were able to conceptualize and simulate a first approach for a continuum-mechanics-based spinal cord regeneration model. Here, observations and findings on molecular and biological aspects of spinal cord regeneration in the zebrafish larvae (from project **B05**) together with mechanical indentation data collected during regeneration in the adult zebrafish (provided by project **B03** [2]) form the cornerstones of the regeneration model.

Figure 14c shows the available mechanical data for the regeneration process of the adult zebrafish at three time points during the course of regeneration and at four locations along the spinal cord axis (as illustrated in Figure 14b). These data show an increase in stiffness of spinal cord tissue close to the lesion site. To incorporate this correlation into a continuum model, an inverse parameter identification routine (developed by project **A01**) based on Finite Element Analysis (Figure 14a) is employed to fit a neo-Hookean material model to the corresponding indentation curves. In this way, a unique set of mechanical material parameters for spinal cord gray and white matter tissue can be calculated for each pair of locations and time points after the lesion. These temporal and spatial profiles of mechanical parameters can then be used to inform the continuum-mechanical regeneration model.

As a first continuum mechanics model, we consider a simplified model by assuming the spinal cord as an assembly of homogeneous concentric cylinders with gray matter, white matter, and meninges arranged radially from the center of the geometry (Figure 14d). The radial stiffness profile is presented in Figure 14e; gray matter in the center is stiffer than the surrounding white matter, while both of the materials are encased in a much stiffer meninges layer. To study how tissue mechanics, affect regeneration, we model regrowth in the spinal cord under the framework of morphoelasticity, where the deformation gradient tensor is multiplicatively decomposed into elastic and growth tensors as $\mathbf{F} = \mathbf{F}_\mathrm{e}\mathbf{F}_\mathrm{g}$. Preliminary results suggest significant variations in morphology as growth is localized in different materials. The resulting morphology of the tissue adjacent to the lesion site by growing only white matter and growing only gray matter are shown in Figure 14f and Figure 14g respectively.

References

[1] **Neumann, O.**, Vardhan Surana, H., **Melly, S.**, **Steinmann, P.**, & **Budday, S.** (2024). Mechanical characterization of spinal cord tissue by nanoindentation. *Journal of the Mechanical Behavior of Biomedical Materials* (accepted).

[2] **Möllmert, S.**, Kharlamova, M. A., Hoche, T., Taubenberger, A. V., Abuhattum, S., Kuscha, V., Kurth, T., Brand, M., & **Guck, J.** (2020). Zebrafish spinal cord repair is accompanied by transient tissue stiffening. *Biophysical Journal, 118*(2), 448–463. https://doi.org/10.1016/j.bpj.2019.10.044

[3] **Hinrichsen, J.**, et al. (2023). Inverse identification of region-specific hyperelastic material parameters for human brain tissue. *Biomechanics and Modeling in Mechanobiology*.

B02 Pre and post metamorphosis spinal cord regeneration in frogs

Maria Tarczewska, Kristian Franze

Objectives

The primary objective of the project work in the report period was to establish a spinal cord injury model in Xenopus laevis tadpoles and establish the methods to be used for imaging spinal cord regeneration. The project also sought to learn and apply Atomic Force Microscopy (AFM) techniques to quantify tissue stiffness in specific regions of the spinal cord.

Main Achievements

Significant progress was achieved in establishing a spinal cord injury model in tadpoles in collaboration with **B05**, with the successful development of a needle-based transection protocol followed by observed regeneration (Figure 15). A major advancement, included implementing a whole-mount tadpole staining protocol [1], primarily using acetylated tubulin, enabling detailed spinal cord visualization for regeneration timeline studies (Figure 16). Additionally, the project successfully incorporated immunohistological staining techniques. Progress was made in learning AFM techniques, a crucial step for quantifying tissue stiffness in the spinal cord lesion site. The project also advanced in swimming behavior analysis methodology, successfully inducing swimming responses and working on optimizing video data analysis to assess functional recovery post-regeneration.

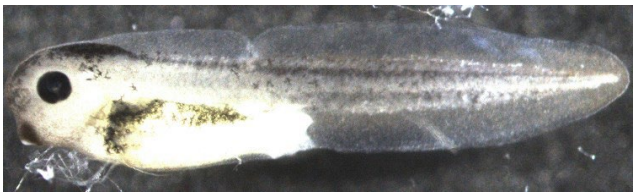

Figure 15: Xenopus laevis tadpole (NF40) day after spinal cord transection. The injury site is visible on the dorsal side.

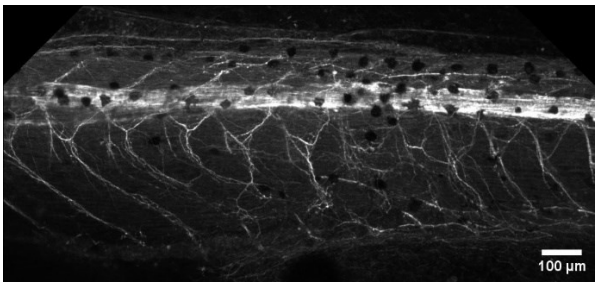

Figure 16: Immunofluorescence imaging of whole-mount Xenopus laevis tadpole stained with acetylated tubulin.

Conclusions

The project has progressed in establishing multiple key protocols for studying spinal cord injury and regeneration in *Xenopus laevis* tadpoles, including transection methods, whole-mount staining, and behavioral analysis. The implementation of AFM techniques and swimming behavior assessment creates a robust foundation for quantifying tissue stiffness, which could provide valuable insights into spinal cord injury regeneration.

Outlook

The next phase of the project will focus on mapping the temporal dynamics of spinal cord regeneration using established microscopy techniques, examining key molecular markers (collagen IV, laminin, GFAP, vimentin, and Sox2/3+ cells) across regenerative and non-regenerative stages [2,3]. Additionally, AFM stiffness mapping of lesion sites will be performed to characterize mechanical changes during regeneration.

References

[1] John, N., **Kolb, J.**, & **Wehner, D.** (2022). Mechanical spinal cord transection in larval zebrafish and subsequent whole-mount histological processing. *STAR Protocols, 3*(1), 101093. https://doi.org/10.1016/j.xpro.2021.101093

[2] Moeendarbary, E., Weber, I. P., Sheridan, G. K., Koser, D. E., Soleman, S., Haenzi, B., Bradbury, E. J., Fawcett, J., & **Franze, K.** (2017). The soft mechanical signature of glial scars in the central nervous system. *Nature Communications, 8*, 14787. https://doi.org/10.1038/ncomms14787

[3] Muñoz, R., Edwards-Faret, G., Moreno, M., Zuñiga, N., Cline, H., & Larraín, J. (2015). Regeneration of *Xenopus laevis* spinal cord requires Sox2/3 expressing cells. *Developmental Biology, 408*, 229–243. https://doi.org/10.1016/j.ydbio.2015.03.009

B03 The determinants of spinal cord mechanics in homeostasis

Jana Bachir Salvador, Stephanie Möllmert, Jochen Guck

Determinants of nervous tissue mechanical properties in homeostasis

Objective

B03 seeks to identify the (bio)chemical and physical determinants that govern a distinct mechanical fingerprint of nervous tissue during homeostasis. This investigation involves a comprehensive quantification of viscoelastic material characteristics *in vivo* and *ex vivo* by using confocal Brillouin microscopy and Atomic Force Microscopy (AFM)-enabled indentation measurements. These mechanical properties are then correlated with the identified factors crucial for maintaining homeostasis. So, we have focused on the cellular constituents of the spinal cord tissue of living zebrafish larvae. Through EBM collaborations, we have expanded our portfolio to include the quantification of mechanical properties of the porcine spinal cord (**B01**), the developing Xenopus neural fold and explants thereof (**A03**), sectioned murine brain tissue (**C02**), and seizing brain tissue in living zebrafish larvae (**C03**). For each species, tissue and measurement technique, we established and optimized sample preparation protocols. We then conducted Brillouin microscopy measurements (*in vivo and ex vivo*) to map the distribution of the Brillouin frequency shift (˜compressibility) and Brillouin linewidth (˜viscosity) optically, and performed indentation measurements to extract an indentation modulus through external compressive loading. One important finding shows that while both AFM and Brillouin microscopy assess key mechanical properties, their differing sensitivities across length- and time-scales provide insights into a broad spectrum of material characteristics, spanning multiple orders of magnitude. Although theoretical relationships between the two techniques can be established, direct empirical comparisons cannot be applied *a priori* [1].

Methodology

In **B03**, the opto-genetic manipulation of tissue structure and composition is based on a targeted ablation of tissue in a transgenic zebrafish line. Using the TetON system [2], a tissue-specific expression of a photosensitizer “KillerRed” (KR) is induced upon incubation with doxycycline (DOX). The specificity of the ablation, such as cell type or spatial dimension, is achieved by combining the exposure of the KR to 561 nm laser light using a confocal fluorescence microscope with fish lines in which only a distinct subset of cells expresses the protein. Using three- and four-day-old larvae, we ablated either entire spinal cord cross-sections, or a cohesive cluster of cells situated at specific spinal cord regions, or only individual motor neurons. KR then generates reactive oxygen species (ROS) which in turn causes irreversible oxidation on cellular components [3]. We proceed by measuring the response of these specimens by Brillouin time-lapse measurements using the Brillouin microscope based on the setup in [4] and AFM-based indentation measurements. The acquired Brillouin microscopy images and indentation curves are analyzed by custom-written software. To facilitate shorter acquisition times and higher throughput, we furthermore are establishing a Brillouin line-scan setup which allows to map the Brillouin frequency shift and linewidth 20x faster than the confocal setup.

Results

Results indicate that one hour following the ablation with 5% laser power of a defined volume of KR-expressing spinal cord tissue, the Brillouin frequency shift is significantly reduced, suggesting a softening of the ablated region that is not observed under control conditions (Figure 17). Additionally, AFM-based indentation measurements were conducted on freshly prepared spinal cord tissue sections subjected to the same ablation protocol (Figure 18). The apparent Young’s modulus did not show significant differences between the various conditions. A TUNEL assay performed post-fixation on ablated specimens demonstrated that this ablation method was insufficient to induce apoptosis, as evidenced by the absence of TUNEL-positive cells in the ablated region. This finding implies that the observed tissue softening cannot simply be attributed to a reduction in cellular density through apoptosis, but rather points towards a detectable mechanical phenotype that precedes cell death and emerges with the dosed occurrence of ROS alone.

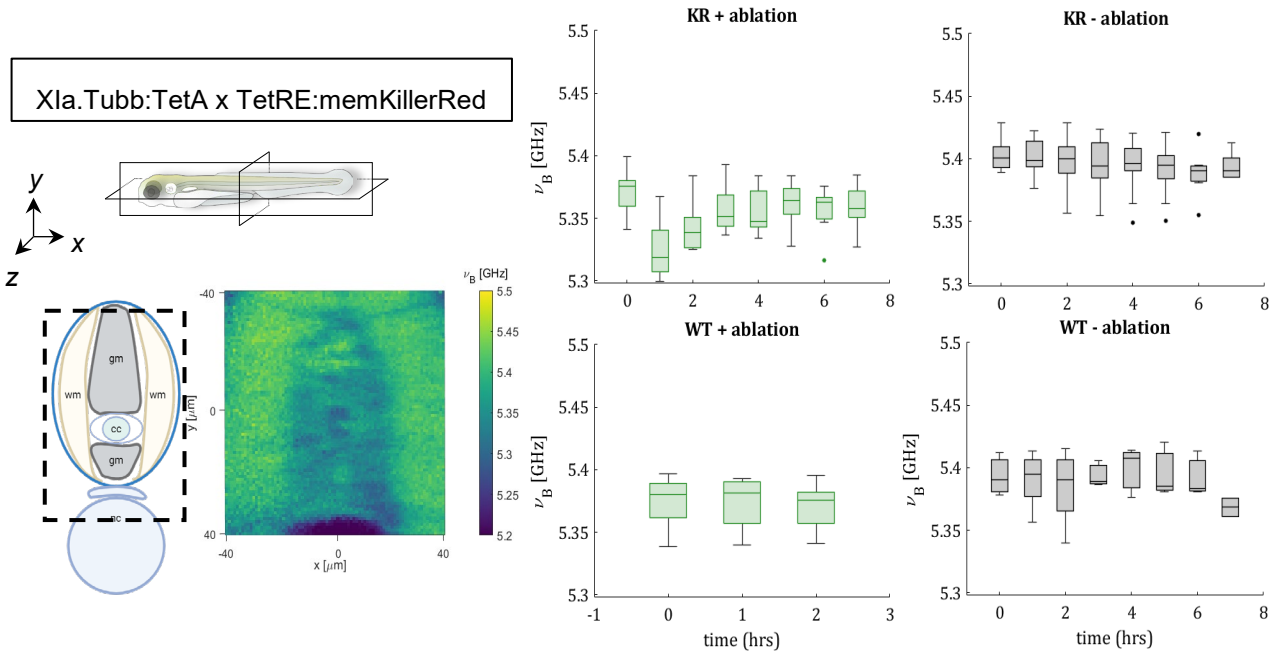

Figure 17: A representative Brillouin frequency shift map of the entirely ablated spinal cord cross-section of KR expressing larva. Dynamic tracking of changes in Brillouin frequency shift of KR expressing larvae subjected to ablation by illumination, and without ablation, as well as wild-type (WT) larvae subjected to the same ablation treatment.

Outlook

Further histological analysis will complement the observed Brillouin frequency shift changes by providing detailed structural and compositional insights. This combination will offer an unparalleled understanding of the factors influencing the mechanical properties of central nervous system (CNS) tissues in the context of homeostasis regulation. A potential link between ROS production, interstitial fluid accumulation, and decreased Brillouin frequency shifts will be investigated further. To address the limitation of slow acquisition inherent to the confocal configuration of Brillouin microscopy, we will finalize a line-scan Brillouin microscope, as described in [5]. This advancement is expected to yield a 20-fold increase in measurement speed, facilitating its application in **B03** and supporting collaborations within the EBM framework.

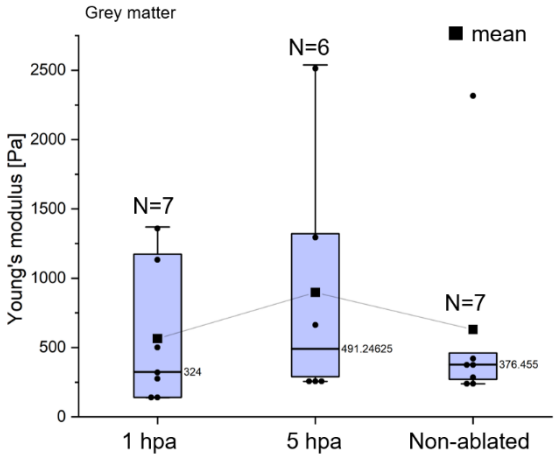

Figure 18: Apparent Young's modulus for gray matter (gm) region for wild-type non-ablated controls, and panneuronal ablated larvae at different hours post ablation (hpa).

References

[1] Gutmann, M., **Bachir Salvador, J.**, et al. (2024). Beyond comparison: Brillouin microscopy and AFM-based indentation reveal divergent insights into the mechanical profile of the murine retina. *Journal of Physics: Photonics, 6*, 035020.

[2] **Wehner, D.**, et al. Use of the Teton system to study molecular mechanisms of zebrafish regeneration. *Journal of Visualized Experiments, (100)*.

[3] Chilakamarthi, U., & Giribabu, L. Photodynamic therapy: Past, present and future. *The Chemical Record, 17*(8), 775–802.

[4] Schlüßler, R., **Möllmert, S.**, et al. Mechanical mapping of spinal cord growth and repair in living zebrafish larvae by Brillouin imaging. *Biophysical Journal, 115*(5), 911–923.

[5] Bevilacqua, C., Gomez, J. M., Fiuza, U. M., et al. High-resolution line-scan Brillouin microscopy for live imaging of mechanical properties during embryo development. *Nature Methods, 20*.

B04 Spinal cord mechanics in a mouse model of multiple sclerosis

Maik Hintze, Rittika Chunder, Stefanie Kürten

Multiple sclerosis (MS) is a chronic autoimmune neuroinflammatory disease of the central nervous system (CNS) that leads to demyelination and neurodegeneration[1]. Infiltration of peripheral immune cells, including antigen-specific T cells and B cells, into the CNS is a major hallmark and potential trigger of neuroinflammation in MS patients[2]. Destruction of myelin triggered by autoreactive immune cells leads to axonal insult, followed by axonal loss and neuronal cell death eventually causing irreversible disease progression[2]. The cell loss during the late phase of MS is accompanied by activation of astrocytes, leading to the formation of a so-called glial scar. Reactive astrocytes are one of the main players in chronic non-resolving glial scar formation pathology[3].

Tissue remodeling in glial scars leads to an overall reduction of tissue stiffness at the lesion site[4], and individual astrocytes have been shown to be “softer” than neurons[5]. Given the wide range of homeostatic, trophic and mechanic functions of astrocytes within the CNS, we hypothesize that astrocytic mechanosensation via the mechanosensory ion channel Piezo1 [6] might be a contributing factor to MS pathology. Piezo1 is known to be expressed on astrocytes and can regulate Ca2+ oscillations and cytokine release *in vitro*[7]. Taken together, these observations suggest that MS-associated tissue remodeling likely leads to altered mechanical properties in MS lesions, which can be sensed by astrocytes and may contribute to further disease progression.

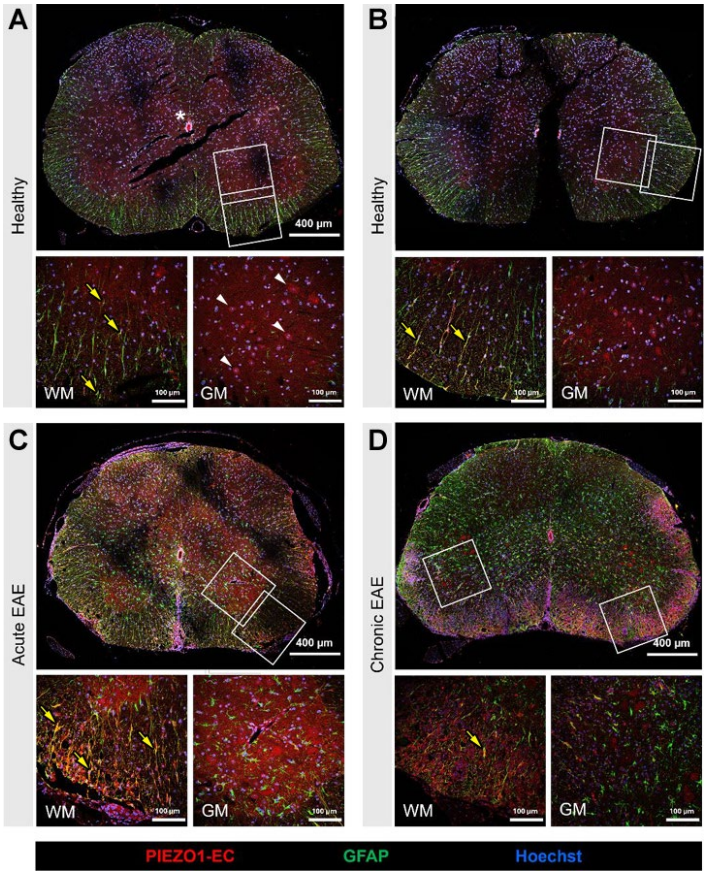

Figure 19: Astrocytic PIEZO1 immunoreactivity is increased in murine spinal cord during EAE. Spinal cord cross-section over-views and magnified views of boxed white matter (WM) and gray matter (GM) areas are shown. A, B, Healthy samples. Immunoreactivity against PIEZO1 extracellular domain (PIEZO1-EC) is most prominently observed in ependymal cells of the central canal (indicated by asterisk in panel A) and ventral horn motoneurons (white arrowheads in magnified GM image of panel A). Healthy mouse spinal cord shows overlap of GFAP and PIEZO1, indicated by yellow staining resulting from GFAP (green) and PIEZO1 (red) color overlap (yellow arrows in magnified WM images A, B). C-D, Spinal cord samples from mice with experimental autoimmune encephalitis (EAE) show increased PIEZO1 immunoreactivity. Specifically, astrocytic PIEZO1 expression seems increased as indicated by intense yellow staining (yellow arrows in magnified WM images C, D). PIEZO1 intensity in chronic EAE is somewhat reduced compared to acute EAE (compare magnified WM images of C and D).

We first set out to test for astrocytic PIEZO1 expression *in vivo* during experimental autoimmune encephalitis (EAE), a mouse model that recapitulates various aspects of the human MS[8]. In mouse spinal cord, we observed overlap between PIEZO1 and the astrocyte marker GFAP (Figure 19A, B), which was increased in spinal cord specimens from animals with acute or chronic EAE (Figure 19C, D) Thus, astrocytic PIEZO1 expression is low in healthy spinal cord and gets upregulated during EAE. We next want to study the function of astrocytic PIEZO1 during EAE in a mouse model where the *Piezo1* gene is ablated specifically in astrocytes (*Piezo1*-cKO mice).

To investigate astrocytic mechanobiology at a molecular level, we currently use iPSC (induced pluripotent stem cell)-derived astrocytes, the human glioblastoma cell line U-87 MG and human patient-derived primary astrocytes *in vitro* (Figure 20). We analyzed cell morphologies on stiff cell culture plastic and found differences between these distinct astrocyte-like cells (Figure 20A-C).

We will use patient-derived astrocytes to study differences between gray and white matter astrocytes *in vitro*. Consistent with their *in vivo* properties, white and gray matter astrocytes exhibit fibrous versus spread-out morphology, respectively, on stiff cell culture plastic (Figure 20D). We will continue

to investigate human gray and white matter astrocyte morphology and function on soft cell culture matrices. We will also use the established protocols to investigate PIEZO1-deficient astrocytes from *Piezo1*-cKO mice to dissect PIEZO1-specific functions of astrocyte mechanobiology.

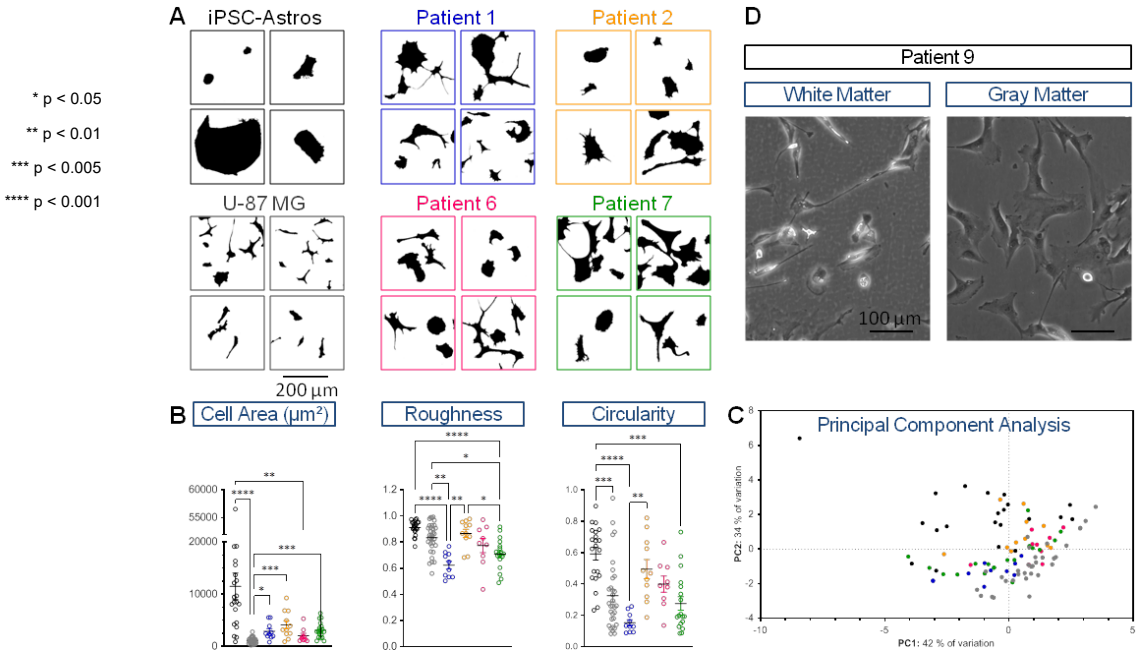

Figure 20: Analysis of astrocyte morphology in vitro. A, Cell shapes of iPSC (induced pluripotent stem cell)-derived astrocytes, U-87 MG glioblastoma, and patient-derived astrocytes are illustrated. Scale bar applies to all images. Color code applies also to panels B and C. B, Morphometric parameters show differences between iPSC-astrocytes, U-87 MG cells, and patient-derived astrocytes. Data points represent individual cells. C, Principal component analysis (PCA) of morphometric parameters shows clear distinction between iPSC-astrocytes (black dots) and U-87 MG cells (gray dots). Patient-derived cells (colored dots) exhibit intermediate morphologies without clear separation of sub-populations. Points represent individual cells. D, separately isolated gray and white matter astrocytes from a single patient sample are morphologically distinct. Scale bar applies to both images.

References

[1] Baecher-Allan, C., Kaskow, B. J., & Weiner, H. L. (2018). Multiple sclerosis: Mechanisms and immunotherapy. *Neuron, 97*(4), 742–768.

[2] Attfield, K. E., Jensen, L. T., Kaufmann, M., Friese, M. A., & Fugger, L. (2022). The immunology of multiple sclerosis. *Nature Reviews Immunology, 22*(12), 734–750.

[3] Lawrence, J. M., Schardien, K., Wigdahl, B., & Nonnemacher, M. R. (2023). Roles of neuropathology-associated reactive astrocytes: A systematic review. *Acta Neuropathologica Communications, 11*(1), 42.

[4] Wang, S., Millward, J. M., Hanke-Vela, L., Malla, B., Pilch, K., Gil-Infante, A., Waiczies, S., Mueller, S., Boehm-Sturm, P., **Guo, J.**, **Sack, I.**, & Infante-Duarte, C. (2020). MR elastography-based assessment of matrix remodeling at lesion sites associated with clinical severity in a model of multiple sclerosis. *Frontiers in Neurology, 10*, 1382.

[5] Lu, Y. B., **Franze, K.**, Seifert, G., Steinhäuser, C., Kirchhoff, F., Wolburg, H., **Guck, J.**, Janmey, P., Wei, E. Q., Käs, J., & Reichenbach, A. (2006). Viscoelastic properties of individual glial cells and neurons in the CNS. *Proceedings of the National Academy of Sciences of the United States of America, 103*(47), 17759–17764.

[6] Chi, S., Cui, Y., Wang, H., Jiang, J., Zhang, T., Sun, S., Zhou, Z., Zhong, Y., & Xiao, B. (2022). Astrocytic Piezo1-mediated mechanotransduction determines adult neurogenesis and cognitive functions. *Neuron, 110*(18), 2984–2999.e8.

[7] Velasco-Estevez, M., Rolle, S. O., Mampay, M., Dev, K. K., & Sheridan, G. K. (2020). Piezo1 regulates calcium oscillations and cytokine release from astrocytes. *Glia, 68*(1), 145–160.

[8] Glatigny, S., & Bettelli, E. (2018). Experimental autoimmune encephalomyelitis (EAE) as animal models of multiple sclerosis (MS). *Cold Spring Harbor Perspectives in Medicine, 8*(11), a028977.

B05 *In vivo* mechanical manipulation of spinal cord regeneration

Julia Kolb, Olga Lyraki, Daniel Wehner

Project **B05** is testing the hypothesis that local mechanical tissue properties are critical for successful nerve fiber (axon) regeneration after spinal cord injury (SCI) and that the specific composition of injury-associated extracellular matrix (ECM) deposits confers these properties. To that aim, **B05** utilizes the vertebrate species zebrafish, which different to humans and other mammals, is capable of long-distance axon regeneration and functional recovery after central nervous system (CNS) injury.

In the first reporting period, together with the EBM projects **A02**, **B03**, **C02**, and **C03**, we provided mechanistic evidence that the ECM in zebrafish spinal cord lesions lacks axon regeneration inhibitory factors present in mammalian CNS scars [1, 2]. We characterized members of the small leucine-rich proteoglycans (SLRPs) family as such inhibitory molecules that govern the permissiveness of the CNS lesion for axon regeneration. We showed that experimental supplementation of the zebrafish injury ECM with SLRPs alters the mechanical properties of the lesion environment (longitudinal modulus, M'; apparent Young's modulus, E; apparent viscosity, η) towards a non-permissive scar-like signature. These results support the hypothesis that the specific composition of the injury ECM confers permissive or adverse mechanical properties to CNS lesions in zebrafish and mammals, respectively. Furthermore, our results identified ECM factors that dictate the ad-verse mechanical tissue properties of mammalian CNS scars.

In the second reporting period, together with the EBM project **B03**, we aimed to identify factors that determine the permissive mechanical properties of the zebrafish injury ECM. To this aim, we used somatic CRISPR/Cas9-mediated gene inactivation of candidate genes and assessed the effect on axon regeneration and mechanical tissue properties using Brillouin microscopy and atomic force microscopy-based nanoindentation measurements. We concentrated on tgm2b, which codes for transglutaminase 2, and on collagen type XII-coding genes col12a1a and col12a1b. These genes were chosen based on their crosslinking functions and documented enrichment in the zebrafish injury ECM. Although CRISPR-manipulated zebrafish larvae showed significantly impaired axon regeneration and functional recovery, we did not detect changes in M' or E.

Altogether, the data obtained in the first two reporting periods suggest that specific ECM factors, which are abundant in mammalian but not zebrafish lesions, predominantly account for the distinct mechanical properties of the lesion environment in zebrafish and mammalian species, respectively.

To test this hypothesis, we are currently generating new transgenic lines that will allow us to conditionally supplement the zebrafish injury ECM with specific human CNS scar components. These include human chondroitin sulfate proteoglycans and the SLRPs LUM and PRELP.

References

[1] **Kolb, J.**, Tsata, V., John, N., Kim, K., Möckel, C., Rosso, G., Kurbel, V., Parmar, A., Sharma, G., **Karandasheva, K.**, Abuhattum, S., **Lyraki, O.**, Beck, T., Müller, P., Schlüßler, R., **Frischknecht, R.**, Wehner, A., Krombholz, N., Steigenberger, B., Beis, D., Tekeoka, A., **Blümcke, I.**, **Möllmert, S.**, Singh, K., **Guck, J.**, **Kobow, K.**, & **Wehner, D.** (2023). Small leucine-rich proteoglycans inhibit CNS regeneration by modifying the structural and mechanical properties of the lesion environment. *Nature Communications, 14*, 6814. https://doi.org/10.1038/s41467-023-43028-3

[2] Möckel, C., Beck, T., Kaliman, S., Abuhattum, S., Kim, K., **Kolb, J.**, **Wehner, D.**, **Zaburdaev, V.**, & **Guck, J.** (2024). Estimations of the mass density of biological matter from refractive index measurements. *Biophysical Reports, 4*(2), 100156. https://doi.org/10.1016/j.bpre.2024.100156

C01 *In silico* modeling of mechanical cell-matrix interactions

Soheil Firooz, Pritha Dolai, Paul Steinmann, Vasily Zaburdaev

Cellular aggregate formation; continuum modeling and computational challenges

Cellular aggregates play a significant role in the evolution of biological systems such as tumor growth, tissue spreading, wound healing, and biofilm formation. In our project, we proposed a non-linear continuum mechanics framework and a corresponding finite element simulation approach to model the physics of cellular aggregate formation. Using our recently developed "Mean Zero Artificial Diffusion" approach applied to the cell number density and pili number density evolution equations, we have successfully captured the behavior of aggregate formation and obtained an equilibrium state consistent with experimental observations. The main advantage of our proposed methodology is that it is capable of circumventing the instabilities associated with convection dominance of the problem and at the same time it facilitates taking higher gradients into account without any requirement to implement C^1continuous elements [1-3].

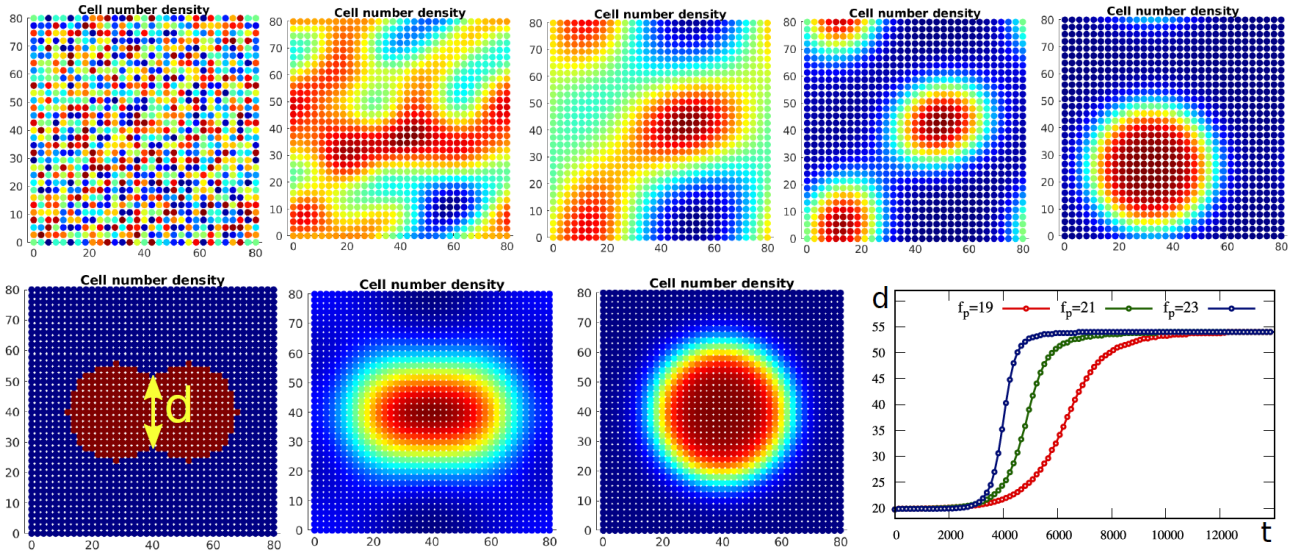

Figure 21: Top: Formation of a colony from a random distribution of cells. Bottom: Coalescence of two micro colonies and investigation of the evolution of the bridge length between them.

Figure 21 (top) renders step-by-step evolution of a cellular aggregate from a random distribution of cells. It is observed that randomly distributed cells form an initial smooth distribution. Further evolution of time leads to the formation of two micro colonies which eventually coalesce and form a single colony. Figure 21 (bottom) examines the coalescence of two microcolonies and investigates the evolution of the bridge length *d* for different pulling forces between the cells.

It is observed that higher pulling forces accelerate the process of coalescence and at the end, all three values yield the same aggregate size signifying the steady state solution.

Modeling neuron growth and role of extra cellular matrix

In another part of the project, we study the role of cell-matrix interactions in the context of brain tissues and the mechanism of neuron growth through the extracellular matrix (ECM). We consider two modes for neurite growth: linear growth by tip extension and growth by the traction force at the tip of the neurite with the ECM. In the linear growth model, the length of a neurite increases linearly with time. In the second mechanism, growth happens solely due to the interaction of the growing appendages with the particles modeling the matrix. With an agent-based model, we recapitulate experimentally observed neuron growth patterns in “healthy” neurons and neurons with mutations corresponding to a disease state performed in organoid models. In experiments (in the group of M. Karow, S. Falk and F. Federica), neuron growth is quantified by the dynamics of the growing tips.

Figure 22(a) shows the neuron growth observed in experiments and Figure 22(b) shows the simulated trajectories using a linear growth model. Figure 22(c) -(d) exhibits simulated neuron trajectories using a linear growth model and growth by traction force under similar conditions.

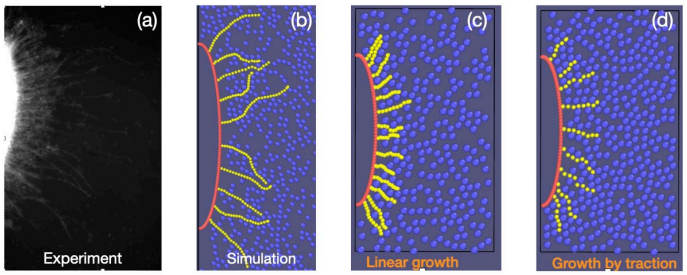

Figure 22(a) Neuron growth dynamics in experiments (in the group of M. Karow, S. Falk and F. Federica). (b) Simulated neurite trajectories. (c) -(d) Simulated neuron growth trajectories using linear growth model and growth by traction force under similar conditions.

We calculated growth characteristics such as track length and velocity of the tip, tortuosity, and angular correlation of growth direction. Figure 23(a)-(c) shows the track length, end-to-end distance, and tortuosity as a function of time for both wild type and mutated one.

Growth speed and angular correlation of growth direction are plotted in Figure 23(d)-(e) for wild type and mutated trajectories of MID1. The next step is to find out the suitable parameters in the simulation model to reproduce the experimentally observed dynamics. Find the role of extracellular matrix (ECM) by changing the density and turnover rate in the traction growth model. In the next few months, we would like to work on developing an agent-based model for neuronal network formation and the role of ECM in the context of brain tissues.

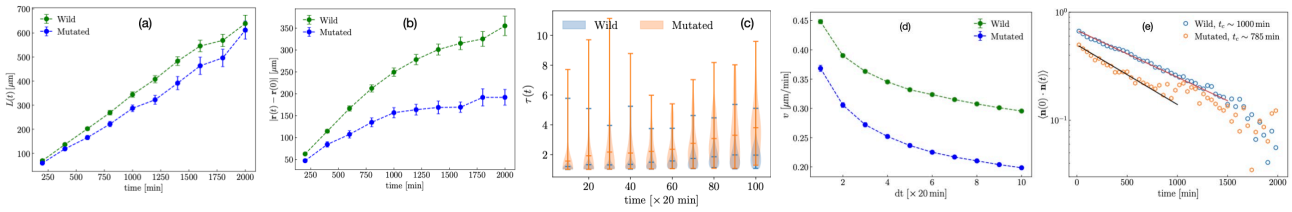

Figure 23: Growth characteristics of MID1 gene plotted for both wild type and mutated one. (a) Track length (b) end-to-end distance and (c) tortuosity as a function of time. (d) Growth speed as a function of timestep (e) Angular correlation of growth direction.

References

[1] **Firooz, S.**, Reddy, B. D., **Zaburdaev, V.**, & **Steinmann, P.** (2024). Mean zero artificial diffusion for stable finite element approximation of convection in cellular aggregate formation. *Computer Methods in Applied Mechanics and Engineering, 419*, 116649. https://doi.org/10.1016/j.cma.2023.116649

[2] **Firooz, S.**, Reddy, B. D., & **Steinmann, P.** (submitted). A novel micromorphic-based artificial diffusion method for stabilization of approximations of convection-diffusion problems. *International Journal for Numerical Methods in Engineering*.

[3] **Firooz, S.**, **Zaburdaev, V.**, Reddy, B. D., & **Steinmann, P.** (in preparation). Cellular aggregate formation: Continuum modeling and computational challenges.

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C02 The role of mechanics for neuronal “plasticity”

Bartomeu Perelló Amorós, Ezgi Erterek, Renato Frischknecht

The role of mechanics for neuronal ‘plasticity’

During postnatal development, neuronal networks in the brain undergo refinement in an activity-dependent manner, enabling adaptation to the challenges of the external environment. This necessitates the formation of new synapses and the elimination of superfluous synapses in response to external stimuli, a process known as neuronal plasticity. Neuronal plasticity, which encompasses the ability of neuronal networks to be readjusted, is particularly pronounced in the juvenile brain, whereas in the adult brain, this capacity is markedly reduced. The perineuronal extracellular matrix (ECM) has been identified as a significant regulator of neuronal plasticity in the adult brain, although the precise mechanisms remain largely unclear.

The objective of this study is to test the hypothesis that the perineuronal ECM in the mature brain restricts neuronal plasticity by creating an unfavorable mechanical environment for structural rearrangements. This hypothesis will be tested in three work packages. WP1 will investigate the mechanical properties of the murine cortex in the presence and absence of ECM. WP2 will develop tools to modify ECM properties *in vitro* and *in vivo*, and evaluate their effects on brain mechanics. Furthermore, hydrogels with various mechanical properties will be tested for their ability to foster neuronal cell growth. WP3 will investigate the influence of tissue stiffness on neuronal plasticity, with a focus on dendritic spine motility.

WP1: Contribution of the ECM to the mechanical properties of cortical layers

In close collaboration with **B03**, we performed measurements of mechanical properties across the layers of the mouse cortex using Brillouin microscopy and AFM indentation. We have established a workflow that includes brain sectioning and ECM degradation using the enzyme chondroitinase ABC, which allows us to measure mechanical properties within 2 h after dissection of the mouse brain.

Measurements of 6 cortices from adult mice showed a difference in the mechanical properties across the cortical layers. While the upper layers appeared homogeneous, the deeper layers differed from those in our measurements. These results correlate with the abundance of perineuronal ECM, which is more highly expressed in deeper cortical layers. However, direct comparison of AFM indentation and Brillouin microscopy results was not straightforward: while AFM indicated "softer" tissue within the perineuronal ECM-rich regions, Brillouin microscopy suggested the opposite. After treatment with chondroitinase ABC, the difference in mechanical properties between layers disappeared in both mechanical tests, suggesting a contribution of the perineuronal ECM to the mechanical properties of cortical layers 4-6. However, several issues remain to be addressed. First and foremost, tissue degradation after preparation has been shown to be a major source of variation in our measurements. This will be addressed in our follow-up experiments with **B03**.

WP2: Development of tools to alter ECM properties *in vitro* and *in vivo*

To assess the role of tissue mechanics during neuronal plasticity, we intend to manipulate the mechanical properties of the extracellular environment of neurons and test their ability to undergo plastic changes. To this end, we are pursuing two strategies to develop tools to modify the mechanical properties of artificial or endogenous ECM without affecting its chemical composition.

In a first approach, in collaboration with **X03**, we tested OHA/GEL (oxidized hyaluronan) hydrogels with different mechanical properties for their ability to promote neuronal outgrowth and maturation. We chose OHA to mimic the perineuronal ECM, which contains hyaluronic acid. Our initial results have been summarized in a recent publication [1]. We are continuing our work with OHA gels, establishing chemical stimulation to mimic synaptic plasticity and viral vectors to visualize the morphology of living cells (Figure 24, WP3). In addition, we plan to implement the progress made in **C03** regarding the composition of the OHA gels and to include collagen as a compound.

A second approach is to optogenetically increase the density of the ECM. We cloned fusion proteins of cryptochrome2 (Cry2) and the abundant hyaluronic acid-binding ECM protein brevican. Unfortunately, this Cry2, which is usually used for intracellular application, formed aggregates within the secretory pathway. We therefore switched to a smaller group of proteins with similar properties to Cry2, called magnets, and generated fusion proteins with brevican and versican. The latter is done by a master's student who is supervised together with **A05**/**B02**. The brevican-magnet fusion proteins are expressed and secreted from the cells, making them suitable for further experiments.

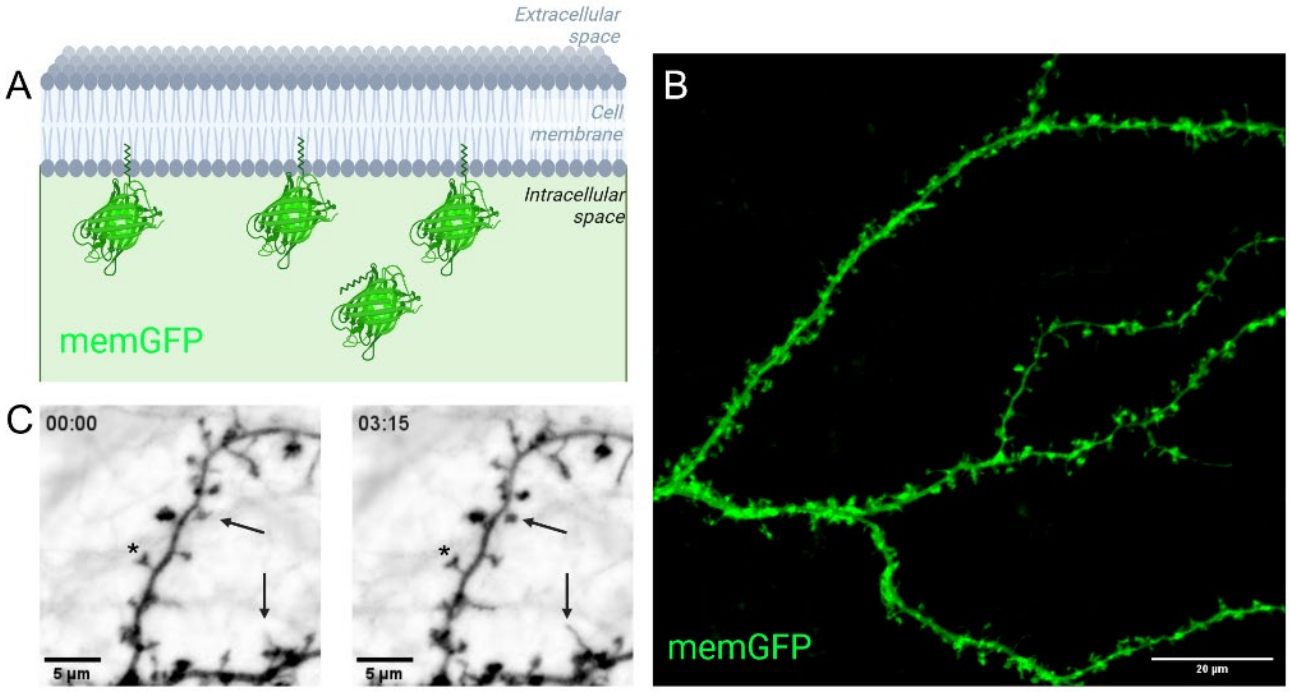


Figure 24: A) Scheme of memGFP with its myristoyl group. B) A neuronal branch that expresses memGFP. C) Live imaging of a dendrite with spines and filopodia. It is noteworthy that some structures undergo morphological changes (indicated by arrows), while others remain stable (indicated by asterisks).

WP 3: Impact of ECM stiffness on neuronal 'plasticity'

During learning and memory formation, new synapses are formed and others are eliminated. This can be observed at the cellular level by the appearance and retraction of dendritic spines. To visualize these, we have engineered an adeno-associated virus (AAV) to express membrane-associated EGFP (memGFP) in neurons. memGFP, as opposed to cytoplasmic EGFP, allows us to reliably visualize and quantify small membrane protrusions as dendritic spines and filopodia (Figure 24). We are currently infecting neurons cultured in OHA gels with different mechanical properties (WP2) to visualize spine dynamics under basal conditions. We are also establishing electrical and chemical stimulation to induce neuronal plasticity. We have shown that this treatment affects ECM integrity and neuronal plasticity Möllmert

. This will be extended to pathological neuronal activity as seen during epileptic seizures in collaboration with **C03** [3].

References

[1] **Kuth, S.**, **Lorke, M.**, **Frischknecht, R.**, & **Boccaccini, A. R.** (2023). Tinten für die Biofabrikation – Druckbarkeit vs. Biokompatibilität? *BIOspektrum, 29*(7), 736-739. https://doi.org/10.1007/s12268-023-2046-0

[2] Singh, J. B., et al. (2024). Activity-dependent extracellular proteolytic cascade remodels ECM to promote structural plasticity. *bioRxiv*. https://doi.org/10.1101/2024.10.28.620597

[3] **Lehner, A.**, **Hoffmann, L.**, **Rampp, S.**, Coras, R., **Paulsen, F.**, **Frischknecht, R.**, Hamer, H., Walther, K., Brandner, S., Hofer, W., Pieper, T., Reisch, L. M., Bien, C. G., & **Blümcke, I.** (2024). Age-dependent increase of perineuronal nets in the human hippocampus and precocious aging in epilepsy. *Epilepsia Open, 9*(4), 1372-1381. https://doi.org/10.1002/epi4.12963

C03 Exploring the mechanics of neuronal network formation

Kristina Karandasheva, Katja Kobow

Aim: To investigate mechano-biological aspects of neuronal circuit function under normal and pathophysiological conditions in mechanically tuneable engineered brain tissue

WP1: Mechanics of primary neuronal network formation

We employed rat primary neuronal cell cultures in both 2D and 3D setups to evaluate and compare the influence of various extracellular environments on neuronal maturation, migration, and network formation. In the 2D setup, neurons were seeded on glass surfaces coated with poly-D-lysine (PDL), either alone or in combination with additional components such as fibronectin or laminin, as well as on a thin layer of Matrigel. For the 3D culture setup, we tested different types of mechanically tunable matrices, including Matrigel (with and without growth factors), Vitrogel (with and without adhesion-promoting molecules), Collagen I (C05), Collagen IV, and hyaluronic acid-based and alginate-gelatin hydrogels (X03).

Our primary objective was to optimize cell viability and facilitate proper network formation while ensuring sample compatibility with imaging techniques and minimizing the number of cells required per experiment. We successfully developed a reproducible protocol for neuronal network formation within Matrigel and Collagen I matrices, achieving cell viability for over 15 days.

The established 3D cultures in Collagen I (2.5 mg/ml) served as a benchmark for time-lapse microscopy and traction force experiments, conducted in collaboration with partner C05 and the Optical Imaging Centre Erlangen (OICE). We analyzed the cellular composition of these samples and utilized 3D microscopy to investigate the anatomy of the neuronal networks. The composition of the established networks was examined using immunofluorescent staining for key markers, including the neuronal marker MAP2, the glial marker GFAP, the immune cell marker CD45, oligodendrocyte progenitor cell marker NG2, the presynaptic active zone protein Bassoon as a synaptic marker, and the clock transcription factor BMAL1, which is found to be highly and exclusively expressed in neuronal nuclei.

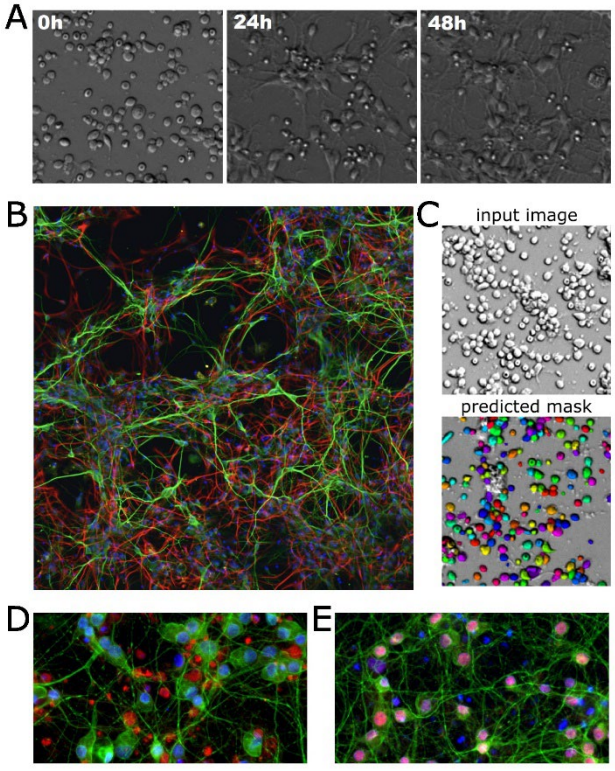


Figure 25: A. Images from timelapse recording on different timepoints (0 h, 24 h, 48 h); B. Immunofluorescent staining of 3D cell culture in collagen I captured at 9 days after seeding: blue – DAPI, green – MAP2; red – GFAP; C. Segmentation result for individual cell tracking; D. Immunofluorescent staining of 2D cell culture: blue – DAPI, green – MAP2; red – NG2; E. Immunofluorescent staining of 2D cell culture: blue – DAPI, green – MAP2; red – BMAL1.

Time-lapse recordings captured dynamic cell movements across distinct time intervals (0–12 hours, n=3425; 0–48 hours, n=32; 24–125 hours, n=14) in 2D cell cultures seeded on poly-D-lysine (PDL). Building on this knowledge, we performed time-lapse brightfield recordings of 3D cell cultures seeded in Collagen I, followed by fixation and immunofluorescent staining using primary cell type markers. The resulting images are utilized as input for deep-learning algorithms designed to support in-silico cell-type prediction based on brightfield microscopy.

We utilized classical computer vision tools, including OpenCV and Fiji/ImageJ, alongside established (Cellpose) and custom-developed deep-learning algorithms based on a U-Net architecture. The custom algorithms were trained on meticulously annotated datasets and achieved a precision of 0.919, recall of 0.842, and accuracy of 0.782. These approaches were employed to extract biologically relevant information from time-

lapse microscopy recordings, such as cell positions and morphologies for monitoring neuronal migration. Detection and tracking of axons and neurites are being actively developed to evaluate the dynamics of network formation.

Additionally, the first traction force microscopy measurements at high resolution (60x, growth cone), but consequently with lack of network information, were conducted on 3D neuronal networks embedded in Collagen I and in combinations of Collagen I with Matrigel, in collaboration with **C05**. Quantification of traction forces was successful but requires technical optimization to be less error prone and compatible with larger fields of view (e.g., 20x).

WP3: Mechanical aspects of epileptogenesis

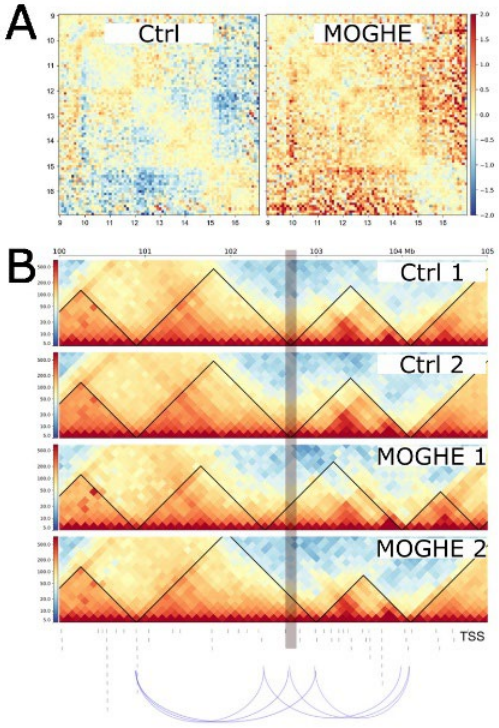


Figure 26: A. Heatmaps illustrating comparisons of Ctrl (left) and MOGHE (right) chromatin folding density; B. A representative example of TAD dynamics, illustrating shifts in chromatin organization between MOGHE and control samples.

In collaboration with **A02**, which focuses on quantitative molecular, structural and mechanical characterization of brain malformations associated with epilepsy, we observed broad structural changes of cellular nuclei in the lesion core of mild malformations of cortical development with oligodendroglial hyperplasia (MOGHE) in conjunction with a specific genotype (1). In electron microscopy, nuclei seemed flooded with heterochromatin or otherwise highly folded chromatin. We therefore investigated 3D chromatin structure using Hi-C sequencing with 1.25 billion unique reads per samples (2.5 bn paired end). Our analysis uncovered distinct differences in chromatin organization between MOGHE samples and no-seizure autopsy controls. Specifically, we identified a broad spectrum of differentially interacting regions, characterized by a loss of short-range interactions and a gain of long-range interactions, resulting in an overall denser chromatin state in MOGHE samples. We further observed significant changes in A/B compartmentalization and the structure and boundary strength of topologically associating domains (TADs). Gene enrichment analysis revealed that the genes affected by these alterations in 3D chromatin structure are involved in several critical biological processes, including the diacylglycerol metabolic process, entrainment of the circadian clock, regulation of chromosome organization, forebrain development, and lipid transporter activity. We will continue to explore how mechanical stresses resulting from, e.g., increased abnormal cell density (i.e., oligodendroglial hyperplasia) in MOGHE transmit into the cell affecting nuclear structure and function. Vice versa we will test whether observed chromosomal changes impact nuclear and cellular mechanical properties (e.g., stiffness).

Reference

[1] Boßelmann, C. M., Leu, C., Brünger, T., **Hoffmann, L.**, Baldassari, S., Chipaux, M., Coras, R., **Kobow, K.**, Hamer, H., Delev, D., Rössler, K., Bien, C. G., Kalbhenn, T., Pieper, T., Hartlieb, T., Becker, K., Ferguson, L., Busch, R. M., Baulac, S., Nürnberg, P., Najm, I., **Blümcke, I.**, & Lal, D. (2024). Analysis of 1386 epileptogenic brain lesions reveals association with DYRK1A and EGFR. *Nature Communications*, *15*(1), 10429. https://doi.org/10.1038/s41467-024-54911-w

[2] **Karandasheva, K.**, **Blümcke, I.**, & **Kobow, K.** (2024). Chromatin conformation changes in focal lesional epilepsy: Insights from Hi-C analysis. *Epilepsia, 65(*S1), 294. (abstract 133). https://doi.org/10.1111/epi.18151

C04 Cellular differentiation in brain tissue-mimicking matrices

Anja Bosserhoff, Shanice Heidenreich

Melanoma is a highly aggressive tumor that originates from the pigment-producing cells, the melanocytes. Melanoma is responsible for the majority of skin cancer-related deaths with brain metastases as one major cause. Due to the poor prognosis resulting from the development of brain metastases in melanoma patients, a deeper understanding of the underlying molecular mechanisms of this process represents a clinical need.

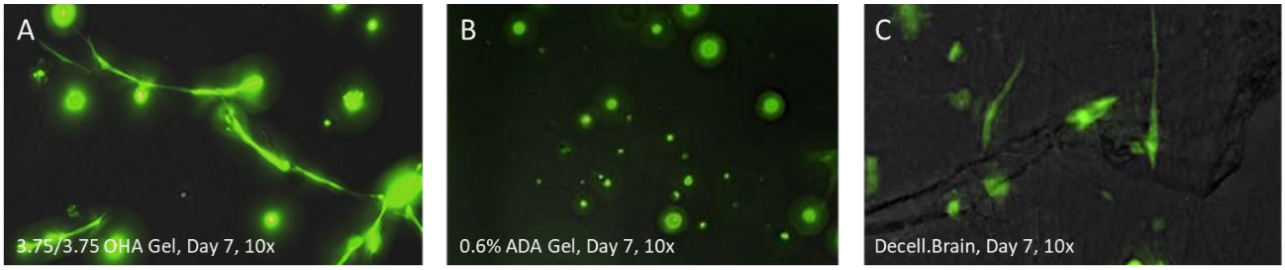


Figure 27: Melanocytes cultivated in 3.75/3.75 OHA Gel (A), in 0.6% ADA Gel (B) and decell. Brain (C) revealed significantly different morphology.

C04 aims to analyze the role of mechanics in cell differentiation and dedifferentiation. For this purpose, cell types of the same embryonic origin as neuronal cells, but different differentiation tracks are used, namely melanocytes and melanoma cells. Comparison of cells from melanocytic origin to neuronal cells with regards to the impact of the different microenvironmental matrices on differentiation is therefore highly interesting. We have started to cultivate melanocytes in brain tissue-mimicking matrix and decellularized brain tissue (supported by **X03**, see Figure 27). The resulting findings indicate an effect of molecular components within the matrices on the cells. Subsequently, analyses of various molecular characteristics were performed, including differentiation-specific genes (MITF, E-cadherin) and hyaluronic acid-binding genes (BCAN, ACAN, and MMP9), using qPCR to define microenvironment-induced changes in the cells. The significant changes in MITF and E-cadherin expression indicate an impact on cell differentiation due to the altered microenvironment. Additionally, BCAN was found to influence the cells' spreading behavior.

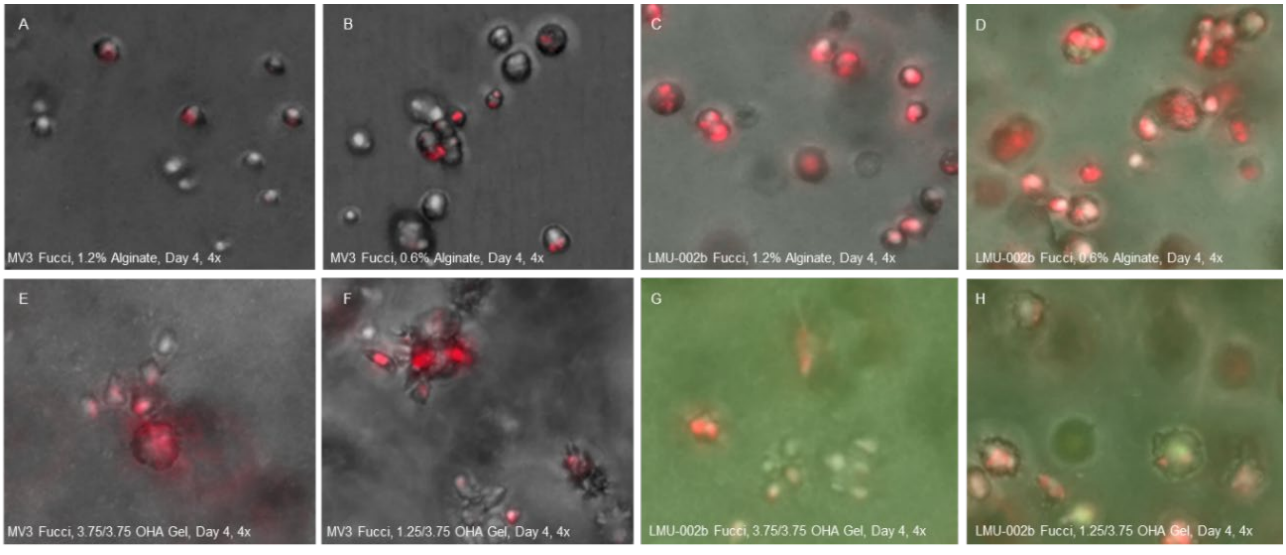


Figure 28: MV3 Fucci cell line cultured in 1.2% alginate (A), 0.3% alginate (B), 3.75/3.75 OHA Gel (E), and 1.25/3.75 OHA Gel (F), as well as LMU-002b Fucci cell line cultured in 1.2% alginate (C), 0.3% alginate (D), 3.75/3.75 OHA Gel (G), and 1.25/3.75 OHA Gel (H), revealed different morphologies.

In addition, the molecular comparison of brain metastases with cells from surrounding tissues regarding the influence of various microenvironment matrices on differentiation represents another important part of the project. The cultivation of melanoma cells derived from brain metastases (HTZ19 and LMU-002b) or from metastases of surrounding tissues (MV3 and Mel Im) in brain tissue-like matrices (supported by **X03**, see Figure 28A-H) marked the beginning of the experimental project

work. The resulting findings, including an increasing proliferation rate and enhanced spheroid formation in hydrogels with reduced stiffness, suggest an influence of mechanical properties on the cells. Additionally, the composition of hydrogels also appears to affect both the proliferation rate and spheroid formation. In a hyaluronic acid-based hydrogel (OHA-Gel), a reduced hyaluronic acid concentration leads to an increased proliferation rate and spheroid formation. The tissue origin of the metastases does not seem to play a role in this specific process.

Furthermore, we observed that the composition of the matrices influences the spreading behavior of the cells. Components such as hyaluronic acid appear to affect brain metastases as well as other metastases with increasing concentration (see Figure 29A-D). In contrast, oxidized alginate (ADA-Gel) seems to induce increased spreading behavior only in brain metastases (see Figure 29E and F).

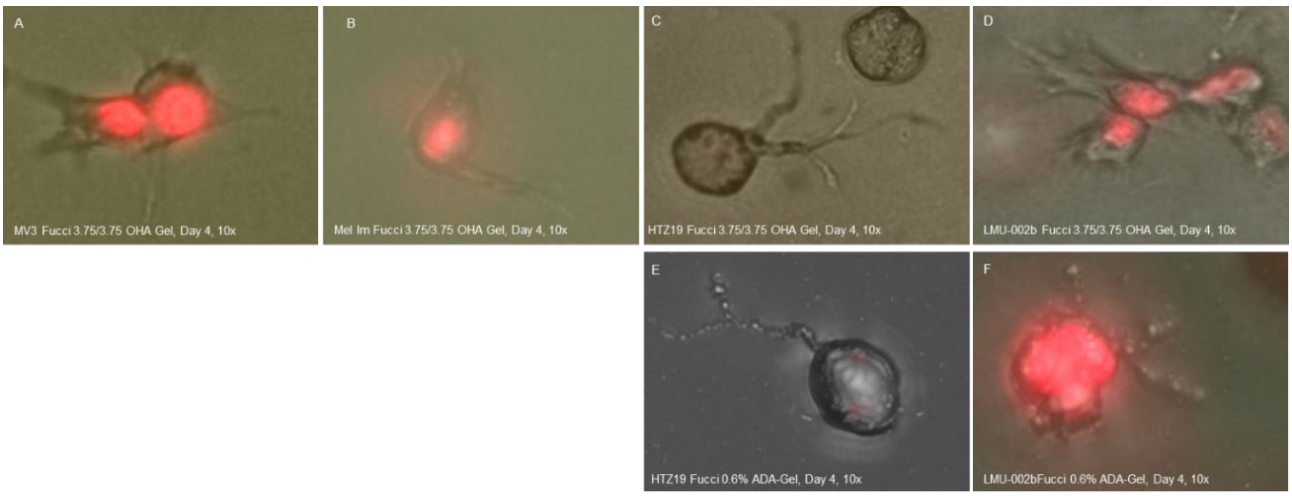


Figure 29: MV3 (A), Mel Im (B), HTZ19 (C), and LMU-002b Fucci cell lines (D) cultured in 3.75/3.75 OHA Gel show similar spread-ing behavior. HTZ19 (E) and LMU-002b Fucci cell lines (F) cultured in 0.6% ADA Gel indicate spreading, in contrast to metastases from surrounding regions.

The use of proliferation markers, markers for transcription and differentiation and an RNA Seq with bioinformatics analyses are considered a future approach to more precisely define cell behavior and differentiation. The aim is to gain insights into the role of mechanics in brain metastasis and finally understand whether the brain, due to its mechanical properties, influences the metastasis, growth and dedifferentiation of tumor cells and thus represent an attractive soil for melanoma cells.

C05 Molecular mechanisms of neuronal mechanotransduction

Lars Bischof, Ben Fabry

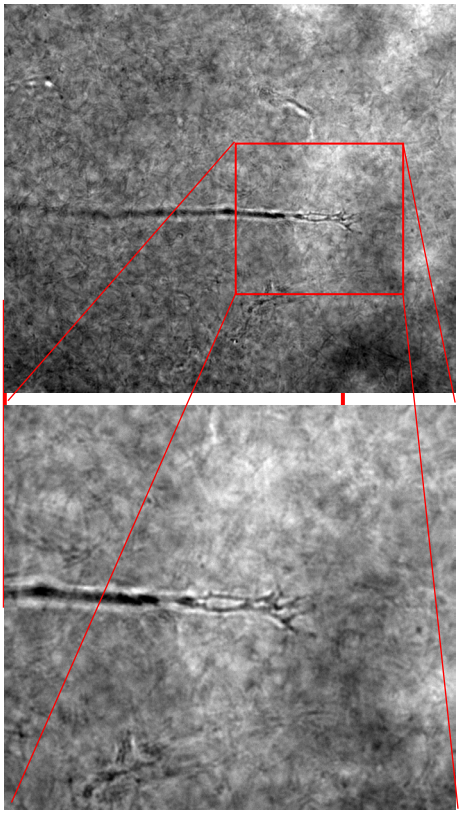


Figure 30: Contrast enhance bright field images; a) single axon growing through collagen matrix; b) Zoom on axonal growth cone.

The main objective of Project **C05** is to investigate molecular mechanisms of mechanosensing and mechanotransduction in primary neurons in 3D environments. In the beginning of the project we established Collagen-I (/Matrigel)- Hydrogels as our 3D culture matrix that allows us to observe neuronal development of primary hippocampal rat neurons up to 14 days. Due to its fibrous structure, these hydrogels allow us to perform traction force microscopy without adding beads as fiducial markers. Typically, this is done recording confocal laser reflection images. However, first experiments were not successful due to photo-damage inflicted by the laser light.

In order to achieve long recording time with reasonable temporal resolution, we try to establish a similar but less invasive imaging method relying only on bright field images. Since good contrast and resolution is needed, experiments were performed using a 60x water immersion objective with a high numerical aperture of 1.1, enabling us to visualize the typical fibrous structure of collagen matrices.

During neurite outgrowth, neuronal cells are expected to sense their environment presumably through mechanical interaction at their growth cones. Hence, we try to observe and record this process. For this purpose, primary hippocampal rat neurons were mixed into 1.2 mg/ml collagen-hydrogels and seeded on top of another already polymerized hydrogel layer. After 48 hours of incubation at 37 °C, single axons could be observed growing through the 3D matrix (see Figure 30). Time laps imaging of three-dimensional z-stacks over periods of 90 min was conducted. Axonal growth cones were found to occasionally exert contractile forces on their environment, causing spatial deformations (see Figure 31).

These deformations are quantified using a 3D particle image velocimetry (PIV) algorithm. The resulting deformation field can be used to calculate cell traction forces using the finite element method.

Further experiments will compare axonal growth in Collagen hydrogels of different concentrations, revealing possible impact of mechanical hindrance due to varying pore sizes and matrix stiffness. Additional stretching of the collagen samples will align the fibers, and we will test if aligned fibers give rise to directional axonal growth. By impairing actomyosin-driven traction forces (e.g. through Blebbistatin), we will further test the significance of traction forces for axonal elongation.

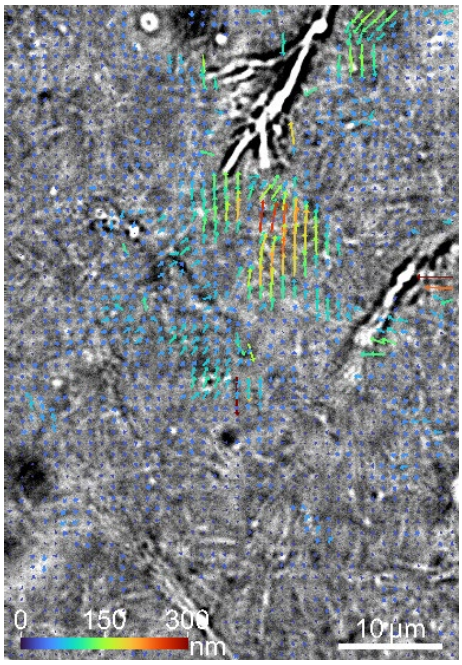


Figure 31: Axonal growth cone in collagen-hydrogel. Colored Arrows represent the 2D-projection of the recorded deformation field.

X01 Model-based reconciliation of *ex vivo* and *in vivo* test data

Laura Ruhland, Kai Willner, Yashasvi Verma, Paul Steinmann, Michael Fedders, Jakob Ludwig, Jing Guo, Ingolf Sack

The mechanical characterization of brain tissue over a wide strain or frequency range is often limited by inconsistent responses from experiments conducted in various time and length scales. To overcome the discrepancies, which are predominantly attributable to the varying boundary conditions of the different experimental setups, a robust identification strategy for all testing methods is crucial.

(LR, KW) The objective of this study is the characterization of a hydrogel based on oxidized hyaluronic acid (OHA) and gelatin (GEL), which has demonstrated potential as a phantom material for brain tissue, over an extended time range. By combining experiments conducted in the quasi-static and high-frequency domains, a comprehensive insight into the frequency dependence of OHA-GEL is provided. The material behavior in the time domain was examined via torsional shear tests at a rheometer, representing the material response at a frequency close to zero. Experiments in the high-frequency domain, from 200 to 2100 Hz, were obtained with a tabletop MRE. Challenges arising during the comparison are firstly attributed to the disparate excitation times and secondly to the nonlinear deformation of the sample in the rheometer, in contrast to the linear deformation in the tabletop MRE. A comparative study based on the storage and the loss modulus obtained from both measurements is presented in Figure 32. The high-frequency modulus was extrapolated to a zero frequency. A close alignment between the MRE and the rheometer measurement can be observed. To complete the entire frequency spectrum, measurements in the medium frequency from 10 to 200Hz range will be included in a further step. These experiments will be conducted using a vibration table, which enables to obtain data ranging from 10 to 200Hz.

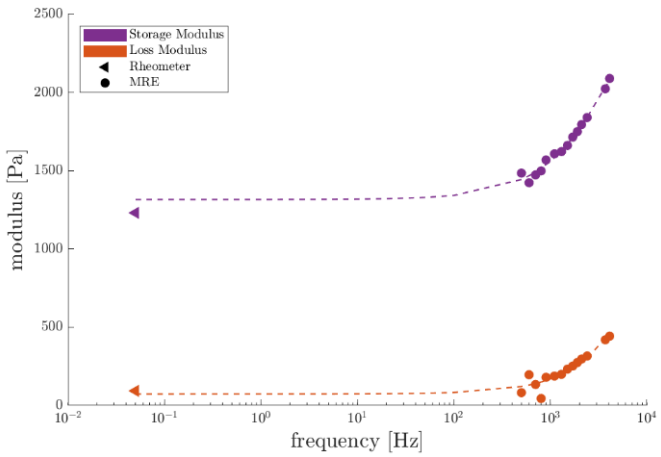


Figure 32: Storage and loss modulus of OHA-GEL for measurements.

The discrepancy in observed mechanical stiffness of brain tissue *in-vivo* and *ex-vivo* has been attributed to the different testing conditions and modalities. In this regard, we hypothesize that the vasculature and associated pressure in the tissue affect the mechanical stiffness.

(YV, PS) We developed a continuum-mechanics-based model with embedded vasculature to investigate the same [1]. A simulated tissue is subjected to shear waves in the small strain regime as would be performed in Magnetic Resonance Elastography (MRE) as shown in Figure 33. The displacement field is fed into an inversion algorithm [2] and the mechanical parameters of the tissue are computed. These retrieved mechanical parameters are compared to those of the simulated tissue. We can recover these parameters with less than 10% relative error, thereby validating our model and proposed scheme. The tissue is then embedded with a vascular inclusion having a particular pressure pulsation. Keeping in mind the error percentage of retrieved parameters, we can still observe an apparent increase in stiffness of the tissue with rising pressure of embedded vasculature.

Further investigation is needed for a comprehensive analysis in this direction. We want to extend our scheme to incorporate more sophisticated material models and to analyze the effect of vascular density and geometry on this observed increase in stiffness

(JL, JG, IS) The functional connectivity of brain networks refers to inter-regional synchrony which has been explored by resting-state functional MRI based on cerebral hemodynamics [3]. The cerebral functional connectivity can be affected by processes such as natural aging, sleep deprivation, epilepsy and Alzheimer's disease [4]. Our study examined for the first time the cerebral biomechanical connectivity using *in vivo* viscoelastic properties, as quantified by MRE, across the mouse lifespan from maturation to aging. Using Leiden community detection algorithm, we determined the integration and segregation of brain subregions for each age group. Based on cerebral stiffness, we observed that the brain segregation increased over maturation which was followed by a de-segregation phase during the aging process, as shown in Figure 34. Furthermore, we observed a clear brain de-segregation over all time points based on the relative change of cerebral stiffness between age groups. Building on these preliminary results, we will extend the analysis to investigate biomechanical cerebral connectivity of the human brain under both physiological and pathological conditions.

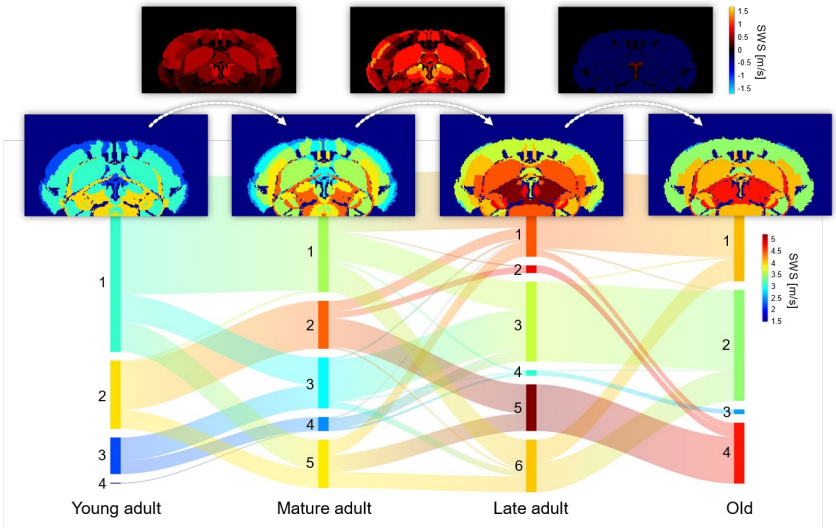


Figure 33: Absolute and relative stiffness Leiden community detection results for the whole lifespan. The Sankey plot corresponds to the absolute communities. We observe a higher brain separation for the mature and late adult age groups and a very low separation for the last relative age transition.

References

[1] Heltai, L., Caiazzo, A., & Müller, L. (2021). Multiscale coupling of one-dimensional vascular models and elastic tissues. *Annals of Biomedical Engineering, 49*, 3243–3254.

[2] Hirsch, S., Braun, J., & **Sack, I.** (2017). *Magnetic resonance elastography: Physical background and medical applications*. WILEY-VCH Verlag GmbH Co. KGaA.

[3] Heeger, D., & Ress, D. (2002). What does fMRI tell us about neuronal activity? *Nature Reviews Neuroscience, 3*, 142–151.

[4] Ferreira, L. K., & Busatto, G. F. (2013). Resting-state functional connectivity in normal brain aging. *Neuroscience & Biobehavioral Reviews, 37*(3), 384–400.

X02 Data analysis and machine learning for heterogeneous, cross-species data

Frauke Wilm, Mathias Öttl, Zhaoya Pan, Mareike Thies, Andreas Maier, Katharina Breininger

The **X02** project focuses on the application of machine learning models on the heterogeneous cross-species data acquired within EBM. In the period covered by this report, members of the **X02** project have performed and published research on different methodological advancements facilitating the development of robust models given challenging data.

The work of FW investigates the **influence of domain shifts** in the input data on downstream tasks such as segmentation. This is particularly relevant in the context of EBM where data is heterogeneous and consistent acquisition protocols over time cannot be guaranteed. It is therefore crucial to develop methods that are resilient to potential shift in the data. FW published a paper on appearance-based debiasing of deep learning models which was an oral presentation at the BVM conference [1]. FW was further involved in the organization and implementation of the MICCAI-MIDOG challenge held in 2023. The results of this challenge have been published in this report's period in the journal Medical Image Analysis [2]. On this year's MICCAI, FW participated in both tracks of an adenocarcinoma segmentation challenge, focusing on improving the generalization capacity of machine learning algorithms in adenocarcinoma segmentation tasks across various organs (track 1) and various scanners (track 2). Her implemented methods [7] ranked 1st place in both tracks and have been presented as a talk at the conference. FW's most recent work investigates the role of skip connections, which are popular in deep learning models, on out-of-distribution performance. This work has been published as a preprint [4].

MÖ has proposed a method on **generation of synthetic images** with specific styles. As an alternative approach to handling scarce and heterogeneous data, synthetic data can enlarge training data sets in a controllable manner, e.g., by providing variable image appearance. This is relevant in the context of EBM as specific anatomical constraints can be defined to condition the generation of images, combined with learning-based image and noise characteristics. The method by MÖ, which has been presented at the ECCV conference this year [3], enables the generation of synthetic data samples with unseen style variations. Adding such synthetic data improves the performance of downstream tasks. In another work, which is currently under review, MÖ investigates the use of probabilistic models for segmentation and how the probabilistic modeling can be adapted to the task of **image segmentation**.

The work of ZP evaluates generalization of **machine learning algorithms for video data** across anatomical sites. One important goal here is the **integration of temporal information** and a comparison of different deep learning strategies and architectures for this aspect (recurrent neural networks, attention-based approaches/transformers, post-hoc aggregation). Here, we have one paper submitted [6] and another report in preparation.

In addition, the **X02** group supervised two student projects within the scope of EBM. The first student investigated stain normalization techniques on domain generalization in downstream tasks such as mitosis detection in histopathological images. This technique worked well for domain shifts introduced by different scanners but was less effective under other types of shifts highlighting the importance of continued research in this direction. The second project focuses on **self-supervised learning** – another interesting technique in the context of EBM because it uses unannotated data to train machine learning models. Labeling acquired data can be a time-consuming, iterative process, and leveraging unannotated data to improve the learning of discriminative features can boost the performance of such algorithms while reducing annotation costs.

The project also focused on integrating machine learning into the EBM consortium, particularly through enhancing the **EXACT online annotation server** by supporting new image formats, annotation types, and visualization of model inference results. Furthermore, the annotation server was extended to enable online prediction of deep learning models on the server side, without users having to install any software on their end (FW, MÖ, MT). With substantial new data acquired and the corresponding need for automated analysis in the **A**, **B**, and **C** projects, task-specific collaborations are being established. State-of-the-art machine learning models were tailored for the first specific EBM applications, implemented by FW and continued by MT. In collaboration with projects **A01** and **A02**, the EXACT platform facilitated the collection of a histology dataset comprising 116 samples. Pre-trained models were then employed to accurately detect neuron cells and calculate cell density

across the dataset. For these experiments, a custom plugin was developed to enable the inference of pre-trained models on these datasets within EXACT, along with the seamless visualization of results directly on the server interface. Figure 35 illustrates these detection results on a representative region of interest. Future efforts will focus on correlating these cell density measurements with the mechanical properties of the tissue, paving the way for potentially discovering novel biomarkers related to cellular mechanics and their influence on tissue behavior. Based on this example, among others, we continue to investigate efficient annotation strategies for fine-tuning models and validation for biomedical research.

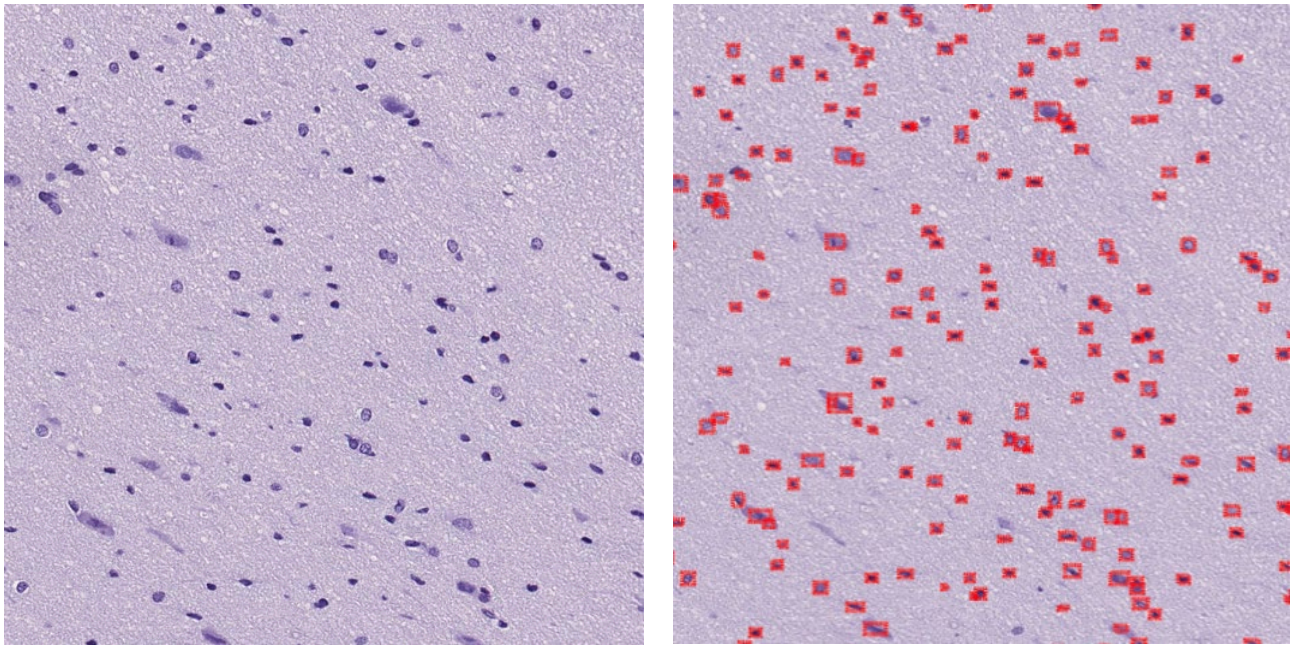


Figure 34: Detection results of machine learning model with original image (left) and detected bounding boxes (right).

References

[1] **Wilm, F.**, et al. (2024). Appearance-based debiasing of deep learning models in medical imaging. In *BVM Workshop* (pp. 1–10). Wiesbaden: Springer Fachmedien Wiesbaden. https://doi.org/10.1007/978-3-658-44037-4_9

[2] Aubreville, M., et al. (2024). Domain generalization across tumor types, laboratories, and species—Insights from the 2022 edition of the Mitosis Domain Generalization Challenge. *Medical Image Analysis, 94*, 103155. https://doi.org/10.1016/j.media.2024.103155

[3] **Öttl, M.**, et al. (2024). Style-extracting diffusion models for semi-supervised histopathology segmentation. *European Conference on Computer Vision (ECCV)*. https://doi.org/10.48550/arXiv.2403.14429

[4] **Wilm, F.**, et al. (2024). Rethinking U-net skip connections for biomedical image segmentation. *Preprint*. https://arxiv.org/abs/2402.08276

[5] **Öttl, M.**, et al. (2024). Analysing diffusion segmentation for medical images. *Preprint, under review*. https://arxiv.org/abs/2403.14440

[6] **Pan, Z.**, et al. (2024). Low-latency classification of malignancy in confocal laser endomicroscopy with automatic nondiagnostic frame detection. *Under review at BMC Medical Imaging*.

[7] **Wilm, F.**, et al. (2024). Domain and content adaptive convolutions for cross-domain adenocarcinoma segmentation. *Challenge manuscript/preprint*. https://arxiv.org/abs/2409.09797

X03 Engineering brain tissue like matrices

Markus Lorke, Aldo R. Boccaccini

Main objectives and achievements

Influence of two different oxidation times of hyaluronic acid on cellular behavior

One of the main challenges in our newly developed OHA/GEL hydrogel system is its relatively low stability upon incubation at cell culture conditions. After establishing an *in situ* crosslinking process, leading to a homogenous crosslinking with higher long-term stability [1], the new approach was to investigate the differences of two different oxidation times and their combination. Longer oxidized HA led to an increase of stiffness compared to the 4-hour oxidation while mixing both in ratios of 1:1 or 2:1 (4h:6h) led to stiffnesses between the different OHA oxidation times. However, the cellular response was altered while combining the different oxidation times when compared to hydrogels with an equivalent stiffness. Further mechanical and chemical investigations are currently ongoing.

Testing different techniques of cell culture

To evaluate cellular behavior in contact with our developed hydrogel matrix, we tested different hydrogels with last year´s established four distinct testing setups tailored to meet the experimental requirements of both our laboratory and our EBM collaborators. Each setup addresses specific objectives and experimental conditions (see Figure 36). In the simplest setup, a thin film or “pillow” of hydrogel matrix is formed in tissue culture plates (TCPs). Following crosslinking, cells are seeded onto the hydrogel surface and cultured in a 2D environment. In the second setup, a more complex “sandwich” structure is created by adding a layer of hydrogel precursor (uncrosslinked polymer solution) on top of cells cultured on the hydrogel matrix. This intermediate layer allows cells to adhere before complete encapsulation by the matrix. The third setup involves directly incorporating cells into the hydrogel precursor solution before cross-linking. Stirring the solution ensures even cell distribution, enabling controlled cell density within a 3D matrix that mimics the extracellular matrix (ECM) environment from the study's onset. In the fourth setup, cell migration into or infiltration of the hydrogel matrix is investigated. Using a 3D printing technique, we create hydrogel strands on coated TCPs, leaving uncovered regions of the plate surface. Cells are seeded onto the plate, and as they spread and proliferate, their interaction with the hydrogel strands is monitored to assess their ability to either bypass or infiltrate the matrix. Each of these approaches has been tested in our laboratory or with EBM collaborators, as further detailed below.

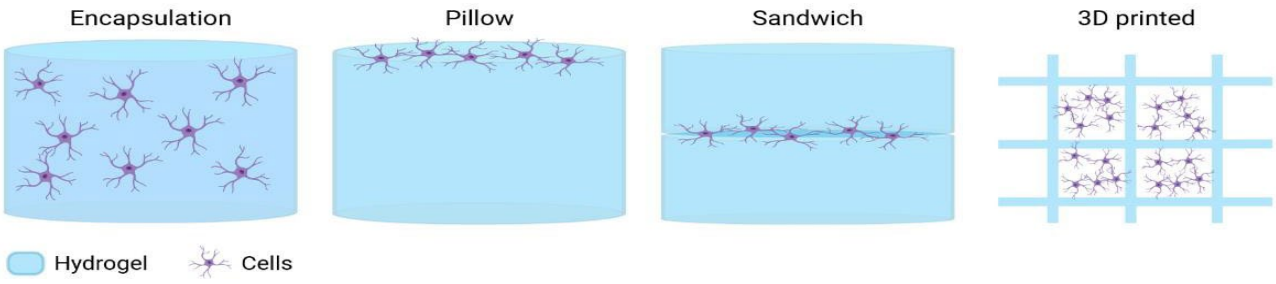


Figure 36: Schematic display of approaches for in vitro cell culture with the developed hydrogel matrix, as established in this project.

3D printing of multiphasic hydrogel constructs

This study aims to identify optimal formulations of mTG crosslinked OHA-GEL hydrogels that closely replicate the mechanical properties of gray and white matter by adjusting the concentrations of mTG, OHA, and GEL. Additionally, these hydrogels must demonstrate adequate printability to facilitate the fabrication of bi-phasic scaffolds through extrusion bioprinting for cell culture applications. The aim was to create bi-phasic hydrogel scaffolds (see Figure 37) to go one step further regarding brain phantom production and closer to mimicking the brain structure with different matrix mechanics.

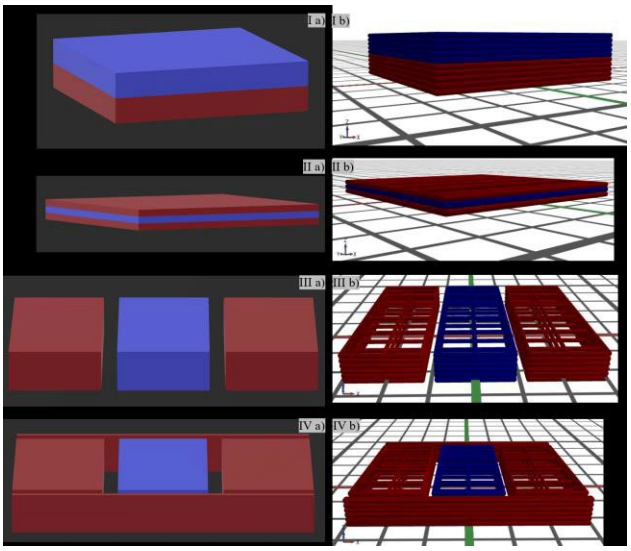


Figure 37: I a) - IV a) designed CAD models, I b) - IV b) corresponding G-Code visualization.

Preliminary testing of established hydrogels in collaboration with different EBM researchers

A03: After assessing the possibilities and requirements of materials provided to **A03**, collaborators of **A03** were trained to the synthesis, sample fabrication, and handling of the hydrogels to allow an extensive collaborative material development in the future.

A04: We provided our established OHA/GEL matrix to **A04** and, in collaboration, succeeded in encapsulating the brain organoids developed in **A04** in a hydrogel bead. We enhanced the encapsulation process and tested different hydrogel concentrations, with altering stiffness.

B02: We have started the development of a suitable 3D hydrogel matrix for the cultivation of amphibian cells. Based on the established hydrogel system, the matrix will be tailored to the needs of Xenopus retinal ganglion cells by creating a matrix with defined storage and loss modulus.

This was part of a joint supervision (Institute of Biomaterials, Institute of Medical Physics, and Micro Tissue Engineering) of a Master's thesis that started in mid-November 23 and ended in May 2024.

C02: In collaboration with **C02** we tested the behavior of primary rat neurons in contact with the established OHA/GEL hydrogel matrix using different aforementioned approaches. We showed that primary neurons can develop in the OHA/GEL matrix provided the network concentration is kept at a low level. Higher concentrations were shown to hinder or deter neuronal development. In lower hydrogel concentrations, neurons can both, develop in a 3D matrix, and actively infiltrate the matrix. Parts of the results of this study were published in 2023 [2].

C04: In collaboration with **C04** we encapsulated melanocytes and melanoma cells in our OHA/GEL matrix. The samples were cultivated and assessed by **C04**.

X01: In collaboration with **X01** we have established a technique for MRE assessment of hydrogel matrices. Requirements that were achieved included bubble-free filling of the test tubes with hydrogel and storability of the filled test tubes without detaching the hydrogel from the test tube walls. The values measured for OHA/GEL hydrogels were similar to those of human brain tissue.

Conclusion and outlook

In summary, the development of neuronal ECM-mimicking hydrogels for use in cell culture was investigated. Several improvements in terms of long-term stability, material combination, and cell culture approaches were developed for many different cell types and their specific requirements, as well as their analysis processes. The developed hydrogel matrix was tested in many collaborations with EBM researchers and showed sufficient results for the first implementation of this type of matrix. In the upcoming development phase, the aim is to establish a more precisely defined matrix, to collect more mechanical data, not only on a macroscopic but also on a microscopic level to further develop the hydrogels into an ECM-mimicking matrix. In addition, an approach for direct printing of cells in the newly created biphasic construct will be investigated. In collaboration with **B02** and **A03**, the use of the matrix for the cultivation of amphibian cells will be extended in addition to the existing mammalian cell cultures.

References

[1] **Kuth, S.**, & **Boccaccini, A. R.** (2024). Enzymatic in situ crosslinking can improve hydrogel stability while maintaining matrix stiffness. *ChemistrySelect, 9*(33), e202401700. https://doi.org/10.1002/slct.202401700

[2] **Kuth, S.**, **Lorke, M.**, **Frischknecht, R.**, **Boccaccini, A. R.** (2023). Tinten für die Biofabrikation – Druckbarkeit vs. Biokompatibilität? *BIOspektrum, 29*, 736–739. https://doi.org/10.1007/s12268-023-2046-0

Y Initialization phase for performing MRE in Erlangen

Guillaume Flé, Frederik Laun, Arnd Dörfler, Jing Guo, Ingolf Sack

Elastography is an imaging technique that maps mechanical properties of tissues *in vivo* non-invasively. As part of EBM project **Y**, we have combined elastography with magnetic resonance imaging to image human brain elasticity in two centers in Erlangen (Zentrum für Medizinische Physik und Technik – ZMPT, and Uniklinikum). Magnetic resonance elastography (MRE) is now available at the Kopfklinik with a Siemens 3 T Vida system and will be recommissioned at ZMPT on a new Siemens 3 T Cima.X system subsequent to recent dismantling of the former Siemens 3 T Prisma scanner.

Following the successful installation of MRE hardware, which began in February 2024, first brain scans were performed on healthy volunteers in our institute. Images of reconstructed brain stiffness, represented by the magnitude of the shear modulus parameter, showed excellent agreement with data obtained by our colleagues at the Elastography Group of the Charité in Berlin, headed by Prof. Ingolf Sack. Figure 38A provides a slice-wise representative example of the stiffness magnitudes and distributions measured in a healthy volunteer. In addition to *in vivo* measurements, MRE is available to EBM projects to characterize *ex vivo* tissues and compare elastography-based estimates with other techniques such as rheometry or tabletop MRE. Beyond MRE, Charité has expanded the range of elastography methods for brain tissue using ultrasound and optical lenses [1,2]. While ultrasound time-harmonic elastography allows the detection of *in vivo* changes in brain stiffness in response to changes in intracranial pressure [1], optical time-harmonic elastography can provide stiffness maps with micrometer resolution in tissue samples [2].

The significant softness of *ex vivo* tissues necessitates the design of specialized tissue-hosting objects that facilitate efficient transmission of elastic waves, while also preventing rigid body motion. Master student Teresa Hidalgo-Gil joined our team and addressed this task as part of her Bachelor's Thesis by creating and 3D-printing an MRE-suitable structure. Figure 38B presents initial findings from a collaboration involving projects **B01** and **X01**, in which *ex vivo* porcine spinal cord bundles (PSCB) were embedded in an agar matrix and examined using MRE. The experimental setup will be optimized, and validation and reproducibility assessments will be carried out to ensure reliable stiffness estimates and to enhance the range of measurements obtained with tabletop MRE.

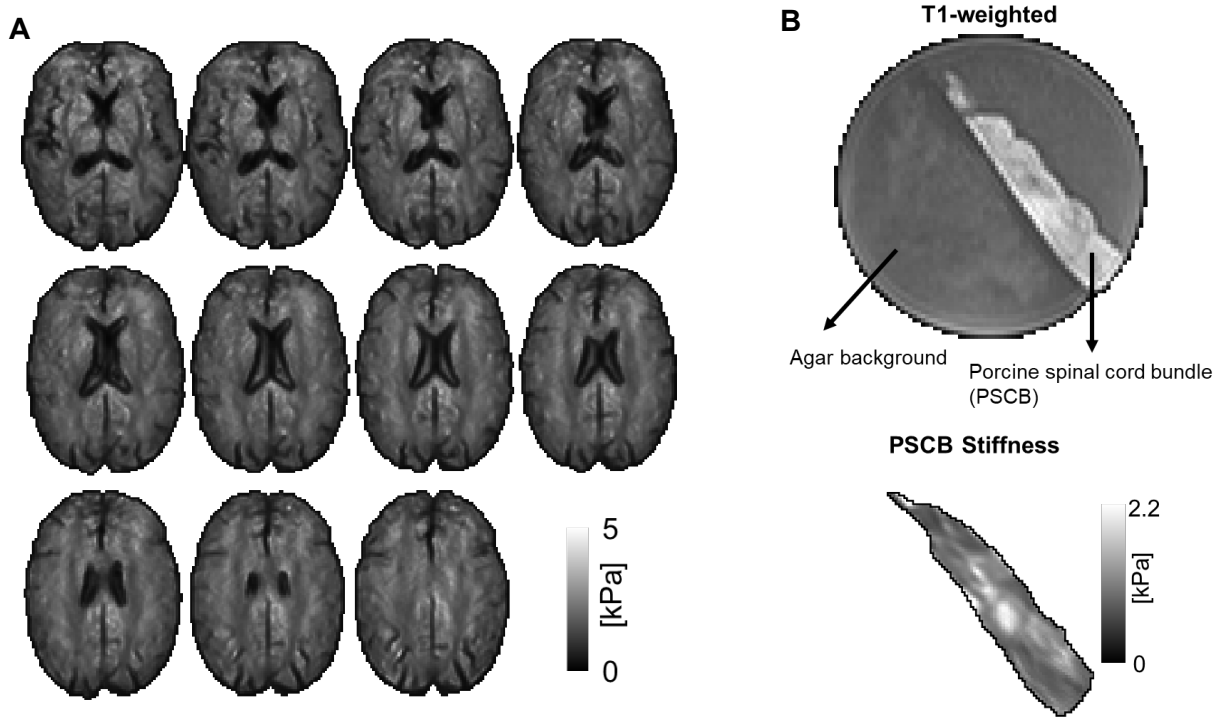


Figure 38: Initial results of MRE imaging. A. Reconstructions of the magnitude of the shear modulus in the healthy brain, representing the tissue stiffness in Pascal unit. B. Anatomical T1-weighted and stiffness images of ex vivo porcine spinal cord bundles embedded in a cylindrical agar matrix.

Further progress was made in establishing MRE in Erlangen by securing clinical scan time at the Kopfklinik. MRE measurements will be conducted on patients with epilepsy and will provide valuable behavioral information regarding the biomechanics of the diseased brain. Additional pre-surgical clinical applications are under discussion with Dr. Stefan Rampp (project **A02**). Finally, we have initiated the development of a new MRE pulse sequence in the context of Mr. Philipp Jeßberger's Master's Thesis with the intention of complementing our elastography toolkit.

References

[1] Klemmer Chandía, S., Schattenfroh, J., Brinker, S. T., Tzschätzsch, H., **Sack, I.**, & **Meyer, T**. (2024). Multimodal assessment of brain stiffness variation in healthy subjects using magnetic resonance elastography and ultrasound time-harmonic elastography. *Scientific Reports*, *14*(1), 28580. https://doi.org/10.1038/s41598-024-79991-y

[2] **Jordan, J.**, Jaitner, N., **Meyer, T.**, Bramè, L., Ghrayeb, M., Köppke, J., Böhm, O., Chandia, S. K., **Zaburdaev, V.**, Chai, L., Tzschätzsch, H., Mura, J., Braun, J., Hagemann, A. I. H., & **Sack, I.** Rapid stiffness mapping in soft biological tissues with micrometer resolution using optical multifrequency time-harmonic elastography. *Advanced Science*, *n/a*(n/a), 2410473. https://doi.org/https://doi.org/10.1002/advs.202410473

1.3 PUBLICATIONS

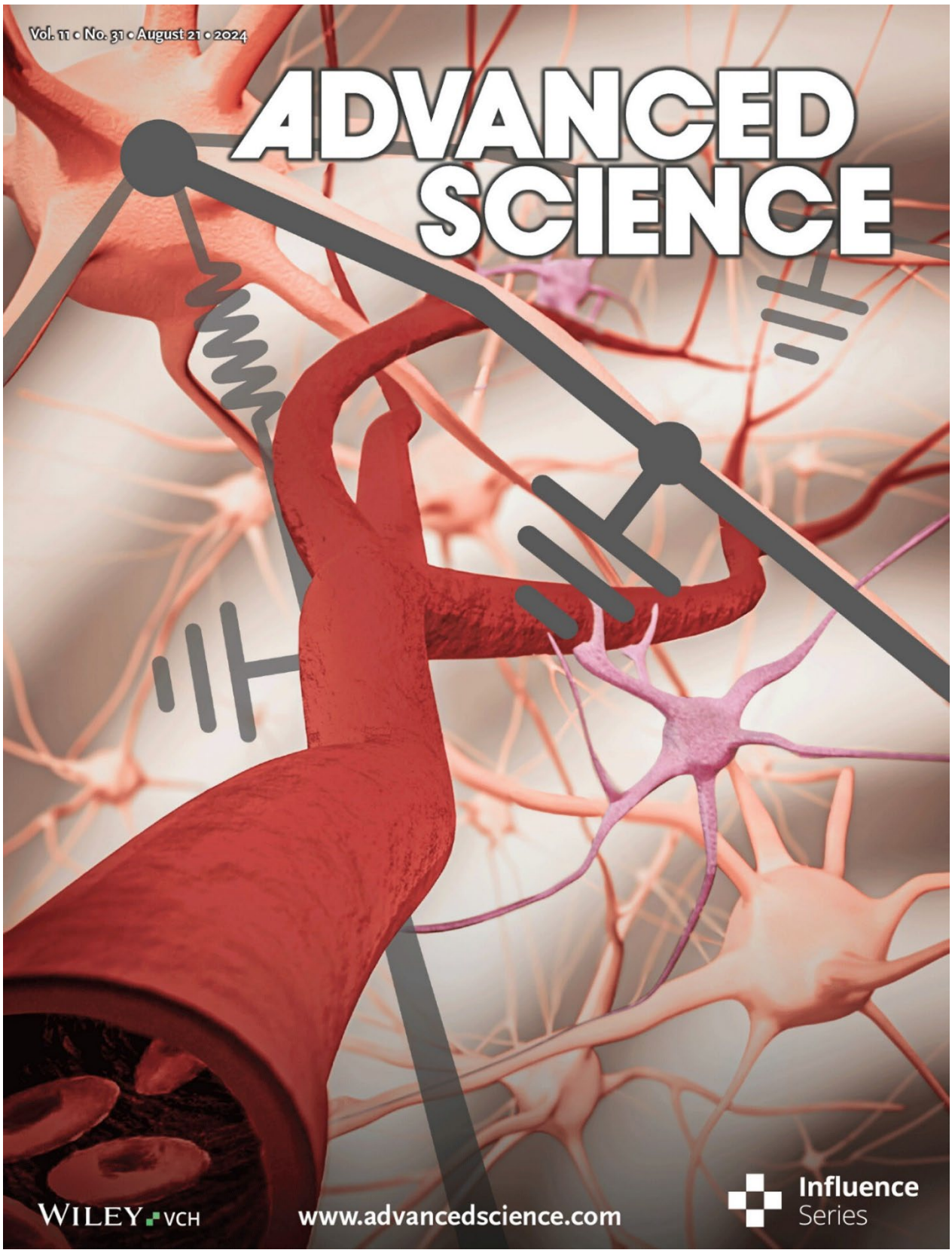


Figure 39: ***Inside Front Cover***

Title: *The Networking Brain: How Extracellular Matrix, Cellular Networks, and Vasculature Shape the ivo Mechanical Properties of the Brain (Adv. Sci. 31/2024).* ***Authors:*** *Judith Bergs, Anna S. Morr, Rafaela V. Silva, Carmen Infante-Duarte, Ingolf Sack.* ***Abstract****: Brain Mechanical Networks: Insight into the brain's mechanical networks sheds light on the relationship between microanatomy and macroscopic biomechanical changes that can be measured by elastography in patients and exploited as novel imaging markers. In article number 2402338, Ingolf Sack and colleagues develop a mechanics-inspired model of four communicating brain networks whose interactions and alterations explain current in vivo elastography findings in normal and diseased human brain.* ***Cover art****: Tom Meyer.*

In the 2024 publication lists, **EBM members** are highlighted in bold. Publication lists are in alphabetical order.

1.3.1 PEER-REVIEWED ARTICLES, CONFERENCE CONTRIBUTIONS, BOOK PUBLICATIONS

[1] Almahayni, K., **Salvador, J. B.**, Conti, R., Widera, A., Spiekermann, M., **Wehner, D.**, Grützmacher, H., & Möckl, L. (2024). Tailored Bisacylphosphane Oxides for Precise Induction of Oxidative Stress-Mediated Cell Death in Biological Systems. *ACS Chem Biol*. https://doi.org/10.1021/acschembio.4c00399

[2] Aubreville, M.**,** Stathonikos, N., Donovan, T. A., Klopfleisch, R., Ammeling, J., Ganz, J., **Wilm, F.**, Veta, M., **Jabari, S.**, Eckstein, M., Annuscheit, J., Krumnow, C., Bozaba, E., Çayır, S., Gu, H., Chen, X. 'A.', Jahanifar, M., Shephard, A., Kondo, S., Kasai, S., Kotte, S., Saipradeep, V. G., Lafarge, M. W., Koelzer, V. H., Wang, Z., Zhang, Y., Yang, S., Wang, X., **Breininger, K.**, Bertram, C. A. (2024). Domain generalization across tumor types, laboratories, and species - Insights from the 2022 edition of the Mitosis Domain Generalization Challenge. *Med Image Anal*, *94*, 103155. https://doi.org/10.1016/j.media.2024.103155

[3] Bergs, J., Morr, A. S., Silva, R. V., Infante-Duarte, C., & **Sack, I.** (2024). The Networking Brain: How Extracellular Matrix, Cellular Networks, and Vasculature Shape the *In Vivo* Mechanical Properties of the Brain. *Adv Sci (Weinh)*, *11*(31), e2402338. https://doi.org/10.1002/advs.202402338

[4] Böhringer, D., Cóndor, M., **Bischof, L.**, Czerwinski, T., **Gampl, N.**, Ngo, P. A., Bauer, A., Voskens, C., López-Posadas, R., **Franze, K.**, **Budday, S.**, Mark, C., **Fabry, B.**, & Gerum, R. (2024). Dynamic traction force measurements of migrating immune cells in 3D biopolymer matrices. *Nature Physics*, *20*(11), 1816-1823. https://doi.org/10.1038/s41567-024-02632-8

[5] Boßelmann, C. M., Leu, C., Brünger, T., **Hoffmann, L.**, Baldassari, S., Chipaux, M., Coras, R., **Kobow, K.**, Hamer, H., Delev, D., Rössler, K., Bien, C. G., Kalbhenn, T., Pieper, T., Hartlieb, T., Becker, K., Ferguson, L., Busch, R. M., Baulac, S., Nürnberg, P., Najm, I., **Blümcke, I.**, & Lal, D. (2024). Analysis of 1386 epileptogenic brain lesions reveals association with DYRK1A and EGFR. *Nature Communications*, *15*(1), 10429. https://doi.org/10.1038/s41467-024-54911-w

[6] Braun, J., Bernarding, J., Snellings, J., **Meyer, T.**, Dantas de Moraes, P. A., Safraou, Y., Wells, R. G., **Guo, J.**, Tzschatzsch, H., Zappe, A., Pagel, K., Sauer, I. M., Hillebrandt, K. H., & **Sack, I.** (2024). On the relationship between viscoelasticity and water diffusion in soft biological tissues. *Acta Biomater*, *182*, 42-53. https://doi.org/10.1016/j.actbio.2024.05.007

[7] Chakraborti, S., & **Zaburdaev, V.** (2024). Transport in cellular aggregates described by fluctuating hydrodynamics. *Physical Review Research*, *6*(4), 043064. https://doi.org/10.1103/PhysRevResearch.6.043064

[8] Fabian, M. S., Rajput, J. R., Schure, J. R., Weinmuller, S., Mennecke, A., Mohle, T. A., **Rampp, S.**, Schmidt, M., **Dörfler, A.**, & **Zaiss, M.** (2024). Comprehensive 7 T CEST: A clinical MRI protocol covering multiple exchange rate regimes. *NMR Biomed*, *37*(5), e5096. https://doi.org/10.1002/nbm.5096

[9] **Firooz, S.**, Javili, A., & **Steinmann, P.** (2024). A versatile implicit computational framework for continuum-kinematics-inspired peridynamics. *Computational Mechanics*, *73*(6), 1371-1399. https://doi.org/10.1007/s00466-023-02415-7

[10] **Firooz, S.**, Reddy, B. D., **Zaburdaev, V.**, & **Steinmann, P.** (2024). Mean zero artificial diffusion for stable finite element approximation of convection in cellular aggregate formation. *Computer Methods in Applied Mechanics and Engineering*, *419*, 116649. https://doi.org/10.1016/j.cma.2023.116649

[11] **Franze, K.** (2024). Tensed axons are on fire. *Proc Natl Acad Sci U S A*, *121*(5), e2321811121. https://doi.org/10.1073/pnas.2321811121

[12] Ganz, J., Marzahl, C., Ammeling, J., Rosbach, E., Richter, B., Puget, C., Denk, D., Demeter, E. A., Tăbăran, F. A., Wasinger, G., Lipnik, K., Tecilla, M., Valentine, M. J., Dark, M. J., Abele, N., Bolfa, P., Erber, R., Klopfleisch, R., Merz, S., Donovan, T. A., **Jabari, S.**, Bertram, C. A., **Breininger, K.**, & Aubreville, M. (2024). Information mismatch in PHH3-assisted mitosis annotation leads to interpretation shifts in H&E slide analysis. *Scientific Reports*, *14*(1), 26273. https://doi.org/10.1038/s41598-024-77244-6

[13] **Greiner, A.**, **Reiter, N.**, **Hinrichsen, J.**, Kainz, M. P., Sommer, G., Holzapfel, G. A., **Steinmann, P.**, Comellas, E., & **Budday, S.** (2024). Model-driven exploration of poro-viscoelasticity in human brain tissue: be careful with the parameters! *Interface Focus*, *14*(6), 20240026. https://doi.org/doi:10.1098/rsfs.2024.0026

[14] Gutmann, M., **Salvador, J. B.**, Müller, P., Kim, K., **Schicht, M.**, Aif, S., **Paulsen, F.**, Meinel, L., **Guck, J.**, & **Möllmert, S.** (2024). Beyond comparison: Brillouin microscopy and AFM-based indentation reveal divergent insights into the mechanical profile of the murine retina. *Journal of Physics-Photonics*, *6*(3). https://doi.org/10.1088/2515-7647/ad5ae3

[15] **Hinrichsen, J.**, Feiler, L., **Reiter, N.**, Bräuer, L., **Schicht, M.**, **Paulsen, F.**, & **Budday, S.** (2024). Identifying composition-mechanics relations in human brain tissue based on neural-network-enhanced inverse parameter identification. *Mathematics and Mechanics of Solids*, *29*(6), 1271-1292. https://doi.org/10.1177/10812865231206544

[16] **Hinrichsen, J.**, Ferlay, C., **Reiter, N.**, & **Budday, S.** (2024). Using dropout based active learning and surrogate models in the inverse viscoelastic parameter identification of human brain tissue [Original Research]. *Front Physiol*, *15*, 1321298. https://doi.org/10.3389/fphys.2024.1321298

[17] **Jordan, J.**, Jaitner, N., **Meyer, T.**, Bramè, L., Ghrayeb, M., Köppke, J., Böhm, O., Chandia, S. K., **Zaburdaev, V.**, Chai, L., Tzschätzsch, H., Mura, J., Braun, J., Hagemann, A. I. H., & **Sack, I.** Rapid Stiffness Mapping in Soft Biologic Tissues With Micrometer Resolution Using Optical Multifrequency Time-Harmonic Elastography. *Advanced Science*, *n/a*(n/a), 2410473. https://doi.org/https://doi.org/10.1002/advs.202410473

[18] Jun, S., Herbst, A., Scheffter, K., John, N., **Kolb, J.**, **Wehner, D.**, & Fattahi, H. (2024). Nonlinear dynamics of femtosecond laser interaction with the central nervous system in zebrafish. *Communications Physics*, *7*(1), 161. https://doi.org/10.1038/s42005-024-01653-2

[19] Kasper, B. S., Archer, J., Bernhardt, B. C., Caciagli, L., Cendes, F., Chinvarun, Y., Concha, L., Federico, P., Gaillard, W., Kobayashi, E., Ogbole, G., Vaudano, A. E., Wang, I., Wang, S., Winston, G. P., & **Rampp, S.** (2024). ILAE neuroimaging task force highlight: Subcortical laminar heterotopia. *Epileptic Disord*, *26*(2), 225-232. https://doi.org/10.1002/epd2.20206

[20] Klemmer Chandía, S., Schattenfroh, J., Brinker, S. T., Tzschätzsch, H., **Sack, I.**, & **Meyer, T**. (2024). Multimodal assessment of brain stiffness variation in healthy subjects using magnetic resonance elastography and ultrasound time-harmonic elastography. *Scientific Reports*, *14*(1), 28580. https://doi.org/10.1038/s41598-024-79991-y

[21] Kreidenhuber, R., Poppert, K. N., Mauritz, M., Hamer, H. M., Delev, D., **Schnell, O.**, & **Rampp, S.** (2024). MEG in MRI-Negative Patients with Focal Epilepsy. *J Clin Med*, *13*(19), 5746. https://doi.org/10.3390/jcm13195746

[22] **Kuth, S.**, & **Boccaccini, A. R.** (2024). Enzymatic Insitu Crosslinking Can Improve Hydrogel Stability While Maintaining Matrix Stiffness. *ChemistrySelect*, *9*(33), e202401700. https://doi.org/10.1002/slct.202401700

[23] **Lehner, A.**, **Hoffmann, L.**, **Rampp, S.**, Coras, R., **Paulsen, F.**, **Frischknecht, R.**, Hamer, H., Walther, K., Brandner, S., Hofer, W., Pieper, T., Reisch, L. M., Bien, C. G., & **Blümcke, I.** (2024). Age-dependent increase of perineuronal nets in the human hippocampus and precocious aging in epilepsy. *Epilepsia Open*, *9*(4), 1372-1381. https://doi.org/10.1002/epi4.12963

[24] Melnyk, O., Quellmalz, M., Steidl, G., Jaitner, N., **Jordan, J.**, & **Sack, I.** (2024). Time-harmonic optical flow with applications in elastography. *Inverse Problems*, *40*(12), 125026. https://doi.org/10.1088/1361-6420/ad9776

[25] **Meyer, T.**, Castelein, J., Schattenfroh, J., Morr, A. S., da Silva, R. V., Tzschätzsch, H., Reiter, R., **Guo, J.**, & **Sack, I.** (2024). Magnetic resonance elastography in a nutshell: Tomographic imaging of soft tissue viscoelasticity for detecting and staging disease with a focus on inflammation. *Progress in Nuclear Magnetic Resonance Spectroscopy*, *144*, 1-14. https://doi.org/10.1016/j.pnmrs.2024.05.002

[26] Mockel, C., Beck, T., Kaliman, S., Abuhattum, S., Kim, K., **Kolb, J.**, **Wehner, D.**, **Zaburdaev, V.**, & **Guck, J.** (2024). Estimation of the mass density of biological matter from refractive index measurements. *Biophys Rep (N Y)*, *4*(2), 100156. https://doi.org/10.1016/j.bpr.2024.100156

[27] **Öttl, M.**, **Wilm, F.**, Steenpass, J., Qiu, J., Rübner, M., Hartmann, A., Beckmann, M., Fasching, P., **Maier, A.**, Erber, R., Kainz, B., & **Breininger, K.** (2025). Style-Extracting Diffusion Models for Semi-supervised Histopathology Segmentation. In A. Leonardis, E. Ricci, S. Roth, O. Russakovsky, T. Sattler, & G. Varol, *Computer Vision – ECCV 2024* Cham.

[28] Pillai, E. K., & **Franze, K.** (2024). Mechanics in the nervous system: From development to disease. *Neuron*, *112*(3), 342-361. https://doi.org/10.1016/j.neuron.2023.10.005

[29] Silva, R. V., Morr, A. S., Herthum, H., Koch, S. P., Mueller, S., Batzdorf, C. S., Bertalan, G., **Meyer, T.**, Tzschatzsch, H., Kuhl, A. A., Boehm-Sturm, P., Braun, J., Scheel, M., Paul, F., Infante-Duarte, C., & **Sack, I.** (2024). Cortical matrix remodeling as a hallmark of relapsing-remitting neuroinflammation in MR elastography and quantitative MRI. *Acta Neuropathol*, *147*(1), 8. https://doi.org/10.1007/s00401-023-02658-x

[30] **Vorndran, J.**, & **Blümcke, I.** (2024). A deep-learning-based histopathology classifier for focal cortical dysplasia (FCD) unravels a complex scenario of comorbid FCD subtypes. *Epilepsia*, *n/a*(n/a). https://doi.org/10.1111/epi.18161

[31] **Wilm, F.**, Reimann, M., Taubmann, O., Mühlberg, A., & **Breininger, K.** (2024). Appearance-based Debiasing of Deep Learning Models in Medical Imaging. In **A. Maier**, T. M. Deserno, H. Handels, K. Maier-Hein, C. Palm, & T. Tolxdorff, Bildverarbeitung für die Medizin 2024. BVM 2024. Informatik aktuell. Springer Vieweg, Wiesbaden Wiesbaden. https://doi.org/10.1007/978-3-658-44037-4_9

1.3.2 OTHER PUBLICATIONS

[32] **Cecchini, E.**, Coras, R., Katoch, M., **Kobow, K.,** Hartlieb, T., Bien, C. G., **Blümcke, I.**, & **Hoffmann, L.** (2024). Brain somatic mosaicism of sex chromosomes defines MOGHE. *Epilepsia*, *65*(S1), 50-51 (abstract 1297). https://doi.org/https://doi.org/10.1111/epi.18151

[33] **Karandasheva, K.**, **Blümcke, I.**, & **Kobow, K.** (2024). Chromatin conformation changes in focal lesional epilepsy: Insights from Hi-C analysis. *Epilepsia, 65(*S1), 294. (abstract 133). https://doi.org/10.1111/epi.18151

1.3.3 SUBMITTED / ACCEPTED / IN PRESS PUBLICATIONS

[34] Almahayni, K., **Bachir, J.**, Jospeh, D. M., Yürekli, N., **Möllmert, S.**, & Möckl, L. From biophysics to biomedical physics. *ACS Bio & Med Chem Au*. (accepted)

[35] Czerwinski, T., **Bischof, L.**, Böhringer, D., Kara, S., Strissel, P. L., Strick, R., Winterl, A., Gerum, R., Wittmann, E., Schneider, M., Beckmann, M. W., Nusser, G., Wiesinger, M., **Budday, S.**, Lux, A., Voskens, C., **Fabry, B.**, & Mark, C. (2024). Immune cells employ intermittent integrin-mediated traction forces for 3D migration. *bioRxiv*, 2023.2004.2020.537658. https://doi.org/10.1101/2023.04.20.537658 (submitted)

[36] Dahl, R., Weier, A. Winter, C., **Hintze, M.**, Rothhamer, V., Tsaktanis, T., Pröbstel, A-K., Neziraj, T., Pössnecker, E., Oechtering, J., Kuhle, J., Kallmann, B.-A., Luber, G., Heider, T., Klotz, L., **Chunder, R.**, **Kuerten, S.** (2024) The ion channel MLC1 is a potential target antigen in multiple sclerosis. Neurology Neuroimmunology & Neuroinflammation. (accepted)

[37] Furlanetto, F., Flegel N., Kremp, M., Spear, C., Alfonsetti, M., Bohl, B., Turan, S., Lie, D.C., Winkler, J., **Falk, S.**, Wegner, M., **Karow, M.** (2024). Establishment of a novel human organoid model system reveals requirement of TCF4 for oligodendroglial differentiation. *Life Science Alliance* (in revision).

[38] **Firooz, S.**, Reddy, B. D., & **Steinmann, P.** A novel micromorphic-based artificial diffusion method for stabilization of approximations of convection-diffusion problems. *International Journal for Numerical Methods in Engineering*. (submitted)

[39] Kreysing, E., Gautier, H., Humphrey, R., Mooslehner, K., Muresan, L., Haarhoff, D., Mukherjee, S., Zhao, X., Winkel, A., Dimitracopoulos, A., Pillai, E. K., Káradóttir, R. T., & **Franze, K.** (2024). Substrate stiffness regulates neuronal maturation via Piezo1-mediated TTR activity. *bioRxiv*, 2024.2007.2025.605128. https://doi.org/10.1101/2024.07.25.605128 (submitted)

[40] Lowinski, A., Dabringhaus, A., Kraemer, M., Doshi, H., Weier, A., **Hintze, M.**, **Chunder, R.**, **Kuerten, S.** (2024) MRI-based morphometric structural changes correlate with histopathology in experimental autoimmune encephalomyelitis. Journal of the Neurological Sciences (accepted)

[41] **Neumann, O.,** Vardhan Surana, H., **Melly, S.**, **Steinmann, P.**, & **Budday, S.** Mechanical characterization of spinal cord tissue by nanoindentation. *Journal of the Mechanical Behavior of Biomedical Materials*. (accepted)

[42] **Öttl, M.**, Mei, S., **Wilm, F.**, Qiu, J., Steenpass, J., Rübner, M., Hartmann, A., Hübner, H., Fasching, P., **Maier, A.**, Erber, R., & **Breininger, K.** Weighted Noise-Range Schedules for Diffusion Segmentation of Medical Image. *Biomedical Signal Processing and Control*. (submitted)

[43] **Öttl, M.**, Mei, S., **Wilm, F.**, Steenpass, J., Rübner, M., Hartmann, A., Beckmann, M., Fasching, P., **Maier, A**., Erber, R., & **Breininger, K.** (2024). *Analysing diffusion segmentation for medical images*. https://doi.org/10.48550/arXiv.2403.14440 (submitted)

[44] **Pan, Z.** et al.: “Low-Latency Classification of Malignancy in Confocal Laser Endomicroscopy with Automatic Nondiagnostic Frame Detection”, under review at BMC Medical Imaging, 2024

[45] Pillai, E. K., Mukherjee, S., **Gampl, N.**, McGinn, R. J., Mooslehner, K. A., Becker, J. M., Thompson, A. J., & **Franze, K.** (2024). Long-range chemical signalling *in vivo* is regulated by mechanical signals. *bioRxiv*, 2024. https://doi.org/10.1101/2024.02.15.580459 (submitted)

[46] **Sipkova, J.**, & **Franze, K.** (2024). Eph/ephrin signalling in the developing brain is regulated by tissue stiffness. *bioRxiv*, 2024.2002.2015.580461. https://doi.org/10.1101/2024.02.15.580461 (submitted)

[47] **Wilm, F.**, Ammeling, J., **Öttl, M.**, Fick, R. H. J., Aubreville, M., & **Breininger, K.** (2024). *Rethinking U-net skip connections for biomedical image segmentation*. https://doi.org/10.48550/arXiv.2402.08276 (submitted)

[48] **Wilm, F.**, **Öttl, M.**, Aubreville, M., & **Breininger, K.** (2024). *Domain and content adaptive convolutions for cross-domain adenocarcinoma segmentation*. https://doi.org/10.48550/arXiv.2409.09797 (submitted)

2 INTEGRATED RESEARCH TRAINING GROUP (IRTG)

As EBM is exceptionally interdisciplinary, integrating disciplines such as experimental analyses, clinical studies, and bioengineering – all informed by advanced modeling and simulation – the integrated Research Training Group (**iRTG**) is particularly important for the CRC to bring the different disciplines together on a common basis.

The **iRTG** of EBM addresses this demanding interdisciplinary challenge by providing a structured mandatory qualification program and ensuring quality management and control for doctoral and postdoctoral researchers. This approach also nurtures their scientific independence and promotes their career development.

The comprehensive program encompasses a range of activities aimed at enhancing theoretical knowledge, methodological skills, soft skills, and fostering a collaborative research environment.

2.1 QUALIFICATION PROGRAM

The qualification program comprises

- EBM (Post-)Doctoral Researchers' Seminars
- EBM Harmonization Workshops (theory and methods)
- EBM Soft Skills Courses
- EBM Annual Retreats and EBM Update Meetings

as basic activities. These components are complemented by active participation in international conferences, the publication of at least one paper, participation in and organization of Lab Shadowing, and writing short contributions for the EBM homepage after organizing EBM-funded activities or travel. In addition, (post-)doctoral researchers have the opportunity to complete research stays abroad as part of the program.

Beyond these essential elements, additional activities are available for all EBM members, including

- EBM Virtual Breakfast Clubs and Lunches
- EBM Virtual Brain Talk
- EBM Seminar Talks

2.1.1 EBM (POST-)DOCTORAL RESEARCHERS' SEMINARS

Every two months, organized by two (post-)doctoral researchers in rotation, these two-hour seminars offer ample opportunities and valuable experiences for (post-)doctoral researchers to present their latest work-in-progress and results. The sessions facilitate discussions on current challenges and future research perspectives within a relaxed and interdisciplinary atmosphere. The seminars aim to foster networks among doctoral and postdoctoral researchers, catalyzing new research directions, approaches, and collaborations.

Originally, the concept was to hold the (post-)doctoral researchers' seminars monthly, with each month featuring a presentation by one (post-)doctoral researcher and the presence of the Principal Investigators. However, early in the EBM program, (post-)doctoral researchers expressed a desire for the seminar to be primarily internal among the doctoral cohort. In a closed circle, the doctoral researchers feel more at ease to ask questions, discuss uncertainties, and share their own experiences, fostering a more open and supportive environment.

Following feedback from the doctoral candidates during the EBM Retreat in September 2023, it was additionally decided to shift the seminar to a bi-monthly schedule due to time constraints. As compensation, it is now organized by two doctoral researchers who also deliver the presentations. This allows for a more efficient use of time for research work and other commitments.

To successfully complete the doctorate within the EBM **iRTG** 1540, it is mandatory to attend at least 4 of the 6 (Post-)Doctoral Researchers' Seminars per year.

Table 2: (Post-)Doctoral Researchers' Seminars

	Date	Organized by (name / project)	Title
01	19.01.24	Erica Cecchini / **A02**	Quantitative characterization of brain malformations – MOGHE
		Soheil Firooz / **C01**	Continuum modeling and simulation of cell aggregation phenomena
02	21.03.24	Shanice Heidenreich / **C04**	Cellular differentiation in brain tissue like matrices
		Michael Tranchina / **A04**	The role of mechanics in orchestrating neural lineage decisions
03	11.06.24	Markus Lorke / **X03**	Engineering brain tissue like matrices
		Clara Froidevaux / **A03**	*In vitro* model for the mechanics of early brain development
04	12.07.24	Laura Ruhland / **X01**	Comparative *ex vivo* testing of brain tissue and substitute materials
		Yashasvi Verma / **X01**	Model-based reconciliation of *ex vivo* and *in vivo* test data
05	08.10.24	Oskar Neumann / **B01**	*In silico* modeling of spinal cord regeneration
		Maria Tarczewska / **B02**	Pre and post metamorphosis spinal cord regeneration in frogs
06	17.12.24	Kristina Karandasheva / **C03**	Exploring the mechanics of neuronal network formation
		Lars Bischof / **C05**	Molecular mechanisms of mechanosensing in primary neurons

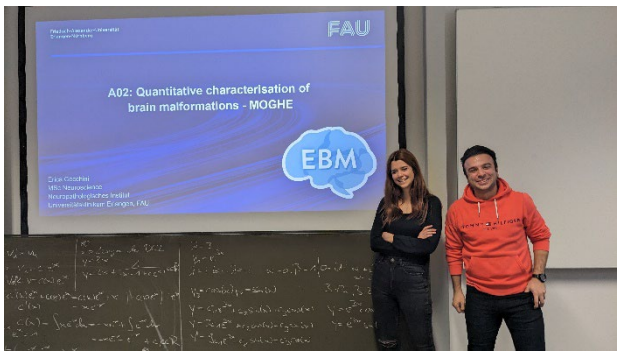
2.1.2 EBM HARMONIZATION WORKSHOPS

Trimestral half-day EBM Harmonization Workshops are focused introductions to interdisciplinary topics of key relevance for EBM. They aim to provide a common theory and methods basis for EBM doctoral researchers. Orchestrated by EBM PIs and postdoctoral researchers from different disciplines, the workshops cover a broad spectrum of theory and methods in various formats (lectures, exercises, laboratories, tutorials, etc.).

To successfully complete the doctorate within the EBM **iRTG** 1540, it is mandatory to attend at least 8 of the 16 Harmonization Workshops (theory and methods) within 4 years.

Table 3: EBM Harmonization Workshops

	Date	Organized by	Subject
01	20.03.24	Alexandra Schambony	Early neural development
02	04.06.24	Silvia Budday / Nina Reiter / Jan Hinrichsen	Mechanical testing
03	19.06.24	Katharina Breininger / Frauke Wilm	Introduction to Deep Learning
04	13.11.24	Stefan Rampp / Arnd Dörfler / Valentin Riedl	Neuroimaging



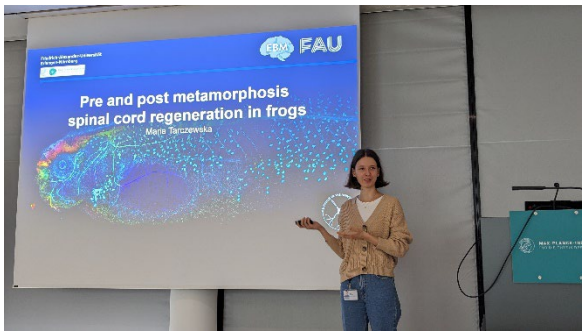


Figure 40: Impressions of the (Post-)Doctoral Researchers' Seminars. (Images: S. Kuth, L. Ruhland, L. Bischof)

2.1.2.1 5th EBM Harmonization Workshop: Early neural development

On March 20, 2024, the 5th EBM Harmonization Workshop took place, where twelve participants of the EBM Integrated Research Training Group recently delved into the intricate processes underlying early brain development during an immersive workshop. Spearheaded by Professor Alexandra Schambony, the session provided insights into early neurogenesis in embryos, along with the pioneering technique of developing neural plate-based brain organoids utilizing eggs from the South African Frog, Xenopus Laevis.

The workshop facilitated hands-on learning opportunities in various aspects of early brain development research, including practical experience in meticulously preparing neural plates, a fundamental step in the generation of brain organoids. Additionally, they were trained in the execution of an in-situ experiment that involves the localization and visualization of specific molecules, such as mRNA

or proteins, within tissues or cells to study their spatial distribution and expression patterns, providing insights into developmental processes.

Furthermore, participants honed their skills in microinjection, a precise technique used to deliver substances such as genetic material or chemicals into cells or tissues. This technique is vital for manipulating gene expression and studying the effects of specific molecules on early brain development. For this station, gelatin-based microbeads were prepared and used as a substitution for the frog embryos.

However, the most memorable aspect for many was the tour of the frog facility, offering a firsthand glimpse into the practical part of amphibian research and an integral part of EBM Project **A03**.

By engaging in these hands-on activities, participants not only deepened their theoretical understanding but also developed practical skills essential for conducting advanced research in the field of embryonic biology and neuroscience.

*(Clara Froidevaux, **A03**)*

Figure 41: EBM'S 5th Harmonization Workshop: Early neural development. (Images: A. Kuhn)

2.1.2.2 6th EBM Harmonization Workshop: Mechanical testing

On July 4, Prof. Silvia Budday and her team hosted an EBM Harmonization Workshop focused on the mechanical testing of brain tissue. Participants learned how constitutive models can be used to develop simulation models that can help with surgical planning and the development of protective equipment.

After a brief introduction to the basics of continuum mechanics, participants had the opportunity to experience the stiffness of brain tissue firsthand by cutting cylindrical samples from pig brains. Does gray matter or white matter feel stiffer? Participants explored our current understanding of the mechanical behavior of the brain, including aspects such as time dependence, preconditioning, and location dependence.

Next, we moved to the lab for another hands-on session. Here, participants learned how to handle tissue samples as they were tested under tension, compression, and torsional shear in the rheometer, under indentation in the nanoindenter, and using the magnetic resonance elastography (MRE) setup. Lively discussions provided valuable input and ideas for future research challenges.

*(Jan Hinrichsen, **A01**)*

Figure 42: EBM'S 6th Harmonization Workshop: Mechanical testing. (Images: S. Budday)

2.1.2.3 7th EBM Harmonization Workshop: Introduction to Deep Learning

On June 19th, Prof. Katharina Breininger and Frauke Wilm invited members of EBM to an introductory workshop on Deep Learning.

In a lively lecture, Katharina Breininger guided the participants through the common deep learning concepts. The EBM members gained insight into the basic structure of neural networks, the importance of reasonable training data, the „pros and cons“ of artificial intelligence, and much more.

In the second half of the afternoon, Frauke Wilm led the participants through a one-hour hands-on course where everyone had the opportunity to train their own neural network. Photos of EBM members presenting different coffee mugs were used as training data.

Frauke Wilm closed the 7th EBM Harmonization Workshop with a short talk on how AI can be successfully used to analyze medical data, promoting collaborations among projects of EBM.

*(Lars Bischof, **C05**)*

Figure 43: EBM'S 7th Harmonization Workshop: Deep learning. (Images: O. Neumann)

2.1.2.4 8th EBM Harmonization Workshop: Neuroimaging

On November 13, a harmonization workshop focusing on neuroimaging was organized by Arnd Dörfler (Department of Neuroradiology) and Stefan Rampp (Department of Neuroradiology and Department of Neurosurgery). The program started with an introduction to neuroimaging from a clinical perspective (Arnd Dörfler), providing the multidisciplinary audience with an overview of neuroanatomy and how different MR techniques are used in clinical applications to diagnose patients with epilepsy, tumors, multiple sclerosis, etc.

This was followed by a joint presentation by Dr. Samira Epp and Dr. Gabriel Castrillon from the group of Valentin Riedl (Department of Neuroradiology) on advanced imaging techniques. The two speakers gave an overview of metabolic and functional imaging techniques such as functional MRI (fMRI),

MRI assessment of tissue oxygenation, and chemical exchange saturation transfer (CEST) for quantitative imaging of metabolites.

In the last part of the workshop, Stefan Rampp presented several clinical cases of focal epilepsy. The participants had to review the MR images on their own laptops and find the epileptogenic lesion. This hands-on session started with easy cases with obvious lesions such as tumors or cavernomas, but then steadily increased in difficulty, ending with a case of subtle focal cortical dysplasia (FCD), a pathology of particular interest to some of the EBM subprojects.

*(Stefan Rampp, **A02**)*

Figure 44: EBM'S 8th Harmonization Workshop: Neuroimaging. (Images: S. Rampp (left), S. Kuth (right))

2.1.3 EBM SOFT SKILLS COURSES

The EBM Soft Skills courses, ranging from half-day to full-day sessions, primarily draw from the portfolio offered by the Graduate Center (GC) of FAU. Additionally, the F³G network (Research Consortia for Promoting Equality at Friedrich-Alexander-Universität Erlangen-Nürnberg) provides a range of gender equality initiatives, including lectures and seminars on topics such as women's advancement and gender sensitivity, which are open to members of affiliated research alliances. EBM doctoral researchers have actively participated in these and other related offerings.

To successfully complete their doctorate within the EBM **iRTG** 1540, doctoral researchers are required to attend at least one course on “Good Scientific Practice”, one course on “Scientific Writing”, and two additional Soft Skills courses within four years.

To meet these requirements, the EBM Coordination organized and offered the “Good Scientific Practice” course exclusively for EBM doctoral and postdoctoral researchers during the first year of the EBM program. In 2024, the second mandatory course, “The Essentials of Scientific Writing”, was likewise organized and offered specifically for EBM doctoral and postdoctoral researchers.

Table 4: Soft Skills Courses with EBM doctoral researcher participation

	Date	Content	Instructor	Offered by
01	17.01.24	Grundlagen der Statistik	Dr. Felix Bauer	GC
02	05.02.24	Zeitmanagement für die Promotion - Erfahrungen und Handlungsempfehlungen	Univ.-Doz. Dr. habil. Tim Alexander Herberger	GC
03	28.02.24	FAU Job Insights live - Career Options outside Academia (engineering/sciences)	Judith Wunschik Mostafa Arghavani	GC
04	28.02.24 + 29.02.24	Giving a memorable presentation	Deborah Bennett	F³G
05	08.03.24	Good Research Practice and Scientific Integrity – An Introduction	Dr. Christian Schmitt-Engel	GC
06	21.03.24	Intercultural Competencies – Recognizing & Realizing Potentials	Dr. Silke Oehrlein-Karpi	F³G
07	09.04.24	Networking - which networks do I need to reach my career goal	Katja Wolter	F³G
08	14.05.24 / 17.05.24	PhD, and next? Career options, skills and orientation for scientists	Dr. Karin Bodewits	F³G
09	17.05.24	Introduction to German Academia	Dr. Christian Schmitt-Engel	GC
10	24.06.24	Increase your employability with a PhD – a workshop on becoming your own marketing manager	Wolfgang Leybold	GC
11	17.07.24 + 18.07.24	Personalführung und Teamentwicklung	Michael Hübler	GC
12	26.09.24 + 27.09.24	Taking the Lead for Postdocs	Matthias Merkelbach	F³G
13	27.09.24	Erfolgreich im Vorstellungsgespräch	Nicole Jakob	GC
14	13.11.24 + 14.11.24	Time and Project Management for Researchers	Dr. Daniel Friedrich	F³G
15	21.11.24 + 22.11.24	Maximizing Publication Potential: The Essentials of Scientific Writing	Dr. Deborah Bennett	EBM
16	10.12.24 + 11.12.24	Women in Academia: The Essentials of Scientific Writing	Dr. Deborah Bennett	EBM

2.1.3.1 Maximizing Publication Potential: Essentials of Scientific Writing

Figure 45: Deborah Bennett presenting the "Essentials of Scientific Writing" seminar to EBM doctoral researchers. (Image: S. Kuth)

As part of the iRTG qualification program, the EBM doctoral researchers participated in the soft skills seminar “Maximizing Publication Potential: Essentials of Scientific Writing” on November 21 and 22, 2024. The seminar, led by lecturer Deborah Bennet, provided an in-depth exploration of the key principles and strategies for crafting compelling scientific texts. Through several sessions, the participants learned how to organize ideas coherently and tailor their writing to engage and inform their target audience.

The seminar began with an overview of foundational concepts, including the different genres of scientific writing, their purposes, and common challenges researchers face when writing. Participants were introduced to practical strategies for overcoming these challenges and achieving professionally written texts. The sessions also addressed the general structure of a scientific publication, helping participants build a solid understanding of how to present their work logically and effectively.

A unique aspect of the seminar was its hands-on approach. Under the lecturer’s guidance, the participants constructed a scientific publication based on their own data from the ground up. This step-by-step process covered all essential stages, starting with identifying the core message or story of their research and moving on to formulating precise, informative, and engaging titles. The researchers also practiced constructing clear and captivating abstracts, describing their results with clarity and flow, and discussing their findings in ways that highlighted their significance and situated them within the broader scientific context. Each stage was accompanied by practical exercises, useful tips, and suggestions to help participants refine their skills.

In addition to these core elements, the seminar focused on enhancing the readability and flow of the scientific texts. Participants explored strategies to avoid the overuse of passive voice and maintain a dynamic and engaging style. Attention was also given to polishing figure captions, ensuring that visual aids were clear, concise, and effective. Throughout the seminar, the emphasis was placed on precision in language, encouraging the researchers to express their ideas accurately and professionally.

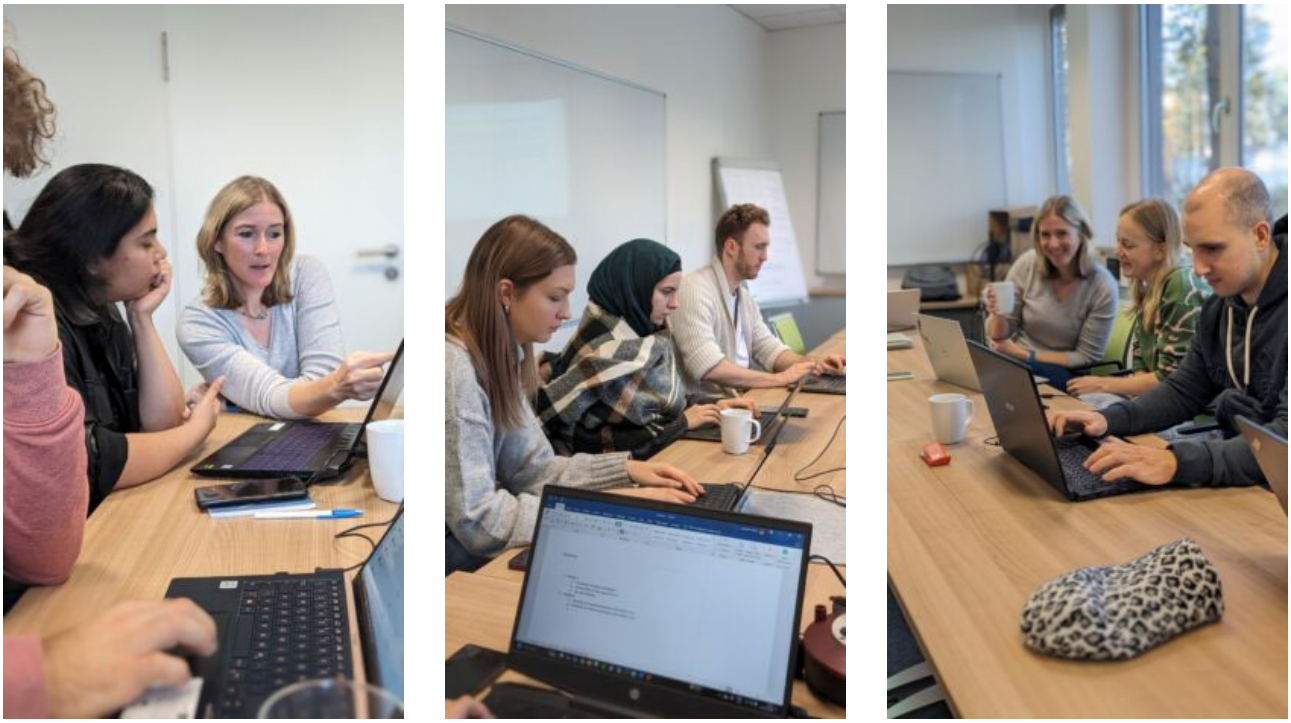


Figure 46: Impression of the "Essentials of Scientific Writing" Seminar. (Images: S. Kuth)

The “Essentials of Scientific Writing” seminar significantly improved participants’ confidence and competence in scientific communication. The insights and skills gained are expected to contribute to the creation of high-quality, impactful publications while supporting the researchers’ academic and professional development as they pursue their doctoral work.

*(Sonja Kuth, **X03**)*

2.1.4 EBM UPDATE MEETING

earch areas and cross-sectional projects. These sessions encompass all projects within the scope EBM, ensuring a thorough review of ongoing initiatives and advancements. The meetings offer a platform for researchers to share developments, exchange ideas, and foster collaboration across various EBM-related fields.

To successfully complete the doctorate within the EBM **iRTG** 1540, it is mandatory to attend all annual Update Meetings.

Table 5: EBM Update Meeting

	Date	Type	Location
01	09.02.24	1. EBM Update Meeting	Max Planck Institute for the Science of Light, Erlangen

Program see Appendix 1

The annual one-day EBM Update Meetings provide comprehensive progress updates on key res

Figure 47: Team Gathering: EBM members pose on the staircase for a group photo. (Image: ITM/FAU)

The 1st EBM Update Meeting of the Consortium on Exploring Brain Mechanics took place on February 9 at the Max Planck Institute for the Science of Light in Erlangen. This meeting provided a comprehensive progress update on all ongoing projects within its purview.

The day began with a meeting of the EBM Executive Board, fostering open dialogue on organizational matters, which seamlessly transitioned into the EBM General Assembly. During the assembly, decisions were made on various aspects, such as social media strategies, plans for further educational workshops and seminars, and comprehensive reviews of the currently ongoing program.

EBM is structured into three focal research areas (FRA) focusing on cerebral (**A**), spinal (**B**), and cellular mechanics (**C**), an overarching cross-sectional research area (**XRA**) and the additional Project **Y**.

Frederik Laun kicked off the presentations, detailing the progress towards establishing MRE at FAU as a key objective of Project **Y**. Following this, Ingolf Sack elaborated on Project **X**, presenting various cross-sectional projects including experimental MRE observations, phantom material testing, computer modeling, and the development of AI-driven identification tools. Moving forward, Kristian Franze reported on FRA **A**, focusing on cerebral research, emphasizing the quantification of brain malformations and the exploration of early neural development through a combination of *in vivo*, *in vitro*, and *in silico* approaches. FRA **B**, focusing on spinal mechanics, was then elucidated by Stephanie Möllmert, who provided insights into spinal cord regeneration, testing protocols, and manipulation techniques across different species. The final round of updates centered on the **C** projects, presented by Vasily Zaburdaev, examining the effects of cell mechanics on neuronal plasticity, activity modulation, mechanotransduction processes, and cell-matrix modeling.

Throughout the presentations, breaks for lunch and coffee provided opportunities for engaging poster presentations from each project, sparking lively debates and discussions among attendees, facilitating a deeper understanding of each project's nuances and fostering further collaborations.

An additional highlight of the day was the celebration of the spokesperson, Paul Steinmann's birthday. A cake was presented to him, which he graciously shared with all participants. Additionally, he received a special gift – a 3D print of his own brain, crafted from MRI scan data – symbolizing appreciation and recognition, and further reinforcing the spirit of collaboration and camaraderie within the consortium.

*(Yashasvi Verma, **X01**)*

Figure 48: Impressions of the 1st EBM Update Meeting. (Images: ITM/FAU, S. Kuth, A. Dakkouri-Baldauf)

2.1.5 EBM RETREAT

Annual two-day EBM Retreats with mandatory attendance for **iRTG** members provide a forum for research progress presentations of the doctoral and postdoctoral researchers. The main focus is on the internal evaluation of scientific progress in the field of EBM and the promotion of the expansion of existing collaborations as well as the establishment of new collaborations between EBM projects.

These events are held at remote locations away from the FAU campus and include social activities to encourage informal interaction between participants.

To successfully complete the doctorate within the EBM **iRTG** 1540, it is mandatory to attend all annual Retreats.

Table 6: EBM Retreat

	Date	Type	Location
01	10.10.24 / 11.10.24	2nd EBM Retreat	Fraunhofer Research Campus Waischenfeld

Program see Appendix 2

Figure 49: EBM members at the 2nd EBM Retreat in Waischenfeld. (Image: A. Dakkouri-Baldauf)

The 2nd EBM Retreat took place on October 10 and 11, 2024, at the Fraunhofer Research Campus in Waischenfeld, nestled in the beautiful Franconian Switzerland. This retreat offered an excellent opportunity for researchers to present their work, engage in networking, and collaboratively explore new ideas.

Day 1: October 10, 2024

The first day of the retreat kicked off with a series of insightful presentations:

Morning Sessions: The day began with presentations focusing on brain malformations and development, covering topics such as *in silico* modeling, quantitative characterization, and both *in vitro* and *in vivo* mechanics of brain development, along with spinal cord regeneration.

Afternoon Activities: After a productive morning, one of the highlights was a scenic hike to Rabenstein Castle, which included speed mentoring sessions. These sessions allowed (post-)doctoral researchers to engage in informal yet valuable conversations with their mentoring teams, providing guidance on both technical issues and broader career advice. The afternoon continued with further presentations on spinal cord mechanics and regeneration, discussing determinants of spinal cord mechanics, regeneration in various models, and mechanical manipulation techniques.

Evening Session: The day concluded with an engaging after-dinner talk by Ben Fabry, who has conducted research multiple times for several months at the Neumayer Station in Antarctica, focusing on the social behavior of emperor penguins. His presentation on the collective behavior of these penguins offered fascinating insights into the mechanisms of the animal world, highlighting the complexities of social interactions in nature.

Figure 50: Ben Fabry during his fantastic talk about emperor penguins. (Image: A. Dakkouri-Baldauf)

Day 2: October 11, 2024

The second day began with a general assembly of EBM, led by the two spokespersons, Paul Steinmann and Silvia Budday. Members discussed recent developments and the future direction of the research consortium. This included announcing and discussing the results of a survey conducted among the doctoral and postdoctoral researchers regarding the EBM **iRTG** 1540. Additionally, a brief presentation was given by the new associated PI, Tomohisa Toda.

Figure 51: Project presentations by the (post)doctoral researchers. (Images: A. Dakkouri-Baldauf)

Morning Presentations: The morning featured discussions on the establishment of magnetic resonance elastography at FAU, followed by presentations on cellular differentiation, molecular mechanisms of mechanotransduction, and model-based reconciliation of test data.

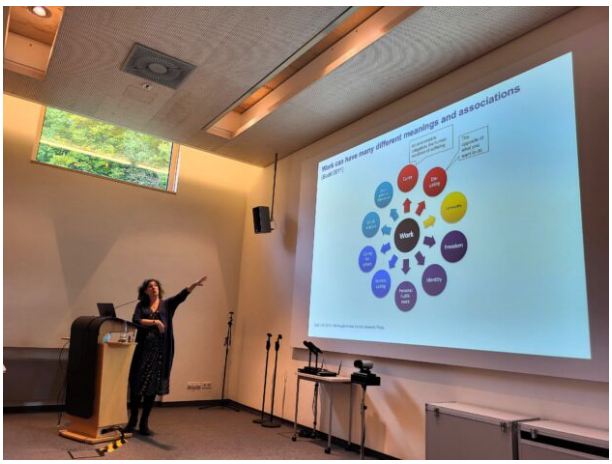


Figure 52: The inspiring guest lecture by Heather Hofmeister. (Image: A. Dakkouri-Baldauf)

Guest Talk: A highlight of the day was the guest lecture by Prof. Dr. Heather Hofmeister from Goethe University Frankfurt. She spoke about the diverse expectations and approaches of different generations in German academia, encouraging reflection on how these factors influence scientific collaboration.

Afternoon Sessions: The retreat wrapped up with additional presentations on data analysis and engineering brain tissue-like matrices, concluding a full agenda that spurred dynamic discussions and collaborative ideas among participants.

Figure 53: Our PI Kristian Franze: Equipped for all conditions. (Image: A. Dakkouri-Baldauf)

Additionally, some associated doctoral researchers and master's students showcased their research through poster presentations. Several sessions were chaired by these early-career researchers, allowing them to gain valuable experience in organizing and leading scientific discussions.

Conclusion

The 2nd EBM Retreat was a resounding success, characterized by a rich exchange of scientific ideas, team-building activities, and new collaborations. The beautiful setting of the Fraunhofer Research Campus in Waischenfeld provided an ideal environment for both formal and informal discussions, fostering new impulses for future research.

Figure 54: Stimulating discussions at various locations and contexts. (Images: A. Dakkouri-Baldauf (top, bottom right), M. Tranchina (bottom left))

Figure 55: Hiking and enjoying the stunning Franconian Switzerland. (Images: A. Dakkouri-Baldauf)


Figure 56: Amazing childcare and happy kids! (Images: P. Steinmann (left), A. Dakkouri-Baldauf (right))

We look forward to the next retreat and the continued scientific progress of the EBM group!

2.1.6 EBM LAB SHADOWING

In 2024, ongoing EBM Lab Shadowing enabled EBM doctoral researchers to conduct short-term collaborative stays at the laboratories of other EBM PIs. These stays provided opportunities to participate in joint experiments, learn experimental, modeling, and computational techniques of common interest, and contribute to overarching, multidisciplinary EBM publications and presentations.

2.1.6.1 Collaborative experiments between **X03** and **C04**/**A04**

How can oxidized hyaluronic acid (OHA)-based hydrogels be synthesized?

Figure 57: Michael Tranchina, Shanice Heidenreich and Markus Lorke casting colorful silicone mats. (Image: S. Kuth)

On July 30, 2024, Shanice Heidenreich (project **C04**, PI: Anja Bosserhoff) and Michael Tranchina (project **A04**, PIs: Marisa Karow / Sven Falk) were invited by Markus Lorke (project **X03**, PI Aldo R. Boccaccini) to join an OHA synthesis experiment in the Boccaccini lab (Department of Materials Science and Engineering). Together, we conducted the oxidation of hyaluronic acid into oxidized hyaluronic acid (OHA) as a key step for producing OHA/GEL-based hydrogels. Additionally, we cast colorful silicone mats for my project, which will simplify the detachment of hydrogels embedded with organoids.

*(Michael Tranchina, **A04**)*

2.1.7 EBM SCHOLARS' VISITS

While EBM Lab Shadowing focuses on facilitating collaborative stays among EBM doctoral researchers within the network, the EBM Scholars' Visit program extends this concept by inviting international researchers to participate in lab shadowing activities.

In 2024, we had the pleasure of hosting **Alireza Sharifzadeh-Kermani**, a PhD student from the University of Auckland's Bioengineering Institute (Animus Lab), as an international EBM scholar. During his visit from August 29th to September 2nd, 2024, Alireza engaged in lab shadowing and fostered cross-institutional collaboration. He met with several colleagues in the lab to discuss key topics, including:

- Poro-viscoelasticity with Alexander Greiner
- Integration of vasculature into full-scale brain models with Yashasvi Verma (**X01**)
- Region-specific mechanical properties of the brain with Nicole Tueni

As part of his visit, Alireza gave a lecture titled "A Mechanistic Approach for Brain Pressure Estimation," in which he presented his innovative computational model for estimating intracranial pressure (ICP). This model integrates brain MR sequences to characterize blood flow and brain tissue deformation, providing a mechanistic analysis of intracranial dynamics. His work aims to offer a non-invasive alternative to traditional invasive ICP measurement techniques, which carry significant risks.

With a background in biomechanical-control engineering from Sharif University of Technology, Alireza is now pursuing his PhD to explore how the brain's fluid pressure influences motor control, driven by his fascination with understanding the 'fishbowl' of the human brain.

Figure 58: Alireza Sharifzadeh-Kermani during his lecture at EBM.

2.1.8 EBM RESEARCH SECONDMENTS AND SHORT-TERM RESEARCH STAYS

EBM Research Secondments, lasting several weeks and involving international academic hosts, including the EBM Mercator Fellows, enable the doctoral and postdoctoral researchers to acquire international experience, perspectives, and exposure. The research secondments support establishing networks for **iRTG** members and thus pave the way for future postdoctoral phases, both early and advanced.

Erica Cecchini

From / to	Institute visited	Local supervisor	Research activities performed and skills acquired during stay
11.02.24 / 16.02.24	Universitätsklinikum Freiburg	n/a	Research secondment for Spatial Transcriptomics with 10x genomics

Guillaume Flé

From / to	Institute visited	Local supervisor	Research activities performed and skills acquired during stay
22.01.24 / 26.01.24	Charité, Berlin	Ingolf Sack	Demonstration of the elastography pipeline including MR sequence, Vibro device, and brain image acquisition
19.08.24 / 23.08.24	Siemens Healthineers	Brian Dale	IDEA Sequence Programming Course

Kristina Karandasheva

From / to	Institute visited	Local supervisor	Research activities and skills acquired during stay
05.02.24 / 01.03.24	d'Aix-Marseille Université	Christophe Bernard	Training for electrophysiology

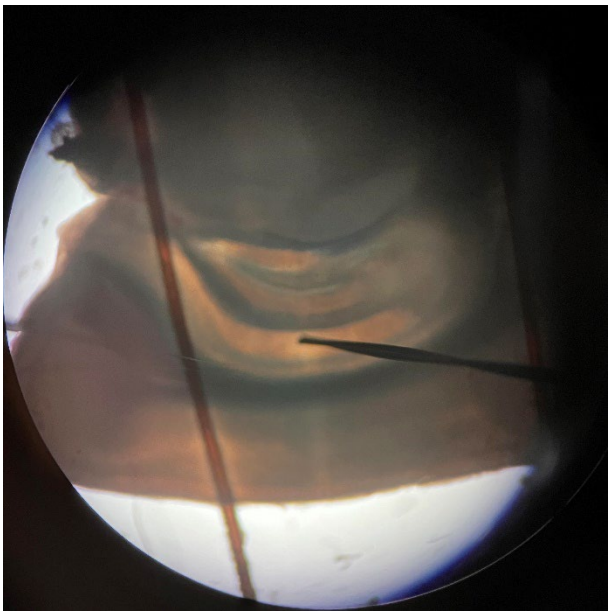


Figure 59: Microscopic view of electrode placement in hippocampal slice for field recording.

From February 5, 2024, to March 1, 2024, I conducted a research stay at d'Aix-Marseille Université in Marseille, France, at the Institut de Neuroscience des Systèmes within the PhysioNet group led by Christophe Bernard. During this time, I received comprehensive training in fundamental electrophysiology techniques, focusing on field potential recordings using murine hippocampal slices as a model system. My work involved stimulating Schaffer collaterals in the CA3 region to elicit synaptic responses in the CA3-CA1 pathway. I gained hands-on experience in precisely recording and analyzing these responses, which provided me with a solid foundation in the principles and methodologies of electrophysiological studies. This research stay significantly enhanced my technical expertise and understanding of neuroscience research methodologies, contributing to my overall development as a researcher.

*(Kristina Karandasheva, **C03**)*

Sebastian Vasquez Sepulveda

From / to	Institute visited	Local supervisor	Research activities and skills acquired during stay
10.03.24 / 20.03.24	PDN, Cambridge	Kristian Franze	Western Blotting of SLC35A2 KD samples
06.07.24 / 13.07.24	PDN, Cambridge	Kristian Franze	Learning AFM usage
03.08.24 / 26.08.24	PDN, Cambridge	Kristian Franze	AFM Measuring of *in vivo Xenopus laevis* brains
21.09.24 / 05.10.24	PDN, Cambridge	Kristian Franze	Differential labelling of dorsal and ventral RGCs.

From March 10 to October 5, 2024, I conducted several research stays at the Franze Lab, Cambridge, focusing on advanced training and experimental work in cellular and molecular neuroscience techniques.

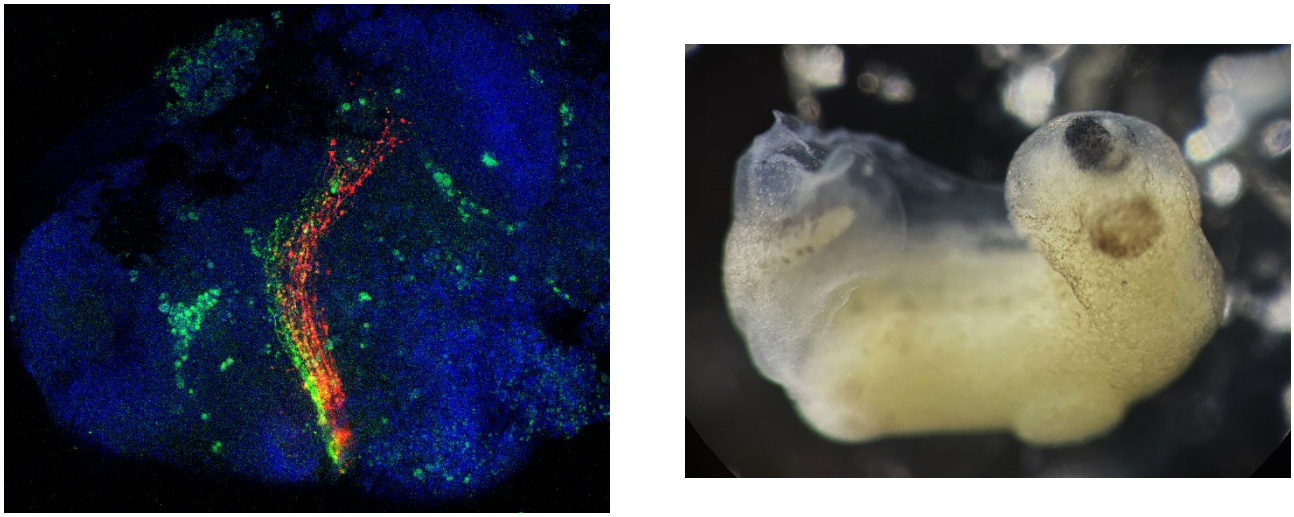


Figure 60: Left: Dual staining of retinal ganglion cells labelling dorsal (DiI-Red) and ventral (DiO-Green), on a stage 42 Xenopus laevis embryo. Right: Malformation on the injected side of SLC35A2 KD embryos, a lack of development of an eye can be observed.

During my first visit from March 10 to March 20, 2024, I trained with lab technician Katrin Mooslehner to perform Western blotting to confirm the knockdown of SLC35A2 via the injection of anti-SLC35A2.S samples. This session gave me with essential expertise in protein detection methods.

From July 6 to July 13, 2024, I underwent extensive training on atomic force microscopy (AFM) usage and data analysis under the guidance of post-docs Alex Winkel and Julia Becker. This laid the groundwork for my subsequent work on AFM-based experiments.

Between August 3 and August 26, 2024, I focused on generating stiffness maps of control and SLC35A2 knockdown tadpole brains at stage 40 using AFM. This experimental work was carried out in collaboration with Alex Winkel and Julia Becker, resulting in the successful production of stiffness maps critical for understanding the mechanical properties of brain tissues.

My final stay from September 21 to October 5, 2024, was dedicated to developing a protocol for differential labeling of dorsal and ventral retinal ganglion cells, originating from the top and bottom of the eye, respectively. Additionally, I attended Katrin Mooslehner's retirement party, which provided an opportunity to connect informally with other members of the Franze Lab.

These research stays significantly expanded my technical skills and understanding of advanced methodologies, particularly in molecular and biomechanical neuroscience. They also enriched my collaborative experience within a leading research environment.

*(Sebastián Vásquez Sepúlveda, **A05**)*

Maria Tarczewska

From / to	Institute visited	Local supervisor	Research activities and skills acquired during stay
02.04.24 / 16.04.24	Cold Spring Harbor Laboratory	n/a	Course: Cell & Developmental Biology of Xenopus: Gene Discovery & Disease
28.06.24 / 30.06.24	Centuri, Turing Centre for Living Systems	Claudio Collinet	Centuri Hackathon for quantitative biology, Participation in the project: EndoTrack: visualizing the movements of intracellular organelles in developing tissues

Figure 61: Group photo from the "Cell & Developmental Biology of Xenopus" course at Cold Spring Harbor Laboratory. (Image: @WalentekLab)

In April 2024 I attended the **"Cell & Developmental Biology of Xenopus: Gene Discovery & Disease"** course at Cold Spring Harbor Laboratory. During the course, I gained both theoretical and hands-on experience working with Xenopus as a model organism. I focused on methods particularly relevant to my work on spinal cord injuries, as well as a broad range of other techniques applicable to Xenopus.

One of the important skills I acquired was learning CRISPR gene editing techniques and microinjections, which I applied to the piezo1 gene. I also explored cell transplantation methods and advanced imaging techniques, such as two-photon microscopy and optical coherence tomography. This course provided a great opportunity to try out methods that I don't typically use in my lab but that could be beneficial for my research.

The curriculum was comprehensive, covering various aspects of Xenopus biology, including maternal control of development, signaling pathways, and organ-specific development such as kidney and limb formation.

One of the most valuable parts of the course was the opportunity to network with other researchers and experts in the field of Xenopus biology. Additionally, we had the chance to visit New York City during our time there. Overall, this course has significantly enriched my knowledge and skills in developmental biology and provided me with hands-on Xenopus skills.

*(Maria Tarczewska, **B02**)*

2.2 FURTHER EBM ACTIVITIES

2.2.1 EBM VIRTUAL BREAKFAST CLUB

The digital format "EBM Virtual Breakfast Club" typically takes place on Monday mornings, except on days when an EBM Lunch is scheduled. All EBM members participate via Zoom in an informal setting. Principal investigators take turns presenting the latest scientific insights and open questions from their projects, sparking collective discussions. These virtual meetings serve as a relaxed forum for informal exchanges on organizational, administrative, and current EBM-related topics.

In 2024, a total of 30 EBM Virtual Breakfasts were held.

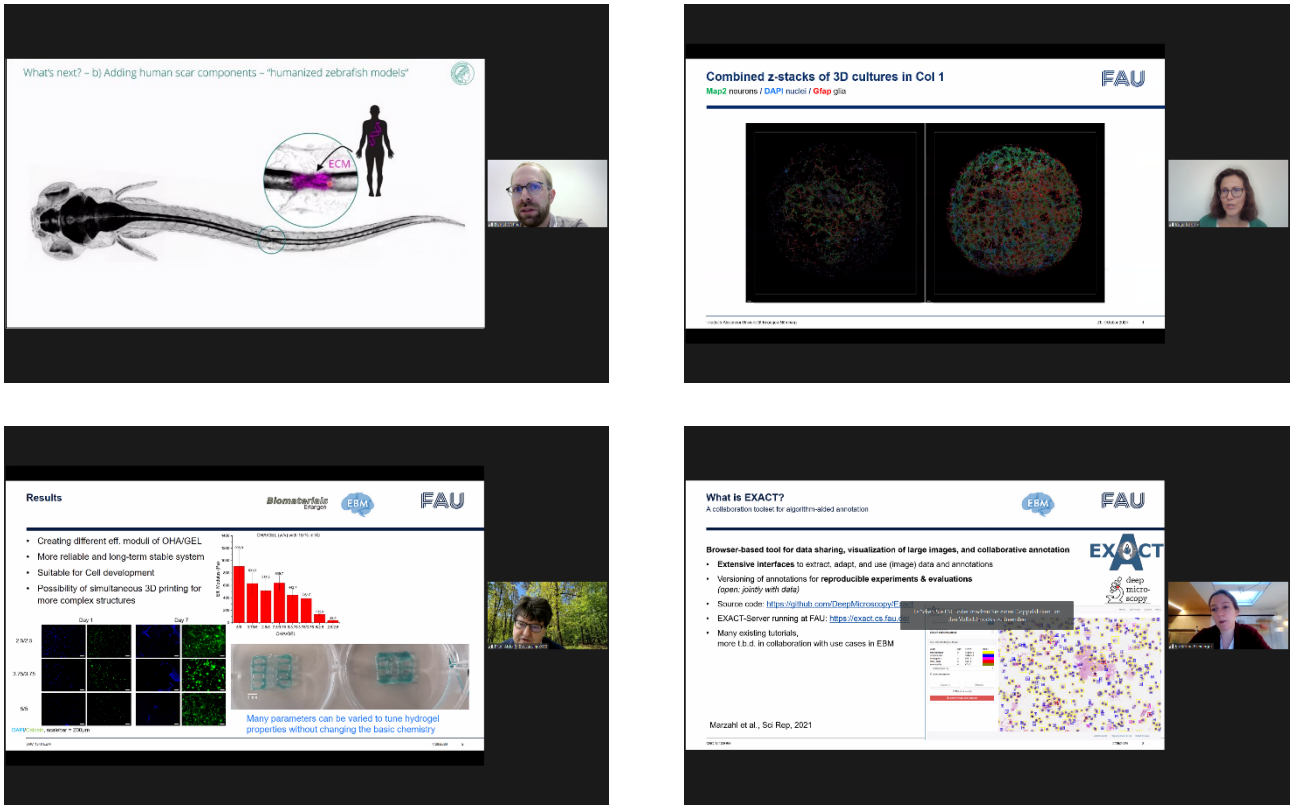


Figure 62: EBM Virtual Breakfast Club: Daniel Wehner (top left), Katja Kobow (top right), Aldo Boccaccini (bottom left) and Katharina Breininger (bottom right).

2.2.2 EBM LUNCH

On the first Monday of each month, all EBM members have the opportunity to gather for lunch, either at a local restaurant or at the FAU campus for the "EBM Synergy Luncheon Meetings," where they can enjoy pizza. These lunches offer a relaxed setting for informal discussions on organizational, administrative, and current EBM-related topics, as well as an opportunity for social networking.

Figure 63: EBM members at their monthly joint lunch. (Images: A. Dakkouri-Baldauf)

2.2.3 EBM VIRTUAL BRAIN TALK SERIES

The EBM Virtual Brain Talk Series is a quarterly virtual, open-access event dedicated to exploring the latest advancements in mechanics-based approaches. Its primary focus is on enhancing our understanding of the functions of the central nervous system, laying the groundwork for future breakthroughs in the diagnosis and treatment of neurological disorders.

The approximately 45-minute presentations, distinguished by their high-quality content, are held by EBM members and invited scholars. These sessions are designed to foster a continuous exchange of results and ideas within the worldwide scientific community.

Despite being in its early stages, the event series has already proven to be a significant success. A substantial number of international participants, surpassing 50 in some instances, enthusiastically followed the engaging presentations by renowned experts and actively engaged in lively discussions.

Table 7: EBM Virtual Brain Talks

	Date	Lecturer	Title
01	28.10.24	Stephanie Willerth (Mechanical Engineering, University of Victoria, BC, Canada)	*3D Printing complex neural tissues*
02	09.12.24	Ingolf Sack (MR-Elastographie, Charité – Universitätsmedizin Berlin, Germany)	*The four-network model: How extracellular matrix, cellular networks, and vasculature shape the in vivo mechanical properties of the brain*

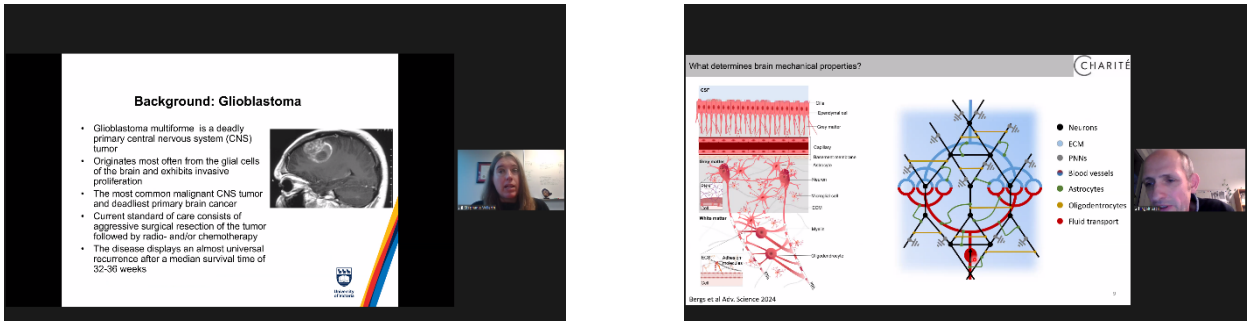


Figure 64: EBM Virtual Brain Talk Series: Stephanie Willerth (left), Ingolf Sack (right).

2.2.4 EBM SEMINAR TALKS

For the EBM Seminar Talks, internationally renowned scientists were invited to give in-depth presentations on EBM-relevant research topics and then to actively engage EBM researchers in discussions and question-and-answer sessions.

Table 8: EBM Seminar Talks

	Date	Lecturer	Title
01	19.04.24	Kevin Linka (Chair and Institute of Applied Mechanics, RWTH Aachen University, Germany)	*Data-driven material modeling for soft biological tissues*
02	19.04.24	Chii Jou Chan (Mechanobiology Institute, National University of Singapore, Department of Biological Sciences, National University of Singapore, Singapore)	*Mechano-hydraulic control of mammalian ovarian follicle development*

Figure 65: Kevin Linka (left, hosted by Silvia Budday) and Chii Jou Chan (right, hosted by Kristian Franze) during their EBM Seminar presentations. (Images: N. Tueni (left), J. Bachir Salvador (right))

2.3 VISITING RESEARCHER PROGRAM

Table 9: Visiting researchers

From / to	Visiting researcher	Topic
19.04.24	**Dr.-Ing. Kevin Linka**, Chair and Institute of Applied Mechanics, RWTH Aachen University, Germany	Invited lecture within the EBM Seminar Talk series: “Data-driven material modeling for soft biological tissues”
19.04.24	**Prof. Chii Jou Chan**, Mechanobiology Institute, National University of Singapore, Department of Biological Sciences, National University of Singapore, Singapore	Invited lecture within the EBM Seminar Talk series: “Mechano-hydraulic control of mammalian ovarian follicle development”
28.10.24	**Prof. Dr. Stephanie Willerth**, Mechanical Engineering, University of Victoria, BC, Canada	Invited lecture within the Virtual Brain Talk Series: “3D Printing complex neural tissues”

3 EQUAL OPPORTUNITY MEASURES

Promoting equal opportunities for both women and men, along with advancing the careers of doctoral and postdoctoral researchers, is a key objective of EBM. This involves supporting early-career female scientists in strategically planning and advancing their careers, as well as facilitating the balance between research commitments and family life.

EBM's commitment to fostering equal opportunities, career advancement, and the holistic development of emerging scientists was underscored by its comprehensive measures under the **EBMequality** concept.

3.1 WORKSHOPS, SEMINARS

The F³G network (Research Associations of Friedrich-Alexander-Universität Erlangen-Nürnberg for the promotion of equality) offers lectures and seminars on women's advancement, gender sensitization, etc., in addition to a variety of other gender equality measures, in which members of the affiliated research associations can participate. Consequently, some EBM members have taken advantage of these training opportunities and participated in the workshops already listed in Table 4.

Figure 66: Deborah Bennett presenting the "Women in Academia: The Essentials of Scientific Writing" seminar to EBM doctoral researchers. (Image: S. Vásquez-Sepúlveda)

Additionally, on December 10 and 11, the EBM coordination organized a workshop titled "Women in Academia: The Essentials of Scientific Writing." This course addressed the unique challenges and opportunities for women in academia, combining essential scientific writing skills with strategies for overcoming gender-specific barriers. Led by lecturer Deborah Bennett, the seminar provided an in-depth exploration of the key principles and strategies for crafting compelling scientific texts, with a particular focus on the challenges women face in academic settings.

3.2 FURTHER MEASURES

3.2.1 EBM FAMILY

Childcare Support

- **KidsBox Acquisition**: Procuring a KidsBox to provide childcare services for the children of EBM members during EBM events.

- **KidsBags Acquisition (1 x Toddler, 1 x School-Age Child)**: Providing mobile toy bags for children to use during EBM events.
- **EBM Update Meeting and EBM Retreat Childcare Expenses**: Covering childcare expenses during the EBM retreat to support participating members.
- **Conference Travel Childcare Coverage**: Providing financial support for childcare expenses incurred by EBM members during conference travel.
- **Financial Support for Holiday Childcare**: Offering financial assistance for vacation care services dedicated to the children of EBM members.
- **Daycare Center Contingent Option**: Securing contingent spots for EBM members at the "Pfauennest II" daycare center.

Support for FAU Childcare Programs

- **F³G Project Funding**: Providing financial support for specific projects under the F³G initiative within FAU holiday childcare programs.
- **Contribution to F³G Coordination Costs**: Supporting the coordination costs associated with F³G initiatives.
- **Pedagogic Enhancement**: Improving the pedagogic infrastructure at FAU daycare facilities to enhance the care provided to children.

Gender Equality and Career Development

- **Organization of Soft Skills Course**: *'Women in Science: The Basics of Scientific Writing'* exclusively for EBM (post)doctoral researchers.
- **Financial Support for 'Women in Science - 3rd Erlanger Symposium'**: Providing funding to support this event.
- **Organization of a Lecture and Plenary Discussion at the 2nd EBM Retreat**: *"If we know better, we can do better"* – addressing generational differences and expectations in German academia.

Figure 67: Young explorers and doctoral researchers in action: The new EBM KidsBox in use at the new location in Fürth. (Images: S. Budday)

3.2.2 EBM ENCOURAGE

CJT (Christoph-Jacob-Treu-Gymnasium) Impulstag – student visit

Figure 68: The students receive an introduction to brain anatomy and function. (Image: S. Rampp)

Building on last year's great success, in October 2024, PD Dr. med. Stefan Rampp, Dr. rer. nat. Nadia Müller-Voggel and cand. med. Emilie Müller from the Department of Neurosurgery and the Department of Neuroradiology once again welcomed 9th-grade students from the Christoph-Jacob-Treu-Gymnasium (Lauf an der Pegnitz). During their visit, they were given a comprehensive introduction to brain anatomy and function, as well as an in-depth look at how these can be affected by brain disorders. The students engaged in lively discussions on brain anatomy and function, brain disorders and how to diagnose and treat them.

As part of the visit, the students examined MR images, identifying various types of lesions, ranging from obvious tumors to subtle focal cortical dysplasia. Surgical approaches were then briefly discussed, including awake surgery.

In the second part of the program, the students visited the magnetoencephalography (MEG) laboratory of the Department of Neurosurgery. Here, patients with epilepsy are examined with EEG and MEG to record epileptic activity. The results are then used to localize the epileptic focus to tailor epilepsy surgery to the individual patient. The students observed how the MEG system operates and even experienced a live demonstration. Volunteers from the group were scanned, allowing their classmates to watch real-time visualizations of brain activity.

The visit provided the students with a unique hands-on experience and a deeper understanding of neuroscience and clinical neurology.

*(Stefan Rampp, **A02**)*

4 SELECTED HIGHLIGHTS

4.1 INES 2024: INTERNATIONAL SUMMER SCHOOL FOR NEUROPATHOLOGY AND EPILEPSY SURGERY

From September 19 to 22, 2024, the 14th International Summer School for Neuropathology and Epilepsy Surgery (INES 2024) took place in Erlangen. This prestigious event provided an excellent platform for advancing knowledge and practical skills in the fields of neuropathology and epilepsy surgery.

EBM was proud to serve as an official partner of INES 2024. The partnership reserved exclusive spots for EBM doctoral researchers and master's students. These participants were given a unique opportunity to learn from leading international experts.

EBM's Principal Investigator, Ingmar Blümcke, played a central role as co-organizer and one of the two course directors. Additionally, EBM PIs Katja Kobow and Stefan Rampp contributed as course faculty, further strengthening EBM's presence and involvement in the program.

INES 2024 offered a comprehensive curriculum featuring lectures and workshops on cutting-edge topics in the diagnosis and treatment of focal epilepsies. A standout feature of the summer school was the hands-on histopathological training in small groups, where participants examined and discussed selected cases under the microscope. This practical component provided a unique learning experience, bridging theoretical knowledge with clinical application.

The event also fostered networking through a group dinner, which allowed participants to engage with peers and experts in an informal setting.

For EBM participants, INES 2024 was recognized as a harmonization workshop within the **iRTG** qualification program.

4.2 AWARDS AND DISTINCTIONS

(in alphabetical order of the award winners)

4.2.1 ALDO R. BOCCACCINI INDUCTED INTO THE 2024 CLASS OF THE AIMBE COLLEGE OF FELLOWS

We are pleased to announce the induction of Prof. Aldo R. Boccaccini, our esteemed EBM PI of subproject **X03**, into the College of Fellows of the American Institute for Medical and Biological Engineering (AIMBE). AIMBE is the authoritative voice and advocate for the value of medical and biological engineering to society. Election to the AIMBE College of Fellows is among the highest professional distinctions accorded to medical and biological engineers. College membership honors those who have made outstanding contributions to „engineering and medicine research, practice, or education" and to „the pioneering of new and developing fields of technology, making major advancements in traditional fields of medical and biological engineering or developing/implementing innovative approaches to bioengineering education."

Figure 69: AIMBE, Annual conference on March 25, 2024 (Image: ©2024 Lloyd Wolf all rights reserved 703-231-6452)

Prof. Boccaccini was nominated, reviewed, and elected by peers and members of the College of Fellows "for his seminal contributions in designing bioactive materials towards regenerative medicine, drug delivery, and 3D bioprinting applications." The induction ceremony was held during the AIMBE Annual Event in Arlington, VA, USA, on March 25, 2024.

Aldo Boccaccini said: „I am very proud of this recognition, which highlights our work on bioactive materials carried out over the years and its impact on biomedical applications. To be a member of the 2024 class of the College of Fellows of AIMBE, the only one based in Germany, means to be in a distinguished group of professionals who have made outstanding contributions to engineering and medicine research, practice, or education. I consider this to be a recognition also to all former and current members of my research team".

Congratulations, Aldo, on this well-deserved honor!

Figure 70: Prof. Dr. Aldo R. Boccaccini. (Image: Euromat2023)

4.2.2 ALDO R. BOCCACCINI: NEW FEMS PRESIDENT

In January 2024, Prof. Aldo R. Boccaccini (**X03** project) started his two-year tenure as president of the Federation of European Materials Societies (FEMS). He has been a member of the Board of FEMS since 2016, representing the German Materials Society (DGM). Speaking of his appointment, Prof. Boccaccini said "I am honored to have been elected President of FEMS and I am looking forward to working together with the Management Team and FEMS Board to enhance FEMS impact and visibility in the materials science community in Europe and worldwide. Materials science and technology are the keys to tackle today's important challenges in all areas; from energy, environment, and transport, to healthcare, and security among others. I hope to contribute to expand FEMS activities so that materials are placed as essential contributors to improve technologies for a better future".

Congratulations, Aldo, on this well-earned recognition!

4.2.3 LEOPOLDINA GREVE PRIZE TO JOCHEN GUCK

Professor Dr. Jochen Guck from the Max Planck Institute for the Science of Light has been awarded the 2024 Greve Prize by the German National Academy of Sciences Leopoldina. The prize honors his groundbreaking work on the movement of tumor cells and metastasis. Along with Professors Dr. Josef Käs and Dr. Bahriye Aktas from Leipzig, Jochen Guck demonstrated how cancer cells transition from a stiff to a softer, more fluid state, allowing them to move through dense tissue and form metastases. This discovery has led to new insights into predicting and preventing metastasis, particularly in breast cancer.

Figure 71 Prof. Jochen Guck got awarded Leopoldina's Greve prize. (© Markus Scholz, Leopoldina)

Their research has identified markers that can better predict the metastatic potential of tumors, paving the way for more personalized cancer treatments. Guck's development of the real-time deformability cytometry (RT-DC) method, which measures cell deformability, plays a key role in finding therapies that can prevent metastasis.

The Greve Prize recognizes the interdisciplinary nature of their research, which has the potential to revolutionize cancer treatment.

Warmest congratulations to Jochen!

4.2.4 SECOND PLACE ITEC STUDENT AWARDS FOR JAKOB JORDAN

Figure 72: Jakob Jordan receives the second-place award in the ITEC Student Awards. (Image source: https://www.elasticityconference.com/)

Jakob Jordan's presentation titled "Optical Multifrequency Time Harmonic Elastography (OMTHE) for High-Resolution, Multiscale Stiffness Mapping" earned him second place in the ITEC Student Awards at the International Tissue Elasticity Conference. His talk highlighted cutting-edge advancements in elastography, offering innovative approaches to map stiffness with exceptional resolution across multiple scales. This recognition underscores the impact of his research in the field of tissue elasticity.

Congratulations to Jakob for this well-deserved achievement!

4.2.5 ANTON WALDEYER PRIZE AWARDED TO FRIEDRICH PAULSEN

Professor Dr. Friedrich Paulsen, Director of the Institute of Functional and Clinical Anatomy at FAU Erlangen, was honored with the prestigious Anton Waldeyer Prize by the Anatomische Gesellschaft and the Anton Waldeyer Foundation. This biennial award recognizes outstanding scientific achievements that underscore the importance of anatomy in medical practice and its close connection to clinical applications.

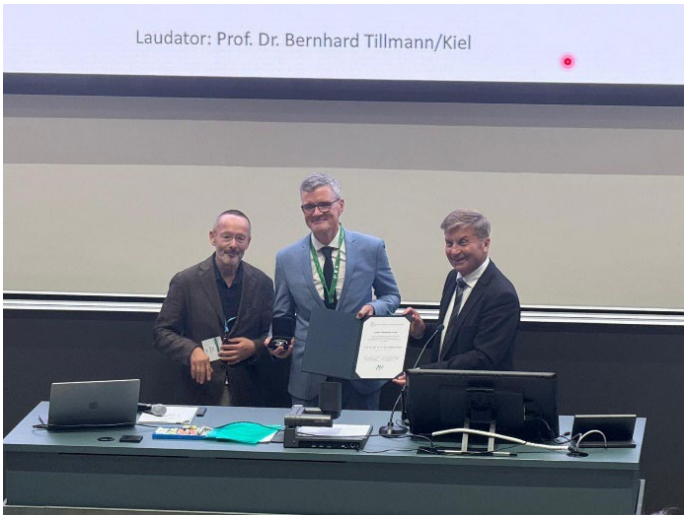


Figure 73: Prof. Dr. med. Dr. h.c. Friedrich Paulsen (center). (Image: L. Bräuer)

The prize highlights Professor Paulsen's significant contributions to the field and his dedication to advancing the integration of anatomical research into clinical contexts. In his acceptance, he expressed gratitude to his colleagues, the nomination committee, and the board of the Anatomische Gesellschaft, led by its president, Prof. Dr. Stefan Britsch (Ulm). He also acknowledged the invaluable support of his team at FAU Erlangen, emphasizing that such an achievement would not have been possible without their collective efforts.

Special thanks were extended to Emeritus Prof. Dr. Bernhard Tillmann (CAU Kiel), who delivered the laudatory speech, highlighting Professor Paulsen's remarkable career and scientific accomplishments.

The award is a testament to Professor Paulsen's leadership in the field of anatomy and his commitment to fostering collaboration between research and clinical practice.!

Congratulations to Friedrich on this great honor!

4.2.6 STUDENT POSTER AWARD TO NINA REITER AT WCCM2024

Congratulations to Nina Reiter for winning the Student Poster Competition in the category 'Computational Biomedical and Biological Systems' at the WCCM2024 conference in Vancouver, Canada, in July 2024! Nina's research on 'Directional Mechanics of the Human Corpus Callosum and Lower Brainstem' has earned her this well-deserved recognition.

Well done, Nina, for your extraordinary work!

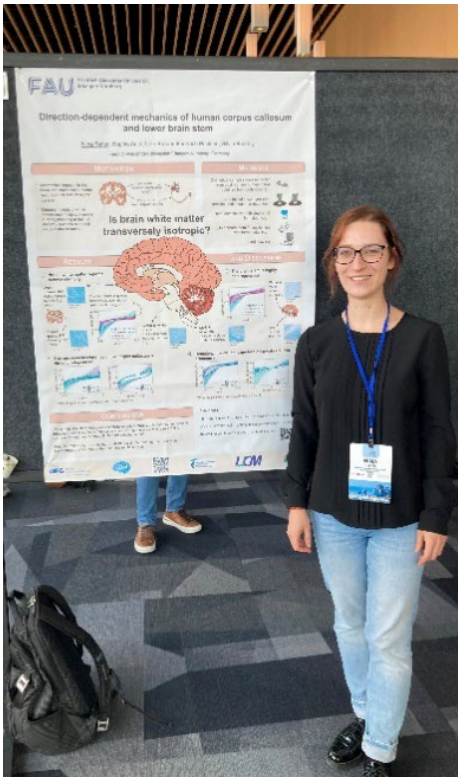


Figure 74: Nina Reiter presenting her award-winning poster. (Image: private)

4.2.7 DANIEL WEHNER RECEIVES THE HILDE MANGOLD SCIENCE PRIZE

We are pleased to announce that our EBM PI Daniel Wehner, research group leader at the Max Planck Institute for the Science of Light, has been awarded the Young Research Award from the German Society of Developmental Biology. The prize recognizes outstanding research and activity in the field of developmental biology and is awarded every two years to early career-stage researchers. Based on his findings in the field of neuroregeneration, Wehner has made a significant contribution to a better understanding of scar formation and regeneration after injuries to the central nervous system.

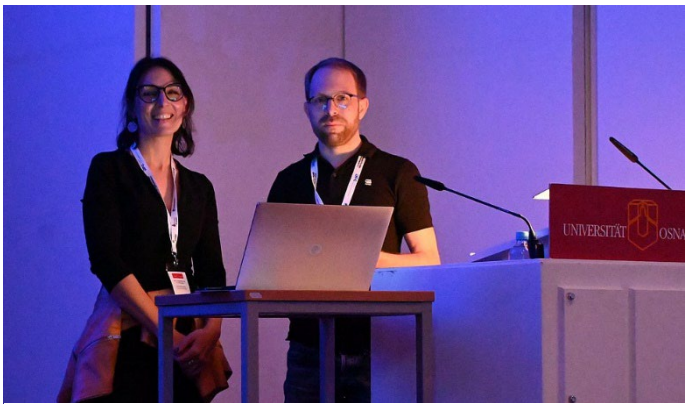


Figure 75: Prof Kerstin Bartscherer (University of Osnabrück) - President of the GfE (Society for Developmental Biology) and Dr. Daniel Wehner (Research Group Leader, Max-Planck-Zentrum für Physik und Medizin. (©Dr. Thomas Thumberger)

Spinal cord injuries can lead to irreparable and permanent loss of function in humans as the injured nerve fibers do not regrow. However, some animal species such as the zebrafish can regenerate severed nerve pathways and restore motor functions. Why this is the case and which biochemical and biomechanical factors play a role in the nervous system's wound healing process is the research topic of Daniel Wehner's team. The biotechnologist has shown that although the different species form scar-like wound tissue after injury, there are crucial differences in its biochemical composition and mechanical properties. The wound tissue in zebrafish is not only permissive to regrowing nerve fibers but also necessary for the regeneration of nerve fibers.

Furthermore, Daniel Wehner was able to identify specific proteins of the small leucine-rich proteoglycans (SLRPs) family as an important factor limiting nerve regeneration in mammals. However, the SLRPs are barely enriched in the wound tissue of zebrafish. The scientist combines methods of genetics with approaches in physics to decipher the biomechanical and biochemical role of the extracellular space in the regenerative context.

The award ceremony took place at the 25th Meeting of the German Society for Developmental Biology together with the Dutch Society for Developmental Biology (DSBD) in Osnabrück. In addition to the Hilde Mangold Science Prize, other honors took place including the best dissertation and honoring the life's work of the renowned Max Planck scientist and Nobel Prize winner Christiane Nüsslein-Vollhard with the Klaus Sander Prize.

Source: Max Planck Institute for the Science of Light: https://mpl.mpg.de/news-events/news-from-the-institute/news-detail/news-detail/news-detail?tx_news_pi1%5Baction%5D=detail&tx_news_pi1%5Bcontroller%5D=News&tx_news_pi1%5Bnews%5D=1263&cHash=493a01e4b5882b4da820c0c9f541d434

The entire EBM family congratulates Daniel on his impressive achievement!

4.2.8 DANIEL WEHNER RECEIVES THE ISRB RISING STAR AWARD 2024

Figure 76: Laureate Dr. Daniel Wehner (right) together with Dr. Mekayla Storer. (©Gilbert Weidinger)

On October 10, 2024, Daniel Wehner was honored with the prestigious Rising Star Award by the International Society for Regenerative Biology (ISRB). This award recognizes emerging scientists who are pioneering new approaches in the field of regenerative biology and whose research has made a lasting impact.

Dr. Wehner, a group leader at the Max Planck Institute for the Science of Light and the Max Planck Center for Physics and Medicine in Erlangen, was awarded for his groundbreaking work on fibroblasts and the extracellular matrix (ECM) in spinal cord regeneration in zebrafish. His research provides valuable insights into the biochemical composition and mechanical properties of ECM that support regeneration. The ultimate goal of his studies is to discover how nerve fiber (axon) regeneration in the central nervous system (CNS) can be enabled in humans.

Dr. Wehner and his team are investigating why some vertebrate species are able to regenerate their spinal cords after injury, while in humans and other mammals, such injuries often lead to permanent dysfunctions, such as paralysis.

In mammals, including humans, the body responds to injury by forming scar tissue produced by specialized cells called fibroblasts. This scar tissue, made up of ECM deposits, presents a significant barrier to nerve regeneration due to its unfavorable biochemical and mechanical properties. However, zebrafish can regenerate axons across long distances after a spinal cord injury, leading to near-complete restoration of movement. Using advanced optical imaging technologies, molecular biology techniques, and innovative humanized fish models, Dr. Wehner's research aims to uncover the factors that influence the differences in scar formation across species.

Source: Max Planck Institute for the Science of Light: https://mpl.mpg.de/de/news-events/neues-aus-dem-institut/news-detail/?tx_news_pi1%5Baction%5D=detail&tx_news_pi1%5Bcontroller%5D=News&tx_news_pi1%5Bnews%5D=1386&cHash=a4f8bc4e187bc0840e20f1a5382bcb2f

Congratulations to Daniel on this outstanding achievement!

4.2.9 FRAUKE WILM WINS 1ST PLACE AT MICCAI ADENOCARCINOMA SEGMENTATION CHALLENGE

Figure 77: Frauke Wilm (left) at the award ceremony at MICCAI. (Image: K. Breininger)

Frauke Wilm achieved outstanding success at the Cross-Organ and Cross-Scanner Adenocarcinoma Segmentation Challenge, held as a satellite event of the International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI). On October 6, 2024, Frauke secured 1st place in both Track 1 and Track 2 of the challenge. In Track 1, she demonstrated the ability of machine learning algorithms to generalize across various organs in adenocarcinoma segmentation tasks. In Track 2, Frauke's work showcased the effectiveness of machine learning in segmenting adenocarcinoma across diverse whole slide image scanners. The developed approaches will also aid the robust analysis of image data across different domains within EBM.

Congratulations, Frauke, on these remarkable achievements!

4.3 SOCIAL ACTIVITIES

PARTY – Peer Assembly for Recreational Time after Yuletide

After an intense and challenging first year of EBM, it was time to celebrate our achievements. On January 12, the PARTY (Peer Assembly for Recreational Time after Yuletide) took place, organized by the doctoral researchers and staff from the Franze Lab.

The event provided a welcome opportunity to kick off the new year in a relaxed and cheerful atmosphere. With an international buffet featuring homemade dishes contributed by the participants, the evening offered a culinary delight. Accompanied by music, engaging conversations, and a vibrant atmosphere, the PARTY was a great success.

It not only marked a fitting end to the previous year but also served as an important moment to strengthen team spirit and recharge for the challenges ahead.

Figure 78: Impressions from the PARTY: Enjoying food, music, and great conversations in a relaxed atmosphere. (Images: A. Dakkouri-Baldauf, L. Zaburdaeva (bottom left))

5 OUTREACH ACTIVITIES

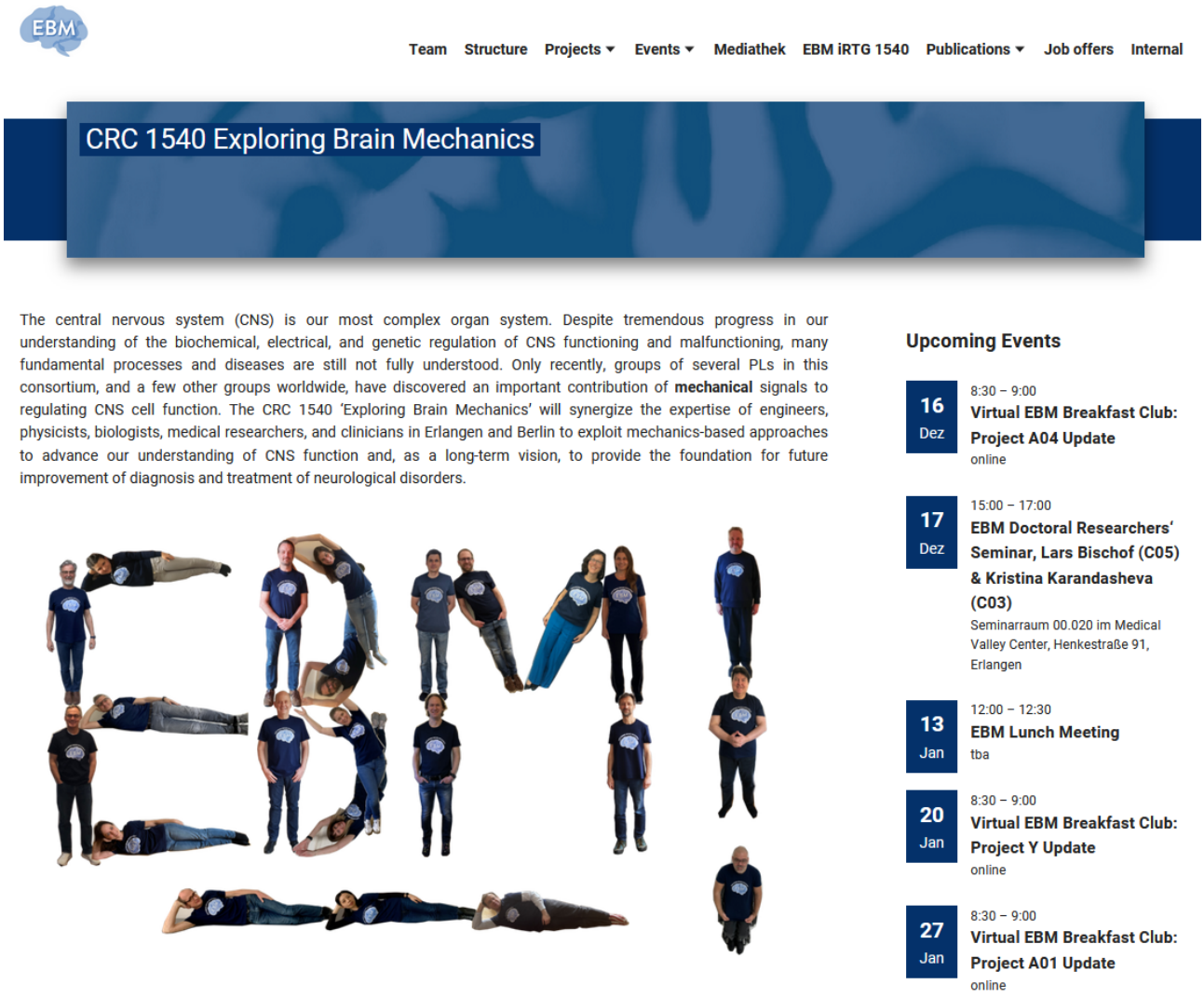
The primary objective of **EBMoutreach** concept is to achieve international, national, and regional visibility. This is intended to be accomplished through disseminating results and activities, thereby engaging both the broader public (**EBM2public**) and the worldwide scientific community (**EBM2peers**).

5.1 EBM2PUBLIC

The **EBM2public** initiative encompasses various channels to enhance public engagement and outreach:

5.1.1 EBM'S WEBPAGE

EBM maintains an informative webpage at www.ebm.fau.de:



5.1.2 EBM SOCIAL MEDIA PRESENCE

- EBM actively manages its social media channels on platforms such as X, Bluesky (which will replace X in the future), LinkedIn, and Instagram.
- The social media team, comprised of EBM doctoral researchers, the co-spokesperson, and the scientific coordinator, regularly updates these platforms.
- Updates on EBM activities, introductions of new publications, achievements of EBM members, and the "#pictureoftheweek" feature were consistently shared.
- Active collaboration with @uni_fau and @itm.fau for the Science and Organ event.

5.1.3 "DAS GEHIRN – MUSIKALISCHE ERKUNDUNGEN"

On September 21, 2024, an extraordinary interdisciplinary event took place at Matthäuskirche in Erlangen. Titled „Das Gehirn – Musikalische Erkundungen," the event merged science and organ music into an impressive audiovisual experience. Organized by the Collaborative Research Center (SFB) 1540 "Exploring Brain Mechanics" (EBM) in collaboration with church music director Susanne Hartwich-Düfel and the media studios of the Institute for Theater and Media Studies (ITM) at Friedrich-Alexander University Erlangen-Nuremberg (FAU), the event guides the audience on a fascinating journey into the world of the brain. This concert, part of the established series "Wissenschaft und Orgel" (Science and Organ), uniquely combined music with scientific presentations and impulse lectures.

Catch a glimpse of the evening by watching the video here: https://go.fau.de/1bdfi

Or simply scan the QR code: (Video/editing by Alexander Becker and Mayla Wind).

Figure 79: Impressions of the event evening. (Image: M.Á. Moreno-Mateos)

Fusion of Science and Music

The evening began with scientific impulse lectures by Professor Dr. Paul Steinmann, spokesperson of EBM, who guided the audience into the complex world of brain anatomy, brain mechanics, and neural networks. Paul Steinmann succeeded in making even complicated scientific topics, such as the folding of the brain and neuronal signal transmission, understandable and fascinating.

> "Just unbelievable experience: exploring mechanics of brain with beautiful visualization, organ music, and accessible explanations by Prof. Paul Steinmann."

> “Imagine Bach, Philip Glass, and stunning brain visuals all coming together in perfect harmony. It was a beautiful reminder of how art and science can connect in unexpected and inspiring ways (and places).”

These lectures were accompanied by impressive visualizations developed by the ITM media studios at FAU. The large-scale projections. displayed on a screen in the altar area and on the walls of the church, ranging from photorealistic animations to live EEG measurements, which visualized the brain activity of a proband visible during Arvo Pärt’s piece “Mein Weg hat Gipfel und Wellentäler”. This harmonious combination of images, sound, and science allowed the audience to immerse themselves deeply in the subject matter and created an emotional connection to the scientific content.

Music as a Reflection of Brain Processes

Figure 80: Paul Steinmann during his impulse lecture on brain anatomy. (Image: M.Á. Moreno-Mateos)

Susanne Hartwich-Düfel provided the musical backdrop for the evening with a program carefully selected by Paul Steinmann that was perfectly aligned with the topics of brain research. The audience was led through various musical moods with works by Johann Sebastian Bach, Arvo Pärt, Philip Glass, and Sofia Gubaidulina, which reflected the complexity of the brain.

Particularly impressive was Bach's "Passacaglia in C Minor" (BWV 582), whose intricate structures are reminiscent of the convolutions and complexities of the brain. Gubaidulina's "Hell and Dark" seemed like a musical image of the nerve pathways, which were colorfully visualized in the video installations. Pärt's "Annum per Annum" subtly musically portrayed the development and increasing complexity of the brain. The expanding sound registers of the organ created an atmosphere of wonder, inviting the audience to reflect on the evolution of human thought and the ever-growing capabilities of the brain. Glass's "Dance No. 4," which rounded off the program, dynamically connected the interdisciplinary topics of the research conducted by the SFB "Exploring Brain Mechanics" (EBM) and brought the diversity of brain mechanics to life.

> “Last night was pure magic! I had the pleasure of diving into the world of brain research and organ music at the „Science and Organ“ event …”

An Experience for the Senses

The interplay of music, science, and visual representations was more than just a concert or a lecture – it was a multisensory experience. A live camera feed of the organist playing was projected onto the barrel ceiling of the church, allowing the audience to visually engage with the artist’s performance. The fusion of the arts and sciences blurred the boundaries between both disciplines and created a completely new perspective on the brain and its processes. Visitors experienced firsthand how music not only evokes emotions but also has a direct influence on our brain activity.

> "Ich kann nur sagen g r a n d i o s ! Herzlichen Dank für einen unvergesslichen Abend!"

The room of the Matthäuskirche, with its impressive organ and simple, neutral interior design, provided the ideal setting to unite science and art in this way.

Figure 81: Impressions of the event evening. (Image: M.Á. Moreno-Mateos)

> "Das Event gestern hat meine Erwartungen übertroffen - richtig klasse gemacht!"

Figure 82: Impressions of the event evening. (Image: V. Zaburdaev)

A Resounding Success

The event "Das Gehirn – Musikalische Erkundungen" thrilled the audience from beginning to end, receiving prolonged and enthusiastic applause. Both the scientific content and the musical performances offered the visitors profound insights into the function of the brain and its significance for our lives. Following the event, guests had the opportunity to engage in conversations with experts from various research areas of EBM during a reception. They could ask questions and explore the fascinating aspects of brain research through the exhibited 3D models of the human brain

Das Gehirn und die Klassik

KONZERT In der Erlanger Matthäuskirche wurden zwei „Elfenbeintürme" verschmolzen.

VON CORA UITTING

ERLANGEN – Wenn man zwei (vermeintlichel) Elfenbeintürme wie die Bio-Mechanik und die klassische Musik nah genug aneinander rückt, dann kann es passieren, dass sich Wendeltreppen wie eine Helix umeinander schlingen und die Menschen auf den Treppen die Themen der Türme fast als Einheit erleben. So geschehen in der voll besetzten Kirche Sankt Matthäus, wo die Kirchenmusikdirektorin, Kantorin und Kulturpreisträgerin Susanne Hartwich-Düfel zusammen mit dem Leiter des Sonderforschungsbereichs „Exploring Brain Mechanics" (EBM) Professor Dr. Paul Steinmann zu „Musikalischen Erkundungen" im Bereich der Hirnforschung eingeladen hatte.

Zunächst beeindruckt der hochprofessionelle Einsatz aktuellster Präsentationstechnik, der für die Visualisierung der unterschiedlichen Aspekte des Gehirns vom Medienstudio des Instituts für Theater- und Medienwissenschaften der FAU bereitgestellt wurde. Eine riesige zentrale Leinwand, Altarraum und Orgel komplett verdeckend, und sechs Video-Animationen, oft fotorealistisch, die gleichzeitig an die Kirchenwände projiziert wurden. Eine Kamera-Aufnahme der spielenden Organistin wurde an das Tonnendach der Kirche übertragen. Dazu kam ein Tablet neben dem Orgelmanual, das die Musikerin informierte, welche Animationen gerade gezeigt wurden.

Konzentriert verfolgten die vielen Zuhörer die Impulsvorträge von Prof. Steinmann, ließen sich hinführen zu überraschenden Zusammenhängen aus dem Bereich der Hirnforschung, staunten über die Wichtigkeit der korrekten Faltung des Gehirns, die schon im frühen Embryonalstadium einsetzt, über Gehirnanatomie und Gewebestrukturen, Nervenbahnen und Hirnströme, die im Live-EEG eines Rodin'schen „Denker"-Probanden zu Arvo Pärts „Mein Weg hat Gipfel und Wellentäler" gemessen und auf die zentrale Leinwand übertragen wurden.

Angesichts der Multivision aus Erkenntnis, Hören und Sehen versinkt der Rest der Welt. Die Sinne sind derart aktiviert, dass man Susanne Hartwich-Düfel zu ihrer Entscheidung, die Forschung mit Minimal Music zu illustrieren, nur gratulieren kann. Philip Glass' „Satyagraha" ist nur scheinbar „minimal", denn unter der einfachen, sich endlos wiederholenden Melodie ändert sich der Bassrhythmus permanent. Die zunehmende Komplexität der Hirnfalten findet ihr Pendant in der unbemerkt anwachsenden Zahl der Orgelregister bei Arvo Pärts „Annum per annum". Genüsslich ent-faltet Susanne Hartwich-Düfel die unbegrenzten Klangmöglichkeiten der Orgel, lässt sie entfernt klingen, lässt sie lärmen, entlockt ihr Naturklänge wie Vogelstimmen.

In der Erlanger Kirche Sankt Matthäus finden regelmäßig spannende Konzerte statt. Beispielsweise die „Musikalischen Erkundungen", die unvereinbar Scheinendes verschmelzen. Foto: Harald Sippel

Irgendwann weiß man nicht mehr, was mehr beeindruckt: Die Vorträge von Professor Paul Steinmann über 90 Milliarden Neuronen und 900 Milliarden Gliazellen im menschlichen Gehirn oder die unendlichen Verschlingungen in Johann Sebastian Bachs hochvirtuoser „Passacaglia" c-Moll (BWV 582).

Paul Steinmann wählt ein Niveau, das die Besucher fordert, dabei aber stets verständlich bleibt. Wie die Organistin, die mit „Hell und dunkel" der russischen Komponistin Sofia Gubaidulina die Visualisierungen der Nervenbahnen im Gehirn umspielt. Die Töne mischen sich zu festen Texturen, und schillern in herrlicher Farbigkeit. Der „Dance No. 4" von Philip Glass entspricht den mechanischen Kräften, die unser Gehirn entstehen und funktionieren lassen.

Das Publikum dankte mit lang anhaltendem Applaus für diesen unvergesslichen Ausflug zu den zwei Türmen.

Figure 83: Event review published in the "Erlanger Nachrichten" on September 27, 2024.

For those interested in further details:

You can download the **event program booklet** here: https://go.fau.de/1bdg-

Or simply scan the QR code.

Read an **article about the event**, including interviews, on the FAU website here: https://go.fau.de/1bdga

Or simply scan the QR code.

> "Das Konzert war grandios und wir sind noch ganz überwältigt von den vielen tollen Eindrücken!"
>
> "Wir gratulieren ... es war ein sehr kurzweiliger Abend mit faszinierenden Bildern und außergewöhnlicher Musik!"

Figure 84: The box office is open. (Image: E. Steinmann)

Figure 85: The ITM media studios team makes final preparations. (Image: E. Steinmann)

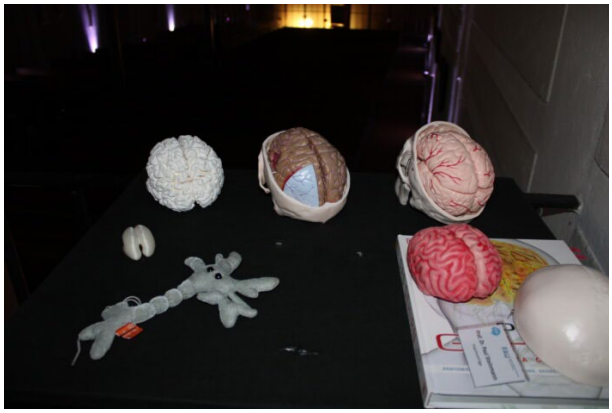


Figure 86: Brainy tools for the impulse lectures. (Image: E. Steinmann)

Figure 87: The subject is being prepared for the live EEG. (Image: E. Steinmann)

Figure 91: Final check. (Image: E. Steinmann)

Figure 90: Engaged audience asks questions to the experts. (Image: E. Steinmann)

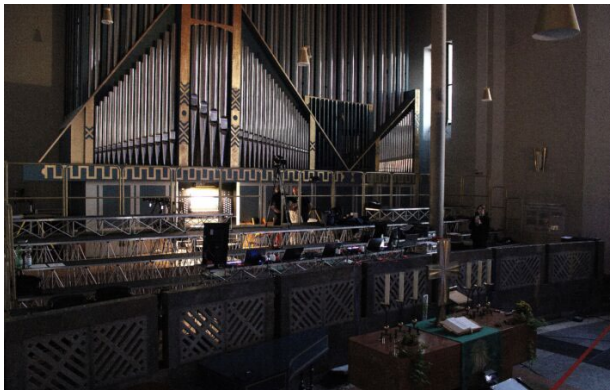


Figure 88: The organ, just before the event. (Image: E. Steinmann)

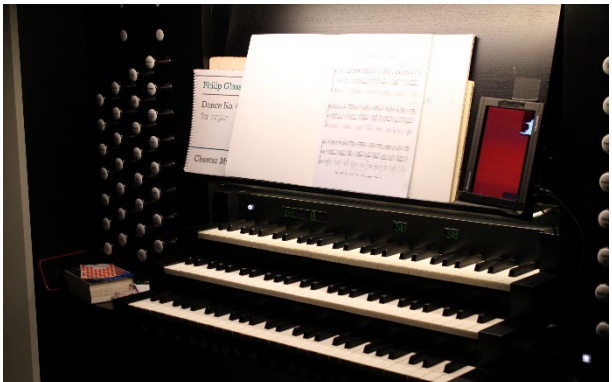


Figure 89: The organ, just before the event. (Image: E. Steinmann)

5.1.4 PODCAST WITH SILVIA BUDDAY

How Do Folds Form in Our Brain?

Silvia Budday participated in an interview featured in the podcast "FELDFORSCHUNG" by the Nürnberger Presse (VPN), which was published in April 2024. The podcast aims to bring FAU researchers into the “real world,” showcasing where their research finds application. The third episode of the series delves into the topic of epilepsy and the brain.

In this episode, the host Lea-Verena Meingast interviews Professor Dr. Silvia Budday and her friend Tina, whose two-year-old son has epilepsy. The conversation explores the connection between the folds in the brain and epilepsy, as well as the hope for improved outcomes for children like Tina’s son and many others. The podcast highlights the potential therapeutic insights that can emerge from understanding the mechanics of brain folding, offering new perspectives on the treatment of neurological conditions.

The episode is available on various podcast platforms, and more details can be found on the FAU website: https://www.fau.de/2024/04/news/podcast-wie-kommen-die-falten-in-unser-gehirn/

Spotify link:
https://open.spotify.com/show/2fh4dOP8JQR3b4Bsb1OCf9?si=PKeMpyq4TXOsj7okk8hHfg&nd=1&dlsi=c2f2af055e9d4a84

5.2 EBM2PEERS

- EBM Scientific Publications (see Section 1.3): All publications are freely accessible. Additionally, supplementary materials such as datasets are publicly available through the "Exploring Brain Mechanics - CRC 1540 EBM" community on the online storage service Zenodo.
- EBM Scientific Presentations at first-class conferences, workshops, and seminars (see Section 6.3
- EBM Virtual Brain Talks (see Section 2.2.3)

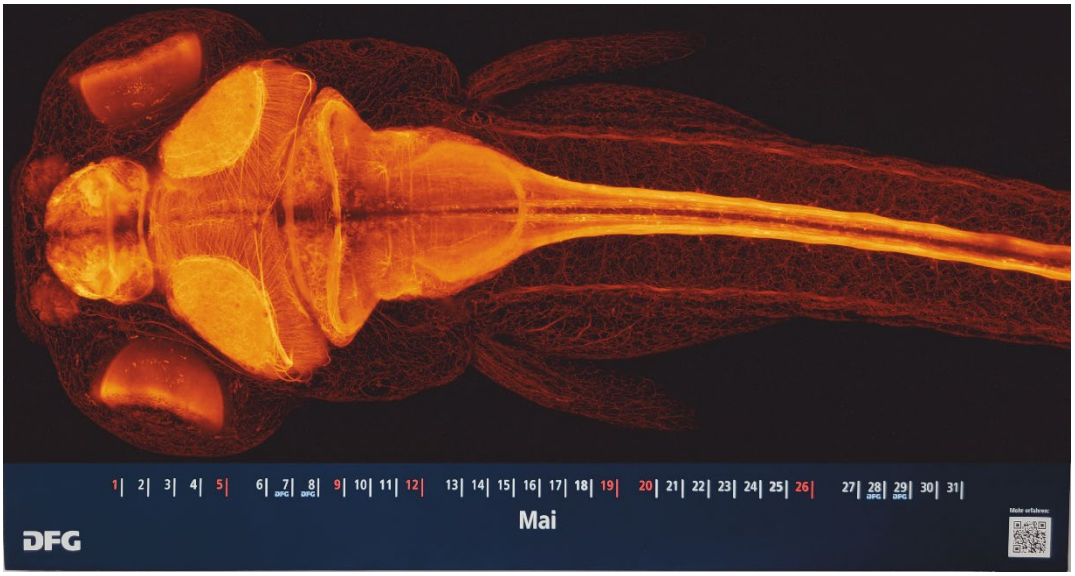


Figure 92: Fascinating insights into science: a zebrafish larva, captured by Daniel Wehner, is the winning image for the May 2024 calendar page in the DFG calendar on the topic 'Wissensspeicher' (knowledge store).

6 GENERAL INFORMATION

6.1 KEY DATA

6.1.1 GOVERNING BODIES OF EBM

Spokesperson
Prof. Dr.-Ing. habil. Paul Steinmann
Institute of Applied Mechanics
Egerlandstr. 5, 91058 Erlangen
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paul.steinmann@fau.de

Co-Spokesperson
Prof. Dr.-Ing. Silvia Budday
Institute of Continuum Mechanics and Biomechanics
Friedrich-Alexander-Universität Erlangen-Nürnberg
Dr.-Mack-Str. 81, 90762 Fürth
+49 9131 8567611
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Scientific Coordination
Dr. rer. nat. Andrea Dakkouri-Baldauf
Institute of Applied Mechanics
Martensstraße 5a, 91058 Erlangen
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EBM Executive Board
The EBM Executive Board consists of the Spokesperson, Co-Spokesperson, Scientific Coordinator, Chairs of the Focal Research Areas (FRA **A**, **B**, **C**) and the Cross-Sectional Research Area (**XRA**), the Principal Executive of the Integrated Research Training Group (**iRTG**), a representative from the Clinics, an Early Career Support Representative, an Equal Opportunity Representative, a (Post-) Doctoral Researchers' Representative, and the EBM assistance.

Members:

Spokesperson	Prof. Paul Steinmann
Co-Spokesperson	Prof. Silvia Budday
Scientific Coordinator	Dr. Andrea Dakkouri-Baldauf
Chair of FRA **A**	Prof. Kristian Franze
Chair of FRA **B**	Prof. Jochen Guck
Chair of FRA **C**	Prof. Ben Fabry
Chair of **XRA**	Prof. Jing Guo / Prof. Ingolf Sack
Clinics Representative	Prof. Arnd Dörfler / Prof. Ingmar Blümcke
Principal Executive of the **iRTG**	Prof. Friedrich Paulsen
Early Career Representative	Prof. Katharina Breininger
Equal Opportunity Representative	Prof. Marisa Karow
(Post-)Doctoral Researchers‘ Representative	Shanice Heidenreich (Deputy: Soheil Firooz)
EBM Assistance	Doris Bittner

6.1.2 PARTICIPATING RESEARCHERS

6.1.2.1 Principal investigators

Table 10: Principal investigators

Principal investigators (PIs)	Faculty	Home institution, location	Project
Blümcke, Prof. Dr. med., Ingmar	FAU-MedFak	Neuropathology, Schwabachanlage 6, 91054 Erlangen	A02
Boccaccini, Prof. Dr.-Ing. habil., Aldo R.	FAU-TechFak	Biomaterials, Cauerstr. 6, 91058 Erlangen	X03
Bosserhoff, Prof. Dr., Anja	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	C04
Breininger, Prof. Dr.-Ing., Katharina	FAU-TechFak	Artificial Intelligence in Medical Imaging, Werner-von-Siemens-Str. 61, 91052 Erlangen	X02
Budday, Prof. Dr.-Ing., Silvia	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Dr.-Mack-Str. 81, 90762 Fürth	A01, B01, Z
Dörfler, Prof. Dr. med., Arnd	FAU-MedFak	Neuroradiology, Schwabachanlage 6, 91054 Erlangen	A02, Y
Fabry, Prof. Dr.-Ing., Ben	FAU-NatFak	Biophysics, Henkestr. 91, 91052 Erlangen	C05
Falk, Dr., Sven	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	A04
Franze, Prof. Dr., Kristian	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05, B02
Frischknecht, Dr., Renato	FAU-NatFak	Animal Physiology, Staudtstr. 5, 91058 Erlangen	C02
Guck, Prof. Dr., Jochen	FAU-NatFak	Biological Optomechanics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B03
Guo, Prof. Dr. rer. nat., Jing	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01, Y
Karow, Prof. Dr. rer. nat., Marisa	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	A04
Kobow, PD Dr. rer. nat. Dr. habil. med., Katja	FAU-MedFak	Neuropathology, Schwabachanlage 6, 91054 Erlangen	C03
Kürten, Prof. Dr. med., Stefanie	FAU-MedFak	Anatomy and Cell Biology, Krankenhausstr.9, 91054 Erlangen and Universität Bonn, Institute of Neuroanatomy, Nussallee 10, 53115 Bonn	B04
Laun, Prof. Dr. rer. nat., Frederik B.	FAU-MedFak	Radiology, Maximiliansplatz 3, 91054 Erlangen	Y
Maier, Prof. Dr.-Ing. habil., Andreas	FAU-TechFak	Computer Science 15, Machine Intelligence, Martensstr. 3, 91058 Erlangen	X02
Möllmert, Dr. rer. nat., Stephanie	MPL	Biological Optomechanics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B03
Paulsen, Prof. Dr. med., Friedrich	FAU-MedFak	Functional and Clinical Anatomy, Universitätsstr. 19, 91054 Erlangen	A02, iRTG
Sack, Prof. Dr. rer. nat., Ingolf	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01, Y
Schambony, Prof. Dr. rer. nat., Alexandra	FAU-NatFak	Schambony Lab, Staudtstr. 5, 91058 Erlangen	A03
Steinmann, Prof. Dr.-Ing. habil., Paul	FAU-TechFak	Applied Mechanics, Egerlandstr. 5, 91058 Erlangen	B01, C01, X01, Z
Wehner, Dr. rer. nat., Daniel	MPL	Biological Optomechanics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B05
Willner, Prof. Dr.-Ing. habil., Kai	FAU-TechFak	Applied Mechanics, Egerlandstr. 5, 91058 Erlangen	X01
Zaburdaev, Prof. Dr., Vasily	FAU-NatFak	Mathematics in Life Sciences, MPZPM, Kussmaulallee 2, 91054 Erlangen	C01

6.1.2.2 Associated principal investigators

Table 11: Associated principal investigators

Associated principal investigators (aPIs)	Faculty	Home institution, location
Gregurec, Prof. Dr., Danijela	FAU-NatFak	Chair for Aroma und Smell Research, Henkestrasse 91, 91052 Erlangen
Hutter, Prof. Dr.-Ing., Jana	FAU-MedFak	Institute of Radiology, Henkestrasse 91, 91052 Erlangen
Nagel, Prof. Dr. rer. nat., Armin M.	FAU-MedFak	Institute of Neuroradiology, Henkestr. 91, 91052 Erlangen
Riedl, Prof. Dr. med., Valentin	FAU-MedFak	Institute of Neuroradiology, Henkestr. 91, 91052 Erlangen
Toda, Prof. Dr., Tomohisa	FAU-MedFak	Professor of Neural Epigenomics, Fahrstr. 17, 91054 Erlangen
Zaiss, Prof. Dr. rer. nat., Moritz	FAU-MedFak	Institute of Neuroradiology, Henkestr. 91, 91052 Erlangen

6.1.2.3 Postdoctoral researchers

Table 12: Postdoctoral researchers and assistant doctors

Postdoctoral researchers (PDRs)	Faculty	Home institution, location	Project
Dolai, Dr., Pritha	FAU-NatFak	Mathematics in Life Sciences, Cauerstr. 11, 91058 Erlangen	C01
Estrella, Dr., Melanie	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01
Flé, Dr., Guillaume	FAU-MedFak	Radiology, Maximiliansplatz 3, 91054 Erlangen	Y
Gopalan Ramachandran, Dr., Rahul	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Dr.-Mack-Str. 81, 90762 Fürth	B01
Hintze, Dr., Maik	FAU-MedFak	Anatomy and Cell Biology, Krankenhausstr.9, 91054 Erlangen and Universität Bonn, Institute of Neuroanatomy, Nussallee 10, 53115 Bonn	B04
Melly, Dr., Stephen	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Egerlandstr. 5, 91058 Erlangen	B01
Rampp, PD Dr. med., Stefan	FAU-MedFak	Department of Neurosurgery, Department of Neuroradiology, Schwabachanlage 6, 91054 Erlangen	A02
Shahryari, Mehrgan	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01
Wellge, Brunhilde	Charité Berlin	Medical Clinic, Department of Cardiology and Angiology, Charitéplatz 1, 10117 Berlin	Y

6.1.2.4 Associated postdoctoral researchers and assistant doctors

Table 13: Associated postdoctoral researchers and assistant doctors

Associated postdoctoral researchers and assistant doctors (aPDRs)	Faculty	Home institution, location	Project
Chunder, Dr. rer. nat., Rittika	FAU-MedFak	Anatomy and Cell Biology, Krankenhausstr.9, 91054 Erlangen and Universität Bonn, Institute of Neuroanatomy, Nussallee 10, 53115 Bonn	B04
Hoffmann, Dr. med., Lucas	FAU-MedFak	Neuropathology, Schwabachanlage 6, 91054 Erlangen	A02

Kolb, Dr., Julia	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Dr.-Mack-Str. 81, 90762 Fürth	A01
Schicht, PD Dr. rer. nat. Dr. habil. med., Martin	FAU-MedFak	Functional and Clinical Anatomy, Universitätsstr. 19, 91054 Erlangen	A02
Scholz, Prof. Dr. rer. nat. Dr. habil. med., Michael	FAU-MedFak	Functional and Clinical Anatomy, Universitätsstr. 19, 91054 Erlangen	A02

6.1.2.5 Doctoral researchers

Table 14: Doctoral researchers

Doctoral Researchers (DRs)	Faculty	Home institution, location	Project
Auer, Sophia	FAU-MedFak	Functional and Clinical Anatomy, Universitätsstr. 19, 91054 Erlangen	A02
Bachir Salvador, Jana	MPL	Biological Optomechanics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B03
Bischof, Lars	FAU-NatFak	Biophysics, Henkestr. 91, 91052 Erlangen	C05
Cecchini, Erica	FAU-MedFak	Neuropathology, Schwabachanlage 6, 91054 Erlangen	A02
Erterek, Ezgi	FAU-NatFak	Animal Physiology, Staudtstr. 5, 91058 Erlangen	C02
Fedders, Michael	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01
Firooz, Soheil	FAU-TechFak	Applied Mechanics, Egerlandstr. 5, 91058 Erlangen	C01
Froidevaux, Clara	FAU-NatFak	Schambony Lab, Staudtstr. 5, 91058 Erlangen	A03
Heidenreich, Shanice	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	C04
Hinrichsen, Jan	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Egerlandstr. 5, 91058 Erlangen	A01
Karandasheva, Kristina	FAU-MedFak	Neuropathology, Schwabachanlage 6, 91054 Erlangen	C03
Kuth, Sonja	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Dr.-Mack-Str. 81, 90762 Fürth	A01
Lorke, Markus	FAU-TechFak	Biomaterials, Cauerstr. 6, 91058 Erlangen	X03
Lyraki, Olga	MPL	Biological Optomechanics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B05
Neumann, Oskar	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Egerlandstr. 5, 91058 Erlangen	B01
Pan, Zhaoya	FAU-TechFak	Chair of Computer Science 5 (Pattern Recognition), Martensstraße 3, 91058 Erlangen	X02
Ruhland, Laura	FAU-TechFak	Applied Mechanics, Egerlandstr. 5, 91058 Erlangen	X01
Sipkova, Jana	FAU-MedFak	Medical Physics, Henkestr. 91, 91052 Erlangen	A05
Tarczewska, Maria Weronika	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05
Thies, Mareike	FAU-TechFak	Chair of Computer Science 5 (Pattern Recognition), Martensstraße 3, 91058 Erlangen	X02
Tranchina, Michael	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	A04
Vásquez Sepúlveda, Sebastián Ignacio	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B02

Verma, Yashasvi	FAU-TechFak	Applied Mechanics, Egerlandstr. 5, 91058 Erlangen	X01
Wilm, Frauke	FAU-TechFak	Chair of Computer Science 5 (Pattern Recognition), Martensstraße 3, 91058 Erlangen	X02

6.1.2.6 Associated doctoral researchers

Table 15: Associated doctoral researchers

Associated doctoral researchers (aDRs)	Faculty	Home institution, location	Project
Greiner, Alexander	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Egerlandstr. 5, 91058 Erlangen	B01
Jordan, Jakob	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01
Ludwig, Jakob	Charité Berlin	Radiology, Charitéplatz 1, 10117 Berlin	X01
Öttl, Mathias	FAU-TechFak	Chair of Computer Science 5 (Pattern Recognition), Martensstraße 3, 91058 Erlangen	X02
Perelló Amorós, Bartomeu	FAU-NatFak	Animal Physiology, Staudtstr. 5, 91058 Erlangen	C02
Reiter, Nina	FAU-TechFak	Institute of Continuum Mechanics and Biomechanics, Egerlandstr. 5, 91058 Erlangen	B01
Welsch, Kathrin	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05

6.1.2.7 Associated master's students / medical doctoral researchers

Table 16: Associated master's student / medical doctoral researchers s

Associated master's students (aMSs) / medical doctoral researchers (medDRs)	Faculty	Home institution, location	Project
Butzke, Julia	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05
Gampl, Niklas	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05
Gataulin, Radik	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05
Görtz-Lizarraga, Matthias	FAU-MedFak	Biochemistry and Molecular Neurosciences, Fahrstr. 17, 91054 Erlangen	A04
Groß, Fabian	FAU-MedFak	Radiology, Maximiliansplatz 3, 91054 Erlangen	Y
Jeßberger, Philipp	FAU-MedFak	Radiology, Maximiliansplatz 3, 91054 Erlangen	Y
Karakuzulu, Buse	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	A05
Lehner, Annika	FAU-MedFak	Functional and Clinical Anatomy, Universitätsstr. 19, 91054 Erlangen	A02
Mager, Miriam	FAU-NatFak	Schambony Lab, Staudtstr. 5, 91058 Erlangen	A03
Mai, Katharina	FAU-MedFak	Medical Physics, MPZPM, Kussmaulallee 2, 91054 Erlangen	B02
Özer, Mert	FAU-TechFak	Chair of Computer Science 5 (Pattern Recognition), Martensstraße 3, 91058 Erlangen	X02
Piehler, Verena	FAU-TechFak	Biomaterials, Cauerstr. 6, 91058 Erlangen	X03

6.1.2.8 Student assistants

Table 17: Student assistants

Name	Supported researchers	Course / field of study	Funded member of EBM (from / to)	Tasks relating to EBM
Abdallah, Farhat	Oskar Neumann, **B01**	Computational Engineering	15.02.24 / 14.08.24	Assistance in data-post processing and the development of a Guided User Interface (GUI) for indentation data analysis
Franke, Lorenz	Alexandra Schambony, Clara Froidevaux, **A03**	Biology	01.01.24 / 30.09.24	Support with Xenopus Laevis handling, support preparation of hydrogel substrates used for **A03**
Gataulin, Radik	Kristian Franze, **A05**	Molecular Medicine	01.01.24 / 31.12.24	Sample preparation and imaging of frog brains
Gottipati, Taraswin	Jan Hinrichsen, **A01**	Computational Engineering	01.01.24 / 31.03.24	Implementing automation tool for rheometer software to improve reproducibility and ease of use.
Hahn, Paula	Kristian Franze, **A05**, **B02**	Cell and Molecular Biology	01.04.24 / 31.03.25	Sample preparation and mechanical manipulation of tissues (in collaboration with **C02**)
Hashemizadeh, Kimia	Silvia Budday, **B01**	Advanced Materials and Processes	15.03.24 / 14.06.24	Mechanical characterization of hydrogels
Karakuzulu, Basak Buse	Kristian Franze, **A05**, **B02**	Molecular Medicine	01.01.24 / 31.12.24	Sample preparation and imaging of frog brains
Kashish Veda, Eluri	Soheil Firooz, **C01**	Computational Engineering	01.01.24 / 30.09.24 15.11.24 /.14.02.25	Programming a coupled-field FEM code for simulating cellular aggregate formation within both Eulerian and Lagrangian frameworks
Khosrobeigi, Rezvan	Soheil Firooz, **C01**	Medical Engineering	15.02.24 / 15.03.24	Poisson ratio study on peridynamic simulation of brain
Krauß, Christina	Markus Lorke, **X03**	Materials Science and Engineering	01.07.24 / 30.09.24	Hydrogel testing. 3D printing, cell experiments
Kuhn, Arne	Alexandra Schambony, Clara Froidevaux, **A03**	Biology	01.01.24 / 31.03.24	Support with hydrogel substrates, preparation of organoids used for **A03**
Lehner, Annika	Ingmar Blümcke, **A02**	Medicine	01.01.24 / 31.03.24	Technical lab support in studying perineuronal nets, sample selection and preparation (e.g. cutting of tissue slices)
Mai, Katharina	Kristian Franze, **A05**, **B02**	Medical Engineering	01.01.24 / 11.03.24 01.04.24 / 11.09.24	Development of soft 3D tissue culture substrates for Xenopus brain tissue (in collaboration with **X03**)
Moradian, Arash	Soheil Firooz, **C01**	Mechanical Engineering	15.06.24 / 13.10.24	Investigation of various peridynamic energy functions together with parameter identification for peridynamic analysis of brain matter
Nasirli, Fatima	Kristian Franze, **B02**	Molecular Medicine	01.01.24 / 31.03.24	Sample preparation

Name	Supported researchers	Course / field of study	Funded member of EBM (from / to)	Tasks relating to EBM
Rahnama Esfahani, Masoud	Soheil Firooz, C01	Computational Engineering	01.01.24 / 30.04.24	Robust modification of multi-neighbor interactions in peridynamic analysis of brain matter – Acceleration of a C++ peridynamic code
Roy, Sohini	Paul Steinmann, B01	Computer Science & Engineering	01.01.24 / 14.02.24	Sample preparation; Uniaxial tension tests; Material characterization; Modification of the experimental setup
Safaei, Behzad	Soheil Firooz, C01	Computational Engineering	01.01.24 / 14.01.24	Implementation of a robust iterative solver in C++
Schaffer, Darius	Ben Fabry, C05	Medical Engineering	01.01.24 / 31.03.24	Developed a user-friendly software for recording time-lapse microscope images; worked on a method for measuring traction forces based on bright-field microscope images
Setayesh, Ardalan	Silvia Budday, A01, B01	Medical Technology	15.05.24. / 31.12.24	Nanoindentation experiments on spinal cord tissue and other EBM materials, preparation of safety documentation related to EBM
Seo, Minsu	Frauke Wilm, Mathias Öttl, X02	Information and Communication Engineering	01.01.24 / 01.06.24	Extension of EXACT server for EBM requirements
Settipalli, Sumanthreddy	Silvia Budday, A01, B01	Mechanical Engineering	01.01.24 / 14.11.24	Support with rheometer experiments
Shah, Rutvi	Jan Hinrichsen, A01	Computational Engineering	01.01.24 / 14.02.24	Setting up Apptainer containers to run deal.ii FE simulations on the FAU HPC
Spear, Chiara	Michael Tranchina, A04	Molecular Medicine	01.03.24 / 31.12.24	Cutting and analysis of brain organoids (either compressed or embedded in hydrogels)
Surana, Harsh Vardhan	Oskar Neumann, B01	Computational Engineering	01.01.24 / 31.07.25	Assistance in the experimental investigation of the mechanical properties of porcine spinal cord using a Nanoindenter
Thattil, Deepu	Soheil Firooz, C01	Computational Engineering	15.03.24 / 14.06.24	Conversion and acceleration of a coupled-field FEM code from Matlab to C++
Tikadar, Mayukh	Markus Lorke, X03	Master's Program Advanced Materials and Processes	01.01.24 / 31.03.24	Hydrogel testing
Valian, Ilia	Soheil Firooz, C01	Computational Engineering	15.03.24 / 14.05.24	Implementation of Arc-length meth-od for minimization of non-convex problems
Vennilavan Thenmozhi, Hariamkumar	Jan Hinrichsen, A01	Computational Engineering	01.07.24 / 30.09.24	Setting up Apptainer containers on the HPC. Running parameter identification for human brain tissue data.

6.1.2.9 EBM Advisory Board

Table 18: EBM Advisory Board

Mercator fellows	Affiliation	Expertise
Franklin, Prof., Robin	Cambridge University, UK	CNS regeneration
Holzapfel, Prof., Gerhard	Institute of Biomechanics, Graz University of Technology, Austria	Mechanical testing and modeling of brain tissue mechanics
Kuhl, Prof., Ellen	Living Matter Lab, Stanford University, USA	Continuum modeling and simulation of the brain
Further board members		
Götz, Prof. Dr., Magdalena	Institute for Physiological Genomics, Ludwig-Maximilians-Universität München & Institute of Stem Cell Research, Helmholtz Zentrum, Munich, Germany	Neuroscience
Jayamohan, Dr., Jayaratnam (Jay)	Consultant Paediatric Neurosurgeon, John Radcliffe Hospital, and private practice at Nuffield Health Oxford, The Manor Hospital, Oxford, UK	Clinician
Schnell, Prof. Dr., Oliver	Neurosurgical Clinic, Chair of Neurosurgery, University Hospital Erlangen, Germany	Neurosurgery

6.1.3 COORDINATION AND ADMINISTRATION

Table 19: EBM Coordination and administration

	Work Address	Contact Data (Tel / Fax, Email, Web)	Work Area
Bittner, Doris	SFB 1540 EBM, Martensstraße 5a, 91058 Erlangen	+49 9131 85 20783 / -20785, doris.bittner@fau.de, www.ebm.fau.eu	EBM Administration
Dakkouri-Baldauf, Dr. rer. nat., Andrea	SFB 1540 EBM, Martensstraße 5a, 91058 Erlangen	+49 9131 85-20782 / -20785, andrea.dakkouri@fau.de, www.ebm.fau.eu	EBM Coordination

6.2 NETWORK AND COOPERATION

Sophia Auer

Partner institute	Researchers involved	Research topic
Institute of Continuum Mechanics and Biomechanics	Silvia Budday, Nina Reiter	Direction-dependent mechanics of human corpus callosum and lower brain stem

Lars Bischof

Partner institute	Researchers involved	Research topic
Institute for Neuropathology, Univ. clinic Erlangen	Katja Kobow, Kristina Karandasheva	Neuronal growth in 2D and 3D matrices

Erica Cecchini

Partner institute	Researchers involved	Research topic
Institute of Continuum Mechanics and Biomechanics	Silvia Budday, Jan Hinrichsen, Nina Reiter	*In silico* modeling of brain malformations
Institut für Funktionelle und Klinische Anatomie	Friedrich Paulsen, Sophia Auer	Deep extracellular matrix (ECM) quantification and phenotyping in healthy human brain and cortical malformations

Epilepsiezentrum Neurochirurgie	Stefan Rampp	Human brain datasets and multi-modal and multiparametric imaging
Neuroradiology	Arnd Dörfler	(Ultra-)High-field imaging of human brain malformations

Guillaume Flé

Partner institute	Researchers involved	Research topic
Institute of Applied Mechanics, FAU (Paul Steinmann – X01)	Laura Ruhland, Yashasvi Verma	In silico modeling of MRE and imaging of porcine spinal cord from tabletop to clinical devices
FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – B01)	Oskar Neumann	Characterization of porcine spinal cord using MRE

Clara Froidevaux

Partner institute	Researchers involved	Research topic
Institute of Biomaterials, FAU	Markus Lorke, Sonja Kuth, Aldo Boccaccini, Project X03	Hydrogels as substrates for explants
Max Planck Institute for the Science of Light, Erlangen	Stephanie Möllmert, Jana Bachir Salvador	AFM and Brillouin Microscopy measurements

Shanice Heidenreich

Partner institute	Researchers involved	Research topic
Institute of Biomaterials, FAU	Markus Lorke, Sonja Kuth (X03)	Development of hydrogel matrices for soft tissue applications

Jan Hinrichsen

Partner institute	Researchers involved	Research topic
FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – A01/ B01)	Nina Reiter	Microstructure - Mechanics relation of human brain tissue
FAU, Institute of Functional and Clinical Anatomy (Friedrich Paulsen – A02, Lars Bräuer, Martin Schicht)	Sophia Auer (A02)	Mechanical characterization of human brain tissue from body donors. Correlation of tissue component concentration with mechanical properties.
Universitätsklinikum Erlangen-Neuropathologisches Institut (Ingmar Blümcke – A02)	Lucas Hoffmann (A02), Erica Cecchini (A02)	Mechanical characterization of human brain tissue from epilepsy surgery. Histological analysis of tested tissue. Investigating links between pathologies and mechanical behavior.
Universitätsklinikum Erlangen-Neurochirurgie (Arnd Dörfler – A02)	Stefan Rampp (A02)	MRT imaging of human brains prior to mechanical testing.
Biophysics Group, Department of Physics (Ben Fabry – C05)	David Böhringer	Mechanical characterization of collagen hydrogels.
ETH Zürich (Laura de Lorenzis)	Moritz Flaschel	Automated hyperelastic model discovery for human brain tissue (publication).
Institute of Medical Physics and Microtissue Engineering (Kristian Franze – B02/ A05)	Julia Becker, Alexander Winkel	Viscoelastic modeling of rat spinal cord AFM data.
FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – A01/ B01)	Alexander Greiner (B01)	Poroviscoelastic characterization of hydrogels.

FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – A01/B01)	Oskar Neumann (B01)	Mechanical characterization of human spinal cord tissue.
FAU, Institute of Applied Mechanics (Paul Steinmann – B01/C01)	Stephen Melly (B01)	Inverse parameter identification for AFM data.

Kristina Karandasheva

Partner institute	Researchers involved	Research topic
Institut für Physik der Kondensierten Materie	Ben Fabry, Lars Bischof	Quantification of neuronal network formation using time-lapse and traction-force microscopy

Markus Lorke

Partner institute	Researchers involved	Research topic
Chair of Animal Physiology, FAU	Renato Frischknecht, Ezgi Erterek, Bartomeu Perelló Amorós,	Cortical neurons in Contact with OHA hydrogels
Chair of Biochemistry and Molecular Neurosciences, FAU	Michael Tranchina	Encapsulated organoids in OHA matrix
Chair of Biochemistry and Molecular Medicine, FAU	Shanice Heidenreich	Reaction of different cell types to OHA encapsulation
Strahlenklinik, UKER	Anja Derer, Rainer Detsch	Cell embedding in different hydrogels for cancer modeling

Oskar Neumann

Partner institute	Researchers involved	Research topic
Institute of Continuum Mechanics and Biomechanics, FAU	Jan Hinrichsen	Inverse identification of material parameters for human spinal cord tissue
Institute of Continuum Mechanics and Biomechanics, FAU	Nina Reiter	Multimodal mechanical testing on human and porcine spinal cord with the rheometer
Institute of Applied Mechanics, FAU	Laura Ruhland	Magnetic resonance elastography (table-top) experiments on porcine spinal cord
Max Plank Institute for the Science of Light	Daniel Wehner	Scientific exchange on the mechano-biological aspects of spinal cord regeneration
Max Plank Institute for the Science of Light	Stephanie Möllmert	Scientific exchange on the mechano-biological aspects of spinal cord regeneration
Institute of Anatomy/Neuroanatomy, Uni Bonn	Maik Hintze	Scientific exchange on the experimental investigation and anatomy of spinal cord (staining, cutting, and general questions)
Max Plank Institute for the Science of Light	Jana Bachir & Stephanie Möllmert	Mechanical experiments on porcine spinal cord tissue with Brillouin Microscopy and Atomic Force microscopy
Max Plank Institute for the Science of Light	Stephanie Möllmert	Scientific exchange and provision of mechanical and biological data of the adult zebrafish during spinal cord regeneration
Institute of Radiology, FAU	Guillaume Flé	Magnetic resonance elastography (1.5 Tesla) experiments on porcine spinal cord
Department of Artificial Intelligence in Biomedical Engineering (AIBE), FAU	Mareike Thies & Katharina Breininger	Image-based counting of axons in the adult zebrafish at different time points over the course of regeneration

Mathias Öttl

Partner institute	Researchers involved	Research topic
FAU, Institute of Continuum Mechanics FAU, Neuropathology	Jan Hinrichsen, Nina Reiter, Silvia Budday (A01) Ingmar Blümcke (A02)	Extension of EXACT for online neuron cell detection and counting

Bartomeu Perelló Amorós

Partner institute	Researchers involved	Research topic
Institute of Biomaterials, FAU	Aldo Boccaccini, Markus Lorke, Sonja Kuth	Engineering brain tissue-like matrices

Nina Reiter

Partner institute	Researchers involved	Research topic
Institute of Functional and Clinical Anatomy	Friedrich Paulsen, Martin Schicht, Sophia Auer	Mechanical characterization and histological analysis of human brain tissue from body donors (connected to B01, A01, A02)
Neuropathology	Ingmar Blümcke, Lucas Hoffmann, Erica Cecchini	Mechanical characterization and histological analysis of human brain tissue samples from epilepsy surgery (connected to A01, A02)

Laura Ruhland

Partner institute	Researchers involved	Research topic
Institute of Continuum Mechanics	Oskar Neumann	MRE experiments on spinal cord
Radiologisches Institut qMRI Lab	Guillaume Flé	MRE experiments

Maria Tarczewska

Partner institute	Researchers involved	Research topic
Max-Planck-Institut für die Physik des Lichts; Die Forschungsgruppe für Neuroregeneration	Daniel Wehner	Spinal cord regeneration

Mareike Thies

Partner institute	Researchers involved	Research topic
FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – A01/ B01)	Jan Hinrichsen, Nina Reiter, Silvia Budday	Neuron cell detection and counting in whole slide images with neural networks (on-going)
FAU, Institute of Continuum Mechanics and Biomechanics (Silvia Budday – A01/ B01)	Oskar Neumann, Silvia Budday	Automatic counting of axons in microscopic images of zebra fish's regenerating spinal cord (new, still in exploration phase)

Michael Tranchina

Partner institute	Researchers involved	Research topic
Institute of Biomaterials, FAU	Aldo Boccaccini, Markus Lorke, Sonja Kuth	Hydrogels
Institute of Continuum Mechanics and Biomechanics, FAU	Nina Reiter, Silvia Budday	Rheometer compressions
Max-Planck-Zentrum für Physik und Medizin (MPZPM)	Sebastián Vásquez-Sepúlveda, Kristian Franze	AFM

Sebastián Vásquez-Sepúlveda

Partner institute	Researchers involved	Research topic
MPZPM, Erlangen, Germany	Nora John, Daniel Wehner	AFM measurements of spinal cord in Zebrafish
University of Manchester, UK	Hamish Gilbert	Mass spectrometry on *Xenopus laevis brains*

Yashasvi Verma

Partner institute	Researchers involved	Research topic
Charité, Berlin, Germany	Ingolf Sack, Jing Guo	MRE testing of brain samples and phantom materials
SISSA, Pisa, Italy	Luca Heltai	Computational modeling of vasculature

Kathrin Welsch

Partner institute	Researchers involved	Research topic
Institute of Biochemistry FAU	Prof. Lie, Dr. Schäffner, Francesco Bambini	Adult neural stem cells and their interactions with their niche

Frauke Wilm

Partner institute	Researchers involved	Research topic
Institute of Continuum Mechanics and Biomechanics (A01) Universitätsklinikum Erlangen-Neuropathologisches Institut (Ingmar Blümcke – A02)	Jan Hinrichsen, Lucas Hoffmann, Nina Reiter, Silvia Budday, Katharina Breininger	Automatic deep learning-based quantification of neurons in histology samples
Technische Hochschule Ingolstadt	Prof. Dr. Marc Aubreville, Jonathan Ganz, Jonas Ammeling	Digital Pathology
Institute of Pathology, University of Veterinary Medicine, Vienna, Austria	Dr. Christof Bertram	Digital Pathology
Institute of Veterinary Pathology, Freie Universität Berlin, Germany	Prof. Dr. Robert Klopfleisch, Chloé Puget	Digital Pathology
Pathology Department, University Medical Centre Utrecht, The Netherlands	Nikolas Stathonikos	Digital Pathology

6.3 PARTICIPATION IN CONFERENCES AND CONGRESSES

6.3.1 CONFERENCES AND RESEARCH STAYS OF PRINCIPAL INVESTIGATORS

Table 20: Conferences and research stays of PIs

PI	Date	Conference	Title of own presentation / participation only
Blümcke, Ingmar	22.01.24 / 26.01.24	EPODES Advanced II, Brno, Czech Republic	*Histopathology basis of human epileptic brain lesions*
Blümcke, Ingmar	18.02.24 / 25.02.24	Epilepsy Center, Cleveland Clinic, USA	*Consultation in histopathology analysis of human epileptic brain lesions*
Blümcke, Ingmar	14.07.24 / 21.07.24	Epilepsy Center, Cleveland Clinic, USA	*Consultation in histopathology analysis of human epileptic brain lesions*

Blümcke, Ingmar	11.09.24 / 15.09.24	Intl. Epilepsy Summit, Cleveland Clinic, USA	Chair and speaker for FCD session
Blümcke, Ingmar	19.09.24 / 22.09.24	Intl. School for Neuropathology and Epilepsy Surgery, Erlangen, Germany	Organizer of hands-on course
Blümcke, Ingmar	03.10.24 / 04.10.24	Neurochirurgische Klinik, Medizinische Universität Wien, Österreich	*Mutational burden and outcome in FCD*
Blümcke, Ingmar	07.11.24 / 09.11.24	Intl. Epilepsy Symposium, University of Calgary, Canada	*Somatic mutations and their relevance to surgical outcome*
Blümcke, Ingmar	11.11.24 / 29.11.24	Epilepsy Center, Cleveland Clinic, USA	*Consultation in histopathology analysis of human epileptic brain lesions*
Blümcke, Ingmar	15.12.24 / 18.12.24	EpiCare European Reference Center Meeting, Rome, Italy	Chair and speaker for FCD session
Bosserhoff, Anja	21.09.24 / 25.09.24	Melanoma symposium 2024, Santorini, Greece	*Quiescence/dormancy in melanoma cells*
Bosserhoff, Anja	16.10.24 / 18.10.24	ESPCR 2024, Marseille, France	*Understanding molecular processes in tumor dormancy, metastasis and therapy*
Breininger, Katharina	11.03.24 / 12.03.24	Bildverarbeitung für die Medizin (BVM), Erlangen, Germany	Different contributions by students
Breininger, Katharina	18.02.24 / 15.03.24	Technische Universität Eindhoven, Netherlands	Research stay
Breininger, Katharina	01.10.24 / 04.10.24	European Congress of Computer Vision, Milan, Italy	*Style-Extracting Diffusion Models for Semi-supervised Histopathology Segmentation*
Breininger, Katharina	06.10.24 / 10.10.24	Medical Image Computing and Computer Assisted Intervention, Marrakesh, Morocco	*Leveraging Image Captions for Selective Whole Slide Image Annotation*
Breininger, Katharina	07.11.24 / 10.11.24	BRAGFOST 2024 Symposium, Piracicaba, Brazil	*Mind the gap: The role of domain generalization for machine learning (in healthcare)*
Budday, Silvia	18.03.24 / 22.03.24	GAMM Annual Meeting 2024, Magdeburg, Germany	Organization of Section S02 “Biomechanics”
Budday, Silvia	11.04.24 / 12.04.2024	Interpore Benelux Chapter, Esch sur Alzette, Luxembourg	*Modeling region-dependent properties of human brain tissue*
Budday, Silvia	26.06.24 / 27.06.24	The Pulsing Brain Meeting, Brighton, UK	*Human brain tissue mechanics: experiments, modeling, and simulation*
Budday, Silvia	21.07.24 / 26.07.24	WCCM 2024, Vancouver, Canada	*Effect of region-dependent material properties of human brain tissue during surgical procedures*
Budday, Silvia	30.07.24 / 01.08.24	CMBBE 2024, Vancouver, Canada	*Combining data-driven and physics-based modeling to predict the behavior of human brain tissue*
Budday, Silvia	04.09.24 / 06.09.24	VPH 2024, Stuttgart, Germany	*Challenges and perspectives in human brain tissue modeling*
Budday, Silvia	09.09.24 / 12.09.24	Evolution and development of nervous system, Zadar, Croatia	*Mechanics in human brain development*
Fabry, Ben	03.06.24 / 05.06.24	IUTAM 2024, Seville, Spain	*High-throughput measurements of viscoelastic cell properties: Potential and limitations*
Falk, Sven	24.06.24	Pre-FENS Meeting, Vienna, Austria	*Overcoming the barriers in making new neurons in the adult brain: lessons from nature*
Franze, Kristian	06.03.24 / 09.03.24	Forces across scales, Porto, Portugal	*The chemo-mechanical regulation of neuronal development and regeneration*
Franze, Kristian	07.05.24 / 08.05.24	2024 BioAFM Conference, Freising, Germany	*Using AFM to Measure and Manipulate Brain Tissue Stiffness In Vivo*

Franze, Kristian	28.05.24	Young Embryologist Network (YEN) Conference, Francis Crick Institute, London, UK	*The chemomechanical regulation of brain development*
Franze, Kristian	25.06.24 / 29.06.24	FENS Forum 2024, Vienna, Austria	*The mechanical regulation of brain development*
Franze, Kristian	01.07.24 / 03.07.24	European Amphibian Conference 2024, Bordeaux, France	*Mechanobiology of nervous system development and pathology*
Franze, Kristian	21.09.24 / 24.09.24	25th Biennial Meeting of the International Society for Developmental Neuroscience, Montpellier, France	*The mechanical regulation of neuronal development*
Franze, Kristian	03.10.24	11th Developing Brains Conference, Karolinska Institute, Stockholm, Sweden	*The chemo-mechanical regulation of neuronal development*
Franze, Kristian	11.10.24 / 14.10.24	Xenopus Resources and Emerging Technologies (XRET) Meeting, Woods Hole, MA, USA	*Measuring and manipulating tissue mechanics to understand brain development in Xenopus laevis*
Frischknecht, Renato	25.06.24 / 29.06.24	FENS Forum 2024, Vienna, Austria	*ECM Remodeling by ADAMTS5 is Critical for Inactivity-Induced Homeostatic Plasticity Mechanisms*
Frischknecht, Renato	11.09.24 / 13.09.24	DGMB Annual Meeting, Regensburg, Germany	*Extracellular proteolytic cascade remodels the ECM to promote structural plasticity*
Guck, Jochen	12.03.24 / 13.03.24	MPHF Selection Symposium, Göttingen, Germany	Member of the Nomination Committee
Guck, Jochen	26.06.24 / 28.06.24	Annual Meeting of Alexander von Humboldt Foundation, Berlin, Germany	*What is a physicist doing in biology and medicine?*
Guck, Jochen	17.07.24	Symposium: Mechanical Interactions of Living Cells with their Environment, University of Bayreuth, Bayreuth, Germany	Participation only
Karow, Marisa	12.03.24 / 15.03.24	SY-Stem, Vienna, Austria	*Dynamic X-chromosomal reactivation enhances female brain resilience in the context of neurodevelopment disorders*
Karow, Marisa	13.10.24 / 16.10.24	EMBO Workshop, Capri, Italy	*Unlocking human brain complexity using 3D culture and single cell omics*
Kobow, Katja	16.08.24 / 24.08.24	GRS + GRC 2024, Waterville Valley, USA	*3D-Chromatin Dynamics in Epilepsy*
Kobow, Katja	06.09.24 / 11.09.24	IEC 2024, Rome, Italy	*Exploring Chromatin Dynamics in Epilepsy through HiC*
Kobow, Katja	19.09.24 / 22.09.24	INES 2024, Erlangen, Germany	*Post-surgical evaluation of human brain tissue*
Kobow, Katja	03.10.24 / 05.10.24	SEEP 2024, Madrid, Spain	*Mutaciones somáticas en MCD*
Kürten, Stefanie	16.05.24	Vortragsreihe am Klinikum St. Marien Amberg in Zusammenarbeit mit der DMSG, Amberg, Germany	*Besser keine Milch bei Multipler Sklerose?*
Kürten, Stefanie	25.09.24 / 27.09.24	Tripartite Anatomy Meeting 2024, Graz, Austria	Participation only
Kürten, Stefanie	06.11.24 / 08.11.24	DGN-Kongress 2024, Berlin, Germany	Presidential lecture: *Entzündliche ZNS-Erkrankungen*
Kürten, Stefanie	22.11.24	B-Zell-Forum November 2024; Online-Meeting	*Mehr als nur Bauchgefühl: Das Mikrobiom und MS*
Laun, Fred	08.05.24 / 10.05.24	#RÖKO2024, Wiesbaden, Germany	Organization and moderation of an MR elastography session: DRG trifft DS-ISMRM: MR-Elastographie
Möllmert, Stephanie	29.02.24 / 01.03.24	Controlled Release Society Conference, Bad Dürkheim, Germany	*Brillouin microscopy - From underlying principles to current applications*

Möllmert, Stephanie	26.01.24 / 01.02.24	SPIE Photonics West, San Francisco, USA	*Current applications of Brillouin microscopy: from sub-cellular mechanics to spinal cord repair*
Möllmert, Stephanie	26.06.24 / 27.06.24	46th NDI3 Conference, Borstel, Germany	*Unveiling the Mechanics of Life: A Cross-Disciplinary Approach to Health and Disease*
Paulsen, Friedrich	25.09.24 / 27.09.24	Tripartite Anatomy Meeting 2024, Graz, Austria	*Extracellular matrix and synaptic alterations in epileptic brain pathologies: A proteomic analysis of MOGHE*
Sack, Ingolf	08.05.24 / 10.05.24	#RÖKO2024, DRG trifft DS-ISMRM: MR-Elastographie, Wiesbaden, Germany	*MR-Elastographie: Grundlagen und Anwendungen in Klinik und Forschung*
Steinmann, Paul	End of February 2024 / End of August 2024	Australian Research Council Industrial Training and Transformation Centre for Joint Biomechanics (ARC ITTC-JB) at Queensland University of Technology (QUT) in Brisbane, Australia	Research stay: Joint research projects with Prof. Peter Pivonka, Prof. Saulo Martelli, and other researchers.
Wehner, Daniel	18.01.24	Ulm University, SFB/CRC1149 Trauma Seminar Series, Ulm, Germany	*Axonal regeneration – a matter of ECM composition, structure, and mechanics*
Wehner, Daniel	20.02.24	University of Manchester, Advances in Bioscience Seminar Series, Manchester, United Kingdom	*Axonal regeneration – a matter of ECM composition, structure, and mechanics*
Wehner, Daniel	12.03.24 / 15.03.24	25th Conference of the Society for Developmental Biology Germany, Osnabrück, Germany	*Axon regeneration in the vertebrate central nervous system: It's all in your ECM*
Wehner, Daniel	30.04.24	University of Bayreuth, Molecular Bioscience Seminar Series, Bayreuth, Germany	*Axonal regeneration – a matter of ECM composition, structure, and mechanics*
Wehner, Daniel	15.05.24	University of Cologne, Regeneration Symposium, Cologne, Germany	*How are regeneration-permissive environments established?*
Wehner, Daniel	20.06.24	Brandenburg University of Technology, Cell Biology Symposium, Senftenberg, Germany	*How are regeneration-permissive environments established?*
Wehner, Daniel	27.06.24	University of Cologne, Institute of Zoology Seminar Series, Cologne, Germany	*ECM composition, structure, and mechanical properties direct axon regeneration in the vertebrate central nervous system*
Wehner, Daniel	17.07.24	Symposium: Mechanical Interactions of Living Cells with Their Environment, University of Bayreuth, Bayreuth, Germany	*How are environments with regeneration-permissive mechanical properties established?*
Wehner, Daniel	11.09.24 / 13.09.24	Annual Meeting of the German Society for Matrix Biology (DGMB), Regensburg, Germany	*ECM composition, structure, and mechanical properties direct axon regeneration in the vertebrate CNS*
Wehner, Daniel	24.09.24 / 27.09.24	Matrix Biology Europe Conference 2024, Lyon, France	*ECM composition, structure, and mechanical properties direct axon regeneration in the vertebrate CNS*
Wehner, Daniel	07.10.24 / 11.10.24	EMBO Conference - The Molecular and Cellular Basis of Regeneration and Tissue Repair, Saint-Jean-Cap-Ferrat, France	*Axon regeneration in the vertebrate central nervous system: It's all in your ECM*

6.3.2 CONFERENCES OF (POST-)DOCTORAL RESEARCHERS

Sophia Auer

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
24.09.24 / 27.09.24	118. Jahrestagung der Anatomischen Gesellschaft	Graz, Austria	Poster: *Extracellular Matrix and Synaptic Alterations in Epileptic Brain Pathologies: A Proteomic Analysis of MOGHE*

Erica Cecchini

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
07.09.24 / 11.09.24	EEC2024	Rome, Italy	Talk 1: *Altered oligodendrocyte function in mild cortical malformation associated with epilepsy* Talk 2: *Brain somatic mosaicism of sex chromosomes defines MOGHE*

Rittika Chunder

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation/participation only
25.09.24 / 27.09.24	Tripartite Anatomy Meeting 2024, Graz, Austria	Graz, Austria	Participation only
09.10.24 / 11.10.24	Hertie MS Symposium	Schloss Liebenberg, Germany	Talk: *You become what you eat" (The gut-brain axis in MS)*

Ezgi Erterek

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
25.06.24 / 29.06.24	FENS Forum 2024	Vienna, Austria	Participation only

Soheil Firooz

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
26.02.24 / 28.02.24	5th African Conference on Computational Mechanics (Africomp)	Cape Town, South Africa	Talk: *Mean zero artificial diffusion for stable finite element approximation of convection dominated problems.*
03.06.24 / 07.06.24	9th European Congress on Computational Methods in Applied Sciences and Engineering, (ECCOMAS)	Lisbon, Portugal	Talk: *Mean zero artificial diffusion for stable finite element approximation of convection dominated problems.*
01.07.24 / 05.07.24	International Workshop on: The coupled nonlinear continuum theory horizon	Castro-Urdiales, Spain	Talk: *Mean zero artificial diffusion for stable finite element approximation of convection dominated problems.*

16.09.24 / 18.09.24	43rd Solid Mechanics Conference, (SolMech)	Wroclaw, Poland	Talk: *Extended General Interfaces.*
25.09.24 / 29.09.24	Advances in peridynamic material modeling	Venice, Italy	Talk: *Nonlocal Elasticity via Continuum-Kinematics-Inspired Peridynamics: Theory, Computation and Applications.*

Guillaume Flé

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
21.10.24 / 23.10.24	ITEC	Lyon, France	Talk: *Imaging the electromechanical properties of the mouse brain during transcranial electrical stimulation: numerical simulations*

Alexander Greiner

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation/participation only
29.01.24 / 02.02.24	ELACTAM	Havanna, Cuba	Talk: *Modeling the Porous Properties of Brain Tissue*
18.03.24 / 22.03.24	GAMM Annual Meeting	Magdeburg, Germany	Talk: *Modeling the Porous Properties of Brain Tissue*

Jan Hinrichsen

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation/participation only
18.03.24 / 22.03.24	GAMM Annual Meeting	Magdeburg, Germany	Talk: *Using dropout-based active learning and surrogate models in the inverse viscoelastic parameter identification of human brain tissue.*
30.06.24 / 03.07.24	ESBiomech 2024	Edinburgh, Scotland	Talk: *Viscoelastic region-specific inverse parameter identification for human brain tissue*

Maik Hintze

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation/participation only
25.09.24 / 27.09.24	Tripartite Anatomy Meeting 2024, Graz, Austria	Graz, Austria	Talk: *Development of an in vitro culture model of astrocytes from human brain biopsies to study astrocyte cell biology*

Jakob Jordan

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
30.09.24 / 2.10.24	Physics of Cancer, POC	Leipzig, Germany	Poster: *Rapid stiffness mapping in soft biologic tissues with micrometer resolution using multifrequency time-harmonic elastography*
21.10.24 / 23.10.24	ITEC 2024	Lyon, France	Talk: *Optical multifrequency time harmonic elastography (OMTHE) for high-resolution, multiscale stiffness mapping*

Kristina Karandasheva

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
07.09.24 / 11.09.24	EEC2024	Rome, Italy	Poster: *Exploring Chromatin Dynamics in Epilepsy through Hi-C*

Julia Kolb

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
12.03.24 / 15.03.24	Joint international GfE/DSDB meeting	Osnabrück, Germany	Poster: *SLRPs inhibit CNS regeneration by modifying structural and mechanical properties of the lesion environment*

Markus Lorke

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
15.09.24 / 18.09.24	CESB 2024	Nuremberg, Germany	Poster: *In situ crosslinked oxidized hyaluronic acid-based hydrogels for neural tissue engineering*

Olga Lyraki

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
18.09.24 / 19.09.24	Grand Opening Symposium, MPZPM	Erlangen, Germany	Participation only

Mathias Öttl

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
13.03.24 / 15.03.24	PRL Symposium	Erlangen, Germany	Poster: *Semantic Zero-Shot-Style Diffusion Models for Semi-Supervised Histopathology Segmentation*
29.09.24 / 04.10.24	ECCV 2024	Milan, Italy	Poster: *Style-Extracting Diffusion Models for Semi-Supervised Histopathology Segmentation*

Zhaoya Pan

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
15.06.24 / 19.06.24	Pattern Recognition Symposium	Obertrum, Austria	Poster*: Towards carcinoma classification via CLE images*

Bartomeu Perelló Amorós

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
25.06.24 / 29.06.24	FENS Forum 2024	Vienna. Austria	Poster: *ECM remodeling by ADAMTS5 is crucial for inactivity-induced homeostatic plasticity mechanisms*

Stefan Rampp

From/to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
07.09.24 / 11.09.24	15th European Epilepsy Congress	Rome, Italy	Talk 1: *MRI physics, sequences and MRI protocol VIREPA MRI* Talk 2: *The current role of MEG within epilepsy surgery*
19.09.24 / 22.09.24	14th International Summer School for Neuropathology and Epilepsy Surgery	Erlangen, Germany	Talk: *Structural and functional neuroimaging*
15.05.24 / 18.05.24	ILAE School on Neuroimaging 2024	Potsdam, Germany	Member of the organizing committee

Nina Reiter

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
18.03.24 / 22.03.24	GAMM Annual Meeting	Magdeburg, Germany	Talk: *Microstructure-informed regional constitutive modeling of human brain tissue* Poster: *Constitutive modeling of human brain tissue*
21.07.24 / 26.07.24	WCCM	Vancouver, Canada	Talk: *Microstructure-informed, region-specific viscoelastic modeling of human brain tissue* Poster: *Direction-dependent mechanics of human corpus callosum and lower brain stem*
30.07.24 / 01.08.24	CMBBE	Vancouver, Canada	Talk: *Influence of postmortem degradation on mechanical properties of human brain tissue*

Laura Ruhland

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
29.05.24 / 31.05.24	EMMC 19	Madrid	Talk: *Viscoelastic characterization of ultrasoft material by unifying different time and length scales*

Maria Tarczewska

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
06.03.24 / 09.03.24	Forces across Scales	Porto, Portugal	Poster: *Spinal Cord Regeneration in Xenopus laevis*

Michael Tranchina

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
12.03.24 / 15.03.24	SY-Stem	Vienna, Austria	Poster: *The role of mechanics in orchestrating neural lineage decisions*
27.05.24 / 30.05.24	Lab retreat	Ofir, Portugal	Talk: *The role of mechanics in orchestrating neural lineage decisions*

Sebastián Vásquez-Sepúlveda

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
06.03.24 / 09.03.24	Forces across Scales	Porto, Portugal	Poster: *In vivo model for the mechanics of brain development*

Yashasvi Verma

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
03.06.24 / 07.06.24	ECCOMAS	Lisbon, Portugal	Talk: *A Continuum Human Brain Model with Embedded Vasculature to Investigate In-Vivo Testing*

Kathrin Welsch

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
29.09.24 / 04.10.24	The cytoskeleton as active matter	Bad Honnef	Poster: *Mechanical interactions between neural stem cells and their niche*

Frauke Wilm

From / to	Name of conference	Location	Title of own presentation / title of own poster presentation / participation only
10.03.24 / 12.03.24	Bildverarbeitung für die Medizin	Erlangen	Talk: *Appearance-based Debiasing of Deep Learning Models in Medical Imaging*
06.10.24 / 08.10.24	MICCAI	Marrakesh	Talk: *Domain and Content Adaptive Convolutions for Cross-Domain Adenocarcinoma Segmentation*

6.4 SUMMER SCHOOLS / AUTUMN SCHOOLS

Sophia Auer

From / to	Name of school	Location
15.05.24 / 16.05.24	ILAE School on Neuroimaging 2024	Online participation

Erica Cecchini

From / to	Name of school	Location
19.09.24 / 22.09.24	INES 2024	Erlangen, Germany

Kristina Karandasheva

From / to	Name of school	Location
07.05.24 / 16.05.24	Deep Learning for Microscopy Image Analysis (EMBO-DL4MIA)	Human Technopole, Milan, Italy
19.09.24 / 22.09.24	INES 2024	Erlangen, Germany

Nina Reiter

From / to	Name of school	Location
15.05.24 / 16.05.24	ILAE School on Neuroimaging 2024	Online participation
15.07.24 / 18.07.24	Discovering Cell Biology	Pisa, Italy
19.09.24 / 22.09.24	INES 2024	Erlangen, Germany

7 APPENDICES

7.1 APPENDIX 1: PROGRAM OF THE 1ST EBM UPDATE MEETING

Program of the
1st EBM Update Meeting
February 9, 2024
Leuchs-Russell Auditorium, A.1.500, Staudtstr. 2, 91058 Erlangen

Organizational Program

Time	Program Segment	Lead
9:30 – 10:30	EBM Executive Board Meeting	Paul Steinmann, Silvia Budday
10:30 – 12:30	EBM Members' General Assembly	Paul Steinmann, Silvia Budday

Scientific Program

Time	Research Progress Report on	Speaker
PROJECT: ESTABLISHING MAGNETIC RESONANCE ELASTOGRAPHY AT FAU		
12:30 – 12:40	**Y**	Frederik Laun
12:40 – 14:00	LUNCH BREAK	
CROSS-SECTIONAL RESEARCH AREA X		
14:00 – 14:30	**X01 – X03**	Jing Guo / Ingolf Sack
FOCAL RESEARCH AREA A: CEREBRAL MECHANICS		
14:30 – 15:00	**A01 – A05**	Kristian Franze
15:00 – 15:30	COFFEE BREAK + POSTER EXHIBITION	
FOCAL RESEARCH AREA B: SPINAL MECHANICS		
15:30 – 16:00	**B01 – B05**	Stephanie Möllmert
FOCAL RESEARCH AREA C: CELLULAR MECHANICS		
16:00 – 16:30	**C01 – C05**	Vasiliy Zaburdaev
16:30 – 18:00	RECEPTION + POSTER EXHIBITION	

7.2 APPENDIX 2: PROGRAM OF THE 2ND EBM RETREAT

Program of the
2nd EBM Retreat
October 10 – 11, 2024
Fraunhofer-Forschungscampus Waischenfeld

Day 1: October 10, 2024			
Time	**Project**	**Title**	**Lecturer**
from 9:00	ARRIVAL		
9:30 – 9:40	A01	*In silico* modeling of brain malformations	Jan Hinrichsen
9:40 – 9:50	A02	Quantitative characterization of brain malformations	Erica Cecchini Sophia Auer Stefan Rampp
9:50 – 10:00		*Discussion*	
10:00 – 10:10	A03	*In vitro* model for the mechanics of early brain development	Clara Froidevaux
10:10 – 10:20	A04	The role of mechanics in orchestrating neural lineage decisions	Michael Tranchina
10:20 – 10:30	A05	*In vivo* model for the mechanics of brain development	Niklas Gampl
10.30 – 11.00	COFFEE BREAK		
11:00 – 11:05	B01	*In silico* modeling of spinal cord regeneration	Oskar Neumann Rahul G. Ramachandran
11:05 – 11:15		*Discussion*	
11:15 – 11:25	B02	Pre and post metamorphosis spinal cord regeneration in frogs	Maria Tarczewska
11:30 – 12:30	**EBM Executive Meeting || Brainstorming Collaborations**		
12:30 – 13:30	LUNCH BREAK		
13:30 – 16:30	**Teambuilding Activity:** Speed Mentoring Hike to Rabenstein Castle Beer Garden		

16:40 – 16:50	**B03**	The determinants of spinal cord mechanics in homeostasis	Stephanie Möllmert
16:50 – 17:00	**B04**	Spinal cord mechanics in a mouse model of multiple sclerosis	Maik Hintze
17:00 – 17:10	**B05**	*In vivo* mechanical manipulation of spinal cord regeneration	Stephanie Möllmert
17:10 – 17:15	**C01**	*In silico* modeling of mechanical cell-matrix interactions	Soheil Firooz Pritha Dolai
17:15 – 17:25		*Discussion*	
17:25 – 17:35	**C02**	The role of mechanics for neuronal ‘plasticity‘	Ezgi Erterek
17:35 – 17:45	**C03**	The role of mechanics in synchronized neuronal activity	Kristina Karandasheva
18:00 – 19:30	DINNER		
from 19:30	**After Dinner Talk:** Speaker: Ben Fabry Title*: ”Collective Behavior of Penguins”*		

Day 2: October 11, 2024			
Time	**Project**	**Title**	**Lecturer**
8:00 – 9:20	BREAKFAST || CHECK-OUT (ROOMS)		
9:20 – 11:10	**EBM General Assembly** incl. brief presentations by the new associated PIs		
11:10 – 11:20		Establishing magnetic resonance elastography at FAU	Guillaume Flé
11:20 – 11:50	COFFEE BREAK		
11:50 – 12:00	C04	Cellular differentiation in brain tissue-like matrices	Shanice Heidenreich
12:00 – 12:10	C05	Molecular mechanisms of neuronal mechanotransduction	Lars Bischof
12:10 – 12:20	X01	Model-based reconciliation of *ex vivo* and *in vivo* test data	Laura Ruhland Yashasvi Verma Jakob Ludwig
12:20 – 12:30		*Discussion*	
12:30 – 13:30	LUNCH BREAK		
13:40 – 15:40	**Guest Talk:** Speaker: Heather Hofmeister (Goethe University Frankfurt) Title: *"When we know better, we can do better" - different generations and expectations in German academic science*		
15:40 – 16:10	COFFEE BREAK		
16:10 – 16:20	X02	Data analysis and machine learning for heterogeneous, cross-species data	Frauke Wilm
16:20 – 16:30	X03	Engineering brain tissue-like matrices	Markus Lorke
16:45	DEPARTURE		

Each EBM (post)doctoral researcher will give a 2-minute presentation, followed by an 8-minute discussion if there is only one presenter per project. If there are two or more presenters per project, a total of 10 minutes will be allocated for discussion.

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