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Erlangen-Nürnberg

EBM Symposium 2025

Exploring Brain Mechanics (EBM)

EBM

BOOK OF ABSTRACTS

September 30 - October 1, 2025
Max Planck Institute for the Science of Light
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Local Scientific Committee:
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CONTENT


EXPLORING BRAIN MECHANICS
EBM
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1 PROGRAM

DAY 1 – SEPTEMBER 30, 2025

08:30 – 09:20
Registration & Welcome Coffee

09:20 – 09:30
Welcome Address

Chairperson: Paul Steinmann

09:30 – 10:00
Medha M. Pathak (Irvine, US)
Forces at play: Deciphering the role of Piezo1 in neural development

10:00 – 10:15
Sudipta Mukherjee (Erlangen, DE)
Mechanical regulation of long-range chemical signaling in the developing Xenopus laevis brain

10:15 – 10:45
Alain Goriely (Oxford, GB)
The multiscale principles of neuronal path-finding

10:45 – 11:15
Coffee Break

11:15 – 11:45
Katie Long (London, GB)
How the extracellular matrix shapes the developing human brain

11:45 – 12:00
Jan Hinrichsen (Erlangen, DE)
Towards an in silico model of brain malformations in FCD II epilepsies

12:00 – 12:30
Roberto Toro (Paris, FR)
Mechanical morphogenesis and the development and evolution of the brain

12:30 – 13:30
Lunch Break & Meet the Mentor

Chairperson: Marisa Karow

13:30 – 14:00
Magdalena Götz (Munich, DE)
Novel mechanisms of neurogenesis and neural repair

14:00 – 14:15
Theo Paillard (Paris, FR)
GPR161 mechanosensitivity at the primary cilium drives neuronal saltatory migration

14:15 – 14:45
Manuel Salmeron-Sanchez (Glasgow, GB)
Mechanical signatures of glioma cells in response to matrix rigidity

14:45 – 16:15
Poster Session + Coffee/Beer

16:15 – 16:45
Daniel M. Suter (West Lafayette, US)
Mechanosensing in neuronal growth and guidance

16:45 – 17:00
Oliver De La Cruz (Barcelona, ES)
Stiffness-regulated microtubule stability controls Tau phosphorylation and nuclear localization in neurons

17:00 – 17:30
Michael Krieg (Barcelona, ES)
Illuminating brain mechanics in an animal without a brain – lessons learned from C. elegans

18:15 – 23:00
Networking Reception & Conference Dinner

DAY 2 – OCTOBER 1, 2025

09:00 – 09:30
Registration & Welcome Coffee

Chairperson: Silvia Budday

09:30 – 10:00
Lynne E. Bilston (Sydney, AU)
In vivo brain mechanics measurements: where are we now?

10:00 – 10:15
Noah Jaitner (Berlin, DE)
Combined MR elastography and 3D MRI deformation mapping towards in vivo assessment of solid stress in glioblastoma

10:15 – 10:45
Philip V. Bayly (St. Louis, US)
Using MRI to estimate mechanical properties, strain and stress in the brain

10:45 – 11:15
Coffee Break

11:15 – 11:45
Mehmet Kurt (Washington, US)
Your brain in motion: How neuroimaging and computer vision transform our understanding of brain biomechanics

11:45 – 12:00
Stefan Rampp (Erlangen, DE)
(Towards) linking mechanical properties with neuronal function

12:00 – 12:30
Matteo Mario Bonsanto (Lübeck, DE)
Mechanical fingerprint: the challenging path to mechanical brain tumor diagnostics

12:30 – 13:30
Lunch Break & Meet the Mentor

Chairperson: Kristian Franze

13:30 – 14:00
Lucy V. Hiscox (Cardiff, GB)
Brain tissue mechanics in dementia: Insights from magnetic resonance elastography

14:00 – 14:15
Vickie Shim (Auckland, NZ)
Brain dynamic changes after mTBI and repetitive head impacts in adolescent rugby players

14:15 – 14:30
Riyi Shi (West Lafayette, US)
Concussive injuries induce neuronal stress-dependent tau mislocalization to dendritic spines with acrolein and functional network alteration in TBI-on-a-chip

14:30 – 15:00
Coffee Break

15:00 – 15:15
Manuel P. Kainz (Graz, AT)
Pores and prejudices: An experimental evaluation of Darcy's permeability in brain tissue with biomimetic hydrogels

15:15 – 15:30
Daniel Garcia-Gonzalez (Leganés, ES)
Mechanical and functional responses in astrocytes under alternating deformation modes

15:30 – 16:00
Paul A. Janmey (Philadelphia, US)
Mechanical properties of the brain and their effect on cell migration

16:00 – 16:30
Conference Closing

2 TALKS

*The talk abstracts are listed in the order of the **speaker**s' presentations, according to the program.*

T01: FORCES AT PLAY: DECIPHERING THE ROLE OF PIEZO1 IN NEURAL DEVELOPMENT

Pathak, Medha M.

Department of Physiology & Biophysics, University of California, Irvine, US

Mechanical forces have long been recognized as fundamental drivers of development, yet the molecular mechanisms remained elusive. The discovery of mechanically gated ion channel Piezo1, recognized with a Nobel Prize, has begun to illuminate some of the underlying mechanisms. We previously demonstrated that Piezo1 directs lineage choice in human neural stem cells, with channel activity promoting neurogenesis while inhibition favors astrogenesis. Here, we demonstrate Piezo1's critical role in neural development through studies spanning molecular to tissue scales. Piezo1 knockout mice exhibit severe brain developmental defects, including disrupted neuroepithelial organization and impaired neuronal differentiation. We traced these defects to downregulated cholesterol biosynthesis, with phenotypes partially rescued by cholesterol supplementation. To study Piezo1 dynamics in human systems, we genetically engineered iPSCs to tag endogenous Piezo1 with HaloTag, enabling measurements of channel localization and activity at single-channel resolution. In hiPSC-derived brain organoids, Piezo1 localizes preferentially to mechanically active regions at the apical border and cell-cell junctions, with knockout organoids showing altered lumen morphology. Our findings establish Piezo1 as a key mechanotransducer linking physical forces to metabolic regulation and cellular fate decisions in neural development, while our HaloTag tools provide new capabilities for studying mechanotransduction dynamics in human tissue models.

T02: MECHANICAL REGULATION OF LONG-RANGE CHEMICAL SIGNALING IN THE DEVELOPING XENOPUS LAEVIS BRAIN

Mukherjee, Sudipta[1,4,6]; Pillai, Eva K.[2,3,4]; Gampl, Niklas[1,6]; McGinn, Ross J.[4,5]; Mooslehner, Katrin A.[1,4,6]; Becker, Julia M.[1,4,6]; Winkel, Alex[4]; Thompson, Amelia J.[4]; Franze, Kristian[1,4,6]

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[6] *Max-Planck-Zentrum für Physik und Medizin, Erlangen, Germany*

Developmental processes rely on both chemical and mechanical signals, but how these two signals interact is still poorly understood. We here identified a crosstalk between tissue stiffness and long-range chemical signaling *in vivo*, in the developing Xenopus laevis brain. Knocking down Piezo1, a mechanosensitive ion channel, either in the brain tissue or in retinal ganglion cells (RGCs) growing through the brain, both led to axon pathfinding errors. Piezo1 knockdown in the neuroepithelium led to decreased expression of the chemical guidance cues semaphorin3A and slit1, as well as to a decrease in brain tissue stiffness. Tissue softening observed in Piezo1 knockdown embryos was mediated by a decrease in the cell-cell adhesion proteins NCAM1 and N-cadherin. Furthermore, tissue stiffness turned out to be a critical regulator of the expression of sema3A and slit1, both *in vitro* and *in vivo*. Decreased environmental stiffness reduced the expression of both chemical guidance cues, while increasing tissue stiffness initiated their ectopic expression. As Sema3A and Slit1 are diffusible cues that act over large distances, local mechanical signals may impact cell function far away from the actual stimulus. Due to the conserved nature of the molecules investigated, the phenomenon is likely relevant across diverse biological systems.

T03: THE MULTISCALE PRINCIPLES OF NEURONAL PATH-FINDING

Goriely, Alain

Mathematical Institute, Oxford, United Kingdom

The guidance of neuronal axons during neurodevelopment is a complex process shaped by biochemical and biomechanical cues. Among these, axonal durotaxis—the directed growth of axons in response to stiffness gradients in the extracellular environment—has emerged as a key factor in neuronal pathfinding. In this talk, we introduce a three-scale model that captures the mechanochemical interactions underlying axonal durotaxis. At the molecular scale, we describe how molecular clutch dynamics mediate the mechanical interaction between the growth cone and its substrate. At the growth-cone scale, we integrate these interactions into a model for traction generation. Finally, at the whole-cell scale, we represent the axon as a filament growing on an adhesive substrate, influenced by durotactic forces. Our model predicts that axons can exhibit both positive and negative durotaxis, leading to the formation of preferential stiffness zones that may influence neural connectivity patterns. Furthermore, we show that axons undergo reflection and refraction at stiffness boundaries, a mechanism that could contribute to the large-scale organization of neuronal networks. To validate our framework, we apply it to a biological scenario where durotaxis has been implicated in *in vivo* axon guidance. These findings provide a fundamental mechanistic theory of axonal mechanotaxis, with implications for understanding neural circuit formation, the emergence of folding patterns in the cerebral cortex, and broader principles of brain development across species.

T04: HOW THE EXTRACELLULAR MATRIX SHAPES THE DEVELOPING HUMAN BRAIN

Long, Katie

Centre for Developmental Neurobiology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE1 1UL, United Kingdom; MRC Centre for Neurodevelopmental Disorders, King's College London, London SE1 1UL, United Kingdom.

The shape of the human brain has long been thought to be important for its function, with many cognitive impairments and neurodevelopmental disorders associated with changes in cortical structure, folding, size, and shape. However, we currently understand relatively little about the morphogenesis of the developing human brain, including how the intricate pattern of cortical folding arises. My lab aims to address this gap in our knowledge using slice cultures of human fetal cortex, examining the role of the tissue environment in a system as physiologically close to the human brain as possible. Our recent work has shown that the extracellular matrix (ECM) is sufficient to drive the formation of cortical folds in this system and is needed to maintain these folds once formed. However, we still know relatively little about the ECM expressed in the fetal brain and its many different functions during development. Our current work has analyzed the composition of the ECM in the human fetal cortex via proteomic and mechanical analysis, providing vital information on not only what ECM is present, but when and where it is expressed. We are now investigating the function of this ECM network in typical development, and in developmental malformations and injury.

T05: TOWARDS AN *IN SILICO* MODEL OF BRAIN MALFORMATIONS IN FCD II EPILEPSIES

Hinrichsen, Jan[1]; Reiter, Nina[1]; Zarzor, Mohammad Saeed[1]; Hoffmann, Lucas[2]; Wilm, Frauke[4]; Thies, Mareike[4]; Blümcke, Ingmar[2]; Breininger, Katharina[3,4]; Paulsen, Friedrich[5]; Delev, Daniel[6]; Budday, Silvia[1]

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[6] *Department of Neurosurgery, University Hospital Erlangen, Germany*

Drug-resistant focal epilepsy can be successfully treated via neurosurgical resection of the carefully located seizure onset zone to minimize additional comorbidity. In the present study, we addressed focal cortical dysplasia ILAE Type 2 (FCD2), which is a common pathology in pediatric patients with focal epilepsy. FCD2 is histopathologically characterized by cytoarchitectonic disturbances of the human neocortex and genetic alterations in the MTOR signaling pathway. Our goal is to develop a model that can explain cortical folding patterns in individual patients by capturing variations in the cell proliferation and migration behavior. To this end, we mechanically tested fresh, surgically resected tissue and identified constitutive parameters using inverse parameter identification. Additionally, we performed histological analysis and cell density estimation via a neural network. We then used these data to inform an *in silico* finite element model describing cortical folding as a finite growth problem coupled with the evolution of cell density. Initial results show that this model can explain how variations in cell proliferation and migration lead to cortical malformations.

T06: MECHANICAL MORPHOGENESIS AND THE DEVELOPMENT AND EVOLUTION OF THE BRAIN

Toro, Roberto

Institut Pasteur, Université Paris Cité, Unité de Neuroanatomie Appliquée et Théorique, F-75015 Paris, France

The development of a complex brain is often assumed to result from genetic and activity-dependent processes. Our work explores the extent to which a third factor – mechanical morphogenesis – can also play a causal role in shaping the development and evolution of the brain. We call mechanical morphogenesis the process leading to the emergence of complex forms in living and non-living matter as a result of growth. Using computational modelling and multimodal imaging data from many time points of the development of a folding brain, and from many primate species across the phylogenetic tree, we study the emergence of brain organization at multiple levels: the changes of the cerebral surface, cortical thickness patterns, and cortico-cortical connectivity. Our results suggest that mechanical morphogenesis could have a causal role in the formation of brain folding patterns, regional differences, and connections. Finally, we show evidence that the same mechanical processes that shape the landscape of brain folds and connections could also influence cognitive behavior.

T07: NOVEL MECHANISMS OF NEUROGENESIS AND NEURAL REPAIR

Götz, Magdalena[1,2,3]; Masserdotti, Giacomo[1,2]; Saghatelyan, Armen[4]

[1] *Biomedical Center, LMU, Planegg-Martinsried, Germany*
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[4] *Brain and Mind Institute, University of Ottawa, Ottawa, Canada*

Cell organelles perform similar functions in all cells, such as centrosomes organizing the cytoskeleton, or mitochondria providing an energy supply. However, we have recently identified profound differences between organelles of even closely related cells. I will describe this for the centrosomes, which differ by more than half of their proteome between neural stem cells and neurons, and mitochondria that differ by a fifth of their proteome between, e.g., astrocytes and neurons. For both, I will also describe the functional relevance of this heterogeneity of organelles between cells for disease and repair. I will then come to a third organelle, the cilium, and discuss how motile cilia of ependymal cells in the adult neural stem cell niche influence the behavior of adult neural stem cells *in vivo*. This influence is mediated by a TrpM-channel, and we propose that beating cilia of neighboring niche cells regulate adult neural stem cell activation and lineage progression by mechano-sensing. Indeed, further mechanical properties specify the adult neural stem cell niche, such as a different stiffness than the rest of the brain, and sheer stress also regulates adult neural stem cell behavior. Taken together, beyond classical signaling pathways and transcriptional regulation, heterogeneity of organelles and mechanical stimulation by cilia beating of neighboring niche cells are novel factors regulating neurogenesis in development and adulthood.

T08: GPR161 MECHANOSENSITIVITY AT THE PRIMARY CILIUM DRIVES NEURONAL SALTATORY MIGRATION

Paillard, Theo[1,2]

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The saltatory migration of neurons is a tightly regulated process critical for brain development, yet the role of mechanical forces in this context remains largely unexplored. We recently uncovered a mechanosensitive pathway in which the primary cilium (PC), a small sensory organelle at the cell surface, functions as a mechanical sensor to regulate neuronal migration. Using ex vivo brain slices and microfluidic systems that apply fluid shear stress, we showed that mechanical stimulation enhances neuronal migration through the G-protein-coupled receptor (GPCR) GPR161, located in the PC. This effect requires GPR161's intracellular Helix 8, a domain essential for the mechanosensitivity of GPCRs. Mechanotransduction through GPR161 activates a cAMP/PKA signaling cascade at the centrosome, leading to phosphorylation of NDE1, a regulator of the dynein complex. This phosphorylation is crucial for proper microtubule organization and the coordination of nucleokinesis during saltatory movement. Disruption of GPR161 or NDE1 function impairs this process, resulting in defective migration and cytoskeletal disorganization. Our work reveals a dynamic, cilium-based signaling axis that converts mechanical stimuli into molecular responses to control the pace of neuronal migration. It highlights a direct link between external mechanical forces and intracellular migration machinery, providing new insights into how brain architecture is shaped during development.

T09: MECHANICAL SIGNATURES OF GLIOMA CELLS IN RESPONSE TO MATRIX RIGIDITY

Dhawan, Udesh[1]; **Salmeron-Sanchez, Manuel**[1,2,3]

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Epithelial-to-Mesenchymal Transition (EMT) plays a key role during embryonic development, tissue regeneration, and immune response. However, EMT signaling is also strongly associated with cancer metastasis, and cells undergoing EMT typically adopt an elongated morphology. Interestingly, this elongated phenotype aligns with the cell morphology on hydrogels of specific stiffnesses. This similarity suggests that matrix stiffness may influence EMT cell signaling, promoting the adoption of an elongated morphology necessary for cell migration and invasion. We engineered polyacrylamide hydrogels of well-defined stiffnesses and demonstrated that placing primary glioma cells in environments mimicking the mechanical properties of the *in vivo* glioma tumor microenvironment activates Rho/ROCK signaling We identified key integrin subunits β1, β7, α1 and αV which might crosstalk with Rho/ROCK kinases to orchestrate an EMT phenotype e.g., an elongated morphology on stiffer substrates (10 and 30 kPa), in contrast to the round morphology observed on softer substrates (0.3 kPa). Consequently, cells cultured on stiffer hydrogels showed significantly higher expression of typical EMT markers N-Cadherin, Vimentin, Transforming Growth Factor Beta-I (TGF-βI), and transcription factor Snail. Furthermore, these cells exhibited markedly elevated expression of cancer stem cell markers such as Sox2, Oct4, ABCG2, Nestin, CD133, and EGFR. This suggests that matrix stiffness may not only promote the invasive properties of glioma cells but also impart them stemness abilities, creating a new bottleneck for existing therapeutic strategies. These findings raise an important question: Can we therapeutically modulate the stiffness of the glioma tumor microenvironment to regulate the gene and protein signatures of cells to prevent overactivation of EMT and acquisition of stemness abilities?

T10: MECHANOSENSING IN NEURONAL GROWTH AND GUIDANCE

Suter, Daniel M.

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Neuronal growth cones constantly sense the environment for cues and transduce them into directional movement. Growth cones can not only respond to well-characterized molecular cues, but also to mechanical, topographical, and electrical ones. Despite the increasing evidence that mechanical properties are critical for nervous system development, there are still significant gaps in our understanding of how neurons respond to the mechanical environment. We have previously shown that Aplysia bag cell neuronal growth cones use substrate-cytoskeletal coupling to advance on adhesive surfaces while producing traction forces. We have modified a computational motor-clutch model based on our experimental data obtained with force-calibrated microneedles. We have found that our modeling results are in good agreement with our experimental data with respect to response time and substrate deformation when growth cones respond to different substrate stiffnesses. Aplysia growth cones respond the fastest to soft substrates with a stiffness of 4 pN/nm. To further investigate growth cone mechanosensing, we cultured these neurons on uniform and gradient polyacrylamide hydrogels and found optimal growth at 3 kPa substrate stiffness. Our results support the idea that neurons engaging in adhesion-mediated growth have a preferred substrate stiffness in the soft range specific to the neuronal subtype.

T11: STIFFNESS-REGULATED MICROTUBULE STABILITY CONTROLS TAU PHOSPHORYLATION AND NUCLEAR LOCALIZATION IN NEURONS

Oliver De La Cruz, Jorge[1]; Guillamat, Pau[1]; Paganetti, Paolo[2,3]; Altadill-Cordero, Mar[1]; Trepat, Xavier[1,4,5]; Roca-Cusachs, Pere[1,6]

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Brain tissue stiffness changes significantly during development, aging, and in pathological conditions. In neurodegenerative diseases such as Alzheimer's disease (AD), these mechanical alterations occur in parallel with neuronal loss, synaptic dysfunction, and inflammation, but a causal relationship has not been established.

To explore this interplay, we developed a model using SH-SY5Y-derived neurons, differentiated through NGN2 overexpression and biochemical induction, and cultured on laminin-coated polyacrylamide hydrogels spanning different stiffnesses. Neurons on softer substrates exhibited reduced spreading, shorter neurites, and impaired axonal microtubule networks, as demonstrated by decreased tubulin acetylation. Pharmacological perturbation of the cytoskeleton revealed that microtubules are key determinants of neuronal morphology and mechanotransduction. Importantly, microtubule disruption in soft matrices led to increased phosphorylation of Tau, which accumulated in the nuclei.

These mechanosensitive effects were recapitulated in human iPSC-derived neurons from an AD patient carrying the APOE4/E4 genotype and an isogenic APOE3/E3 control. APOE4 neurons on soft substrates showed exacerbated AD-related phenotypes, including perinuclear and nuclear accumulation of phosphorylated Tau, suggesting a synergistic interaction between genetic risk and mechanical cues.

Our findings reveal a link between brain stiffness, cytoskeletal instability, and Tau pathology, suggesting that targeting mechanosensitive pathways could provide new therapeutic strategies for Alzheimer's disease.

T12: ILLUMINATING BRAIN MECHANICS IN AN ANIMAL WITHOUT A BRAIN – LESSONS LEARNED FROM *C. ELEGANS*

Krieg, Michael

IICFO - Institut de Ciències Fotòniques, Castelldefels, The Barcelona Institute of Science and Technology, Barcelona, Spain

The mechanical properties of the nervous system are fundamental to mechanosensing and mechanoprotection. Research over the last decades has suggested that the way a neuron responds to a mechanical signal is highly cell-type specific. If true, the universal principle of how cells respond to force will remain elusive, highlighting that the response is as diverse as the cell types subjected to it. This is partly due to the diverse mechanosensors and ion channels expressed in neurons, which respond to the same stress by inducing either membrane polarization or depolarization. During this talk, I will highlight some of the recent findings from my lab studying the response of *C. elegans* to mechanical forces. In particular, I will emphasize how the known wiring diagram of the nervous system enabled a systems-understanding of how mechanical stresses on the level of individual molecules relate to animal behavior. I will further touch upon the mechano-metabolon and the role of mitochondria in mechanophysiology.

T13: *IN VIVO* BRAIN MECHANICS MEASUREMENTS: WHERE ARE WE NOW?

Bilston, Lynne E.

Prince of Wales Medical Research Institute, UNSW, Sydney, Australia

It has been known for decades that the mechanical behavior of the brain is important for its normal physiological function, with neurological disorders arising when brain mechanics are disturbed. Brain mechanical behavior also plays a role in the pattern and extent of neurological damage during traumatic injury, due to its nonlinear and strain-rate sensitive behavior. Characterizing the complex mechanical behavior of brain tissue across the broad range of loading conditions that are of scientific and medical interest, especially in living humans, is a major challenge. Imaging-based methods such as Magnetic Resonance Elastography can provide quantitative estimates of linear viscoelastic properties at infinitesimal strains *in vivo*, and recently, approaches combining MRE with diffusion tensor imaging may enable the anisotropic behavior of brain white matter to be measured. However, these techniques do not provide us with low-strain-rate or large deformation brain properties, and properties measured using MRE have been difficult to adapt as inputs for parameterizing reliable constitutive models. Translating methods for measuring brain mechanical behavior to the clinic so they can be used as a marker of pathology and treatment response, using is slowly evolving. This presentation will provide an overview of the current state-of-the-art in human brain *in vivo* brain mechanics methods, and a perspective on future developments and research gaps in the field.

T14: COMBINED MR ELASTOGRAPHY AND 3D MRI DEFORMATION MAPPING TOWARDS *IN VIVO* ASSESSMENT OF SOLID STRESS IN GLIOBLASTOMA

Jaitner, Noah; Shahryari, Mehrgan; Schattenfroh, Jakob; Ludwig, Jakob; Meyer, Tom; Sack, Ingolf

Charité – Universitätsmedizin Berlin, Germany

Glioblastoma, an aggressive and rapidly growing brain tumor, affects surrounding tissue properties by exerting mechanical stress. While MR elastography (MRE) can measure tissue stiffness *in vivo*, assessing solid stress additionally requires 3D deformation analysis. In this study, we combined MRE and 3D MRI deformation mapping to quantify, for the first time, solid stress in patients with glioblastoma. Therefore, twenty-one patients and sixteen healthy controls underwent MRE at four frequencies between 20 and 40 Hz and T1-weighted MRI. Imaging examinations were performed using a 32-channel head coil in a 3T-MRI scanner. Shear wave speed maps, as a surrogate for brain stiffness, were generated, and brain displacement fields were calculated via image registration to a standard brain atlas. Peritumoral regions exhibited significantly greater strain than distant brain areas or those observed in healthy controls ($p < 0.001$). Stiffness correlated with volumetric strain in peritumoral regions ($R = -0.55$, $p = 0.009$), suggesting that tumor-induced solid stress leads to heterogeneous hyperelastic stiffening. A significant negative correlation between solid stress and days of survival was found ($R = -0.65$, $p = 0.02$), indicating the clinical relevance and prognostic potential of solid stress in glioblastoma patients.

T15: USING MRI TO ESTIMATE MECHANICAL PROPERTIES, STRAIN, AND STRESS IN THE BRAIN

Bayly, Philip V.

Mechanical Engineering and Materials Science, Washington University, 1 Brookings Drive, St. Louis, MO 63130, USA

The human brain undergoes large deformations, sometimes very quickly in traumatic brain injury (TBI), and or very slowly during brain development. Computer simulations of brain biomechanics offer enormous potential for understanding both TBI and brain development. However, models require biomechanical measurements to define the constitutive behavior of bulk tissue and interfaces. In addition, theoretical models should ideally be evaluated by comparison of their predictions to corresponding experimental measurements. Brain tissue may exhibit nonlinear, anisotropic, viscoelastic, and heterogeneous behavior, and the intricate connections between the brain and skull are also important in understanding brain mechanics. While studies of animal brains and ex vivo brain tissue have led to important insights, measurements of the response of the intact human brain are necessary and complementary. Efforts to understand the motion of the human brain *in vivo* are complicated by the fact that it is delicate, hidden, and well-protected by the skull. I will describe MR imaging techniques to characterize brain deformation, estimate brain material properties, and illuminate the mechanical stresses in brain tissue, all aimed at improving the understanding of both injury and development.

T16: YOUR BRAIN IN MOTION: HOW NEUROIMAGING AND COMPUTER VISION TRANSFORM OUR UNDERSTANDING OF BRAIN BIOMECHANICS

Kurt, Mehmet

Department of Mechanical Engineering, University of Washington, Seattle, WA, USA

The human brain is the continuous subject of extensive investigation aimed at understanding its behavior and function. Despite an overwhelming interest and major research initiatives on how our brain operates, comparatively little is known about how it functions at the mechanical level. Recent findings have directly linked major brain development, mechanisms, and diseases to the mechanical response of the brain, both at the cellular and tissue levels. Despite clear evidence that mechanical factors play an important role in regulating brain activity, current research efforts focus mainly on the biochemical or electrophysiological activity of the brain, mostly due to the difficulty of probing the brain physically.

In this talk, I will present how a combination of novel computational, deep learning, and neuroimaging methods can provide insights into the world of brain biomechanics. I will introduce novel neuroimaging tools that can measure and track how the brain moves inside the skull, even during physiological processes. I will demonstrate how studying the motion of the brain *in vivo* is useful in several important clinical applications, enabling earlier diagnosis and intervention of brain pathologies such as traumatic brain injury, hydrocephalus, Chiari Malformation, Alzheimer's disease, and other degenerative diseases.

T17: (TOWARDS) LINKING MECHANICAL PROPERTIES WITH NEURONAL FUNCTION

Rampp, Stefan [1,2]; Flé, Guillaume [3]; Laun, Frederik [3]; Delev, Daniel [2]; Schnell, Oliver [2]; Hinrichsen, Jan [4]; Budday, Silvia [4]; Doerfler, Arnd [1]

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Investigations on the mechanical properties of brain tissue show significant differences between brain regions, linked to local microstructural, cellular, and molecular characteristics. Mechanics plays a role in normal brain development and disease, e.g., neurodegeneration. However, whether mechanics are correlated to functional characteristics/neuronal activity, still remains unclear.

The present study aims to link post-mortem mechanical testing data with neuronal activity using magnetoencephalography (MEG) and magnetic resonance diffusion-weighted imaging (MR-DWI).

MR-DWI fractional anisotropy (FA) acquired at 3T in healthy individuals is compared to graph-theoretical metrics (node degree) derived from cortical MEG resting-state connectivity and material parameters of brain tissue (shear modulus, nonlinearity parameter) derived from fitting a hyperelastic Ogden model to mechanical data of post-mortem tissue from body donors.

We found significant (negative) correlations between regional FA and shear modulus, but not with the nonlinearity parameter in DWI. FA exhibited significant negative correlations with cortical MEG node degree. These results suggest that higher functional connectivity is related to lower anisotropy of the underlying cortical microstructure and to higher mechanical stiffness, as reflected by higher shear modulus values.

Further *in vivo* multimodal MRI studies are planned, combining MR elastography techniques, functional MRI, DWI, and EEG/MEG to further elucidate the link between brain mechanics and function.

T18: MECHANICAL FINGERPRINT: THE CHALLENGING PATH TO MECHANICAL BRAIN TUMOR DIAGNOSTICS

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Understanding and leveraging the mechanical properties of brain tissue may offer neurosurgeons valuable intraoperative guidance—particularly in glioma surgery, where the distinction between infiltrative tumor and healthy brain is often ambiguous. Parameters such as tissue stiffness and viscoelasticity can provide objective, spatially resolved biomarkers for tumor identification and resection planning, complementing existing imaging and navigation systems.

On a microscopic level, glioma progression involves fundamental changes in tissue architecture. Glioblastoma, for instance, is characterized by loss of cytoarchitectural organization, increased cell density, altered extracellular matrix composition, and reduced crosslinking, resulting in mechanically softer and more heterogeneous tissue compared to healthy brain parenchyma [Friedrich et al., Cells, 2022].

Despite the diagnostic potential of these mechanical signatures, *in vivo* measurement remains challenging. While Magnetic Resonance Elastography provides non-invasive preoperative stiffness maps, its utility is limited intraoperatively due to skull-induced wave attenuation and low resolution near cortical surfaces [Murphy et al., Neuroimage Clin, 2017]. Intraoperative ultrasound Elastography/Vibrography offers real-time visualization but suffers from limited contrast, operator dependence, and distortion due to brain shift, reducing its accuracy during extended resections [Skjerpe et al., Acta Neurochir, 2024; Kataoka et al., BMC Med Inform Decis Mak, 2022].

To evaluate mechanical contrast directly, indentation-based techniques have been explored. In recent ex vivo studies, glioblastoma tissue exhibited reduced stiffness and differences in relaxation behavior compared to adjacent and peritumoral brain tissue [Kren et al., Acta Neurochir, 2024]. Furthermore, intraoperative indentation measurements confirmed the feasibility of using local mechanical properties to assist in tumor identification [Skambath et al., Acta Neurochir, 2024].

To translate these insights into a high-resolution, intraoperative-compatible modality, we developed a MHz-range Optical Coherence Elastography (OCE) platform using a flow-controlled air-jet to induce localized mechanical excitation. In the latest analysis of brain tumor data acquired with this system [Detrez et al., SPIE Proc., 2023], we introduced a framework for quantitative stiffness interpretation, combining air-jet dynamics, optical phase data, and tissue response modeling. Using tailored phase unwrapping algorithms, we achieved robust stiffness mapping at the microscale, resolving tumor borders and mechanical gradients not evident in histology.

In conclusion, mechanical tissue properties may be used as clinically relevant intraoperative biomarkers in glioma surgery. The air-jet-based OCE platform combines high spatial resolution, contactless measurement, and real-time applicability, making it a promising tool to enhance surgical precision and reduce residual tumor burden. By incorporating biomechanical feedback

into the neurosurgical workflow, we aim to support more informed, tissue-specific resection strategies in neuro-oncology.

T19: BRAIN TISSUE MECHANICS IN DEMENTIA: INSIGHTS FROM MAGNETIC RESONANCE ELASTOGRAPHY

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What if the brain's "mechanical fingerprint" could reveal the earliest signs of Alzheimer's disease—years before memory loss or cognitive decline? Using magnetic resonance elastography (MRE), we can measure the stiffness and damping of brain tissue in vivo, providing a unique perspective on microstructural health. While reduced tissue stiffness in Alzheimer's disease patients is well documented, little is known about mechanical changes during the disease's long, silent preclinical phase, which can span decades. In this talk, I will present our latest findings from healthy midlife adults with and without a genetic predisposition to Alzheimer's disease, defined by the APOEε4 variant, focusing on subtle hippocampal changes—one of the first regions to accumulate tau pathology. Our results suggest that MRE can detect region-specific mechanical alterations in at-risk individuals long before symptoms appear. I will discuss what these changes could mean for early diagnoses, evaluating the effectiveness of disease-modifying treatments, as well as the possibility that brain mechanics themselves could play a role in Alzheimer's disease pathogenesis.

T20: BRAIN DYNAMIC CHANGES AFTER MTBI AND REPETITIVE HEAD IMPACTS IN ADOLESCENT RUGBY PLAYERS

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Adolescent rugby players face risks from head impacts, including mild traumatic brain injuries (mTBI) and repetitive subconcussive events, which may have long-term effects. This study explored the connections between head impact exposure, brain dynamics, and strain patterns in these young athletes.

In a longitudinal study, 33 male rugby players (mean age 16.22 ± 0.94 years) underwent MRI scans, including diffusion tensor imaging (DTI), to monitor brain changes throughout a rugby season. Instrumented mouthguards measured head acceleration events during both games and practices. For 15 players, including two with clinically diagnosed mTBI, subject-specific finite element (FE) models were generated using T1-weighted MRI and DTI.

Dynamic impact simulations were performed using a representative 300-ms impact profile derived from measured linear and angular accelerations. This enabled analysis of spatiotemporal changes in brain dynamics during head impacts over the season, utilizing dynamic mode decomposition (DMD).

Key findings indicated that DMD-derived metrics, specifically mode energy and damping ratio, correlated more strongly with head kinematic measures ($r = 0.72$ and $r = 0.74$, respectively) compared to cumulative strain damage measures. This suggests that brain dynamics could be crucial in understanding longitudinal alterations in brain behavior following both mTBI and repeated subconcussive impacts.

T21: CONCUSSIVE INJURIES INDUCE NEURONAL STRESS-DEPENDENT TAU MISLOCALIZATION TO DENDRITIC SPINES WITH ACROLEIN AND FUNCTIONAL NETWORK ALTERATION IN TBI-ON-A-CHIP

Rogers, Edmond A.[1,2,3]; Diorio, Tyler C.[1,2,3]; Beauclair, Timothy[1,2,3]; Martinez, Jhon[1,2,3]; Mufti, Shatha J.[1,2,3]; Kim, David[4]; Krishnan, Nikita[1,3]; Rayz, Vitaliy L.[1,5]; **Shi, Riyi**[1,2,3]

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Traumatic Brain Injuries (TBI) are a risk factor for Alzheimer's Disease (AD), and share several important pathological features, including the development of neurofibrillary tangles (NFT) of tau protein. While this association is well established, the underlying pathogenesis is poorly defined, and current treatment options remain limited, necessitating novel methods and approaches. In response, we developed "TBI-on-a-chip", an *in vitro* trauma model utilizing murine cortical networks on microelectrode arrays (MEAs), capable of reproducing clinically relevant impact injuries while providing simultaneous morphological and electrophysiological readout. Here, we incorporate a digital twin of the TBI-on-a-chip model to resolve cell-scale mechanical deformation via shear stresses and demonstrate direct connections between impact forces with aberrations in tau and synaptic deficits, and correlate these changes with elevations of oxidative stress, a suspected key contributor to both trauma and neurodegeneration. This multi-disciplinary investigation combines computational modeling, electrophysiology, and imaging to explore tau mislocalization and functional deficits as a function of force, in the context of a potential mechanism via acrolein. We hope that this novel, integrative approach will help improve our mechanistic understanding of trauma and neurodegeneration, solo and in concert, and ultimately assist in generating more effective treatment options.

T22: PORES AND PREJUDICES: AN EXPERIMENTAL EVALUATION OF DARCY'S PERMEABILITY IN BRAIN TISSUE WITH BIOMIMETIC HYDROGELS

Kainz, Manuel P.[1]; Terzano, Michele[1]; Sommer, Gerhard[1]; Greiner, Alexander[2]; Budday, Silvia[2]; Steinmann, Paul[3,4]; Holzapfel, Gerhard A.[1,5]

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Accurate biomechanical models of brain tissue are essential for understanding neurological disorders and enabling simulations for injury prediction, neurosurgery, and drug delivery. Brain tissue is an ultra-soft, highly hydrated material whose mechanical response is strongly influenced by the movement of interstitial fluid. It is increasingly modeled as a biphasic medium, coupling solid deformation to fluid flow. While porosity and permeability are key parameters in such models, direct experimental determination, particularly of permeability, remains challenging. Darcy's permeability is often used as a representative parameter, but this is rarely validated due to difficulties measuring fluid transport and coupled deformation in ultra-soft materials.

Here, we present a novel experimental setup that mimics classical conditions of Darcy's law. The system uses a cylindrical chamber to simultaneously measure hydrostatic pressure, fluid flow, and global deformation. Using brain tissue-mimicking hydrogels with varying stiffness and porosity, we quantitatively investigate the pressure-dependent permeability. We demonstrate how stiffness and porosity affect the applicability of Darcy's law and identify conditions where it fails.

This approach allows direct derivation of permeability and is transferable to brain tissue. Applied to animal tissue samples, we provide the first direct measurements under Darcy-like conditions and offer new insights for biomechanical modeling of soft porous tissues.

T23: MECHANICAL AND FUNCTIONAL RESPONSES IN ASTROCYTES UNDER ALTERNATING DEFORMATION MODES

Garcia-Gonzalez, Daniel[1]; Gomez-Cruz, Clara[1]; Fernandez-de la Torre, Miguel[1]; Lachowski, Dariusz[1,2]; del Rio, Armando[1,2]; Perea, Gertrudis[3]; Muñoz-Barrutia, Arrate[1]

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This work introduces NeoMag, a system designed to enhance cell mechanics assays in substrate deformation studies. NeoMag uses multidomain magneto-active materials to mechanically actuate the substrate, transmitting reversible mechanical cues to cells. The system boasts full flexibility in alternating loading substrate deformation modes. The multidomain substrates facilitate mechanobiology assays on 2D and 3D cultures. The integration of the system with nanoindenters allows for precise evaluation of cellular mechanical properties under varying substrate deformation modes. The system is used to study the impact of substrate deformation on astrocytes, simulating mechanical conditions akin to traumatic brain injury and ischemic stroke. The results reveal local heterogeneous changes in astrocyte stiffness, influenced by the orientation of subcellular regions relative to substrate strain. These stiffness variations, exceeding 50% in stiffening and softening, and local deformations significantly alter calcium dynamics. Furthermore, sustained deformations induce actin network reorganization and activate Piezo1 channels, leading to an initial increase followed by a long-term inhibition of calcium events. Conversely, fast and dynamic deformations transiently activate Piezo1 channels and disrupt the actin network, causing long-term cell softening. These findings unveil mechanical and functional alterations in astrocytes during substrate deformation, illustrating the multiple opportunities this technology offers.

T24: MECHANICAL PROPERTIES OF THE BRAIN AND THEIR EFFECT ON CELL MIGRATION

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The mechanical properties of central nervous system tissue are different from those of most other soft tissues in part because they lack a three-dimensional fibrous collagen matrix. The response of the brain to mechanical stresses depends on the direction of the applied force, especially at large deformations. The shear modulus of the brain slightly decreases with increasing shear strain, but it strongly increases under uniaxial compression. Compression stiffening is likely to contribute to damage caused by solid stress developed in growing tumors, even when the shear modulus of the uncompressed tissue remains low. The crowded compression-stiffening environment of the brain affects the way that cells migrate through the tissue. A limiting factor in cell migration through dense matrices is often the deformation of the nucleus. Recent experiments show that the chromatin remodeling motors BRG1 is essential for cell migration through constrictions. For example, the outgrowth of LN 18 glioma cell spheroids through a matrix is almost completely abrogated when the BRG1 motor is inhibited. The unique mechanical properties of the brain and their effect on the way that cells move through this tissue illustrate the importance of mechanical features to provide diagnostic information and potentially suggest therapeutic strategies.

3 POSTERS

Posters are listed in alphabetical order by the **presenting author**.

P01: QUANTIFICATION OF PERINEURONAL NETS IN FOCAL CORTICAL DYSPLASIA TYPE IIB

Auer, Sophia[1]; Hoffmann, Lucas[2]; Schicht, Martin[1]; Blümcke, Ingmar[2]; Paulsen, Friedrich[1]

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Introduction
Focal cortical dysplasia type IIb (FCD IIb) is a frequent cause of pharmacoresistant epilepsy in children and is histopathologically characterized by cortical dyslamination, dysmorphic neurons, and balloon cells. Although somatic mutations in the mTOR signaling pathway are implicated in a subset of FCD IIb cases, the contribution of extracellular matrix (ECM) alterations to its pathophysiology remains poorly understood. Perineuronal nets (PNNs) are specialized ECM structures that primarily enwrap parvalbumin-expressing (PV+), GABAergic inhibitory interneurons and are essential for maintaining synaptic stability and regulating cortical excitability. While PNN alterations have been reported in various forms of epilepsy, their presence and distribution in FCD IIb have not been systematically investigated.

Methods
Human brain tissue samples from FCD IIb patients and non-epileptic controls were examined using immunohistochemistry and immunofluorescence with specific markers for PNNs, GABAergic interneurons, PV+ interneurons, dysmorphic neurons, and balloon cells. PNN density and cellular association were quantified in lesional, perilesional, and subcortical white matter regions.

Results
We observed a region-specific increase in PNN density within FCD IIb lesions compared to perilesional cortex and control tissues. Furthermore, an age-dependent increase in PNN density was detected across both cohorts, with overall higher levels in FCD IIb tissue.

Conclusion
These findings demonstrate abnormal PNN accumulation in FCD IIb lesions, pointing to ECM remodeling as a potential contributor to cortical hyperexcitability seen in epilepsy. These results underscore the importance of the ECM in epilepsy and suggest PNNs as modulators of epileptogenicity in FCD IIb.

P02: AUTOMATED CLASSIFICATION OF NUCLEI IN WHOLE SLIDE BRAIN TISSUE SAMPLES

Aust, Oliver[1]; Hinrichsen, Jan[2]; Hoffmann, Lucas[3]; Thies, Mareike[1,4]; Öttl, Mathias[1,4]; Wilm, Frauke[1,4]; Blümcke, Ingmar[3]; Breininger, Katharina[1,5]

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With the final goal of being able to fully automatically count nuclei in whole-slide brain tissue samples and classify them based on the cells they originate from, two experts annotated 5 regions of interest in three images, each originating from a different dataset. Approximately 650 objects were annotated and divided into 6 different classes (corpora amylacea, endothel, glia, hematopoietic, neuron, and "unclear"). As a first step, we compared the two expert annotators irrespective of the classification of the nuclei, where we found a high IoU (0.86). However, we observed substantially lower IoU values when the classification of the nuclei was taken into account: 0.605 (corpora amylacea), 0.561 (endothel), 0.540 (glia), 0.000 (hematopoietic), 0.508 (neuron), and 0.137 (unclear). The relatively low values resulted from a mismatch of the cell type classification of each annotator. As a next step, we will compare these annotations with predictions from existing deep learning (DL) methods for nuclei detection, including the Hovernet architecture, to provide an initial benchmark for future model selection. This initial experiment using a smaller amount of annotated images allowed us to obtain valuable insights for generating larger amounts of annotations to be able to train or adapt existing DL models for cell differentiation.

P03: PIEZO1 IS A MECHANOTRANSDUCER OF SOFT MATRIX VISCOELASTICITY

Azevedo Gonzalez Oliva, Mariana[1,2]; Ciccone, Giuseppe[1,2]; Flaschner, Gotthold[1]; Vassalli, Massimo[2]; Roca-Cusachs, Pere[1]; Salmeron-Sanchez, Manuel[1,2]

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Mechanosensitive ion channels, such as Piezo1, have emerged as having fundamental roles in sensing the mechanical properties of the extracellular matrix (ECM). However, whether and how Piezo1 senses viscoelasticity—the time-dependent mechanical behavior characteristic of soft tissues like the brain—remains unclear. To address this question, we combined an immortalised mesenchymal stem cell (MSC) line in which Piezo1 expression can be modulated with soft and stiff viscoelastic hydrogels that have independently tunable elastic and viscous moduli. We demonstrate that Piezo1 is a mechanosensor of viscoelasticity in soft ECMs, both experimentally and through simulations using a modified viscoelastic molecular clutch model that incorporates Piezo1. Using RNA sequencing, we also identify the transcriptomic phenotype of MSC response to matrix viscoelasticity and Piezo1 activity, identifying gene signatures that modulate MSC's mechanobiology in soft and stiff viscoelastic hydrogels. These findings advance our understanding of how cells interpret time-dependent mechanical cues and position Piezo1 as a central transducer of viscoelasticity in soft tissues. Given the highly viscoelastic nature of brain tissue, our work provides a potential mechanistic framework for Piezo1's involvement in neural tissue physiology and pathophysiology, and offers new avenues for engineering brain-like *in vitro* models to probe neural mechanobiology and disease.

P04: MECHANICAL MODULATION OF THE CENTRAL NERVOUS SYSTEM DUE TO OXIDATIVE STRESS

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Oxidative stress significantly impacts the viability of central nervous system (CNS) cells and tissues, influencing neurodegenerative diseases and injury responses. Given that CNS structure is closely linked to its function, understanding how oxidative stress alters its mechanical properties is crucial. However, the underlying biomechanical mechanisms remain poorly understood.

This study examines oxidative stress-induced mechanical changes in the CNS at both cellular and tissue levels using *in vitro* and *in vivo* models. We employ Brillouin microscopy (BM) and atomic force microscopy (AFM)-assisted indentation to quantify mechanical responses under oxidative stress. *In vitro*, cultured neural cells and tissue slices undergo controlled oxidative stress, enabling stiffness and viscoelasticity assessment via BM and AFM. *In vivo*, zebrafish larvae serve as a model to investigate dynamic CNS mechanical modulation under optogenetically induced oxidative stress in a physiologically relevant, regenerative environment. By correlating mechanical alterations with oxidative stress markers and biochemical modifications, we aim to elucidate the relationship between oxidative stress and CNS biomechanics.

Our findings indicate an increase in Young's modulus in the soma of primary cortical neurons following oxidative stress induction, as measured by AFM. *In vivo*, BM-based dynamic monitoring of optogenetically induced oxidative stress reveals a decrease in the Brillouin frequency shift. Together, AFM and BM provide complementary insights into oxidative stress-induced CNS mechanical remodeling. These results advance our understanding of CNS mechanobiology under early oxidative stress and may inform therapeutic strategies aimed at mitigating mechanical effects associated with injury and disease progression.

Keywords: Oxidative stress, central nervous system, biomechanics, Brillouin microscopy, atomic force microscopy, zebrafish.

P05: MECHANOSENSITIVITY OF AXONAL GROWTH OF PRIMARY RAT NEURONS IN FIBROUS 3D MATRICES

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Axonal pathfinding is influenced by various environmental cues, including substrate stiffness, a process referred to as durotaxis. Axonal response to changing mechanical surroundings is of interest for developmental neuroscience and regenerative medicine. During growth, neuronal cells are thought to sense their environment through mechanical interaction at the growth cone. We test this by seeding primary hippocampal rat cells in three-dimensional collagen hydrogels and observing growing axons over several hours. We find that collagen fibers are pulled towards the tip of the growth cones, which is indicative of traction forces exerted by the cells onto the matrix. We use particle image velocimetry to quantify these matrix deformations, and then apply 3-D traction microscopy to compute cell-generated forces. These forces are in the range of 0.5 - 3 nN, which is much smaller than the forces generated by other cells. We perform these experiments in three different collagen concentrations, resulting in different stiffness and pore sizes of the extracellular matrix. We are currently analyzing whether traction forces change in response to these matrix properties. However, we found that axons of primary rat neurons grow straighter in stiffer matrices with smaller pore sizes, demonstrating clear signatures of mechano-sensitivity of axonal growth processes.

P06: THE GENETIC SIGNATURE OF MOGHE: THE SOMATIC SLC35A2 BRAIN VARIANT AND THE Y CHROMOSOME MOSAICISM

Cecchini, Erica[1]; Coras, Roland[1]; Katoch, Mitali[1]; Kobow, Katja[1]; Karandasheva, Kristina[1]; Hartlieb, Till[2,3]; Bien, Christian G.[4]; Blümcke, Ingmar[1]; Hoffmann, Lucas[1]

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Mild Malformation of Cortical Development with Oligodendroglia Hyperplasia in Epilepsy (MOGHE) is a recently defined neuropathological entity associated with drug-resistant frontal lobe epilepsy in children. MOGHE is defined by oligodendroglia hyperplasia, myelin loss, and heterotopic neurons in the white matter. Approximately half of affected individuals harbor somatic brain variants in the X-linked SLC35A2 gene, which encodes a UDP-galactose transporter involved in glycosylation. Our studies demonstrated reduced SLC35A2 protein expression and altered subcellular localization in tissues with pathogenic variants, particularly nonsense mutations. However, hypomyelination was observed irrespective of SLC35A2 mutation status, indicating additional myelin-associated mechanisms. Copy number variation analyses revealed mosaic gains of the Y chromosome in male and, unexpectedly, in female patients, confirmed by in situ hybridization and PCR. These findings suggest that MOGHE pathogenesis may arise from the interplay between somatic SLC35A2 mutations and sex chromosome mosaicism, both potentially impacting oligodendroglia function, glycosylation processes, and myelin integrity. Notably, SLC35A2 mutations have not been identified in any other epileptogenic lesion to date, highlighting the specificity of this mechanism for MOGHE and its potential as a distinguishing genetic marker. The detection of Y-chromosome in female brains and Y-chromosome gain in males uncovers a previously unrecognized form of sex chromosome mosaicism in the brain, raising key questions about its origin and role in epileptogenesis.

P07: MECHANICAL PROPERTY MAPPING OF BRAIN TUMOR TISSUE VIA AIR-JET BASED OPTICAL COHERENCE ELASTOGRAPHY

Detrez, Nicolas[1]; Burhan, Sazgar[2]; Matschke, Jakob[4]; Theisen-Kunde, Dirk[1]; Bonsanto, Matteo Mario[3]; Huber, Robert[2]; Brinkmann, Ralf[1,2]

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Objective:
Measuring the mechanical properties of brain tumor tissue provides critical insights into tissue characterization. Optical coherence elastography (OCE) has shown success in breast cancer delineation. We explore its use in brain tumor analysis and will present a demonstrator system that quantifies basic tissue properties in brain tumor biopsies.

Methods:
The OCE system integrates a custom air-jet to apply and measure force with a 3.2 MHz optical coherence tomography (OCT) system that tracks tissue displacement using phase data. Tissue samples are excited with 200-ms air-jet pulses at a 70 µN load. Based on this data, Pixel-wise mechanical properties within OCT B-scans are computed. The longer excitation allows steady-state analysis, and sharp pulse edges enable dynamic assessment.

Results:
Key mechanical properties — bulk stiffness, creep constant, and regression constants — are extracted and classified as elastic, ductile, or viscous. These are visualized through pixel-wise spider plots for intuitive interpretation. Contrast maps aligned with OCT scans facilitate correlation with histological data and support mechanical-tissue research.

Conclusion:
We demonstrate the capability to measure and visualize critical mechanical parameters of brain tumor samples. This technique supports AI-based classification and opens new avenues for investigating tissue mechanics. A clinical in situ study is planned.

P08: EFFECTS OF DIFFERENT 3D BIOMATERIAL HYDROGEL ENVIRONMENTS ON HUMAN IPSC-DERIVED ASTROCYTE MORPHOLOGY, TRANSCRIPTOME, AND REPROGRAMMING

Distler, Thomas[1,2]; Konrad Daga, Katherina[1]; Bürkle, Martina[1]; Simon, Tatiana[1]; Vásquez-Sepúlveda, Sebastian[3,4]; Franze, Kristian[3,4,5]; Götz, Magdalena[1,2,6]; Masserdotti, Giacomo[1,2]

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Astrocytes show a pronounced morphological and molecular heterogeneity in the mammalian central nervous system. However, the influence of their 3D environment and their surrounding extracellular matrix on astrocyte behavior is poorly understood, while their composition and mechanics change upon brain injury. Here, we examined the morphology, gene expression, and direct neuronal reprogramming of human iPSC-derived astrocytes (hAstro) in different 3D fibrin-based hydrogel environments.

Our results show that hAstro obtains a higher ramification complexity in a stiffened fibrin alginate (FA) interpenetrating network hydrogel compared to soft pristine fibrin, highlighting the impact of the culturing environment on hAstro growth. Bulk RNA-sequencing results further strengthen this observation, as we observe striking differences between soft pristine fibrin and FA hydrogel. Interestingly, direct conversion of hAstro is mitigated in the latter, while hAstro successfully reprograms into induced neurons in the other hydrogel.

Together, these results highlight the impact of the cell environment and its properties to shape the morphology and function of human iPSC-derived astrocytes, and their potential to be converted into neurons in 3D environments of different stiffness.

P09: CAN WE MODEL CHANGES IN BRAIN FLUID DYNAMICS WITH A 0D MODEL?

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Metabolic waste produced by neuronal cell activity in the brain is eliminated by two distinct physiological systems coupled by mechanical interactions: the microvasculature and the system including cerebrospinal fluid (CSF) and interstitial fluid (ISF). Previous studies on mice have shown an increase in brain ISF volume during sleep, which was associated with an enhanced clearance. These results have been reproduced in humans using electrical impedance spectroscopy (Dagum et al. 2025). However, the role of sleep in metabolic waste clearance is still under debate, and it remains unclear how the large-scale dynamics of blood and CSF/ISF may change. Here, we work on a brain-scale 0D model inspired by Linninger et al. (2009) and Toro et al. (2022). We include a cardiac-type pulsatile pressure at the inlet, drainage through the jugular veins, reabsorption in the venous sinuses, and a biphasic brain tissue. With a simplified but robust seven-compartment resistance/compliance model, we first reproduce numerical and experimental dynamics of blood and CSF pressures, arterial and venous blood flows, and velocity in the spinal canal reported in the literature. Then, we test the impact of the hypothetized sleep-associated changes in the brain tissue on blood and CSF/ISF circulations, and, potentially, on brain clearance.

P10: THE ROLE OF MECHANICS FOR 'NEURONAL PLASTICITY'

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Neuronal plasticity, an essential mechanism underlying learning and memory, declines during adulthood. This reduction is partly mediated by the perineuronal extracellular matrix (ECM), which restricts structural remodeling of synaptic contacts. ECM maturation correlates with altered brain tissue mechanics, which may contribute to reduced neuronal plasticity. The objective of this study is to investigate how ECM-related mechanical cues affect neuronal plasticity and neuronal network organization. We used atomic force microscopy on adult mouse brain sections to measure cortical stiffness in a layer-by-layer approach, considering the heterogeneity of the ECM. Additionally, the effect of ECM digestion on these changes was examined. Increased stiffness was found to correlate with higher ECM density, thereby underscoring the mechanical contribution of ECM. Moreover, we investigated the influence of OHA/GEL (oxidized hyaluronan) hydrogel stiffness on neuronal outgrowth. Actin intensity in dendrites was analyzed under various mechanical conditions, given its role in dendritic spine formation. Furthermore, dendritic spine length was measured before and after forskolin-induced long-term potentiation (LTP), as LTP selectively increases the size of small spines. The results demonstrated that neurons responded differently to environments with varying stiffness. Together, these results underscore the impact of ECM properties on brain mechanics and neuronal plasticity.

P11: DYNAMIC COMPRESSIBILITY OF THE *IN VIVO* HUMAN BRAIN ACROSS A WIDE RANGE OF ACOUSTIC FREQUENCIES

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From a mechanical perspective, the human brain is a poro-viscoelastic material, whose dynamic response to deformation is dictated by solid-fluid interactions. There are two deformation modes: shear strain, which is volume-conservative and represented by the curl field, and compression, the divergence of the deformation field, which signifies volumetric changes and relates to tissue pressure. MR elastography (MRE) typically utilizes shear waves in the frequency range of 20-50Hz to measure shear modulus. However, MRE simultaneously induces compression waves that remain unused despite their mechano-biological relevance in quantifying tissue pressure. In this study, we demonstrate that the divergence of MRE wave fields at very low frequencies (<20Hz) can be deduced and potentially exploited as a proxy for tissue pressure when normalized over shear strain in a group of healthy volunteers. We observed relatively large divergence values of 23.9x10-3 [12.5-32.7]x10-3 at low frequencies (12.5Hz) compared to 1.1x10-3 [1.1-1.3]x10-3 at higher frequencies (35Hz) as well as large compression-over-shear-wave amplitude ratios of 0.34 [0.31-0.47] and 0.16 [0.12-0.18], respectively. These results suggest that externally stimulated brain oscillations within the lower range of MRE frequencies can induce significant solid-fluid poroelastic interactions, which could serve as biomarkers for neurovascular compliance, intracranial pressure, and glymphatic system integrity.

P12: SQUISHY BRAIN: A POROELASTIC MATHEMATICAL MODEL OF THE BRAIN TISSUE TO STUDY PARENCHYMAL FLUID FLOW AND CLEARANCE

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Unraveling the complex functioning of brain perfusion and waste clearance is essential for understanding several neurodegenerative pathologies. The perivascular space (PVS) is known to efficiently deliver cerebrospinal fluid (CSF) deep into the brain tissue (parenchyma). However, little is understood about how, from the delivery point in the PVS, the CSF permeates the parenchyma, removing waste. Here, we model the portion of brain parenchyma between a penetrating arteriole and a venule as a highly deformable poroelastic medium, where solute transport is strongly influenced by fluid flow, which itself depends on tissue deformation. We then apply a mechanical forcing corresponding to arteriolar pulsations as experimentally observed *in vivo*. We explore several parameters (such as tissue properties and amplitudes and frequencies of the arterial pulsations), with a particular focus on their changes between different stages of wake and sleep. We see that the specific arterial pulsations observed in each vigilance state (e.g., wake, REM, and NREM sleep) lead to different poromechanical responses of the brain parenchyma, in terms of mechanical deformation, fluid-flow, and solute transport. The model can therefore provide important insights into the physics of brain perfusion and clearance.

P13: CELLULAR AGGREGATE FORMATION: CONTINUUM MODELING AND COMPUTATIONAL IMPLEMENTATION

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Cellular aggregates play a crucial role in various biological processes, including tumor growth, tissue expansion, wound healing, and biofilm formation. The study of such systems necessitates an analysis of the interplay between cell–cell and cell–matrix interactions, which collectively govern the dynamics of cellular aggregates, an inherently out-of-equilibrium phenomenon.

In this presentation, we introduce a nonlinear continuum mechanics framework alongside a finite element simulation approach to model the physics underlying cellular aggregate formation. As a representative case, we focus on bacterial colony formation, and conceptualize the aggregation process as an active phase separation phenomenon. The problem is formulated with both Eulerian and Lagrangian continuum descriptions. Furthermore, a robust and efficient finite element implementation is elaborated for the computational implementation of the problem.

To further enhance numerical stability, we present our recently developed micromorphic-based artificial diffusion method to mitigate instabilities stemming from the convective nature of the problem. This approach improves the robustness of the numerical scheme while preserving the essential physics of the system.

Finally, through a series of numerical examples, we investigate how different parameters influence the dynamics of cellular aggregate formation. The proposed methodology provides a comprehensive framework for exploring the rheology and non-equilibrium behavior of cellular aggregates.

P14: REPRODUCIBILITY STUDY OF MAGNETIC RESONANCE ELASTOGRAPHY OF THE HUMAN BRAIN

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Magnetic resonance elastography (MRE) offers a unique framework for the mechanical characterization of the human brain under small strains, *in vivo* and non-invasively. Since the introduction of MRE in 1995, significant advancements have been made in designing appropriate MR pulse sequences, intuitive and reliable hardware, as well as robust image analysis methods for reconstructing spatially distributed mechanical parameters.

MRE methodologies are diverse, and assessments of methodological reproducibility are sparse in the literature, although some variability in measured mechanical properties across individual approaches is expected due to varying physical assumptions.

This study discusses the robustness of a human brain MRE pipeline recently established at the University Hospital Erlangen, which involved two repeated measurements from thirteen participants across two sites. The MRE device, supplied by the Elastography Group at Charité in Berlin, involves a dual-actuation system operating in phase opposition, an echo-planar-based MR sequence, and a multifrequency wavenumber approach to provide estimates of the brain stiffness. Whole brain images were acquired to sample eight evenly spaced timesteps across each of four actuation frequencies (20, 25, 30, 35 Hz) using velocity-compensated motion-sensitizing-gradients applied in three orthogonal spatial directions. Preliminary analysis indicates high reproducibility while maintaining short scan times and minimal processing overhead.

P15: AORTIC CARBOXYPEPTIDASE-LIKE PROTEIN CONTROLS FIBROTIC SCARRING AFTER SPINAL CORD INJURY

Fleming, Thomas[1]; John, Nora[1]; Battistella, Alice[1]; Parmer, Asha[1]; Kolb, Julia[2]; Štěpánková, Kateřina[3]; Smejkalová, Barbora[3]; Jendelová, Pavla[3]; Singh, Kanwarpal[4]; Kobow, Katja[5]; Guck, Jochen[1]; Wehner, Daniel[1]

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Following spinal cord injury (SCI), locally forming scar tissue prevents axon regeneration. In contrast, zebrafish undergo successful axon regeneration after SCI, supported by an injury ECM lacking most known inhibitory ECM components in mammals. We identify aortic carboxypeptidase-like protein (ACLP; encoded by the AEBP1 gene) as enriched in mammalian (including human) CNS lesions but absent in zebrafish. We developed a humanized zebrafish model to dissect the role ACLP in SCI *in vivo*. Targeting human AEBP1 expression to fibroblasts led to ACLP enrichment in the injury ECM, impaired axon regeneration and recovery of swim function after spinal cord transection, and increased accumulation and proliferation of fibroblasts in the lesion site. Single-cell transcriptomic profiling of the lesion site revealed an upregulation of core matrisome gene expression—most prominently collagens—in fibroblast-like cell populations in ACLP-enriched fish. The changes in matrisome gene expression were accompanied by structural changes and softening of the lesion site, as measured *in vivo* by cross-polarized optical coherence tomography and atomic force–enabled nanoindentation. Together, these data suggest ACLP drives aberrant fibroblast behavior after SCI, which leads to changes to the injury ECM and impaired axon regeneration, suggesting ACLP is an upstream regulator of mammalian CNS scarring.

P16: *IN VITRO* MODEL FOR THE MECHANICS OF EARLY BRAIN DEVELOPMENT

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The physical properties of the cellular environment are essential in guiding early developmental processes, yet recreating these conditions in vitro remains a significant challenge.

In our research, we introduce a mechanically flexible hydrogel-based system designed to support the growth and differentiation of early neural tissues derived from Xenopus laevis embryos. By tuning the material properties and incorporating biological cues, we examined how mechanical and adhesive factors influence the development of neural structures in a controlled setting. Using a combination of imaging and biomechanical analyses, we observed that specific material conditions promoted more organized tissue architecture and neural patterning. Our approach also demonstrated stability and reproducibility under experimental conditions relevant to developmental biology. These findings highlight the potential of customizable hydrogel platforms to model complex tissue behaviors *in vitro* and offer new opportunities for studying the interplay between mechanics and neuronal morphogenesis.

P17: MECHANICAL REGULATION OF TRACTION FORCES AND GUIDANCE CUE EXPRESSION IN EMBRYONIC BRAIN TISSUE

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During embryogenesis, chemical and mechanical signals regulate many biological processes, ensuring precise organ formation and functioning. Understanding the interplay between these signals and how cells integrate them is essential for elucidating the complex mechanisms that drive development. Using Xenopus laevis embryos as a model system, where neural extensions in the brain are guided by both chemical signals and stiffness gradients *in vivo*, we investigated the interplay between tissue stiffness and long-range chemical guidance cues. Using atomic force microscopy (AFM)-based stiffness mapping and hybridization chain reaction-fluorescence in situ hybridization (HCR-FISH), we found a strong correlation between tissue stiffness and gene expression patterns of the chemical guidance cues sema3A and slit1. *In vitro*, 3D traction force microscopy revealed tissue-generated tensile forces, which increased in stiff compared to soft matrices. Soft brain tissue increased the expression of sema3A and slit1 in stiff environments compared to soft matrices, indicating a mechanosensitive response to environmental stiffness. Our findings elucidate the complex interplay between tissue mechanics, cellular forces, and chemical signaling, which interact to regulate diverse biological processes throughout embryonic development.

P18: MODELING MECHANICS-INDUCED DAMAGE OF BRAIN TISSUE

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Surgery is used to treat many neurological disorders. However, these procedures can result in large deformations and possibly damage, due to the ultra-soft nature of brain tissue. It is therefore important to develop a thorough understanding of the large-strain mechanical behavior of brain tissue and the resulting damage. A hyperelastic damage model for simulating damage to brain tissue is presented, and extensions to a viscoelastic material model are discussed. Cyclic load experimental data is used to fit the model parameters.

P19: FINITE ELEMENT MODELING OF SPINAL CORD REGENERATION IN ZEBRAFISH LARVAE

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Traumatic spinal cord injury (SCI) is a non-regenerative condition in humans that can cause loss of motor function and disability. In contrast, adult and larval zebrafish exhibit remarkable spinal cord regeneration after SCI, recovering significant motor abilities. Recent experiments have shown that, in adult zebrafish, the stiffness of spinal cord tissue near the injury site increases over time during regeneration. Furthermore, in recent research, we have provided the first evidence that tissue mechanics affect axonal regeneration. To further study this correlation, zebrafish larval spinal cords were imaged at regular time points after transection at 10× and 20× magnification. Upon transection, the spinal cord tissue retracted, indicating residual tension. The mechanical state of the regenerating spinal cord was then modeled using finite element simulations, approximating its geometry first as a homogeneous cylinder and subsequently as a radially layered cylinder. Tension was incorporated by decomposing the deformation gradient into elastic and residual stretch components. We introduce axial variation in stiffness through a function $\theta(x)$, such that the local shear modulus $\mu(x) = \mu_0\, \theta(x)$. Comparison between simulated tissue morphology and experimental images enabled adjustment of $\theta(x)$ to match the observed regeneration dynamics.

P20: CHARACTERIZATION OF THE EXTRACELLULAR MATRIX DURING BRAIN DEVELOPMENT IN XENOPUS LAEVIS

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The extracellular matrix (ECM) plays a central role in the regulation of cell and tissue mechanics, cell behavior and cell fate decisions during embryonic development. For a comprehensive understanding of the contributions of mechanical cues to brain development, it is therefore essential to investigate the composition and localization of the ECM in the developing brain at different developmental stages. While studies on the ECM of the embryonic brain are already available in several model organisms, knowledge of its role in Xenopus laevis (African clawed frog), particularly in the early stages of brain development, is limited.

In this study, we aimed to qualitatively and quantitatively characterize the ECM composition in early Xenopus laevis embryos. Combining FastCAT and quantitative LC/MS-MS mass spectrometry allows absolute quantification of target proteins. Here, we adapted protocols for qualitative and quantitative analyses to the special requirements of early Xenopus laevis embryos, which contain large amounts of lipid and yolk. To optimize sample preparation, we have established and validated metabolic labelling of different glycans in Xenopus laevis embryos. In addition, the temporal and spatial expression of glycans and ECM components was investigated using different staining and imaging methods.

P21: A COUPLED MECHANICS-AI PREDICTION FRAMEWORK FOR SPORTS-RELATED MILD TRAUMATIC BRAIN INJURY

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Finite Element Head Models (FEHMs) have been extensively used to explore injury risk in different head impact scenarios. Many FEHMs exist, with a variety of simplifications and assumptions, making direct comparisons between studies challenging. Even the most advanced patient-specific FEHMs cannot currently account for variations in brain properties between individuals, along with other non-mechanical factors that influence the probability of injury (e.g., age, medical history, etc.). Furthermore, to date, there is no consensus on the best mechanistic injury criteria (stress, strain, etc.) or their respective thresholds to predict injury risk.

Injury risk has also been predicted with machine learning (ML) algorithms, using multimodal datasets related to brain injuries. However, these ML methods lack insight into the mechanisms of injury, limiting our ability to prevent future injuries through targeted protective equipment.

Recent efforts have thus combined both approaches by supplying the results of FEHMs to ML methods, hence simultaneously capturing intrinsic mechanistic phenomena (e.g., stress propagation upon impact) and patient-specific prediction (e.g., concussion risk at a given age, with a given medical history). Here, we apply this approach to a multimodal sports-related mild traumatic brain injury dataset and demonstrate the ability of the approach to go beyond traditional techniques.

P22: CELLULAR DIFFERENTIATION IN BRAIN TISSUE-LIKE MATRICES

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Metastasis to the central nervous system, especially the brain, is one of the most dangerous forms of metastasis in malignant melanoma. The mechanisms and influencing factors that contribute to brain metastasis remain poorly understood. Both tumorigenic factors and the mechanical and molecular properties of the cerebral microenvironment may affect metastatic behavior. This study investigates how these environmental factors influence melanoma cell metastasis and whether the origin of metastases (brain metastases or metastases from other extracranial sites) is relevant.

For this purpose, four melanoma cell lines - two from brain metastases and two from non-cerebral metastases - were cultured in hydrogels with variable stiffness and defined molecular components. Cell behavior was assessed by quantitative imaging to evaluate migration, invasion, and proliferation. We revealed that soft matrices with a Young's modulus up to 1 kPa were associated with increased cell proliferation, while hyaluronic acid-enriched environments promoted cell spreading. In addition, different behavioral patterns were observed between cell lines of different metastatic origins. A complementary hydrogel migration assay showed preferential migration into certain hydrogel types, suggesting selective colonization. These findings demonstrate the complex interplay between melanoma cells and their microenvironment and may contribute to the development of improved therapeutic strategies targeting brain metastasis.

P23: *IN VITRO* CULTURE MODEL OF WHITE AND GRAY MATTER ASTROCYTES FROM HUMAN BRAIN BIOPSIES TO STUDY ASTROCYTE CELL BIOLOGY

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Astrocytes can contribute to the development and progression of neuroinflammatory and neurodegenerative disorders. White and gray matter of the central nervous system host different astrocyte populations, which contribute to tissue homeostasis, mechanics, and disease in context-dependent ways. Most *in vitro* studies focus on astrocytes isolated without specifying white or gray matter origin. We obtained and characterized astrocytes from adult human brain biopsies and investigated differences between gray and white matter astrocytes.

White and gray matter were manually dissected from human brain tissue samples, followed by single-cell dissociation and magnetic astrocyte enrichment. The purity of the astrocyte culture was tested by flow cytometry. Further characterization was done by PCR as well as immunofluorescence.

Human white and gray matter astrocytes from brain biopsies were successfully isolated with high purity and grown in serum-containing media. Cells could subsequently be cultured and maintained for several passages. Further characterization of the cells revealed astrocyte-like properties.

Differences between human gray and white matter astrocytes are preserved *in vitro*. Cellular complexity in the mature human brain and interindividual differences impair data comparison between commonly used generic isolation protocols, giving additional value to the study of white and gray matter astrocytes from human brain biopsies.

P24: INVESTIGATING THE BIOMECHANICAL PROPERTIES OF THE AGING MOUSE BRAIN USING AN ELASTOGRAPHIC ATLAS

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Viscoelastic properties of brain tissue serve as biophysical markers of structural integrity of the nervous system. MR elastography (MRE) can quantify cerebral biomechanics *in vivo* and capture structural changes. However, the aging brain's biomechanical changes remain unclear. This study analyzes cerebral biomechanical properties in elderly mice, as depicted in an elastographic atlas of the mouse brain.

In vivo multifrequency MRE was applied to groups of 30 female C57BL/6J mice (aged six to 18 months), and changes of shear wave speed (SWS, stiffness) and penetration rate (PR, inverse viscosity) were analyzed. MRE parameter maps were registered to the DSURQE mouse brain atlas.

Mice brain showed age-related global softening (-11.0±12.3%, p=0.02) and an increase in viscosity (20.2±14.0%, p=0.01). While the viscosity of white matter and gray matter showed the same course of change, stiffness reduction was more pronounced in WM (-29.4±11.5%, p=0.02) than GM (-5.5±9.2%, p=0.06).

Our study provides an elastographic atlas of the elderly mouse brain *in vivo* with detailed anatomical information and age-related changes. Brain softening with increasing viscosity during aging indicates a progressive degradation of brain tissue to a more fluid-like state. Proteomics data will be correlated to identify structural elements and changes associated with the mechanical integrity of neural tissue over aging.

P25: REAL-TIME VISUALIZATION OF THE CELLULAR RESPONSES TO MECHANICAL LOADING

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Cellular behavior and function are significantly influenced by mechanical stimuli, including the mechanical properties of their environment and forces exerted on them. These forces can lead to local tissue deformation and potential damage, depending on the applied loading, its direction, magnitude, duration, and rate, which can surpass functional tolerance.

Current research lacks comprehensive data on how complex three-dimensional (3D) loading scenarios impact processes on the cellular level, limiting the examination of biochemical effects on cells in deeper tissue layers in response to loading. Multiphoton microscopy provides a solution allowing for deeper penetration depths, reduced phototoxicity, and enhanced 3D resolution compared to commercially available integrated systems.

To address this, we have combined, for the first time, a rheometer for multi-modal large-strain mechanical measurements with a customized 2-photon microscope for simultaneous imaging. This new setup enables us to investigate how tissue-scale mechanical loading translates to the cellular scale, allowing real-time assessment of cellular behaviors, such as dysfunction or death, in their 3D environment, including tissue or *in vitro* systems, such as 3D cell cultures or organoids.

Overall, this combined approach aims to enhance our understanding of mechanically-induced cellular responses and identify 3D thresholds for tissue and cell damage under multi-modal loading.

P26: MODELING NEURON GROWTH DYNAMICS AND ROLE OF EXTRACELLULAR MATRIX

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Biological tissues are composed of cells embedded in extracellular matrix (ECM) and extracellular fluid. We study the role of cell-matrix interactions in the context of brain tissues and the mechanism of neuron growth through this matrix. We consider a traction-based model for the neurons, in which growth happens solely due to the interaction of the growing appendages with the particles modeling the matrix. Working with experiments performed on organoid models with healthy and diseased neurons, we aim to recapitulate the observed differences in the neuron growth patterns between the states. We compare numerous growth characteristics, such as mean square displacement, tortuosity, and velocity correlation, to gain further insight into the neuron growth mechanics using our simulation model.

P27: IN SITU CROSSLINKED OXIDIZED HYALURONIC ACID-BASED HYDROGELS FOR SOFT TISSUE ENGINEERING

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Mechanical cues at the cellular level are critical in shaping the development, behavior, and function of neural cells. Understanding how microscale mechanical forces interact with the cellular microenvironment is essential for revealing mechanisms of neural injury and disease progression. Biomaterials that mimic the extracellular matrix (ECM) and offer tunable mechanical properties are vital for advancing neural tissue engineering. Hyaluronic acid (HA), a natural component of the brain ECM, presents a promising platform due to its biocompatibility and biological relevance.

In this study, we engineered ECM-inspired hydrogels using oxidized hyaluronic acid (OHA) with adjustable mechanical properties for neural cell culture. HA was oxidized with sodium periodate ($NaIO_4$), enabling Schiff base bonding with gelatin (GEL). The resulting hydrogel network was further stabilized by enzymatic crosslinking using microbial transglutaminase (mTG), forming a dual-crosslinked matrix. Physicochemical analysis revealed that increasing GEL content significantly enhanced mechanical stiffness, while higher OHA levels mildly influenced stiffness and primarily affected swelling behavior. Hydrogels with a Young's modulus near 0.5 kPa supported the 3D culture of primary neurons, indicating an ECM-like and cell-friendly environment. These findings underscore the potential of OHA-GEL hydrogels for replicating neural tissue mechanics and advancing applications in soft tissue engineering.

P28: BRAIN MECHANICAL COMMUNITIES: *IN VIVO* REGIONAL REPRESENTATION AND LIFETIME CHANGES IN THE MOUSE BRAIN

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The mechanical connectivity of brain regions forms the structural basis of cerebral functional networks. Therefore, we hypothesize that cerebral functional connectivity is influenced by mechanical networks, which can be probed *in vivo* by MR elastography (MRE), and which are affected by physiological processes such as aging. Our study focuses on the biomechanical connectivity of the mouse brain *in vivo* and the changes that occur due to aging across the lifespan.

Cerebral MRE was applied to 87 mice in age phases of adolescence (N=30, 1-4 months), mature adult (N=34, 4-10 months), late adult (N=12, 10-14 months), and old age (N=11, 14-24 months). For each age, group-mean maps of stiffness and tissue fluidity normalized to the standard brain atlas were analyzed using the Leiden community detection algorithm.

Patterns of stiff biomechanical communities overlapped with midbrain and thalamus regions, while fluidity properties predominantly connected midbrain and striatum. The change in the number of detected communities suggested that the viscoelastic networks of the brain undergo significant differentiation patterns from adolescence towards old age.

In summary, our results show that biomechanical communities change across the lifespan, independent of anatomically defined regions, but with differentiation patterns similar to functional brain networks.

P29: LAMIN B1 AND CELL NUCLEAR MECHANICS IN THE REGULATION OF ADULT NEUROGENESIS DURING CHRONIC STRESS

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Brains adapt their structure and function to environmental changes or pathology. These changes range from the tissue to the cellular level, although their interplay remains largely elusive. For instance, in major depressive disorder (MDD), the dentate gyrus (DG) of the hippocampus shrinks at onset but recovers after therapy, despite varying outcomes in cell density, implying structural dynamics drive brain resilience alongside cellular signaling. To address this knowledge gap, we investigated how chronic stress, a major MDD risk factor, reshapes DG architecture and its neurogenic niche in the mouse hippocampus. We developed an imaging pipeline to quantify nuclear shape alongside local tissue topology. We found that nuclei in DG were shrunk and local tissue topology became more constricted after chronic stress, which likely contributes to limited integration and migration of neural progenitor cells (NPCs) in DG. At the cellular level, chronic stress-related signals reduced lamin B1 levels, a key nuclear structural protein, resulting in altered NPC deformability and nuclear mechanics as measured by AFM and Brillouin microscopy. Lamin B1 knockout recapitulated stress-induced mis-migration and changes in nuclear mechanics. These findings highlight lamin B1 as a crucial mechanistic link between chronic stress and structural plasticity of the DG from the cellular to the tissue level.

P30: TOWARDS SEX SPECIFIC BIOMECHANICS OF TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) affects 30 million women globally each year. However, women remain underrepresented in TBI research, despite reporting worse symptoms, longer recovery time, and prolonged symptom durations compared to men. Our work focuses on sex-specific TBI biomechanics in young adults (22-25 years old), motivated by the highest reported incidence of TBI in people under the age of 25 years old.

Finite element brain models (FEBMs) have revolutionized our understanding of TBI biomechanics. However, the majority of FEBMs have been developed using single-subject male data, limiting our understanding of TBI biomechanics to the adult male demographic. Our preliminary work has shown that there are sex-specific brain morphologies in the thalamus, caudate, brainstem, putamen, pallidum, optic chiasm, and corpus callosum. It is hypothesized that these structural and volumetric differences could explain the sex-divergent TBI sequelae.

Here, the progress towards the development of sex-specific FEBMs will be detailed. A pipeline for the construction of morphologically averaged, age and sex specific brain model templates will be presented, and our preliminary results of the sex specific morphology and model development will be discussed.

P31: COMPUTATIONAL MODELING OF CEREBRAL VENOUS COLLAPSE AND ITS IMPACT ON INTRACRANIAL PRESSURE DYNAMICS

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The brain is enclosed within a rigid skull, making it highly sensitive to changes in intracranial volume. Even small variations in CSF, blood, or tissue volume can significantly affect intracranial pressure (ICP), potentially causing tissue damage or impaired perfusion. Cerebral compliance mechanisms buffer these fluctuations, and the collapsibility of cerebral veins is hypothesized to play a key role. However, their mechanical behavior and contribution to brain compliance are not fully understood, as they are difficult to observe *in vivo* with current imaging techniques. To address this, we developed a computational model of intracranial fluid dynamics.

The model uses a lumped-parameter framework representing CSF dynamics, coupled to vascular compartments, a simplified systemic circulation, and cerebral autoregulation. Venous collapse is modeled using Starling resistor analogues or nonlinear pressure–area relationships, reflecting the compliant and collapsible nature of cerebral veins.

Simulation results qualitatively match experimental and clinical data, capturing trends in venous pressure, flow, and ICP. Sensitivity analyses indicate that venous collapse has a significant impact on ICP behavior and system compliance.

The model offers a foundation for further investigation and requires validation across physiological and pathological conditions.

P32: MECHANICAL AND MICROSTRUCTURAL ALTERATIONS IN THE BRAIN DUE TO AGE AND PARKINSON'S DISEASE

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Magnetic resonance elastography (MRE) is a non-invasive method to measure the mechanical properties of tissue, such as the brain. By investigating how these properties change due to Parkinson's disease (PD), we aim to obtain a greater understanding of the disease. In this study, we investigated a combination of MRE and other microstructural metrics obtained via multidimensional diffusion MRI (MD-dMRI). Although several studies have made great efforts in coupling the microstructure of tissue to its mechanical properties, the underlying mechanisms remain poorly understood. We acquired MRE and MD-dMRI data on a cohort of 29 subjects (12 with PD and 17 healthy controls), and analyzed how mechanical and microstructural properties correlate in various brain regions and how these are affected by PD. In several cerebral regions, we found a significant reduction in stiffness, viscosity, microscopic FA(μFA), and an increase in mean diffusivity (MD) and normalized variance of MD due to increased age. These results imply that, due to aging effects, these regions are softened due to the replacement of neurons with extracellular water. In general, the cerebrum was softened due to PD; however, apart from an increase in MD, the other microstructural parameters were not as significantly affected.

P33: EFFECTS OF POSTMORTEM DEGRADATION ON HUMAN BRAIN TISSUE MECHANICS

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Computational models of the brain rely on material parameters from large-strain experiments that cannot be performed in vivo. Human brain tissue from body donations usually only becomes available after 9-24 hours post-mortem. Here, we assess the effect of postmortem degradation on the tissue response of 13 human brains in compression, tension, and shear within a postmortem interval (PMI) ranging from 18 to 98 hours.

To assess how individual brains degrade mechanically, we compare samples from opposite hemispheres that were extracted at different times. To assess general changes, we group samples of all brains according to their anatomical region and correlate their viscoelastic material parameters with the PMI. In addition, we compare ex vivo samples from the cortex to samples from surgically resected cortex tissue that were tested directly after resection. We further relate mechanical parameters to degradation-related histological changes, such as changes in cell morphology and increases in perivascular and pericellular spaces.

The results will enable us to improve experimental planning by prioritizing the most vulnerable brain regions and optimizing storage conditions. Furthermore, insights into relations between degradation-related microstructural changes and viscoelastic parameters may make it possible to establish correction factors for material parameters obtained from ex vivo experiments.

P34: INVESTIGATING THE RELATIONSHIP BETWEEN NUCLEAR MORPHOLOGY AND LOCAL TISSUE ORGANIZATION IN ADULT HIPPOCAMPAL NEUROGENESIS

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The mammalian brain is a highly organized, subdivided, and interconnected structure. This organization is believed to be important to maintain proper brain function, as disorganization of brain structure is often associated with age-dependent functional decline. This is particularly interesting in the dentate gyrus (DG) of the hippocampus, where the organization is preserved despite the continuous adult neurogenesis. Adult-born DG neurons have to be integrated into the tightly organized DG by squeezing their nuclei without disturbing tissue organization. Nevertheless, how DG structural organization is maintained remains poorly understood. Recent findings suggest that nuclear morphology in DG is impaired with age, along with an age-dependent decline in adult neurogenesis. In order to investigate the relationship between age-dependent changes in nuclear morphology and tissue (dis)organization, we have developed a custom nuclear morphology analysis pipeline. Our systematic quantification will provide insights into the role of nuclear morphology in the maintenance of DG tissue organization.

P35: NUMERICAL AND EXPERIMENTAL CHARACTERIZATION OF BRAIN TISSUE ACROSS TIME SCALES AND PHYSIOLOGICAL CONDITIONS USING MRE

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To better understand the characterization of brain tissue properties, we analyzed different testing modalities and conditions. To bridge the gap among the different time scales, brain tissue and substitute materials were characterized at a rheometer and a tabletop MRE. The material behavior in the different regimes was combined by calculating the storage and loss modulus from the experimental responses. At the rheometer, the quasi-static material behavior under multiple loading modes was examined. In an inverse parameter identification, the mechanical parameters of a hyper-viscoelastic material model were determined. The high-frequency response was studied at a tabletop MRE, and the viscoelastic moduli were identified by fitting the measured shear wave to an analytical solution. To understand the difference in *in vivo* and ex vivo testing conditions, we modelled the tissue with and without vascular pulsation. This was based on the hypothesis that blood pressure stiffens the surrounding tissue. The tissue domain was simulated with vascular inclusions that were pressurized and coupled using the reduced Lagrange multiplier method in the 3D-1D regime. An *in silico* MRE experiment was performed on this domain to capture the effect of pressure on the shear modulus. The re-extraction of material properties using direct inversion techniques gave stiffened shear moduli.

P36: *IN VIVO* WIDEBAND MR ELASTOGRAPHY OF THE HUMAN BRAIN

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In vivo stiffness mapping of the brain by MR elastography (MRE) is usually restricted to a limited dynamic range of 30–50 Hz. However, a wideband MRE approach with a broader frequency spectrum could aid multi-frequency dispersion analysis, potentially enhancing our understanding of age- and disease-related microstructural tissue changes.

Therefore, a dual-actor wideband-MRE setup for 5-50 Hz frequencies was developed and tested in the brains of two groups of healthy volunteers assigned to younger adults (N=15: 29.7±4.1years) and older adults (N=10: 56.5±3.8years). Dispersion analysis was performed by fitting a spring-pot viscoelastic model to frequency-resolved shear wave speed (SWS).

Frequency-averaged SWS as a proxy for stiffness was lower in the older group (1.16±0.03m/s) than in the younger group (1.22±0.04m/s; $p<0.001$). SWS decreased linearly with age (SWS=1.28-0.0021×age; $p=0.002$). Spring-pot shear modulus decreased ($p=0.005$) while power law exponent α increased ($p=0.019$) with age. Lower drive frequencies were more sensitive to age-related brain softening than higher frequencies.

Our novel dual-actuator system enabled wideband MRE of the brain over more than three octaves. The age-related decrease in SWS and the associated changes in spring-pot parameters suggest sensitivity to microstructural tissue degradation (e.g., loss of neural and vascular integrity) associated with physiological aging.

P37: CHALLENGES IN MECHANICAL CHARACTERIZATION OF BRAIN ORGANOIDS

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Organoids are valuable *in vitro* models for neurological development. Although mechanical stimuli are assumed to impact organoid development, measurements of their mechanical response are currently limited to AFM -- brain organoids in particular have yet to be characterized.

This lack of data hinders the determination of stress states experienced by organoid cells and thus the understanding of organoid mechanobiology.

We aim to develop a robust testing protocol to characterize the mechanical response of organoids.

Testing of organoids is impeded by their small size, inherent softness, and fragility.

Unconfined compression tests up to 60\% strain at 37°C and 40 um/s using a rheometer have been performed in drops of nutrient solution.

Testing in fluid is necessary to avoid their desiccation and limit adhesion to the testing machine. However, measured forces are strongly affected by hydrodynamic effects. We use a simple hydrodynamic model to discriminate between organoid and fluid response. Visual determination of the contact point prior to testing is hampered by refraction in the fluid; therefore, it is fitted to the loading curve.

Qualitatively, the results show strain hardening, hysteresis, and a preconditioning effect similar to native brain tissue.

Determining mechanical properties will aid the quantification of mechanical stimuli in *in vitro* studies.

P38: MECHANICS OF SPINAL CORD REGENERATION IN XENOPUS LAEVIS

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The African clawed frog (Xenopus laevis) can regenerate central nervous system (CNS) neurons during its early life stages - pre-metamorphosis. However, this ability is lost post-metamorphosis, after the frog transitions into its adult form. Biochemical differences between pre- and post-metamorphosis frog spinal cord tissue identified so far cannot fully explain the differences in their regenerative capacity, suggesting that other signals may contribute to regulating wound healing and neuronal regeneration. Following spinal cord injury (SCI), the composition of the extracellular matrix changes, and scar tissue forms. In mammals, this scar tissue, which is softer than healthy tissue, inhibits axon regeneration. In contrast, in zebrafish, whose CNS neurons regenerate after SCI, tissue stiffens after injury. Mechanical properties of frog spinal cord tissue have not been measured yet. Because mechanosensing of tissue stiffness is critical for axon growth, we here test the hypothesis that tissue stiffness is a critical factor facilitating or impeding axon regeneration after SCI. We investigate the mechanical differences in the spinal cord lesion environment in pre- and post-metamorphosis Xenopus laevis. By examining factors such as tissue stiffness and molecular changes, we will illuminate the relationship between these factors and the regenerative capabilities.

P39: THE ROLE OF MECHANICS IN ORCHESTRATING NEURAL LINEAGE DECISIONS

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The mature central nervous system consists of a vast number of neurons and macroglial cells, all derived from a small population of neural stem cells (NSCs). The regulation of stem cell decisions, enabling both the expansion of the initial NSC pool and the precise production of differentiated cells at the correct time and place, is essential for generating the appropriate cell types. Notably, changes in extracellular matrix (ECM) expression patterns in NSCs are associated not only with the evolutionary increase in brain size from rodents to humans but also with the differentiation potential of NSC subtypes within a species. Since ECM composition determines the physical properties of a niche, this raises the intriguing question of whether and how the physical environment influences NSC lineage decisions. Our work explores how mechanical forces guide NSC lineage decisions and neuron formation in human brain organoids, a 3D model of early human brain development. We show that applying short acute physical stress on brain organoids induces cellular and molecular changes in NSCs, increases the protein level of the NSC factor SOX2 in a spatial-dependent manner, and decreases the rate of neuron formation. Using bulk and single-cell RNA sequencing, we dissect the molecular changes triggered by mechanical stress, showing it deregulates patterning processes and disrupts mitochondrial metabolism. Our findings reveal a hitherto unappreciated feedback loop, where the physical environment directs NSC patterning processes, and in turn, these processes shape the physical environment. This bidirectional interaction highlights the profound role of mechanics in brain development.

P40: REGIONAL MATERIAL PARAMETERS IN CEREBRAL ATROPHY SIMULATIONS

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Cerebral atrophy, characterized by a progressive reduction in brain volume, can be accelerated by the accumulation of neurotoxic proteins. To better understand the mechanical response of the brain during this process, we employed finite element simulations using regionally heterogeneous brain models. Brain images from the OASIS dataset were processed and segmented into 17 regions, each assigned specific material properties based on experimental data. Comparative models with reduced heterogeneity (9, 4, 2, and 1 region) were developed to evaluate the impact of regional simplification. Atrophy was modeled as a multiplicative decomposition of the deformation gradient, accounting for both natural and protein-induced shrinkage.

Stress analysis showed large discrepancies between simplified models (1R, 2R, 4R) and the 17R model, especially in the corpus callosum, with residual differences in the cortex and basal ganglia still present in the 9R model. Stretch patterns revealed persistent deviations between 9R and 17R in the corpus callosum, internal brain structures, and cortex. Morphological changes were largely consistent across models, except in the corpus callosum and ventricles. These results underscore the importance of regional heterogeneity in biomechanical modeling for the accurate representation of brain deformation due to atrophy.

P41: EVALUATING ADVANCED DIFFUSION IMAGING AS A PREDICTOR OF BRAIN TISSUE STIFFNESS

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Magnetic resonance elastography (MRE) of the brain has shown a reduction in brain stiffness in patients with Parkinson's and Alzheimer's disease. However, the microstructural changes that lead to this reduction are not fully understood. Meanwhile, multidimensional diffusion imaging (MD-dMRI) provides an extended set of diffusion parameters that reveal the differences in brain microstructure at sub-voxel level. In this study, we investigate whether the variation in these parameters can be linked to differences in the mechanical response of brain tissue. To achieve this, we implemented different sets of MD-dMRI parameters within a finite element model of the brain tissue and evaluated the mechanical response by altering the distribution of the brain's material properties. Each distribution corresponded to a unique set of four MD-dMRI parameters. We modeled the brain as a linear poroelastic material and evaluated its response under both constant and periodic (50 Hz) loading. Changing the permeability distribution led to variations in deformation, reaching up to 20% under static loading and less than 1% under periodic loading. Our results indicate that the mechanical characterization method influences the outcomes. This motivates further analysis of the boundary conditions and expansion of the current study to include additional poroelastic material parameters.

P42: THE MECHANICAL ROLE OF THE UDP-GALACTOSE TRANSPORTER SLC35A2 IN BRAIN MALFORMATIONS

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In humans, somatic mutations of the UDP-galactose translocator protein Slc35A2 have been identified as the cause of malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE). This condition is characterized by loss of the gray-white matter barrier and heterotopic neurons in the white matter. How Slc35A2 contributes to brain malformations remains poorly understood. Here, we investigated the effect of Slc35A2 loss of function on the onset of malformations in the developing Xenopus laevis brain. Preliminary results show that Slc35A2 knockdown in one brain hemisphere causes severe morphological phenotypes, with smaller and bent embryos and loss of eye development. Moreover, AFM measurements showed that knockdown of Slc35A2 results in stiffer brain tissue. As tissue mechanics is tightly linked to brain folding, these mechanical changes might be critically involved in the disorder. Future work will reveal molecular mechanisms linking galactose transport to tissue mechanics and brain folding.

P43: MODELING BRAIN DEVELOPMENT THROUGH A CELL-TYPE-DRIVEN GROWTH COMPUTATIONAL FRAMEWORK

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The human brain, our most complex organ, serves as the center of knowledge, language, and logic, defining what makes us uniquely human. Its structural complexity is evident, but its cellular intricacy is even more remarkable. Researchers aim to understand how cellular composition influences the formation of cortical folds, which emerge around mid-gestation and are closely linked to cognitive ability. Despite this, the connection between microscopic cellular processes and large-scale brain morphology remains unclear. Experimental evidence suggests that cortical folding arises from internal forces within the brain. Once these forces exceed a critical threshold, they trigger mechanical instability, resulting in cortical buckling. This study introduces a computational multifield model that links cellular dynamics to large-scale brain growth. Morphological development is captured using a continuum mechanics framework that incorporates finite deformation and growth. Cellular processes are represented by a system of advection-diffusion equations, each reflecting the behavior of a specific cell type and regulating localized tissue growth. The model successfully captures essential features of brain development, such as the outer subventricular zone, and distinguishes the roles of various brain cell types. This integrative framework enhances our understanding of brain development and may ultimately help uncover the origins of cortical malformations.

4 APPENDIX

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