GÖTTINGEN

21ST-24TH MAY

11TH BIENNIAL NEUROSCIENCE CONFERENCE

NEURIZONS

Event Booklet

GEORG-AUGUST-UNIVERSITÄT GÖTTINGEN

IMPRS for Neurosciences

INTERNATIONAL MAX PLANCK RESEARCH SCHOOL

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EVENT BACKGROUND

Message from the Organizing Committee

Welcome to **NEURIZONS 2024**, the 11th biennial neuroscience conference organized by the students of the International Max Planck Research School (IMPRS) for Neurosciences, Göttingen.

In this edition of **NEURIZONS**, we would like to bring the focus on the young scientists who have started to contribute to the vast and fascinating field of Neuroscience. As such we have created opportunities for early career scientists to display their work and attend talks by renowned scientists, exploring every subcategory of Neuroscience, from detailed molecular work to brain-wide network dynamics. We encourage you, the participants, to form connections and share your work with peers and experts alike. To this end we would like to highlight our poster session, from which we have selected some particular meritorious early scientists to present their work in front of an international audience. Moreover, our carrier fair provides the perspective of less–known career paths outside of academia.

We hope that you have a lovely and scientifically-invigorating time at **NEURIZONS 2024**.

Your 2024 NEURIZONS Organizing Team

Welcome Note from the Program Coordinator

It is a pleasure for me to welcome all participants of **NEURIZONS 2024** on behalf of the International Max Planck Research School for Neurosciences to our venue at the Max Planck Institute for Multidisciplinary Sciences!

The longstanding tradition of our biennial conference has its roots in the year 2004, when PhD students of the International MSc/PhD/MD-PhD Program and IMPRS for Neurosciences organized the first meeting in Göttingen. Over the years, **NEURIZONS** further developed its unique character as a small conference with a family-like atmosphere, encouraging direct personal interactions between participants and especially bringing young PhD students at the beginning of their scientific careers in contact with renowned neuroscientists.
Since 2015, **NEURIZONS** is featuring a career fair to highlight the multiple career opportunities. Also involving alumni of the IMPRS, the students have not only the chance to attend interesting talks with intensive Q&A sessions, but also join workshops to further develop their individual career choices.

NEURIZONS is traditionally an in-person event, but **NEURIZONS 2020** had to be shifted to an online format on a very short notice due to the pandemic and the conference in 2022 was planned as a hybrid event. Even though both formats worked well and attracted many interested participants worldwide, **NEURIZONS 2024** is coming back as a pure on-site conference focusing on

personal interactions among participants and speakers.

This year's organizing team has invited internationally renowned speakers who will provide insights in their recent research activities. The scientific talks are clustered into five topics (Molecular and Cellular Neuroscience, Computational and Systems Neuroscience, Cognitive Neuroscience, Clinical Neuroscience, and Emerging Techniques) comprising all fields of neurosciences and highlighting experts in the respective research areas. Additionally, early career researchers are encouraged to present their own research during the poster session and take part in the young investigator contest to be selected for short presentations alongside the invited speakers or pitch talks to highlight their posters for the poster session. The panel discussion will focus on neuroprosthetics, inviting all participants to actively take part in the discussion with the panelists. The scientific program is flanked by two keynote lectures presenting the highlights of **NEURIZONS 2024** to open and close the conference.

Traditionally, the Otto Creutzfeldt PhD Award for the best doctoral graduates of the last years is awarded during the **NEURIZONS** closing ceremony. Ever since the price was launched in 2007, it has been sponsored by the Göttingen based company Sartorius with a cash price documenting the company's commitment and close cooperation with the Neuroscience Program.

Several companies are continuously supporting **NEURIZONS** since many years. Thanks to their contribution, participation in **NEURIZONS 2024** is free of charge, which is especially attractive for early career researchers as they can join the meeting without relying on the budget of their host institutions. The conference would not be

possible without our sponsors, whose generous support is very much appreciated and will contribute to make **NEURIZONS 2024** a success.

Dr. Jonas Barth

About Us

The Neurizons 2024 organizing team is a group of MSc/PhD students from the International Max Planck Research School (IMPRS) for Neurosciences. The IMPRS for Neurosciences program is a member of the Göttingen Graduate School of Neurosciences and Molecular Biosciences (GGNB), funded by the German Excellence Initiative, under the umbrella of the Georg-August University School of Science (GAUSS). It is conducted jointly by the Georg-August University Göttingen, the Max Planck Institute for Multidisciplinary Sciences, the Max Planck Institute for Dynamics and Self-Organization, the German Primate Center, and the European Neuroscience Institute Göttingen.

Mels Akhmetali

Yixuan Chen

Maren Cremer

Tarannom Taghavi

Thanh Thao Do

Elisa Panzeri

Uğur Coşkun

Eren Diniz

Marina Saade

Robert Haret

Ege Kingir

Vladyslav Ivanov

Ranjit Pradhan

Varsha Ramakrishna

Asude Tura

Lucia Rojas

Göttingen, City of Science

Welcome to Göttingen, the city of science. Founded in the 10th century, it is one of the oldest university towns in Germany. Among its 119.000 inhabitants, around 20% are students. They study alongside researchers from various illustrious research institutes, including 4 instutes belonging to the Max Plank Society (founded in Göttingen in 1948):

- Max Planck Institute for Multidisciplinary Sciences (previously Max Planck Institute for Biophysical Chemistry and Max Planck Institute for Experimental Medicine)
- Max Planck Institute for Dynamics and Self-Organization
- Max Planck Institute for Solar System Research
- Max Planck Institute for the Study of Religious and Ethnic Diversity
-

The city's other scientific establishments include the German Primate Center, the German Aerospace Center, the Private University of Applied Sciences, and the University of Applied Sciences and Arts. The city boasts more than 40 Nobel Prize winners who have lived or worked here in the last century. Of those, 13 were awarded with the prize for research done in the city. Other notable inhabitants include mathematicians Carl Friedrich Gauss, Bernhard Riemann, David Hilbert and Hermann Minkowski, as well as the physicists Wilhelm Weber, Max Born, Werner Heisenberg and Georg Lichtenberg. Take a tour through the old town and have a look on the walls of the houses for plaques commemorating their famous dwellers.

Göttingen has a uniquely well-preserved old town with half-timber houses with precipitous roofs, typical of German architecture, as well as important university buildings like the Great Assembly Hall at Wilhelmsplatz (William's Square) and the Old Botanic Garden. Other interesting locations are the Jacobikirche (St. Jacob Church), and the Old Town Hall. In the center of the Old Town Hall stands a young girl holding a goose: The Gänseliesel. She is central to the Göttingen PhD life: students look forward to the day when, after completing their thesis defense, they get to be carried to the market square in wagons decorated with balloons and flowers, where they climb the fountain and kiss "the most kissed girl in the world".

In spite of its historic roots, Göttingen is home to a young, international scene. Much of the night life is focused within the old town. There are various clubs, ranging from Latin (Sausalitos), pop, hip-hop and electro (Savoy, JT-Keller) to alternative (Cafe Kabale), as well as jazz and live music (Noergelbuff). Göttingen also offers many pubs and bars (Duke, Thanners, Trou, Nautibar) with a cozy atmosphere if you are looking to be surrounded by good company and good beer. The restaurants offer various kinds of cuisine from traditional German (Zum Szultenburger) to international (Zak, Myer's, Kartoffelhaus), Asian (Gamie, Vietal Village, India Haus), Italian (Tante Giulia, Fellini, Vapiano), Greek (Hellas), to African (Abessina). You can find further information about Göttingen on www.goettingen-tourismus.de.

Venue Information

Neurizons 2024 will take place at the Max Planck Institute for Multidisciplinary Sciences, Faßberg Campus, am Faßberg 11, 37077 Göttingen. The scientific talks and the career fair seminars will be held in the Manfred-Eigen Lecture Hall. The registration desk will be located in the entrance foyer, alongside our sponsors' industry exhibitions. Poster sessions will take place in the Ludwig Prandtl Hall. Lunch will be held in the canteen ("Mensa") located in the basement under the foyer (see image on the next page).

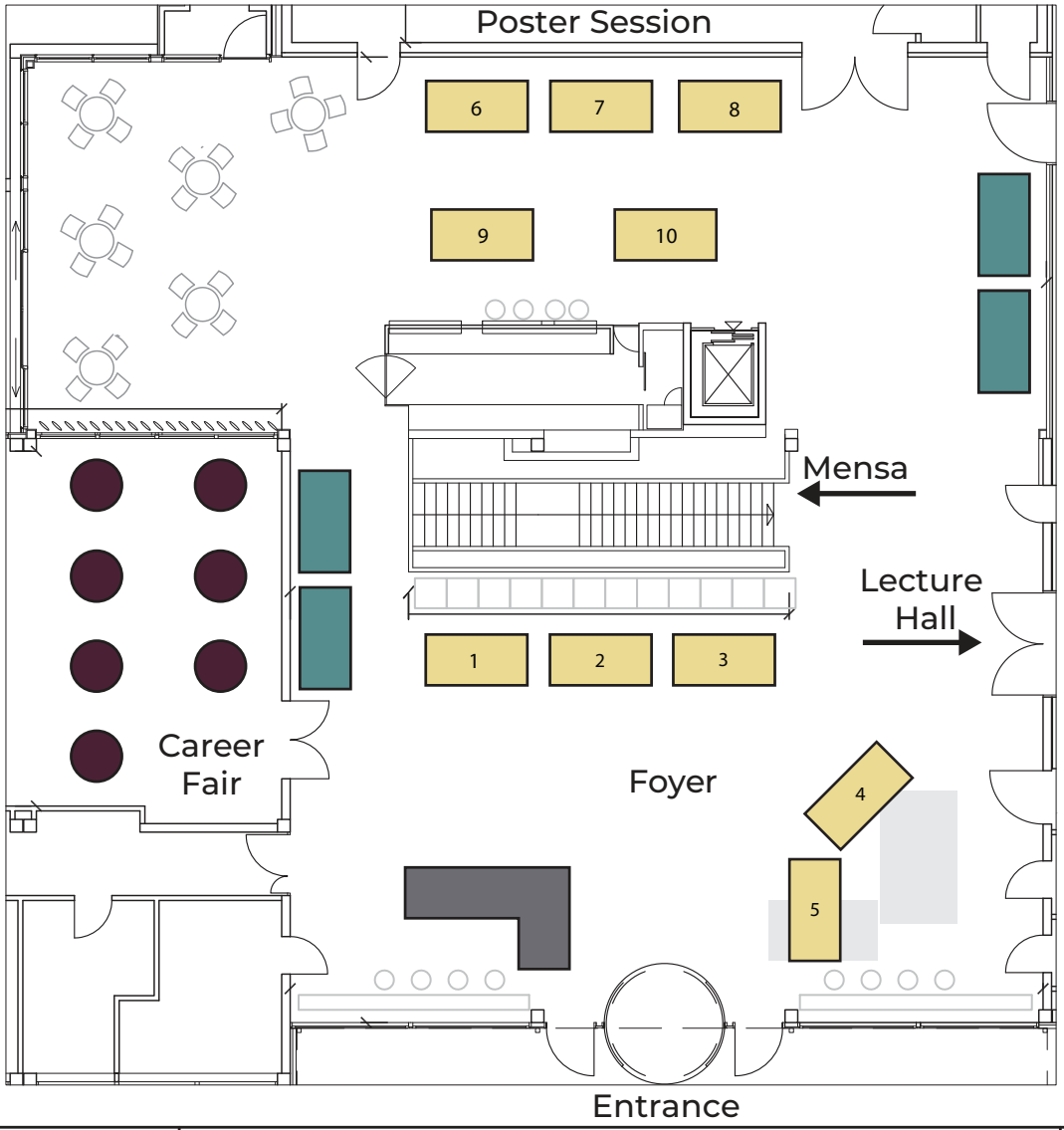
Please take care of your personal belongings. The Organizing Committee takes no responsibility for accidents or damages to participants' belongings. Feel free to approach the Neurizons Organizing Team if you need any further information or assistance. The organizers are the ones wearing Neurizons T-shirts!

Bus Lines

Buses no. 21, 22 and 23 connect the Max Planck Institute for Multidisciplinary Sciences, Faßberg Campus with the city center and the railway station. On the map above, you can see the route that buses 21 and 23 follow from the railway station to the venue. To reach the venue, take the bus in the direction "Nikolausberg" (for no. 21/22) or "Faßberg" (for no. 23) and get off at the bus stop "Faßberg". From there it is a minute's walk to the first large administration building on the opposite side of the street. There are buses departing from Faßberg towards the city center approximately every

NEURIZONS 2024 VENUE LAYOUT

- Sponsor Desk
- Snack Tables
- Organizer Desk
- Career Fair Tables



15 minutes. The last bus departs at 23:21. You can also consult Google® Maps, selecting the option for Public Transport. You can buy tickets from the driver: the single ticket for adults (Einzelfahrkarte) is €2.40. The day ticket (Tageskarte) is €5.80. For more information about the bus fares please visit the bus company's webpage: www.goevb.de.

Name Tags

Every participant of Neurizons will receive a name tag. These name tags should be worn throughout the conference, as they will be required for admission to all events.

Lunch and Refreshments

Lunches are included in the conference fee. In order to receive your lunch, you will need to present a valid voucher. Cold refreshments, coffee and tea will be provided during each break.

Internet Access

Free WiFi connection will be available throughout the conference. Please ask for the password at the registration desk. Additionally, in many areas across Göttingen you may find connection to the eduroam wireless network. Scientists and students from participating institutions can log in with their personal or institutional eduroam account.

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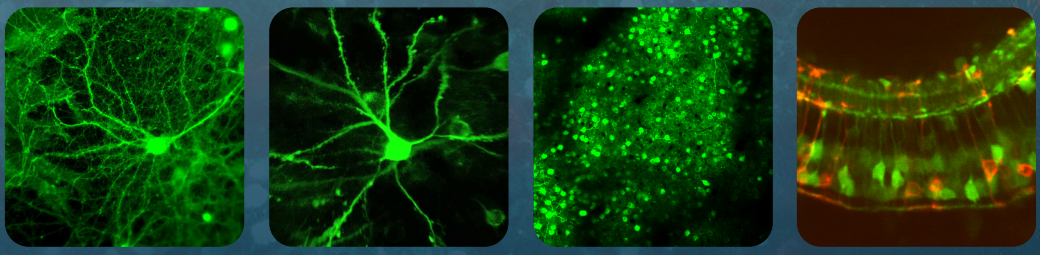

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EVENT HIGHLIGHTS

Career Fair

Tuesday, 21st of May 2024

At our career fair, you will have the opportunity to learn about the variety of jobs available after the PhD. Here you can benefit from the expertise of successful scientists who chose to continue their path in the industry. Whether you have already decided on your future career path or not, don't miss out on this chance to hear some interesting stories and opinions, and to grow your professional network. So join us on the first day of Neurizons 2024, Tuesday, May 21st, and interact with scientists who have been through the same dilemmas to find out what career path suits you the best. We hope to give you a taste of what is out there!

Dr. Andreas Görlich

German Research Foundation (DFG), Germany

From funded to funder: working for the German Research Foundation (DFG)

Dr. Andreas Görlich studied biophysics at the University of Kaiserslautern and did his diploma and PhD thesis in neurobiology there. For his postdoc, he went to the Rockefeller University in New York to the lab of Nathaniel Heintz. His scientific work focused, among other things, on the neurobiological basis of the auditory system and nicotine addiction, using electrophysiological methods in brain slices.

After a 10-month parental leave he started his work at the German Research Foundation (DFG). Here he processes research proposals in the basic neurosciences, advise applicants and is involved in various projects to adapt the application process.

Dr. Fernando Cross Villasana

Brain Products, Germany

Insights from a journey between academia and industry

As a scientific consultant at Brain Products, Dr. Fernando Cross Villasana's main task is to support their users about EEG data processing and analysis using their software. This involves helping them to adapt analysis strategies that fit the particular characteristics of their data and the research aims, but can also include questions on experimental design or about the particular use of their software. Another important task is to produce educational materials. This involves writing articles, imparting seminars and webinars or generating data for demonstration, all with the aim to help researchers make the best use of their products.

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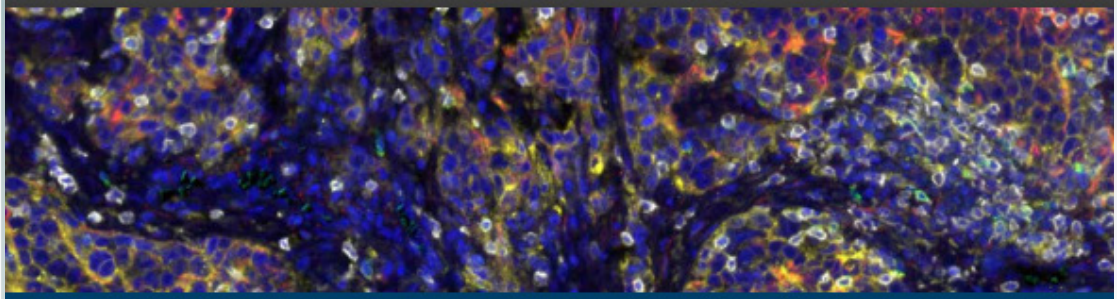

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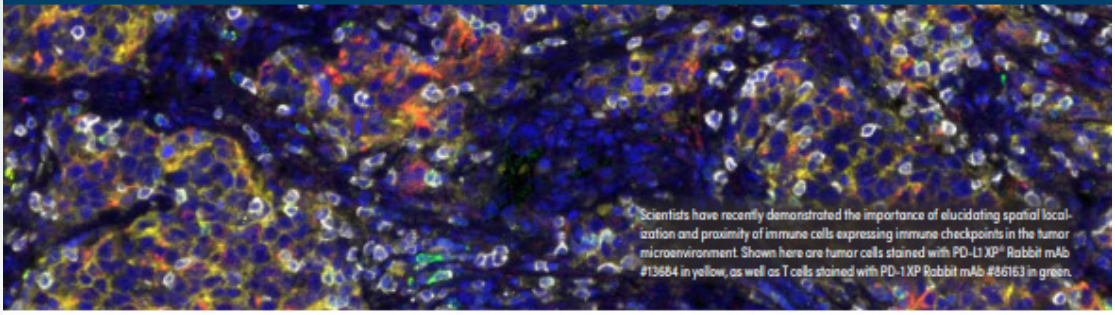

Scientists have recently demonstrated the importance of elucidating spatial localization and proximity of immune cells expressing immune checkpoints in the tumor microenvironment. Shown here are tumor cells stained with PD-L1 XP® Rabbit mAb #13684 in yellow, as well as T cells stained with PD-1 XP Rabbit mAb #86163 in green.

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Dr. Olga Babaev

Boehringer Ingelheim Pharma, Germany

Career opportunities in drug development

Dr. Olga Babaev received Dr.rer.nat (summa cum laude) from Göttingen University in Germany and a B.Pharm (summa cum laude) from Ben-Gurion University in Israel. Prior to joining Boehringer Ingelheim Pharma, she worked as a Post-Doctoral Researcher at the Max Planck Institute for Experimental Medicine in Göttingen. During this time, she led several multidisciplinary projects to discover novel therapeutic targets for anxiety treatment and established an in-vivo lab in her department. Additionally, Dr. Babaev wrote four papers, successfully secured two grants, and led a Public Relations team for two international conferences. Dr. Babaev then moved to Boehringer Ingelheim Pharma in Biberach, Germany, and became a Post-Doctoral Researcher in the Department of CNS Diseases Research. During this time, she established novel paradigms to evaluate pre-clinical models of depression and proposed two novel therapeutic concepts for the treatment of motivation-related deficits in depression and schizophrenia. In this role, she supported the CNS research portfolio and initiated external collaborations. After 12 years in research, she started a new role as a Medical Writer in Clinical Development at Boehringer Ingelheim. She now works with biostatisticians, physicians, patent attorneys, clinical trial leaders, and research scientists to organize the preparation and submission of clinical documents required for the approval of new drugs for the treatment of cardiometabolic disorders.

Dr. Tal Dankovich

Nucleai, Israel

Academia to Tech: Code your way through your PhD

Immediately after leaving academia, Dr. Tal Dankovich began to work at Nucleai, a cancer research company that utilizes deep learning to gain insights into biopsy images. During her initial months, she worked on developing a deep learning-based image analysis pipeline for analyzing multiplex immunofluorescence microscopy images. Later on, she became the main developer in charge of spatial feature calculation within their software team. Spatial features are quantitative values derived from analyzing the results of their deep-learning models. These can be fairly basic values like 'density of tumor cells' to more complex features such as measures of cell clustering. The position she holds involves both the development of the software branch in charge of this feature calculation, as well as the research and integration of new features they (or their clients) wish to calculate.

Dr. Sandy Rathod
NeuroReality, Netherlands

From Academia to Industry: A Journey of Learning, Growth, and Impact

NeuroReality transforms cognitive rehabilitation through VR experiences rooted in neuropsychology. As CEO, Dr. Sandy Rathod merges scientific rigor with strategic vision, leveraging her PhD in Consumer Behavior from Purdue University to drive innovation. Her academic background informs her approach to business, making rehabilitation engaging for patients and seamless for clinicians while delivering economic impact. This fusion of science and business has fueled her success across diverse sectors in the US and Europe, where she has collaborated with diverse companies from start-ups to industry giants like KLM and Lucent Technologies.

Drawing on her expertise in marketing, strategy, and product development, she has navigated complex challenges to create tangible value. Beyond the boardroom, she is deeply committed to social good, serving on non-profit boards and fostering environments where creativity flourishes. Her goal as a leader is to inspire teams to achieve collective success, driven by clarity, empathy, and an unwavering commitment to excellence. Every endeavor is propelled by purpose and passion, rooted in the fusion of academia and business.

Workshops

Tuesday, 21st of May 2024

Neurizons 2024 brings you two compelling workshops. The first workshop, 'What to do with a PhD?', addresses the career trajectories post-PhD, offering participants a practical guide on navigating career options with insights into transitioning from academia to industry. The second workshop, 'Communicating animal research to public', focuses on the ethical dimensions and communication strategies related to animal research. This workshop aims to equip scientists with the skills to effectively address public concerns and communicate the critical role of ethical considerations in animal studies.

Dr. Gaby Schilling

KEPOS

“What to do with a PhD?”

At the end of their PhD young scientists are confronted with the question whether to remain in science and look for a postdoc position or whether to change direction and start a career outside academia. At the time, when they focus on their dissertation they are confronted with essential questions for their professional career.

This workshop will give the participants an overview of various career paths in academia, the public service, NGOs and the private industry and addresses the issues that postgraduates face at the end of their PhD: What are the cultural differences between private industry and academia? What are the advantages/disadvantages of public and private business? What kind of jobs are out there and what sort of personality/mindset is necessary to be successful in industry? How can I apply for a job if I don’t even understand what the job offers mean? And where shall I start looking for a job? These and other questions will be addressed in this mini-workshop.

Dr. Roman Stilling

Tierversuche Verstehen

“Communicating Animal Research to Public”

In this workshop, scientists will be encouraged to foster a thoughtful dialogue on the complex and critical issue of animal use in scientific experiments. With this, the participants will learn how to address the questions from public concerning their research with animals, while also practicing their scientific communication skills. Join us as we learn the ethical guidelines of animals in research, while exploring the important balance between discoveries and the moral responsibility to minimize harm.

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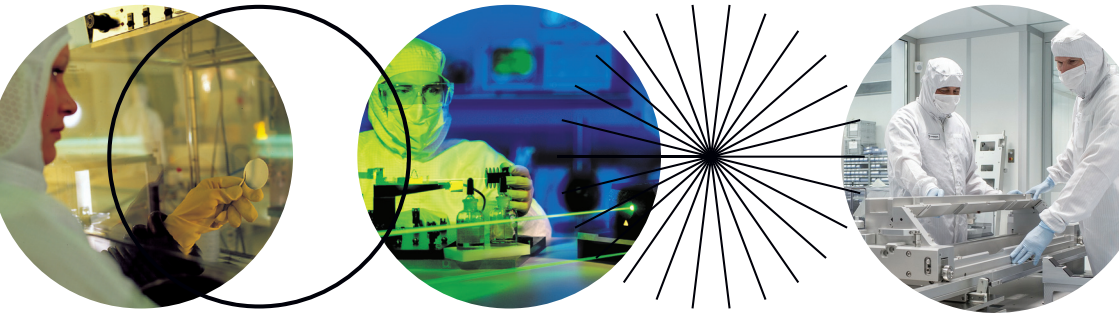

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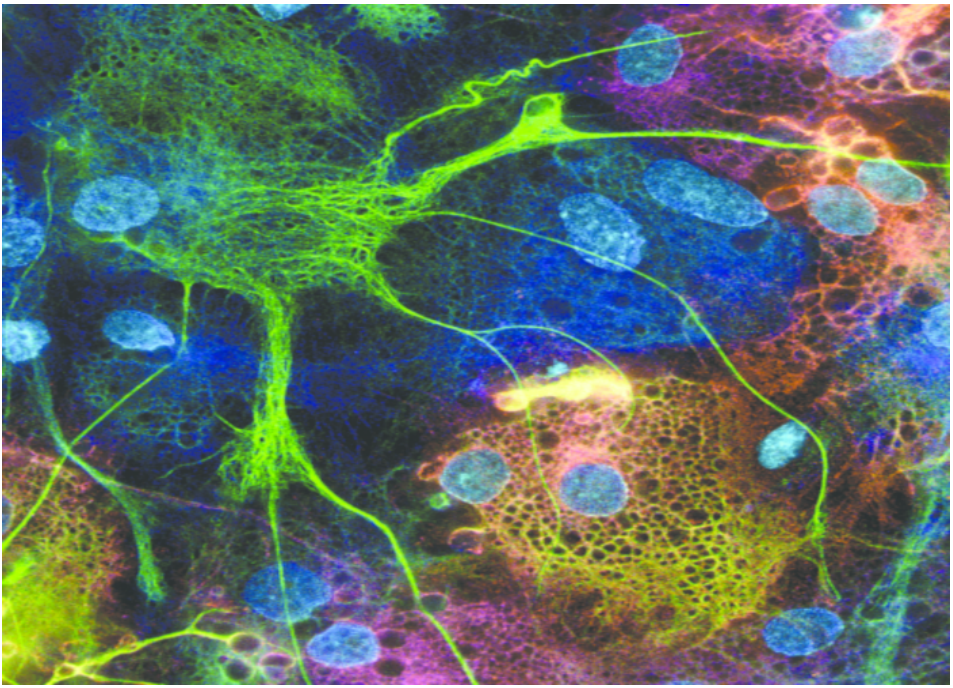

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Scientific Lectures

Wednesday - Friday, 22nd - 24th of May 2024

This year, we have five main categories of talks to cater to the diverse subdisciplines of neuroscience: molecular and cellular neuroscience, computational and systems neuroscience, emerging techniques, cognitive neuroscience, and clinical neuroscience. There will also be two keynote lectures by Dr. Li-Huei Tsai and Dr. Peter Dayan.

Keynote Lecture 1

Wednesday, 22nd May 2024

Prof. Dr. Li-Huei Tsai

Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, USA

Enhancing gamma oscillations in Alzheimer's disease: mechanism and pilot study in humans

Rhythmic neural activity in the gamma range (30-80 Hz) is modulated during various aspects of cognitive function and is disrupted in several neurological conditions, including Alzheimer's disease (AD). We developed an approach which we term Gamma ENtrainment Using Sensory stimuli (GENUS), using patterned light and sound stimulation at 40 Hz in AD model mice to evaluate the effects of boosting gamma oscillations. We showed GENUS augmented gamma power in multiple brain regions. Moreover, daily application markedly reduced amyloid and tau pathology, attenuated degeneration of neurons and synapses, and improved cognitive function in multiple AD mouse models. In addition, GENUS induced morphological and gene expression changes of various cell types, including microglia and enhanced vasodilation. GENUS also enhanced glial-mediated and lymphatic-like brain waste clearance, known as glymphatic clearance, in a VIP interneuron dependent manner. We showed evidence that the enhanced glymphatic clearance is necessary for the reduction of amyloid burden following GENUS in mouse cortex. Multisensory gamma stimulation has now been administered to human subjects in multiple studies. I will discuss the outcome of these human studies and the feasibility of using this non-invasive sensory stimulation approach to treat neurological disorder.

Keynote Lecture 2

Friday, 24th May 2024

Prof. Dr. Peter Dayan

Max-Planck-Institute for Biological Cybernetics; University of Tübingen, Germany

‘Liking’ as a First Draft of the Affective Future

Humans and other animals are excellent at improving their otherwise unfortunate lot in life - often described in terms of optimizing utility. However, understanding utility in a non-circular manner is surprisingly difficult. One example of the complexity is the important psychological and neural distinction made most prominently by Kent Berridge between concepts of ‘liking’ and ‘wanting’, with the former characterizing an immediate hedonic experience; and the latter the motivational force associated with that experience. How could it be that we could `want’ something that we do not `like’, or `like’ something that we would not be willing to exert any effort to acquire? Furthermore, what role do neural systems associated with reinforcement such as the neuromodulator dopamine play in these concepts? Here, we suggest a framework for answering these questions through the medium of reinforcement learning. We consider ‘liking’ to provide immediate, but preliminary and ultimately cancellable, information about the true, long-run worth of a good. Such preliminary estimates, viewed through the lens of what is known as potential-based shaping, generally facilitate the temporally complex learning problems that we face.

Molecular and Cellular

Prof. Dr. Dietmar Schmitz

German Center for Neurodegenerative Diseases, Germany

Synchronization of neuronal networks at high speed

One of the most intriguing open questions in neuroscience is how the brain captures and stores information in such an efficient and long-lasting way. To do so, it has to perform a tremendous task: it has to process a continuous input from our sensory organs and at the same time it must be able to store memories, sometimes even for a lifetime. What are network-level foundations of this long-term information storage capacity? In a concert between the hippocampal formation and cortical areas specific forms of memories are established. Differential roles of synchrony of neuronal networks are thought to be important for both the encoding as well as the consolidation of memory traces. I will consider how brain rhythms at the network level contribute in processes of information storage and by what means they participate. Furthermore, I we examine memory consolidation at the system level during processes of sleep.

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Molecular and Cellular

Prof. Dr. Isabelle Mansuy

Brain Research Institute, University of Zurich;
Institute of Neurosciences, ETH Zurich, Switzerland

Epigenetic inheritance: How traumatic experiences in early life can affect descendants via the germline

Behavior and physiology in mammals are strongly influenced by childhood experiences. While positive factors favor proper development and mental and physical health in adulthood, early life adversity increases the risk for psychiatric, metabolic and autoimmune diseases and cancer. Such disorders can affect directly exposed individuals and their descendants in some cases across several generations. The biological mechanisms underlying the inheritance of environmentally-induced (acquired) traits are thought to involve factors independent from the DNA sequence in the germline. We developed a mouse model of postnatal stress that causes persistent symptoms across generations.[1-3] The symptoms include increased risk-taking, depressive-like behaviors, cognitive and social deficits, metabolic and cardiovascular dysfunctions in adulthood. Some symptoms also manifest in the offspring of exposed individuals, up to the 5th generation i.e. risk-taking behaviors.[4] In humans, comparable symptoms affect people exposed to childhood trauma, suggesting conserved effects across species.[5] At a molecular level, exposure is associated with epigenetic changes involving RNA and DNA methylation in somatic cells across the body and in germ cells, with sperm RNA being causally linked to symptoms transmission.[2] MiRNAs are also affected

in extracellular vesicles in blood and the reproductive tract.[6] Circulating factors were identified as mediators of alterations in germ cells. Chronic injection of serum from trauma-exposed mouse males into control males recapitulates metabolic phenotypes in the offspring, suggesting information transfer from serum to germ cells. Pathways involving peroxisome proliferator-activated receptor (PPAR) are causally involved, with pharmacological PPAR activation in vivo affecting sperm transcriptome and metabolic functions in the offspring and grand-offspring.5 These results suggest the existence of an ensemble of factors and mechanisms that can carry information about past experiences from the periphery to germ cells for the inheritance of acquired traits.[7,8]

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5. van Steenwyk, G. et al. Involvement of circulating factors in the transmission of paternal experiences through the germline. EMBO J. 39, e104579 (2020).
6. Alshanbayeva, A., Tanwar, D. K., Roszkowski, M., Manuella, F. & Mansuy, I. M. Early life stress affects the miRNA cargo of epididymal extracellular vesicles in mouse. Biol Reprod 105, 593–602 (2021).

7. Arzate-Mejia R.G., Carullo N.V.N. and Mansuy I.M. The epigenome under pressure: On regulatory adaptation to chronic stress in the brain. Current Opinion in Neurobiology. 84:102832 (2024).
8. Arzate-Mejia, R. G and Mansuy, I.M. Remembering through the genome: The role of chromatin states in brain functions and diseases. Transl Psy 13:122 (2023).

Computational and Systems

Dr. Fabien Wagner

French National Centre for Scientific Research; University of Bordeaux, France

Neuroprosthetic modulation of distributed spinal cord and brain networks for restoring motor and cognitive functions in neurological disorders

Neuroprosthetics is a multidisciplinary field at the interface between neurosciences and biomedical engineering, which aims at replacing or modulating parts of the nervous system that get disrupted in neurological disorders or after injury. Although neuroprostheses have steadily evolved over the past 60 years in the field of sensory and motor disorders, their application to higher-order cognitive functions is still at a relatively preliminary stage. Nevertheless, a recent series of proof-of-concept studies suggest that electrical neuromodulation strategies might also be useful in alleviating some cognitive and memory deficits, in particular in the context of dementia.

In this talk, I will first introduce neuroprosthetic technologies for restoring motor function after spinal cord injury, based on the principle of spatially and temporally specific spinal cord stimulation protocols. These technologies were first developed in preclinical models, in particular non-human primates, which led to their translation into patients with either incomplete or complete spinal cord injury. Next, I will propose a translational path for the development of invasive cognitive neuroprostheses that could interface with large-scale brain network oscillations. Specifically,

I will present the technological development of brain implants targeting distributed brain areas involved in memory processes, and preliminary testing in non-human primates trained to perform a short-term memory task. This parallel between motor and cognitive neuroprostheses highlights important common principles such as the need for neuroprosthetic systems that enable multisite bidirectional interactions with the nervous system.

Computational and Systems

Prof. Dr. Jorge Mejias

University of Amsterdam, Netherlands

Towards virtual brain models with cognitive functionalities

Computational models of large-scale brain networks, or 'virtual brain models', have been traditionally focused on reproducing brain dynamics such as resting state activity. However, embedding the mechanisms and structure needed to reproduce brain functions related to perception and cognition, in a way that also matches the neuroanatomical and electrophysiological evidence, has been more challenging. In this talk, I will present two recent examples of computational models of brain networks which include rudimentary but behaviorally relevant functions. The first example will focus on how the delay activity underlying working memory may emerge as a distributed phenomenon across multiple regions of the macaque and human brains - rather than restricted to prefrontal areas as assumed in classical computational models. For the second example, I will shift the focus to decision making and present simulations of the macaque brain in a framework where the evidence accumulation needed for perceptual decisions is brain-wide distributed. These results, obtained with models strongly constrained by anatomical and electrophysiological data, successfully explain multiple experimental observations, suggest that both working memory and decision making are intrinsically distributed phenomena in the brain. Our work also opens the door of using virtual brain approaches to study cognitive functions and disorders.

Computational and Systems

Prof. Dr. Anthony Holtmaat

Department of Basic Neuroscience,
Geneva University, Switzerland

Higher-order thalamocortical feedback regulates pyramidal cell excitability and plasticity

The neocortex plays a critical role in higher cognitive functions and learning, which involves the integration of various feedforward and feedback information streams. In primary sensory cortices, an important source of input originates from first-order and higher-order thalamic nuclei, with the former relaying principal sensory information and the latter conveying contextual or behavioral information. The functional interaction between higher-order thalamocortical feedback and the cortical synaptic circuitry is poorly understood. I will summarize work over the last decade in which we have characterized some of the unique properties of higher-order thalamocortical input for synaptic integration and plasticity in the primary somatosensory cortex. I will further support this with recent data from dendritic patch clamp recordings ex vivo, Ca2+ imaging experiments in vivo, and correlative light and electron microscopy.

Emerging Techniques

Assoc. Prof. Dr. Laura Huckins

Yale University, USA

Dr. Laura Huckins is an Associate Professor in the Molecular Psychiatry Division at Yale University. Her research group is dedicated to understanding the roles of genetics and environment in psychiatric disorders, with a particular emphasis on Eating Disorders and PTSD. Her lab develops novel approaches to identify and characterize genetic regulation of higher order biology, primarily focusing on eQTLs (SNPs that regulate gene expression). Dr. Huckins' group has applied these models to identify novel risk genes associated with schizophrenia, PTSD, and most recently, anorexia nervosa, as well as answering key questions about developmental risk periods, tissue- and pathway-level involvement, and identifying metabolic and psychiatric risk factors in eating disorders. Most recently, students in Dr. Huckins' lab have pioneered the study of interaction-QTLs, identifying variants that regulate gene expression only in certain environmental contexts.

Dr. Huckins was awarded the highly prestigious Ted Reich Young Investigator Award from the International Society of Psychiatric Genetics in 2023. She is an elected member of the Brain and Behaviour Research Foundation, and the Connecticut Academy of Science and Engineering.

Emerging Techniques

Prof. Dr. Emilie Maće

University Medical Center Göttingen, Germany

Functional ultrasound imaging: application to vision

Functional ultrasound imaging (fUS) is a powerful neuroimaging tool that can measure brain-wide vascular signals linked to neuronal activity with high spatial and temporal resolution. Notably, fUS is among the limited methods that facilitate real-time imaging of activity deep within the brains of behaving rodents. In this presentation, I will highlight recent technical advancements of fUS used in our laboratory, such as the ability to image the entire mouse brain while manipulating specific neuronal circuits with optogenetic. I will exemplify the potential of fUS for advancing our understanding of the neural basis of behavior. Specifically, I will explain how we used fUS to investigate object vision within the mouse brain. Mice depend on vision for various behaviors, such as hunting crickets or evading predators; however, whether they are capable of object recognition and how visual objects are processed in their brains remains unclear. Through our unbiased approach, we unexpectedly found object selectivity in regions traditionally associated with the spatial navigation system in mice, a discovery that we validated with electrophysiology. Our findings call for a reconsideration of the role that spatial navigation systems play in object vision.

Emerging Techniques

Asst. Prof. Nako Nakatsuka

École polytechnique fédérale de Lausanne, Switzerland

Aptamer Nanotechnologies for Neurochemical Detection

Advancing our understanding of brain (dys)function necessitates novel nanotools that can monitor chemical signaling with high spatial resolutions. While advanced methods to record electrical signaling from neurons are prevalent (e.g., microelectrode arrays, MEAs), tools to monitor chemical signaling have been limited. We have tackled this challenge by coupling the inherent selectivity of DNA-based recognition elements termed aptamers, with nanoscale pipettes with openings of ca. 10 nm. Aptamers are systematically designed oligonucleotide receptors that exhibit highly specific and selective recognition of targets. Aptamers that recognize small-molecule neurotransmitters, including serotonin and dopamine, have recently been isolated. Upon reversible target binding, aptamers undergo a rearrangement of the negatively charged backbone, and these dynamic structural changes can be transduced as measurable changes in current through the nanoscale orifice of the sensors. Nanoscale confinement of the sensor surface results in single-molecule sensitivity while simultaneously reducing biofouling for long-term recordings in complex environments, overcoming a critical bottleneck for clinical biosensors. We have demonstrated the capacity to detect physiologically relevant differences in neurotransmitter amounts released by live neurons in complex media with

unprecedented sensitivity. Further, through seamless integration into patch clamp setups, our sensors have been deployed to track endogenous dopamine release in acute brain slices. Through collaboration, we are currently tracking serotonin while simultaneously recording electrical responses of neural tissue cultured on MEAs. Thus, we demonstrate the translatability of these sensors to other neuroscience groups and the possibility to conduct continuous recordings in localized regions with nanoscale resolution.

Cognitive Neuroscience

Prof. Dr. Arno Villringer

Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences; Cognitive Neurology, University of Leipzig Medical Center, Germany

The Relationship of Cardiovascular and Mental Function

Medicine today is still strongly influenced by the dualistic view that diseases are either 'somatic' or 'psychological'. However, epidemiological studies show that mental and somatic illnesses, and in particular cardiovascular and mental illnesses, often co-occur. There are many explanations for this co-occurrence, generally involving reciprocal pathophysiological influences. In our studies, we test an extrapolation / generalization of findings from animal studies that cardiovascular and psychological functions not only influence each other, but are even more closely related in that they represent different dimensions of integrated cardiovascular-mental states. In human studies, this view is supported by beat-to-beat tight heart-brain interactions, integrated states during emotions, but also longer-lasting states such as stress. In this view, the co-occurrence of cardiovascular and mental illness is only a logical consequence, i.e., the tip of the iceberg.

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Cognitive Neuroscience

Prof. Dr. Emrah Düzel

Otto von Guericke University Magdeburg; German Center for Neurodegenerative Diseases, Germany

Episodic memory circuitry and its impairment in Alzheimer's disease

Alzheimer's Disease causes pathology to spread along neural pathways that serve specific cognitive processes, such as pattern separation and pattern completion in memory. These neural pathways not only reflect distinct cognitive processes, but also specialize in different representational contents, such as object information and spatial properties. Recent research has revealed that an association of pathology spread and content-specific impairment of memory processes can be observed in early Alzheimer's disease. This helps to generate mechanistically specific cognitive signatures of clinical stages and patterns of pathology in Alzheimer's disease. In this talk, I will present data from large disease cohorts, and functional and molecular imaging to provide an overview of the current state of this research. I will also discuss how these insights can be translated into new digital technologies to support diagnosis and monitoring.

Cognitive Neuroscience

Prof. Dr. Fabian Grabenhorst

Department of Experimental Psychology, University of Oxford, UK

A view-based decision mechanism for rewards in primate amygdala neurons

Primates make decisions visually by shifting their view from one object to the next, comparing values between objects, and choosing the best reward, even before acting. Here we show that when monkeys make value-guided choices, amygdala neurons encode their decisions in an abstract, purely internal representation defined by the monkey's current view but not by specific object or reward properties. Across amygdala subdivisions, recorded activity patterns evolved gradually from an object-specific value code to a transient, object-independent code in which currently viewed and last-viewed objects competed to form a view-based choice. Using neural-network modelling, we identified a sequence of computations by which amygdala neurons implemented view-based decision-making and eventually recovered the chosen object's identity when the monkeys acted on their choice. These findings reveal a neural mechanism in the amygdala that derives object choices from abstract, view-based computations, suggesting an efficient solution for decision problems with many objects.

Clinical Neuroscience

Prof. Dr. Chris Mathys

Aarhus University, Denmark

Change of Mind - Computational Approaches to (Mal)adaptive Changes in Beliefs

As the world around us changes continually, we need to adapt our beliefs to keep with environmental changes. This has both a 'where' and a 'what' aspect. On the 'where' side, we need to track how things move in space, be that movements in a concrete space (e.g., an object in our field of vision) or in an abstract one (e.g., the probability of a certain event). In the past decade, many connections between psychopathology and maladaptive belief updates in this domain have been found. I will go into some of them and will cover recent advances in creating computational models of this kind of belief update. Specifically, I will introduce generalizations to hierarchical Gaussian filtering which allow for the extension of this approach to arbitrarily large networks of nodes coupled not only via their variance but also their means, where this latter coupling may also be nonlinear. In a second part of the talk, I turn to the 'what' side, where we need to update beliefs about categories, which is especially interesting in the case of categories of events that have the same explanation or cause. This is especially relevant in the computational modelling of delusions, where events are attributed to causes in a maladaptive way. I will go into recent advances in this field, specifically such involving hierarchical Dirichlet process mixture models.

Clinical Neuroscience

Dr. Marina Chekulaeva

Berlin Institute of Medical System Biology, Germany

RNA regulation in neurons and neurodegeneration

Neurodegeneration disorders are devastating incurable diseases, predicted to become the second leading cause of death by 2040 due to population ageing. A common theme across neurodegenerative disorders is that they begin with the loss of neuronal extensions (neurites – axons and dendrites). The formation and function of neurites relies in large part on the asymmetric subcellular localization and translation of mRNAs. mRNA localization is mediated by specific sequences in their 3'UTRs, known as localization elements. These elements are bound by trans-acting factors, RNA-binding proteins (RBPs), that link their targets to transport machinery or regulate their stability and translation in a localization-dependent manner. Although thousands of mRNAs are known to be localized in neurons, only a small number of localization elements have been identified so far. Addressing this knowledge gap, we developed a compartmentalized neuronal culture enabling the separation of cell bodies and neurites (Zappulo et al. Nature Comm 2017, Ciolli Mattioli et al. NAR 2019, Ludwik et al. Methods 2019), coupled with a massively parallel reporter assay for mapping RNA localization elements transcriptome-wide (Mendonsa et al. Nature Neuro 2023). Using this technique, we identified localization elements in one-third of the analyzed transcripts and provided the first evidence of miRNA let-7 affecting mRNA localization.

Our further work revealed that a high mRNA half-life reliably predicts localization to neurites, a mechanism that is essential for the localization of housekeeping mRNAs and plays a critical role in local translation and neuronal activity (Loedige et al. Mol Cell 2023). Our current research focuses on understanding the mechanisms of axonal vulnerability in neurodegenerative diseases such as ALS and CMT (Charcot-Marie-Tooth disease, Mendonsa et al. NAR 2021).

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Clinical Neuroscience

Prof. Dr. Mathias Jucker

University of Tübingen; German Center for Neurodegenerative Diseases (DZNE), Germany

Proteopathic seeds in neurodegenerative diseases

The commonality of many neurodegenerative disorders is the progressive temporal and spatial aggregation of specific proteins in the brain. The quintessential proteopathy is Alzheimer's disease (AD), in which the aggregation and seeded propagation of amyloid-B peptide (AB) triggers AD pathogenesis, including neuronal Tau inclusions and neurodegeneration. Current therapeutic strategies focus on early disease stages and aim to inactivate AB seed propagation before the onset of neurodegeneration. However, to develop such primary prevention approaches a mechanistic understanding of early disease stages is essential.

Panel discussion

Thursday, 23rd of May 2024

"Integration of Neuroprosthetics into our Daily Lives"

The technological developments in the neuroprosthetics and brain-computer interface has ushered a new era of innovation that will have a significant impact on the lives of the individuals that are suffering from neural impairments and disorders. However, integration of these rapidly developing technologies to our lives raises some questions about how would these developments affect humanity. In this panel discussion, leading experts from various fields will discuss the borders that define neuroprosthetic concepts to answer questions that arise from the emergence and integration of these new technologies. Following that, topics such as feasibility of neuroprosthetics, the latest developments, the problems that neuroprosthetics help to solve and the problems they might impose in the future will be discussed.

Moderator:

Prof. Dr. Alexander Gail

German Primate Center,
Göttingen, Germany

Prof. Dr. Alexander Gail is interested in the neural processes underlying goal-directed behavior. His lab investigates the basis of movement planning and decision making in different areas in the cerebral cortex of primates. They have a particular focus on the interplay between frontal and parietal lobe areas in the context of rule-guided behavior. Their research in fundamental neuroscience goes hand in hand with research towards modern neuroprostheses and development of neurotechnology tools. Additionally they advance methods with the goal of improving animal welfare.

Panelists:

Prof. Dr. Silke Schicktanz

University Medicine Göttingen, Germany

Prof. Dr. Silke Schicktanz's current research focus is the ethical and cultural studies of Bio-medicine. The primary goals of her research are to address:

- Cultural differences within bioethics, globalization of life science research
- Concepts of collectivity in bioethics
- Public and stakeholder engagement in bioethics – methods and concepts
- Relationship of ethics and empirical studies.

Prof. Dr. Loes Van Dam

Technical University of Darmstadt, Germany

Prof. Dr. Loes Van Dam is currently chairing the Sensorimotor Control and Learning Group at the Technical University of Darmstadt. Her group is interested in human multisensory perception and goal-oriented movement behavior in virtual reality (VR) as well as the real world. Her research group focuses on how our sensorimotor system selects and combines relevant pieces of information for the perception of our environment, the perception of our own body, as well as for guiding goal-oriented movements. To this end, they investigate the interactions between visual, proprioceptive and tactile feedback for movement control. The more cognitive aspects included in their work concerns

the use of prior knowledge and learned relationships between an object's shape and the appropriate behavior to interact with it.

Furthermore, their work investigates how our senses, our motor control system and our prior experiences combine to help form a sense of ownership over our own body, an avatar, or a tool and a sense of agency about our actions and their perceptual consequences. To study these topics they combine experimental work (e.g. psychophysics, game-like sensorimotor control tasks) with modeling approaches such as optimal multisensory integration and optimal control theory.

Understanding these processes informs the development and use of sensory substitution devices in general and is therefore also of relevance for neuroprosthetics. They believe that the naturalness of their use and the acceptance of such devices depends on how the feedforward processes from movement planning and feedback processes linked to these movements can interact and how this information is represented and learned.

Dr. Fabien Wagner

French National Centre for Scientific Research;
University of Bordeaux, France

Trained first as an engineer and then as a neuroscientist, Dr. Fabien Wagner conducts research at the intersection between neuroscience and neuroengineering. He is interested in understanding how the dynamics of neuronal networks become altered in neurological disorders or after injury, and how to restore their natural behavior using neuromodulation approaches.

During his Ph.D. at Brown University (USA), working with Profs. Arto Nurmikko and Wilson Truccolo, he developed new tools to record and stimulate the brain simultaneously and investigated the cortical dynamics that underlie the transition to epileptic seizures in rodent models and epileptic patients. During his postdoctoral work with Prof. Grégoire Courtine and Jocelyne Bloch at the Ecole Polytechnique Fédérale de Lausanne (EPFL, Switzerland), he pioneered neuroprosthetic technologies to restore locomotion, first in non-human primates (Nature 2016; Nature Protocols 2018), and then in patients with chronic spinal cord injury as part of a first-in-human clinical trial (Nature, 2018, Nature Medicine 2022).

In 2020, he was awarded a Neurocampus chair for young group leaders funded by the Nouvelle-Aquitaine Region and the University of Bordeaux, which allowed him to create the “Neuromodulation and Neuroprosthetics” team at the Institute of Neurodegenerative Diseases. Their goal is to expand neuroprosthetic systems beyond their current applications in motor disorders, towards neurocognitive impairments. He recently obtained a permanent position at the French National Centre for Scientific Research (CNRS) and an ERC starting grant to pioneer these approaches in non-human primates.

Young Investigator Contest

Thursday, 23rd of May 2024

In the Young Investigator Contest, participants (PhD students and Post-doctoral researchers) will have the opportunity to give a 20 minute presentation of their own research to the audience of Neurizons 2024, followed by 5 minutes for questions. The best presentation will win an exciting prize! This year's three candidates are:

- **Zulvikar Syambani Ulhaq** (National Research and Innovation Agency, Indonesia)
- **Paulina Wanken** (University Medicine Göttingen, Germany)
- **Hyojin Kim** (Institute for Auditory Neuroscience Göttingen, Germany)

Power Pitch Talks

Thursday, 23rd of May 2024

In the Power Pitches, 10 participants will have the opportunity to share their ideas in very short talks of duration 2-3 minutes + 2 minutes for questions, to convince the audience to come to their poster and know their research.

Poster Sessions

Thursday, 23rd of May 2024

The Neurizons talks cover a broad range of neuroscientific topics. We would like to offer the same variety in our poster session, and broaden our horizons with a multitude of techniques and ideas. The speakers and participants will vote for the best poster according to its design, display and the presenter's skills. Seize the chance to be evaluated for your work and evaluate others. There will be 3 winners to get prizes!

Göttingen City Tour

Wednesday, 22nd of May 2024

Participants will have the opportunity to explore Göttingen through city tours. 'Around the Gänseliel - highlights of Göttingen's old town' will be a tour of the cultural and historical highlights of the city center such as the Gänseliesel, the Old Town Hall, and the half-timbered houses. 'History of science in Göttingen' and 'History of the University of Göttingen' tours will take participants through the scientific history of the University of Göttingen, founded in 1734, which attracted numerous bright minds like Gauss, Hilbert, Born, Heisenberg, Oppenheimer, and Planck.

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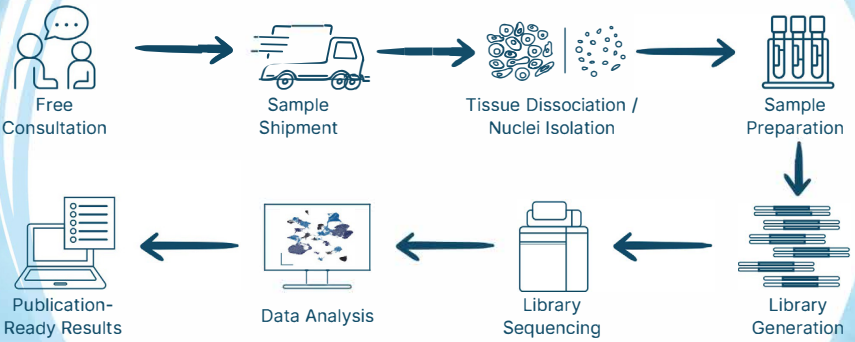

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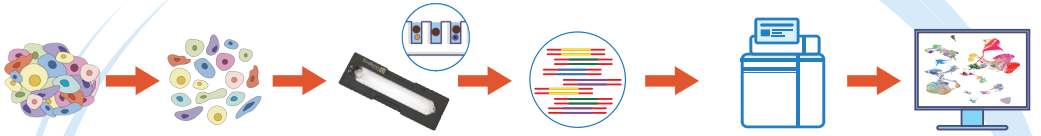

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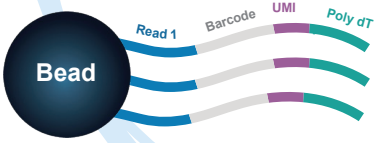

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ABSTRACTS

Young Investigator Contest

Zulvikar Syambani Ulhaq

National Research and Innovation Agency, Indonesia

"Polr1c Deficiency Leads to Photoreceptor Degeneration and Vision Impairment in a Zebrafish Model of POLRIII-Related Leukodystrophy"

The POLR1C gene encodes both RNA polymerase I (POLR1) and RNA polymerase III (POLR3). While recessive mutations in POLR1C have long been associated with Treacher Collins syndrome (TCS), recent findings indicate their association with RNA polymerase III-related hypomyelinating leukodystrophy (POLR3-HLD). However, our understanding of how POLR1C contributes to intraocular defects in POLR3-HLD remains limited. Here, we present the first investigation into the localization and function of polr1c in the retina using a zebrafish model of POLR3-HLD. Our study employed morphological analysis, sox10 lineage tracing, and neurological assessments to confirm whether depletion of polr1c recapitulates the clinical features of both TCS and POLR3-HLD. Through double staining-immunohistochemistry, we determined the localization of polr1c in the retina. Additionally, we utilized various techniques including qRT-PCR, immunostaining, in-situ hybridization, TUNEL assays, and behavioral analysis to elucidate the molecular mechanisms underlying photoreceptor degeneration in polr1c–/– mutants. Our results display attributes similar to both characteristic of TCS-3 and POLR3-HLD in polr1c–/– zebrafish. Furthermore,

these mutants exhibited alterations in eye-to-body ratio, affecting retinal layers, leading to myopia, optic nerve (ON) atrophy, and diminished retinal nerve fibers. Polr1c was found to be exclusively expressed in photoreceptor outer segments (OS) and sensory cilia, impacting photopigments, particularly severely affecting blue opsin among other cone photopigments. Depletion of polr1c led to increased apoptosis in photoreceptor cells. Additionally, behavioral changes in polr1c–/– zebrafish correlated with shifts in photopigment expression. In conclusion, our findings highlight the importance of polr1c in photoreceptor survival, and its absence may lead to secondary diseases related to photoreceptor function.

Young Investigator Contest

Paulina Wanken

University Medicine Göttingen, Germany

"Whole-brain activity patterns underlying uninstructed behavioral switching in mice"

The ability to switch between different behaviors is essential to all animals' survival. The selection of a behavior is guided by multiple factors, such as sensory inputs, internal states, and memory, which suggests that many regions across the brain are involved in the decision to switch between them. While whole-brain information is necessary to investigate the neural basis of behavioral switching, brain-wide imaging in behaving mice has proved challenging so far. We employed functional ultrasound imaging (fUS) to record large-scale neural dynamics in head-fixed mice while simultaneously tracking their behavioral state. Our aims to identify brain regions that predict self-initiated behavioral transitions that occur in the absence of external triggers. Accordingly, we utilized the virtual burrow assay in which head-fixed mice are placed in an air-floating tube, from which they can voluntarily egress. Leveraging the unsupervised behavior segmentation framework VAME, we found that mice (N = 11, 60 sessions) robustly exhibit distinct, uninstructed behavioral states in this assay that include egress, whisking, inactivity, and grooming. Utilizing brain-wide fUS, we subsequently observed activity patterns associated with these distinct behavioral states and performed whole-brain time-resolved decoding around behavioral transitions. Remarkably, our

results revealed that whole-brain activity can predict an uninstructed switch in behavior several seconds before its onset, indicating that a change in behavior is preceded by a detectable change in brain state. Furthermore, region-wise decoding and fiberphotometry revealed specific brain areas that drive the prediction of behavioral transitions. Through this unbiased approach, our work sheds light on the neural dynamics receding uninstructed transitions of behavioral state.

Young Investigator Contest

Hyojin Kim

Institute for Auditory Neuroscience Göttingen, Germany

“Molecular simulation of Ca2+-triggered synaptic vesicle release in presynaptic active zone of inner hair cells”

Hearing impairment is growing in prevalence, significantly affecting people ś quality of life. It is often caused by dysfunction in auditory processing from sensory hair cells to the spiral ganglion neurons (SGNs). Experimentally, a great deal of detailed structural and functional properties of the inner hair cells (IHCs) has revealed that various presynaptic molecular properties can affect SGN function. Yet, experimental data cannot solely elucidate the intricate signal transmission mechanisms between IHCs and SGNs. To address this challenge, we have integrated experimental data from various imaging techniques into a unified 3D cellular model. In this study, we focused on the presynaptic active zone (AZ) of IHC where Ca2+-dependent signaling triggers synaptic vesicle (SV) release. We investigated how the following presynaptic AZ properties affect the vesicle release rate: i) the number of Ca2+ channels and ii) the coupling distance between Ca2+ channels and SV sensors. To stimulate Ca2+ diffusion and binding to SVs, we used a Monte
Carlo simulation tool reflecting the molecular structure of presynaptic AZ. The size of Ca2+ clusters was set to 67 nm x 420 nm while the number of channels varied from 14 to 150. Additionally, we varied the coupling distance between

Ca2+ channels and SV sensors within the range of 15nm. Results show that the coupling distance may have a greater impact on the vesicle release rate compared to the number of Ca2+ channels. Furthermore, the predicted vesicle rate was not fully aligned with experimental measurements, suggesting that additional presynaptic factors may also play a role, such as the distance between Ca2+ channels and the arrangement of Ca2+ channel clusters.

Power Pitch Talk

Josiane Kelly Siemund

"Investigating Synaptic Degeneration in a Mouse Model of Amyotrophic Lateral Sclerosis"

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by the loss of upper and lower MNs leading to muscle atrophy, paralysis, and death. The causes of ALS are mostly sporadic, with only about 10% of cases being inherited. Since 1993, over 200 SOD1 gene mutations have been identified in ALS patients, and studies have revealed MN degeneration in familial ALS resulting from dominant gain-of-function mutations in the SOD1 gene. Recent findings from patients and mouse models of ALS suggest synaptic dysfunction as an early event in this pathology. However, the crosstalk between MN loss and synaptic dysfunction in ALS is still not well established. Our study applied immunohistochemistry and confocal microscopy to perform a time course analysis coupling MN and synaptic degeneration in the SOD1G93A mouse model of ALS. We characterized MNs from the lumbar spinal segments 1, 4, and 5 of mutant and control groups at different disease stages. The L1 segment mostly innervating proximal muscles demonstrated a significant loss of MNs only at the disease end-stage, whereas L4 and L5 segments which innervate distal muscles were already affected at postnatal day 80. Interestingly, quantifying proprioceptive synapses (major excitatory sensory inputs unto MNs) in proximal motor circuits demonstrated synaptic degeneration earlier than MN loss in the L1 segment. Proprioceptive synapses on MNs of the L4 and

L5 segments significantly degenerated towards the onset of MN death. Additionally, analysis of further excitatory (c-boutons and VGluT2+ synapses) and inhibitory VGAT+ synapses revealed significant aberrations in all three segments. Taken together, our findings demonstrate the correlation between MN loss and synaptic impairment in both vulnerable and resistant motor circuits in ALS mice, highlighting the key role central synapses play in investigating fundamental mechanisms underpinning motor circuit pathology both in ALS mice and patients.

Power Pitch Talk

Seth Talyansky

"Genetic markers of disease severity in a rodent model of CMT1A"

Aims: Charcot-Marie-Tooth disease subtype 1A (CMT1A) is the most common hereditary peripheral neuropathy. Caused by a duplication of the PMP22 gene, CMT1A manifests with a high variability in clinical severity, even between close relatives. The biological basis of this variability is unknown. In this work, we set out to identify genes marking CMT1A disease severity at the level of the peripheral nerve. Methods: We studied a transgenic rat model of CMT1A shown to recapitulate the phenotypic variability observed in human patients. We isolated sciatic nerve from four wildtype (WT) and four CMT1A rats at embryonic day 21 (E21) and postnatal days 6 (P6) and P18. At 16 weeks, we tested the clinical phenotype in the CMT1A rat cohort and classified the four least and most burdened rats as mildly (MA) and severely affected (SA). We then isolated sciatic nerve from the MA and SA rats and from eight age-matched WT rats. We performed RNA-Seq on the samples collected at E21, P6, and P18, in each case analyzing the WT and CMT1A samples in one batch. We also performed RNA-Seq on the MA and SA samples, analyzing the MA and four WT samples in one batch and the SA and four other WT samples in another batch. Results: There were 2,226 differentially expressed genes between WT and MA rats and 1,546 between WT and SA rats, with 1,232 genes in common. Of the genes with human orthologues, expression of Tmc5, Cabp2, and Pnlip increased the most

from WT to MA, and from MA to SA (comparing WT to MA and WT to SA fold change), while expression of Erbb4, Rlbp1, Ntsr2, Rab15, and Vsig2 decreased the most. Cabp2 and Pnlip were also upregulated in CMT1A rats relative to WT at P18. Conclusions: The genes identified may be robust markers of CMT1A severity. Cabp2 and Pnlip expression may be involved in disease pathogenesis. Tmc5, Cabp2, and Ntsr2 all relate to calcium signaling, making this pathway a candidate for determining disease severity.

Power Pitch Talk

Shashwat Sridhar

"Modeling spatial contrast sensitivity in responses of primate retinal ganglion cells to natural movies"

The retina encodes incoming light into neural signals through a complex circuit of cells arranged in layers, from the input photoreceptors to the output retinal ganglion cells (RGCs). Predictive models of RGCs aim to understand this coding. One such model, the Spatial Contrast (SC) model, was developed as an extension of the widely used Linear-Nonlinear (LN) model to study the influence of contrast on the firing response of the cell. For each cell, the model computes the mean luminance and local contrast in the stimulus and linearly combines them using a learned parameter that determines the importance of local contrast to the cell. The resulting value is passed through a non-linear activation function. However, this model was originally tested only on stimuli consisting of flashed natural images (i.e. without any temporal dynamics).In this paper, we extend the SC model to the temporal domain and apply it to ex-vivo electrophysiological data obtained using microelectrode arrays from marmoset retinas. We find that the SC model outperforms the LN model in predicting RGC responses to both spatio-temporal white-noise and naturalistic movies, and that this improvement is due to the additional information provided by local spatial contrast. Furthermore, we find that the improvement varies with the cell type and size of the RGC. Finally, we use the SC model to identify the optimal scale at which each cell integrates

contrast information. Interestingly, this optimal scale remains consistent across cells when exposed to white-noise stimulation, but not when exposed to naturalistic movie stimulation, highlighting the influence of the spatial frequencies present in the stimuli. Thus, we present the SC model as a powerful alternative to the LN model that not only provides a better benchmark against which more complex models of the retina can be compared, but also serves as a useful tool for understanding non-linear spatial integration in the retina.

Power Pitch Talk

Bernardo Andrade Ortega

“Bimodal multistability during perceptual detection in the ventral premotor cortex ”

How does the brain manage to process and integrate information from different sensory modalities? This intriguing question has been explored in this study by recording the activity of the Ventral Premotor Cortex (VPC) in two trained macaques (Macaca mulatta) while performing a Bimodal Detection Task (BDT) (Parra et al., 2022). In BDT, subjects were required to identify and report the modality, or the absence thereof, of a near-threshold stimulus that could be either tactile or acoustic. An initial approach on single cells revealed the presence of neurons that were responsive to tactile and/or acoustic stimuli. Moreover, some units predominantly demonstrated sensory responses, while others exhibited sustained activity during the decision maintenance delay—i.e., between the onset of the stimulus and the motor execution. To delve deeper, we employed dimensional reduction techniques to scrutinize the population dynamics. These analyses in biological networks were also compared with theoretical models based on Recurrent Neural Networks (RNN), where a striking finding was the clear divergence between tactile and acoustic responses during the stimulation period. This phenomenon was consistent across both the VPC and the RNN models. During the delay, the neural trajectories rotated within a subspace orthogonal to the initial sensory responses, effectively preserving the decision memory. This suggests that the network can sustain different stable

responses that correlate with the three potential outcomes of the task. In summary, our findings indicate that the VPC is equipped with neurons capable of bimodal coding. Likewise, its neuronal population possesses the remarkable ability to integrate competing sensory information and preserve a decision regarding the modality throughout a delay period.

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Power Pitch Talk

Ilona Vieten

“Attentional modulation of single-unit activity in the human medial temporal lobe”

The human medial temporal lobe (MTL) is populated by single neurons showing remarkable stimulus selectivity and response invariance, sometimes called concept cells. Involved in conscious perception and working memory, their particular response properties have led to the hypothesis that they constitute the building blocks of human episodic memory. The brain organizes and guides perception of relevant stimuli through attentional mechanisms. Extensive work in non-human primates has shown modulation of single-unit responses to preferred stimuli by attention, mostly in the visual system. Functional imaging in humans has similarly shown attention modulation in different brain regions involved in sensory processing. However, the interplay between attention and visual processing on a single-unit level the human MTL has not been investigated.

In our study, 37 epilepsy patients with microwire electrodes embedded in four MTL regions performed a task designed to isolate the effect of attention on single-unit activity. Subjects followed a rapid and pseudo-randomized stream of eight images previously found to specifically activate the recorded neurons, and to count the occurrence of a different particular stimulus in each run of one minute duration. In total, we recorded from 172 stimulus-selective units in the amygdala (59 units), the hippocampus (32), the entorhinal cortex (11), and the parahippocampal cortex (70).

Throughout the MTL, we find that stimulus-related activity is attention-modulated in 25-37% of these units, with no statistically significant difference between regions.
Our results suggest a functional division among stimulus-selective neurons in the human MTL, with a large minority being sensitive to attentional signals. These subpopulations could play different roles in the transfer of experiences into long-term memory.

Power Pitch Talk

Andrei Kalinichenko

“Chemogenetic emulation of intraneuronal oxidative stress affects synaptic plasticity”

Oxidative stress (OS) is a known contributor to age-related brain disorders: dementia and Alzheimer’s disease. Nevertheless, studying the direct effects of OS on neurodegeneration remains challenging due to the absence of an appropriate in vivo model of isolated OS [1]. We introduced a novel chemogenetic technique employing the yeast flavoprotein d-amino acid oxidase (DAAO) [2] to generate hydrogen peroxide (H202) in neuronal cells in a controlled manner. By co-expressing DAAO with HyPer7, an H2O2 biosensor [3], in cultured neuronal cells, we induced and measured intracellular H2O2 production activated by added d-norvaline, a substrate of DAAO, thus validating our chemogenetic model. Subsequent experiments on acute
brain slices demonstrated that this controlled induction of oxidative stress does not alter basal synaptic transmission or the probability of neurotransmitter release but notably impairs long-term potentiation, indicating a detrimental effect on synaptic plasticity at the single-cell level. In sum, our findings expand the existing toolkit for studying normal brain redox regulation and the mechanisms by which oxidative stress contributes to cognitive aging and early neurodegenerative disease stages. Our approach also offers a potential platform for identifying early oxidative stress markers and screening potential antioxidant treatments targeting neuronal oxidative damage.

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Power Pitch Talk

Pia Schweineberg

“How can we differentiate two approved anti-CD20 preparations for multiple sclerosis”

Multiple sclerosis (MS) is defined as a chronic inflammatory demyelinating disease of the central nervous system (CNS). B cell-depleting monoclonal antibodies (mabs) are now in focus as potent treatment options for MS (Torke et al., 2020).Ocrelizumab (OCR) and ofatumumab (OFA), two anti-CD20 mabs, are approved for the treatment of MS. These mabs differ in their application, dosage, and administration interval (Florou et al., 2020). Hence, this project aims to differentiate OCR and OFA, with a particular focus on disease activity, CNS damage, B cell depletion kinetics, and long-term effects on serum IgM and IgG levels. Experimental autoimmune encephalomyelitis (EAE), an animal model of MS will be induced in human CD20 transgene mice. Different concentrations of OCR and OFA will be applied, according to their usage in the human. Subsequently, flow cytometry analysis, histological analysis, measurements of serum neurofilament light chain levels, antibody levels, and several cytokines will be performed.

In preliminary data, we analyzed the B cell depletion capacity of OCR and OFA. Therefore, we applied a single dose of either OCR or OFA and examined the blood, bone marrow, inguinal lymph nodes, and spleen. OCR use resulted in a nearly complete depletion, while in OFA treated mice approximately 5-10 % of B cells remained.

Overall, the aim is to analyze differences between both

anti-CD20 medications, possibly leading to a more specific and educated use of the respective medication.

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Power Pitch Talk

Josiane Kelly Siemund

Investigating Synaptic Degeneration in a Mouse Model of Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by the loss of upper and lower MNs leading to muscle atrophy, paralysis, and death. The causes of ALS are mostly sporadic, with only about 10% of cases being inherited. Since 1993, over 200 SOD1 gene mutations have been identified in ALS patients, and studies have revealed MN degeneration in familial ALS resulting from dominant gain-offunction mutations in the SOD1 gene. Recent findings from patients and mouse models of ALS suggest synaptic dysfunction as an early event in this pathology. However, the crosstalk between MN loss and synaptic dysfunction in ALS is still not well established. Our study applied immunohistochemistry and confocal microscopy to perform a time course analysis coupling MN and synaptic degeneration in the SOD1G93A mouse model of ALS. We characterized MNs from the lumbar spinal segments 1, 4, and 5 of mutant and control groups at different disease stages. The L1 segment mostly innervating proximal muscles demonstrated a significant loss of MNs only at the disease end-stage, whereas L4 and L5 segments which innervate distal muscles were already affected at postnatal day 80. Interestingly, quantifying proprioceptive synapses (major excitatory sensory inputs unto MNs) in proximal motor circuits demonstrated synaptic degeneration earlier than MN loss in the L1 segment. Proprioceptive synapses on MNs of the L4 and

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Power Pitch Talk

Anna Marie Muellen

Extraction and characterization of the motor hand knob from central sulcus deflection profiles in >1000 human brains

The human central sulcus (CS) is located between the primary motor cortex (M1) in the precentral gyrus and the primary somatosensory cortex in the postcentral gyrus. Anatomical landmarks of M1 are thus partly reflected in the CS morphology. The hand knob [1], a prominent folding of the precentral gyrus marking the M1 hand area, presents as a posterior deflection of the CS. Here, aspects of the CS morphology will be analysed in a large cohort to extract and characterize the hand knob and set it into context with known landmarks in the CS depth.
Structural T1-weighted magnetic resonance imaging data from 1112 subjects of the Human Connectome Project S1200 Data Release were pre-processed with BrainVISA (V4.6.0). Cortical sulci were computed as attributed relational graphs (Morphologist 2015), and all graphs of the CS were identified. Selected CS graphs were reconstructed and parametrized (Sulcus Parametrization 2015) resulting in a 3D CS mesh, its deflection and depth profile. The deflection profile approximates the deviations of the CS towards anterior and posterior at discrete positions from the medial start to the lateral end of the CS. The depth profile approximates the CS depth from surface to fundus at the same positions. To extract the hand knob, fast Fourier transformation was applied to deflection profiles and band pass filtered. The extracted hand knob is set into context

with the CS depth profile where a small elevation at the CS fundus, the pli-de-passage fronto-pariétal moyen (PPfpm), has been characterized previously.

Preliminary results indicate that this method enables a characterization and quantification of the hand knob in >1000 human brains. Further, a close association with the PPfpm is indicated. Together, this presents as a first step to assess the CS morphology at the height of the hand knob in individual human brains.

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Power Pitch Talk

David Ehrlich

Analyzing Class-wise Differences between Neural Representations using Partial Information Decomposition

The selective encoding of task-relevant information is crucial for both biological and artificial neural systems. Despite its significance, understanding how information is distributed among individual neurons remains incomplete. Bridging this gap requires quantifying encoding characteristics of the intermediate representations using a common framework. While Information Theory has been utilized to track information flow, existing approaches struggle to differentiate between unique, redundant, and synergistic contributions. Partial Information Decomposition (PID) offers a solution by enumerating and quantifying these non-overlapping information atoms.

In previous work [1], we utilized PID to introduce Representational Complexity (C) to measure the difficulty of extracting information. We found that in Deep Neural Networks solving the MNIST handwritten digit recognition task, representational complexity decreases over training and through hidden layers.

Here, we refine our analysis by dissecting PID contributions for each class. We observe that representational complexity varies for individual digits based on image similarities, reflecting the network's struggle in discerning certain digits. In future work, we aim to apply Representational Complexity to biological neural circuits, shedding light on similarities and differences with artificial networks, aiding

in the design of more biologically inspired structures.

[1] DA Ehrlich, AC Schneider, V Priesemann, M Wibral, A Makkeh, A measure of the complexity of neural representations based on partial information decomposition. Transactions on
Mach. Learn. Res. (2023).

Poster Presentation

Timo Walter, *Lucas Rudelt , Fabian A. Mikulasch , Viola Priesemann*

Attention-based gain modulation for rapid adaptation in neural networks

Neural networks in the brain utilize an internal model of the world to filter out relevant information out of noisy stimuli. By doing so these networks need to distinguish between uncertainties induced by ambiguities in the environment and uncertainties based on relevant novel information e.g. through sudden environmental changes. As a result, they engage in a trade-off between favouring internal predictions for sensory stimuli and favouring the integration of sensory information. This raises the need for an algorithmic explanation for how neural networks can resolve this trade-off and deal with abrupt changes in the environment. Therefore we propose a multi model adaptive algorithm for attentional gain modulation. The algorithm is able to detect change points and quickly adapt to sudden state changes. We achieve this by implementing a likelihood- weighted filter algorithm based on the Kalman filter. It is designed to assign weights to state estimates either in favour of relying on the algorithm's history or integrating novel information. We show in simulations that our method successfully estimates ground truth signals from noisy data as well as quickly reacts and adapts to abrupt state changes. We interpret this weighting process as the brain either emphasizing top-down predictions about upcoming sensory information or bottom-up encodings of sensory information in response to novel sensory stimuli.

Finally, we argue that this filtering mechanism may be implemented as bottom-up attentional gain modulation on the apical dendrites of pyramidal cells and hypothesize about a microcircuit motif using SST and VIP interneurons which could facilitate the desired effect.

Poster Presentation

Chrystalleni Vassiliou, Rina Patel, Shimon Jude Swer, Matthias Haberl, Silvia Viana da Silva, Camin Dean

The Role of the Transient Receptor Potential Vanilloid 1 (TRPV1) Channel in Sharp Wave Ripples, Place Cells, and Spatial Memory

Sharp-wave ripples (SWRs) are hippocampal oscillations important for memory consolidation that appear during sleep and awake immobility. During SWRs, neuronal firing patterns formed during previous exploration are reactivated, which allows strengthening of synaptic connections between the firing cells, i.e., long-term potentiation (LTP). The transient receptor potential vanilloid 1 (TRPV1) protein is a cation channel that in the hippocampus is specifically expressed in oriens lacunosum moleculare (OLM) interneurons, which participate in SWRs. Because TRPV1 knockout (KO) mice have impaired hippocampal LTP, another fundamental process of memory consolidation, we hypothesized a similar impairment in SWRs. However, SWRs recorded from hippocampal slices were longer, while SWRs in tetrode-implanted mice were larger; hence, both in vivo and in vitro recordings pointed towards enhanced SWRs in TRPV1 KO mice instead. From recordings in behaving animals, we also examined spatial properties of hippocampal place cells and found larger and less stable place fields in TRPV1 KOs. Next, we examined spatial memory using a dry land version of the water maze, the cheeseboard maze task. Even though WT and TRPV1 KO mice learned the first reward location at similar rates, KO mice took longer to reach the new reward

location when the location was switched to the opposite quadrant of the maze on all days after reversal. This was at least partly because TRPV1 KO mice visited the original reward location before going to the new one, which might hint at an impairment in memory extinction or forgetting.

Poster Presentation

Richmond L. Crisostomo, Shreya Agarwal, U lrich Egert, and Samora Okujen

Exploring the Impact of Inhibition on Activity-Dependent Neuronal Growth and Migration in Developing Networks

The maturation of inhibition in neuronal networks is considered crucial for stable activity dynamics that support normal brain function. In parallel, morphological and functional differentiation of such networks are regulated by activity-dependent structural plasticity, suggesting opposing influences of excitatory and inhibitory signals on this process. In idealized models with activity-dependent regulation of neurite growth, network activity can be regulated homeostatically. Under such control, the interplay between neuronal growth and migration shapes synaptic connections and fosters variety in network architecture, clustering, and modularity. Still, how maturation of inhibition interferes with this process remains to be understood. To explore the role of inhibition, we adopted growth models that recapitulate many aspects in the development of cultured neuronal networks. Varying the ratio of excitatory and inhibitory neurons, we investigated its impact on network structure stabilization and spatial embedding of neurons. Under activity-dependent neurite growth, increased proportion of inhibitory neurons prolongs morphogenic period of neurite field expansion, neuronal migration, and clustering. Furthermore, inhibition increased the level of connectivity and reduced the extent of developmental

pruning of connections - consequently reducing network modularity. Interestingly, networks with more than 20% inhibitory neurons - above typical proportions in cortical networks - exhibited instability in structure and dynamics. Here, developing connectivity is driven towards runaway scenarios. The challenge now is to better understand the role of these asymmetric interactions in the self-organized spatial embedding of inhibitory neurons and the resulting consequences for tractable dynamics of spiking neuronal networks.

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Poster Presentation

Anna Katharina Kau, Bojana Kuzmanovic , Yasmina Saadi, Lionel Rigoux, Julian Koenig, Soyoung Q Park , Jens Claus Brüning , Marc Tittgemeyer

Metabolic regulation of adaptive behaviour - the role of sensory perception

In hungry mice, sensory detection of food cues elicits motivational behaviours and preparatory physiological processes for food intake (Berrios et al., 2021). These anticipatory responses include rapid modulation of hypothalamic activity and fat metabolism via an enhanced sympathetic activity (Brandt et al., 2018). How do hungry humans manage this fast-forward energy balance process? Based on mice models, we expect that food cues relative to neutral cues will increase sympathetic activity and modulate hunger reports and reinforcement learning. In a cross-over pilot study, 30 overnight fasted healthy participants were presented with a food cue on one day (hot sandwich), and with a neutral cue on another day (newspaper). Before and after the cue presentation, we assessed subjective hunger and sympathetic activity using cardiac activity, blood pressure, electro- and impedance cardiogram, and the computation of the pre-ejection period.

Furthermore, 15 minutes after the cue presentation, participants completed a reinforcement learning task. As predicted, participants reported to be more hungry after seeing and smelling the food relative to the neutral cue, $F(1,48) = 10.45$, $p = .002$. Furthermore, a preliminary analysis indicated a trend toward a modulation of the sympathetic

activity in response to the food relative to neutral cue. Moreover, participants' learning behaviour relied stronger on negative prediction errors after the food cue relative to the neutral cue, $F(2,117) = 3.99$, $p = .02$. The behavioural adaptation of hungry participants in response to the sensory detection of a food source is quite remarkable. In order to understand these changes in behavioural adaptation and the associated physiological processes, we are currently finalising analysis of heart activity data.

Poster Presentation

David A. Ehrlich, Teresa Monteiro, Andreas C. Schneider, Michael Wibral, Viola Priesemann, Abdullah Makkeh

Analyzing Class-wise Differences between Neural Representations using Partial Information Decomposition

The selective encoding of task-relevant information is crucial for both biological and artificial neural systems. Despite its significance, understanding how information is distributed among individual neurons remains incomplete. Bridging this gap requires quantifying encoding characteristics of the intermediate representations using a common framework. While Information Theory has been utilized to track information flow, existing approaches struggle to differentiate between unique, redundant, and synergistic contributions. Partial Information Decomposition (PID) offers a solution by enumerating and quantifying these non-overlapping information atoms.

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Complexity to biological neural circuits, shedding light on similarities and differences with artificial networks, aiding in the design of more biologically inspired structures.

[1] DA Ehrlich, AC Schneider, V Priesemann, M Wibral, A Makkeh, A measure of the complexity of neural representations based on partial information decomposition. Transactions on
Mach. Learn. Res. (2023).

Poster Presentation

Ruslan Kalimullin, Ekaterina Antipushina , Maxim Sharaev , Maria Boyko, Milena Gazdieva, Alexander Korotin

Rest2Task: Generate task based fMRI using resting state fMRI image-to-image task Resting State to Task-based fMRI Generator

Contemporary research in functional magnetic resonance imaging (fMRI) highlights challenges associated with the time-consuming nature of data acquisition during motor tasks. In response, the application of deep generative models is proposed to streamline the data acquisition process. These models facilitate the transformation of fMRI signals from resting states to active motor tasks. This study explores examples of various generative models, including Variational Autoencoders (VAE), Conditional Generative Adversarial Networks (cGAN), and Neural Optimal Transport. The advantages and limitations of each model are analyzed concerning efficiency and accuracy in transforming fMRI signals. The proposed approach has the potential to significantly reduce data acquisition time, offering a more efficient and precise method for analyzing brain motor activity. This opens avenues for a deeper understanding of neurophysiological mechanisms related to motor functions. This innovative method enhances the processing and interpretation of fMRI signals, representing a critical step in advancing neuroscience research.

Poster Presentation

Chopra A., Yin F., Xylaki M., Castro-Hernández R., Fischer A., Outeiro T.

The role of N6-Methyladenine modification in A30P Parkinson's disease mutation

Parkinson's disease (PD), typically characterized by rigidity, tremor, and bradykinesia, is estimated at ~1% of the population >60 years of age [1]. The main pathological hallmarks of PD include alpha Synuclein (aSyn) pathology and Lewy bodies (LBs) and Lewy neurites (LNs) [2]. Only 10-15% of the PD cases that have been reported are familial. These mutations are most commonly present in the SNCA and LRRK2 gene including A53T, A30P, and E46K. A30P aSyn mutation marks a late onset PD with mild form of dementia [3]. Post-transcriptional regulatory markers are present on - mRNAs, tRNAs, rRNAs, circRNAs, miRNA, and lncRNAs. m6A modification is the most abundant and conserved transcriptional modifications in eukaryotic RNA. m6A modification plays important roles in regulating RNA splicing, translation, stability, translocation, and the high-level structure [4,5,6]. This study focuses on understanding the differences in the m6A modification in the brains from control vs. A30P aSyn PD mutation mouse models. We have compared the expression of m6A modification on mRNA from the mouse brain striatum in A30P vs. control mice. We observed m6A hyper-methylation in several genes at the synapse in in young PD mouse model. This hyper- methylation is lost during ageing as we observe that more synaptic genes are hypomethylated in aged mice. The localization of METTL3, m6A writer protein is

observed at the post-synaptic terminal in both PD and control cortical neuron cultures. We would further like to observe the expression levels of m6A regulatory proteins in different regions of mouse brain.

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Poster Presentation

Michael Gabriel, Marcin Lipiec, Joanna Bem, Marta Wiśniewska

Unravelling TCF7L2 isoform-specific contributions to thalamic development

TCF7L2 is an evolutionarily conserved transcription factor that is crucial for thalamic development by regulating genes involved in patterning, cell-cell adhesion, axon guidance/growth and signal transmission. Two main isoforms of TCF7L2 exist, a full-length (fl-TCF7L2) and a short (sh-TCF7L2) isoform that differs respectively by the presence and absence of a B-catenin activation domain in the N-terminal for canonical Wnt signalling. Although both isoforms are formed by alternative promoter usage, it is unknown whether they play redundant or specific roles during thalamic development.

In this study, we examined two mouse models, a fl-TCF7L2 isoform-specific knockout model and a total TCF7L2 (t-TCF7L2) knockout model, to understand the roles of TCF7L2 isoforms during thalamic development

The results of the experiments showed that thalamic morphology and boundary formation were affected in both fl-TCF7L2 and t-TCF7L2 knockout mice coupled with a significant decline in the expression of some sub-regional thalamic markers at embryonic day (E) 18.5. Growth and fasciculation of thalamocortical axons were altered in the fl-TCF7L2 and more dramatically in the t-TCF7L2 knockout mice suggesting a level of functional overlap between the fl-TCF7L2 isoforms and sh-TCF7L2. To verify this, a transcriptomic analysis of the thalamo-habenular

region of both fl-TCF7L2 and total TCF7L2 knockout mice was conducted. The result showed that the expression of many genes was affected by t-TCF7L2 knockout but not by fl-TCF7L2 knockout, implying redundancy between the isoforms. Nevertheless, correlation analysis showed an expression correlation in a population of differentially expressed genes, indicating that they are regulated mainly by the fl-TCF7L2. This study suggests that while the fl-TCF7L2 isoform is crucial for regulating thalamic developmental events, the sh-TCF7L2 isoform may play partly similar roles to the fl-TCF7L2 in performing TCF7L2-mediated roles during thalamic development.

Poster Presentation

Alex Roxin, Federico Devalle, Licheng Zou, Gloria Cecchini

Representational drift as the consequence of ongoing memory storage

Memory systems with biologically constrained synapses have been the topic of intense theoretical study for over thirty years. Perhaps the most fundamental
and far-reaching finding from this work is that the storage of new memories implies the partial erasure of already-stored ones. This overwriting leads to a decorrelation of sensory-driven activity patterns over time, even if the input patterns remain similar. Representational drift (RD) should therefore be an expected and inevitable consequence of ongoing memory storage. We tested this hypothesis by fitting a network model to data from long-term chronic calcium imaging experiments in mouse hippocampus. Synaptic turnover in the

model inputs, consistent with the ongoing encoding of new activity patterns, accounted for the observed statistics of RD. This mechanism also provides a parsimonious explanation for the recent finding that RD in CA1 place cells has two distinct components: one which depends only on the passage of time, and another which depends on the time spent exploring a given environment. Furthermore, in the context of ongoing learning, the drift rate of any one memory depends on its repetition rate, a mechanism which can reproduce the diverse effects of experience on drift found in experiment. Our results suggest that RD should be observed wherever neuronal circuits are involved in a process of ongoing learning or memory storage.

Poster Presentation

Ismael Fernández-Hernández, André Fiala

SUSTAINED REGENERATION OF NEURONS IN ADULT Drosophila

Promoting adult neurogenesis in aging has the potential to rejuvenate neural circuits and restore associated functions. Establishing tractable models of adult neurogenesis can significantly expedite the identification of compounds and their cellular mechanisms promoting nervous system regeneration in aging. We have established the fruit fly Drosophila melanogaster as an easily scalable, highly tractable and genetically conserved platform to analyze nervous system regeneration. Particularly, by developing and implementing genetically-encoded lineage tracing systems, as well as molecular and imaging methods, we have captured sustained regeneration of olfactory sensory neurons in adult flies. Furthermore, our platform allows for the screening of compounds promoting neuron regeneration, and the evaluation of their functional contribution in the adult. By leveraging this novel platform, our current efforts are aimed at identifying clinically-relevant compounds promoting rejuvenation of the aging nervous system. Ultimately, this approach has the potential to expedite the development of regenerative therapies to treat otherwise irreversible neurodegenerative conditions, affecting an increasingly growing aging population and bearing a significant socioeconomic impact.

Poster Presentation

Martha N. Havenith+, Max Leidenberger+, Jelena Brasanac*+, Mafalda Corvacho, Inês Carmo Figueiredo, Leonie Schwarz, Malin Uthaug, Simona Rakusa, Marijan Bernardic, Lili Vasquez-Mock, Sergio Pérez Rosal, Robin Carhart-Harris, Stefan M. Gold, Henrik Jungaberle, Andrea Jungaberle
+ equal authorship

End-tidal CO2 saturation during circular breathwork supports the emergence of altered states of consciousness

Non-ordinary states of consciousness (NOSCs), induced e.g. during psychedelic-assisted therapy, show great potential to treat highly prevalent mental health disorders like depression and posttraumatic stress disorder. However, such treatment approaches are not widely accessible due to legal, medical and financial limitations. Here we explore the potential of circular breathwork as a non-pharmacological and accessible alternative to engage similar therapeutic mechanisms. Scientific studies investigating the effects of breathwork on mental health are only just emerging and the underlying physiological and psychological mechanisms are largely unknown. In this study, we aim to address these questions by for the first time tracking physiological and experiential dynamics throughout the time course of a breathwork session, comparing two popular forms of breathwork: Holotropic and Consciously-Connected breathwork. We show that reducing CO2 pressure due to deliberate hyperventilation is instrumental in catalysing NOSCs during breathwork. The NOSCs evoked

by breathwork were comparable to those produced by psychedelics, and their depth predicted psychological and physiological follow-on effects, including reduced symptoms of depression and improved well-being. Further analysis showed that different breathwork traditions engaged similar physiological mechanisms as well as experiential and psychological outcomes. Our findings for the first time identify physiological boundary conditions in which NOSCs can arise in a non-pharmacological context, offering insights into the functional mechanisms of breathwork and its potential as a psychotherapeutic tool.

Poster Presentation

Aleyna M. Diniz, Lennart Roos, Mostafa Aakthe, Jan Huisken, Tobias Moser

Investigating synaptic heterogeneity in the mouse cochlea using high-resolution light sheet microscopy

High-resolution microscopy techniques are imperative in investigating the morphology of synapses. However, in large-scale systems, like tissues or organs, these approaches are lacking scalability. Light sheet fluorescence microscopy (LSFM) has been widely used and greatly improved for imaging these large systems, such as whole mouse brains, retinae, kidneys, and cochleae, albeit sacrificing resolution. Here, we utilized a newly developed high-resolution Cleared Tissue Light Sheet Microscope together with a specialized iDISCO+ sample preparation protocol for visualization of synapses in the whole mouse cochlea. We utilized specific antibodies against different Spiral Ganglion Neurons (SGN) subtypes and inner hair cell (IHC) synapses for visualization of different SGN synapses with IHCs throughout the whole mouse cochlea volume. With this approach, the cell and synapse counts as well as SGN subtype targeting throughout the entire tonotopic axis of mouse cochlea can be addressed at once. These findings will help answer how different sound frequencies are encoded in IHC-SGN synapses in relation to synaptic heterogeneity. This technique is also compatible with different animal models (i.e. gerbil and marmoset) and further imaging techniques such as post-LS confocal slice imaging and correlative LS-EM as well as X-ray tomography.

Poster Presentation

Pablo Del Olmo-Encabo, Paola Fuentes-Claramonte, Núria Ramiro, Llanos Torres, Pilar Salgado-Pineda, Joan Soler-Vidal, María Ángeles García-León, Francesco Panicalli, Josep Tristany, Salvador Sarró, Raymond Salvador, Peter J McKenna, Edith Pomarol-Clotet

Neural correlates of the disorganization syndrome in schizophrenia during a goal management task

The disorganization syndrome, whose principal symptom is incoherence of speech or 'formal thought disorder', has been established as one of the symptom dimensions of schizophrenia by factor analytic studies [1]. Formal thought disorder has also been linked to deficits in executive function in neuropsychological studies [2]. The aim of this study was to examine the brain functional correlates of disorganization during performance of a novel executive function task, the computerised multiple elements test (CMET) [3], which is designed to be sensitive to goal neglect. 91 right-handed patients with a DSM-5 diagnosis of schizophrenia underwent 3T fMRI during performance of the CMET. Following Wallwork et al [1], scores for disorganization were obtained for each patient by summing the items conceptual disorganization (P2), poor attention (N5) and difficulties in abstraction (G11) of the Positive and Negative Syndrome Scale (PANSS). Analysis was carried out at the whole-brain level, with correction for multiple comparisons. At a threshold of $z>3.1$, a cluster of negative correlation between CMET-related activation and disorganization was seen in the right frontal superior frontal and

dorsolateral prefrontal cortex. These results support the conclusion that disorganization symptoms in schizophrenia are underpinned by executive dysfunction.

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Poster Presentation

Minyu Chan, Georg Ramm, Satoshi Ogawa

Characterization of the habenula-raphe circuit in gpr139 crispant zebrafish using multimodal imaging approaches

The habenula-raphe circuit is a subcomponent of the dorsal diencephalic conduction system (DDCS), a phylogenetically conserved pathway that bridges the basal forebrain to the monoaminergic systems and brainstem, which contributes mainly to the neurophysiology of reward processing, fear learning, sleep, social behaviours, reproductive behaviours, and more. Within this context, G-protein-coupled receptor 139 (GPR139) expression is reportedly unique to the thalamus, i.e. concentrated at the striatum and habenula in primates and non-primate vertebrates. GPR139 has been conventionally classified as an orphan receptor due to a lack of understanding of its physiological role and is highly conserved across virtually all vertebrates, including the sea lamprey, suggesting a critical functional role in the thalamus. Since its identification in 2002, studies employing gpr139 ablation models are sparse across literature, however, most notable are the gpr139 knockout mice model and pharmacological modulation models using GPR139-specific compounds. This study reports the functional connectivity changes in the DDCS of gpr139 crispant zebrafish using a multimodal imaging approach including synchrotron radiation micro-computed tomography (sr-microCT), lattice light sheet microscopy, and volume electron microscopy techniques. This study is significant in contributing an advanced

understanding of the habenula-raphe circuit, which has wide implications towards clinical applications of neuropsychiatric disorders and comorbid diseases.

Poster Presentation

Madiha Merghani, Ellen Gerhardt, Tiago Fleming Outeiro

The interplay between LRRK2/LRRK1 and Rab7 in the degradation of alpha-synuclein.

Parkinson's disease (PD) is the Second most common neurodegenerative disease after Alzheimer's disease. PD is characterized by the loss of dopaminergic neurons in substantia pars compacta (SNpc) and the presence of abnormal protein aggregates called Lewy bodies (LB) and Lewy neurites [1]. Leucine-rich repeats kinase 2 (LRRK2) gene mutations are the most common cause of familial PD, and variations in the chromosomal locus that includes LRRK2 are linked with an increased risk of developing sporadic PD. Within neurological diseases, PD is the most common diagnosis for LRRK2 mutation [2,3]. Leucine-rich repeat kinases (LRRKs) are exceptional proteins not only due to their unusually large size but also because they contain two distinct enzymatic domains and two different sets of phosphorylation sites. In humans, two proteins from this family have been identified: LRRK2 and LRRK1. Despite sharing a similar structure, mutations in these proteins lead to different diseases. LRRKs play an important role in different cellular processes including autophagy, cytoskeleton dynamics, vesical dynamics, mitochondria dynamics, and regulation of the immune system[4]. LRRKs are involved in regulating this process by modulating the phosphorylation of Rabs protein. Given the significant role of autophagy in PD, our study aims to unravel how LRRK2 modulates the autophagy process by regulating

the activity of LRRK1 and how defects in LAS contribute to the accumulation of aSyn. Our preliminary date show that losing kinase activity of LRRK2 lead to increase Autophagic activity and throw BiFC system we found that LRRK1 interact with LRRK2 forming heterodimer.

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Poster Presentation

Stella Mayer, Mary Katherine P. Joyce, Pavel Truschow, Stefan Treue & Jochen F. Staiger

Noradrenaline receptor expression in macaque striate and extrastriate cortex

Visual attention is a critical mechanism that enhances the processing of behaviorally relevant stimuli in the visual cortex, hypothesized to involve neuromodulators like noradrenaline.In this project, the expression of three of the most common noradrenaline receptor subtypes (A2A,B1 and B2) on inhibitory interneuron subtypes (parvalbumin,PV;calretinin,CR;calbindin,CB) and pyramidal neuron markers (SMI-32,Neurogranin) in rhesus macaques was examined in the visual cortical areas V1 and MT.Brain sections of 2 male rhesus macaques were used.A standard dual-immunofluorescence staining was performed on serial coronal sections.Scans were taken with a microscope with a 10x, 40x and 63x objective.We observed that in macaque visual cortex, all three noradrenaline receptor subtypes were abundantly expressed in all layers.We found that A2A and B2 adrenergic receptors were more frequently expressed than B1 adrenergic receptors in both areas. The experiments revealed higher CR- and CB-neurons density in layers II–III compared to layers IV–VI in V1 and MT.In V1,we found that CR and CB-immunoreactive neurons appear in less density.Regarding the PV expression, we found it evenly expressed across layers II–VI in all areas,although in less density in MT.Considering the pyramidal neuron markers,SMI-32 is expressed in layers III-IV and V-VI in both areas. Neurogranin is evenly expressed in all layers except

for layer I and V in both areas.The detailed Airyscan images revealed that A2A,B1, and B2 show a strong signal close to the cell membrane and partly within the cell bodies.B1 and B2 label the nucleus at a higher frequency than the A2A antibody, which shows the strongest signal close to the cell membrane.Also, A2A,B1 and B2 are co-expressed with all cell markers.These findings support a model of noradrenergic modulation in macaque visual areas V1 and MT,enriching our understanding of the neuropharmacology of attention.

Poster Presentation

Pinar Yurt, Antonino Calapai, Roger Mundry, Stefan Treue

Assessing cognitive flexibility in rhesus macaques and humans with a novel multidimensional set-shifting task

Cognitive flexibility (CF) is an executive function helping individuals to adjust their behavior based on changes in the environment and internal needs. Paradigms for set shifting and reversal learning are successful in measuring CF in a variety of species but their transferability is low due to differences in how these tasks are adapted to each species. Here we assess CF for both rhesus macaques and humans without species-specific task modifications, with a novel computerized paradigm combining elements of set shifting (intradimensional (ID) and extradimensional (ED) shifts) and reversal learning (discrimination and reversal stages) tasks. Four stimuli, target, distractor and two neutrals, appear on a touchscreen. Each stimulus combines a shape, color and motion direction, the latter used in a set shifting paradigm for the first time. In each cycle, discrimination-reversal pair, one of the features is relevant and subjects find the target by trial and error. A trial ends when a target or distractor is touched. With neutrals, we allow for a foraging approach as they disappear upon touch without terminating the trial. We assessed cognitive flexibility of 11 rhesus macaques and 25 adult humans, which required little to no training. CF remains consistent across different feature dimensions in both species, suggesting that the same mechanism is responsible for rule change,

regardless of the feature dimension of the sensory input. Thus, visual motion is a suitable feature dimension for CF tasks. We observed that humans perform better during ID compared to ED shifts. As we do not see such a difference for monkeys, the two species might be using disparate strategies to solve the task, with humans showing a level of flexibility that is categorically different from that of monkeys.

Poster Presentation

Perianen Ramasawmy, Olga Lucia Gamboa Arana, Frank Petzke, Andrea Antal

Testing a brief tailored mindfulness intervention in fibromyalgia- a preliminary therapeutic and mechanistic account from a single-arm open-label study.

Recently, mindfulness-based interventions (MBIs) have gained attention in the treatment of fibromyalgia syndrome (FMS) and other chronic pain conditions. Previous studies have stressed the need for shorter interventions tailored to the condition to increase the accessibility and feasibility of the therapy. In this open-label single-arm study, we aimed to test the preliminary therapeutic effects of a four-week online MBI tailored for FMS, which included weekly online group meetings and daily mindfulness home-based practices. Due to the incomplete understanding of the mechanisms governing mindfulness-induced analgesia in chronic pain, we investigated its effects on cortical excitability using single- and paired-pulse transcranial magnetic stimulation (TMS) protocols. Forty-six FMS patients (30-72 years) completed the intervention. Assessments encompassed self-reports of affective pain, pain intensity, quality of life (QOL), sleep quality, mood, mindfulness level, emotional regulation, and psychological impairment, utilizing a German battery of questionnaires. Verbal fluency was evaluated by the Regensburg test. We compared the post-MBI measures to baseline. The findings revealed showed modest to moderate small to medium reductions in pain, particularly in affective

pain, which exhibited a greater response compared to pain intensity. Additionally, and improvements were observed in QOL, mindfulness level, verbal fluency, and resilience post-intervention. Following the MBI, the long-interval intracortical inhibition– a measure of gamma-aminobutyric acid (GABA)Bergic inhibition– increased, hinting at the restoration of the often-observed cortical hyper-excitability in FMS patients. Our results support the therapeutic benefits of a four-week online MBI in FMS. However, a future randomized placebo-controlled clinical trial with longer follow-up is required to confirm our findings.

Poster Presentation

Amirmohammad Naderi, Adrián Palacios Muñoz, Sarath Ravindran, Jan Clemens

Higher-order social interactions shape courtship behavior in Drosophila

Social interactions in groups of animals arise from pairwise as well as higher-order interactions. For instance, courtship is commonly considered a pairwise interaction between a single male and a single female, but third parties such as rival courters and alternative mating targets can influence the interaction. The contribution of these higher-order interactions to the social dynamics in animal groups is only poorly understood. Here, we analyzed the courtship behavior in groups of the fruit fly Drosophila melanogaster to understand the influence of third parties and higher-order social interactions. We recorded interactions in mixed groups of 4 males and 4 females from two wild-type strains and defined a dynamical social interaction network based on the proximity and alignment of flies. We then used graph- and information-theoretic methods to characterize the interaction dynamics and the role of higher-order interactions. Information theoretical measures show that higher-order interactions strongly shape social dynamics: Flies are more likely to form male-female pairs than expected by a maximum entropy model that only takes into account independent links between flies. Only a model with higher-order interactions is able to explain the patterns of interactions in our data. Interestingly, the importance of higher-order interactions depended on the strain: The NM91 strain exhibited larger group sizes

and stronger higher-order interactions compared to the CantonS strain. NM91 courts more but discriminates less between males and females. However, the levels of female-directed courtship in both strains are similar, suggesting that different strategies can yield the same level of mating efficiency. Our results offer a framework for studying social behavior in groups of flies to identify the underlying neural circuits with the help of genetic or anatomical manipulations.

Poster Presentation

Luca Büschgens, Aditi Methi, Andrew Octavian Sasmita, Thomas Meyer, Sascha Weggen, André Fischer, Klaus-Armin Nave, Oliver Wirths

Loss of Interferon-gamma & -alpha signaling ameliorates Alzheimer's disease-like pathology in 5xFAD mice in an age-dependent manner

The transgenic mouse model 5xFAD resembles hallmarks of Alzheimer's disease (AD), such as amyloid-B deposition, chronic neuroinflammation, and behavioural deficits. Activated microglia cluster around B-amyloid deposits, suggesting that phagocytosis by these cells is important for either the formation or clearance of amyloid plaques. Chronic inflammatory activation of microglia (e.g. by interferon-A or -G signalling) and associated cytokine production is largely mediated through STAT ("Signal Transducer and Activator of Transcription")-dependent transcription of cytokine-responsive genes. By crossing 5xFAD with STAT1-deficient (STAT1-/-) mice, we aimed at studying a presumed inflammation-modulating effect by suppressing interferon-A and -G signalling, focussing on microglial function & phagocytic activity, amyloid plaque pathology, and behavioural deficits at different time points. Following behavioural analysis focussing on recognition memory tasks, immunohistochemical analyses of disease-associated markers were conducted on brain samples from 5xFAD and 5xFAD/STAT1-/- mice. Extracellular amyloid-B plaque pathology was assessed with 3D lightsheet fluorescence microscopy of brain hemispheres. In addition, electrochemiluminescence assays and gene expression

analyses were carried out in brain samples. A deficiency in interferon-A and -G signalling significantly ameliorated memory deficits in 5xFAD mice. Immunohistochemical analyses and electrochemiluminescence assays revealed an unchanged overall amyloid pathology at later stages. Interestingly, young 5xFAD/STAT1-/- mice showed a lower AB plaque load, linked to an altered phagocytic phenotype of immune cells. A bulk transcriptome analysis of the hippocampus and subsequent qPCR validation demonstrated various differentially expressed genes associated with neurogenesis, protective immune response and reduced cellular damage. These findings point to microglia and their activation as a disease-modulating target in AD.

Poster Presentation

Akshay Edathodathil, Stefan Treue

Adaptive and closed-loop sampling methods for a rapid estimation of receptive fields in macaque visual cortex area MST

How the physical world is represented in the activity of cortical neurons is a key question in neuroscience. Typically, for the visual system, this relationship is studied by presenting well-defined visual stimuli multiple times and then averaging the neuronal response to obtain a neuron's stimulus preferences (tuning curves, spatial receptive fields). For 2-dimensional visual receptive field (RF) estimation, visual stimuli (such as random dot patterns (RDPs)) are repeatedly presented for a few seconds at different positions, followed by an offline analysis of neuronal responses and a RF map is computed (traditional method). We study the macaque visual cortical area MSTd, which contains neurons selective for linear and for complex motion patterns (expansion, rotation & spirals) which are crucial for optic flow perception. In this study, we use a 'closed-loop electrophysiology' approach aimed at a faster estimation of the preferences of a neuron using 'adaptive sampling' methods. In this approach, the stimulus for an experimental trial is based on the neural data collected from previous trials. We evaluate two adaptive sampling methods: the Nelder-Mead Simplex Algorithm (Nelder & Mead, 1965) and the Bayesian Active Learning (BAL) approach (Pillow & Park, 2016) for estimating the 2-D preference profile (RF) of an MST neuron. The simplex algorithm method was able to estimate the RF center

with an error as low as 20-30% of the RF width, in less than 40 seconds of stimulus, compared to ~120 seconds in the traditional method. The BAL method was also able to estimate the center and the map of the RF in ~40 seconds, providing a more detailed description of the RF compared to the simplex method. The RF center estimate error using the BAL method was ~15-25% of the RF width and it showed less fluctuation compared to the simplex method. In summary, our data show that adaptive methods are substantially faster in estimating stimulus preferences compared to traditional methods.

Poster Presentation

Björn Hendrik Schott, Joram Soch, Jasmin M. Kizilirmak, Anni Richter

Preserved inhibitory temporo-parietal effective connectivity predicts explicit memory performance in older adults

Background: Successful encoding of novel information into episodic memory traces is associated with increased activation of the hippocampus and temporo-occipital cortical structures like the parahippocampal place area (PPA). On the other hand, midline brain structures like the precuneus, which is prominently involved in memory retrieval, typically show encoding-related deactivations. Older adults exhibit lower episodic memory performance and reduced precuneus deactivations. However, it is still unclear how the hippocampus interacts with temporo-occipital and medial parietal structures to facilitate successful memory formation and whether these interactions are affected by aging. Methods: Here, we used dynamic causal modeling (DCM) of functional magnetic resonance imaging (fMRI) data from three independent cohorts to elucidate the information flow between the hippocampus, the PPA, and the precuneus during episodic memory formation for visual scene stimuli. We then tested the relationship between effective connectivity of the memory network using Bayesian robust correlations. Results: In 117 young, healthy adults, we observed pronounced excitatory connectivity from the PPA to the hippocampus and inhibitory connections from the PPA to the precuneus. Both were further up-regulated during

successful encoding. This pattern could be replicated in two cohorts of young and older adults (N = 58 young, 83 older; 64 young, 84 older). Older adults exhibited attenuated negative PPA-precuneus connectivity, which correlated negatively with memory performance. Discussion/ Conclusion: Our results provide insight into the network dynamics underlying encoding-related activations and deactivations and suggest that age-related differences in memory-related network activity manifest in altered temporo-parietal neocortical rather than hippocampal connectivity.

Poster Presentation

Midea M. Ortiz-Rios, Kevin Sicking, Tat Cheng, Mary Xylaki, Brit Mollenhauer, Christine Stadelmann, Rubén Fernandez-Busnadiego

Workflow for ASyn Aggregate Analysis in Nasal Cells from PD patients using Cryo-ET

Parkinson's disease (PD), Dementia with Lewy Bodies (DLB), and Multiple System Atrophy (MSA) are distinct neurodegenerative disorders sharing a common feature: misfolded alpha-synuclein (ASyn) protein aggregates in patients' brains. Recent cryo-electron microscopy studies revealed structural differences in ASyn aggregates among these diseases, suggesting a link between ASyn structure and clinical presentation. However, traditional methods for protein analysis from patients involve post-mortem delay, tissue fixation and chemical purification, potentially confounding results. Here, we introduce a novel workflow to directly examine ASyn aggregates in nasal cells from PD patient, bypassing post-mortem delay, chemical fixation and purification. By collaborating with the Paracelsus-Elena clinic, we obtained nasal cells from PD patients, applied amyloid-specific live cell staining and plunge-froze them within two hours of collection. Preliminary results from screening and examination of these cells using cryo-light and cryo-electron microscopes are presented, marking a significant step towards structural analysis of ASyn aggregates in patients.

Poster Presentation

Mingyu Zhu, Adam Harris, Mark Walton, Thomas Akam, Tim Behrens, Mohamady El-Gaby

Ventral Hippocampal-Medial Prefrontal Cortical Pathway in Encoding Goal Progress

Our world is structured – akin to a 2-D map, navigating in the real world is similar to moving through the world coordinates. Likewise, abstract rules often underlie the structure of tasks in life, and progression through tasks could be seen as traversing task coordinates. Past studies have shown how medial prefrontal cortex (mPFC) neurons' activities tile the progress to goals in such task coordinates (1,2), and suggested that these activity sequences could act as the fundamental building blocks of task structure schemata (1). Nevertheless, how such goal progress sequences form remains unclear, and the distance in task coordinates does not necessarily equate that in world coordinates. It is possible that the distance to goal in the real world contributes to task progress coding – the further the goal, the longer it takes to reach it, the slower the network shall move in task space. Our group has illustrated how the mPFC seems to compute the online distance-to-goal signal prior to the start of the trajectory towards goal. This further raises the question of the origin of this distance-to-goal signal. We hypothesised that the ventral hippocampus (vHPC) could be a strong candidate, as it sends direct projections to mPFC and its activities have been shown to correlate with goal proximity (3). Using the dataset from Bolkan et al. (4), we showed that inhibiting vHPC input to mPFC leads the mPFC neurons to

fire earlier than in control conditions in a goal navigation task, suggesting an overestimation of task progress. Furthermore, we hope to further interrogate the circuit in a task that separates euclidean distance to goal with task progress, hoping to interrogate that vHPC-mPFC input is indeed translated into task progress information to guide animals' behaviour.

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Poster Presentation

Merle Fricke, Christina Lehnen, Hans-Wolfgang Klafki, Barbara Morgado, Sandra Lehmann, Jens Wiltfang, Thomas Liepold, Olaf Jahn, Sascha Weggen, Oliver Wirths

Amino-terminally elongated Abeta-6/-3-x peptides can be generated by the secreted metalloprotease ADAMTS4 and deposits in the brain of a subset of Alzheimer's disease patients

Objectives: The aggregation and deposition of amyloid-B (AB) peptides in the brain is thought to be the initial driver in the pathogenesis of Alzheimer's disease (AD). In addition to full-length AB peptides starting with an aspartate residue in position 1, both N-terminally truncated and elongated AB peptides are produced by various proteases from the amyloid precursor protein (APP), and have been detected in brain tissues and/or body fluids. We had demonstrated recently that the particularly abundant N-terminally-truncated AB4-x peptides are generated by ADAMTS4, a secreted metalloprotease that in the brain is exclusively expressed in the oligodendrocyte cell population. Methods: We employed a previously developed electrochemical sandwich immunoassay and immuno-precipitation (IP) followed by mass spectrometry to determine AB-3-40 and AB-6-40 levels in the supernatants of a variety of cell lines, in addition to a detailed immunohistochemical analysis of human brain samples. Results: In this study, we describe two additional ADAMTS4 cleavage site in APP N-terminal to Asp(1) between residues Glu(-4) and Val(-3) and Glu(-7) and Ile(-6), resulting in the release of N-terminally elongated AB-6-40 and AB-3-40 peptides,

from which the later serve as a component in a promising AB-based plasma biomarker assay. These elongated AB-6/-3-40 peptides were detected in supernatants of various cell lines, and ADAMTS4 enzyme activity promoted the release of AB-6/-3-x peptides. In addition, extracellular and vascular localization of N-terminally elongated AB-6/-3-x peptides were identified in a subset of AD patient cases with immunohistochemistry. The results indicated that ADAMTS4 facilitates the generation of N-terminally elongated AB-6/-3-x peptides, which were also identified in parenchymal and vascular deposits in brain samples of a subset of AD patients.

Poster Presentation

Thanh Thao Do, Arsen Petrovic, Rubén Fernández-Busnadiego

Using cryo-electron tomography (cryo-ET) to study the molecular architecture of synapses

Neurons communicate at specialized terminals called synapses, where hundreds of molecules work together in harmony to ensure proper and efficient signal transmission, which is crucial for normal brain functions. Aberrant synaptic signalling is involved in many neurodevelopmental and neurodegenerative diseases such as autism and Parkinson's disease. This highlights the need to understand the organization and interactions of molecular complexes at the synapse [1]. Cryo-electron tomography (cryo-ET) offers a close-to-native preservation of biological specimen and the unique possibility to capture both the cellular context and the molecular details, and thus can be utilized to advance structural understanding of the synapse [2, 3]. However, it is challenging to access sufficiently thin synapses for high-resolution cryo-ET. We address this problem by employing cryo-focused-ion beam milling to produce electron transparent slices containing intact synapses in cultured neurons. We obtained high-quality cryo-tomograms of synapses, showing unprecedented molecular details. In order to target synapses, we also apply correlative light and electron microscopy. Preliminary results show that fluorescence labelling is useful to localize synaptic elements in the crowded cryo-electron micrographs and 3D-tomograms. These technical developments pave the way for studies on the molecular architecture of synapses,

such as the structural basis of synaptic plasticity.

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