neurizons 2018

fire wire inspire

29th May - 1st June 2018

Göttingen, Germany

Welcome to Neurizons 2018

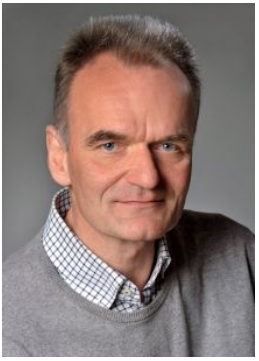
Message from the Organizing Committee

Welcome to Neurizons 2018, the 8th biennial Neuroscience conference organized by the students of the International Max Planck Research School (IMPRS) for Neurosciences, Göttingen.

Modern Neuroscience encompasses countless research approaches, from fundamental molecular investigations to large-scale explorations of networks and cognition, all converging to tackle issues of the mind. At Neurizons we invite young researchers to behold the latest research in the field from a multitude of neuroscientific disciplines. In addition to hosting renowned researchers, Neurizons promises a stage for young scientists to bring forward their own ideas, and a platform for learning and scientific exchange with the masters in the field. Neurizons provides the perfect milieu for stimulating discussions and networking during talks, poster sessions and in the more informal settings of the various social events.

Join us to fire, wire, inspire!
The Neurizons 2018 Organizing Team

Message from the Program Coordinator



Prof. Dr. Michael Hörner
Coordinator of the
International Max Planck Research
School for Neurosciences, Göttingen.

Since the start of NEURIZONS in the year 2004 the meeting is now held in Göttingen for the 8th time in 2018. Despite its growing size the meeting is still entirely organized by the PhD students of the International MSc/PhD/MD-PhD Program and International Max Planck Research School for Neuroscience Göttingen. Over the years, NEURIZONS has preserved its unique character as a small meeting encouraging direct personal interactions between participants and especially bringing young PhD students at the beginning of their scientific career in contact with renowned neuroscientists. More and more NEURIZONS integrates the alumnae and alumni who contribute both with their scientific talks and with their personal engagement by interacting with our Master and young PhD students, for instance in career-related workshops.

This year's conference certainly is special again due to its unique speakers and diverse accompanying activities. And it also marks the transition of the Neuroscience Program from its long-time host, namely the Max Planck Institute for Biophysical Chemistry to its new 'homebase', the Max Planck Institute for Experimental Medicine. With its new leadership, the Neuroscience Program successfully applied for a new round of funding which has recently been granted, securing financial support until the end of 2024.

The NEURIZONS 2018 organizing team has again been very successful to compose an attractive program with internationally renowned speakers, who – together with all other participants – will provide the scientific input to the meeting by communicating their newest findings. Consequently, the conference has again attracted participants not only from Göttingen or Germany but also from worldwide locations underlining the degree of internationalization reached on the Göttingen Campus.

In this respect, we especially welcome our guests from the Weizmann Institute in Rehovot/Israel and participants from the European Neuroscience Campus representing our joint Master and PhD training network with Amsterdam, Bordeaux and Berlin. As a tradition, the Otto Creutzfeldt PhD Price will be awarded to the best female and male doctoral graduate during the NEURIZONS opening. Ever since the price was launched in 2007, it has been sponsored by Sartorius stedim documenting the company's commitment and close cooperation with the Neuroscience Program.

We are very happy that NEURIZONS again is continuously sponsored by several companies and we are proud to announce that we do have a new record number of exhibitors this year. It is important to mention here, that a meeting like this would not be possible without our sponsors, whose generous support is very much appreciated and will contribute to make NEURIZONS 2018 a success.

About us

The Neurizons 2018 Organizing Team is a group of MSc/PhD students from the International Max Planck Research School (IMPRS) for Neurosciences. The IMPRS for Neurosciences 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 Biophysical Chemistry, the Max Planck Institute for Experimental Medicine, the Max Planck Institute for Dynamics and Self-Organization, the German Primate Center and the European Neuroscience Institute Göttingen.

GEORG-AUGUST-UNIVERSITÄT
GÖTTINGEN

MAX-PLANCK-GESELLSCHAFT

DPZ
Deutsches Primatenzentrum
Leibniz-Institut für Primatenforschung

The Neurizons 2018 Organizing Team

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Göttingen, City of Science

Göttingen, founded in the 10^{th} century, is one of the oldest university towns in Germany, with 20% of its 120.000 inhabitants being students. Except for the "Georgia Augusta" - the oldest and biggest university in Lower Saxony, the city also boasts numerous other research institutions. The prestigious Max Planck Society was founded here in 1948 and is still represented by five institutes:

- Max Planck Institute for Biophysical Chemistry
- 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.

In the last century more than 40 Nobel Prize winners lived or worked here. Of those, 13 were awarded with the prize for research done in the city. It has been a home to a number of great individuals, such as the 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. Many of the city's buildings display plaques commemorating their famous former residents.

Göttingen's well-preserved old town is now an attractive place for tourists. The half-timber houses with precipitous roofs, typical of German architecture, create a unique atmosphere in the inner city. The city center also holds some of the most 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), the Old Town Hall and in front of it, the Gänseliesel fountain. The sculpture on top of the fountain depicts a young girl holding a goose, and is associated with a curious local tradition: after completing their final examination, all PhD students are carried to the market square in wagons decorated with balloons and flowers, where they climb the fountain and kiss the goose girl on her bronze cheek, thereby making her "the most kissed girl in the world".

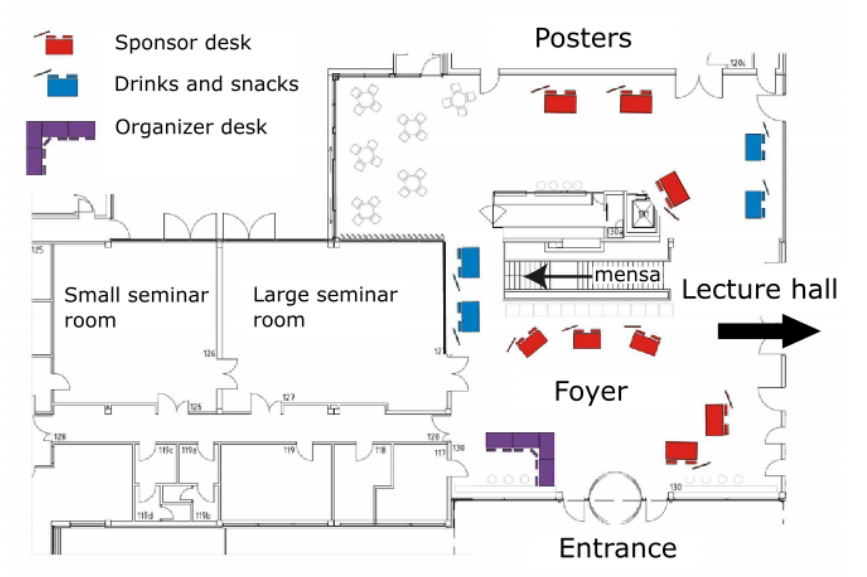
In spite of its historic roots, Göttingen is home to a young, international scene. Much of the night life is focused within the old town

walls, which makes it all the more lively and convenient for locals and visitors. 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 (Nörgelbuff). Göttingen also offers many pubs and bars (Irish Pub, Thanners, Trou, Nautibar) with a cosy atmosphere if you are looking for good company and good beer. The restaurants offer various kinds of cuisine from traditional German (Zum Szultenburger) through international (Zak, Meyer's, Kartoffelhaus), Italian (Nudelhaus, Fellini, VaPiano), Greek (Hellas) to African (Sambesi). You can find further information about Göttingen on www.goettingen-tourismus.de.

Venue Information

Location

Neurizons 2018 will take place at the Max Planck Institute for Biophysical Chemistry, am Faßberg 11, 37077 Göttingen.

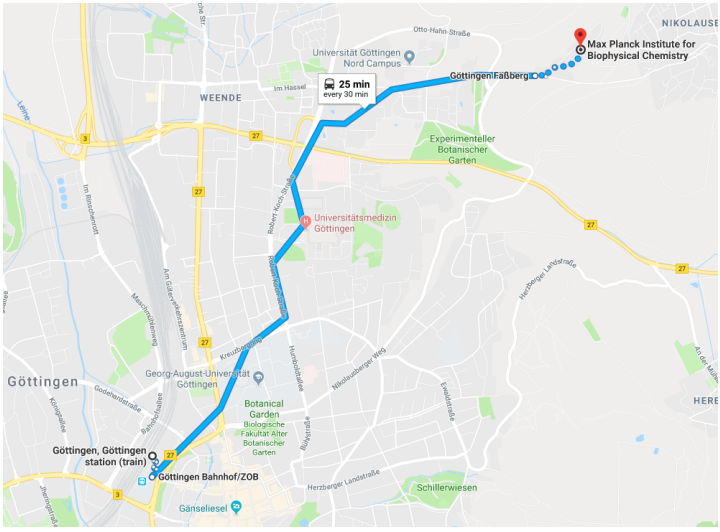


The scientific talks and the career fair seminars will be held in the

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. CoachMe will be held in the canteen ("Mensa") located in the basement under the foyer (see image above).

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 bright Neurizons T-shirts!

Buses



Buses No. 21, 22 and 23 connect the Max Planck Institute for Biophysical Chemistry 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 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 €2.30, while a 4-single-ride ticket (Viererkarte) costs €8.30. The day ticket (Tageskarte) is €5.60. For more information about the bus fares please visit the bus company's webpage www.goevb.de.

Name badges

Every participant of Neurizons will receive a badge. The badges should be worn throughout the conference, as they will be required for admission to all events.

Lunch and refreshments

Three lunches are included in the conference fee. On Wednesday, Thursday and Friday the meals will be served in the canteen located in the basement under the foyer. 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.

Highlights

Career Fair

When: Tuesday, May 29th

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 both prominent young group leaders who chose to continue in academic research, and from successful scientists who chose the path to 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 Tuesday May 29th, 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!

We would like to highlight our soft skill workshop **"Communication and Career Planning" by "Schiller & Mertens"**. The workshop is designed in a fun, interactive setting to gain insights into communication problems and provide the participants with strategies for better career planning.

Career fair is open to all without registration. For the soft skill workshop, prior registration is required. Ask at the registration desk whether there are any vacant spots.

Panel discussion: "Are animals conscious?"

When: Thursday, May 31st, 11:20

Neurizons will offer a platform for young scientists not only to learn from masters in a scientific field, but also to bring forward their own ideas and engage in a scientific exchange with these experts. We are inviting three speakers who are leading scientists in their field to introduce a scientific topic for discussion. This year's topic is "Are animals conscious?". The introduction will be followed by a 30-minute long interactive discussion between the speakers and the participants. Join us and share your ideas!

Speakers:

- Prof. Nicholas Humphrey
- Dr. Irene Pepperberg
- Prof. Dr. Melanie Wilke

Young Investigator Contest

When: Friday, June 1st, 12:00

In the Young Investigator Contest, participants (PhD students and Post-doctoral researchers) will have the opportunity to give a 10 minute presentation of their own research to the audience of Neurizons 2018. The best presentation will win the speaker a Coolpix W100 Nikon camera! This year's four candidates are:

- Thomas Chartier, EMBL, Heidelberg
- Lihi Gibor, Weizmann Institute of Science, Rehovot
- Liubov Sokhranyaeva, Russian Academy of Science, Moscow
- Katja Sporar, University of Göttingen

Poster Sessions

When: I (posters 1-20): Wednesday, May 30th, 16:20
II (posters 20-39): Thursday, May 31st, 17:00

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 2 winners! Our prizes this year include a Nikon Coolpix W1000 camera and a framed piece of original graphic art from Brain Buds. First place winner gets to choose between the two!

CoachMe

When: Wednesday, May 30th, 16:20

Speed dating for scientists! In 10 minutes, you can fire, wire and inspire. At Neurizons, we offer a once-in-a-lifetime experience to interact with world renowned scientists. CoachMe allows you to come face-to-face with the Neurizons 2018 speakers of your choice in a 'speed-dating' format. Have you wondered what makes a good scientist? Are you interested in what goes on behind the scenes of academic research? Do you want to know how to best apply for a post-doctoral position? Raise all of your questions and concerns directly with senior, successful and experienced scientists, who will share their experiences to help you with your future career in academia.

Participation in CoachMe is possible only after prior registration for this event.

Methods Workshops

Neurizons brings to you methods workshops, for state of the art and emerging techniques in Neuroscience. It is an opportunity to get hands-on practical training and an introduction to the new trends in scientific methods. Experience the work atmosphere and learn first-hand the techniques you read about and always wanted to try.

Prior registration is necessary for participation. Ask at the registration desk whether there are any vacant spots.

Expansion Microscopy

Offered by: Dr. Sven Truckenbrodt (S.O. Rizzoli Lab)

When: Wednesday, May 30th, 10:30

Number of participants: 8

Duration: 2 hours

Expansion Microscopy (ExM) is a recent addition to the biologist's toolkit for super-resolution imaging. All super-resolution imaging techniques used so far (e.g. STED, PALM/STORM) circumvented Abbe's resolution limit by separating fluorophores in time, by detecting neighboring fluorophores separately one after another. ExM instead separates fluorophores in space, by increasing the physical distance between neighboring fluorophores. This is achieved by embedding the sample

in a swellable gel matrix after immunostaining. The gel matrix can then be expanded equally in all three dimensions to obtain a resolution of at least ≈ 80 nm, and up to ≈ 25 nm (depending on the ExM technique used).

ExM has undergone rapid development since its introduction in 2015 (Chen et al., 2015). It can now be used with conventional antibodies (Chozinsky et al., 2016; Tillberg et al., 2016), and obtains a resolution that rivals STED and PALM/STORM (Chang et al., 2017). ExM has the following advantages over other super-resolution techniques:

- No specialized instrumentation required, a resolution of up to 25 nm can be obtained on conventional epifluorescence microscopes
- Multi-colour super-resolution imaging in 3-4 channels is possible without any additional effort, with almost identical resolution in all channels
- ExM can be performed on any conventional immunostaining (with the restriction that not all fluorophores are compatible with ExM)

We will perform ExM on exemplary samples provided during the course: COS7 cells (Tubulin), neuron culture (SVs, AZ, PSD), and rat brain slices.

FlyGym: Tracking *Drosophila* Optomotor Responses

Offered by: Sebastian Molina Obando and Madhura Ketkar (M. Silies Lab)

When: Tuesday, May 29th, 09:00

Number of participants: 7-8

Duration: 3 hours

With a variety of sophisticated tools available for its genetic manipulation, the fruit fly *Drosophila melanogaster* offers many advantages as a model organism. Combining genetic manipulations in specific neuronal subsets together with behavioural assays can help us to address a wide range of neuroscientific questions. The aim of the workshop is to present how an animal's locomotion can be tracked during behavioural experiments. We will track the responses of the *Drosophila* during visual stimulation in a virtual reality setup. In the first part (1.5 hours) of the workshop we will discuss the theory behind this approach and explain how measurements acquired from a fly walking on an air-supported ball can be used to compute the fly's walking velocity. Afterwards, participants will have a 'hands-on' experience with our behavioral setup, and will be guided through a real experiment, including analysis and visualisation of the results. Participants will also have a chance to learn how these experiments are designed in our lab to efficiently address our scientific interests.

Social Events

Pub Quiz

When: Tuesday, May 29th, 19:00

Where: "Escape" bar, Gutenbergstrasse 32, 37075 Göttingen

Break the ice with some friendly competition in our very own Neuro-themed trivia pub quiz! Split up into teams to answer a series of geeky questions contrived by our talented Quiz Master, all the while enjoying refreshing beer to enhance your cognitive performance. The winning team will receive a small prize and street cred for the rest of the conference.

This event is open to all and does not require prior registration. You would have to pay for your own drinks though ;)

City Tour

When: Thursday, May 31st, 20:00

Where: Old Town Hall (Altes Rathaus)

The meeting point is the Gänseliesel Fountain in front of the Old Town Hall. A professional guide will show you around Göttingen's historic old town and its various attractions. This trip is a wonderful

opportunity to learn about the history of this traditional and beautiful university town.

This event is included in the registration fee (with the exception of day passes), but prior registration is required. Ask at the registration desk whether there are any vacant spots.

Neurizons Party

When: Thursday, May 31st, 21:00

Where: "EinsB", Nikolaistrasse 1B, 37073 Göttingen

Following a long day of engaging talks, your brain will need an opportunity to rest and digest. The NEURIZONS PARTY will allow just that! Whether you want to have a stimulating conversation over drinks, or just dance and enjoy the music – don't miss out on this event.

This event is included in the registration fee, with the exception of day passes. In that case, an additional amount has to be paid.

BBQ

When: Friday, June 1st, 17:00

Where: Main conference venue

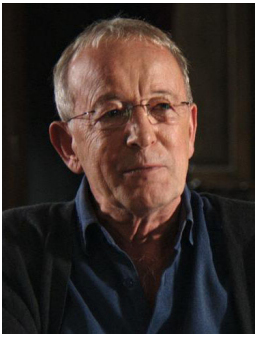
What better way to say goodbye after a long and satisfying conference than with food. At the BBQ you can eat, compete, drink, laugh, and enjoy the company of the Neurizons participants and speakers before departing! Don't miss out on this closing event, which will also include a Lab Olympics! Details will be announced soon.

This event is included in the registration fee, with the exception of day passes. In that case, an additional amount has to be paid.

Plenary Lectures

Keynote Lecture

Nicholas Humphrey



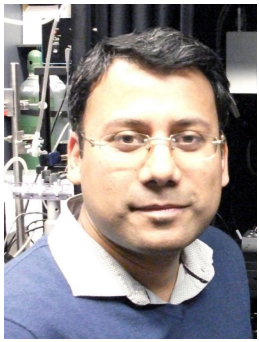
London School of Economics.
New College of the Humanities.
Darwin College, Cambridge.

The invention of consciousness

In English we use the word "invention" in two ways. First, to mean a new device or process developed by experimentation, and designed to fulfill a practical goal. Second, to mean a mental fabrication, especially a falsehood, developed by art, and designed to please or persuade. In this talk I'll argue that human consciousness is an invention in both respects. First, it is a cognitive faculty, evolved by natural selection, designed to help us make sense of ourselves and our surroundings. But then, second, it is a fantasy, conjured up by the brain, designed to change the value we place on our own existence.

Molecular Neuroscience and Neurogenetics

Amit Agarwal



Institute for Anatomy and Cell Biology,
Heidelberg University

Decoding Calcium Signals in Glial Cells

Research interest

Our brain is the most networked organ in the entire body and consists of two equal populations of broadly classified groups of cells called neurons and glia. A single neuron or a glia (such as an astrocyte) makes thousands of synaptic contacts, and thereby exhibits the highest level of cellular connectivity known to us. However, very little is known about the molecular and cellular mechanisms by which neurons and glia interconnect, and how these intricate connections are

maintained and fine-tuned over our entire lifespan. This can be partly attributed to the fact that unlike neurons, glial cells do not exhibit electrical excitability, and the widely used electrophysiological methods to probe the connectivity of neurons are not ideal for studying glia. But, glial cells show a distinct form of "excitability" based on variation in intracellular calcium ion (Ca^{2+}) concentrations. Although glial Ca^{2+} transients were discovered more than two decades ago, the mechanisms that generate these transients and their function in the brain remain a mystery.

Recent advancements in genetically encoded ions and molecular sensors, optophysiology and in vivo microscopic techniques, single-cell genetics, mouse transgenics, and computational methods are changing the landscape of glial biology. The Agarwal laboratory uses these tools and technologies to decipher cellular connectivity and molecular pathways by which neurons and glia interact, interconnect and integrate into the neural networks. The focal aim of the laboratory is to understand the functional significance of these neuron-glia connections in the neural circuits, and their role in cognition, learning, and memory; and study how disturbances in these fine cellular interactions can contribute to various neurological and psychiatric disorders ranging from multiple sclerosis to autism.

Katja Burk

University Medical Center, Göttingen

Re-routing of the Calcium-Sensing-Receptor from recycling to late endosomes by TrkB enhances BDNF-mediated neurite growth

Research interest

One of the most intensely studied areas in biology is how neurons establish and maintain functional neural circuits. However, the precise molecular mechanisms of this regulation and how neurons maintain their circuits in vivo remain incompletely understood.

Dr. Burk's main scientific interest is to understand and decipher trafficking mechanisms as part of these underlying mechanisms. Her team investigates activated receptor trafficking during development, when axons navigate through their environment and connect with their respective targets but also in disease context such as Parkinson's disease, frontotemporal dementia and Charcot-Marie-Tooth, where functional receptors fail to traffic correctly.

The lab addresses the following questions:

- What are the mechanisms of activated receptor sorting and can receptors re-route?
- Which proteins are regulating the intracellular sorting machineries and how does dysfunction of these proteins lead to neurological diseases?
- What are the exact dynamics of endosomes during activated

receptor sorting and are these dynamics compromised in disease states?

Dr. Burk's group uses an interactome and biochemistry approach as well as live-cell and high-resolution imaging to investigate these questions. In addition, they study endogenous dynamics using CRISPR in iPSC- lines from patients.

Hermona Soreq

The Edmond and Lily Safra Center for Brain Sciences (ELSC)

The impact of non-coding RNAs on cholinergic reactions to trauma

Research interest

Dr. Hermona Soreq was trained at The Weizmann Institute of Science and the Rockefeller University. She joined the faculty of The Hebrew University in 1986, where she holds a University Slesinger Chair and is a founding member of the Edmond and Lily Safra Center for Brain Science. Dr. Soreq's research pioneered the application of molecular biology and genomics to the study of cholinergic signaling, with a recent focus on its microRNA regulation and on signaling changes in health and disease. She is the elected head of the International Organization of Cholinergic Mechanisms, and served as the elected Dean of the Faculty of Science from 2005-2008. Dr. Soreq authored hundreds of publications, including 55 published in Science, Nature, PNAS and other high-impact journals. Dr. Soreq studies the

molecular regulators of acetylcholine (ACh) functioning with a recent focus on MicroRNAs (miRNAs), which rapidly emerge as global regulators of gene expression, yet the full scope of their roles in brain and body functioning is largely unknown. She combines advanced sequencing technologies with computational neuroscience and transgenic engineering tools to investigate miRNA functions in the healthy and diseased brain, with a focus on acetylcholine-related processes. Her studies discovered cholinergic brain-to-body regulation of anxiety and found "CholinomiR" miRNA silencers of multiple genes that compete with each other on suppressing anxiety and metabolic targets.

Plasticity, Learning and Memory

Christopher Colwell

Department of Psychiatry and Biobehavioral Sciences, UCLA

Circadian regulation of learning & memory and possible links to disease

Research interest

Dr. Christopher Colwell is a Professor at the Department of Psychiatry and Biobehavioral Sciences in the University California in Los Angeles School of Medicine. He has started his research career with studying the neural mechanisms of photic regulation on circadian rhythm. After his PhD and postdoctoral fellowship at the University of Virginia, Dr. Colwell started working at the University of California in Los Angeles as postdoctoral fellow and he has continued his academic career in the UCLA. The Colwell laboratory has worked with different techniques including behavioral analysis, electrophysiology and lumi-

nescence reporter gene assay to reveal the interactions between the circadian timing system and physiological functions including learning and memory. The laboratory is presently engaged in pre-clinical research designed to understand the circadian dysfunction common to a variety of diseases including neurodevelopmental and neurodegenerative disorders. Using mouse models, the Colwell laboratory has been exploring the mechanisms underlying the disease-evoked circadian dysfunction and developing new therapeutic approaches.

Alexander Dityatev

German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

Extracellular matrix and neuroplasticity

Research interest

Alexander Dityatev is a Professor at the head of the German Center for Neurodegenerative Diseases site in Magdeburg, where he heads the Molecular Neuroplasticity research group. He has co-authored more than 130 papers (h-index=48 in Google Scholar), and is co-editor of books "Molecular Mechanisms of Synaptogenesis" (2006) and "Brain Extracellular Matrix in Health and Disease" (2014).

Prof. Dityatev's group explores the role of the extracellular environment of the brain in processes of learning and memory. The formation and and ongoing activity of synaptic connections between neurons require adhesive interactions between cells and their extracellular environment, which include both cell adhesion and extracellular matrix

(ECM) molecules. These molecules regulate synaptogenesis, synaptic and extrasynaptic transmission and plasticity. In fact, a synapse can be viewed as a tetrapartite system composed of pre- and postsynaptic specializations, glial terminals and (peri)synaptic ECM. The Molecular Neuroplasticity research group aims to uncover novel mechanisms by which the ECM and cell adhesion molecules (CAMs) control learning-induced synaptic plasticity and homeostatic regulations in the brain, to characterize how dysregulation in expression and posttranslational modifications of these molecules, their receptors and ectoproteases may induce neuroinflammation and synaptic dysfunctions in major neurodegenerative and psychiatric diseases, and to develop new CAM- and ECM-targeting strategies for restoration of synaptic and cognitive functions in animal models of these diseases.

Scott Waddell

Centre for Neural Circuits & Behaviour,
University of Oxford

Neural mechanisms of memory re-evaluation

Research interest

Scott Waddell is a Professor of Neurobiology and Wellcome Trust Principal Research Fellow in Basic Biomedical Sciences at the University of Oxford, where he is Vice-Director of the Centre for Neural Circuits & Behaviour. Scott is an elected member of EMBO and was the 2014 recipient of the Liliane Bettencourt Prize in Life Sciences.

Scott's research pursues one of the great challenges in neuroscience

– to understand how molecular processes code experience within the neural networks of the brain, and how these circuits operate to ensure that memories are retrieved at the right time to guide appropriate behaviour. His research has generated a cellular resolution view of memory formation, consolidation and retrieval by combining genetic, molecular biology, two-photon microscopy and behavioural approaches in the relatively small brain of the fruit fly. Much of the work has converged on discrete groups of dopaminergic neurons that innervate the brain structure called the mushroom bodies. Different combinations of these dopaminergic neurons write sweet and nutritious sugar or water memories, and provide hunger state-dependent control of the expression of food-seeking memory. In addition, recent work has shown that these networks also allow the fly to re-evaluate memory at the time of retrieval. The Waddell group also investigates transposition in the brain and whether it contributes to neural function.

Sensory Systems

Ruben Portugues

Max Planck Institute of Neurobiology,
Martinsried

Research interest

Ruben Portugues is the research group leader at the Max Planck Institute of Neurobiology in Martinsried, Germany, for the group of sensorimotor control. After Dr. Portugues started his studies in Mathematics with a Master's, he continued with his PhD in theoretical physics at the University of Cambridge. Dr. Portugues then went to Chile for a postdoctoral fellowship in theoretical physics at Centro de Estudios Cientificos. From 2006 until 2014 Dr. Portugues did a postdoctoral fellowship in neurobiology at Harvard University in the laboratory of Florian Engert. Since 2014 he is a successful group leader at the Max

Planck Institute of neurobiology. His team investigates motor learning and sensory integration with a key focus on brain adaptation to new learning rules, unravelling the underlying neural circuits by studying the behavioural algorithms. To investigate this, the group is using larval zebrafish with self-programmed virtual reality experiments in a swim-simulator.

Yoshihiro Yoshihara

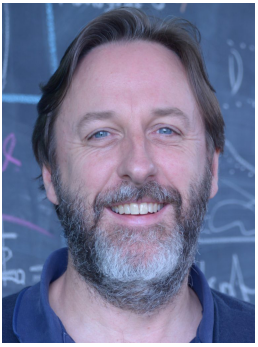
RIKEN Brain Science Institute, Japan

Research interest

Yoshihiro Yoshihara is a Team Leader of the Laboratory for Neurobiology of the Synapse at the RIKEN Brain Science Institute in Japan. He did his PhD in Pharmacology at Kyoto University in 1989 followed by a postdoctoral fellowship in the department of Neuroscience at the Osaka Bioscience Institute. From 1992 until 1998 Dr. Yoshihara worked at the Osaka Medical College in the department of Biochemistry as a lecturer and Associate Professor. Since 1998 he has been at RIKEN Brain Science Institute as a Team Leader and since 2009 Senior Team Leader. Dr. Yoshihara was awarded the Young Investigator Award in 2006 from the Japanese Association for the Study of Taste and Smell. His team is working on the molecular, cellular and circuit mechanisms underlying the development and functional architecture of the zebrafish and mouse olfactory system. His work focuses on the

neural circuits mediating various olfactory behaviors such as searching for mates, finding mates, and escaping from danger.

Jason Kerr



Department of Behaviour and Brain Organization, Caesar, Bonn, Germany

Research interest

The primary aim of the Department of Behavior and Brain Organization (BBO) is to understand how mammals use vision to make decisions and what the underlying neural processes are. BBO combines imaging, computation, behavioral analysis, electrophysiological recordings, and anatomical mapping to explore the connection between behavior and neuronal activity. The research of BBO can be divided into two broad regions. The first develops tools and techniques, which have single cell and single action-potential resolution, for recording and analyzing neuronal activity from large populations of cortical neurons in the awake and freely moving mammal. The second is focused on understanding the neuronal mechanisms underlying vision-based decision making in freely moving mammals. This involves the development of special multiphoton microscopes and of optics-based head and eye tracking techniques that can be used on freely behaving animals from a range of mammalian species. The use of different species allows, for example, the comparison of how the eye movements of different animals vary in coordination and nature. The

overall aim of this approach is to generate a thorough understanding of mammalian vision and the organization of the underlying neuronal circuits.

Evolutionary and Developmental Neuroscience

Gregor Bucher

Georg-August-University Göttingen

Conservation and divergence in brain development

Research interest

The projects of the Bucher lab center on the developmental genetics and the evolution of the arthropod head and brain using the red flour beetle *Tribolium castaneum* as model. This species shows an insect typical mode of head development while the *Drosophila* larval head is turned outside into the thorax and shows a derived genetic control. Further, *Tribolium* develops some parts of the brain during embryogenesis like most insects while in *Drosophila*, these are formed

postembryonically.

With respect to head development, the lab aims at identifying the genes required for insect head patterning and their interactions. Further, the morphogenetic movements are studied that shape the head. These data provide the basis for evolutionary comparisons within and beyond arthropods.

The central complex is a higher order integration center of the insect brain involved in spatial orientation and other tasks. However, this neuropil develops only after embryogenesis in *Drosophila* while it forms during embryogenesis in the beetle. Therefore, the lab is using *Tribolium* to identify the genes and cell lineages required for embryonic formation of the central complex. The comparison of the development of homologous cells between these two species is used to reveal the developmental and genetic basis of these evolutionary differences.

Besides testing a number of candidate genes the lab has been leading the genome wide RNAi screen "iBeetle" in order to comprehensively identify all genes required for these and other processes in an unbiased way. With this project, the red flour beetle has become the second insect model with tools for genome wide phenotypic screening.

Suzana Herculano-Houzel

Departments of Psychology and Biological Sciences, Vanderbilt University

Research interest

Dr. Suzana Herculano-Houzel is a Brazilian neuroscientist mainly focusing on comparative neuroanatomy. Dr. Herculano-Houzel did her Bachelor's degree in biology and genetics in Rio de Janeiro, to continue her education in Cleveland with a Master's degree in Neuroscience and a PhD in Paris at the Université Pierre et Marie Curie. After a Postdoctoral fellowship at the Max-Planck-Institute for Brain Research in Frankfurt, Dr. Herculano-Houzel is now an associate Professor at Vanderbilt University in Nashville. She published several books on neuroscience for the general public and her role as an advocate for science has earned her the José Reis Prize of Science Communication in 2004. She continues to spread her passion of neuroscience by writing a biweekly column about neuroscience in everyday life for a major newspaper in Brazil.

Her main research interest is the evolutionary origin of diversity in the nervous system, comparing the human brain to other species by investigating the numerical relations of neurons and glia cells, as well as brain size and folding across species. She is interested in the variation in cellular composition of the brain over evolution, across species and the relation to cognitive abilities. Dr. Herculano-Houzel's laboratory of Comparative Neuroanatomy uses quantitative morpholog-

ical approaches, namely the Isotropic Fractionator, developed by Dr. Herculano-Houzel in the lab in 2005, to investigate neuronal numbers.

Daniel Kronauer

The Rockefeller University

Communication and social behavior in ants

Research interest

Insect societies are socially integrated to such an extent that they are often portrayed as "superorganisms" in which different morphological or behavioral castes have different functions, similar to the tissues of an organism. The Kronauer lab uses ants to study a number of broad questions: How did complex animal societies evolve from solitary ancestors? How does behavioral and developmental plasticity give rise to division of labor? How do individual ants produce, perceive, and process social signals? And how does the composition and network structure of social groups affect emergent group-level properties and fitness?

To address these questions, the lab uses molecular genetics and neuroscience in combination with quantitative behavioral and morphological measurements under controlled laboratory conditions. In particular, the researchers are developing and using the clonal raider ant *Ooceraea biroi* as a new model system for social behavioral genetics. The

clonal raider ant is a powerful model system because it uniquely combines the rich biology of social insects with unparalleled experimental accessibility. For example, the species' unusual biology makes it possible to control and replicate the size, genotypic composition, and age structure of colonies—the three central factors affecting individual behavior, division of labor, and social networks in ants. The Kronauer lab has recently published the species' genome and has developed protocols for genome editing along with automated tracking setups that allow precise quantification of individual and group behavior, as well as social interaction networks.

Theoretical and Computational Neuroscience

Dean Buonomano

Brain Research Institute, UCLA

How does the brain tell time? Computational and Experimental Studies.

Research interest

Much of the information the brain processes and stores is temporal in nature—a spoken word or a handwritten signature is defined as much by how it unfolds in time as by its spatial structure at any moment. The brain seamlessly assimilates and processes temporal information, an ability critical to most behaviors, from understanding speech to anticipating events such as when a traffic light will change colors. Because timing and temporal processing are so fundamental to brain

function, the Buonomano lab has proposed that that there is no single brain area responsible for timing, but rather that most neural circuits are intrinsically able to process temporal information.

To study the neural basis of timing and temporal processing on the scale of milliseconds to seconds the Buonomano lab uses computational, electrophysiological, optogenetic, and psychophysical techniques. The lab's research supports the state-dependent network model, that postulates that sensory timing (e.g. interval discrimination) is encoded in the intrinsic neural dynamics of cortical networks, specifically that timing emerges from the interaction of the time-varying internal state of neural networks with external stimuli.

Keith Hengen

Washington University in St. Louis

Active self organization in the brain: stable function from neurons to networks

Research interest

Keith Hengen's research is focused on the mechanisms and parameters of homeostatic plasticity in the intact brain. While these processes are traditionally investigated as exclusively cellular and molecular phenomena, nothing in the brain works without the capacity to self-organize and maintain stable function across dynamic and variable environments. As a result, Keith aims to understand how cellular mechanisms of dynamic stabilization can give rise to robust emergent properties

that are truly the biological underpinnings of cognition and behavior. As a newly formed group, the Hengen Laboratory is concerned with understanding homeostatic plasticity in normal brains as well as how failures of homeostasis are instrumental in disease. Currently, Keith is investigating the role of sleep and wake in shaping neural dynamics and thereby gating the expression of distinct plasticity mechanisms.

Anthony Leonardo

Janelia Farm Research Campus, HHMI

Components of the neural circuitry for an internal model

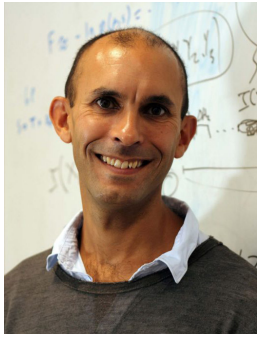
Research interest

The quest of Neuroscience is to explain how cognition arises from the microscopic circuitry within the brain. Of the endless mental feats we engage in, predictions are amongst the most fundamental and the least noticed. They are so pervasive that they underlie not only highly complex decisions, but even mundane actions, like lifting a glass. Motor control in particular is riddled with prediction and planning because fine control of the body is complex. The implementation of predictive control requires internal models, representations from which we can infer the future state of something from its past states. Decades of work have provided evidence supporting the existence of predictions and internal models underlying behavior. These models are also a pillar of modern control systems. Anthony Leonardo's work is focused on understanding the neuronal structure and function of such predictive

internal models and how they are integrated with reactive feedback to generate complex and robust behaviors. At present his lab studies this in the context of prey capture in dragonflies. A broad range of tools are employed, ranging across outdoor recordings, feedback-controlled behavioral environments, measurements of kinematics and neurons in freely moving animals, neuroanatomy, conventional intracellular and extracellular electrophysiology, and electron microscopy. These different levels of description, which span microscopic to macroscopic phenomena, are linked together with systems level quantitative models.

Higher Brain Functions

Anil Seth



University of Sussex, Brighton, UK

Real problems and beast machines: predictive processing and conscious experience

Research interest

Anil Seth is a Professor of Cognitive and Computational Neuroscience at the University of Sussex, where he is also Co-Director (with Prof. Hugo Critchley) of the Sackler Centre for Consciousness Science. He sits on the steering group and advisory board of the Human Mind Project.

He is the Editor-in-Chief of Neuroscience of Consciousness, editor and co-author of 30 Second Brain and consultant for Eye Benders (winner of the Royal Society Young People's Book Prize 2014). He contributes regularly to a variety of media including the New Scientist,

The Guardian, the BBC and writes the popular blog NeuroBanter.

His research pursues one of the great challenges for 21st century science – of understanding the biological basis of conscious experience. He uses a highly multidisciplinary approach to study complex brain networks by bringing together research across neuroscience, mathematics, computer science, psychology, philosophy and psychiatry.

Billions of neurons are working together to create a conscious perception of the world and of ourselves within it. How does this happen? What are the biophysical mechanisms that underpin our experiences of self and world? According to neuroscientist Anil Seth, we're all hallucinating all the time; it's just that when we agree about our hallucinations, we call it "reality". Join us in a stirring keynote address at Neurizons 2018 to question the very nature of your existence!

Robin Carhart-Harris

Centre for Neuropsychopharmacology, Division of Brain Sciences, Faculty of Medicine, Imperial College London

Research interest

The Psychedelic Research Group at Imperial focuses on two main research areas: 1) the action of psychedelic drugs in the brain, and 2) their clinical utility, e.g. as aides to psychotherapy, with a particular focus on depression. The group is lead by Dr. Robin Carhart-Harris with oversight from Professor David Nutt. Robin Carhart-Harris has

studied effects of LSD, psilocybin (magic mushrooms), and MDMA on the brain, conducting some of the first brain imaging studies of these drugs. Most recently he has been running a clinical trial looking at the potential of psilocybin to treat depression.

Joseph Paton

Champalimaud Foundation, Lisbon

Research interest

Animals are exposed to countless sensory stimuli, which must be processed and filtered so as to make the appropriate behavioural adjustments. A fundamental part of this process is determining which cues hold predictive value of relevant events. How animals figure this out is dubbed the credit assignment problem. Joe Paton's group at Champalimaud Research takes on the problem by investigating the time encoding mechanisms of the brain, for temporary proximity of the cues to important events determines their usefulness and thus, whether they warrant learning about. To delve into the problem, his group makes use of a wide array of computational, electrophysiological and molecular techniques to observe and manipulate the neurophysiology of rodents performing tasks that force them to estimate intervals.

Ursula Voss

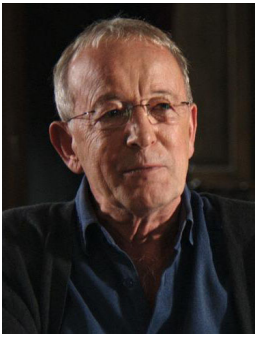
Goethe University, Frankfurt (Main)

Research interest

Ursula Voss is currently Professor at Goethe University in Frankfurt am Main, Germany and head of a special outpatient clinic at Vitos Waldkrankenhaus Köppern in Friedrichsdorf, Germany. Her research centers on attention, endocrine changes in sleep, information processing and vigilance, psychological sleep research, states of consciousness, stress and coping, and sleep in neurodegenerative disease.

Panel Discussion: "Are animals conscious?"

Nicholas Humphrey



London School of Economics.
New College of the Humanities.
Darwin College, Cambridge.

How is it for them?

What's it like to be a dog, a spider, an earthworm or an intelligent robot? Are the lights on? What difference would it make? Many theorists assume that the phenomenal quality of consciousness emerges as an accidental side-effect of complex information processing by the brain, and that it has no consequences for cognition or behaviour. I argue, to the contrary, that phenomenal quality, if and where it exists, is a super-added feature of consciousness that has evolved because of

the biological benefit it brings. In the case of human beings, it enhances the value of lived experience and thus changes humans' sense of self-worth and their outlook on the material and social world. The question is: for which if any nonhuman animals does – or could – consciousness play this adaptive role? We can seek evidence at two levels: 1. Does the animal's brain have the additional circuitry? 2. Does the animal's behaviour demonstrate the additional commitment to life? My own reading of the evidence is that the majority of animals are not conscious in this way. The lights are off. If we apply the same criteria to intelligent machines, we can be sure that at the present stage of development the same is true.

Irene Pepperberg

Harvard University in Cambridge, MA

Arguments for human consciousness usually derive from introspective reports; we lack such reports for nonhumans. Given the absence of confirmatory data, I argue that nonhumans have an awareness distinct from human consciousness; the extent to which it approaches human consciousness is the subject of ongoing study. I propose that this awareness is required for complex tasks and is a form of higher order cognition, sensu Delacour (1997), who posits consciousness as a "...certain style of cognition, characterized by a particular integra-

tion of different processes. . . " For some nonhumans, this awareness involves the capacity not only to process perceived data, but also to choose, from among various possible sets of rules that have been acquired or taught, the set that appropriately governs the current processing of that data (Pepperberg 1999). Simple associative processes probably require only basic perception. In contrast, complex comparative psychology tasks (e.g., transfer, hierarchical category formation) require integrating perception, centralized monitoring, and behavioral control; for some tasks, however, even this information-processing account cannot explain observed data. I will review one of several studies that provide evidence not for nonhuman consciousness equivalent to that of humans, but possibly for some of its elements: evidence concerning a Grey parrot's derivation of a zero-like concept.

Melanie Wilke

Cognitive Neurology Department at the
University Medical Center Göttingen.
German Primate Center.

Visual consciousncess and its losses

At every moment when we are awake, our brains create an 'inner world', filled with percepts, imaginations and feelings. How does physical matter such as neurons in our brains lead to these subjective states and is there a special 'hardware' or dynamic required? Drawing conclusions from neuroscientific experiments in humans and animals, this talk will address the question where and how activity in the brain

correlates with our subjective perception. In addition, the talk will discuss how damage to the brain, due to local inactivation of brain structures in animals or due to stroke in humans, can impair conscious perception. By better understanding the symptoms of patients we are learning more and more about the neural mechanisms underlying such failures and recovery of consciousness.

Abstracts

Young Investigator Talks

Bidirectional control over impulsive behavior through optogenetic modulation of prefrontal circuits [YI 1]

Lihi Gibor[1], and Ofer Yizhar[1]

[1]Weizmann Institute of Science

The capacity to withhold a response when confronted with negative consequences is crucial for cognitive function, and is a hallmark of goal-directed behavior. Frontostriatal circuits, linking the medial prefrontal cortex (mPFC) and the striatum, have been implicated in the regulation of impulsive behavior. However, it remains unclear how intact behavior is maintained, and which mPFC neuron populations mediate these behavioral responses. To better understand the contribution of frontostriatal circuit components to behavioral control, we trained mice in a 5-choice serial reaction time task for sustained attention and cognitive control. We then incorporated optogenetic inhibition into behavioral sessions to silence the mPFC during task performance. Silencing of the ventral mPFC caused an impairment in the ability of mice to adapt to changes in task structure, suggesting the mPFC is required for flexible control of goal-directed behavior. Next, we targeted nucleus accumbens-projecting neurons in the mPFC, utilizing a novel optogenetic inhibitory tool, soma-targeted GtACR2. Inhibition of this subpopulation led to reduced impulsivity, without changes in performance and motivation. Finally, we incorpo-

rated behavioral testing with extracellular recordings and optogenetics for photostimulation-assisted identification of recorded neurons, based on their projection target. Our preliminary results reveal that mPFC neurons show diverse, yet stable, responses to behavioral events in the task (e.g., correct response). We are currently performing analyses to determine whether accumbens-projecting neurons demonstrate unique patterns of neuronal activity compared with mPFC neurons in general. These results could serve to delineate the cell type-specific mechanisms involved in mPFC regulation of cognitive control.

[YI 2] Distinct properties and functions of first-order interneurons in the *Drosophila* visual system

Katja Sporar[1], Madhura Ketkar[1], Marvin Seifert[1], Burak Gür[1], and Marion Silies[1]

[1]European Neuroscience Institute (ENI-G)

In many sensory systems including the visual system of *Drosophila melanogaster*, there are distinct ON and OFF pathways. In *Drosophila*, these pathways split postsynaptic to photoreceptors, where the two first-order interneurons L2 and L3 are the major inputs to circuitry that detects OFF edge motion, whereas the ON pathway receives input from the L1 neurons. The functional role of the distinct OFF pathways is not known. Here, we show that the physiological properties of the L2 and L3 input neurons are very different. When we use *in vivo* two photon imaging to record calcium signals in L2 or L3 axon terminals in response to prolonged light stimuli, L2 responses are transient, whereas L3 calcium signals are sustained. Using a range of visual stimuli we could show that L2 is contrast sensitive as it provides downstream circuits with information about recent changes in luminance, whereas L3 is luminance sensitive and responds strongest at low luminance. Thus, the two cells in the OFF pathway respond to fundamentally different features of the visual scene. To understand these early differences in visual processing, we tested the contribution

of different photoreceptors inputs, lateral circuit inputs and downstream feedback mechanisms. Together, our data argue that lamina neuron properties are shaped by cell autonomous mechanisms and are not a result of circuit interactions. We are currently working towards identifying the mechanisms that shape the distinct physiological properties, as well as the probing the specific behavioral roles that these two OFF pathways play in motion detection.

Calcium responses of head chemosensory organs in the marine annelid *Platynereis dumerilii* [YI 3]

Chartier T.[1], Dürichen W.[1], Deschamps J.[1], Jékély G.[2], and Arendt D.[1]

[1]Developmental Biology Unit, EMBL Heidelberg, Germany; [2]Max Planck Institute for Developmental Biology, Tübingen, Germany

Chemosensation drives animal behavior. Adapting to different habitats, animals possess chemosensory systems of diverse morphology and cellular architecture, and using distinct types of molecular receptors. To elucidate the early evolution of chemosensation, it is essential to study chemosensory systems in their original environment, the sea. Yet, most animals investigated so far are terrestrial or freshwater species. Here, we test the role of candidate chemosensory head organs in *Platynereis dumerilii*, a marine annelid worm. Using a customized microfluidic setup for precise delivery of chemical compounds, we perform calcium imaging of whole heads to visualize neuronal activity in 6-days-old larvae. We find evidence of chemosensitivity in all types of adult organs, but not in the larval apical organ. Antennae appear to be the main chemosensory organs, whereas nuchal organs and palps appear more specialized, and tentacular cirri show low chemosensitivity. The apical organ, a brain region thought to be responsible for larval settlement and metamorphosis, shows prominent oscillatory activity. Interestingly, we find chemically-induced activity in the Mushroom

Bodies, a brain structure potentially involved in learning. Other previously unknown regions or cells are described which were activated by chemical stimulation, and sensory integration between organs is analyzed. We provide the first comprehensive study of head chemosensory organs in an annelid, establishing the 6-days-old *Platynereis* larvae as a model for the study of annelid chemosensory systems.

[YI 4] Patterns of Post-Translational Histone H3 Modifications in Human Temporal Lobe Epilepsy

Sokhranyaeva L.[1], Aniol V.[1], Trifonov I.[2], and Gulyaeva N.[1]

[1]Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russia; [2]University clinic of Yevdokimov Moscow State University of Medicine and Dentistry N.V., Moscow, Russia

Temporal lobe epilepsy (TLE) is the most widespread type of epilepsy. About 75% of TLE cases appear to be drug resistant (refractory). It has been proposed that epigenetic modifications, including post-translational chromatin modifications, play a critical role in etiology and refractoriness of TLE. The aim of this study was to describe patterns of histone H3 modifications in brain tissue of patients with refractory TLE.

Tissue samples were collected from patients after amygdalohippocampectomy. Histones were extracted with trichloroacetic acid and modifications were analyzed using Western blotting. The levels of following modifications of lysine residues (K) were measured: acetylation (ac) of H3K9, H3K14 and H3K18 and mono-, di- and trimethylation (me1, me2, me3) of H3K4, H3K9 and H3K27. The research was focused on regional differences in modification patterns (temporal lobe vs. hippocampus) as well as on changes in these patterns associated with hippocampal sclerosis and antiepileptic drugs intake (valproate, carbamazepine, levetiracetam and lamotrigine).

We found that most modifications were more expressed in the temporal lobe in comparison to the hippocampus. In patients with hippocampal

sclerosis me3H3K4, me2H3K9 and me2H3K27 were decreased, but me3H3K27 was increased. Valproate and lamotrigine did not affect H3 modifications. In patients treated with carbamazepine the level of me1H3K4 was decreased, while levetiracetam intake was associated with the increase in me1H3K4.

We suggest that modifications of histone H3 are involved in development and maintenance of drug resistant TLE. In the future we intend to find specific genes regulated by these epigenetic modifications.

The study was supported by RFBR grant #16-04-01513.

Poster Session I

Exploring the function of an uncharacterized transmembrane protein for chronic pain [1]

Meike Hütte[1], Julia Sondermann[1], Tom Rouwette[1], Luca Avenali[1], David Gomez-Varela[1], and Manuela Schmidt[1]

[1]Max Planck Institute of Experimental Medicine, Göttingen

An adequate treatment of chronic pain is not feasible yet, because available drugs exhibit limited efficacy and are often accompanied by strong side effects. In order to try to improve therapies, one would ideally know the molecular mechanisms, which are specific for chronic pain states without affecting key physiological functions. These could serve as target for novel drugs to increase the treatment efficacy of pain and to reduce side effects.

Applying state-of-the-art technology in proteome analysis (‚DIA-MS': data-independent acquisition mass spectrometry) we were able to generate data, which allows a unique insight in the regulation of protein networks in dorsal root ganglia (DRG) during inflammatory and neuropathic pain.

Differentially expressed proteins could be identified including those, which are commonly known in the context of chronic pain as well as many novel candidates that were specifically regulated in one of the pain paradigms. Among the latter group was TM, a completely un-

characterized transmembrane protein. In order to explore the function of TM in the context of somatosensation and chronic pain, we generated transgenic knockout mice, and use diverse *in vitro* methods. Our results show that TM affects mitochrondrial function and attenuates mechanical hypersensitivity upon inflammatory pain *in vivo*.

While further work is needed to fully understand the role of TM in the somatosensory system, our findings validate the utility of comparative proteomics to reveal novel players of pain.

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[2] Stimulus polarity differentially influences cortical network activation in *in vivo* intracortical microstimulation

Mathias B. Voigt[1], and Andrej Kral[1]

[1]Institute for AudioNeuroTechnology (VIANNA), Hannover Medical School, Germany

Intracortical microstimulation (ICMS) is widely used in clinical and basic neuroscientific research. Earlier work from our group showed the possibility to combine ICMS with neuronal recordings on the same shank of multi-electrode arrays and consequently inside the same cortical column *in vivo*. The gold standard stimulus pulse shape for ICMS is a symmetric, biphasic current pulse. In the present study we investigated the role of the leading-phase polarity (cathodic- vs. anodic-leading) of single ICMS pulses on the activation of the cortical network.

We recorded local field potential and multi-unit responses from the auditory cortex of adult guinea pigs ($n = 15$) under ketamine/xylazine anesthesia, using 16 channel Neuronexus multi-electrode arrays. Physiological responses of A1 were recorded during acoustic click stimulation (50 μs condensation clicks, 15-95 dB). ICMS was performed with varying current and polarity on any one of the 16 electrodes while recording at the same time with the 15 remaining electrodes.

In general, cathodic-leading and anodic-leading electric stimulation showed comparable activation patterns, with stronger influences of the stimulation strength and depth than the leading-phase polarity. But cathodic-leading ICMS consistently led to higher response amplitudes. Intracortical electric stimulation, regardless of polarity, was found to have a strongly reduced dynamic range in comparison with acoustic stimulation, in consistence with the literature on electric stimulation of subcortical auditory pathway structures.

A detailed analysis of the directly activated cortical structures, based on the current-source density sink distribution, revealed a granular activation which was exclusive to cathodic-leading ICMS of deep cortical tissue. This supports the results of simulations and *in vitro* studies, reporting a differential activation of fibers of passage, i.e. cathodic-leading stimulation are preferential for the activation of thalamo-cortical fibers.

Supported by Deutsche Forschungsgemeinschaft (Cluster of Excellence Hearing4all).

Mapping brain-wide inputs to Parvalbumin-expressing interneurons with intersectional rabies virus tracing [3]

Georg Hafner[1], Mirko Witte[1], Julien Guy[1], and Jochen Staiger[1]

[1]Institute for Neuroanatomy, Universitätsmedizin Göttingen, Georg-August-Universität Göttingen

Parvalbumin (PV)-expressing interneurons are the largest subpopulation of inhibitory neurons in the mouse neocortex and are indispensable for controlling the activity level of principal cells. We wanted to visualize brain-wide inputs to PV neurons in the barrel cortex to investigate what areas and cell types can activate PV neurons. Rabies virus tracing holds the potential to map both local and long-range inputs to a class of neurons. It utilizes adeno associated viruses (AAVs) to express proteins for rabies virus entry and spread together with

a modified rabies virus to label monosynaptic inputs. To achieve a very specific tracing, we employed an intersectional strategy. We generated Vgat-Cre/PV-Flp transgenic mice, which co-express Cre and Flp in PV interneurons. We combined this line with a Cre- and Flp-dependent AAV, which expresses its proteins only in the presence of both recombinases. We thoroughly tested this new viral construct for Cre/Flp-independent leak expression and found it to be very specific for mapping long-range inputs, while local inputs were slightly confounded by leak expression of the construct for rabies virus entry. We mapped the brain-wide long-range inputs to PV interneurons in the barrel cortex and found input cells in several distant cortical areas and thalamic nuclei. Surprisingly, layer IV sent an equal number of projections from distant areas to PV neurons as supra- or infragranular layers; in visual cortex layer IV even sent the most projections, questioning its mere role as an input layer. We mapped local inputs within the barrel cortex, too, and analyzed them with respect to layer distribution and molecular markers. Local inputs were mainly from layer IV and mainly excitatory. A small number of inputs originated from layer I, a previously unknown source of input. In conclusion, this study provides a fine-grained analysis of the inputs PV neurons integrate.

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[4] Mechanisms of activity-dependent modulation of *Drosophila* muscles by a neuropeptide

JaeHwan Jung[1], Amanda Kornel[1], and Joffre Mercier[1]

[1]Brock University

Neuropeptides are the most diverse group of transmitters in the nervous system, with over 100 in human brain and several thousands in invertebrates. Neuropeptides can be released at synapses, where they as co-transmitters by enhancing the effectiveness of classical transmitters, or they can be released into the circulation to act as neurohormones, altering efficacy of chemical synapses. We are examining the physiological effects of the peptide, proctolin (RYPLT),

which can be released in *Drosophila* as both a neurohormone and a co-transmitter. We previously reported that bath application of proctolin enhances nerve-evoked contractions and that increasing stimulus frequency in the motor neurons decreases threshold and EC50 for this effect. This activity dependence suggest a secondary level of modulation, or "metamodulation". Our results are surprising because there is only one known proctolin receptor in *Drosophila*. Two hypotheses could account for our observations. Increasing neural activity may release higher amounts of proctolin and other co-transmitters from the motor neurons. Alternatively, proctolin's ability to enhance contractions may depend on increased release of the classical transmitter, glutamate, and the resulting increased levels of depolarization of the muscle fibers. We are currently testing the latter hypothesis by inducing contractions with glutamate and determining whether or not the EC50 and threshold for proctolin to enhance glutamate-evoked contractions decrease with increasing glutamate concentrations. Data to date do not support a postsynaptic mechanism. These results will provide a better understanding of the mechanisms underlying metamodulation of chemical synapses. Supported by NSERC Canada.

The role of PSD-95 in the response of neuronal networks to hypoxia [5]

Joana-K. Duda[1], Michael Müller[2], and Oliver M. Schlüter[1]

[1]Department of Psychiatry and Psychotherapy, University Medical Center Göttingen; [2]Institute of Neuro- and Sensory Physiology, University Medical Center Göttingen

The postsynaptic density protein-95 (PSD-95) and PSD-93 belong to a major family of scaffolding proteins at glutamatergic synapses, namely the DLG-MAGUK family. Its members play essential roles in synaptic development, transmission and plasticity, especially by regulating the function and trafficking of the most abundant neurotransmitter receptor in the CNS: the AMPA receptor. PSD-95 has also been

linked to neurotoxic signaling pathways. Peptides predicted to prevent the NMDA receptor/PSD-95/nNOS (neuronal NO synthase) complex formation were demonstrated to reduce infarct volumes in mouse and primate stroke models. To investigate the role of PSD-95 in the response of neuronal networks to metabolic compromise, we performed an hypoxia-induced spreading depression (HSD) assay using extracellular field potential recordings in acute hippocampal slices of adult PSD-95 knock-out (KO) and PSD-93 KO mice. Spreading depression (SD) appears as a depolarizing wave, shutting down neuronal function and is associated with stroke, migraine and epilepsy - to name prevalent examples. It is electrophysiologically and also optically visible. Performance of the HSD assay demonstrated a lower susceptibility to hypoxia of mice lacking PSD-95 (not PSD-93), indicated by increased times to HSD-onset and reduced HSD-propagation velocities. Supporting this phenomenon, PSD-95 KO mice also showed a slower, less complete synaptic failure during hypoxia and earlier synaptic recovery after reoxygenation. Thus, the absence of PSD-95 in the mouse hippocampus was partly protective against hypoxia, possibly linked to the reported higher number of AMPA-silent synapses persisting into adulthood. This mimics the brain in a less mature stage and might lead to improved hypoxia tolerance.

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[6] Behavioral and Physiological Responses to Optogenetic Stimulation of the Cochlea

Alexander Dieter[1], Marcus Jeschke[1,2], Christian Wrobel[1,3,4], Vladan Rankovic[1,2], Daniel Keppeler[1], Christian Vogl[1,3,5], Gerhard Hoch[1], and Tobias Moser[1,2,3]

[1]Institute for Auditory Neuroscience and InnerEarLab, University Medical Center Göttingen, Göttingen, Germany; [2]Auditory Neuroscience and Optogenetics, German Primate Center, Göttingen, Germany; [3]Collaborative Research Center 889, University of Göttingen, Göttingen, Germany; [4]Department of Otolaryngology, Ruhr University Bochum, Bochum, Germany; [5]Presynaptogenesis and Intracellular Transport in Hair Cells Group, University Medical Center Göttingen, Göttingen, Germany

Investigating the Neural Similarity of False Memories and True Memories using Electrocorticography Data [7]

Chelsea Nnebe[1,2], Lukas Kunz[2], and Andreas Schulze-Bonhage[2]

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Recent research has found many similarities between the neural behavior of true and false memories. False memories are memories that commonly arise in neuroscience research when participants respond to new stimuli as though they have seen it before during encoding trials when in fact they have not. False memories can be induced by exposing subjects to similar stimuli, then exposing them to new stimuli that fits into the same category as the stimuli that was encoded. Data suggests that the underlying reason why false memories occur is that the brain analyzes similar stimuli in similar ways. Thus far, this research has mainly been conducted using fMRI. The objective of this study is to look at the same phenomenon using electrocorticography data, which provides greater temporal resolution, and the ability to perform time-frequency decomposition on data which have been collected from the hippocampi of subjects performing cognitive tests. In addition, the type of test given to the subjects used in this study allows us to investigate whether the neural similarity that causes false memories is also influenced by the Von Restorff effect, which states that when homogenous stimuli are presented in the midst of a novel stimulus, the novel stimulus is more likely to be remembered. Our hypothesis is that false memories will have the highest neural representational similarity to the encoded stimuli that is most similar to it based on their structural similarity index results, and that false memories will have a higher level of neural similarity to encoded items than correct rejections, but still less neural similarity to hits, or true memories. Moreover, we hypothesize that the von Restorff effect will decrease the level of neural similarity found for expected versus unexpected items.

[8] Synaptic Adaptor Protein-2 Clathrin coated vesicles differ in their half lives, contributing to the synaptic plasticity

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Deficiency in the sigma1B-adaptin of the tissue-specific Adaptor Protein -1/sigma1B AP-1 complex, leads to severe learning, memory, and motor coordination deficits in the knockout mice. Sigma1B-knockout synapses lacking the AP-1/sigma1B AP-1 complex, display two major phenotypes. Firstly, synaptic vesicles (SV) recycling is impaired and early endosomes accumulate. The ubiquitous AP-1/sigma1A complex binds to these endosomes and stimulates their maturation into late, multi-vesicular-body endosomes, upregulating endolysosomal protein transport. Secondly, the endocytic Adaptor Protein-2 (AP-2) clathrin-coated-vesicles (CCV) accumulate, a surprise given the reduction in the major vesicular transport route, SV recycling. This indicated that clathrin-mediated-endocytosis (CME) is a major mechanism of synaptic plasticity. AP-2 CCV accumulation could be caused by up-regulation of CME and by the stabilization of AP-2 CCV extending their half-life. We characterized these AP-2 CCV biochemically. The data demonstrate that two populations of AP-2 CCV exist in synapses. One formed by canonical CME and one formed by a specialized pathway. The latter one is characterized by a stabilized CCV coat. Both CME routes are upregulated two-fold in AP-1/sigma1B deficient synapses. In addition, the longer-lived AP-2 CCV are stabilized by three distinct molecular mechanisms compared to the respective AP-2 CCV from wt synapses. The stabilized AP-2 CCV are enriched in the active zone proteins stonin2 and Git1. The AP-1/sigma1B deficient synapses contain more Git1 than wt synapses, indicating Git1

redistribution from the active zone into the synapse. Git1 stimulates SV recycling by unknown molecular mechanisms. Thus, two CME routes characterised by specific lifetimes and specific cargo proteins contribute to the synaptic plasticity.

The time dependence of firing behavior and its relation to internal clock in disassociated hippocampal neurons [9]

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The circadian rhythm is an internal time-keeping mechanism. The consensus view is that every cell integrates a circadian clock input with internal information to generate its own cellular function, which is adapted to the molecular clock rhythm. It has been repeatedly shown that Suprachiasmatic Nucleus and some other cell types can maintain their time dependent behavior in a Petri dish. However, not much is known about hippocampal neurons. We would like to understand the time dependent firing behavior in disassociated hippocampal cultures in relation to their internal clock. As a starting point, we confirmed that time series relative mRNA amounts of Period 2 (Per2) and Brain and muscle Arnt-like protein 1 (BMAL 1) indicate that disassociated hippocampal rat neurons maintain an oscillatory molecular clock expression even at 21 days after culturing. Subsequently, we would like to learn how spiking behavior is connected to the molecular clock, and how the internal clock is preserved over time without any Zeitgeber, by integrating electrophysiological recordings and Per2 and BMAL1-dependent live imaging.

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[10] Characterization of cochlear optogenetics

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Activation of the auditory pathway by cochlear optogenetics has been shown to be feasible. Given the fact that light can be better confined than electric current, its application to cochlear prosthetics provides an alternative to currently employed electrical cochlear implants with a greater number of independent stimulation channels. In addition, cochlear optogenetics can be used as a research tool to answer fundamental questions in auditory research, bypassing cochlear micromechanics and its changes with stimulus level. The plethora of light-sensitive channels that are currently available offers different possibilities — not only regarding their biophysical properties, but also in terms of excitation wavelength which implies different light propagation profiles. We aim to build a computational model that combines the light distribution profile from our emitter through the cochlear tissues with electrophysiological responses of light-activated spiral ganglion neurons (SGN). To study the light propagation, we have conducted Monte Carlo ray tracing simulations using structurally realistic data from X-ray tomography, optical parameters obtained from literature and the emission profile of our emitters. In preparation for a biophysical constrained SGN model, we are using the whole-cell patch clamp technique to characterize the properties of various opsins with different spectral properties in postnatally AAV-transduced SGNs *in vitro*. Finally, this model will enable us to test and study different strategies *in silico* that will finally assist in the development of future optogenetic cochlear implants.

GABAergic mechanisms shape visual motion processing in *Drosophila* [11]

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Many animals use visual information and especially motion cues to navigate their environment. The underlying circuits need to compare luminance changes over space and time to compute direction selective (DS) signals. Two models have proposed how this can be achieved, the *Hassenstein-Reichardt-Correlator (HRC)* and the *Barlow-Lewick model (BL)*. The HRC relies on a non-linear amplification of motion in the preferred direction. In contrast, the BL model supresses signals that move in the non-preferred, or null direction. Recent studies showed that a combination of these two mechanisms is implemented in the *Drosophila* brain (Fisher et al., 2015, Leong et al., 2016, Haag et al., 2016). Using *in vivo* calcium imaging of the first DS cells of the fly visual system, T4 and T5, it was additionally shown that direction selectivity and orientation tuning require inhibitory GABAergic circuits (Fisher et al. 2015). However, loss of the GABAA receptor in DS neurons themselves does not affect DS responses, arguing that GABAergic signaling is required in upstream circuitry. Therefore, we aimed to identify upstream inhibitory cells that are required for DS responses. Reasoning that a loss of DS responses would also lead to a loss of motion guided behaviors, we used data from a behavioural forward genetic screen in which we identified InSITE Gal4 driver lines that lead to a deficit in behavioural responses to moving stimuli, when synaptic activity is blocked in the Gal4 pattern (Gohl et al., 2011; Silies et al., 2013). Using immunohistochemistry and an intersectional strategy, we identified four GABA-ergic cell types that repeatedly occurred in the Gal4 expression patterns, including the columnar feedback neurons C2 and C3. We are currently investigating the response characteristic of these cell types to visual stimuli and their role in shaping DS responses in the fly visual system.

[12] Cannabinoid 1 receptor-expressing interneurons in mouse medial prefrontal cortex

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Aberrant endocannabinoid signaling through cannabinoid 1 (CB1) receptors has been implicated in schizophrenia-related cognitive impairments. Indeed, such CB1 receptors are highly expressed on a subpopulation of inhibitory interneurons, which are believed to fine-tune network activity to promote cognitive functioning. However, their function is only poorly understood. We therefore assessed electrical firing properties and synaptic connectivity patterns of CB1+ interneurons in mouse medial prefrontal cortex (mPFC), an important structure for cognitive function, using parvalbumin-expressing (PV+) interneurons as reference, a major mPFC interneuron cell type with an established role in network refinement. To this aim, we performed patch-clamp electrophysiological recordings in acute mPFC slices using a double reporter mouse line, in which CB1+ and PV+ interneurons are tagged with tdTomato and YFP, respectively. We found that CB1+ interneurons were regular- or irregular-spiking and displayed similar connection probability onto local mPFC pyramidal (PN) neurons as fast-spiking PV+ interneurons. Notably, PV+ interneurons exerted rather stereotyped inhibitory control over local PNs, with connections being characterized by low failure rates and paired-pulse depression. By contrast, CB1→PN connections were highly diverse, ranging from strong to rather weak and unreliable connections, possibly pointing to a higher degree of synaptic plasticity. Interestingly, CB1+ interneurons showed substantially higher excitability and therefore might be more readily recruited during specific network operations than PV+ interneurons.

Together, these results suggest that CB1+ and PV+ interneurons provide two functionally distinct, parallel sources of inhibition to fine-tune mPFC neural activity.

Molecular mechanisms that shape neuronal responses in early visual processing [13]

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Neural circuits in sensory systems implement a diverse array of computations which highly depend on circuit interactions and cell-intrinsic properties. A versatile model to study neural computations is the fruit fly, where the circuits for motion vision have been extensively characterized. Visual processing in *Drosophila* is separated into two parallel ON and OFF pathways, similar to the vertebrate retina. Both pathways include circuit elements that exhibit different spatial and temporal tuning properties. Despite the extensive knowledge about the circuitry, the biophysical mechanisms that shape circuit elements are unknown. We investigated the mechanisms that confer distinct physiological properties to the two OFF pathway inputs, the first order interneurons L2 and L3. Receiving the same photoreceptor inputs, L2 responses are transient, whereas L3 shows sustained responses. Previous studies revealed that these neurons contribute non-redundantly to motion induced behaviors and process information for different speeds of motion. Using *in vivo* two photon calcium imaging we measured neural activity from L2 and L3 axon terminals while applying genetic and pharmacologic perturbations for different ion channels. A block of distinct potassium channels mediating Ka currents changed the kinetics of L2 responses but did not affect L3. We further show that the Ka mediating channel Shal is localized to L2 neurons. These data suggest that the computational role of Ka currents is to mediate responses to fast changes in the stimulus. The identified mechanism

can reveal a common molecular implementation within cells that are tuned to different aspects of a stimulus.

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[14] Linear and nonlinear natural image encoding in retinal ganglion cells

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In the vertebrate retina, each retinal ganglion cell encodes information about a specific region of the visual scene that corresponds to the spatial receptive field of the cell. When probed with artificial visual stimuli with fine spatial structures, many ganglion cells integrate light contrasts in their receptive fields nonlinearly. Thus, it has been suggested that linear receptive field models are inadequate to describe the retinal function during natural vision. However, there is little evidence of whether such linear encoding models hold under actual natural stimuli.

Using multielectrode array recordings of spiking activity from isolated mouse retinas, we show that a linear encoding model fails to capture the responses of many ganglion cells under flashed natural images. By presenting blurred versions of natural images, we show that the responses of such nonlinear cells are sensitive to the spatial structures of natural images. In addition to nonlinear cells, we find cells whose responses can be sufficiently described by a linear encoding model and are resistant to blurring. Finally, we identify some functional ganglion cell types with artificial stimuli and show that cells of the same type are equally sensitive to the spatial structures of natural images.

We conclude that the different output channels of the retina are specialized in conveying either linear or nonlinear spatial transformations of the natural visual signals.

Deciphering the role of acetylcholine in shaping the response properties of distinct retinal ganglion cell types in the mouse retina [15]

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Visual processing begins in the retina, where the information is split into 40 channels carried by different subtypes of retinal ganglion cells (RGCs), each of which encodes a different modality of the visual scene, such as edges, contrast or motion. So called direction-selective ganglion cells (DSGCs) respond with increased firing rate to objects moving in one (preferred) direction as opposed to the opposite (null) direction. Responses of DSGCs are mediated by starburst amacrine cells (SACs), which form synapses onto DSGCs. SACs co-release GABA and acetylcholine (ACh). While the inhibitory GABAergic synapses onto DSGCs are asymmetric — stronger in the null side— and mediate the directional response, the cholinergic synapses onto DSGCs are symmetric and their contribution to the computation of direction is debatable. Furthermore, although previous studies reported effects of ACh on several RGC subtypes, it is not yet understood how responses of distinct RGC subtypes are shaped by ACh.

Here, we developed a two-photon calcium imaging setup to study the responses of a population of RGCs to visual stimuli and to investigate how ACh differentially affects their response properties. We projected commonly used stimuli consisting of light increments and decrements, as well as moving bars and sinusoidal gratings, onto the isolated retina of transgenic mice expressing GCaMP6f in RGCs while recording their responses. We blocked nicotinic ACh receptors (nAChRs) to study how RGC responses are differentially affected by this perturbation. To verify cell identity, specific RGCs that were affected by blocking nAChRs were filled after the recording to analyse their morphology.

Our approach will allow studying the effect of a certain neurotransmitter or -modulator on the retinal code, both on the population and single cell level. As opposed to grouping all RGCs together, we can now study how specific subtypes of RGCs are differentially affected by perturbations in neurotransmitter signalling.

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[16] After aversive olfactory conditioning Drosophila larvae form a larval anesthesia-resistant memory (lARM) in the dependency of the internal physilogical state.

Annekathrin Widmann[1,2], Nazli Güllü[1], Melanie Eschment[1], and Andreas Thum[1]

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Establishing a memory is a highly complex and dynamic process. It consists of different memory phases, which dependent on molecular and structural changes within neurons. For example, changes in intracellular signalling cascades alter synaptic efficiency and provide the feature of transforming learned behaviours into memories. Recently, it was shown that *Drosophila* larvae are able to form different memory phases, which exist in parallel but with different stabilities. After aversive olfactory conditioning larvae establish a longer lasting larval anesthesia resistant memory (lARM), which is resistant to cold shock treatment, independent to the requirement of protein synthesis and initially co-exists with a larval short-term memory (lSTM), but becomes the predominant memory component after a short time interval. The formation of different memory phases requires the timely controlled activity of different cellular components. For example lARM relies heavily on the radish (rsh) gene and protein kinase C (PKC). In *Drosophila* adults two consolidated memory phases ARM and LTM compete with each other. A LTM gating mechanism prevents the adult *Drosophila* from forming an energetic costly LTM in favour to a less costly, but less stable ARM under critical nutritional circumstances. However, the biochemical underpinnings of this gating mechanism are

poorly understood. Due to the fact of the occurrence of only larval ARM after aversive olfactory conditioning may shed light upon molecular basis of switching between two different memory phases in dependency of the physiological state. By defining the physiological state of a larva by feeding sucrose prior to the training regime held some promising findings. The internal physiological state acts as a binary switch between the formation of lARM and another memory component. We were able to show that insulin singling within the Mushroom body Kenyon cells (MBKCs) could be involved in this binary switch between two different memory phases in *Drosophila* larvae.

Cell assembly creation and retention by interaction of synaptic and structural plasticity [17]

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Memory is stored in the synaptic connections between neurons. Accordingly, synaptic connectivity changes with time and experience. Mechanisms that are responsible for these changes can be separated in two categories: synaptic plasticity refers to changes of synaptic efficacies, whereas structural plasticity refers to the creation and elimination of synapses. Hereby, most existing synaptic memory models only consider synaptic plasticity and assume a fixed connectivity between neurons.

By enabling structural plasticity, a neural network may attain qualitatively new aspects to its dynamics due to the potential to adapt the connectivity by the turnover of synapses. While theoretical studies predict that structural plasticity enhances a network's memory-related

capabilities, the exact impact of a network's rewiring ability on its dynamics and memory storage is still largely an open question.

In our work, we therefore explore the interaction between synaptic and structural plasticity with respect to memory formation and retention. We use a network of firing-rate coded neurons with static inhibitory connections and plastic excitatory connections. Synaptic plasticity is modeled by a combination of the basic Hebb rule and a weight-dependent synaptic scaling term. We use a stochastic structural plasticity mechanism for excitatory connections, that preferably removes synapses with small weights. New synapses are created based on a constant creation probability. We show that our network stores information about an external input by forming a cell assembly, which is strongly interconnected both by strong weights and a large number of synapses.

We then analyze how the heterogeneity and stochastic turnover of the connectivity, which is induced by structural plasticity, influences assembly formation and transformation into long-term stable network structures. We show that structural plasticity adds new qualities to the network dynamics that allow for a deeper understanding of memory formation and retention.

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[18] The role of FoxQ2 in insect brain development

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The central complex (CX) is a higher order structure in the insect brain that is involved in sky compass orientation, flight control, locomotor behavior, courtship and memory. It consists of neuropils including protocerebral bridge (PB), central body (CB) with upper (CBU) and lower unit (CBL), also called fan-shaped body (FB) and ellipsoid body (EB). Both CX function and development are highly studied in *Drosophila*

melanogaster. However, in *Drosophila*, the CX develops during late larval stages which prohibits to study its embryonic development. As consequence, the genetic signals specifying the identity of the neuroblasts arising in the anterior region remain poorly studied. Therefore, we use *Tribolium castaneum* to study CX development. In *Tribolium* it is partially formed during embryogenesis and this model system offers a number of experimental possibilities. (Efficient systemic RNAi, transgenic approaches, tools for gene misexpression).

The aim of this project is to identify the neuroblasts and their lineages that contribute to central complex development and understand the genes that are required for their spatial specification. We have shown by RNAi that Tc-foxQ2 is required for CX development. We are developing tools for analyzing neural development in *Tribolium* (e.g. generation of an antibody against FoxQ2 and of an enhancer trap line with CRISPR/Cas9 strategy to mark foxQ2 expression *in vivo*) with which we will study the phenotype.

The impact of brands and food labels on prefrontal cortex activity - A fNIRS- study [19]

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Not only the taste of a product influences our decision for or against it, but also brands and food labels. In various functional Magnetic Resonance Imaging (fMRI) studies, strong brands caused greater neuronal activation in different areas of the prefrontal cortex compared to weak brands. Due to the limitations of fMRI for real-world situations, the aim of this study was to examine the feasibility of a mobile functional Near-Infrared Spectroscopy (fNIRS) system, a non-invasive optical brain imaging technique, for neuroeconomic research. This study sets up two experiments, both dealing with the impact of brands' respective labels in a food related context. Thirty-one subjects had to

decide which modification of different products (organic label, regional label, product not labelled) they would buy. Afterwards a taste test with two strong and two weak coke brands was performed. In both experiments, significant differences in prefrontal cortex activity were measured. The organic food label led to a higher activation than the regional label, and both of them led to an increase in activation compared to the same products without any labelling. The strong coke brands, Coca-Cola and Pepsi, led to an increase in activation while drinking and viewing the respective brand cue compared to the weak brands Topstar and Vita Cola. It is also interesting that although there were no differences between the coke beverages, the subjects made deviating pleasantness ratings. Summarizing the results, it is possible to measure prefrontal cortex activation using a mobile fNIRS system for brand and label related food decision experiments. This leads to the belief that fNIRS could become a promising new tool for neuromarketing research.

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[20] **The Sense of Touch in the Ageing Mouse**

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Mechanosensation remains to be the least understood sensory system in vertebrates. It requires the activation of specialised neurons which innervate the skin and internal organs. The somatosensory neurons facilitating the senses of touch and proprioception express Piezo2, which has been found to be the key player in these sensory functions. This mechanosensitive ion channel has only been discovered in the recent past and accomplishes mechanotransduction, the conversion of mechanical stimuli into electrical signals.

While mechanosensory decline with age is evident in humans, corresponding findings in the mouse have been inconsistent in the case of

light touch. Moreover, the role of molecular mechanotransduction in the age-dependency of mechanosensation is unexplored in mice and man.

We compared mechanically activated whole-cell currents of cultured sensory neurons of juvenile, adult and middle-aged mice (4, 12 and 34 weeks old, respectively). Interestingly, juvenile neurons show 55 % higher Piezo2-mediated mechano current amplitudes than adult neurons, suggesting that extensive maturational processes may be at play. Surprisingly, the amplitudes in middle-aged neurons were higher than in adult ones as well, matching those in juvenile neurons.

In future experiments we wish to investigate the implication of Piezo2-mediated mechanotransduction in age-dependent mechanosensitivity.

Poster Session II

Time-dependent changes of hippocampal representations underlying long-term spatial memory [21]

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Therapeutic Potential of Psychedelic Drugs and Stimulants: an Overview [22]

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Psychedelics induce an altered state of consciousness with changes in perception, state of euphoria, visual, auditory and tactile hallucinations, the experience of unity with the world and dissolution of self-boundaries. Stimulants produce no hallucinations, but are characterized by enhanced mental or physical function. These substances have been proposed as a novel treatment for a variety of psychiatric and neurological conditions, including depression, anxiety, post-traumatic stress disorder, obsessive-compulsive disorder, addiction,

cluster headaches, and chronic pain. A vast amount of scientific literature points towards the therapeutic potential of psychedelics. Despite that, they remain classified as United Nations Schedule I drugs. Drugs classified as Schedule I are considered to have a high potential for abuse and harm, and no medical value. Furthermore, compared to Schedules II-IV, Schedule I drugs have the most restrictive regulations, requiring special permits for the use in research that are time-consuming and expensive to obtain, presenting an obstacle for scientific investigation. This poster presentation draws from a comprehensive literature review that I conducted for my Master's thesis. With it, I aim to contribute to a better understanding of Schedule I psychedelics and stimulants, and point to their usefulness in treating several disorders, which could markedly increase the quality of life for patients and reduce patient burden. Furthermore, to present a balanced overview, I also present the health risks associated with the use of these substances as potential treatments.

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[23] PKC alpha regulates ER beta activity in a medulloblastoma cell line

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Lecithin therapy ameliorates disease progression in Charcot Marie Tooth disease type 1A [24]

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Duplication of the peripheral myelin protein 22 gene (PMP22) causes the most frequent subform Charcot–Marie–Tooth 1A (CMT1A). In contrast to previous reports stating that CMT1A manifests in the second decade of life, moderate walking disability and electrophysiological abnormalities are already present during childhood. The early onset and developmental nature of the disease is also supported by findings derived from a Pmp22 transgenic rat model for CMT1A (CMT rat), which displays a reduced number of myelinated fibers per peripheral nerve already postnatally and never reaches a wildtype level throughout development. In line, CMT rat Schwann cells show a strongly impaired lipid biogenesis required for myelination as assessed by RNA-seq and lipid profiling of peripheral nerve transcriptomes and myelin composition, respectively. Importantly, Pmp22 overexpressing Schwann cells also reflect an impaired myelination competence *in vitro*, when co-cultured with dorsal root ganglia neurons. A noticeable improvement of Schwann cell myelination upon supplementation with phosphatidylcholine *in vitro* has led to the hypothesis that exogenous

supplementation with lipids *in vivo* may improve disease progression. Indeed, we observed an improved disease progression on the histological, electrophysiological and behavioral levels in CMT rats which were fed with a chow enriched in lecithin from P2 to adulthood. Moreover, disease amelioration is also evident after late long term (P21-P112) and early short term treatment (P2 to P21), but the effect is fading after treatment cessation. Therefore, continuously supplying patients with exogenous lipids may be considered as a promising therapeutic approach for CMT1A disease.

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[25] The influence of frequency-distance and behavioral valence on discrimination learning and generalization of tone frequency

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Subjects need to identify stimuli they are exposed to in order to respond to them. To identify a stimulus presented in isolation is more difficult than recognizing it when it appears among other stimuli and it is believed to depend on long-term representations. Little is known, however, about how these representations are formed, how they interact with each other and how they are used to respond to novel stimuli (generalization).

Here, we trained mice to discriminate isolated tones in an automatic behavioral apparatus, the Audiobox, in which one frequency was negatively reinforced while another was positively reinforced. We evaluated how changes in the frequency-distance between these two stimuli influenced discrimination learning and generalization.

Mice learnt to avoid the negative stimulus readily. We found that the degree by which mice approached the positive stimulus was determined largely by the frequency-distance between this stimulus and the negative one. When the distance was half an octave or smaller, even though the positive stimulus was easily discriminable, mice tended to avoid it more and to generalize less around it. Generalization around the negative stimulus also became narrower, although to a lesser extent, as its distance to the positive stimulus shortened.

Overall, responses to familiar (discrimination) and novel (generalization) stimuli depended fundamentally on how different the discriminative feature (frequency) was from the negative stimulus and less on the behavioral experience the animal had with these tones.

Locomotor activity in *Drosophila melanogaster* with altered function of gene swiss cheese [26]

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Gene swiss cheese (sws) in *Drosophila melanogaster* is orthologue of human gene Neuropathy target esterase (NTE also known as PLPLA6), disorders in which lead to development of hereditary motor neuron disease — Spastic Paraplegia, first symptoms of which characterized by locomotor disorders. Mutations in sws gene lead to neuron degeneration and glia hyperwrapping. Sws functioning are critical for nervous system aging, especially for glia maintenance. The aim of our study was to describe climbing activity of old *Drosophila* males with altered sws function.

We used mutant line sws1 (kindly provided by Dr. D. Kretzschmar), Oregon-R, Repo-Gal4, MHC-Gal4 (Bloomington Drosophila Stock Center) and UAS-sws-RNAi (VDRC). Climbing test was used as a behavioral assay in 21-days old tested flies. Climbing test is based on negative geotaxis. At least 100 males of each genotype were tested. The

significance of intergroup differences was checked using the two-factor T-test with different dispersions (Microsoft Office Excel 03 software).

We discovered that sws1 line showed reduction of motor activity by 22,7% ($p \leq 0{,}004$**) in comparison with control. Flies with knockdown of sws in glia UAS-sws-RNAi/Repo-Gal4 had lower level of motor activity in comparison with control and that difference is 15,6% ($p \leq 0.017$*). Flies with knockdown of sws in muscles UAS-sws-RNAi/MHC-Gal4 had by 65,1% ($p \leq 0{,}00004$***) lower motor activity in comparison with control.

Our data suggest that sws involved in motor behavior control in *Drosophila* adults. As the lowest motor activity we saw in flies with reduction of SWS in muscles, we plan to study the morphology of these muscles.

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[27] Learning in and from Invertebrates - Influence of Temperature on Synaptic Plasticity in Octopus vulgaris

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Octopods belong to the most intelligent invertebrates, being capable of higher cognitive functions including the use of tools, self-awareness and observational learning. Essential for these abilities is the vertical lobe in their central brain – a structure resembling the mammalian hippocampus and which is important for learning, as lesion studies and electrophysiological experiments indicate. Even though octopods are cold-blooded marine organisms and prefer a certain ambient water temperature, the influence of temperature on synaptic plasticity and therefore the octopus' ability to learn has not been investigated yet.

We measured field potentials at the synaptic junctions between the superior frontal lobe (SFL) neurons and the amacrine cells in the vertical lobe of *Octopus vulgaris*. Ensuring to cover the seasonal variation

in ambient water temperature of the octopus' natural habitat, we recorded under different but constant temperature conditions, varying between 9° and 24° Celsius. We used linear mixed effects models to account for the nested data structure.

The applied triple pulse stimulation protocol induced short-term facilitation of the postsynaptic field potentials (fPSP) in all conditions. Moreover, increasing the temperature decreased the duration of the tract potential and the fPSP ($Q_{10} = 1.8$) but did not change the integrated amount of fPSP. These results indicate that temperature influences channel kinetics, ion flow and transmitter release machinery equally, resulting in the same total postsynaptic potential. This simple characteristic might allow the octopus to adapt to different temperatures without losing its performance to establish synaptic plasticity and hence learning.

Myelin is an important factor in the establishment of handedness [28]

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The neuronal development of a growing mammal is punctuated by brief time-specific windows, called critical periods, during which already wired circuits are said to undergo fine-tuning. One hypothesis is that myelin helps consolidate these circuits by preventing axonal sprouting thereby facilitating the closure of these critical periods. The aim of this project is to study the consequences of myelination on critical period plasticity. The corpus callosum, a heavily myelinated CNS white matter track, plays an essential role in the development of

handedness. Previous work in the lab has shown in mice that while the absence of myelin (shiverer mouse) hinders the natural development of handedness, demyelination in the adult brain after the peak of myelination doesn't affect this behavior. Myelin is, thus, important for the establishment but not the maintenance of handedness. The behavioral study of handedness and the underlying corpus callosum circuitry are, therefore, a useful model to study the role of myelin on critical period plasticity. Here, we show data on the development of handedness in the first 8 weeks of the life of wild-type mice and shiverer mice. The data suggest that repetitive training in the paw preference task during the weeks 4 to 8 of life may be sufficient to allow for lateralization to develop at the same rate in the shiverer mice as the wild-type controls. We conclude that while myelin is important for the spontaneous establishment of handedness during normal development, its absence does not hinder learnt lateralization.

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[29] Mover: a presynaptic protein buffering short-term synaptic plasticity at the Hippocampal Mossy Fiber Synapse

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The increase in the complexity of brains in evolution is accompanied by a surprisingly small number of new synaptic proteins. However, a few vertebrate-specific synaptic proteins arose. One of these vertebrate-specific proteins, Mover, is strongly upregulated in schizophrenia.

Mover is a synaptic vesicle-attached phosphoprotein, regulated by activity, and binds the conserved Calmodulin and the vertebrate-specific protein Bassoon. Mover is differentially expressed at subsets of synapses. Knockdown of Mover in the calyx of Held leads to an increased calcium sensitivity of release.

In this study, we used a Mover knockout mouse line to investigate the role of Mover in the hippocampus. While Schaffer collateral synapses

were unchanged by the knockout, the mossy fibers showed strongly increased facilitation. The effect of Mover knockout in facilitation was both calcium- and age-dependent, having a stronger effect at higher calcium concentrations and in younger animals. Increasing cAMP levels by forskolin potentiated equally both wildtype and knockout mossy fiber synapses. However, forskolin-potentiation and Kainate receptor blockade independently occluded most of the increased facilitation observed in the knockout.

These discoveries suggest that a) Mover has distinct roles at different synapses; b) generally acts to dampen the extent of presynaptic events; c) acts as a brake that can be released during low activity. I suggest a model in which Mover inhibits the Kainate receptor/cAMP pathway, which explains the observed results and supports the proposed role of Mover dynamically buffering synaptic strength.

Anesthesia optimization for rat fMRI [30]

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Functional Magnetic Resonance Imaging (fMRI) in rats usually necessitates the use of anesthesia, with the anesthetic of choice being medetomidine, a drug known to produce long-lasting sedation while preserving neurovascular coupling. Most researchers apply medetomidine subcutaneously (SC), starting with a bolus loading dose followed by continuous infusion. However, the exact timing, dose, and route of administration vary across studies, impairing their comparability. We aimed to identify the impact of different dosing practices on the strength and temporal stability of fMRI responses.

Three groups of female adult Wistar rats (6 animals each) were anesthetized for up to six hours in order to compare the standard SC protocol with two intravenous (IV) variants of it: one with no change

in the dosing scheme, and another lacking the bolus loading dose. We continuously monitored physiological parameters and performed fMRI at 20 minute intervals using an electrical forepaw stimulation paradigm. The stimulus-related percent signal change at the contralateral primary somatosensory cortex (S1) served as a measure of response strength.

The fMRI responses under the standard SC protocol were strong, yet highly varied in the first 1.5 hours, reaching a steady state of weaker, but consistent responses thereafter. The overall trend was the same with the two IV protocols, but the time to reach steady state differed: the presence of a bolus dose resulted in earlier stabilization within the first hour, while its absence delayed the steady state for 2.5 hours.

Our data show that the temporal evolution of stimulus-evoked fMRI responses in medetomidine-anesthetized rats can be significantly affected by the anesthetic's dosing scheme. The overall time-course of responses can be explained by an inverse relationship with the drugś blood concentration. This motivates us to improve on current protocols by testing lower doses in future work.

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[31] Luminance and contrast sensitive neurons shape behavioral response to visual motion.

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Motion vision is crucial for an animal's survival. Sensory circuits computing visual motion are a research focus since a few decades and a considerable progress has been made understanding these circuits in insects. In the fruit flies *Drosophila melanogaster*, visual neurons responsible for motion computation constitute two pathways comparable with those in the vertebrate systems: one detecting motion from contrast increments ('ON' pathway) and the other from contrast decrements ('OFF' pathway). Downstream of photoreceptors, L1 is the

major input to the ON pathway, while L2 and L3 are inputs to the OFF pathway. How these parallel OFF-pathway inputs differentially shape motion-guided behaviors is not fully understood.

Response characteristics of L2 and L3 neurons suggested that the two neuron classes encode different stimulus features — contrast and luminance — respectively. To determine significance of these neuronal properties in behavior, we silenced output of individual lamina neurons and tested the flies' optomotor response to rotational motion stimuli. Silencing was achieved by expressing temperature-sensitive, dominant negative dynamin allele (shibire^{ts}) in a cell-type specific manner using the Gal4-UAS system. While L2 silencing led to deficits in OFF-motion responses under all luminance conditions, L3 neurons were necessary specifically in low luminance. These observations corroborated the differential encoding properties of L2 and L3 and confirmed that they translate to behavior. Furthermore, flies lacking functional L3 neurons were able to respond to rotating gratings with much lower contrasts than wildtype flies did, suggesting a role of luminance sensitivity in biologically relevant contrast computation. Intriguingly, silencing the ON-pathway input, L1, also resulted in altered OFF-motion responses, providing evidence for crosstalk between ON and OFF pathways. Collectively, these findings indicate that the early visual neurons are not simple relay stations, but help extracting specific aspects of the visual input statistics that prime the downstream motion calculations.

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[32] Age-related intracranial volume — A longitudinal study

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Brain aging is a natural process that is manifested, mostly, as atrophy of both white and gray matter, as well as in other pathophysiological processes that operate from the cellular to the system level. These brain changes have been associated with cognitive changes. Excessive atrophy, beyond normal aging, has been found in brain diseases such as dementia, with their global impact on public health. Most neuroimaging studies that aim at identifying brain aging processes use total intracranial volume (IC) as a confounder. However, IC is an important biological marker in itself that can represent the integrity of the brain as a whole. It is not known whether and if so to which extent, IC changes with brain aging.

We measured IC in magnetic resonance imaging (MRI) brain scans using a unique longitudinal design. Each subject was scanned at three different time points with an average time interval of 3 years between scans (at time-1, time-2, time-3 the number of individuals was 563, 363 and 323; their mean ages were 27.13$\pm$7.23, 30.07$\pm$7.15 and 33.67$\pm$7.57 years). By applying an automatic in-house-made algorithm for IC volume, we measure individual trajectories of IC volume changes between 16 and 62 years. This procedure allows us to detect within-individual changes in IC with increasing age if present. Using this approach, we hope to detect subtle but consistent senescence process of the IC already during adulthood.

Behavioral and neural mechanisms of perceptual and interoceptive metacognition [33]

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During metacognition, humans evaluate decisions by assessing the reliability of information associated with different cognitive processes, e.g. how confident they are about having done a correct decision?. However, certainty might also increase owning to error detection. Indeed, our recent study demonstrated that humans can wager adaptively after their decisions (post-decision wagering) by reading out both certainty directions: certainty of being correct and certainty of being incorrect (Moreira et al., 2018). Bold & Yeung (2015) proposed that shared neural mechanisms underlie readouts of both certainty directions. To further investigate these two metacognitive processes, we used fMRI to identify brain areas that might encode both certainty directions.

Twenty participants performed a visual delayed match-to-sample task followed by a post-decision wagering during scanning. BOLD activity was analyzed using event-related GLMs in combination with parametric regressors which were derived from perceptual and metacognitive outcomes.

Several brain areas in the frontal, parietal and cingulate cortices encoded certainty readouts in a bi-directional way (i.e. both certainty of being correct and certainty of being incorrect) during the wagering event. Most of the areas previously related to certainty of being correct were activated in the bi-directional contrast, suggesting that our task requirements prompted those areas to encode the information suitable for behaving in the most adaptive way (i.e. gain more when correct and avoid losses when incorrect).

While most work on metacognition focused on monitoring of cognitive processes related to sensorimotor interactions with the external

world, humans also evaluate their internal, interoceptive sensations (e.g. heart rate, breathing) that might influence decision making (Dunn et al., 2010). Our recent experiments investigate the relationship between perceptual metacognition and interoceptive abilities, in particular the question if a high interoceptive accuracy correlates with better perceptual performance monitoring.

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[34] Analysis of visual evoked potentials in the diagnosis of demyelinating diseases and other diseases with similar symptoms

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Introduction: Visual evoked potentials (VEP) are very sensitive neurophysiological method for diagnosis of demyelinating diseases. The most important part is analysis of P100 latency, which increased value, especially in the clinically silent lesions, makes the diagnosis easier. It is crucial for early stage disease detection, especially in multiple sclerosis.

Aim: The aim of this study is analysing VEP P100 latency for diagnosis of demyelinating diseases and for prediction in slight clinical state of diseases.

Material and Methods: The study included 60 patients (17 men and 43 women), divided in 3 groups, 20 in each: 1) with multiple sclerosis (44.0 ± 11.71 years) 2) retrobulbar neuritis (40.85 ± 17.32 years) 3) clinically isolated syndrome (CIS) and diseases with similar symptoms (paresthesia, dizziness or walking difficulty) (37.75 ± 8.46 years). VEP latencies were measured with pattern method and the obtained data were statistically analyzed (SPSS statistical program).

Results: These diseases are more frequent in women, between 38 and 44 years. The highest P100 values were at the second group and the

lowest in the third group. VEP latency is prolonged in majority of the patients, but significant difference between them is not found.

Conclusions: VEP is a sensitive method in the diagnosis of demyelinating diseases, but also other diseases which does not give visual disorders. VEP latencies values probably correlate with the severity and type of the disease.

A microfluidic approach facilitates a more dynamic study of the ionic mechanism of neurotransmitter tranporters [35]

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Synaptic vesicles are the storage units of neurotransmitters, which are necessary for communication between neurons. Disrupted neurotransmission is a suggested cause of several diseases. The transmission is heavily influenced by the number of neurotransmitters transported into the synaptic vesicles by transporters. However the precise ionic mechanisms of the neurotransmitter transporters, such as VGAT, VGLUT and VNUT remain largely unknown. Furthermore the methods currently available do now allow us to study the update via transporters in more details. Here we show a new microfluidic approach to study neurotransmitter uptake into synaptic vesicles, facilitating quick solution changes for more reliable results in the dynamics of the neurotransmitter transporters.

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[36] Time lapse of individualized repetitive transcranial magnetic stimulation effects on resting state functional connectivity of healthy brains

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Numerous studies have suggested that a single session of repetitive transcranial magnetic stimulation (rTMS) is effective at manipulating the brain's functional connectivity. While it is possible to manipulate functional connectivity by stimulating at several accessible cortical targets, the DLPFC as an rTMS target is of particular importance due to its therapeutic use in the alleviation of depressive symptoms. To detect differences in rTMS induced effects related to time lapsed after stimulation targeted at the left DLPFC in healthy brains, we recruited healthy volunteers for three experimental sessions. In the initial session, the resting state (rs)-fMRI scan is utilized to select the strongest node within the overlap of two components, one spanning the DLPFC (positive correlation), and the other the anterior cingulate cortex (negative correlation), which then becomes the target for individualized rTMS intervention. The next two sessions, at least a week apart, involve either real or sham rTMS intervention delivered using real time neuronavigation. A pre-rTMS rs-fMRI session and three subsequent post-rTMS sessions are acquired upon completion of rTMS. The data is analyzed for differences in functional connectivity during resting state, both within the three rs-fMRI scans acquired post-rTMS and between the pre-rTMS and post-rTMS resting state scans, to answer how long the rTMS effects are sustained and which resting state networks are involved over time, also complimenting the work by Tik et al. 2017. Additionally, we also aim to utilize the rs-fMRI scan from the first session and the two pre-rTMS rs-fMRI scans from next two sessions to test the stationarity of target selection across sessions.

Importance of Calcium-Permeable AMPA receptors for drug-induced reinstatement [37]

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The persistence of drug-associated memories constitutes a hallmark of drug addiction, which renders individuals vulnerable to relapse even after years of abstinence. Cocaine injections have been shown to generate silent synapses, an early brain development marker, in key regions of the adult reward circuitry. During long-term withdrawal from cocaine, calcium-permeable AMPA receptors (CP-AMPARs) are incorporated into maturing silent synapses in drug-related networks. CP-AMPARs lack the GluR2 subunit and are implicated in several types of plasticity. They are also considered necessary for certain drug-related behaviours, such as incubation of craving, to manifest. It has recently been shown that CP-AMPARs are required for morphine-induced reinstatement. We asked whether CP-AMPARs are a general requirement for reinstatement by other drugs of abuse. We used the conditioned place preference (CPP) paradigm to approach this question. Pharmacological removal of CP-AMPARs did not block cocaine-induced reinstatement. Moreover, CPP reinstatement was not altered in SAP 102 knock-out mice, which do not express CP-AMPARs. Overall, our results indicate that CP-AMPARs are not absolutely required for reinstatement, that mechanisms of reinstatement may differ between different drugs of abuse, or that CP-AMPARs may regulate the sensitivity for reinstatement.

[38] Molecular mechanism that shape ON-pathway responses in the Drosophila visual system

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Motion detection has served as a model to understand how specific neural computations are implemented in the brain. In the *Drosophila* visual system, the core circuits that extract motion cues have been mapped. With this knowledge at hand, we can now tackle the question which molecular and biophysical properties shape essential physiological circuit characteristics. In the fly visual system, information about moving ON (brightness increments) and moving OFF (brightness decrements) stimuli is processed in two distinct ON and OFF pathways. These pathways split downstream of photoreceptors, where the lamina neurons L1 is the major input to the ON pathway, whereas L2 and L3 give input to the OFF pathway. As all of these cellular components depolarize to OFF and hyperpolarize to ON flashes, a sign inversion is necessary for downstream components to preferentially respond to ON. Accordingly, inhibitory synapses are expected to mediate this step. Since the ON pathway input neuron L1 is the only glutamatergic first order interneuron, glutamate gated chloride channels (GluCls) are the main candidates. Using *in vivo* 2-photon calcium imaging, we recorded the visual response properties of ON-pathway neurons postsynaptic to L1, or of downstream direction-selective cells. A pharmacological block of GluCls abolished all ON responses in these neurons. We are currently using genetic approaches to both show the specificity of the pharmacological approach, and to disentangle cell-autonomous and non-autonomous functions of GluCls. Our work will not only elucidate the biophysical mechanisms of a core visual computation, but also serve as a tool to study ON and OFF pathway interactions in a cell type specific manner.

GluK2-NETO2 signalling regulates dendritic spine morphology in developing hippocampus [39]

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Kainate receptors (KARs) are a subtype of ionotropic glutamate receptors, composed of five different subunits (GluK1-5) in tetrameric assemblies. They are highly expressed during early brain development to modulate synaptic transmission, network excitability and synaptogenesis. In particular, recent evidence highlights a robust increase in axonal filopodia by overexpression GluK1-GluK5 while shRNA-mediated knockdown of GluK2/5 reduces the density of filopodia, suggesting a role for KARs in structural plasticity of synaptic contacts. NETO2 is an auxiliary subunit of KARs which modulates their functional properties. In this study, we showed that absence of NETO2 significantly reduced the proportion of dendritic spines in cultured hippocampal neurons, and it was rescued by the overexpression of GluK2. We also studied the effect of NETO2 on the actin dynamics using live-cell imaging. Indeed, the absence of NETO2 had a significant effect on actin dynamics by increasing the stability of F-actin filaments in dendritic spines of hippocampal cultures. In conclusion, our results demonstrate that GluK2-NETO2 signalling developmentally regulates dendritic spine formation and its stability.

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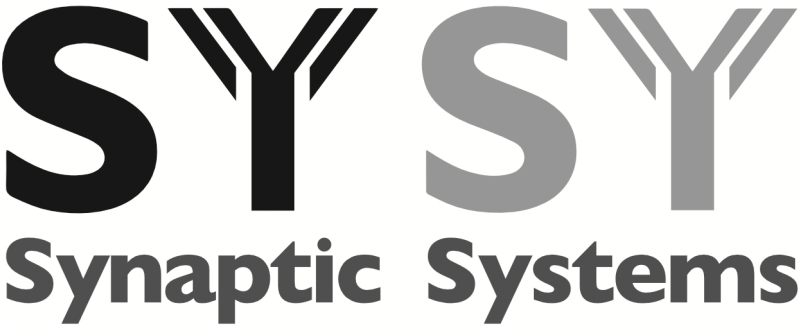
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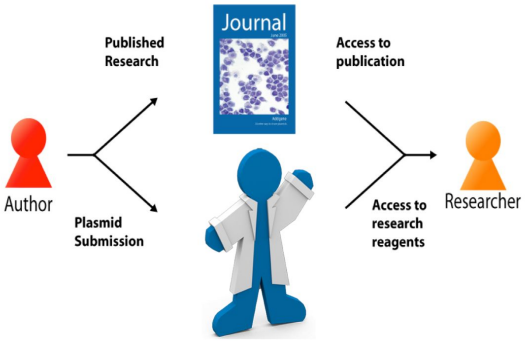

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