European Neuroscience Institute Göttingen

A Joint Initiative of the University Medical Center Göttingen and the Max Planck Society

UNIVERSITÄTSMEDIZIN GÖTTINGEN : UMG

MAX-PLANCK-GESELLSCHAFT

Imprint

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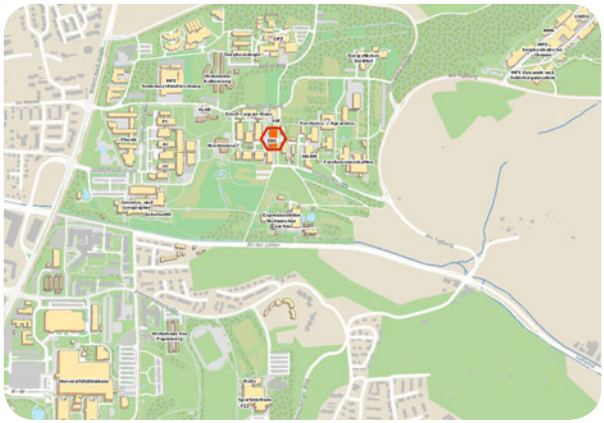
Content

The ENI-G

The European Neuroscience Institute Göttingen (ENI) is situated in the lively NordCampus of the University of Göttingen. Founded and run as a partnership between the University Medical Center Göttingen (UMG) and the Max-Planck-Society (MPG), ENI is embedded into the administrative infrastructure of UMG. Promising young investigators in the field of neuroscience have the opportunity to build a research team and independently perform ambitious scientific research in an attractive multifaceted environment.



With its modular and adaptable working conditions and basic support by a small team of permanent staff, ENI facilitates the work of young researchers in the period of their life considered to be the most important for a productive future career. A position as group leader at the ENI is given in a competitive selection process to excellent postdocs between the third and sixth year after receiving their PhD. The ENI position can be secured with a top-ranking grant proposal written to win a major grant from third party funding agencies. As the record shows, these very best young investigators at the forefront in their fields generate comprehensive and far-reaching new insights/knowledge in the neurosciences, and they attain associate/full professorship level by the end of their appointment at the ENI.

Ample professional support and networking opportunities are provided through the rich neuroscientific environment of Göttingen comprising the UMG, the Max-Planck-Institute (MPI) for Biophysical Chemistry, the MPI for Experimental Medicine, the MPI for Dynamics and Self-Organisation, the German Primate Center (DPZ), the Center for Biostructural Imaging of Neurodege-

neration (BIN), the Schwann-Schleiden-Zentrum, the Göttingen Center for Molecular Biosciences (GZMB), the German Center for Neurodegenerative Diseases (DZNE), the Heart and Brain Center, the Cluster of Excellence (Multiscale Bioimaging: from Molecular Machines to Networks of Excitable Cells), Collaborative Research Centers (e.g. SFB 889 Cellular Mechanisms of Sensory Processing, SFB 1190 Compartmental Gates and Contact Sites in Cells or SFB 1286 Quantitative Synaptology), as well as associated spin-off companies.

This concentration of scientific expertise is within walking distance. Recruitment of Master and PhD students as well as optional training in teaching is facilitated by the International Max Planck Research School (IMPRS) „Neuroscience" at the ENI, and „Molecular Biology" at the GZMB as well as university-affiliated MSc programs. Unsurprisingly, the independent ENI group leaders prove to be very successful in this stimulating environment.

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A representative of the group leaders

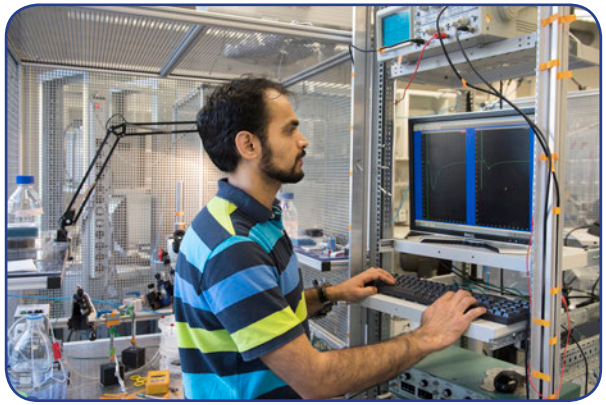
Research in Fundamental Neuroscience

The ENI young investigator groups focus on many research areas within the neurosciences, covering systems and computational neuroscience, and molecular and cellular questions regarding central and/or peripheral nervous systems with the aim of increasing our understanding of the mechanisms associated with healthy and diseased states. The research topics range from synaptic vesicle dynamics, trans-synaptic signaling, visual and auditory processing, neural computation and behavior, to neural circuits, perception and cognition.

Groups work with fruit flies, nematodes, rodents, human and non-human primates using psychophysical, electrophysiological and molecular approaches. The acquired knowledge will not only increase the understanding of brain function but is also anticipated to underpin the development of future treatments for neurological and neurodegenerative diseases.

The ENI building provides plenty of room for six to nine independent groups on three floors, each with two laboratory wings and interconnecting offices and social rooms. Each group leader is assigned up to 150 square meters of individually furnished laboratory space, three offices and additional shared rooms for undergraduates. In addition to common lab space for centrifuges, freezers, incubators, autoclaves, washers and dryers, there are various specialized rooms equipped with high-end microscopes, electrophysiology set-ups in various configurations, and molecular biology, histology and biochemistry equipment including cryostats, ultramicrotomes, RT-PCR machines, HPLC/FPLC, and bioanalysers for common use. Additionally, fully equipped cell culture rooms, an S2 level lab

for the professional handling of viruses and a yeast lab exist. A specialized low noise area for psycho-physics experiments furnished with cabins is also available. Two additional floors with seminar rooms, two lecture theatres, a precision mechanical workshop, administration offices and teaching labs as well as a self-contained animal facility exist within the building. The infrastructure of the building is designed for high flexibility which allows to make adaptations in the laboratories required by specific technical demands.

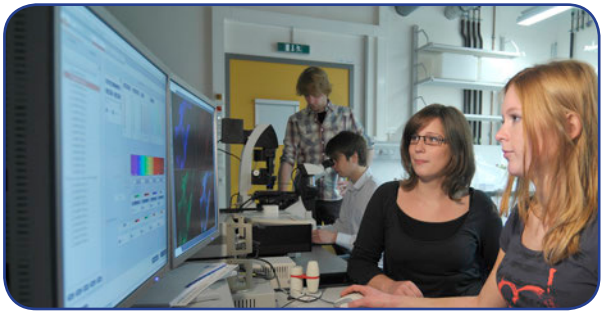


Electrophysiology and Optogenetics

A wide variety of electrophysiology set-ups are used in the institute by a number of groups to record ionic currents in slices, whole cells or isolated patches. These include upright and inverted microscopes equipped with either field stimulation capabilities, or single or double whole cell patch clamp systems for intracellular recordings of ionic currents. These systems are used to stimulate and measure the activity of single interconnected neurons or populations of neurons and enable functional studies of the developing and mature nervous system in normal conditions, in response to perturbations in activity, following manipulation of protein expression levels, or in the aging or diseased brain. Voltage-sensitive fluorescent dye imaging approaches are used to optically monitor neuronal activity patterns in brain circuits. Fluorescence imaging using confocal or two-photon microscopy is also utilized to monitor intracellular ion and membrane potential changes, as well as vesicular fusion. Optogenetics approaches are being used to photo-stimulate neuronal activity in various preparations. The ENI currently houses more than ten electrophysiology set-ups that enable investigations on a wide range of cellular applications, which can be used on a short term or test basis.

Microscopy and Electron Microscopy

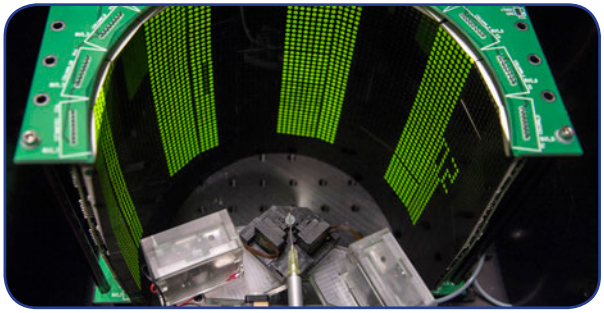
A unique feature of the ENI is the availability of advanced optical instrumentation with high-end specialized microscopes, which include two confocal laser scanning microscopes and several types of preparative and analytical microscopes. In addition, two spinning disc microscopes, a TIRF microscope and three individualized two-



photon set-ups exsist. Other super-resolution microscopes such as STED and light-sheet microscopes can be booked easily.
Additionally, several vibratomes, cryostats and microtomes as well as a paraffin embedding station are available. Sections embedded for electron microscopy can be further processed in the Göttingen campus which offers ready access to EM, freeze-fracture-EM and cryo-EM facilities.

Animal and Behavior Facility

The ENI houses a large animal facility. In a clean environment, mice are bred under controlled conditions. The animal facility is also equipped with special units for behavioral studies. Isolated rooms with separate computer desks and cameras allow undisturbed observation of animals under various experimental conditions and si-

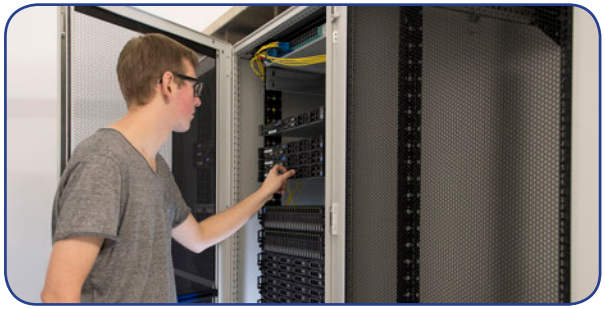


multaneous recording of studies with computer-based video tracking. In addition, ENI houses a Drosophila fly facility and supports research on nematodes, zebrafish, Xenopus and other model systems. ENI's research groups also focus on systems neuroscience, neural computation, cognition and behavior in model organisms as well as in human and non-human primates. To support this research, extra rooms are alloca-

ted and in addition to cabins for psychophysics tests, specialized new equipment is developed with the help of ENI's precision mechanics.

Information Technology

The ENI IT service uses the local IT service, GWDG (www.gwdg.de), which serves as a data center and provides core IT services for the University and the Max-Planck-Institutes in Göttingen. Necessary ENI infrastructure is maintained to provide the expertise, maintenance and development of a modern scientific network. Two IT specialists support the ENI group leaders. Due to the requirements for fast and stable storage connections by an increasing number of imaging and psychophysics set-ups, well-equipped independent storage was established at ENI while assuring synchronization and data integrity with GWDG.



Precision Mechanics Workshop

The technical development and adaptation of equipment is a prerequisite of unhindered scientific progress. To address this need, ENI runs its own machine shop staffed with two precision mechanics to design and develop innovative scientific instruments serving the needs of the rapidly developing scientific fields. These instruments range from Drosophila behavioral and imaging equipment, temperature controlled chambers for electrophysiology and microscopes, brain tissue slicers, and xy-stages and micromanipulators, to behavior analysis and training equipment.

Team support

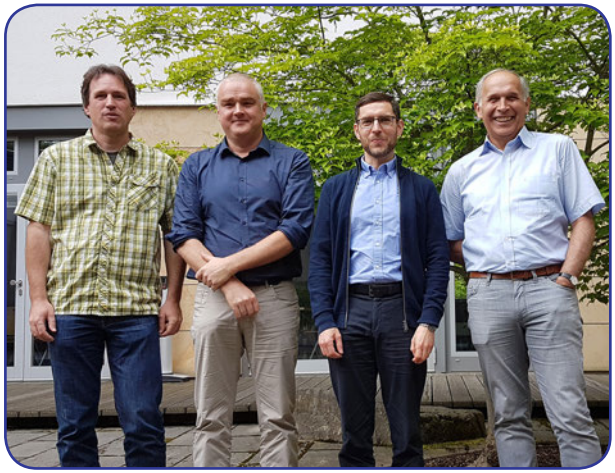
To afford the group leaders the greatest possible scientific freedom, the ENI is not overseen by a senior director. Each research team organises its daily laboratory and administrative tasks supported by well-trained permanent staff. Group leaders are backed by their scientific mentors and the ENI Board of Directors provides further support. The daily support encompasses advice regarding the balance between scientific needs and formal necessities of administrative accounting, as the young investigators take responsibility for the administration of their groups. To facilitate this, the group leaders receive an introduction to budget responsibility and third party funding reporting regulations. With regard to equipment maintenance, common and basic equipment is overseen and serviced with the help of technical staff, although self-reliance (autonomy) of the ENI groups plays a major role.

Researchers selected by the ENI receive specific help in their preparation of a solid grant proposal. Group leaders then are assisted with grant administration and guided in matters of international funding, particularly in regard to regulations associated with Horizon 2020, the current Research Framework Programme of the European Union.

Additionally, they are regularly informed of current funding opportunities in the field of neurosciences. The third party funds for a five-year period have mostly been obtained from the Emmy-Noether-Program financed by the German Research Foundation (DFG), various European Union programs, especially the European Research Council (ERC) grants and the Sofja-Kovalevskaja award from the Alexander-von-Humboldt-Foundation. Additi-

onal funds have been awarded from the former Excellence Cluster, Center for Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), and from the Collaborative Research Centers of the DFG. This is topped up by contributions from the Federal Ministry of Education and Research (BMBF), the Volkswagen Foundation, the Leibniz Campus „Primate Cognition“ and private foundations.

ENI Advisory Board



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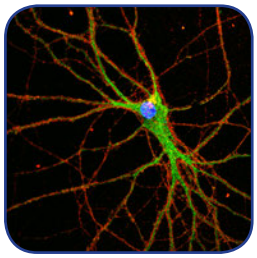
Synaptic Physiology in Health and Disease



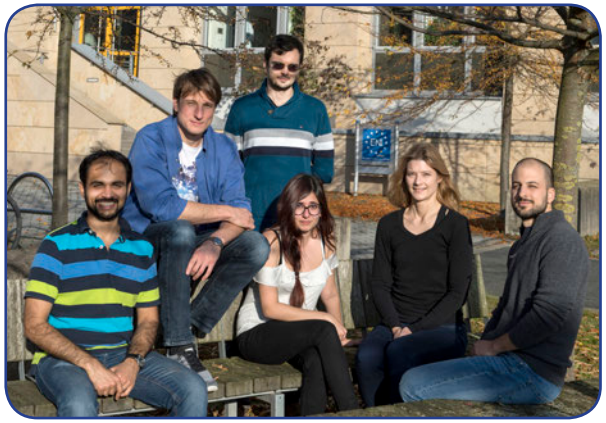
Transsynaptic Signaling

Neuronal circuits involved in memory encoding are located within high-level brain regions that integrate and process information from multiple sensory areas. These circuits must be reliable, but also highly dynamic to add or delete information. However, surprisingly little is known about the molecular switches that determine if something is remembered or forgotten. The hippocampus is a key area of focus; it is a high-level brain region consisting of a unidirectional trisynaptic circuit, where information from multiple sensory cortices is integrated. The hippocampus is crucial for memory, which is an ideal higher brain function to study because memory performance can be quantified. Clinically, the hippocampus is the brain area first and most severely affected by dementia and Alzheimer's disease. As synapse degeneration is an early (and reversible) hallmark of neurodegenerative diseases, new neurodegenerative disease therapies could also target the hippocampus.

The „Transsysnaptic Signaling" group of Camin Dean analyzes synaptic, cellular and circuit-based mechanisms of memory. Imaging, electrophysiology, biochemistry and behavior methodologies are combined to identify the molecules and distinct cell types (specified by their molecular composition) that promote memory, recall, or forgetting, using rats and mice as a model system. At the level of synapses, dissociated hippocampal cultures are used to study pre- and post-synaptic function optically by quantifying live antibody-labeling of recycling synaptic vesicles or post-synaptic receptors. Using time-lapse imaging of hippocampal neurons, the trafficking and recruitment of fluorescently-tagged molecules to synapses in response to changes in neuronal activity is examined. In this way, the rapid recruitment of dense core vesicles to synapses, which release neuropeptides to modulate synaptic strength, can be monitored

in response to increased neuronal activity, for example.

The imaging work is complemented by electrophysiological recordings to assess synaptic transmission. To examine intact circuits, acute hippocampal slices are used to measure long-term potentiation (LTP) or long-term depression (LTD) electrophysiologically by field recordings, which correlate with learning/remembering or forgetting, respectively. Genetically-encoded calcium indicators are also used both to image the activity of populations or specific types of cells in hippocampal slices. Acute hippocampal slices are also used to measure sharp-wave ripples (SWRs) – the most synchronous oscillation in the brain, which promotes memory consolidation during sleep following learning. Normal SWRs have highly stable durations. Too many SWRs, or inadequate separation between them, may degrade spatial information. The goal is to investigate the molecular and cell-type specific mechanisms that limit the duration of SWRs in the hippocampus to promote memory consolidation.



Finally, the effects of synaptic and cellular function and dysfunction on memory, is examined by assessing behavioral tasks in mice. The Morris water maze is a well-established behavioral task for spatial memory, in which mice are trained to swim to a hidden platform based on visual cues surrounding a pool. This task allows quantitation of learning (how quickly mice learn to find the platform), recall (how well the mice continue to remember the route to the platform), and forgetting (how quickly the mice forget the position of a previous platform position). Other animal behavioral assessments available at the ENI include novel object recognition and fear conditioning, which check different aspects of memory, and the open field and elevated plus mazes, which test anxiety.

In summary, the Dean group aims to identify the underlying mechanisms of memory encoding at the molecular, cellular, circuit and behavioral levels. This will provide an understanding of the functional dynamic range of memory circuits and potentially the means to counteract aberrant brain states by improving memory or promoting forgetting.

Synaptic Vesicle Recycling

Even with modest levels of neuronal activity, the hundreds of synaptic vesicles (SVs) typically present at the neuronal synapse would be used up rapidly without equally robust mechanisms of SV renewal. The existence of SVs allows neuronal synapses to sustain high rates of activity and to maintain their key properties: directionality of the signal, quantal release and synaptic modulation. Consequently, synapses must be capable of regenerating SVs locally with high efficiency and fidelity in order to meet the demand associated with various levels of neuronal activity. The uniquely homogeneous size of SVs, as well as their defined protein composition, suggest the existence of very precise mechanisms of SV formation and release that are intimately linked with the endocytic machinery.

Proper nervous system function relies on the controlled recycling of SV membrane and proteins after each exocytic event to ensure subsequent rounds of SV fusion. Although it has been more than four decades after it was originally proposed that SVs are formed and recycled locally at the presynaptic terminals, the mechanistic aspects of the endocytic processes at the synapse are still heavily debated. Therefore it is vital to better understand the molecular mechanisms of neuronal communication at synapses, as well as to recognize how such communication is affected in the diseased brain. Using morphological and functional assays, the „Synaptic Vesicle Dynamics" group of Ira Milosevic studies a

number of aspects of synaptic function and performs in depth analyses of neuronal function. Neurological and psychiatric illness is thought to arise, at least in part, as a result of imbalances in neuronal communication. Thus, studies of synaptic and neuronal functions in the context of major neurodegenerative conditions including Parkinson's disease (PD) are also pursued.

Novel properties of two proteins central to SV recycling have been uncovered. These proteins, as a result of specific post-translational modifications, divert from their defined endocytotic role and join the autophagy-lysosome pathway. The main pathway of SV recycling relies on the formation and dissociation of a clathrin coat around the vesicle to effect clathrin-mediated endocytosis. Studies in mouse neurons and in clonal cell-lines derived either from patients or mutant mouse models are conducted. The studies are complemented with elaborate neuronal cell biology, physiology and RNA sequencing, that enable assessment of the molecular mechanisms of the vesicle trafficking pathways in healthy and diseased situations. Significantly, mammalian models of defective endocytosis show accumulation of recycling intermediates at their synapses and prominent neurodegeneration and/or early lethality.

In recent years, mutations in two important clathrin uncoating factors have been found in patients with early-onset PD. The first of these factors (auxilin) is recruited to the clathrin coats via the action of the second factor (synaptojanin-1), which is itself colocalized to clathrin-coated pits by endophilin-A, a key endocytic adaptor that belongs to the family of BAR-domain proteins and interacts with hallmark PD-proteins: the ubiquitin ligase, Parkin, and leucine-repeat rich kinase (LRRK2). The Milosevic group continues to investigate the link of these key endocytic proteins to neurodegenerative diseases and PD. Given the importance of efficient SV recycling, it can be anticipated that new developments in

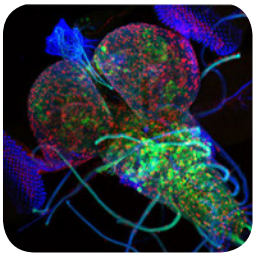
this research area will advance both the field of synaptic transmission and also have broad implications for neurophysiology and medicine.

Synaptic Physiology and Plasticity

Neurons have adapted the use of ion channels to generate electrical signals, which underlie the ability of the brain to sense the world, process and compute information, and design appropriate behavioral responses. These processes occur through networks of neurons that communicate via fast chemical synapses at which electrically active presynaptic 'sending' neurons release neurotransmitter molecules that are sensed by postsynaptic 'receiving' cells to regenerate, integrate, and propagate an electrical signal. In response to experience, the strength of a synapse can undergo long-term plastic change, a cellular mechanism of information storage, which is thought to underlie the processes of learning and memory.

The „Synaptic Physiology and Plasticity" group of Brett Carter seeks to understand how synaptic plasticity alters the physiology of a synapse, what patterns of synaptic activity lead to long-term plastic changes, the essential signals involved in this change, and how changes are expressed at the synapse. To address these questions, the group studies the synapse between layer 4 and layer 2/3 neurons in the rodent somatosensory cortex, which is involved in the development of cortical receptive fields. Electrophysiology and 2-photon imaging of neurons in the acute brain slice preparation allows the study of intact neuronal circuits at the level of single synapses.

Sensory Coding in Genetic Model Organisms



Many different animals use sensory cues to inform their behavioral decisions. It is a central question as to how sensory cues are recognized and the information processed in neuronal circuits to guide behavioral motor programs. In particular, ENI groups seek to understand how relevant neural circuit computations are implemented not only at an algorithmic level, but also how networks of neurons are organized, how they interact within intricate microcircuits and how complex physiological properties of individual neurons or even individual synapses contribute to network function and thus shape specific features of neural computation. Invertebrate systems are composed of relatively few neurons and are thus often considered “simple”. While functional and physiological studies have shown that invertebrate circuits can actually be quite complex, they can serve to reveal fundamental principles of circuit function. To name just one example, the stomatogastric system of the leech has led to the identification of mechanisms such as long-range neuromodulation, electrical coupling and bursting neurons, which have subsequently also been found in large brains. Indeed, many basic functional principles are incredibly similar between invertebrate and vertebrate brains and the list is expanding as more circuits are being characterized in more detail.

At the ENI, the fruit fly model organism, Drosophila melanogaster, has been chosen by two group leaders to investigate neuronal circuitry. This organism is simple enough to be able to modify its behavior and record the activity of its neurons in vivo, as well as perform precise genetic manipulations with cell type specific accuracy such that a single neuron within a microcircuit can be targeted. It is also possible to quantitatively measure fly behavior in a single fly or in a population of flies. This can be combined with precise sensory stimulation and/or genetic manipulations. Importantly, genetic tools exist that can be used to express

different transgenes in any pattern of interest, and in principle in every single neuron or cell type in the fly brain. Transgenes that can be expressed with this level of specificity include reporter and effector genes. It is therefore possible to label cells using GFP or other fluorescent molecules that change their fluorescence with the state of neuronal activity. This therefore allows different aspects of neuronal activity to be monitored, including intracellular calcium signals, vesicle release, or membrane voltage. In addition to labeling neurons with such reporter genes, it is also possible to modulate the activity of such reporters using effector genes or other genetic tools, which can inactivate or ectopically activate neurons. The most popular approaches rely on genetic tools to either block neuronal activity (by hyperpolarizing a neuron or preventing vesicle recycling), or ectopically activate neurons using thermo- or optogenetics. At the ENI, sensory coding in two distinct areas in Drosophila – the auditory and visual systems are currently under study.

Sensory Coding in the Fly Visual System

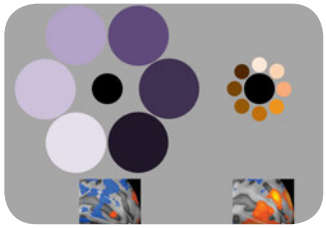
The „Visual Processing" group of Marion Silies is interested to understand how visual cues in the fly are processed, and thereby to link behavior to cellular and circuit mechanisms. The group is primarily focusing on the microcircuitry of a behaviorally critical computation, name-

ly, the extraction of directional information by motion-detection circuits in the visual system. To understand how a specific computation is implemented in the fly nervous system, cell biological and genetic approaches are used to manipulate critical neurons in motion detecting circuits. In combination with physiological measurements, in particular in vivo 2 photon calcium imaging experiments, and quantitative behavioral analysis, the group aims to identify the cellular and molecular mechanisms that guide behavioral responses to motion.

Sensory Coding in the Fly Auditory System

The „Neural Computation and Behavior" group of Jan Clemens works on how acoustic communication signals are processed in Drosophila to inform behavior. Acoustic communication is widespread in the animal kingdom – yet its neural basis is poorly understood. Like songbirds or crickets, fruit flies also produce mating songs during courtship. The group uses high-throughput behavioral assays and computer vision to precisely quantify how song influences fly behavior on multiple time scales – from changes in locomotion in response to the song over tens of milliseconds to mating decisions based on song accumulated over several minutes of courtship. The genetic toolbox available in Drosophila is also utilized to identify the neural substrates of these behaviors. Using optogenetics, individual neurons in the fly brain can be activated or inactivated during courtship interactions – quantitative models of the behavior then allow the identification of the time scales and components of the behavior controlled by these neurons. Having found individual neurons involved in processing song, electrophysiology and two-photon calcium imaging can be used to interrogate the dynamic neural representations of song to determine how song is encoded in the brain and determine how such neural codes give rise to the resultant behavior.

The Neural Basis of Cognition and Behavior in Human and Non-Human Primates



Understanding human cognition has been the subject of philosophical and scientific investigations ever since humans developed writing (the brain was first mentioned in a papyrus dating back to 17th century BC). The famous sentence Cogito ergo sum (I think therefore I am) reflects the key reason why the study of the human mind is such a fascinating endeavor: understanding how we think is equivalent to understanding ourselves. How close have we come to ‚understanding ourselves' after almost 3700 years? Modern-day neuroscientists may be hesitant to answer this question: unlike early philosophers who daringly proposed grand, all-explaining theories, they focus on specific aspects of human cognition and are aware that even within these specialized areas we know little about the exact mechanisms that underlie cognition. This is despite the fact that today, more than any other era in history, there is a pressing need to arrive at a more global understanding of human cognition that transcends the boundaries of specific disciplines. For instance, while we are experiencing an artificial intelligence (AI) revolution, science and society need to determine whether there are diagnostic features that distinguish human thought from what is happening in artificial neural networks that are now able to execute many tasks as well as or better than human performance levels. How can these seemingly incompatible goals, i.e., a mechanistic understanding of cognitive functions using specialized methodologies on the one hand, and an interdisciplinary and general-purpose understanding of human cognition on the other be achieved? At the ENI theoretical frameworks and empirical techniques of Cognitive Neuroscience are used to help realize these goals.

Cognitive Neuroscience is an interdisciplinary field encompassing methods and theories of neuroscience, psychology, biology, mathematics, and computational modeling. The diverse set of skills and tools available to cognitive neuroscientists will allow the unraveling of the biological and computational basis of the

mind. At the ENI, two groups capitalize on the following tenets to guide their studies, namely, 1. Understanding brain functions necessarily entails detailed understanding of behavior. 2. Understanding human brain-behavior mechanisms is greatly aided by understanding how other organisms encode and process information, which

also reaches out to various groups at the ENI using model organisms to understand the principles of neural coding. 3. Some cognitive functions are best addressed in animal models that naturally employ these cognitive functions. The closest available model system fulfilling this requirement is the non-human primate. Here, direct electrophysiological recordings and inactivation techniques can foster insight at a depth and level of granularity that is unavailable with noninvasive techniques in humans; at the same time, assessing similarities and differences in behavior and brain activity between species provides deep insights into the evolution of our cognitive abilities and behaviors. Thus, research in non-human primates is an indispensable component for the advancement of the scientific goals in this field.

Hence, multiple techniques of behavioral, electrophysiological and neuroimaging experimentation in humans as well as similar techniques in non-human primates are used at ENI and in collaboration with the DPZ (German Primate Center) and the MRI facility of the UMG (University Medical Center Göttingen), to advance our

understanding of the neural basis of cognitive and perceptual functions.

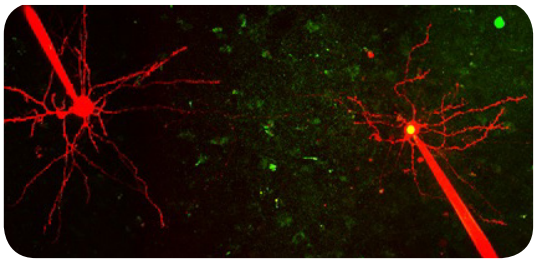
Perception and Cognition in Humans

The „Perception and Cognition" group of Arezoo Pooresmaeili focusses on testing how the stimulus value signaled by different sensory modalities modulates perception within or across senses. Whether or not we move our eyes towards a sudden flash of light depends on both physical characteristics of the stimuli (e.g. brightness of lightbeam) as well as their relevance to our current goals (e.g. we may want to avoid moving our eyes elsewhere while giving a presentation in front of an audience). One important determinant of relevance is the amount of gain or loss that is associated with the occurrence of a stimulus, referred to as stimulus value. A large body of research has shown that the stimulus value affects the encoding of sensory information at the earliest stages of processing, for instance at the level of thalamus and primary sensory areas. This means that the flash of light in the example above may even not be registered or conversely become strongly amplified by our sensory organs if it is associated with a certain negative or positive hedonic value. Despite ample evidence for the effect of value on sensory perception, the exact underlying mechanisms are largely unknown. For instance, the value associated with a flash of light or a burst of sound can affect visual or auditory perception, thus influencing information processing within or across senses. Importantly, these effects occur even under conditions when a stimulus is no more associated with an explicit value and is subconsciously registered. To understand the underlying mechanisms of these behavioral effects the group uses eye-tracking, electroencephalography (EEG) and neuroimaging (functional MRI) techniques. These methods allow the elucidation of the temporal characteristics of value effects on perception (eye-tracking and EEG) and their underlying brain networks (fMRI). Stimulus value not only affects perceptual and value-based decisions in a single person but also determines the nature and dynamics of social interactions. To this end, computational modeling techniques are used to gain insight into how perceived gains and costs of actions are evaluated and parsed by humans during social interactions.

Neural Circuits and Cognition in Humans and Non-Human Primates

The „Neural Circuits and Cognition" group of Caspar Schwiedrzik focusses on the visual system to investigate various aspects of learning. Learning is a core building block of intelligent behavior. It endows complex systems with the flexibility to adjust to changing environments and with the capacity to generalize to novel situations. Generalization is a hallmark of intelligent computation in humans and machines alike, but only brains can generalize on the basis of only one example. How do minds/brains achieve such a feat, and what is so remarkable about the brain that sets it apart from computers? Answers to these questions are still in their infancy, as little is known, e.g., about the neural machinery underlying the ability to generalize. The Schwiedrzik group pursues the idea that inroads into understanding learning and generalization can be made by studying the visual system, where these complex problems can be broken down into tractable hypotheses. Visual processing hierarchies provide an ideal testing ground and offer unique opportunities to unravel the role of feedforward and feedback message passing along the processing hierarchy as a function of learning and generalization. To this end, the group capitalizes on combining noninvasive neuroimaging with electrophysiological recordings and causal manipulations of brain activity in awake, behaving macaque monkeys, and parallel experiments using fMRI in humans. The group studies learning over multiple time scales, from learning effects that build up within seconds to those that take days and weeks to materialize, and across various levels of complexity, for example, from discriminating simple visual features to high-level associative and statistical learning. The group's goal is to determine the neural basis of the visual system's capacity to learn and generalize through an explicitly comparative approach – a necessary prerequisite step towards understanding the human mind and its complexity.

Selected Publications



Brett Carter, *Group Leader Synaptic Physiology and Plasticity since 2017*

Sun W, Wong JM, Gray JA, Carter BC (2018). „Incomplete block of NMDA receptors by intracellular MK-801." Neuropharmacology 143: 122-129.

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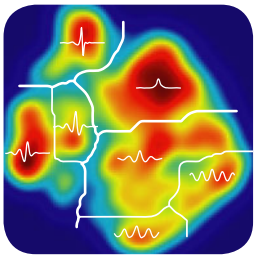

Jan Clemens, *Group Leader Neural Compuation and Behaviour since 2017*

Christa A. Baker, Jan Clemens*, and Mala Murthy* (* co-corresponding authors) (2019) Acoustic Pattern Recognition and Courtship Songs: Insights from Insects. Annual Reviews of Neuroscience, 42

Jan Clemens*, Philip Coen*, Frederic A. Roemschied*, Talmo Pereira, David Mazumder, Diego Pacheco, and Mala Murthy (2018). Discovery of a new song mode in Drosophila reveals hidden structure in the sensory and neural drivers of behavior. Current Biology, 28:2400–2412

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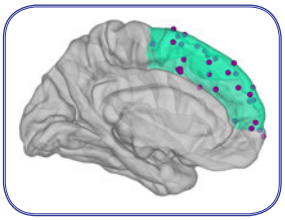

Caspar Schwiedrzik, *Group Leader Neural Circuits and Cognition since 2017*

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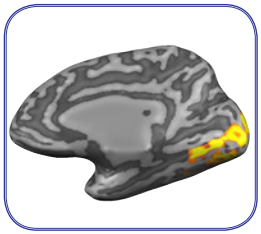

Arezoo Pooresmaeili, *Group Leader Perception and Cognition since 2015*

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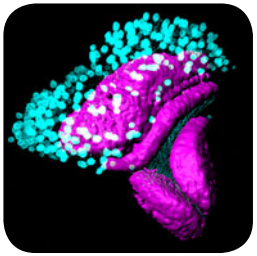

Marion Silies, *Group Leader Visual Processing 2014-2018; since 2019 Professor at Johannes Gutenberg University Mainz*

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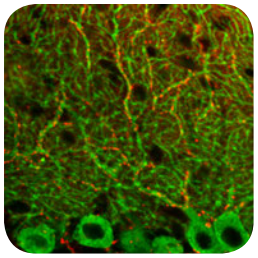

Ira Milosevic, *Group Leader Synaptic Vesicle Dynamics 2012-2019*

Murdoch JD, Rostsoky C, Gowrisankaran S, Arora AS, Soukup SF, Vidal R, Capece V, Freytag S, Fischer A, Verstreken P, Bonn S, Raimundo N, Milosevic I (2016) Endophilin-A deficiency induces the FoxO3a-Fbxo32 network in the brain and causes dysregulation of autophagy and the ubiquitin-proteasome system. Cell Rep 17(4), 1071-86

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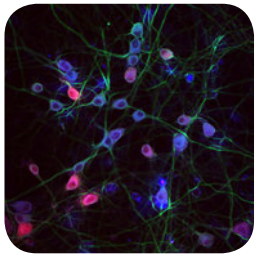

Camin Dean, *Group Leader Trans-synaptic Signaling 2010-2018;* since 2018 Group Leader at German Center for Neurodegenerative Diseases (DZNE) Göttingen

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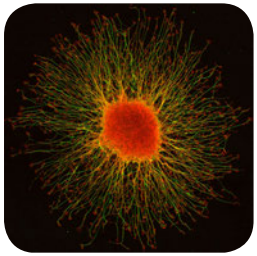

Till Marquardt, *Group Leader Developmental Neurobiology 2007-2016; since 2016 Professor at Klinik für Neurologie, RWTH Aachen*

Müller D, Cherukuri P, Henningfeld K, Poh CH, Wittler L, Grote P, Schlüter O, Schmidt J, Laborda J, Bauer SR, Brownstone RM, Marquardt T (2014) Dlk1 promotes a fast motor neuron biophysical signature required for peak force execution. Science 343(6176): 1264-6

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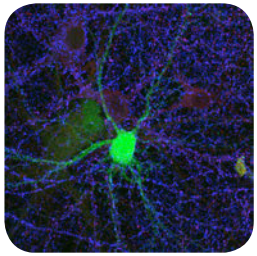

Oliver Schlüter, *Group Leader Molecular Neurobiology 2006-2015; since 2015 Associate Professor at the Department of Neuroscience, Pittsburgh and Guest Professor at the Clinic of Psychiatry and Psychotherapy at UMG*

Huang X, Stodieck SK, Goetze B, Cui L, Wong MH, Wenzel C, Hosang L, Dong Y, Löwel S, Schlüter OM (2015) Progressive maturation of silent synapses governs the duration of a critical period. Proc. Natl. Acad. Sci.USA 112(24): E3131-40

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Lars Kuhn, *Group Leader NMR Spectroscopy 2008-2013 ; until 2016 Senior Research Scientist at the Spanish National Biotechnology Centre (CNB) – CSIC, Madrid; since 2017 NMR Staff Scientist at the University of Leeds*

Kuhn, Lars T (2013) Photo-CIDNP NMR Spectroscopy of Amino Acids and Proteins. Top Curr Chem 338: 229-300

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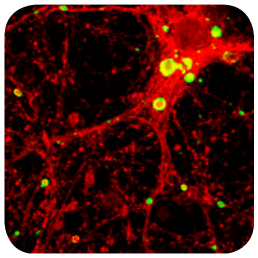

Silvio Rizzoli, *Group Leader STED Microscopy of Synaptic Function 2007-2012; since 2012 Professor of Physiology, Department of Neuro- and Sensory Physiology, University Medical Center, University Göttingen; since 2014 Head of Department of Neuro- and Sensory Physiology, Center for Physiology and Pathophysiology, University Medical Center, University Göttingen.*

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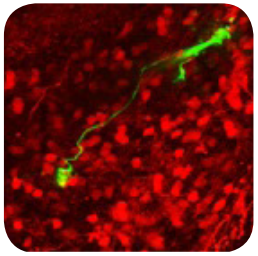

Stefan Hallermann, *Group Leader High Frequency Signalling 2011-2013; since 2013 Professor of Neurophysiology and Head of Department I „Physiology“, Carl-Ludwig-Institute for Physiology, University Leipzig*

Ritzau-Jost A, Delvendahl I, Rings A, Byczkowicz N, Harada H, Shigemoto R, Hirrlinger J, Eilers J, Hallermann S. (2014) Ultrafast action potentials mediate kilohertz signaling at a central synapse. Neuron. 2014 Oct 1;84(1):152-163

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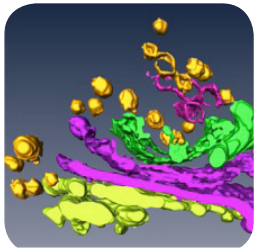

Stefan Eimer, *Group Leader Molecular Neurogenetics 2005-2012; 2012-2017 Professor of Cellular Structural Neurobiology, Institut for Biology II, Center for Biological Signalling Studies (BIOSS), University Freiburg since 2018 Professor for Structural Cell Biology, Institute for Cell Biology and Neurosciences, Goethe University Frankfurt/Main*

Kittelmann M, Hegermann J, Goncharov A, Taru H, Ellisman MH, Richmond JE, Jin Y, Eimer S (2013) Liprin-α/SYD-2 determines the size of dense projections in presynaptic active zones in C. elegans. J Cell Biol 203(5): 849-63

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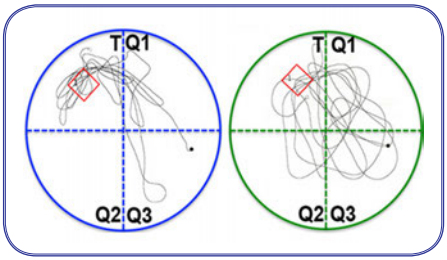

André Fischer, *Group Leader Laboratory for Aging and Cognitive Diseases 2007-2011; 2011 Professor of Epigenetics, Department for Psychiatry and Psychotherapy, University Medical Center, University Göttingen and German Center for Neurodegenerative Diseases (DZNE), Goettingen.*

Agis-Balboa RC, Arcos-Diaz D, Wittnam J, Govindarajan N, Blom K, Burkhardt S, Haladyniak U, Agbemenyah HY, Zovoilis A, Salinas-Riester G, Opitz L, Sananbenesi F, Fischer A (2011) A hippocampal insulin-growth factor 2 pathway regulates the extinction of fear memories. EMBO J 30(19): 4071-83

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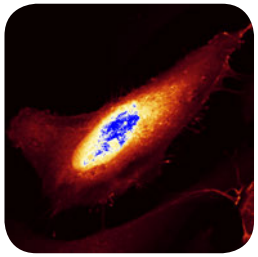

Fred Wouters, *Group Leader Cell Biophysics 2001-2007; 2007-2014 Professor of Molecular Microscopy, Department of Neuro- and Sensory Physiology, University Medical Center, University Göttingen, since 2014 Department of Neuropathology, Center for Pathology and Legal Medicine, University Medical Center, University Göttingen.*

Esposito A, Dohm CP, Bähr M and Wouters FS (2007) Unsupervised fluorescence lifetime imaging microscopy for high content and high throughput screening. Mol Cell Proteomics 6, 1446-54

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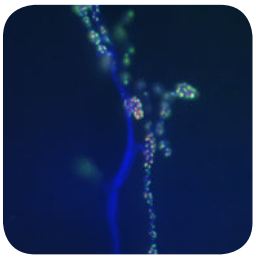

Stephan Sigrist, *Group Leader Neuroplasticity 2001-2005; 2006-2008 Professor for Experimental Biomedicine and Bio-Imaging, Rudolf Virchow Center of Excellence, University of Würzburg, since 2009 Professor in Genetics, Institute of Biology, Freie Universität Berlin, and affiliated with the Neurocure Cluster of Excellence, Charité, University Medicine Berlin*

Schmid A, Hallermann S, Kittel RJ, Khorramshahi O, Frölich AM, Quentin C, Rasse TM, Mertel S, Heckmann M, Sigrist SJ (2008). Activity-dependent site-specific changes of glutamate receptor composition in vivo. Nat Neurosci. 6, 659-666.

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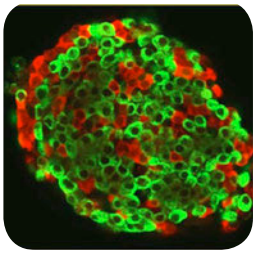

Marjan Rupnik, *Group Leader Neuroendocrinology 2000-2005; 2004-2009 Assistant Professor of Physiology, Medical Faculty University Maribor; since 2009 Professor and Head of Institute of Physiology, Medical Faculty University Maribor*

Speier S, Gjinovci A, Charollais A, Meda P and Rupnik M (2007) Cx36-mediated coupling reduces beta-Cell heterogeneity confines the stimulating glucose concentration range and affects Insulin release kinetics. Diabetes. 56, 1078-86

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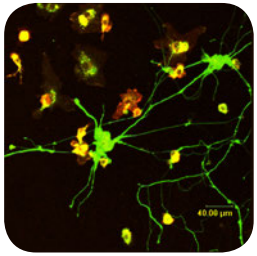

Harald Neumann, *Group Leader Neuroimmunology 2001-2004; since 2004 Professor, Neural Regeneration Group, Institute of Reconstructive Neurobiology, Life & Brain Center University Bonn*

Takahashi K, Rochford CD and Neumann H (2005) Clearance of apoptotic neurons without inflammation by microglial triggering receptor expressed on myeloid cells-2. J Exp Med. 201, 647-57

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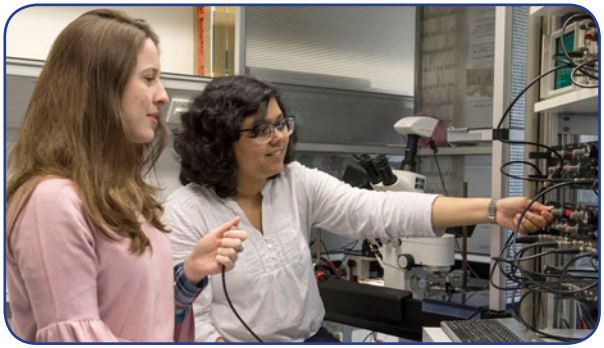
Study Program

The Neurosciences study program located on ENI's ground floor consists of rooms for coordination and administration of the program, a seminar room, a computer room, and teaching laboratories in the north wing, and free access to ENI's lecture theatres. Each year 500 students with a Bachelor's degree in life sciences/biosciences from across the world apply; of which up to 20 are selected to enter the program. Particular emphasis is put on teaching electrophysiology with labs fully equipped with two electrophysiological set-ups to measure currents in oocytes, two set-ups to allow recordings from leeches, two whole cell patch clamp set-ups and two set-ups for calcium imaging techniques. Group leaders can contribute to teaching in the courses which stands for a high degree of internationalization and scientific excellence.



History

The initiative to found the European Neuroscience Institute in Göttingen and to develop a Network of European Centers of Competence in the Neurosciences arose in 1997 following several European study reports, which called for an increased European effort in the Neurosciences. Nobel Laureate Erwin Neher from the Max-Planck-Institute of Biophysical Chemistry and his colleagues, Diethelm Richter from the University Medical Center and Walter Stühmer from the Max-Planck-Institute of Experimental Medicine, realized the potential for a Göttingen based effort to strengthen the study of Neuroscience with new centers of competence embedded in a European network. Göttingen offered a rich scientific environment and multiple interactions had evolved following receipt of international, national and thematic research programs. In 2001, the European Neuroscience Institute was officially opened in Göttingen by the European Commissioner Philippe Busquin for four independent young investigators and their teams. This achievement in the field of neuroscience was then rewarded with its own new building provided by the state of Lower Saxony with support from UMG and MPG in 2005 for up to nine independent groups.