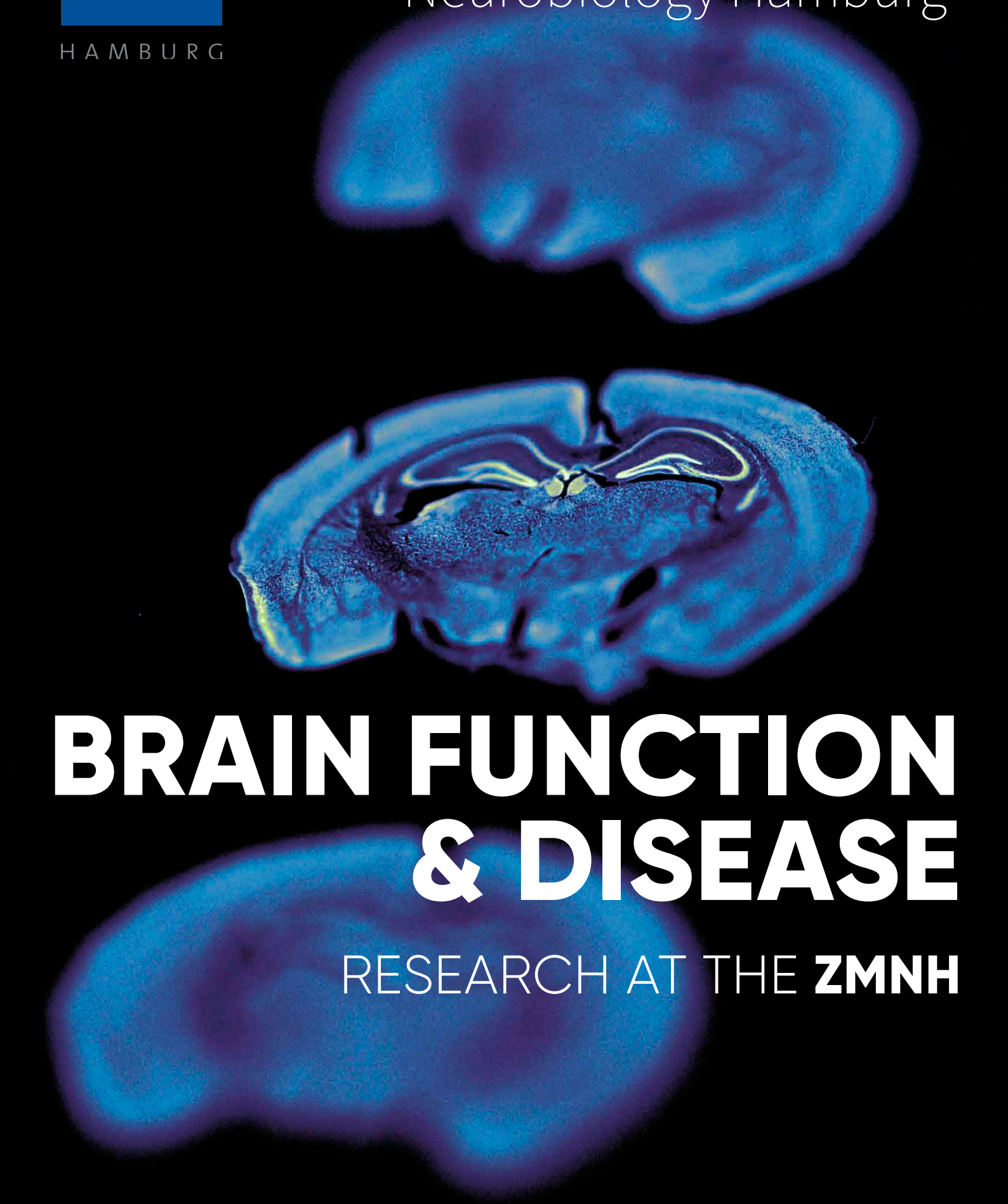
UKE
HAMBURG

Center for Molecular Neurobiology Hamburg



BRAIN FUNCTION & DISEASE

RESEARCH AT THE **ZMNH**

Strong basic science powers new translational and clinical developments that generate true impact for society

The brain is the most complex organ in the body. Around 100 billion neuronal connections are formed and maintained as we grow up and age, and collectively they determine nervous system function. We explore the rules and mechanisms that shape and modify neuronal circuits during learning and behavior. Because of its dazzling complexity, we need top-notch technology and a multidisciplinary approach to unravel brain function.

We use electrons and lasers to visualize subcellular structures and molecules in nerve cells, to measure activity patterns in the brain, and to control the activity of specific neuronal populations. We generate and study mouse models of human neuropsychiatric and neurodegenerative diseases to obtain insights into pathological processes and to identify new biomarkers and therapeutic targets. We develop machine learning approaches to discover hidden patterns in large datasets.

To make all of this possible, we support and train young scientists at all stages of their career to become critical and independent researchers.

In collaboration with partners from other disciplines such as psychology, physics and informatics, we develop interdisciplinary approaches to understand the brain from different perspectives. We believe that strong basic science powers new translational and clinical developments that generate true impact for our society.

Our Center participates in national and international networks to propel discovery and innovation and is a strong partner in the scientific environment within Hamburg.

This brochure provides an overview of our science and the people that make it happen. We hope it inspires you to join us in our mission.

Matthias Kneussel
Director

Thomas Oertner
Vice-director

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Cover legend: Mouse brain slices. The hippocampal formation (middle, white) is an important brain area involved in memory consolidation. Image by Simon Wiegert.

MISSION

Our Center investigates the molecular processes and cellular communication underlying nervous system function and dysfunction in health and disease.

As a center for basic research at the University Medical Center Hamburg-Eppendorf (UKE), the ZMNH deciphers fundamental principles of brain and nervous system function including its homeostasis and disruption in disease.
We aim to improve our understanding of how genetic, molecular and cellular processes, as well as environmental factors, affect brain function and the communication between cells of the nervous system.

We investigate molecular units, processes and pathways, underlying the physiology and pathophysiology of neurons within neuronal circuits. Our investigations range from the developing to the aged brain, include the analysis of intellectual functions, learning, memory, decision making, attention, as well as sensory and motor skills. They yield insights for translational neuroscience to fight neuronal disease and neurodegeneration, and deliver the basis for new and more effective strategies for diagnosis, therapy and prevention.

Stefan **Bonn**

Institute of Medical Systems Biology

Our group uses computational approaches on big biomedical data to elucidate mechanisms of human pathology, with a particular focus on neurodegeneration. While we use various probabilistic, statistical, and graph-based approaches to achieve our aims, we currently explore how deep learning-based architectures can help us understand human disease.

"Our efforts in database creation and curation enable meaningful analysis of omics, opening up new routes to predicting and curing human disease. We have built SEAweb, a searchable database for the expression of small RNA and pathogens. Our curated, ontology connected metadata enables powerful searches within this database."

Manuel **Friese**

Institute of Neuroimmunology and Multiple Sclerosis

We want to understand the etiology and pathogenesis of multiple sclerosis and other neuroimmunological or neuroinfectious diseases and to translate this knowledge into efficacious treatments. We investigate the immune and the central nervous system and their interactions to understand mechanisms of immune cell dysregulation and neurodegeneration.

"We were able to identify inflammation-induced neuronal response patterns that resulted in ion channel dysfunction, energy deficit and toxic protein deposition, together driving neuronal injury and resembling findings reminiscent of primary neurodegenerative diseases. These can now be therapeutically targeted."

Ileana **Hanganu-Opatz**

Institute of Developmental Neurophysiology

Our research focuses on the mechanisms underlying the development of neuronal networks under physiological and pathophysiological conditions. In particular, we aim to elucidate how patterns of early electrical activity control local and long-range wiring in the brain in relationship with the emergence of cognitive behavior and (multi)sensory perception.

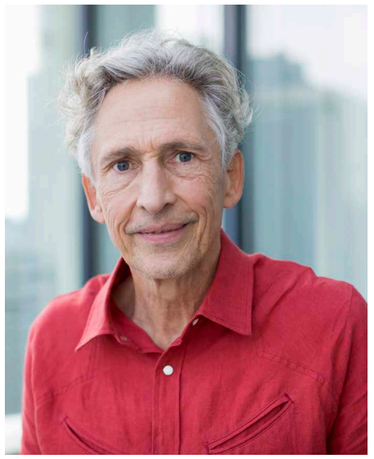
"We have pioneered the functional dissection of neuronal circuits during development using in vivo electrophysiology and optogenetics. We showed that dynamic interactions between neurons early in life not only shape the adult brain function and behavior but are also of paramount importance for circuit miswiring and disabilities in mental disorders."

Matthias **Kneussel**

Institute of Molecular Neurogenetics

We investigate how neuronal activity and intracellular trafficking of synaptic molecules intertwine. We ask how synapses crosstalk to cytoskeletal elements to direct plasticity-related proteins across neurons. Combining biochemical, cellular and mouse behavioral approaches, we also study non-canonical neuronal communication through extracellular vesicles and unravel mechanisms of neuronal dysfunction.

"We recently identified a subcellular mechanism that controls the direction of protein targeting from synapses to either the lysosome or multivesicular body/exosome pathway. Our lab showed that posttranslational modification of tubulin controls neuronal transport underlying the regulation of working and associative memory."



Dietmar **Kuhl**

Institute of Molecular and Cellular Cognition

Our laboratory takes an integrative approach to study the physiology and pathophysiology of synaptic plasticity and learning and memory. We investigate the molecular, cellular and network mechanisms of learning and memory using mouse genetics to bridge molecular biology, biochemistry, in-vitro and in-vivo electrophysiology, systems biology, and behavior.

"We pioneered the identification of genes whose activity-dependent expression is vital for long-term plastic events in the brain. One example is Arc/Arg3.1, which we discovered and demonstrated to be essential for the consolidation of memories. Recently, we found that Arc/ Arg3.1, in addition, is crucial for establishing memory circuits during brain development."

Thomas **Oertner**

Institute of Synaptic Physiology

We study the mechanisms of information processing in the brain. We focus on long-lasting changes in the strength of synaptic connections, which we follow over several days with optical methods, and the role of glia cells in this process.

"Our genetically encoded sensor SynTagMA allows us to freeze the activity state of thousands of synapses with a flash of light. For the first time, we are able to monitor all inputs to a neuron simultaneously and decipher synaptic activity patterns in intact brain tissue."

Immo **Prinz**

Institute of Systems Immunology

Our goal is to understand the immunological changes and challenges emerging from the vast majority of more than a quadrillion potential adaptive immune receptor combinations in T cells and B cells.

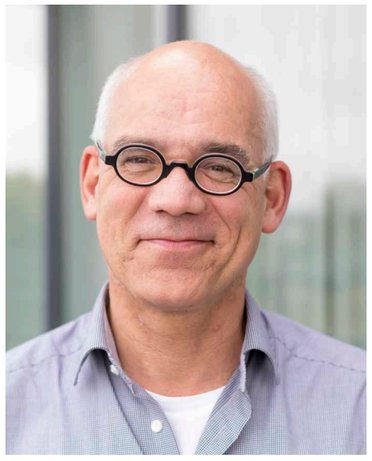
“We developed systems for high-throughput monitoring of T cell receptor repertoires and found that certain γδ T cells mount an adaptive immune response to viral infection in humans. Our current research focusses on systems to identify specific antigens based on T cell response sequence information.”

Froylan **Calderon de Anda**

Research Group Neuronal Development

We study how neurons acquire their morphology. This is a fundamental topic in neurobiology given that the shape of a neuron supplies valuable clues to its function. Little is known about the mechanisms of axon and dendrite specification in vivo and how intracellular and extracellular programs cooperate to define neuronal cytoarchitecture.

“We have been contributing to the understanding of how neurons differentiate in vivo. Moreover, our work uncovers that neuronal cytoarchitectural abnormalities might lead to neurological disorders. We are generating insight into the cellular and molecular events that may underlie neuropsychiatric diseases, such as autism.”



Christoph **Heesen**

Clinical and Rehabilitative Multiple Sclerosis Research Unit

We focus on the development of behavioral interventions for MS, from psychological Ehealth interventions to exercise trials. Novel drugs to treat MS relapses and further development of autologous hematopoietic stem cell transplantation are key treatment approaches. New outcomes and effective study designs are another focus of our research.

“We apply evidence-based patient education methods and interactive EHealth tools. We could show high acceptance of a matching algorithm approach comparing individual patient disability evolution with natural cohort data. We showed that Ehealth interventions alleviate depression and fatigue as key neuropsychiatric complaints in randomized controlled trials for MS.”

Meliha **Karsak**

Research Group Neuronal and Cellular Signal Transduction

Based on our long-standing interest in the role of the endocannabinoid system in human diseases, we are currently studying the molecular mechanisms caused by dysfunction of GPCRs and other membrane associated proteins in selected neurological diseases.

“In an ongoing study we are investigating how newly identified mutations in a gene encoding for a GPCR-associated protein disturb receptor signaling and cause a neurodevelopmental disease.”

Michael R **Kreutz**

Leibniz-Group Dendritic Organelles & Synaptic Function

Our laboratory investigates how microsecretory systems and organelles like amphisomes, autophagosomes, lysosomes and Golgi satellites in neurites are involved in synaptic function.

“We discovered neuronal amphisomes – hybrid organelles of autophagosomes and signaling endosomes. We could show that the enormous complexity of neuronal cytoarchitecture has enabled ways of long-distance protein transport that combine degradative with signaling functions.”

Fabio **Morellini**

Research Group Behaviorial Biology

We investigate how mouse behavior develops and is controlled, and how it is affected in disease. We aim to implement the validity of behavioral analyses and to understand causations using transgenic, pharmacological and optogenetic approaches.
We study a broad spectrum of behavioral functions and, in particular, the neuronal correlates of prospective representation and decision making.

“We provided the first evidence that mice process episodic-like memories, which allowed us to identify a new physiological correlate of learning in the dentate gyrus. We also showed that genetically identical mice have distinct individual coping strategies that affect their decision making and problem-solving under conflictual situations.”

Axel **Neu**

Guest Group Experimental Neuropediatrics

Our research is focused on the role of ion channels in epileptogenesis during early brain development. In addition to elucidating the basic pathophysiological mechanisms, the ultimate goal is to offer targeted treatment options for the cure of genetic ion channel dysfunction.

“Our translational approach with humanized mouse models and high throughput drug screening allows us not only to investigate the processes underlying developmental and epileptic encephalopathy, but also to develop novel therapeutic strategies for our pediatric patients.”

Ole **Pless**

Guest Group Fraunhofer ITMP

The Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP) works on the development and application of novel technologies for diagnosis and therapy of diseases. One focus of the guest group at the ZMNH is the determination of efficacy and toxicity of therapeutic molecules based on cell types derived from human pluripotent stem cells.

“Recently, we were able to significantly improve the ‘embryonic stem cell test (EST)’ for the assessment of teratogenicity of small molecule substances on a technological level and to automate crucial process steps.”

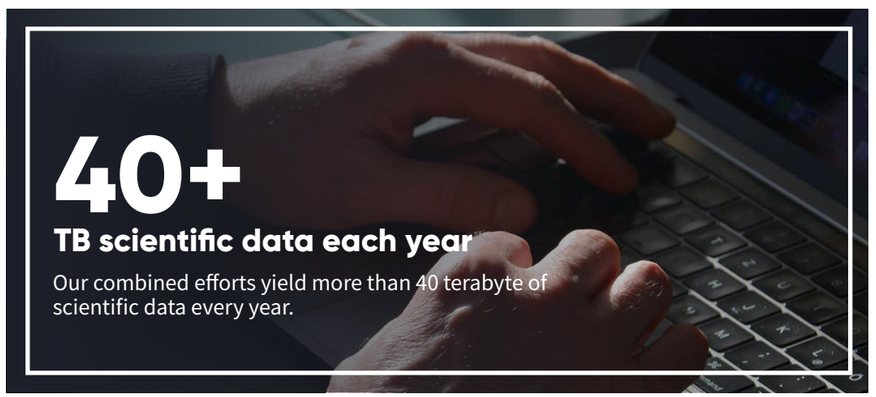
Simon **Wiegert**

Research Group Synaptic Wiring and Information Processing

We ask how information is encoded and stored in the brain and how these processes are influenced by the main neuromodulatory systems, reflecting different states of the animal. We address these questions at various levels ranging from single hippocampal synapses to cellular ensembles.

“To have a better way to control identified neuronal populations in the brain, we recently developed a novel optogenetic tool termed BiPOLES that allows bidirectional manipulation of neural activity. BiPOLES can be used to both optically silence and activate the exact same neurons with light of different color, enabling gain-of-function and loss-of-function experiments in the same animal.”

ZMNH IN NUMBERS

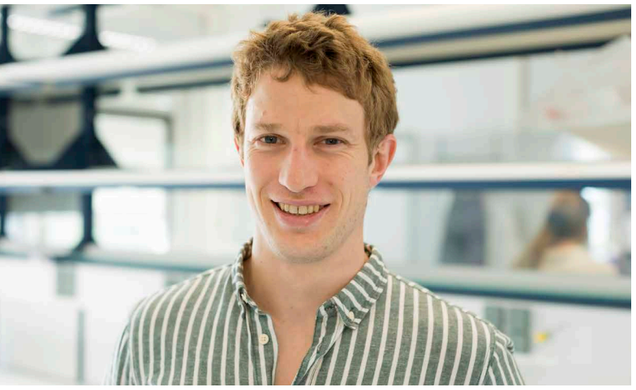


Rescuing developmental miswiring in a mouse model of cognitive impairment

It has been long postulated that cognitive problems associated with mental disorders result from network dysfunctions that develop long before symptom onset, but the mechanisms controlling such abnormal maturation remain unclear. A team led by **Ileana Hanganu-Opatz** found that in a mouse model of mental disease, early deficits in neuronal networks in the prefrontal cortex are responsible for cognitive impairment. Interestingly, the new findings also open up new potential therapeutic avenues for disease prevention.

Using a mouse model that mimics the dual genetic-environmental etiology of psychiatric disorders, the team found that early bouts of beta/gamma activity were a biomarker for whether the mice would follow a healthy developmental trajectory or would develop cognitive dysfunction later in life. These alterations turned out to depend on deficits affecting the pyramidal neurons of the superficial layers.

First author **Mattia Chini** explains: "We uncovered that this defect was at least partially due to excessive synaptic pruning by microglia cells, so we wanted to know if we could rescue some of the defecits by inhibiting the phagocytic activity of microglia."



A pharmacological intervention that reduces microglia phagocytosis also restored the alterations that affected the pyramidal neurons and the beta/gamma oscillations that depend on them.

"The very last step was to go back and check whether the rescue of the physiology would also rescue the cognitive defects," says Chini. "This turned out to be at least partially the case."

Scientific exchange at ZMNH and UKE was important for this work. "At the ZMNH there is freedom to pursue your own questions, and there is a truly collaborative atmosphere among the different groups. The research topics are very diverse, which has the big advantage that if you have a question you want to pursue with different techniques, you can always find an expert in house."

In the long-term, the team wants to study the gut microbiome and neuro-immune axis and look for what is upstream of the microglial alterations.

"This work brings us closer to one of the goals of network psychiatry: the identification of key neurobiological targets amenable to tailored therapies, that not only treat but also prevent disease-related cognitive and behavioral symptoms."

Chini et al. Neuron 2020
Resolving and rescuing developmental miswiring in a mouse model of cognitive impairment

Taking snapshots of synaptic activity

Information within the brain travels from neuron to neuron across billions of synapses. A team led by Thomas Oertner came up with a way to freeze the activity state of thousands of synapses with a flash of light. Their new method opens up new avenues to decipher synaptic activity patterns in the living brain.

There are billions of synapses in the brain, but at any given moment, only a small subset of neurons and synapses are active. Finding the active synapses in brain tissue has been a technical challenge, but Thomas Oertner and his team devised a way to tag active synapses in a user-defined time window.

"As intracellular calcium levels are a good proxy for activity, genetically encoded calcium indicators provide good temporal resolution of synaptic activity," explains **Alberto Perez-Alvarez**, postdoc in the Oertner lab and co-first author on the study. "However, due to the limited field of view of light microscopes, which monitor just a few synapses in 2D, you need to know beforehand where exactly activity takes place."

To circumvent this limitation, the team targeted a photoconvertible calcium sensor to synaptic compartments and named it SynTagMA, for 'Synaptic Tag for Mapping Activity'.

Perez-Alvarez: "Upon violet light illumination, this genetically encoded reporter converts irreversibly from green to red if, and only if, it is bound to calcium — i.e. during neuronal activation."

Targeted to presynaptic terminals, preSynTagMA allows discrimination between active and silent axons. Targeted to the postsynaptic compartment of excitatory synapses, postSynTagMA provides a still frame of synapses, active and inactive, just before photoconversion.

"To aid in the analysis of the typical large datasets that we generated, we also developed software to identify and track the fluorescence of thousands of individual synapses in tissue," adds Perez-Alvarez. "Together, these tools provide an efficient method for repeatedly mapping active neurons and synapses in cell culture, slice preparations and in vivo during behavior."

Perez-Alvarez, Fearey et al. Nature Communications 2020
Freeze-frame imaging of synaptic activity using SynTagMA

Neuronal circuit development defects in autism spectrum disorder

A microdeletion of the chromosomal region 16p11.2 contributes to approximately 1% of all cases of autism spectrum disorder, while a reciprocal microduplication of the same region is linked to schizophrenia. TAOK2 is one of 31 genes located in 16p11.2, but whether and how it contributes to neurodevelopmental disorders was unknown. A team led by **Froylan Calderon de Anda** explored how TAOK2 contributes to disease and if its deregulation could be restored.

Despite several studies suggesting a link between TAOK2 and neurodevelopmental disorders, concrete evidence of a causative role in mouse or human models was lacking. Through whole-genome and exome sequencing of different families with autism spectrum disorder, Calderon de Anda and his team identified novel mutations in the TAOK2 gene, underscoring its relevance to disease.

These team went on to confirm the importance of TAOK2 through behavioral experiments. “Using both Taok2 heterozygous and knockout mice, we found gene-dosage dependent impairments in cognition, anxiety and social interaction,” says Melanie Richter. “The Taok2 knock out mice also had an abnormally large brain, with deficits in dendrite and synapse formation and reduced excitatory neurotransmission.”

Three different clinical mutations in TAOK2 were found to impair protein stability, dendrite growth and synapse development in mice and in human cells.

Since TAOK2 encodes a protein kinase, Richter and her colleagues looked into the downstream pathway. “Loss of Taok2 activity caused a reduction in RhoA activation,” explains Richter. “By pharmacologically enhancing RhoA activity, we could rescue the synaptic phenotypes.”

Calderon de Anda: “Our results do not only provide evidence that TAOK2 is indeed a neurodevelopmental disorder risk gene, they also offer insight into how mutations impact brain function and development. Since RhoA activity could rescue some of the phenotypes, it could be a potential therapeutic target.”

Richter et al. Mol Psychiatry 2019
Altered TAOK2 activity causes neurodevelopmental and cognitive abnormalities through RhoA signaling

Toxic protein aggregates congest inflamed neurons

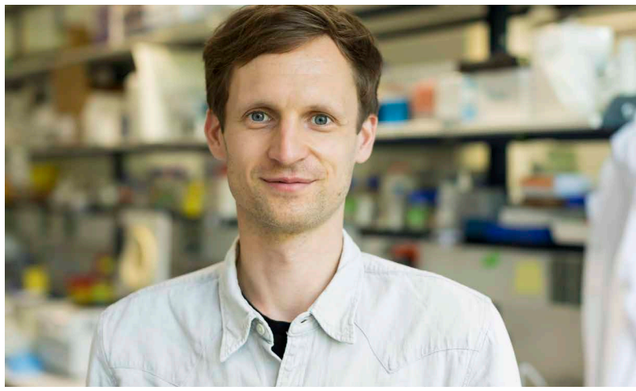
In multiple sclerosis, inflammation in the nervous system leads to damage and loss of neurons. However, little is known about how neurons themselves respond to the inflammatory insult. By profiling ribosome-bound transcripts of motor neurons confronted with inflammation, the lab of **Manuel Friese** uncovered toxic intracellular aggregation of the presynaptic protein Bassoon as a novel pathological hallmark.

Multiple sclerosis is characterized by inflammatory lesions in the central nervous system. “Although these inflammatory insults drive neuroaxonal injury und ultimately disease progression, our knowledge about neuron-intrinsic responses to inflammation is still very limited,” says Manuel Friese.

“To explore how neurons react to inflammation, we genetically tagged spinal cord motor neurons for profiling of ribosome-bound transcripts. This approach allowed us to gain insight into these neurons in mice undergoing experimental autoimmune encephalomyelitis, a widely used animal model of multiple sclerosis,” explains **Jan Broder Engler**, a systems biology postdoc in the lab.

Surprisingly, the team discovered an increased expression and toxic aggregation of the presynaptic protein Bassoon in neuronal cell bodies. Similar protein aggregates are typically observed in primary neurodegenerative diseases like Parkinson’ s or Alzheimer’ s disease.

“We were astonished when we first saw the microscopy images of these aggregates being triggered by inflammation,” remembers Benjamin Schattling, a neurobiologist in the lab. “But as soon as we learned that these aggregates were toxic for the neurons, we started thinking about ways to remove them.”



After validating their findings in human material and proving the connection of Bassoon aggregates and neuronal loss in overexpression and knockout experiments, the team went on to devise a therapeutic approach.

“Finally, we used a substance called IU1, which boosts the activity of the proteasome, an important trash removal system in the cell,” explains Manuel Friese. Using this approach, the team could dissolve Bassoon aggregates, reduce neuronal loss and improve the neurological outcome.

“Our findings reveal protein aggregation as a universal feature in both inflammatory and primary neurodegeneration,” concludes Manuel Friese. “Beyond that, boosting protein clearance appears to be a promising therapeutic approach with broad applicability.”

Schattling, Engler et al. Nature Neuroscience 2019
Bassoon proteinopathy drives neurodegeneration in multiple sclerosis

Coordinating prion protein trafficking and exosome release

Prion diseases are deadly infectious neurodegenerative disorders that cause synaptic impairment, neuronal loss and brain spongiform vacuolation. A research team led by Matthias Kneussel uncovered how Muskelin coordinates the trafficking of cellular prion protein PrP^c, the central player in prion disease.

Cellular prion protein (PrP^c) modulates cell adhesion and signaling in the brain. Conversion of PrP^c to its infectious isoform causes neurodegeneration and prion disease, such as Creutzfeldt-Jakob disease in humans.

PrP^c undergoes rapid turnover and extracellular release via exosomes. However, the intracellular transport of PrP^c, and its potential impact on prion disease progression is barely understood.

Kneussel and his team identified critical components of PrP^c intracellular and extracellular trafficking.

"We found that PrP^c associates with muskelin, dynein and KIF5C at transport vesicles," says **Frank Heisler**, a postdoc in Kneussel' s team. Muskelin coordinated bidirectional PrP^c transport and facilitated lysosomal degradation over exosomal PrP^c release.

Heisler: "We found that knocking out the Muskelin gene caused PrP^c to accumulate at the neuronal surface and on secreted exosomes. When we injected these mice with pathogenic prions, we saw an accelerated onset of prion disease."

The work is the result of a fruitful collaboration with colleagues at the Institute of Neuropathology and UKE and the inhouse expertise in electron microscopy.

The identification of this essential checkpoint in PrP^c turnover has important implications, concludes Kneussel: "Our findings propose a novel connection between intracellular lysosome targeting and extracellular exosome trafficking, relevant to the pathogenesis of neurodegenerative conditions. Since PrP^c also binds Aß oligomers as well as tau and α-synuclein aggregates, this pathway may serve as a novel target for the development of neuroprotective treatment strategies."

The team now wants to address how changes in synaptic activity and plasticity affect the intracellular trafficking of PrP^c.

Heisler et al. Neuron 2018
Muskelin Coordinates PrP^c Lysosome versus Exosome Targeting and Impacts on Prion Disease Progression

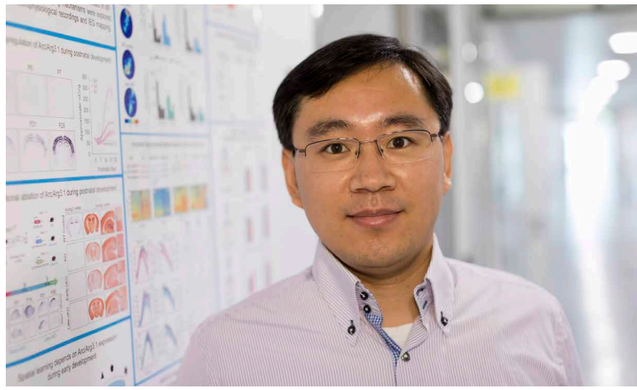
Timing spatial learning, long-term memory and hippocampal network activity

During early postnatal development, sensory regions of the brain undergo periods of heightened plasticity. This sculpts neural networks and lays the foundation for adult sensory perception. The team of **Dietmar Kuhl** and **Ora Ohana** addressed whether such critical periods of plasticity also occur during learning and memory by capitalizing on the unique properties of Arc/Arg3.1, an activity-regulated gene essential for long-term memory.

Co-first author **Xiaoyan Gao**: "Arc/Arg3.1 is transiently upregulated in the hippocampus during the first three postnatal weeks, well before the ability to store long-term memories emerges. We generated conditional Arc/Arg3.1 knockout mice in which the gene was deleted either early or late during postnatal development to learn more about its dynamic role in learning and memory."

The team used biochemical and molecular tools, behavioral analysis, and in vivo electrophysiology to investigate the consequences of postnatal Arc/Arg3.1 deletion on adult cognition, and found that early removal of the gene permanently alters hippocampal oscillations and diminishes spatial learning capacity of the mice throughout adulthood. In contrast, the post-developmental removal of Arc/Arg3.1 left learning and network activity patterns intact.

"Long-term memory storage continues to rely on Arc/Arg3.1 expression throughout life," explains Gao. "These results demonstrate that Arc/Arg3.1 mediates a critical period for spatial learning, fostering the maturation of hippocampal network activity necessary for future learning and memory storage."



"These findings shed light on how the regulation of Arc/Arg3.1 by genetic, environmental factors, as well as experiences during childhood can determine adult cognitive capacity," says **Ora Ohana**. "Ultimately, these insights can help to inform therapeutic development for neuropsychiatric and neurodevelopmental conditions."

Gao, Castro-Gomez et al. PNAS 2018
Arc/Arg3.1 mediates a critical period for spatial learning and hippocampal networks

COLLABORATIVE NETWORKS

RESEARCH UNIT FOR 2419
German Research Foundation

Speaker: Matthias Kneussel

PLASTICITY VERSUS STABILITY
MOLECULAR MECHANISMS OF SYNAPTIC STRENGTH

The processing, storage and retrieval of information in the brain depends on neural circuits and the synapses connecting all the different elements within these circuits. While the gross structure of synaptic networks is stable for years, synaptic strength can change within minutes in response to particular patterns of activity.

This synaptic plasticity is thought to underlie learning and memory, forming the basis for cognitive function. How the balance between stability and flexibility at the synapse is maintained is barely understood, especially as synaptic proteins turnover rapidly, in minutes to hours, whereas memories may last decades.

It is largely unknown, for instance, how synaptic activation or silencing regulate the dynamic equilibrium of synaptic molecules or the long-term survival of dendritic spines. The list of cognitive and psychiatric disorders that are thought of as "synaptopathies" is growing and includes autism spectrum disorder and schizophrenia.

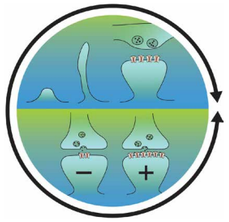
The DFG Research Unit FOR 2419 applies anatomical, biochemical, physiological, genetic and optogenetic approaches to address the conflict between plasticity and stability at the synaptic level. The consortium combines expertise in molecular, cellular and systems neuroscience to ask how stable synaptic transmission is achieved, considering the constant turnover of synaptic constituents. Focusing on activity-dependent trafficking of mRNAs, proteins and organelles, all FOR 2419 projects investigate molecular and cellular mechanisms that set synaptic lifetime and underlie memory.

"Our research focusses on highly topical questions at the core of human identity and provides a basis for understanding neuronal disease."

Matthias Kneussel, FOR 2419 speaker

"This collaborative grant provides a lot of opportunities for interaction, from the use of a facility, to discussions with other PhD students and postdocs."

Daniele Stajano, FOR 2419 PhD Student



Some of the ZMNH PhD students working on FOR 2419
Daniele Stajano, Noelia Sanchez-Rodriguez, Daniela Hacker, Cynthia Rais, Tomas Fanutza and Rui Wang

5.42
million EUR

This consortium received 2.65 million EUR in the first funding period and 2.75 million EUR in the second

13
projects

Scientists linked to FOR 2419 at ZMNH and the Universities of Hamburg and Mainz collaborate in 13 projects

20+
collaborators

Different national and international teams closely interact with FOR 2419 scientists

SYNERGY GRANT
European Research Council

Thomas Oertner and collaborators

MICROGLIAL CONTROL OF PHYSIOLOGICAL BRAIN STATES

A consortium with Thomas Oertner at ZMNH, Nils Brose (Germany), Anne Schaefer (US) and Antoine Triller (France) has been funded by an ERC Synergy grant of 10 million EUR to investigate the role of microglia in the brain.

Reciprocal signalling between neurons and microglia is critical for a healthy brain. The language of this intercellular communication is largely unknown. By combining their complementary expertise, the consortium hopes to paint a more complete picture of how the brain works, shedding light on some of its complex mysteries and advancing the fight against neurological disorders.

COLLABORATIVE RESEARCH CENTER 936
German Research Foundation

Speakers: Andreas Engel and Christian Gerloff

MULTI-SITE COMMUNICATION IN THE BRAIN

Scientists from both theoretical and clinical departments at the UKE, including the ZMNH, and the University of Hamburg, as well as the Universities of Lübeck, Berlin, and Gießen, join forces in Collaborative Research Center grant 936 on multi-site communication and interaction during brain development and disease. The overarching hypothesis pursued by the scientists in this consortium is that the crucial determinant of behavior is neuronal network interaction and not local processing. The research is structured in three thematic areas:

- Multi-site communication as a basis of cognition
- Multi-site interactions during development, plasticity and learning
- Altered multi-site communication in brain disorders

HERTIE NETWORK OF EXCELLENCE
Hertie Foundation

Speakers: Christian Gerloff and Manuel Friese

CLINICAL NEUROSCIENCE

We are part of the Hertie Network of Excellence in Clinical Neuroscience and the Hertie Academy of Clinical Neuroscience, a network and junior researcher support programme for clinical neurosciences. The Hertie Foundation is the biggest private supporter of brain research in Germany and the third-largest in Europe.

"Although there is a lot of speculation about possible additional functions of microglia, the knowledge about these cells is still very fragmented."

Thomas Oertner, ERC Synergy grantee

"The SFB936 network is the most ambitious multi-disciplinary consortium I have ever experienced. Collaborations and communications are highly effective."

Paul Lamothe, Postdoc CRC/SFB 936

"Excellent research requires, in addition to the necessary funding, a great team, time, creativity, perseverance and a good network."

Sina Rosenkranz, Hertie fellow

CORE FACILITIES

ELECTRON MICROSCOPY
MICHAELA SCHWEIZER

The Electron Microscopy Core Facility provides expertise, training and support in ultrastructural visualization technologies. We design EM experiments and develop novel techniques to further research in collaboration with groups from within and outside the ZMNH. Projects have included the ultrastructural analysis of genetically engineered primary cell cultures, numerous analyses of synaptic structure in the central nervous systems of knock out mouse models and analysis of many other tissues including bone. We localize gene products including RNA and proteins using immunohistochemistry and advanced labeling techniques and perform both conventional EM and 3D electron tomography.

IT SERVICE & DEVELOPMENT
SIEGFRIED KOLOSCHIN &
HANS-MARTIN ZIETHEN

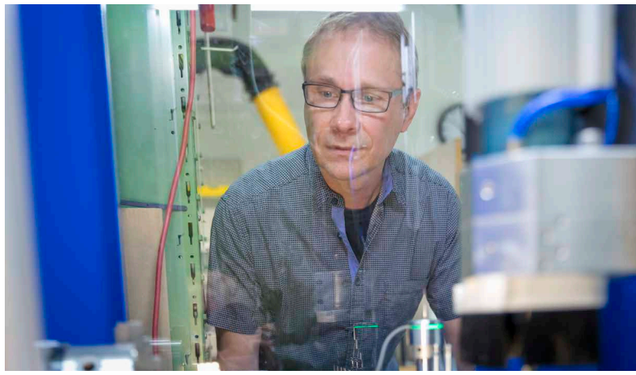
The ZMNH IT service is dedicated to providing each research group the resources and technologies relevant to their work. That includes the purchase and installation of soft and hardware, supporting and consulting the scientists in all IT matters, as well as the assembly of specialized computer and software systems tailored to perform specific tasks. We also provide assistance in data evaluation, archiving and software development.

BIOANALYTICS
SABINE HOFFMEISTER-ULLERICH

The Core Facility Bioanalytics offers sequence analyses services. Routinely the chain-termination method is performed using fluorescently labeled dideoxynucleotides (Big Dye). We are also responsible for the maintenance of two RT-PCR cyclers, and offer support in any respect of the use of the instruments. Moreover, together with the ZMNH Transgenic Mouse Core Facility, we also developed several assays for genotyping genetically altered mice. We offer introductions and services for a broad range of other assays as well, including copy number variation analysis, expression analysis, high resolution melting as well as FISH and thermal shift analysis.

SCIENTIFIC WORKSHOP
TORSTEN RENZ &
FRITZ KUTSCHERA

Our scientific workshop constructs the components of electrophysiological or microscopy set-ups. The facility uses metal, wooden and plastic material to support our scientific equipment and experiments.
Our experts have helped furnish our mouse behavioral facilities, for example by building mazes, and also deal with the electronics of our scientific equipment.

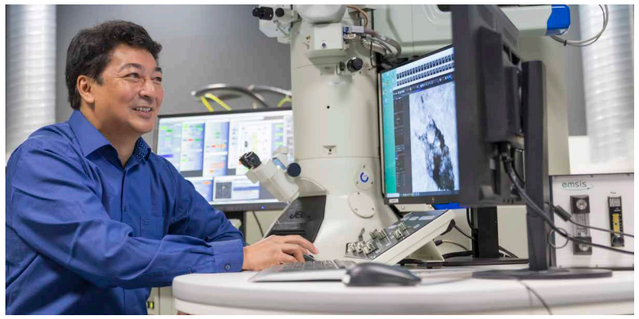


TRANSGENIC MICE
IRM HERMANS-BORGMEYER

Our aim is to support scientists in all aspects of transgenic mouse generation. While some projects still require ES cell targeting or classical transgenesis, most projects involve gene editing via CRISPR/Cas to introduce mutations relevant for human disease into the mouse genome. We provide the necessary techniques, are involved in developing the experimental design and molecular workflow. We help ZMNH researchers to establish their mouse lines and manage their colonies.

SUPPORT STAFF

Our experiments can run smoothly thanks to the dedicated support of many: from technicians to animal-caretakers and organizational support. Their instrumental help with all of the day-to-day lab logistics makes sure our researchers can concentrate on science.



FINANCE DEPARTMENT
KATJA HUSEN

Running successful research labs comprises much more than science alone. At ZMNH we can rely on our administrative staff, who make sure the rest of us are able to focus on doing exciting research. One of these instrumental figures is the head of our Finance Department Katja Husen.

Managing director
Katja Husen

BEHAVIORAL FACILITY

Over the last years, we have strengthened our expertise in animal behavior and became the primary partner for UKE scientists interested in mouse behavioral analyses.

The Behavioral Biology Unit was established at ZMNH in 2013, under the direction of Fabio Morellini.

MORELLINI: We have three facilities fully dedicated to the study of a broad spectrum of behavioral systems, ranging from cognition to addiction."

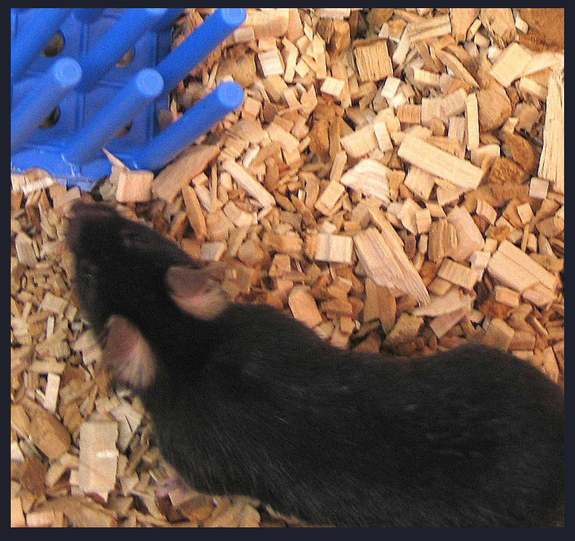
Each of the reseach teams at ZMNH has established paradigms to provide functional correlates to their specific scientific questions of interest.

Fabio
Morellini

Several groups also combine behavioral analyses with optogenetic approaches or in vivo imaging to dissect the neuronal and network substrates underlying the expression of specific behavioral responses.

MORELLINI: "We continuously develop and validate new behavioral paradigms, not only to enhance the validity of our results, but also to allow in vivo imaging, electrophysiology, and optogenetics in freely behaving or head-fixed mice."

Morellini believes that in order to understand the complexity of brain function, the future challenge will be to benefit much more from computational and mathematical analysis when modeling behavior: "Machine vision and deep learning will help us to extract and quantify a considerable amount of behavioral variables that will be shared in large datasets combining genomic, proteomic and behavioral data."



MEDICAL SYSTEMS BIOLOGY

A newly joined group led by Stefan Bonn brings new expertise to ZMNH

The prime focus of the Institute for Medical Systems Biology, led by Stefan Bonn, is to understand human pathology, especially in the central nervous system. The team integrates and curates ‘big’ biomedical data using automated systems and extracts disease-relevant information using statistical and machine learning approaches. These insights and tools help us to understand, predict and potentially cure human disease.

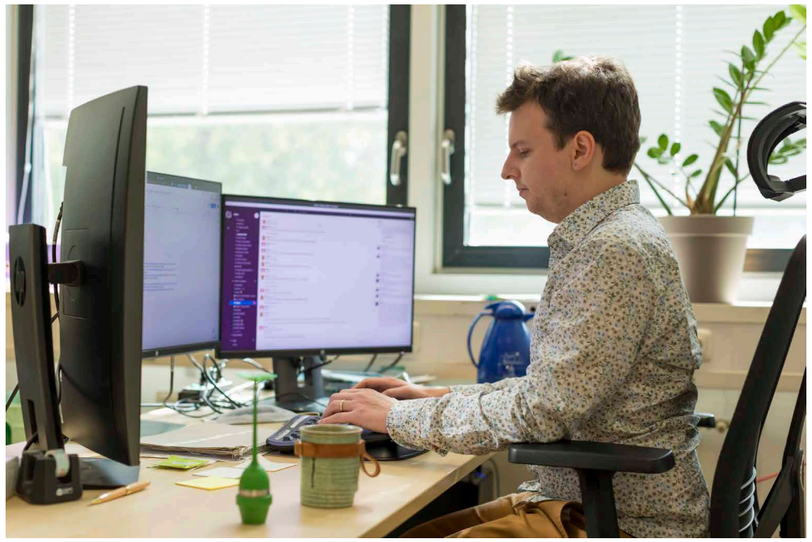
BONN: “Our research is based on the premise that the exploration of big biomedical data using smart algorithms is key to achieve essential improvements in healthcare. That is why we create and curate knowledge bases for medical deep sequencing data in the context of aberration and disease.”

BONN: “With SEA, we were able to identify novel pathogenic infections across diseases as diverse as Crohn’ s disease, dementia or schizophrenia. In addition, we determined a blood biomarker specific for Parkinson’ s disease that is based on sRNAs linked to neuronal differentiation and intracellular signal transduction.”

Using deep neural networks, the researchers de-bias and generate omics data. They developed cscGAN (conditional single-cell generative adversarial neural networks) for augmentation of sparse scRNAseq data, for instance, supporting and enabling the analysis and interpretation of gene expression profiles.

BONN: “Another deep neural network model, Scaden (single-cell-assisted deconvolutional deep neural network), deconvolves differential gene expression from changes in cell composition such as cell proliferation and cell death for example. With Scaden, we were able to link Braak stages to fractional neuronal loss in brain samples affected by Alzheimer’ s disease.”

“The exploration of big biomedical data using smart algorithms is key to achieve essential improvements in healthcare.”



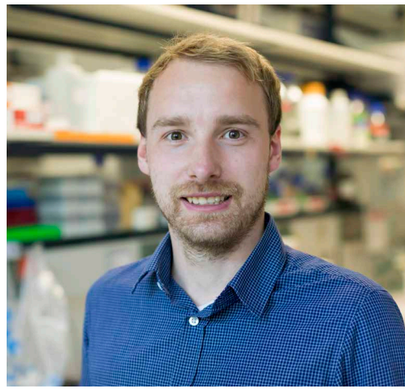
Stefan Bonn

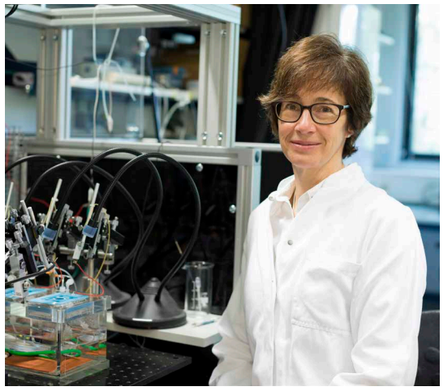
Bonn and his team have developed OASIS (oasis.dzne.de), a web application for the detection, differential expression, and classification of small RNAs from deep sequencing data, and SEA (small RNA expression atlas, www.sea.ims.bio), which uses OASIS for ontology-based interactive querying, visualization, and analysis of over 4000 published sRNA samples.

In the context of bAIome, the center for biomedical AI at UKE (www.baiome.org), the Institute for Medical Systems Biology is one of the main motors for translation of mature AI methods into a clinical setting.
Recently, the team used their methods to decipher cell specific infection of SARS-COVID 2 in the brain.

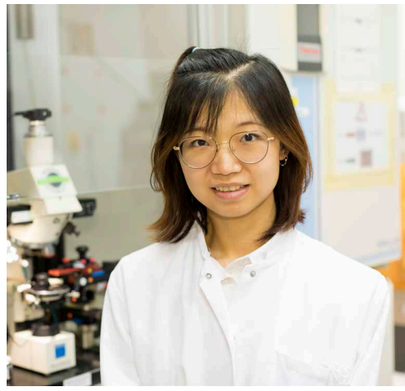
MORE THAN THE SUM OF OUR PARTS

We combine fundamental neurobiology with clinical and translational research. That is why in addition to PhD students and postdocs, we have MDs like **Mark Walkenhorst** (right) and **Timo Schwarze** (below) who do research at our Center.



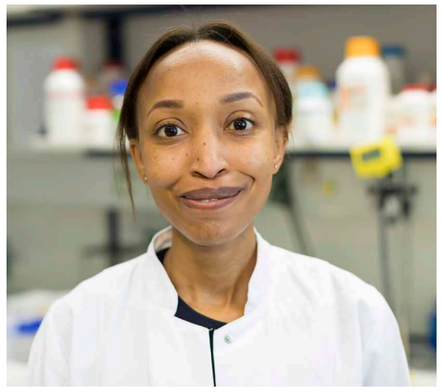


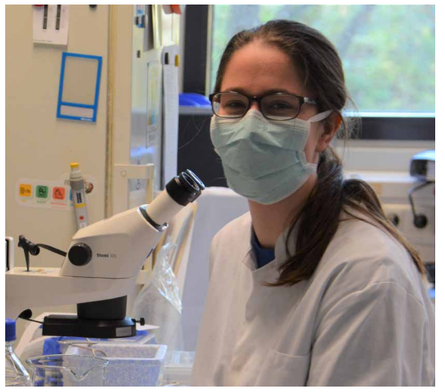
Christine Gee heads a scientific working group at the Institute for Synaptic Physiology. She aims to understand the impact of synaptic plasticity on the function of brain circuits and studies the role of second messengers in synaptic function and brain inflammation.



Hadjilaou Alexandros is a clinical scientist at ZMNH. His research project represents one of many links between ZMNH and the clinic.

Postdoc **Mary Muhia** is a behavioral scientist at ZMNH. She investigates molecular and synaptic mechanisms underlying cognitive function, through behavioral experiments in mouse models on conditioning, spatial learning, anxiety, exploration, depression or social interaction.





NEW INSTITUTE DIRECTOR

Ileana Hanganu-Opatz was recently promoted to Director of the newly established Institute of Developmental Neurophysiology at the ZMNH. On this occasion, she reflects on what made her want to become a scientist, and how she eventually became one, leading her own team at ZMNH—a journey that started more than 10 years ago.

INTERVIEW WITH ILEANA HANGANU-OPATZ

Coincidence and resilience

Hanganu-Opatz' love for neurophysiology was sparked when she read Solomon Snyder' s book Drugs and the Brain. "I was incredibly fascinated and wanted to understand how chemicals act in the brain. No one in my family had any connection to neural science, and I thought studying biochemistry would be a perfect way in. When I discovered physiology, I was immediately convinced this is what I wanted to do. These lectures tackled exactly the questions that I wanted to understand and address."

Studying in Romania, Hanganu-Opatz sought out international opportunities. "I applied for a 7-month internship to learn a fascinating method: the patch clamp technique that allows to "watch" neurons at work. I worked with professor Schwarz, who is now an emeritus at ZMNH, here at UKE in Hamburg."

"I continued in science working on brain development with a supervisor whose enthusiasm was extremely contagious. The work itself was focused on sensory systems of the rodent. I wanted to go back to my childhood questions on psychiatric disorders that were inspired by Snyder' s book. Therefore, I wrote my first grant on the developmental mechanisms of schizophrenia in animal models. Well, the grant was rejected, with some harsh comments, but it was this rejection that triggered me to push forward."

"Schizophrenia has a strong developmental background and we need to understand what goes wrong early on. We are in the dark about the disease mechanisms, because we simply don' t know what is going right in the healthy brain in the first place. I am focused on these questions for more than eight years now, but still we are only scratching the surface."

In a nutshell, Hanganu-Opatz says she ended up working on developmental neurophysiology through a combination of luck, coincidence but also resilience. "A lot in science is about simply not giving up," she says.

A great team in Hamburg

Through an Emmy Noether fellowship from the DFG and a BMBF award, she was able to start her own team at the ZMNH in 2009.

"When I arrived at ZMNH there were mainly molecular scientists here, while I was doing system neuroscience. I was considered "the exotic one" in the Center, but in fact it gave me a refreshing perspective. The questions I got from colleagues were really different from the ones I was used to. These interdisciplinary discussions have been directing my research approach for years."

Over the past decade, Hanganu-Opatz has had several outside offers, but she declined all and stayed in Hamburg, citing the good atmosphere at ZMNH as an important reason.

"It is not only a question of competition and collaboration, but of whether you can have a beer with your colleagues. Hamburg is absolutely fantastic in this regard. Quite soon after my arrival, I got the opportunity to take part in several research consortia and immediately established very tight links, not only with other scientists at the ZMNH but also in the UKE."

"Another reason why I am so happy here is my team. I have had the chance to work with such great people over the years. They reward me in a way that I never imagined was possible. I learned as much from them as they from me."

Hanganu-Opatz confesses she sometimes misses bench work. "I know it is a good day if someone knocks on my door to tell me things are not working. It means I can leave the computer and help at the bench. I used to have an office in the middle of the lab so I always knew what was running." Her office moved recently, but her door is still open.

"My direct PhD supervisor taught me that in order to have good people in your team, it is not enough that they are enthusiastic, they need someone to take their hand and take them through the problem—to digest science together. That is why I don' t want my institute to grow too big: I want to be able to give everyone in my team this hand when they need it."

Diving deeper

When it comes to the science, she hopes that the upgrade from research group to institute will allow her to dive deeper, and pursue more risky research opportunities. "I have an ERC consolidator grant, which for the first time allowed me to start more innovative and risky projects; projects with a fifty-fifty chance of working out. If you have an institute with more manpower, you can take such riskier pathways."

"I will definitely keep on investigating neurodevelopment and the function of neural networks. We want to try and understand the underlying molecular pathways much better, in both health and disease. In other words: basic research with a translational flavor."

Brain development is so little understood, she says. "There are topics that nobody touched before, so this is work that will accompany me for the next decade."

Hanganu-Opatz is a big fan of diversity in neuroscience, in all possible ways: "At the ZMNH we address a lot of questions, and it is one of the reasons we are successful."

The same applies at the level of individual researchers. There are very few rules to be successful in science, according to Hanganu-Opatz: "You need to be enthusiastic, resilient, hard-working... All this is true, but I don' t think there is one golden way, there are so many forks in the road. I always tell my students: my way is my may, don' t copy it!"

"A lot in science is about simply not giving up"

“There are so many examples of how basic research informs clinical practice”

INTERVIEW WITH EMERITUS JÜRGEN SCHWARZ

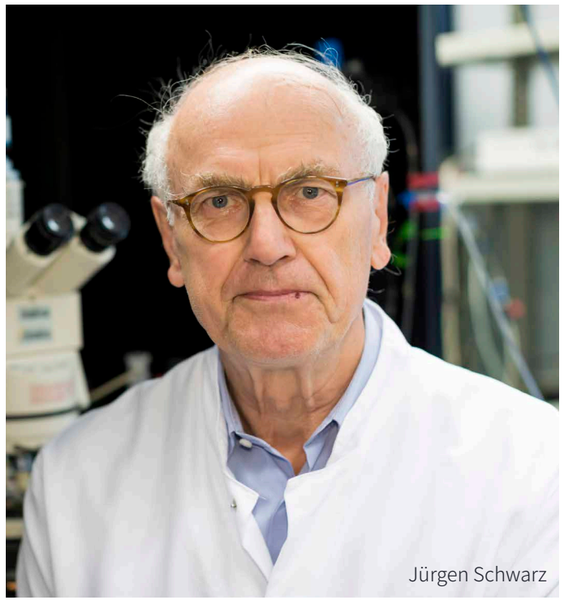
One of the emeriti at ZMNH is electrophysiologist Jürgen Schwarz. Fifteen years past retirement and nearly 50 years after publishing his first manuscript, he keeps submitting grants, conducting experiments and publishing papers.

What drives you to return to the lab each day?

SCHWARZ: “One word: Curiosity! I still want to know more about nerve fibers and action potentials. There are still so many unanswered questions. I’ m currently working on an exciting collaboration unravelling the function of a particular leakage channel in the node of Ranvier together with Roderick McKinnon at Rockefeller, who won the 2003 Nobel Prize for his structural and mechanistic studies of ion channels. As part of the Kneussel group, I am also involved in the research topics of our team. I am always happy to contribute my electrophysiology expertise to answer fascinating questions about molecular events at the synapse.”

What has changed over the years in science?

“I started my studies in medicine and wanted to become a neurologist or psychiatrist, combining clinical work and basic research. At that time it was almost impossible to do. I started a lab, but basically could only run experiments at night. My wife made me choose between the two, so I ended up going back to the clinics and became a neurologist. Perhaps today my decision would be a little different.
When I was a neurologist, many disorders were just called ‘undefined diseases’ . Now it has become evident that many neurological diseases are caused for example by mutations in channels, so the translational link has become stronger and basic science is also much more incorporated in the clinics.”



Jürgen Schwarz

How did you end up at the ZMNH?

“The ZMNH was founded a long time ago. When I was head of the Department of applied physiology at UKE, I was always envious of all the methods available to my colleagues here at ZMNH and collaborated with them whenever I could. After retiring in 2006 it was an easy decision to join.
As a professor you are a member of the university for life, you can teach as long as you want, apply for grants and train PhD students. However, as an emeritus you do need to team up and embed yourself in an existing team. As the head of a big department it may seem like a step back, but in fact it is quite nice to be free of all administration and extra responsibilities.”

What do you consider the biggest strength of the ZMNH?

“The strength of the center is the successful merger of basic and clinical questions in neuroscience. It all starts from primary scientific questions, and this is really important. There are so many examples of how basic research informs clinical practice. Of course, more and more clinical questions are asked and answered as well. For example, the institute on MS is relatively new. I think we have a very nice working model here, doing basic research on a disease in close collaboration with the clinic. That is why I think it is important that we also have clinical scientists and MDs at the ZMNH.”

What would be your advice to young aspiring researchers?

“I would advise clinicians to spend several years doing basic research in their field of specialization. If you want to become a neurologist, for example, why not spend 3 to 5 years doing neurophysiology? If you are open to ask questions and have the freedom to do research, enjoy it. To spend your time doing research is fascinating and rewarding. Your paper is like a work of art: everyone can look at it, think about your results and learn from them.”

MEET OUR ALUMNI

MARINA MIKHAYLOVA

Professor at the Humboldt-Universität zu Berlin

Marina Mikhaylova started her own lab as a junior group leader at ZMNH in 2015, with support of a prestiguous Emmy-Noether fellowship. In 2020, she was appointed professor for Optobiology at the Humboldt University in Berlin. **Her team studies neuronal protein transport and organelle trafficking using the latest fluorescence imaging techniques.**

MIKHAYLOVA: “Research in our laboratory is focused on understanding how local calcium signalling is transduced to the cytoskeleton and motor proteins. Compartmentalized calcium signalling plays a central role in connecting synaptic activity to local actin remodelling, allowing for selective stabilization and strengthening of active dendritic spines. For example, we could recently show that that the calcium sensor caldendrin orchestrates nano-domain actin dynamics in the early phase of long-term potentiation.”

“With super-resolution imaging we discovered a periodic sub-membranous F-actin cytoskeleton in the neck of dendritic spines, as well as dense F-actin patches associated with excitatory shaft synapses in adult principal neurons. The latter structures serve as hubs for the docking of secretory trafficking organelles such as endo-lysosomes and Golgi satellites. Interestingly, we found that an interplay between kinesin and myosin motors allows for long-term organelle stalling near excitatory shaft synapses or recruitment of organelles into active dendritic spines, diversifying the molecular composition of individual synapses.”

“In ongoing work, we are exploring this diversity with a particular focus on dendritic spines invaded by the endoplasmic reticulum and synapses containing differential “bar codes” of major synaptic scaffolding proteins.”

How do you look back on your time at ZMNH?

MIKHAYLOVA: “My time as an independent junior group leader has been an important step in my career, allowing me to pursue my own ideas, to create my scientific network and get recognition in the field of neuroscience. It has prepared me for this next exciting step as professor in Berlin. I am very grateful to my team members, mentors, colleagues and friends at ZMNH.”

STEFAN GOLD

Professor of Neuropsychiatry, Charité Universitätsmedizin Berlin, Center for Neurology, Neurosurgery and Psychiatry

Stefan Gold was group leader at ZMNH, and has been appointed professor at Charité Universitätsmedizin Berlin in 2014. **His team is interested in neuro- endocrine-immune networks and their role in the pathogenesis and progression of neuroinflammatory and neuropsychiatric disorders.**

GOLD: “We are interested in how the immune system and the brain communicate and what happens if this communication is dysregulated as a consequence of inflammatory or neurodegenerative processes. We are particularly interested in the ‘common biology’ of behavioral symptoms seen in many neuropsychiatric disorders such as depressive symptoms or cognitive impairment. To this end, we employ disease models as well as cross-sectional and longitudinal studies in clinical cohorts.

“We aim to use this knowledge to develop and test novel therapeutic approaches including behavioral and pharmacological interventions and to explore the underlying biological mechanisms that may mediate therapeutic effects.”

How do you look back on your time at ZMNH?

GOLD: “Even though I came from a quite different scientific background and our institute at the time was the only one with a focus on immunology and clinical research, people would enjoy to sit down and ask interesting questions or offer technical assistance with new methods. Often their thoughts would help me move my research in an unexpected and surprisingly rewarding direction.”

What would be your advice to young scientists pursuing a research career?

GOLD: “Don’ t be afraid to apply new or even unusual methods to your research and don’ t stick to a method just because you are good at it. As long as you are asking a question that fascinates you, you’ ll be alright. Methods change all the time, the big questions remain the same. Get technical help if you need it and make sure you always acknowledge this help publicly. On a more practical note: never submit a grant before a smart colleague from an entirely different field has read and understood it!”

FUTURE RESEARCH

ZMNH leadership (from left to right): Ileana Hanganu-Opatz, Matthias Kneussel, Thomas Oertner, Stefan Bonn, Manuel Friese and Dietmar Kuhl.

We integrate expertise in molecular, synaptic, cellular, circuit, system, behavioral and clinical neuroscience

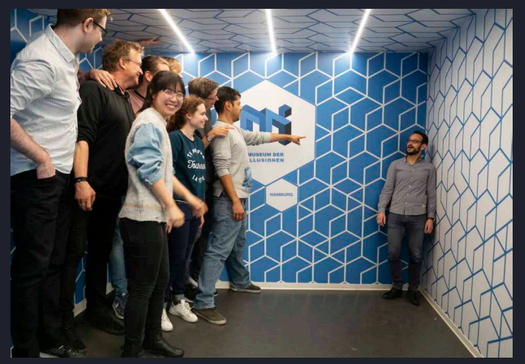
Looking into the future at what lies ahead for ZMNH, we envision a research center that focusses on two central topics:

- **Multiscale analysis of stability versus flexibility in brain function and behavior**
  These questions range from development to adulthood. They include functional aspects of neurons, synapses and circuits underlying cognition, as well as neurological and neuropsychiatric disease.
- **Neuro-immune interactions**
  We study neurons, glia and immune cells to unravel the interplay of the nervous and immune system and investigate the etiology of neuroimmunological and neuroinfectious diseases.

We integrate complementary expertise to understand the dynamics and trade-offs at different levels in the healthy and diseased nervous system.

In addition to these two key topics in our research, we keep our eyes on the emerging field of non-canonical communication in the brain (extracellular vesicles, exosomes) and the interference of neuronal function through infectious agents such as viruses, bacteria and parasites.

OUT & ABOUT



When we don’ t need to practice social distancing, we regularly get together outside of our labs. From dinner and drinks to games and activities, at the beach, on the water, high up in the trees, you name it, we are game!

In addition to various lab outings, all researchers assemble for an annual retreat to get to know each other - and each other’ s research - better. With guest speakers, talks and lots of posters, it is always one of the highlights of the year.

ZMNH

Where scientific talent thrives

Simon Wiegert has been awarded an **ERC Starting grant** to study the role of synapses in memory. Together with his team, he aims to fill a wide gap in our understanding of how synapses contribute to the formation and storage of memories.

The physical nature of memory – or engram – is probably one of the longest studied mysteries in neuroscience, and yet it still remains elusive.

The engram could be defined as the subset of neurons necessary and sufficient to cause recall of a specific memory when activated. But where is the engram when the neurons are not active? Most likely, 'lasting alterations' during memory formation are encoded in the synaptic connections between nerve cells, whose connection pattern and strength determine the flow of information.

WIEGERT: "The central aim of this project is to identify synapses participating in the engram and to study their morphological stability and functional properties, but also to identify general rules that determine the lifetime of synapses and their participation in information processing."

Wiegert' s team is developing new approaches to precisely control synaptic circuits and neuronal networks with light (optogenetics) or targeted pharmacological interventions (chemogenetics).

WIEGERT: "We use these techniques in combination with molecular markers of synaptic and neuronal activity to investigate functional synapses and neuronal populations in their native circuit over the time scale of weeks, relevant for memory encoding and long-term storage."

"By connecting functional long-term analysis of single synapses and neuronal circuits with morphological observations, we hope to understand if and how memory traces - or engrams - can be encoded and stored in the brain."

The **Hamburg Brain School** nurtures the next generation of neuroscientists

Training and mentoring young scientists is one of our main priorities. In addition to our in house activities, all ZMNH graduate students are connected to the Hamburg Brain School, the highly acclaimed graduate training program at the Medical Faculty of the University of Hamburg.

The Hamburg Brain School connects the neuroscientific activities at the UKE from the molecular level to clinical research. It works in close collaboration with the UKE departments of neuroanatomy, neurophysiology, neuropathology, neurology and psychiatry, offering numerous opportunities for interaction with colleagues within our extended local scientific network. The Hamburg Brain School unites over 400 scientists and PhD students from 18 different institutes and clinics at UKE, including ZMNH.

JOIN US IN HAMBURG

Founded in 1987, the ZMNH is an internationally renowned research center of the Medical School at the University of Hamburg. We are part of the University Medical Center Hamburg-Eppendorf (UKE), the medical faculty of the University of Hamburg. With 506,697 patients, 11,348 employees and 3,338 students, the UKE is one of the largest university medical centers in Germany. Neuroscience is one of its main research focus areas.

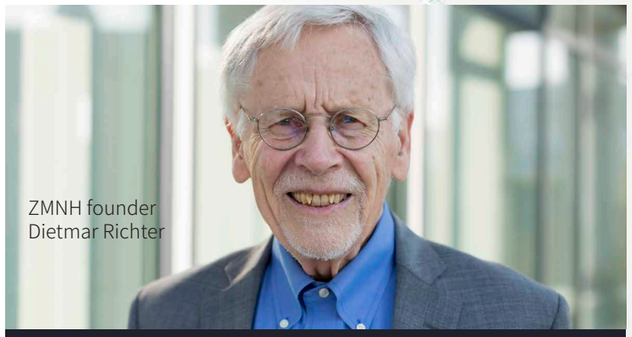
As a young and dynamic institute, we are a fertile ground for neuroscience research. We have close ties with our local partners, and forged strong collaborations with researchers at the nearby Fraunhofer Institute and the Hamburg University of Technology. The ZMNH is part of the Hamburg Center of Neuroscience community (HCNS) and actively participates in graduate teaching at the Hamburg Brain School.

"The ZMNH has been a focus of innovation on the UKE campus, bridging molecular analysis of brain function and clinical translation."

Blanche Schwappach-Pignataro
Dean UKE

"Major advances in neuroscience will only be possible by bridging the gap between human and animal models. The ZMNH provides the necessary and complementary expertise to our research in humans."

Andreas Engel,
Director Department of Neurophysiology and Pathophysiology, UKE



ZMNH founder
Dietmar Richter

BLANKENESE CONFERENCE

ZMNH founder and emeritus **Dietmar Richter** organizes the famous Blankenese Conference, an annual event covering topics in cell biology, genetics, virology and neurobiology. Richter founded this meeting series in 1979, together with the late Gebhard Koch.

By design, the conference headlines two distinct topics, bringing together key investigators from different fields to exchange ideas. The conferences are held in Blankenese, a suburb of Hamburg, at the beautiful Elsa-Brändström-Haus.

CITY OF SUPERLATIVES

As Germany' s second-largest city, Hamburg has been a gateway to the world for centuries. It has a rich architectural heritage and vibrant cultural scene. Hamburg is home to the biggest and busiest harbor in Germany, most of Germany' s major media, the oldest stock exchange in Germany and more bridges than Venice!

"Our collaborations with the ZMNH are extremely valuable, because they provide us with highly innovative optogenic tools and allow us to build even better bridges between systems neuroscience and cellular-molecular neuroscience."

Christian Büchel,
Director Department of Systems Neuroscience, UKE

Center for Molecular Neurobiology Hamburg **ZMNH**

University Medical Center Hamburg-Eppendorf **UKE**

Hamburg, Germany

www.uke.de/zmnh

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